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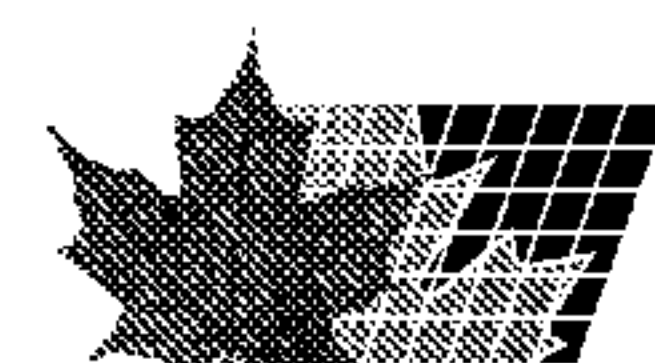
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(54) Titre : PROCEDES D'UTILISATION DE MODULATEURS PI3K ETMEK
(54) Title: METHODS OF USING PI3K AND MEK MODULATORS

(57) **Abrégé/Abstract:**

The invention provides methods of treating cancer with a combination of compounds which inhibit kinases, more specifically MEK and PI3K.



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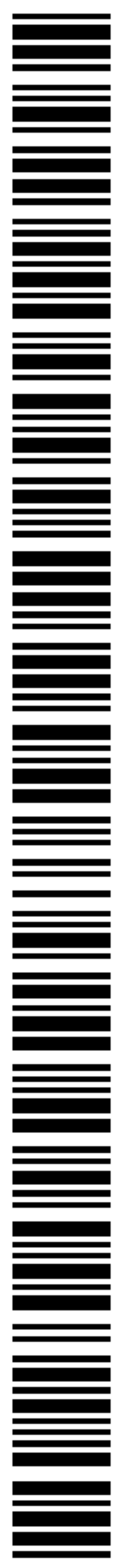
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(54) Title: USING PI3K AND MEK MODULATORS IN TREATMENTS OF CANCER

(57) Abstract: The invention provides methods of treating cancer with a combination of compounds which inhibit kinases, more specifically MEK and PI3K.



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METHODS OF USING PI3K AND MEK MODULATORS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] This invention relates to methods of treating cancer with a combination of compounds that modulate protein kinase enzymatic activities and the resultant modulation of cellular activities (such as proliferation, differentiation, programmed cell death, migration, chemoinvasion and metabolism). In particular, this invention relates to a compound that inhibits mitogen activated protein kinase (MEK) used in combination with a compound that inhibits phosphatidylinositol 3-kinase (PI3K) signaling pathways.

State of the Art

[0002] Improvements in the specificity of agents used to treat cancer is of considerable interest because of the therapeutic benefits which would be realized if the side effects associated with the administration of these agents could be reduced. Traditionally, dramatic improvements in the treatment of cancer are associated with identification of therapeutic agents acting through novel mechanisms.

[0003] Protein kinases are enzymes that catalyze the phosphorylation of proteins, in particular, hydroxy groups on tyrosine, serine and threonine residues of proteins. The consequences of this seemingly simple activity are staggering; cell differentiation and proliferation; i.e., virtually all aspects of cell life in one-way or another depend on protein kinase activity. Furthermore, abnormal protein kinase activity has been related to a host of disorders, ranging from relatively non-life threatening diseases such as psoriasis to extremely virulent diseases such as glioblastoma (brain cancer).

[0004] Protein kinases can be categorized as receptor type or non-receptor type. Receptor-type tyrosine kinases have an extracellular, a transmembrane, and an intracellular portion, while non-receptor type tyrosine kinases are wholly intracellular. They are comprised of a large number of transmembrane receptors with diverse biological activity. In fact, about 20 different subfamilies of receptor-type tyrosine kinases have been identified. One tyrosine kinase subfamily, designated the HER subfamily, is comprised of EGFR (HER1), HER2, HER3, and HER4. Ligands of this subfamily of receptors identified so far include epithelial growth factor, TGF-alpha, amphiregulin, HB-EGF, betacellulin and heregulin. Another subfamily of these receptor-type tyrosine kinases is the insulin subfamily, which includes INS-R, IGF-IR, and IR-R. The PDGF subfamily includes the PDGF-alpha and beta receptors, CSFIR, c-kit and FLK-II. In addition, there is the FLK family, which is

comprised of the kinase insert domain receptor (KDR), fetal liver kinase-1 (FLK-1), fetal liver kinase-4 (FLK-4) and the fms-like tyrosine kinase-1 (flt-1). The PDGF and FLK families are usually considered together due to the similarities of the two groups. For a detailed discussion of the receptor-type tyrosine kinases, see Plowman et al., *DN&P* 7(6): 334-339, 1994, which is hereby incorporated by reference.

[0005] The non-receptor type of tyrosine kinases is also comprised of numerous subfamilies, including Src, Frk, Btk, Csk, Abl, Zap70, Fes/Fps, Fak, Jak, Ack, and LIMK. Each of these subfamilies is further sub-divided into varying receptors. For example, the Src subfamily is one of the largest and includes Src, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr, and Yrk. The Src subfamily of enzymes has been linked to oncogenesis. For a more detailed discussion of the non-receptor type of tyrosine kinases, see Bolen, *Oncogene*, 8:2025-2031 (1993), which is hereby incorporated by reference.

[0006] Since protein kinases and their ligands play critical roles in various cellular activities, deregulation of protein kinase enzymatic activity can lead to altered cellular properties, such as uncontrolled cell growth associated with cancer. In addition to oncological indications, altered kinase signaling is implicated in numerous other pathological diseases. These include, but are not limited to: immunological disorders, cardiovascular diseases, inflammatory diseases, and degenerative diseases. Therefore, both receptor and non-receptor protein kinases are attractive targets for small molecule drug discovery.

[0007] One particularly attractive target for small-molecule modulation, with respect to antiangiogenic and antiproliferative activity is MEK. The MEK-ERK signal transduction cascade is a conserved pathway which regulates cell growth, proliferation, differentiation, and apoptosis in response to growth factors, cytokines, and hormones. This pathway operates downstream of Ras which is often upregulated or mutated in human tumors. It has been demonstrated that MEK is a critical effector of Ras function. A large portion of human cancers, including 80% pancreatic, 50% colorectal, and 40% lung cancers, harbor activating Ras mutations. It has been shown that inhibition of the ERK pathway, and in particular inhibition of MEK kinase activity, results in anti-metastatic and anti-angiogenic effects largely due to a reduction of cell-cell contact and motility as well as downregulation of vascular endothelial growth factor (VEGF) expression. Furthermore, expression of dominant negative MEK, or ERK reduced the transforming ability of mutant Ras as seen in cell culture and in primary and metastatic growth of human tumor xenografts *in vivo*. Therefore, the MEK-ERK signal transduction pathway is an appropriate pathway to target for therapeutic intervention.

[0008] Accordingly, the identification of small-molecule compounds that specifically inhibit, regulate and/or modulate the signal transduction of kinases, particularly MEK, is desirable as a means to treat or prevent disease states associated with cancer and is an object of this invention.

5 [0009] Phosphatidylinositol 3-kinase (PI3K α), a dual specificity protein kinase, is composed of an 85 kDa regulatory subunit and a 110 kDa catalytic subunit. The protein encoded by this gene represents the catalytic subunit, which uses ATP to phosphorylate PtdIns, PtdIns4P and PtdIns(4,5)P2. PI3K α has been implicated in the control of cytoskeletal reorganization, apoptosis, vesicular trafficking, proliferation and differentiation processes.
10 Increased copy number and expression of PIK3CA is associated with a number of malignancies such as ovarian cancer, cervical cancer, breast cancer, colorectal cancer, and glioblastomas, among others. The tumor suppressor PTEN inhibits cell growth through multiple mechanisms. PTEN can dephosphorylate PIP3, the major product of PIK3CA. PIP3, in turn, is required for translocation of protein kinase B (AKT1, PKB) to the cell
15 membrane, where it is phosphorylated and activated by upstream kinases. The effect of PTEN on cell death is mediated through the PIK3CA/AKT1 pathway.

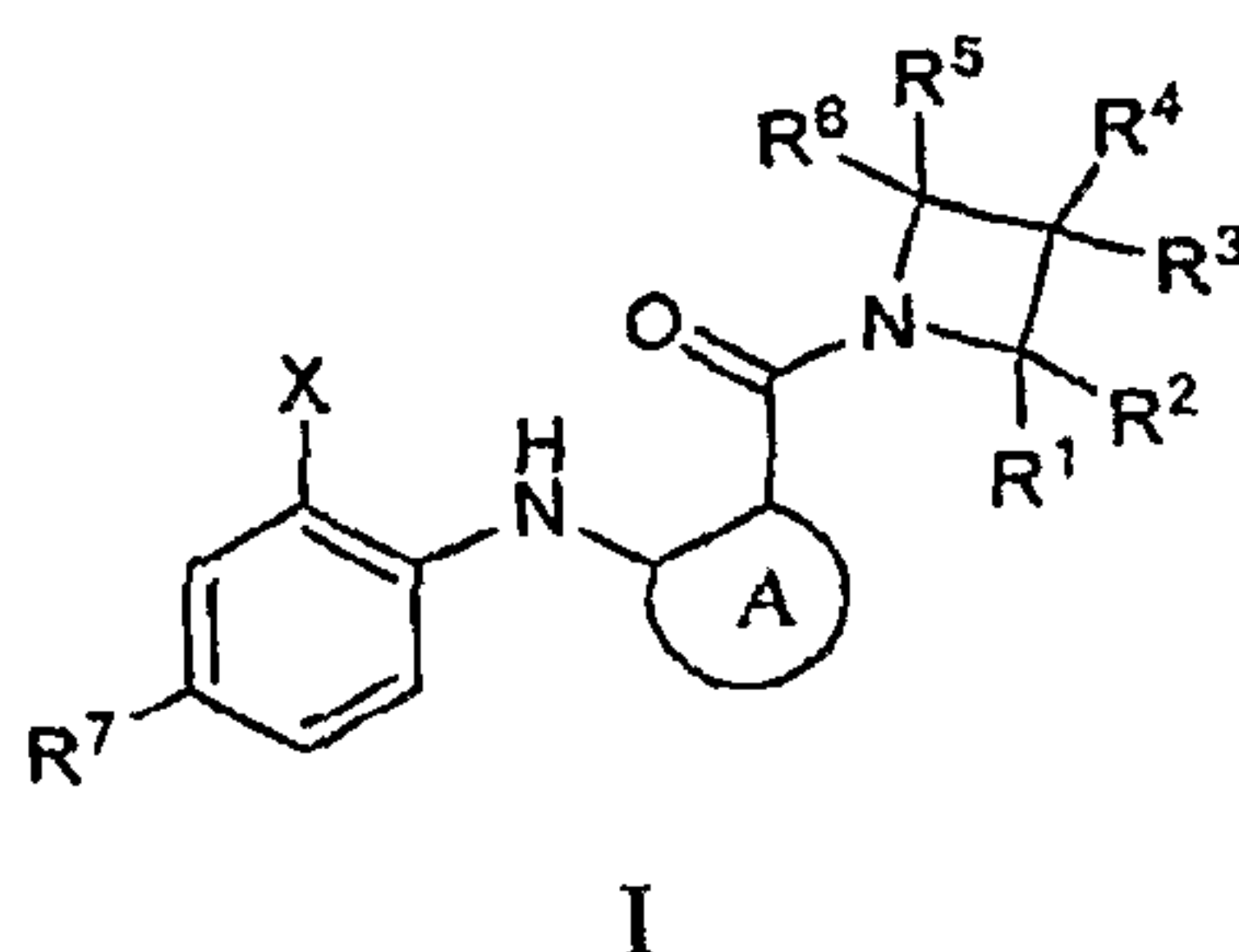
[0010] Thus, an object of this invention is the identification of small-molecule compounds that specifically inhibit, regulate and/or modulate the signal transduction of kinases, particularly phosphatidylinositol 3-kinase, in order to treat, prevent, and/or inhibit
20 diseases and conditions associated with cancers.

[0011] Combination therapy has been commonly utilized to overcome drug resistance. Clinical trials of dasatinib or nilotinib (AMN-107) in combination with the current standard CML therapy, ie., imatinib (Gleevec®), are ongoing (ClinicalTrials.gov). Dasatinib in combination with Gleevec® has shown improved efficacy against various Abl mutants except
25 for T315I in preclinical studies (O'Hare T, Walters DK, Stoffregen EP, et al., "Combined Abl inhibitor therapy for minimizing drug resistance in chronic myeloid leukemia: Src/Abl inhibitors are compatible with imatinib", *Clin Cancer Res.* 11, 6987-6993 (2005)). Recently, specific mutations in B-RAF have been shown to confer reduced sensitivity to treatment of cells and tumors with compounds that inhibit MEK (Solit et al. *Nature* online, pgs 1-5
30 November 6, 2005). Combination therapies treating multiple kinases pathways should eliminate this reduced sensitivity.

SUMMARY OF THE INVENTION

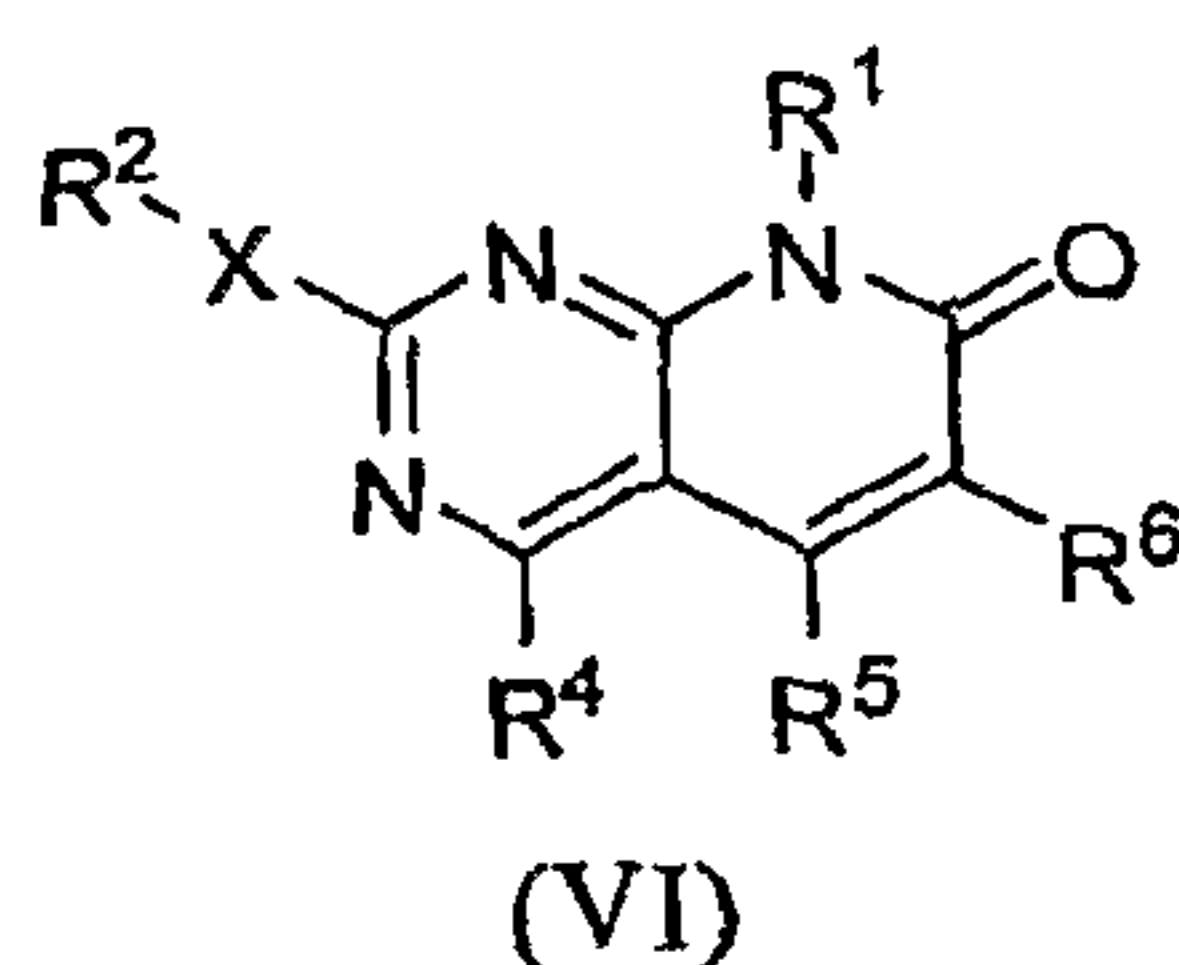
[0012] This invention provides a method of using an MEK inhibitor of Formula I, Ia, Ic, Id, II, III, IV, or V in combination with a PI3K inhibitor of Formula VI, VIa, VIb, or VII, or in combination with a PI3K inhibitor of Formula VIII, VIIIa, VIIIb, IX, X, XI or XII for the treatment of hyperproliferative disorders, such as cancers.

[0013] In one embodiment, in section I an MEK inhibitor of Formula I is as follows:



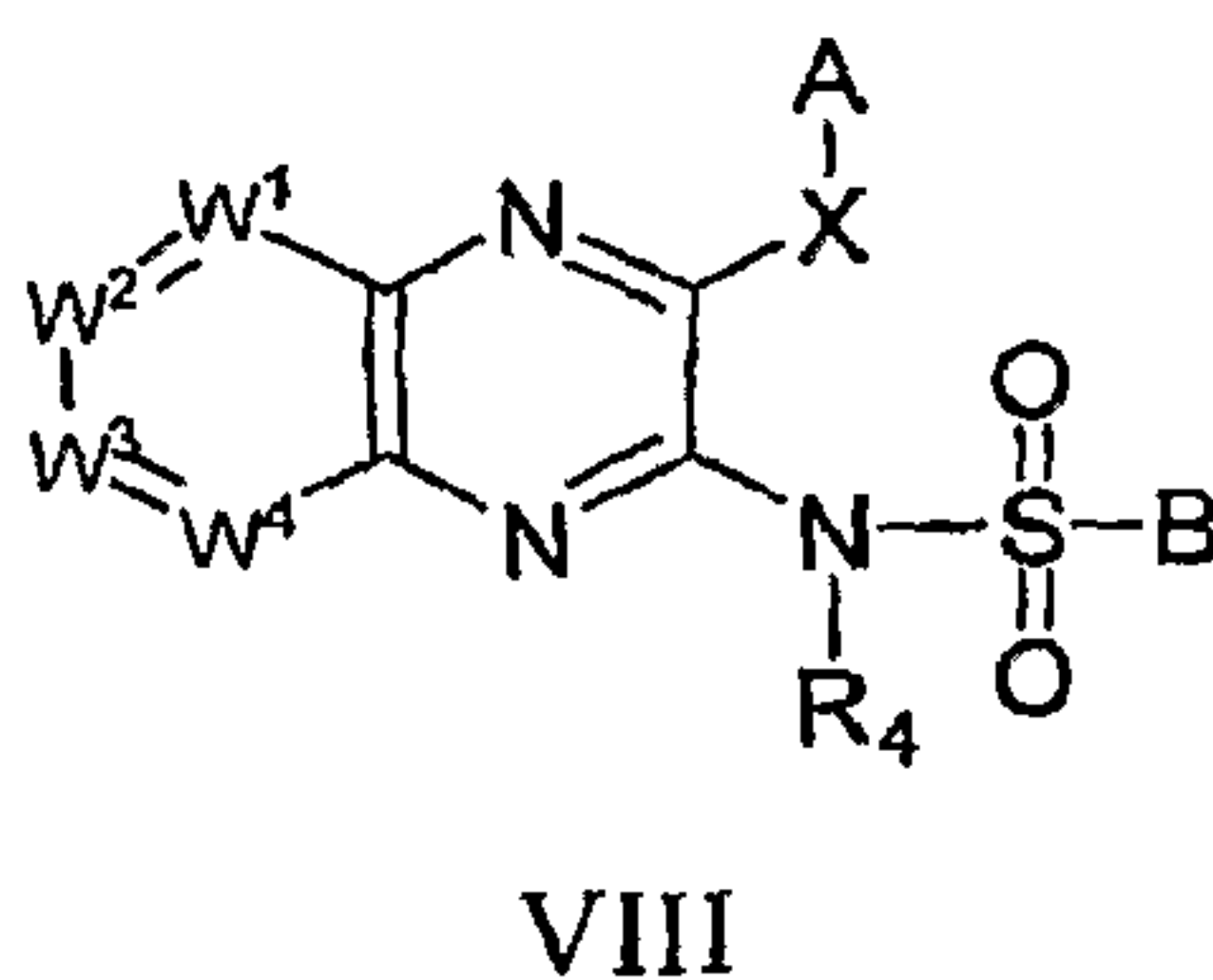
and optionally a pharmaceutically acceptable salt or solvate thereof, wherein the A ring, X, R¹, R², R⁴, R⁵, R⁶, and R⁷ are as defined below in Section I.

[0014] In one embodiment, in section II a PI3K inhibitor of Formula VI is as follows:



and optionally a pharmaceutically acceptable salt hydrate or solvate thereof, wherein X, R¹, R², R⁴, R⁵, and R⁶ are as defined below in Section II.

[0015] In one embodiment, in section III a PI3K inhibitor of Formula VIII is as follows:



and optionally a pharmaceutically acceptable salt hydrate or solvate thereof, wherein W¹, W², W³, W⁴, A, X, R⁴, and B are as defined in Section III.

[0016] The invention encompasses using the MEK inhibitor disclosed in Section I in combination with the PI3K inhibitor of section II or section III to treat a hyperproliferative diseases and disorders and in particular cancers comprising administering to a patient a compound of Formula I, Ia, Ic, Id, II, III, IV, or V, with a compound of the Formula VI, VIa,

VIb, or VII, or a compound of the Formula VIII, VIIIa, VIIIb, IX, X, or XI, or a pharmaceutical composition thereof.

[0017] The foregoing merely summarizes certain embodiments of the invention and is not intended to be limiting in nature. These embodiments and other embodiments and
5 embodiments are described more fully below. The patent and scientific literature referred to herein establishes knowledge that is available to those with skill in the art. The issued patents, applications, and references that are cited herein are hereby incorporated by reference to the same extent as if each was specifically and individually indicated to be incorporated by reference. In the case of inconsistencies, the present disclosure will prevail.

10 DETAILED DESCRIPTION OF THE INVENTION

[0018] The following applies to all three sections.

[0019] "Yield" for each of the reactions described herein is expressed as a percentage of the theoretical yield.

15 [0020] Some of the compounds of the invention may have imino, amino, oxo or hydroxy substituents off aromatic heterocyclyl systems. For purposes of this disclosure, it is understood that such imino, amino, oxo or hydroxy substituents may exist in their corresponding tautomeric form, *i.e.*, amino, imino, hydroxy or oxo, respectively.

20 [0021] Compounds of the invention are named according to systematic application of the nomenclature rules agreed upon by the International Union of Pure and Applied Chemistry (IUPAC), International Union of Biochemistry and Molecular Biology (IUBMB), and the Chemical Abstracts Service (CAS).

[0022] The compounds of the invention, or their pharmaceutically acceptable salts, may have asymmetric carbon atoms, oxidized sulfur atoms or quaternized nitrogen atoms in their structure.

25 [0023] The compounds of the invention and their pharmaceutically acceptable salts may exist as single stereoisomers, racemates, and as mixtures of enantiomers and diastereomers. The compounds may also exist as geometric isomers. All such single stereoisomers, racemates and mixtures thereof, and geometric isomers are intended to be within the scope of this invention.

30 [0024] It is assumed that when considering generic descriptions of compounds of the invention for the purpose of constructing a compound, such construction results in the creation of a stable structure. That is, one of ordinary skill in the art would recognize that

there can theoretically be some constructs which would not normally be considered as stable compounds (that is, sterically practical and/or synthetically feasible, *supra*).

[0025] When a particular group with its bonding structure is denoted as being bonded to two partners; that is, a divalent group, for example, $-\text{OCH}_2-$, then it is understood that either of the two partners may be bound to the particular group at one end, and the other partner is necessarily bound to the other end of the particular group, unless stated explicitly otherwise. Stated another way, divalent groups are not to be construed as limited to the depicted orientation, for example “ $-\text{OCH}_2-$ ” is meant to mean not only “ $-\text{OCH}_2-$ ” as drawn, but also “ $-\text{CH}_2\text{O}-$ ”.

[0026] In addition to the preferred embodiments recited hereinabove, also preferred are embodiments comprising combinations of preferred embodiments.

[0027] Methods for the preparation and/or separation and isolation of single stereoisomers from racemic mixtures or non-racemic mixtures of stereoisomers are well known in the art. For example, optically active (R)- and (S)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. Enantiomers (R- and S-isomers) may be resolved by methods known to one of ordinary skill in the art, for example by: formation of diastereoisomeric salts or complexes which may be separated, for example, by crystallization; via formation of diastereoisomeric derivatives which may be separated, for example, by crystallization, selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where a desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step may be required to liberate the desired enantiomeric form. Alternatively, a specific enantiomer may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents or by converting one enantiomer to the other by asymmetric transformation. For a mixture of enantiomers, enriched in a particular enantiomer, the major component enantiomer may be further enriched (with concomitant loss in yield) by recrystallization.

[0028] “Patient” for the purposes of the present invention includes humans and other animals, particularly mammals, and other organisms. Thus the methods are applicable to both

human therapy and veterinary applications. In a preferred embodiment the patient is a mammal, and in a most preferred embodiment the patient is human.

[0029] “Kinase-dependent diseases or conditions” refer to pathologic conditions that depend on the activity of one or more protein kinases. Kinases either directly or indirectly participate in the signal transduction pathways of a variety of cellular activities including proliferation, adhesion, migration, differentiation and invasion. Diseases associated with kinase activities include tumor growth, the pathologic neovascularization that supports solid tumor growth, and associated with other diseases where excessive local vascularization is involved such as ocular diseases (diabetic retinopathy, age-related macular degeneration, and the like) and inflammation (psoriasis, rheumatoid arthritis, and the like).

[0030] While not wishing to be bound to theory, phosphatases can also play a role in “kinase-dependent diseases or conditions” as cognates of kinases; that is, kinases phosphorylate and phosphatases dephosphorylate, for example protein substrates. Therefore compounds of the invention, while modulating kinase activity as described herein, may also modulate, either directly or indirectly, phosphatase activity. This additional modulation, if present, may be synergistic (or not) to activity of compounds of the invention toward a related or otherwise interdependent kinase or kinase family. In any case, as stated previously, the compounds of the invention are useful for treating diseases characterized in part by abnormal levels of cell proliferation (*i.e.* tumor growth), programmed cell death (apoptosis), cell migration and invasion and angiogenesis associated with tumor growth.

[0031] “Therapeutically effective amount” is an amount of a compound of the invention, that when administered to a patient, ameliorates a symptom of the disease. The amount of a compound of the invention which constitutes a “therapeutically effective amount” will vary depending on the compound, the disease state and its severity, the age of the patient to be treated, and the like. The therapeutically effective amount can be determined routinely by one of ordinary skill in the art having regard to their knowledge and to this disclosure.

[0032] “Cancer” refers to cellular-proliferative disease states, including but not limited to: Cardiac: sarcoma (angiosarcoma, fibrosarcoma, rhabdomyosarcoma, liposarcoma), myxoma, rhabdomyoma, fibroma, lipoma and teratoma; Lung: bronchogenic carcinoma (squamous cell, undifferentiated small cell, undifferentiated large cell, adenocarcinoma), alveolar (bronchiolar) carcinoma, bronchial adenoma, sarcoma, lymphoma, chondromatous hamartoma, mesothelioma; Gastrointestinal: esophagus (squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, lymphoma), stomach (carcinoma, lymphoma, leiomyosarcoma), pancreas (ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma,

carcinoid tumors, vipoma), small bowel (adenocarcinoma, lymphoma, carcinoid tumors, Karposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, fibroma), large bowel (adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, leiomyoma); Genitourinary tract: kidney (adenocarcinoma, Wilm's tumor [nephroblastoma], lymphoma, leukemia), bladder and urethra (squamous cell carcinoma, transitional cell carcinoma, adenocarcinoma), prostate (adenocarcinoma, sarcoma), testis (seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, lipoma); Liver: hepatoma (hepatocellular carcinoma), cholangiocarcinoma, hepatoblastoma, angiosarcoma, hepatocellular adenoma, hemangioma; Bone: osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocyoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochondroma (osteochondrosarcoma), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors; Nervous system: skull (osteoma, hemangioma, granuloma, xanthoma, osteitis deformans), meninges (meningioma, meningiosarcoma, gliomatosis), brain (astrocytoma, medulloblastoma, glioma, ependymoma, germinoma [pinealoma], glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, congenital tumors), spinal cord neurofibroma, meningioma, glioma, sarcoma); Gynecological: uterus (endometrial carcinoma), cervix (cervical carcinoma, pre-tumor cervical dysplasia), ovaries (ovarian carcinoma [serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma], granulosa-thecal cell tumors, Sertoli-Leydig cell tumors, dysgerminoma, malignant teratoma), vulva (squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, melanoma), vagina (clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma (embryonal rhabdomyosarcoma), fallopian tubes (carcinoma); Hematologic: blood (myeloid leukemia [acute and chronic], acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome), Hodgkin's disease, non-Hodgkin's lymphoma [malignant lymphoma]; Skin: malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Karposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, psoriasis; Adrenal Glands: neuroblastoma; and breast cancer. Thus, the term "cancerous cell" as provided herein, includes a cell afflicted by any one of the above-identified conditions.

[0033] "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise

undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like, as well as organic acids such as acetic acid, trifluoroacetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like.

[0034] "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Exemplary salts are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglucamine, theobromine, purines, piperazine, piperidine, N-ethylpiperidine, polyamine resins, and the like. Exemplary organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline, and caffeine. (See, for example, S. M. Berge, et al., "Pharmaceutical Salts," J. Pharm. Sci., 1977;66:1-19 which is incorporated herein by reference.).

[0035] "Metabolite" refers to the break-down or end product of a compound or its salt produced by metabolism or biotransformation in the animal or human body; for example, biotransformation to a more polar molecule such as by oxidation, reduction, or hydrolysis, or to a conjugate (see Goodman and Gilman, "The Pharmacological Basis of Therapeutics" 8.sup.th Ed., Pergamon Press, Gilman et al. (eds), 1990 for a discussion of biotransformation). As used herein, the metabolite of a compound of the invention or its salt may be the biologically active form of the compound in the body. In one example, a prodrug may be used such that the biologically active form, a metabolite, is released *in vivo*. In another example, a biologically active metabolite is discovered serendipitously, that is, no prodrug design *per se* was undertaken. An assay for activity of a metabolite of a compound of the present invention is known to one of skill in the art in light of the present disclosure.

[0036] In addition, the compounds of the present invention can exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the

like. In general, the solvated forms are considered equivalent to the unsolvated forms for the purposes of the present invention.

[0037] In addition, it is intended that the present invention cover compounds made either using standard organic synthetic techniques, including combinatorial chemistry or by biological methods, such as bacterial digestion, metabolism, enzymatic conversion, and the like.

[0038] "Treating" or "treatment" as used herein covers the treatment of a disease-state in a human, which disease-state is characterized by abnormal cellular proliferation, and invasion and includes at least one of: (i) preventing the disease-state from occurring in a human, in particular, when such human is predisposed to the disease-state but has not yet been diagnosed as having it; (ii) inhibiting the disease-state, *i.e.*, arresting its development; and (iii) relieving the disease-state, *i.e.*, causing regression of the disease-state. As is known in the art, adjustments for systemic versus localized delivery, age, body weight, general health, sex, diet, time of administration, drug interaction and the severity of the condition may be necessary, and will be ascertainable with routine experimentation by one of ordinary skill in the art.

[0039] One of ordinary skill in the art would understand that certain crystallized, protein-ligand complexes, in particular IRK, IGF1R, c-Met, c-Kit, KDR, flt-3, or flt-4-ligand complexes, and their corresponding x-ray structure coordinates can be used to reveal new structural information useful for understanding the biological activity of kinases as described herein. As well, the key structural features of the aforementioned proteins, particularly, the shape of the ligand binding site, are useful in methods for designing or identifying selective modulators of kinases and in solving the structures of other proteins with similar features. Such protein-ligand complexes, having compounds of the invention as their ligand component, are an embodiment of the invention.

[0040] As well, one of ordinary skill in the art would appreciate that such suitable x-ray quality crystals can be used as part of a method of identifying a candidate agent capable of binding to and modulating the activity of kinases. Such methods may be characterized by the following embodiments: a) introducing into a suitable computer program, information defining a ligand binding domain of a kinase in a conformation (*e.g.* as defined by x-ray structure coordinates obtained from suitable x-ray quality crystals as described above) wherein the computer program creates a model of the three dimensional structures of the ligand binding domain, b) introducing a model of the three dimensional structure of a candidate agent in the computer program, c) superimposing the model of the candidate agent

on the model of the ligand binding domain, and d) assessing whether the candidate agent model fits spatially into the ligand binding domain. Embodiments a-d are not necessarily carried out in the aforementioned order. Such methods may further entail: performing rational drug design with the model of the three-dimensional structure, and selecting a potential candidate agent in conjunction with computer modeling.

[0041] Additionally, one skilled in the art would appreciate that such methods may further entail: employing a candidate agent, so-determined to fit spatially into the ligand binding domain, in a biological activity assay for kinase modulation, and determining whether said candidate agent modulates kinase activity in the assay. Such methods may also include administering the candidate agent, determined to modulate kinase activity, to a mammal suffering from a condition treatable by kinase modulation, such as those described above.

[0042] Also, one skilled in the art would appreciate that compounds of the invention can be used in a method of evaluating the ability of a test agent to associate with a molecule or molecular complex comprising a ligand binding domain of a kinase. Such a method may be characterized by the following embodiments: a) creating a computer model of a kinase binding pocket using structure coordinates obtained from suitable x-ray quality crystals of the kinase, b) employing computational algorithms to perform a fitting operation between the test agent and the computer model of the binding pocket, and c) analyzing the results of the fitting operation to quantify the association between the test agent and the computer model of the binding pocket.

General Administration

[0043] Administration of the compounds of the invention, or their pharmaceutically acceptable salts, in pure form or in an appropriate pharmaceutical composition, can be carried out via any of the accepted modes of administration or agents for serving similar utilities. Thus, administration can be, for example, orally, nasally, parenterally (intravenous, intramuscular, or subcutaneous), topically, transdermally, intravaginally, intravesically, intracisternally, or rectally, in the form of solid, semi-solid, lyophilized powder, or liquid dosage forms, such as for example, tablets, suppositories, pills, soft elastic and hard gelatin capsules, powders, solutions, suspensions, or aerosols, or the like, preferably in unit dosage forms suitable for simple administration of precise dosages.

[0044] The compositions will include a conventional pharmaceutical carrier or excipient and a compound of the invention as the/an active agent, and, in addition, may include other

medicinal agents, pharmaceutical agents, carriers, adjuvants, etc. Compositions of the invention may be used in combination with anticancer or other agents that are generally administered to a patient being treated for cancer. Adjuvants include preserving, wetting, suspending, sweetening, flavoring, perfuming, emulsifying, and dispensing agents.

5 Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, and the like. It may also be desirable to include isotonic agents, for example sugars, sodium chloride, and the like. Prolonged absorption of the injectable pharmaceutical form can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

10 **[0045]** If desired, a pharmaceutical composition of the invention may also contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, antioxidants, and the like, such as, for example, citric acid, sorbitan monolaurate, triethanolamine oleate, butylated hydroxytoluene, etc.

[0046] Compositions suitable for parenteral injection may comprise physiologically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, and sterile powders for reconstitution into sterile injectable solutions or dispersions. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (propyleneglycol, polyethyleneglycol, glycerol, and the like), suitable mixtures thereof, vegetable oils (such as olive oil) and injectable organic esters such as ethyl
15 oleate. Proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersions and by the use of surfactants.

[0047] One preferable route of administration is oral, using a convenient daily dosage regimen that can be adjusted according to the degree of severity of the disease-state to be
20 treated.

[0048] Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound is admixed with at least one inert customary excipient (or carrier) such as sodium citrate or dicalcium phosphate or (a) fillers or extenders, as for example, starches, lactose, sucrose, glucose, mannitol, and
25 silicic acid, (b) binders, as for example, cellulose derivatives, starch, alginates, gelatin, polyvinylpyrrolidone, sucrose, and gum acacia, (c) humectants, as for example, glycerol, (d) disintegrating agents, as for example, agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, croscarmellose sodium, complex silicates, and sodium carbonate, (e) solution retarders, as for example paraffin, (f) absorption accelerators, as for example, quaternary

ammonium compounds, (g) wetting agents, as for example, cetyl alcohol, and glycerol monostearate, magnesium stearate and the like (h) adsorbents, as for example, kaolin and bentonite, and (i) lubricants, as for example, talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, or mixtures thereof. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents.

[0049] Solid dosage forms as described above can be prepared with coatings and shells, such as enteric coatings and others well known in the art. They may contain pacifying agents, and can also be of such composition that they release the active compound or compounds in a certain part of the intestinal tract in a delayed manner. Examples of embedded compositions that can be used are polymeric substances and waxes. The active compounds can also be in microencapsulated form, if appropriate, with one or more of the above-mentioned excipients.

[0050] Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs. Such dosage forms are prepared, for example, by dissolving, dispersing, etc., a compound(s) of the invention, or a pharmaceutically acceptable salt thereof, and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, ethanol and the like; solubilizing agents and emulsifiers, as for example, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propyleneglycol, 1,3-butyleneglycol, dimethylformamide; oils, in particular, cottonseed oil, groundnut oil, corn germ oil, olive oil, castor oil and sesame oil, glycerol, tetrahydrofurfuryl alcohol, polyethyleneglycols and fatty acid esters of sorbitan; or mixtures of these substances, and the like, to thereby form a solution or suspension.

[0051] Suspensions, in addition to the active compounds, may contain suspending agents, as for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, or mixtures of these substances, and the like.

[0052] Compositions for rectal administrations are, for example, suppositories that can be prepared by mixing the compounds of the present invention with for example suitable non-irritating excipients or carriers such as cocoa butter, polyethyleneglycol or a suppository wax, which are solid at ordinary temperatures but liquid at body temperature and therefore, melt while in a suitable body cavity and release the active component therein.

[0053] Dosage forms for topical administration of a compound of this invention include ointments, powders, sprays, and inhalants. The active component is admixed under sterile conditions with a physiologically acceptable carrier and any preservatives, buffers, or

propellants as may be required. Ophthalmic Formulations, eye ointments, powders, and solutions are also contemplated as being within the scope of this invention.

[0054] Generally, depending on the intended mode of administration, the pharmaceutically acceptable compositions will contain about 1% to about 99% by weight of a compound(s) of the invention, or a pharmaceutically acceptable salt thereof, and 99% to 1% by weight of a suitable pharmaceutical excipient. In one example, the composition will be between about 5% and about 75% by weight of a compound(s) of the invention, or a pharmaceutically acceptable salt thereof, with the rest being suitable pharmaceutical excipients.

[0055] Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington's Pharmaceutical Sciences, 18th Ed., (Mack Publishing Company, Easton, Pa., 1990). The composition to be administered will, in any event, contain a therapeutically effective amount of a compound of the invention, or a pharmaceutically acceptable salt thereof, for treatment of a disease-state in accordance with the teachings of this invention.

[0056] The compounds of the invention, or their pharmaceutically acceptable salts, are administered in a therapeutically effective amount which will vary depending upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of the compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular disease-states, and the host undergoing therapy. The compounds of the present invention can be administered to a patient at dosage levels in the range of about 0.1 to about 1,000 mg per day. For a normal human adult having a body weight of about 70 kilograms, a dosage in the range of about 0.01 to about 100 mg per kilogram of body weight per day is an example. The specific dosage used, however, can vary. For example, the dosage can depend on a number of factors including the requirements of the patient, the severity of the condition being treated, and the pharmacological activity of the compound being used. The determination of optimum dosages for a particular patient is well known to one of ordinary skill in the art.

General Synthetic Section

[0057] The compounds of the invention, or their pharmaceutically acceptable salts, may have asymmetric carbon atoms or quaternized nitrogen atoms in their structure.

[0058] It is assumed that when considering generic descriptions of compounds of the invention for the purpose of constructing a compound, such construction results in the

creation of a stable structure. That is, one of ordinary skill in the art would recognize that theoretically some constructs which would not normally be considered as stable compounds (that is, sterically practical and/or synthetically feasible, *supra*).

[0059] The compounds of the invention and their pharmaceutically acceptable salts may exist as single stereoisomers, racemates, and as mixtures of enantiomers and diastereomers. The compounds may also exist as geometric isomers. All such single stereoisomers, racemates and mixtures thereof, and geometric isomers are intended to be within the scope of this invention.

[0060] Methods for the preparation and/or separation and isolation of single stereoisomers from racemic mixtures or non-racemic mixtures of stereoisomers are well known in the art. For example, optically active (R)- and (S)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. Enantiomers (R- and S-isomers) may be resolved by methods known to one of ordinary skill in the art, for example by: formation of diastereoisomeric salts or complexes which may be separated, for example, by crystallization; via formation of diastereoisomeric derivatives which may be separated, for example, by crystallization, selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where a desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step may be required to liberate the desired enantiomeric form. Alternatively, specific enantiomer may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents or by converting one enantiomer to the other by asymmetric transformation. For a mixture of enantiomers, enriched in a particular enantiomer, the major component enantiomer may be further enriched (with concomitant loss in yield) by recrystallization.

[0061] In addition, the compounds of the present invention can exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like. In general, the solvated forms are considered equivalent to the unsolvated forms for the purposes of the present invention.

[0062] In addition, it is intended that the present invention cover compounds made either using standard organic synthetic techniques, including combinatorial chemistry or by

biological methods, such as bacterial digestion, metabolism, enzymatic conversion, and the like.

Abbreviations and their Definitions

[0063] The following abbreviations and terms have the indicated meanings throughout:

Abbreviation	Meaning
Ac	acetyl
br	broad
°C	degrees Celsius
c-	cyclo
CBZ	CarboBenZoxy = benzyloxycarbonyl
d	doublet
dd	doublet of doublet
dt	doublet of triplet
DIPEA	<i>N,N</i> -diisopropylethylamine
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
EI	Electron Impact ionization
Et	Ethyl
g	gram(s)
GC	gas chromatography
h or hr	hour(s)
HOAc	acetic acid
HOBt	Hydroxybenzotriazole
HPLC	high pressure liquid chromatography
L	liter(s)
M	molar or molarity
m	Multiplet
Me	Methyl
mesyl	Methanesulfonyl
mg	milligram(s)
MHz	megahertz (frequency)

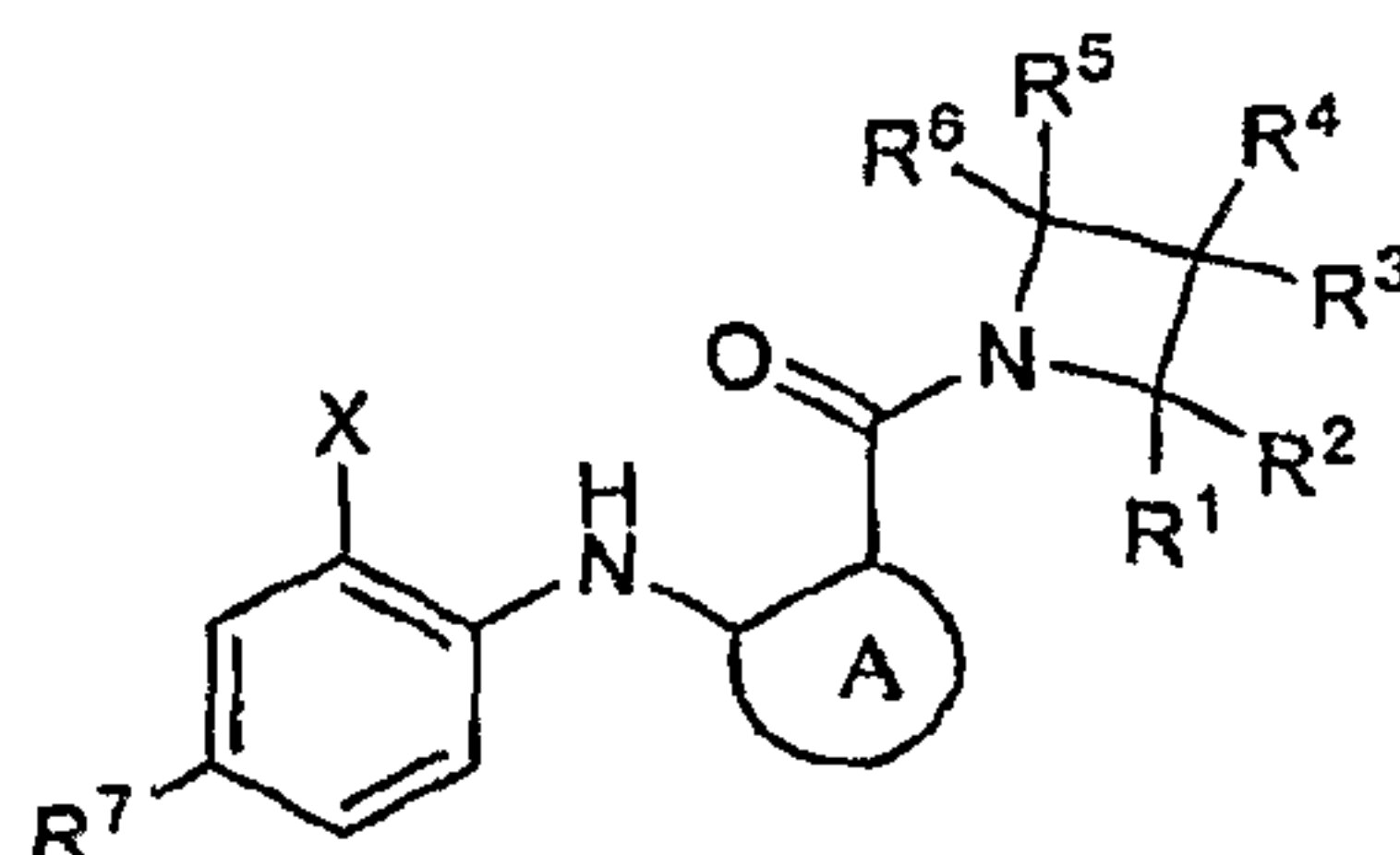
Min	minute(s)
mL	milliliter(s)
mM	Millimolar
mmol	millimole(s)
mol	mole(s)
MS	mass spectral analysis
MTBE	methyl t-butyl ether
N	normal or normality
NBS	<i>N</i> -bromosuccinimide
NCS	<i>N</i> -chlorosuccinimide
nM	Nanomolar
NMO	<i>N</i> -methyldmorpholine oxide
NMR	nuclear magnetic resonance spectroscopy
PEG	polyethylene glycol
pEY	poly-glutamine, tyrosine
Ph	Phenyl
PhOH	Phenol
PfP	Pentafluorophenol
PfPy	Pentafluoropyridine
PPTS	Pyridinium p-toluenesulfonate
Py	Pyridine
PyBroP	bromo-tris-pyrrolidino-phosphonium hexafluorophosphate
q	Quartet
RT	Room temperature
Sat'd	Saturated
s	Singlet
s-	Secondary
t-	Tertiary
t or tr	Triplet
TBDMS	<i>t</i> -butyldimethylsilyl

TES	Triethylsilyl
TFA	trifluoroacetic acid
THF	Tetrahydrofuran
TMOF	trimethyl orthoformate
TMS	trimethylsilyl
tosyl	<i>p</i> -toluenesulfonyl
Trt	triphenylmethyl
uL	microliter(s)
uM	Micromole(s) or micromolar

Section I

[0064] As noted above, this invention relates to compounds of Formula I and which inhibit MEK.

5 [0065] In one embodiment, in section I the invention provides a compound of Formula I below:



I

and optionally a pharmaceutically acceptable salt or solvate thereof, wherein the A ring

10 represents an arylene or heteroarylene group and the A ring is optionally substituted with one, two, three or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} where R^{10} , R^{12} , R^{14} , and R^{16} are independently hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, halo, haloalkoxy, hydroxy, lower alkoxy, amino, alkylamino, dialkylamino, haloalkyl, $-NHS(O)_2R^8$, $-CN$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$ or $-NR^8C(O)R^8$;

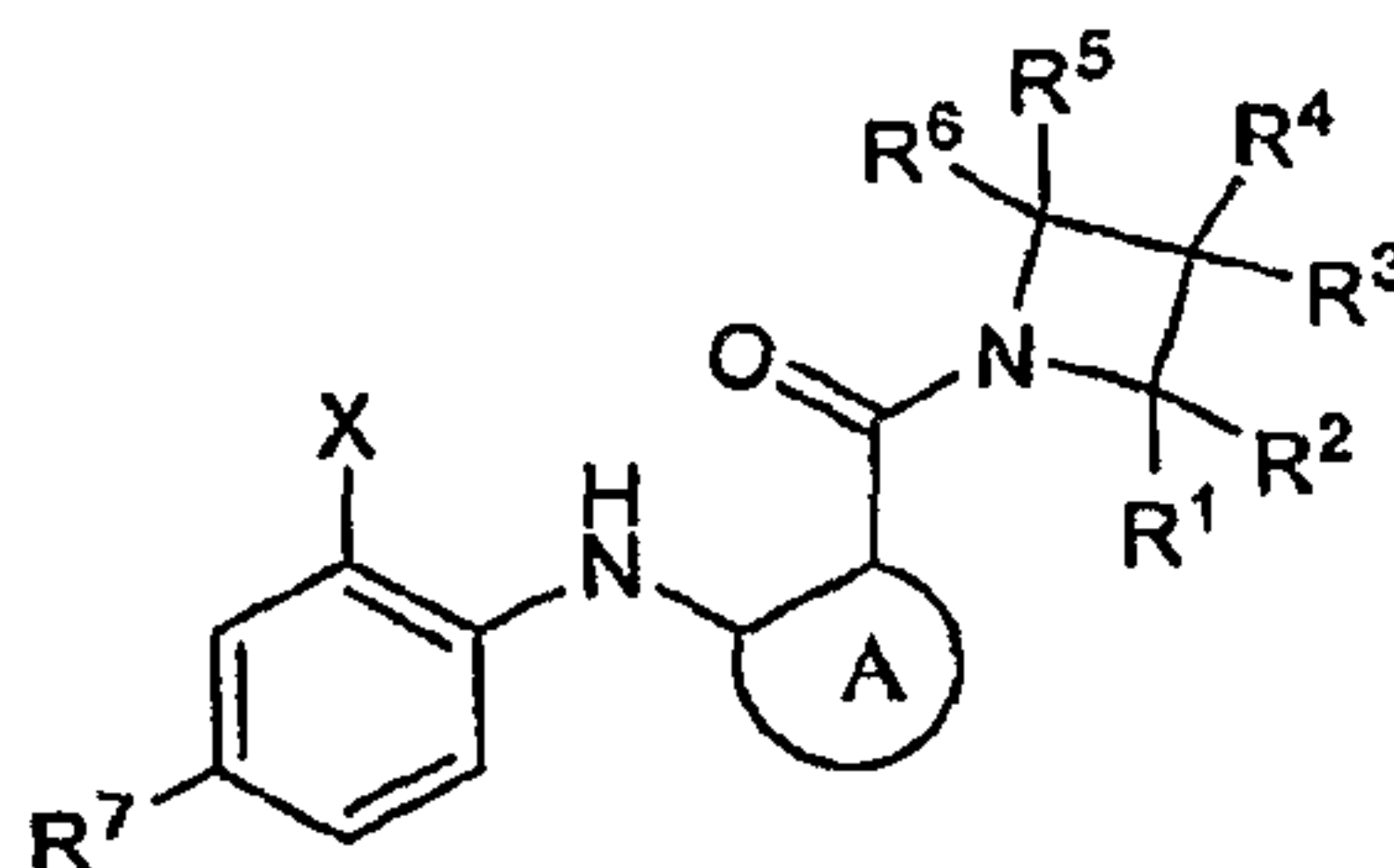
15 X is lower alkyl, halo, haloalkyl, or haloalkoxy;

R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, or $-NR^8C(O)R^8$; or

- R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are independently lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, and $-NR^8C(O)R^{8'}$, or
- one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;
- m is 1 or 2;
- R^7 is hydrogen, halo or lower alkyl; and
- R^8 , $R^{8'}$ and $R^{8''}$ are independently hydrogen, hydroxy, alkoxy, substituted alkoxy, lower alkanyl, haloalkyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from lower alkanyl, halo, hydroxy, hydroxyalkyl, lower alkoxy, substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and R^{31} is alkyl, substituted alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{34}SO_2R^{34a}$ (where R^{34} is hydrogen or lower alkyl and R^{34a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl), $-SO_2NR^{35}R^{35a}$ (where R^{35} is hydrogen or alkyl and R^{35a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, aryloxy, arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (where R^{32} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, lower

alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (where R^{33} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl).

[0066] In one embodiment, in section I the invention provides a compound of Formula Ia below:



Ia

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein the A ring represents an arylene or heteroarylene group and the A ring is optionally substituted with one, two, three or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16}

where R^{10} , R^{12} , R^{14} , and R^{16} are independently hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, halo, haloalkoxy, hydroxy, lower alkoxy, amino, alkylamino, dialkylamino, haloalkyl, $-NHS(O)_2R^8$, $-CN$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$ or $-NR^8C(O)R^8$;

X is lower alkyl, halo, haloalkyl, or haloalkoxy;

R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NHS(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, and $-NR^8C(O)R^8$; or

one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

m is 1 or 2;

R^7 is hydrogen, halo or lower alkyl;

R^8 , $R^{8'}$ and $R^{8''}$ are independently hydrogen, hydroxy, alkoxy, substituted alkoxy, lower alkanyl, haloalkyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl,

5 cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from lower alkanyl, halo, hydroxy, hydroxyalkyl, lower alkoxy, substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and R^{31} is alkyl, substituted alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{34}SO_2R^{34a}$ (where R^{34} is

10 hydrogen or lower alkyl and R^{34a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl),

$-SO_2NR^{35}R^{35a}$ (where R^{35} is hydrogen or alkyl and R^{35a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, aryloxy, arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (where R^{32} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, lower

15 20 alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (where R^{33} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl); and

R^9 is lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or

heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, or five groups selected from lower alkanyl, halo, hydroxy, haloalkoxy, haloalkyl, amino, alkylamino, and dialkylamino.

25

[0067] In another embodiment, the invention provides a compound of Formula I or Ia where R^7 is halo and all other groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, R^7 is iodo or bromo. In another embodiment, R^7 is iodo. In another embodiment, the compound is that where R^7 is iodo or bromo; the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; and all other groups are as defined for a Compound of Formula I or Ia, respectively.

30

[0068] In another embodiment, the invention provides a compound of Formula I or Ia where X is halo and all other groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, X is fluoro or chloro. In another embodiment, X is fluoro. In yet another embodiment, the compound is that where X is fluoro or chloro; the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶; and all other groups are as defined for a Compound of Formula I or Ia, respectively.

[0069] In another embodiment, the invention provides a compound of Formula I or Ia where R¹, R², R⁵, and R⁶ are hydrogen and all other groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, R¹, R², R⁵, and R⁶ are hydrogen; the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶; and all other groups are as defined for a Compound of Formula I or Ia, respectively.

[0070] In another embodiment, the invention provides a compound of Formula I or Ia where the A ring is a phenylene ring optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶ where R¹⁰, R¹², R¹⁴, R¹⁶, and all groups are as defined for a Compound of Formula I or Ia, respectively.

[0071] In another embodiment, the invention provides a compound of Formula I or Ia where R⁷ and X are halo and all other groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, R⁷ is iodo and X is fluoro.

[0072] In yet another embodiment (A1), the compound of Formula I or Ia is that where R⁷ and X are halo; the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶; and all other groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, R⁷ is iodo and X is fluoro; the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶; and all other groups are as defined for a Compound of Formula I or Ia, respectively.

[0073] In another embodiment (A2), the invention provides a Compound of Formula I or Ia where the A ring is phenylene; R¹⁴ and R¹⁶ are hydrogen; R¹⁰ and R¹² are independently hydrogen or halo; and all other groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, R¹⁰ and R¹² are independently hydrogen or fluoro. In another embodiment, R¹⁰ is 3-fluoro and R¹² is hydrogen. In another embodiment, R¹⁰ and R¹² are fluoro. In another embodiment, R¹⁰ and R¹² are 3-fluoro and 4-fluoro, 4-fluoro and 5-fluoro, or 4-fluoro and 6-fluoro.

[0074] In another embodiment of the invention (A3), the compound of Formula I or Ia is that where R^1 , R^2 , R^5 and R^6 are hydrogen; the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; and all other groups are as defined for a Compound of Formula I or Ia, respectively.

5 [0075] In another embodiment (A4), the invention provides a Compound of Formula Ia where the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; X, R^7 , R^{10} , R^{12} , R^{14} , and R^{16} are as defined for a Compound of Formula Ia; and

10 one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups
15 independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NHS(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; and
20 the others of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are as defined for a Compound of Formula Ia; or

one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached forms $C(O)$ or $C(=NOH)$; the others of R^1 , R^2 , R^3 , R^4 , R^5 , and
25 R^6 are as defined for a Compound of Formula Ia; and

all other groups are as defined in Formula Ia.

[0076] In another embodiment (A5), the invention provides a Compound of Formula Ia where the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; X, R^7 , R^{10} , R^{12} , R^{14} , and R^{16} are as defined for a
30 Compound of Formula Ia; and

R^3 is halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl,

heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, -OR⁸, -NR⁸R^{8'}, -NHS(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; and R⁴ is as defined in Formula Ia; or

R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in Formula Ia.

10 [0077] Another embodiment of embodiment A5 is that where R¹, R², R⁵ and R⁶ are hydrogen.

[0078] In another embodiment (A6), the Compound of Formula Ia where the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R¹⁰, R¹², R¹⁴, and R¹⁶; X, R⁷, R¹⁰, R¹², R¹⁴, and R¹⁶ are as defined for a Compound of Formula Ia; and R³ and R⁴ are independently halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in Formula Ia.

[0079] Another embodiment of embodiment A6 is that where R¹, R², R⁵ and R⁶ are hydrogen.

30 [0080] In another embodiment (A7), the invention provides a Compound of Formula Ia where the A ring is phenylene optionally substituted with R¹⁰, R¹², R¹⁴, and R¹⁶ where R¹⁴ and R¹⁶ are hydrogen and where R¹⁰ and R¹² are independently hydrogen or halo; X and R⁷ are halo; R¹, R², R⁵ and R⁶ are hydrogen; and

R^3 is hydrogen and R^4 is $-NR^8R^{8'}$ (where R^8 is hydrogen, hydroxy, lower alkanyl, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl and $R^{8'}$ is hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl), $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$,
 5 $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$,
 $-NR^8C(O)R^{8'}$, lower alkenyl, and lower alkynyl; where the lower alkenyl and lower alkynyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$,
 10 $-NHS(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^{8'}$ and $-NR^8C(O)R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

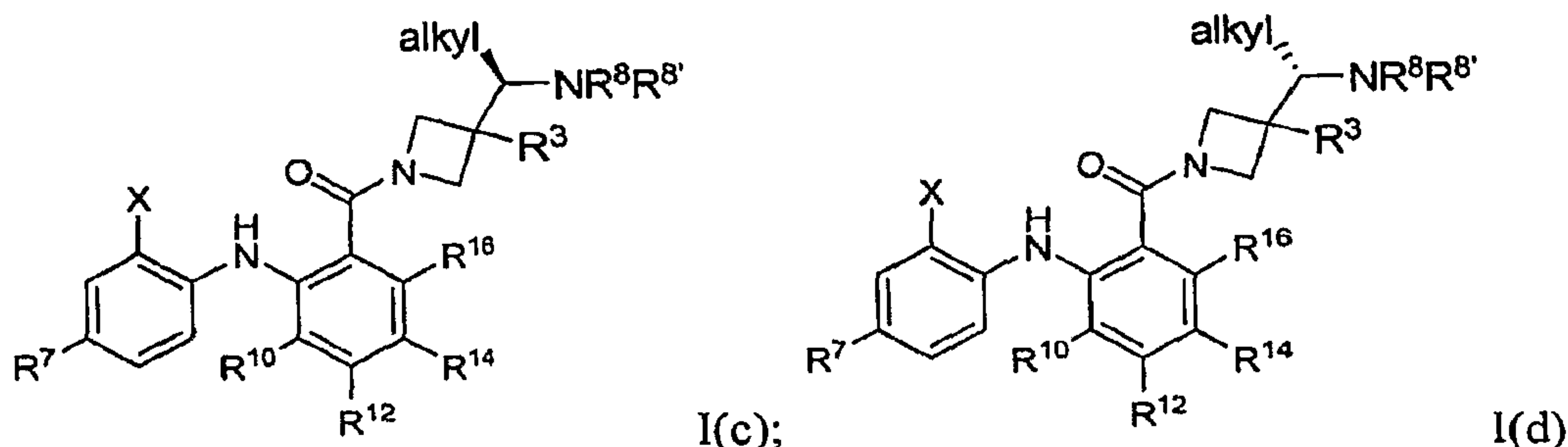
15 m , $R^{8''}$, and R^9 are as defined for a Compound of Formula Ia; and unless otherwise specified in this embodiment, R^8 and $R^{8'}$, and all other groups, are as defined in the Summary of the Invention for a Compound of Formula Ia.

[0081] In another embodiment of the Invention (A8), the invention provides a Compound of Formula I or Ia where the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; R^3 is hydrogen, halo, hydroxy, alkoxy, or amino; and all other groups are as defined in Formula I or Ia, respectively. In another embodiment, R^3 is hydrogen, fluoro, hydroxy, methoxy, or amino. In yet another embodiment, R^3 is hydrogen or hydroxy. In another embodiment, R^3 is hydroxy.

25 [0082] In another embodiment of embodiment A8, X and R^7 are halo; A is phenylene optionally substituted with R^{10} , R^{12} , R^{14} , and R^{16} where R^{14} and R^{16} are hydrogen and where R^{10} and R^{12} are independently hydrogen or halo; R^1 , R^2 , R^5 and R^6 are hydrogen; and R^4 is as defined in Formula I or Ia, respectively.

30 [0083] In another embodiment of the Invention (A9), the invention provides a Compound of Formula Ia where the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; R^1 , R^2 , R^5 and R^6 are hydrogen; R^3 is hydrogen, halo, hydroxy, alkoxy, or amino; and R^4 is heterocycloalkyl, heteroaryl, or alkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ and all other groups are as defined in Formula Ia.

[0084] Another embodiment of embodiment A9 is that where R^4 is alkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ and all other groups are as defined in Formula Ia. In another embodiment, the compound is of Formula I(c) or I(d):



5 where R^3 is as defined in A9; X , R^7 , R^8 , $R^{8'}$, R^{10} , R^{12} , R^{14} , and R^{16} are as defined in Formula Ia.

[0085] Another embodiment of embodiment A9 is that where R^4 is heterocycloalkyl.

[0086] In another embodiment of embodiment A9, the compound is that where X and R^7 are halo; A is phenylene optionally substituted with R^{10} , R^{12} , R^{14} , and R^{16} where R^{14} and R^{16} are hydrogen and where R^{10} and R^{12} are independently hydrogen or halo; R^3 is hydroxy; and R^4 is alkyl substituted with $-NR^8R^{8'}$ or R^4 is heterocycloalkyl optionally substituted with one, two, or three groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NHS(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8''}$, $-NR^8C(O)OR^8$ and $-NR^8C(O)R^8$; and where m , R^3 , R^8 , $R^{8'}$, $R^{8''}$, and R^9 are as defined in Formula Ia.

[0087] In another embodiment of the Invention (A10), the invention provides a Compound of Formula Ia where the A ring is phenylene optionally substituted with one, two, three, or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} ; R^4 is

- hydrogen;
- lower alkanyl;
- lower alkanyl substituted with one or two $-OR^8$ where R^8 is hydrogen, aryl, or lower alkanyl where the lower alkanyl in R^8 is substituted with one or two hydroxy;
- lower alkanyl substituted with one, two, or three halo;
- lower alkanyl substituted with nitro;
- lower alkanyl substituted with $-S(O)_mR^9$ (where m is 0 and R^9 is aryl);
- lower alkanyl substituted with optionally substituted heterocycloalkyl;

- h) lower alkenyl;
- i) $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen; lower alkanyl; lower alkenyl; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with one or two $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; lower alkanyl substituted with optionally substituted heteroaryl; or lower alkanyl substituted with optionally substituted cycloalkyl);
- 5 j) $-C(O)NR^8R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl; and $R^{8'}$ is hydrogen; hydroxy; lower alkanyl; lower alkenyl; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with optionally substituted heterocycloalkyl; lower alkanyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, alkyl, or hydroxyalkyl; or alkoxy);
- 10 k) $-NR^8C(O)OR^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl);
- l) lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, or lower alkanyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; hydroxy; alkoxy; lower alkanyl; lower alkenyl; lower alkynyl; alkoxy; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with one or two alkoxy; lower alkanyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl; lower alkanyl substituted with one or two hydroxy and one or two $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl; lower alkanyl substituted with one, two, three, four, or five halo; lower alkanyl substituted with optionally substituted cycloalkyl; lower alkanyl substituted with optionally substituted aryl; lower alkanyl substituted with one or two hydroxy and one optionally substituted aryl; lower alkanyl substituted with optionally substituted heterocycloalkyl; lower alkanyl substituted with optionally substituted heteroaryl; heteroaryl; aryl; aryl substituted with one or two hydroxy; aryl substituted with one or two alkoxy; aryl substituted with one or two halo; aryl substituted with one or two $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or lower alkanyl and R^{32a} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl; aryl substituted with $-NR^{34}SO_2R^{34a}$ where R^{34} is hydrogen or lower alkanyl and R^{34a} is lower alkanyl, lower alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl; cycloalkyl; cycloalkyl substituted with one or two hydroxy; cycloalkyl substituted with one or two hydroxy and one or two hydroxyalkyl; cycloalkyl substituted with one or two alkoxy; cycloalkyl substituted with carboxy;
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- 30

cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or lower alkanyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl; lower alkanyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or lower alkanyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl; cycloalkyl substituted with optionally substituted cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted with lower alkanyl; heterocycloalkyl substituted with alkoxycarbonyl; heterocycloalkyl substituted with optionally substituted arylalkyl; heterocycloalkyl substituted with one or two hydroxy; heterocycloalkyl substituted with one or two alkoxy;

heterocycloalkyl substituted with one or two hydroxyalkyl; heterocycloalkyl substituted with one or two hydroxy, one or two alkoxy, and one or two hydroxyalkyl; lower alkanyl substituted with optionally substituted aryloxy; lower alkanyl substituted with $-S(O)_nR^{31}$ where n is 0 and R^{31} is lower alkanyl; lower alkanyl substituted with carboxy; lower alkanyl substituted with alkoxycarbonyl; or lower alkanyl substituted with $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or lower alkanyl and R^{32a} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl);

m) $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl; and $R^{8'}$ is hydrogen; lower alkanyl; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with optionally substituted heterocycloalkyl; lower alkanyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, hydroxyalkyl, or lower alkenyl);

n) cycloalkyl;

o) cycloalkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl;

p) heterocycloalkyl;

q) heterocycloalkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl;

r) heterocycloalkyl substituted with one or two lower alkanyl;

s) heterocycloalkyl substituted with $-C(O)OR^8$ where R^8 is lower alkanyl or lower alkenyl;

t) lower alkanyl substituted with $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl and $R^{8'}$ is lower alkanyl; lower alkenyl; or lower alkanyl substituted with alkoxy, aryl, and one, two, or three halo);

u) heteroaryl;

- v) heteroaryl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl; lower alkanyl substituted with optionally substituted heteroaryl;
- w) lower alkanyl substituted with $-NR^8S(O)_2R^9$ where R^8 is hydrogen, lower alkanyl, or lower alkenyl and R^9 is lower alkanyl or lower alkenyl;
- x) lower alkanyl substituted with $-NR^8C(O)OR^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl;
- y) lower alkanyl substituted with one aryl and one $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl; or
- z) lower alkanyl substituted with one or two $-OR^8$ (where R^8 is hydrogen) and one or two $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl; and

all other groups are as defined for a Compound of Formula Ia.

[0088] Another embodiment of embodiment A10 is that wherein X and R^7 are halo; A is phenylene optionally substituted with R^{10} , R^{12} , R^{14} , and R^{16} where R^{14} and R^{16} are hydrogen and where R^{10} and R^{12} are independently hydrogen or halo; R^1 , R^2 , R^5 and R^6 are hydrogen; and R^3 is hydrogen, halo, hydroxy, alkoxy, or amino.

[0089] Another embodiment of embodiment A10 is that where R^3 is hydrogen and R^4 is

- a) hydrogen;
- b) $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen; lower alkanyl; lower alkenyl; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with one or two $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl; lower alkanyl substituted with optionally substituted heteroaryl; or lower alkanyl substituted with optionally substituted cycloalkyl);
- c) $-C(O)NR^8R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl; and $R^{8'}$ is hydrogen; hydroxy; lower alkanyl; lower alkenyl; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with heterocycloalkyl; lower alkanyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl; alkoxy; or substituted alkoxy);
- d) $-NR^8C(O)OR^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl);
- e) $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl; and $R^{8'}$ is hydrogen; lower alkanyl; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with optionally substituted heterocycloalkyl; lower alkanyl

substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, hydroxyalkyl, or lower alkenyl);

f) lower alkanyl;

g) lower alkanyl substituted with one or two $-OR^8$ (where R^8 is hydrogen);

5 h) lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, or lower alkanyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; lower alkanyl; lower alkenyl; lower alkynyl; lower alkanyl substituted with one or two hydroxy; heterocycloalkyl substituted with lower alkanyl; or lower alkanyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen,
10 lower alkanyl, or hydroxyalkyl);

i) heterocycloalkyl; or

j) heterocycloalkyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl).

[0090] Another embodiment of embodiment A10 is that where R^3 is alkoxy and R^4 is
15 lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl). In another embodiment, R^3 is methoxy and R^4 is lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl).

[0091] Another embodiment of embodiment A10 is that where R^3 is halo and R^4 is lower
20 alkanyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl). In another embodiment, R^3 is fluoro and R^4 is lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl).

[0092] Another embodiment of embodiment A10 is that where R^3 is amino and R^4 is
25 lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl).

[0093] Another embodiment of embodiment A10 is that where R^3 is hydroxy and R^4 is

a) hydrogen;

b) lower alkanyl;

30 c) lower alkenyl;

d) lower alkanyl substituted with one or two $-OR^8$ where R^8 is hydrogen, aryl, or lower alkanyl where the lower alkanyl in R^8 is substituted with one or two hydroxy;

e) lower alkanyl substituted with one, two, or three halo;

f) lower alkanyl substituted with nitro;

- g) lower alkanyl substituted with $-S(O)_mR^9$ (where m is 0 and R^9 is aryl);
- h) lower alkanyl substituted with optionally substituted heterocycloalkyl;
- i) lower alkanyl substituted with $-NR^8R^{8'}$ (where R^8 is hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, or lower alkanyl substituted with one or two hydroxy; and $R^{8'}$ is hydrogen; hydroxy; alkoxy; lower alkanyl; lower alkenyl; lower alkynyl; alkoxy; substituted alkoxy; lower alkanyl substituted with one or two hydroxy; lower alkanyl substituted with $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl; lower alkanyl substituted with one or two hydroxy and one or two $-NR^{30}R^{30'}$ where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl; heterocycloalkyl substituted with lower alkanyl, alkoxycarbonyl, or optionally substituted arylalkyl; lower alkanyl substituted with one, two, three, four, or five halo; lower alkanyl substituted with optionally substituted cycloalkyl; lower alkanyl substituted with optionally substituted aryl; lower alkanyl substituted with one or two hydroxy and one optionally substituted aryl; lower alkanyl substituted with optionally substituted heterocycloalkyl; lower alkanyl substituted with optionally substituted heteroaryl; heteroaryl; aryl; aryl substituted with one or two hydroxy; aryl substituted with one or two alkoxy; aryl substituted with one or two halo; aryl substituted with one or two $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or lower alkanyl and R^{32a} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl; aryl substituted with $-NR^{34}SO_2R^{34a}$ where R^{34} is hydrogen or lower alkanyl and R^{34a} is lower alkanyl, lower alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl; cycloalkyl; cycloalkyl substituted with one or two hydroxy; cycloalkyl substituted with one or two hydroxy and one or two hydroxyalkyl; cycloalkyl substituted with one or two alkoxy; cycloalkyl substituted with carboxy; cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl; cycloalkyl substituted with optionally substituted cycloalkyl; heterocycloalkyl; heterocycloalkyl substituted with one or two hydroxy; heterocycloalkyl substituted with one or two alkoxy; heterocycloalkyl substituted with one or two hydroxyalkyl; heterocycloalkyl substituted with one or two hydroxy, one or two alkoxy, and one or two hydroxyalkyl; lower alkanyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or alkyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl; lower alkanyl substituted with optionally substituted aryloxy; lower alkanyl substituted with $-S(O)_nR^{31}$ where n is 0 and R^{31} is lower alkanyl; lower alkanyl substituted with carboxy; lower alkanyl substituted with

- alkoxycarbonyl; or lower alkanyl substituted with $-NR^{32}C(O)R^{32a}$ where R^{32} is hydrogen or lower alkanyl and R^{32a} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl);
- j) heterocycloalkyl;
- 5 k) $-C(O)NR^8R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl; and $R^{8'}$ is hydrogen; lower alkanyl; lower alkenyl; or substituted with one or two hydroxy;);
- l) lower alkanyl substituted with $-NR^8C(O)R^{8'}$ (where R^8 is hydrogen, lower alkanyl, or lower alkenyl and $R^{8'}$ is lower alkanyl; lower alkenyl; or lower alkanyl substituted with alkoxy, aryl, and one, two, or three halo);
- 10 m) cycloalkyl;
- n) cycloalkyl substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl;
- o) cycloalkyl substituted with $-C(O)NR^{33}R^{33a}$ where R^{33} is hydrogen or lower alkanyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl;
- 15 p) heterocycloalkyl;
- q) heterocycloalkyl substituted with one or two lower alkanyl;
- r) heterocycloalkyl substituted with $-C(O)OR^8$ where R^8 is lower alkanyl or lower alkenyl;
- s) heteroaryl;
- 20 t) heteroaryl optionally substituted with $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl;
- u) lower alkanyl substituted with optionally substituted heteroaryl;
- v) lower alkanyl substituted with $-NR^8S(O)_2R^9$ where R^8 is hydrogen, lower alkanyl, or lower alkenyl and R^9 is lower alkanyl or lower alkenyl;
- 25 w) lower alkanyl substituted with $-NR^8C(O)OR^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl;
- x) lower alkanyl substituted with one aryl and one $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl; or
- y) lower alkanyl substituted with one or two $-OR^8$ (where R^8 is hydrogen) and one or
- 30 two $-NR^8R^{8'}$ where R^8 and $R^{8'}$ are independently hydrogen, lower alkanyl, or lower alkenyl.

[0094] Another embodiment of the Invention (A11) provides a compound of Formula I or Ia where the A ring is phenylene optionally substituted with R^{10} , R^{12} , R^{14} , and R^{16} ; R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and all other

groups are as defined for a Compound of Formula I or Ia, respectively. In another embodiment, X and R⁷ are halo; A is phenylene optionally substituted with with R¹⁰, R¹², R¹⁴, and R¹⁶ where R¹⁴ and R¹⁶ are hydrogen and where R¹⁰ and R¹² are independently hydrogen or halo; R¹, R², R⁵ and R⁶ are hydrogen; and R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH).

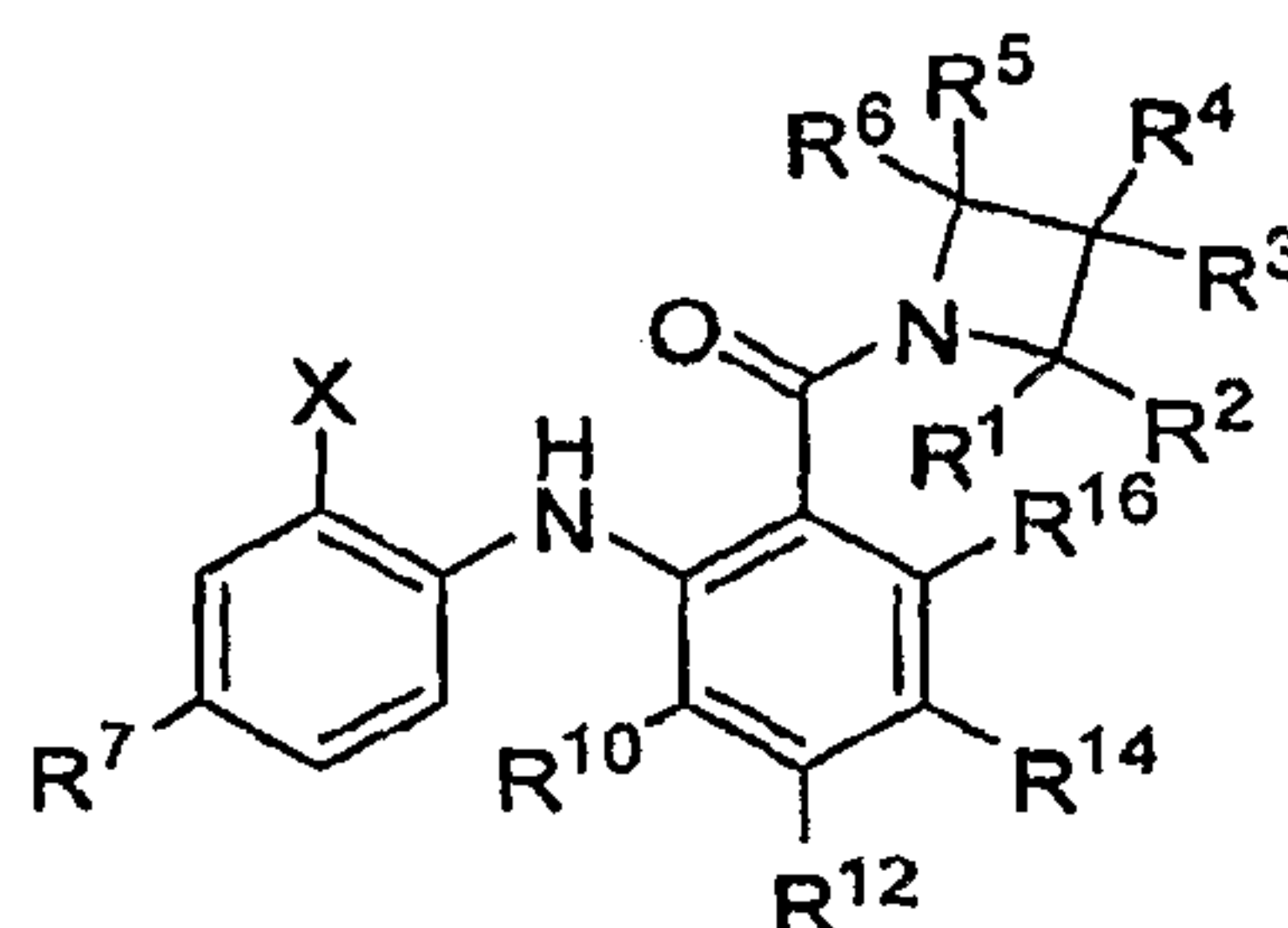
[0095] Another embodiment of the Invention (A12) provides a Compound of Formula I or Ia where the A ring is phenylene optionally substituted with R¹⁰, R¹², R¹⁴, and R¹⁶ where R¹⁴ and R¹⁶ are hydrogen and where R¹⁰ and R¹² are independently hydrogen or halo; X and R⁷ are halo; and R¹, R², R⁴, R⁵ and R⁶ are hydrogen; and all other groups are as defined in Formula I or Ia, respectively.

[0096] Another embodiment of the Invention (A14) provides a Compound of Formula I or Ia where the A ring is phenylene optionally substituted with R¹⁰, R¹², R¹⁴, and R¹⁶; R¹ is hydrogen; and R² is alkyl substituted with -NR⁸R^{8'}; where R⁸ and R^{8'} and all other groups are as defined in Formula I or Ia, respectively.

[0097] Another embodiment of the Invention (A15) provides a Compound Formula I or Ia where the A ring is phenylene optionally substituted with R¹⁰, R¹², R¹⁴, and R¹⁶; R⁷ is iodo or bromo; X is fluoro or chloro; R¹, R², R⁵, and R⁶ are hydrogen; and R¹⁰, R¹², R¹⁴, and R¹⁶ are independently hydrogen or fluoro; and all other groups are as defined in Formula I or Ia, respectively. In another embodiment, R¹⁰ is 3-fluoro and R¹², R¹⁴, and R¹⁶ are hydrogen or halo; R¹⁰ is 3-fluoro, R¹² is 4-fluoro, and R¹⁴ and R¹⁶ are hydrogen; R¹⁰ is 4-fluoro, R¹² is 5-fluoro, and R¹⁴ and R¹⁶ are hydrogen; R¹⁰ is 4-fluoro, R¹² is 6-fluoro, and R¹⁴ and R¹⁶ are hydrogen; or R¹² is 4-fluoro and R¹⁰, R¹⁴, and R¹⁶ are hydrogen.

[0098] In another embodiment, the invention is a compound of Formula I or Ia where the A ring is phenylene optionally substituted with R¹⁰, R¹², R¹⁴, and R¹⁶; R³ is hydroxy and R⁴ is heterocycloalkyl, lower alkanyl, or heteroaryl, where the lower alkanyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or lower alkanyl and R^{8'} is hydrogen, lower alkanyl, or cycloalkyl where the cycloalkyl is optionally substituted with groups independently selected from hydroxy and lower alkanyl) and the heteroaryl is optionally substituted with lower alkanyl; and all other groups are as defined in Formula I or Ia, respectively. In another embodiment, R³ is hydroxy and R⁴ is heterocycloalkyl or lower alkanyl, where the lower alkanyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or lower alkanyl and R^{8'} is hydrogen, lower alkanyl, or cycloalkyl where the cycloalkyl is optionally substituted with groups independently selected from hydroxy and lower alkanyl).

[0099] Another embodiment of the invention is a compound of Formula II:

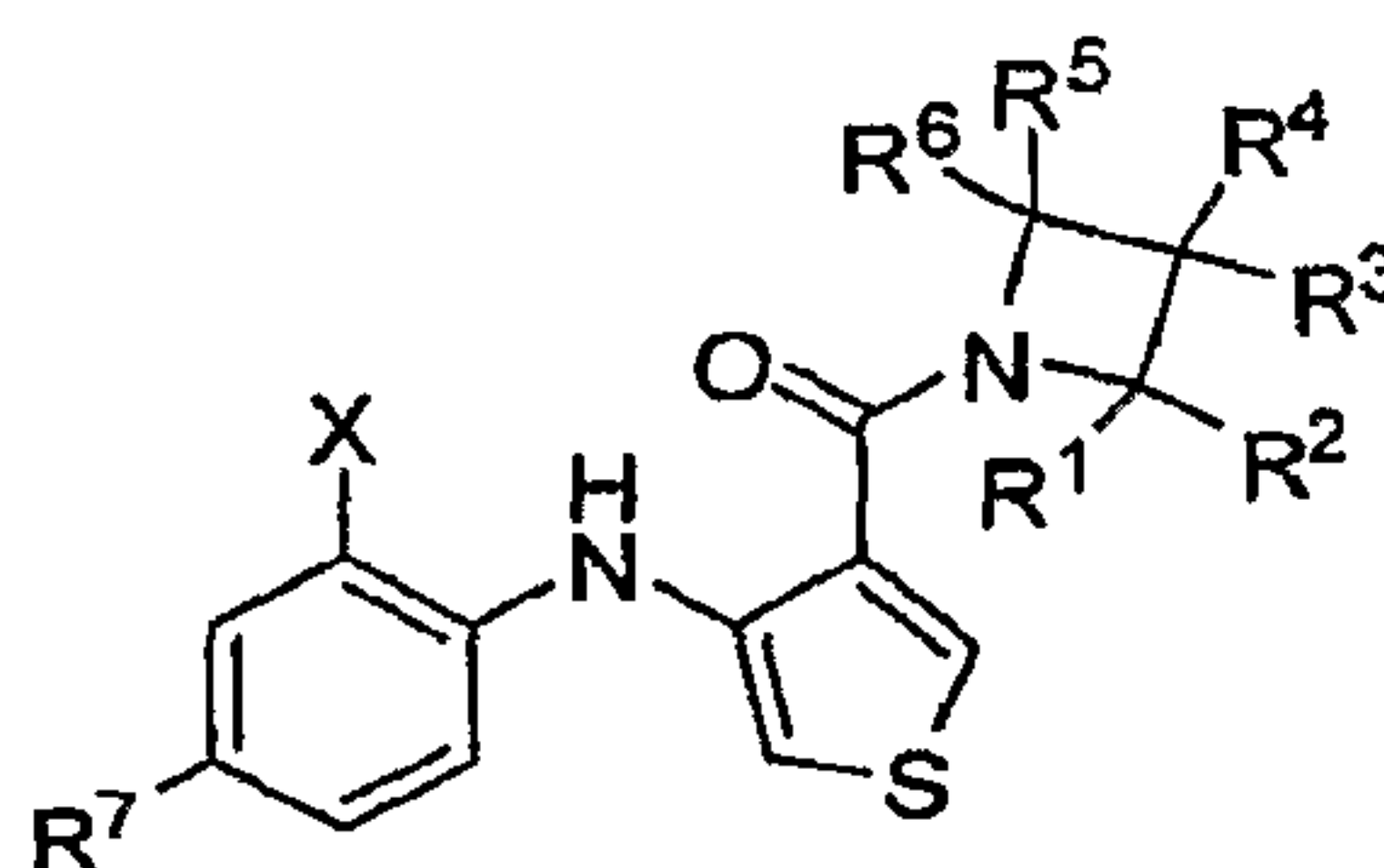


II

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein X, R¹, R², R³, R⁴, R⁵, R⁶, and R⁷ are as defined above for Formula I, and R¹⁰, R¹², R¹⁴ and R¹⁶ are independently selected from hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, halo, haloalkoxy, hydroxy, lower alkoxy, amino, alkylamino, dialkylamino, haloalkyl, -NHS(O)₂R⁸, -CN, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'} and -NR⁸C(O)R^{8'}.

[00100] In another embodiment of Formula II, R⁷ and X are halo and R¹⁰, R¹², R¹⁴ and R¹⁶ are independently selected from hydrogen and halo.

[00101] Another embodiment of the invention is a Compound of Formula III:



III

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein X, R¹, R², R³, R⁴, R⁵, R⁶, and R⁷ are as defined above for a Compound of Formula I.

[00102] In another embodiment of Formula III, X and R⁷ are halo. In another embodiment, X is fluoro or chloro and R⁷ is iodo or bromo.

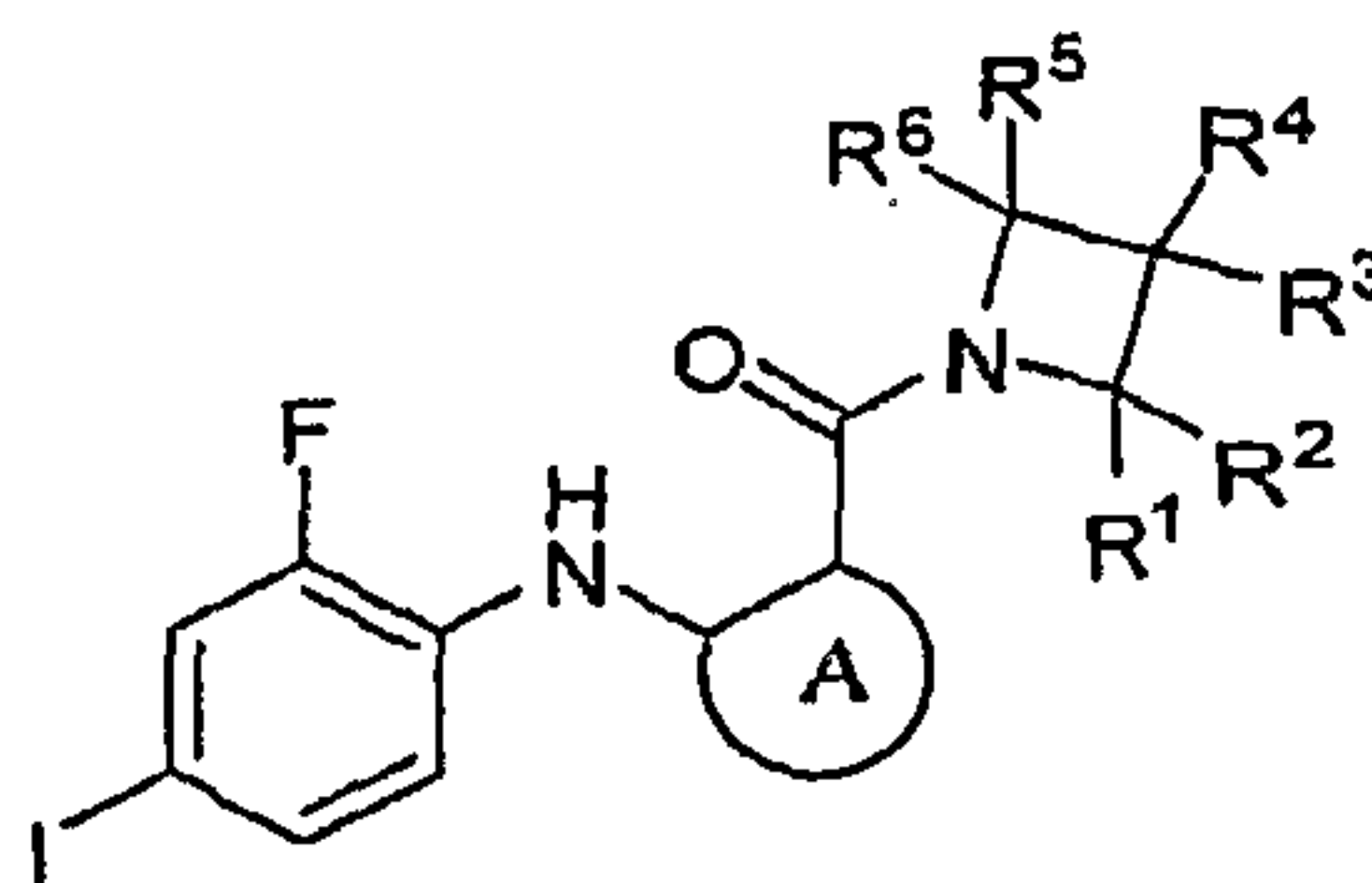
[00103] In another embodiment of Formula III, R³ is halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from

halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'} and R⁴ is as defined in Formula III; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in Formula III. More specifically, R¹, R², R⁵ and R⁶ are hydrogen; and X and R⁷ are halo.

[00104] In another embodiment of Formula III, R³ and R⁴ are independently halo, nitro, -NR⁸R^{8'}, -OR⁸, -NHS(O)₂R⁸, -CN, -S(O)_mR⁸, -S(O)₂NR⁸R^{8'}, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'}, -NR⁸C(O)R^{8'}, lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, -OR⁸, -NR⁸R^{8'}, -NR⁸S(O)₂R⁹, -CN, -S(O)_mR⁹, -C(O)R⁸, -C(O)OR⁸, -C(O)NR⁸R^{8'}, -NR⁸C(O)NR^{8'}R^{8''}, -NR⁸C(O)OR^{8'} and -NR⁸C(O)R^{8'}; or R³ and R⁴ together with the carbon to which they are attached form C(O) or C(=NOH); and all other groups are as defined in Formula III. In another embodiment, R¹, R², R⁵ and R⁶ are hydrogen; and X and R⁷ are halo.

[00105] In another embodiment of the invention (B5), the invention provides a Compound of Formula I where the A ring is thien-diyl and X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R¹⁰, and R¹² are as defined in Formula I. In another embodiment, the A ring is thien-3,4-diyl; R¹⁰ and R¹² are hydrogen; X and R⁷ are halo; and R¹, R², R⁵, and R⁶ are hydrogen. In another embodiment, X is fluoro or chloro; R⁷ is iodo or bromo; R³ is hydrogen or hydroxy; and R⁴ is -NR⁸R^{8'} (where R⁸ and R^{8'} are independently hydrogen or lower alkanyl), heterocycloalkyl, heteroaryl (optionally substituted with lower alkanyl), or lower alkanyl where the lower alkanyl is optionally substituted with -NR⁸R^{8'} (where R⁸ is hydrogen or lower alkanyl and R^{8'} is hydrogen, lower alkanyl, or cycloalkyl where the cycloalkyl is optionally substituted with one or two groups independently selected from hydroxy and lower alkanyl).

[00106] Another embodiment of the invention is a compound of Formula IV:

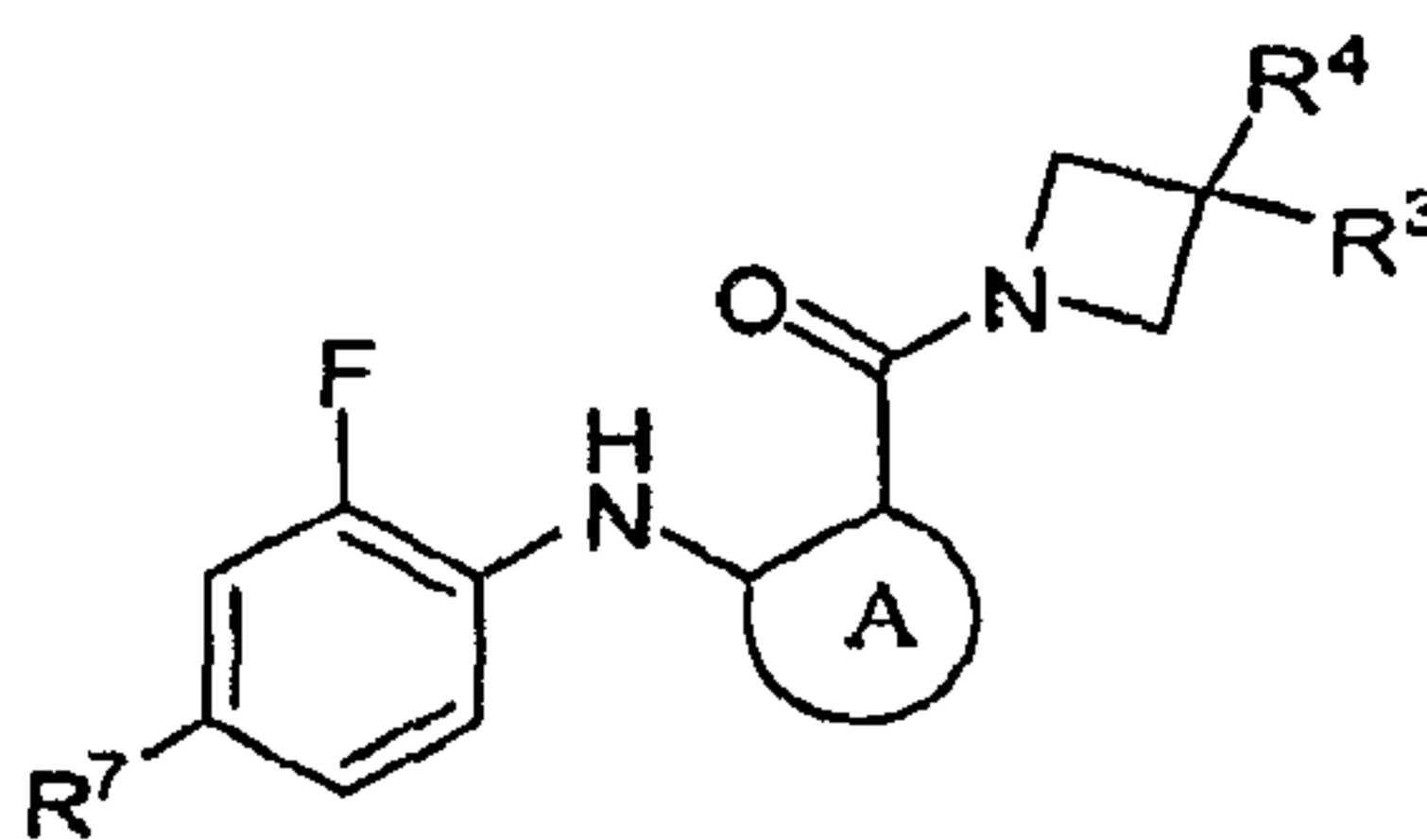


IV

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein the A ring,

5 R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are as defined above for Formula I.

[00107] Another embodiment of the invention is a compound of Formula V:



V

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein the A ring,

10 R^3 , R^4 , and R^7 are as defined above for Formula I.

[00108] Another embodiment of the Invention (E) is directed to a Compound of Formula Ia where

the A ring is phenylene optionally substituted with one or two groups selected from R^{10} , R^{12} , R^{14} , and R^{16} where R^{10} , R^{12} , R^{14} and R^{16} are independently hydrogen or halo;

15 X is halo;

R^1 , R^2 , R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, alkoxy, or amino;

R^4 is hydrogen, halo, $-NR^8R^{8'}$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^{8'}$, lower alkanyl, lower alkenyl, cycloalkyl, heterocycloalkyl, or heteroaryl; where the R^4 lower alkanyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, nitro, $-S(O)_mR^9$, optionally substituted heterocycloalkyl, $-NR^8R^{8'}$, $-NR^8C(O)R^{8'}$,

20 $-NR^8S(O)_2R^9$, $-NR^8C(O)OR^8$, and aryl; where the R^4 cycloalkyl is optionally substituted with one or two groups selected from $-OR^8$ and $-NR^8R^{8'}$; where the R^4

25 heterocycloalkyl is optionally substituted with one or two groups independently

selected from lower alkanyl and $-C(O)OR^8$; and where the R^4 heteroaryl is optionally substituted with $-NR^8R^{8'}$; or

R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; m is 1 or 2;

5 R^7 is halo;

[00109] R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, lower alkanyl, lower alkenyl, lower alkynyl, aryl, heterocycloalkyl, heteroaryl, and cycloalkyl;

where the R^8 and $R^{8'}$ alkyl are independently optionally substituted with one, two, or three

10 groups indendently selected from hydroxy, $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl), optionally substituted heteroaryl, optionally substituted cycloalkyl), alkoxy, substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR^{33}R^{33a}$ (where R^{33} is hydrogen or alkyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl), optionally substituted aryloxy, $-S(O)_nR^{31}$ (where n is 0 and R^{31} is alkyl), 15 carboxy, alkoxycarbonyl, and $-NR^{32}C(O)R^{32a}$ (where R^{32} is hydrogen or alkyl and R^{32a} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl); or where the lower alkanyl is optionally substituted with one, two, three, four, or five halo;

20 where the R^8 and $R^{8'}$ heteroaryl are independently optionally substituted with one or two groups indendently selected from amino and lower alkanyl;

where the R^8 and $R^{8'}$ heterocycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from lower alkanyl, alkoxycarbonyl, optionally substituted arylalkyl, hydroxy, alkoxy, and hydroxyalkyl;

25 where the R^8 and $R^{8'}$ aryl are independently optionally substituted with one or two groups indendently selected from hydroxy, alkoxy, halo, $-NR^{32}C(O)R^{32a}$ (where R^{32} is hydrogen or lower alkanyl and R^{32a} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl), and $-NR^{34}SO_2R^{34a}$ (where R^{34} is hydrogen or alkyl and R^{34a} is lower alkanyl, lower alkenyl, cycloalkyl, aryl, heteroaryl, or heterocycloalkyl); and

30 where the R^8 and $R^{8'}$ cycloalkyl are independently optionally substituted with one, two, or three groups indendently selected from hydroxy, hydroxyalkyl, alkoxy, carboxy, $-C(O)NR^{33}R^{33a}$ (where R^{33} is hydrogen or alkyl and R^{33a} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl), and optionally substituted cycloalkyl; and R^9 is lower alkanyl or aryl.

[00110] Another embodiment of Embodiment (E) is directed to a Compound of Formula Ia where

R^3 is hydrogen, halo, hydroxy, or alkoxy;

R^4 is hydrogen, halo, $-NR^8R^{8'}$, $-NHS(O)_2R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$,

5 $-NR^8C(O)R^{8'}$, lower alkanyl, lower alkenyl, or heterocycloalkyl; where the R^4 lower alkanyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, optionally substituted heterocycloalkyl, and $-NR^8R^{8'}$; and where the R^4 heterocycloalkyl is optionally substituted with one or two groups independently selected from lower alkanyl and $-C(O)OR^8$; or

10 R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

m is 1 or 2;

R^7 is halo;

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, lower alkanyl, and lower

alkenyl; where the R^8 and $R^{8'}$ lower alkanyl are independently optionally substituted

15 with one, two, or three groups indendently selected from halo, hydroxy, and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl); and

all other groups are as defined in Embodiment E.

[00111] Another embodiment (F) of the Invention is a Compound of Formula Ia where

the A ring is phenylene optionally substituted with one or two groups selected from R^{10} , R^{12} ,

20 R^{14} , and R^{16} where R^{10} , R^{12} , R^{14} and R^{16} are independently hydrogen or halo;

X is halo;

R^1 , R^2 , R^5 and R^6 are hydrogen;

R^3 is hydrogen, halo, hydroxy, or alkoxy;

R^4 is $-NR^8R^{8'}$, $-NHS(O)_2R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$,

25 $-NR^8C(O)R^{8'}$, lower alkanyl, lower alkenyl, or heterocycloalkyl; where the R^4 lower alkanyl is optionally substituted with one, two, or three groups independently selected from $-OR^8$, halo, optionally substituted heterocycloalkyl, and $-NR^8R^{8'}$; and where the R^4 heterocycloalkyl is optionally substituted with one or two groups independently selected from lower alkanyl and $-C(O)OR^8$; or

30 R^3 and R^4 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$; and

R^8 and $R^{8'}$ are independently selected from hydrogen, hydroxy, lower alkanyl, and lower

alkenyl; where the R^8 and $R^{8'}$ lower alkanyl are independently optionally substituted

with one, two, or three groups indendently selected from halo, hydroxy, and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, lower alkanyl, or hydroxyalkyl).

[00112] Another embodiment (G) of the Invention is directed to a Compound of Formula Ia where

the A ring is thien-3,4-diyl optionally substituted with one, two, or three groups

independently selected from R^{10} , R^{12} , R^{14} , and R^{16} where R^{10} , R^{12} , R^{14} and R^{16} are

5 independently hydrogen, lower alkanyl, halo, or amino;

X is halo;

R^1 , R^2 , R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-OR^8$, $-NR^8R^{8'}$, heterocycloalkyl, heteroaryl, or lower alkanyl; where the lower alkanyl

10 is optionally substituted with $-NR^8R^{8'}$ and where the heteroaryl is optionally substituted with lower alkanyl;

R^7 is halo;

R^8 is hydrogen or lower alkanyl; and

$R^{8'}$ is hydrogen, lower alkanyl, or cycloalkyl; where the cycloalkyl is optionally substituted

15 with one or two groups independently selected from hydroxy and lower alkanyl.

[00113] Another embodiment of the Invention (H) is directed to a Compound of Formula Ia where

the A ring is thien-3,4-diyl;

X is halo;

20 R^1 , R^2 , R^5 and R^6 are hydrogen;

R^3 is hydrogen or hydroxy;

R^4 is $-OR^8$, $-NR^8R^{8'}$, heterocycloalkyl, or lower alkanyl; where the lower alkanyl is optionally substituted with $-NR^8R^{8'}$;

R^7 is halo;

25 R^8 is hydrogen or lower alkanyl;

$R^{8'}$ is hydrogen or lower alkanyl; and

all other groups are as defined in Embodiment E.

[00114] Another embodiment of the invention is a pharmaceutical composition comprising a compound according to any of Formulas I, Ia, Ic, Id, II, III, IV, and V or a compound as
30 depicted in Table 1, and a pharmaceutically acceptable carrier. In another embodiment, the Compound is according to Formula Ia, according to Formula V, or according to Embodiment G.

Section I Definitions

[00115] As used in this section, the following words and phrases are generally intended to have the meanings as set forth below, except to the extent that the context in which they are used indicates otherwise or they are expressly defined to mean something different.

5 [00116] The symbol “-” means a single bond, “=” means a double bond, “≡” means a triple bond, and “—” means a single bond and optionally a double bond. When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four. Sometimes a particular atom in a structure is described in textual Formula as having a hydrogen or
10 hydrogens as substitution (expressly defined hydrogen), for example, -CH₂CH₂-. It is understood by one of ordinary skill in the art that the aforementioned descriptive techniques are common in the chemical arts to provide brevity and simplicity to description of otherwise complex structures.

[00117] “Alkyl” or “lower alkyl” means a (C₁-C₂₀) linear, branched, or cyclic hydrocarbon group and combinations thereof, inclusively. For example, “C₈ alkyl” refers to an *n*-octyl, *iso*-octyl, cyclohexylethyl, isobutenyl, and but-2-ynyl groups and the like. Examples of lower alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, *s*-butyl, *t*-butyl, isobutyl, pentyl, hexyl and the like. Exemplary alkyl groups are those of C₂₀ or below.

[00118] In this application, alkyl includes alkanyl, alkenyl, alkynyl, and cycloalkyl
20 residues (and combinations thereof); it is intended to include cyclohexylmethyl, vinyl, allyl, isoprenyl, and the like. Thus when an alkyl residue having a specific number of carbons is named, all geometric isomers having that number of carbons are intended to be encompassed; thus, for example, either “butyl” or “C₄ alkyl” is meant to include *n*-butyl, *sec*-butyl, isobutyl, *t*-butyl, isobutenyl and but-2-ynyl groups; and for example, “propyl” or “C₃ alkyl”
25 each include *n*-propyl, propenyl, and isopropyl.

[00119] “Alkanyl” means a linear saturated monovalent hydrocarbon radical of one to twenty carbon atoms or a branched saturated monovalent hydrocarbon radical of three to 20 carbon atoms, e.g., methyl, ethyl, propyl, 2-propyl, butyl (including all isomeric forms), or pentyl (including all isomeric forms), and the like. “Lower alkanyl” means alkanyl having
30 one to six carbons atoms.

[00120] The term “cycloalkyl” means a monocyclic or polycyclic hydrocarbon radical having three to thirteen carbon atoms. The cycloalkyl can be saturated or partially

unsaturated, but cannot contain an aromatic ring. Cycloalkyl includes fused, bridged, and spiro ring systems. Examples of such radicals include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

[00121] "Optionally substituted cycloalkyl" means a cycloalkyl radical, as defined herein, that is optionally substituted with one, two, three, or four groups independently selected from C₁-C₆ alkanyl, C₁-C₆ alkoxy, halo, haloalkyl, haloalkoxy, oxo, hydroxy, cyano, nitro, amino, mono(C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono(C₁-C₆)alkylamino(C₁-C₆)alkyl di(C₁-C₆)alkylamino(C₁-C₆)alkyl, carboxy, carboxy ester, cycloalkyl, hydroxyalkyl, -C(O)NR'R'' (where R' is hydrogen, alkyl, hydroxy, or alkoxy and R'' is hydrogen, alkyl, aryl, or heterocyclyl), optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -NR'C(O)R'' (where R' is hydrogen or alkyl and R'' is alkyl, aryl, or heterocyclyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heterocyclyl).

[00122] "Alkenyl" means a straight or branched hydrocarbon radical having from 2 to 20 carbon atoms and at least one double bond and includes ethenyl, propenyl, 1-but-3-enyl, 1-pent-3-enyl, 1-hex-5-enyl and the like. "Lower alkenyl" is alkenyl having 2-6 carbon atoms.

[00123] "Alkynyl" means a straight or branched hydrocarbon radical having from 2 to 20 carbon atoms and at least one triple bond and includes ethynyl, propynyl, butynyl, pentyn-2-yl and the like. "Lower alkynyl" is alkynyl having 2-6 carbon atoms.

[00124] "Alkylene" means a straight or branched divalent group consisting solely of carbon and hydrogen atoms, containing no unsaturation and having from one to ten carbon atoms, for example, methylene, ethylene, propylene, *n*-butylene and the like. Alkylene is a subset of alkyl, referring to the same residues as alkyl, but having two points of attachment and, specifically, fully saturated. Examples of alkylene include ethylene (-CH₂CH₂-), propylene (-CH₂CH₂CH₂-), dimethylpropylene (-CH₂C(CH₃)₂CH₂-), and cyclohexylpropylene (-CH₂CH₂CH(C₆H₁₃)).

[00125] "Alkylidene" means a straight or branched, divalent group consisting solely of carbon and hydrogen atoms, having from two to ten carbon atoms, and containing at least one double bond. Representative examples include ethylidene, propylidene, *n*-butylidene, and the like.

[00126] "Alkylidyne" means a straight or branched chain divalent group consisting solely of carbon and hydrogen atoms having from two to ten carbon atoms, and containing at least one triple bond, for example, propylid-2-ynyl, *n*-butylid-1-ynyl, and the like.

[00127] "Alkoxy" or "alkoxyl" means -O-alkyl, where the alkyl group includes from one to eight carbon atoms of a straight, branched, cyclic configuration, unsaturated chains, and combinations thereof attached to the parent structure through an oxygen atom. Examples include methoxy, ethoxy, propoxy, isopropoxy, cyclopropyloxy, cyclohexyloxy and the like.

5 Lower-alkoxy refers to groups containing one to six carbons.

[00128] "Substituted alkoxy" means an -OR radical where R is substituted alkyl as defined herein. Representative examples include groups such as -OCH₂CH₂OCH₃, and glycol ethers such as polyethyleneglycol and -O(CH₂CH₂O)_xCH₃, (where x is an integer of between two and twenty, preferable, between two and ten, and more preferably, between two and five). Another exemplary substituted alkoxy group is hydroxyalkoxy or -OCH₂(CH₂)_yOH (where y is an integer of between one and ten, in another example y is an integer of between one and four).

[00129] "Alkoxyalkyl" means a lower alkyl group, as defined herein, substituted with at least one, preferably one, two, or three, alkoxy groups as defined herein. Representative examples include methoxymethyl and the like.

[00130] "Alkoxycarbonylamino" means a -NR'C(O)OR" group where R' is hydrogen, alkyl, hydroxy, or alkoxy and R" is alkyl.

[00131] "Alkylcarbonyloxy" means an -OC(O)R group where R is alkyl, as defined herein.

20 [00132] "Acyl" means a -C(O)R radical where R is alkyl (i.e., one to ten carbon atoms of a straight, branched, or cyclic configuration, and is saturated or unsaturated) or R is optionally substituted aryl or optionally substituted heteroaryl. One or more carbons in the R residue may be replaced by nitrogen, oxygen or sulfur. Examples include acetyl, benzoyl, propionyl, isobutyryl, *t*-butoxycarbonyl, benzyloxycarbonyl, and pyridinylcarbonyl, and the like. Lower-acyl refers to groups containing one to six carbons.

[00133] "Acylamino" means a -NRR' group where R is acyl, as defined herein, and R' is hydrogen or alkyl.

[00134] "Alkylamino" means a -NHR radical where R is alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., methylamino, ethylamino, *n*-, *iso*-propylamino, *n*-, *iso*-, *tert*-butylamino, or methylamino-N-oxide, and the like.

30 [00135] "Alkylaminoalkyl" means an alkyl group substituted with one or two alkylamino groups, as defined herein.

[00136] "Alkylaminocarbonyl" means a $-C(O)NHR$ radical where R is lkyl, as defined herein.

[00137] "Aryl" means a monovalent six- to fourteen-membered, mono- or bi-carbocyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the bicyclic ring is aromatic. Representative examples include phenyl, naphthyl, and indanyl, and the like.

[00138] "Optionally substituted aryl" means an aryl group, as defined herein, which is optionally substituted with one, two, three, four, of five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, $-C(O)NR'R''$ (where R' is hydrogen or alkyl and R'' is hydrogen, alkyl, aryl, or heterocyclyl), $-NR'C(O)R''$ (where R' is hydrogen or alkyl and R'' is alkyl, aryl, or heterocyclyl), and $-NHS(O)_2R'$ (where R' is alkyl, aryl, or heteroaryl).

[00139] "Arylalkyl" means a residue in which an aryl moiety is attached to a parent structure via one of an alkylene, alkylidene, or alkylidyne group. Examples include benzyl, phenethyl, phenylvinyl, phenylallyl and the like. "Lower arylalkyl" refers to an arylalkyl where the "alkyl" portion of the group has one to six carbons; this can also be referred to as C₁₋₆ arylalkyl.

[00140] "Optionally substituted arylalkyl means an alkyl group substituted with one or two optionally substituted aryl group(s) as defined herein. In addition the alkyl group may itself be substituted as described under "substituted alkyl".

[00141] "Arylalkyloxy" means an $-OR$ group where R is arylalkyl, as defined herein.

[00142] "Carboxy ester" means a $-C(O)OR$ group where R is lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, aryl or arylalkyl, each of which is defined herein. Representative examples include methoxycarbonyl, ethoxycarbonyl, and benzyloxycarbonyl, and the like.

[00143] "Dialkylamino" means a $-NRR'$ radical where R and R' are independently alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., dimethylamino, diethylamino, *N,N*-methylpropylamino or *N,N*-methylethylamino, and the like.

[00144] "Dialkylaminoalkyl" means an alkyl group substituted with one or two dialkylamino groups, as defined herein.

[00145] "Dialkylaminocarbonyl" means a $-C(O)NRR'$ group where R and R' are alkyl.

[00146] “Exo-alkenyl” refers to a double bond that emanates from an annular carbon, and is not within the ring system.

[00147] In some examples, as appreciated by one of ordinary skill in the art, two adjacent groups on an aromatic system may be fused together to form a ring structure. The fused ring structure may contain heteroatoms and may be optionally substituted with one or more groups. It should additionally be noted that saturated carbons of such fused groups (*i.e.* saturated ring structures) can contain two substitution groups.

[00148] “Fused-polycyclic” or “fused ring system” means a polycyclic ring system that contains bridged or fused rings; that is, where two rings have more than one shared atom in their ring structures. In this application, fused-polycyclics and fused ring systems are not necessarily all aromatic ring systems. Typically, but not necessarily, fused-polycyclics share a vicinal set of atoms, for example naphthalene or 1,2,3,4-tetrahydro-naphthalene. A spiro ring system is not a fused-polycyclic by this definition, but fused polycyclic ring systems of the invention may themselves have spiro rings attached thereto via a single ring atom of the fused-polycyclic.

[00149] “Haloalkoxy” means an -OR’ group where R’ is haloalkyl as defined herein, e.g., trifluoromethoxy or 2,2,2-trifluoroethoxy, and the like..

[00150] “Halogen” or “halo” means fluoro, chloro, bromo or iodo.

[00151] “Haloalkyl” and “haloaryl” mean an alkyl and an aryl group, respectively, that are substituted with one or more halogens, preferably one to five halo atoms. Thus, “dihaloaryl,” “dihaloalkyl,” and “trihaloaryl” etc. refer to aryl and alkyl substituted with a plurality of halogens, but not necessarily a plurality of the same halogen; thus 4-chloro-3-fluorophenyl is within the scope of dihaloaryl.

[00152] “Heteroatom” refers to O, S, N, or P.

[00153] “Heterocyclyl” means a stable three- to fifteen-membered ring substituent that consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, phosphorus, oxygen and sulfur. For purposes of this invention, the heterocyclyl substituent may be a monocyclic, bicyclic or tricyclic ring system, which may include fused or bridged ring systems as well as spirocyclic systems. The terms “heterocycloalkyl” and “heteroaryl” are groups that are encompassed by the broader term “heterocyclyl.” The nitrogen, phosphorus, carbon and sulfur atoms in the heterocyclyl group may be optionally oxidized to various oxidation states. In a specific example, the group -S(O)₀₋₂-, refers to -S- (sulfide), -S(O)- (sulfoxide), and -SO₂- (sulfone). For convenience, nitrogens, particularly

but not exclusively, those defined as annular aromatic nitrogens, are meant to include their corresponding *N*-oxide form, although not explicitly defined as such in a particular example. Thus, for a compound of the invention having, for example, a pyridyl ring; the corresponding pyridyl-*N*-oxide is meant to be included as another compound of the invention. In addition,

5 annular nitrogen atoms may be optionally quaternized; and the ring substituent may be partially or fully saturated or aromatic. Examples of heterocyclyl groups include, but are not limited to, azetidiny, acridiny, benzodioxoly, benzodioxany, benzofurany, carbazoy, cinnoliny, dioxolany, indoliziny, naphthyridiny, perhydroazepiny, phenaziny, phenothiaziny, phenoxaziny, phthalaziny, pteridiny, puriny, quinazolinyl, quinoxaliny,

10 quinoliny, isoquinoliny, tetrazoy, tetrahydroisoquinolyl, piperidiny, piperaziny, 2-oxopiperaziny, 2-oxopiperidiny, 2-oxopyrrolidiny, 2-oxoazepiny, azepiny, pyrroly, 4-piperidony, pyrrolidiny, pyrazoly, pyrazolidiny, imidazoly, imidazoliny, imidazolidiny, dihydropyridiny, tetrahydropyridiny, pyridiny, pyraziny, pyrimidiny, pyridaziny, oxazoly, oxazoliny, oxazolidiny, triazoly, isoxazoly, isoxazolidiny, morpholiny,

15 thiazoly, thiazoliny, thiazolidiny, isothiazoly, quinuclidiny, isothiazolidiny, indoly, isoindoly, indoliny, isoindoliny, octahydroindoly, octahydroisoindoly, quinoly, isoquinoly, decahydroisoquinoly, benzimidazoly, thiadiazoly, benzopyrany, benzothiazoly, benzoxazoly, furyl, tetrahydrofuryl, tetrahydropyrany, thienyl, benzothienyl, thiamorpholiny, thiamorpholiny sulfoxide, thiamorpholiny sulfone, dioxaphospholany, and

20 oxadiazoly.

[00154] “Optionally substituted heterocyclyl” means a heterocyclyl group, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, oxo (valency rules permitting), lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, optionally substituted cycloalkyl, optionally substituted

25 heterocycloalkyl, optionally* substituted aryl, optionally substituted heteroaryl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, carboxy ester, -C(O)NR'R" (where R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, or heterocyclyl), -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, or heterocyclyl), amino, alkylamino, dialkylamino, and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

30 **[00155]** “Heteroalicyclic” and “heterocycloalkyl” mean a non-aromatic heterocyclyl group, as defined herein. A “heteroalicyclic” or “heterocycloalkyl” may be fully saturated or may contain unsaturation, but is not aromatic. “Heteroalicyclic” or “heterocycloalkyl” may be monocyclic or bicyclic (including fused, bridged, and spiro ring systems).

[00156] "Optionally substituted heteroalicyclic" and "optionally substituted heterocycloalkyl" mean, respectively, a heteroalicyclic and heterocycloalkyl ring, each as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, oxo, lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, optionally substituted cycloalkyl, heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, carboxy ester, -C(O)NR'R" (where R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, or heterocyclyl), -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, or heterocyclyl), amino, alkylamino, dialkylamino, and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

[00157] "Heteroaryl" means a 5- to 12-membered, monocyclic aromatic heterocyclyl (where heterocyclyl is defined herein) or bicyclic heterocyclyl ring system (where at least one of the rings in the bicyclic system is aromatic) where the monocyclic ring and at least one of the rings in the bicyclic ring system contains one, two, three, four, or five heteroatom(s) selected from nitrogen, oxygen, phosphorous, and sulfur. Representative examples include pyridinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, tetrazolyl, furyl, thienyl, isoxazolyl, thiazolyl, oxazolyl, isothiazolyl, pyrrolyl, quinolinyl, isoquinolinyl, indolyl, benzimidazolyl, benzofuranyl, cinnolinyl, indazolyl, indoliziny, phthalazinyl, pyridazinyl, triazinyl, isoindolyl, pteridinyl, purinyl, oxadiazolyl, triazolyl, thiadiazolyl, thiadiazolyl, furazanyl, benzofurazanyl, benzothiophenyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, and furopyridinyl. Fused, bridged, and spiro moieties are also included within the scope of this definition.

[00158] "Optionally substituted heteroaryl" means a heteroaryl group, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, hydroxy, oxo (valency rules permitting), carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, heteroaryl, optionally substituted aryl, -C(O)NR'R" (where R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, or heterocyclyl), -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, or heterocyclyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

[00159] "Optionally substituted heterocyclalkyl" means an alkyl group substituted with an optionally substituted heterocyclyl group, as defined herein.. Examples include (4-methylpiperazin-1-yl) methyl, (morpholin-4-yl) methyl, (pyridin-4-yl) methyl, 2-(oxazolin-2-yl) ethyl, 4-(4-methylpiperazin-1-yl)-2-butenyl, and the like. In addition, the alkyl portion of a heterocyclalkyl group may be substituted as described in the definition for "substituted".

“Lower heterocyclalkyl” means a heterocyclalkyl where the “alkyl” portion of the group has one to six carbons. “Heteroalicyclalkyl” or “lower heterocycloalkylalkyl” means a heterocyclalkyl where the heterocycl portion of the group is non-aromatic; and “heteroarylalkyl” means a heterocyclalkyl where the heterocycl portion of the group contains an aromatic ring. Such terms may be described in more than one way, for example, “lower heterocyclalkyl” and “heterocycl C₁₋₆alkyl” are equivalent terms. Additionally, for simplicity, the number of annular atoms (including heteroatoms) in a heterocycle may be denoted as “C_x-C_y” (as in “C_x-C_y-heterocycl” and “C_x-C_y-heteroaryl” (and the like)), where x and y are integers. So, for example, C₅-C₁₄-heterocycl refers to a 5 to 14 membered ring system having at least one heteroatom and not a ring system containing 5 to 14 annular carbon atoms.

[00160] Preferred heterocycls include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, pyridotriazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolyl, carbazolyl, 4aH-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2H,6H-1,5,2-dithiazinyl, dihydrofuro[2,3-b]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indoliziny, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinoliziny, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,3,4-triazolyl, and xanthenyl.

[00161] “Hydroxyalkyl” means an alkanyl, alkenyl, or alkynyl radical, as defined herein, substituted with at least one, preferably one, two, or three, hydroxy group(s), provided that if two hydroxy groups are present they are not both on the same carbon atom. Representative

examples include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 1-(hydroxymethyl)-2-hydroxyethyl, 2,3-dihydroxybutyl, 3,4-dihydroxybutyl and 2-(hydroxymethyl)-3-hydroxypropyl, preferably 2-hydroxyethyl, 2,3-dihydroxypropyl, or 1-(hydroxymethyl)-2-hydroxyethyl, and the like.

[00162] "Optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. One of ordinary skill in the art would understand that with respect to any molecule described as containing one or more optional substituents, only sterically practical and/or synthetically feasible compounds are meant to be included. "Optionally substituted" refers to all subsequent modifiers in a term. So, for example, in the term "optionally substituted arylC₁₋₈ alkyl," both the "C₁₋₈ alkyl" portion and the "aryl" portion of the molecule may or may not be substituted. A list of exemplary optional substitutions is presented below in the definition of "substituted."

[00163] "Saturated bridged ring system" refers to a bicyclic or polycyclic ring system that is not aromatic. Such a system may contain isolated or conjugated unsaturation, but not aromatic or heteroaromatic rings in its core structure (but may have aromatic substitution thereon). For example, hexahydro-furo[3,2-b]furan, 2,3,3a,4,7,7a-hexahydro-1H-indene, 7-aza-bicyclo[2.2.1]heptane, and 1,2,3,4,4a,5,8,8a-octahydro-naphthalene are all included in the class "saturated bridged ring system."

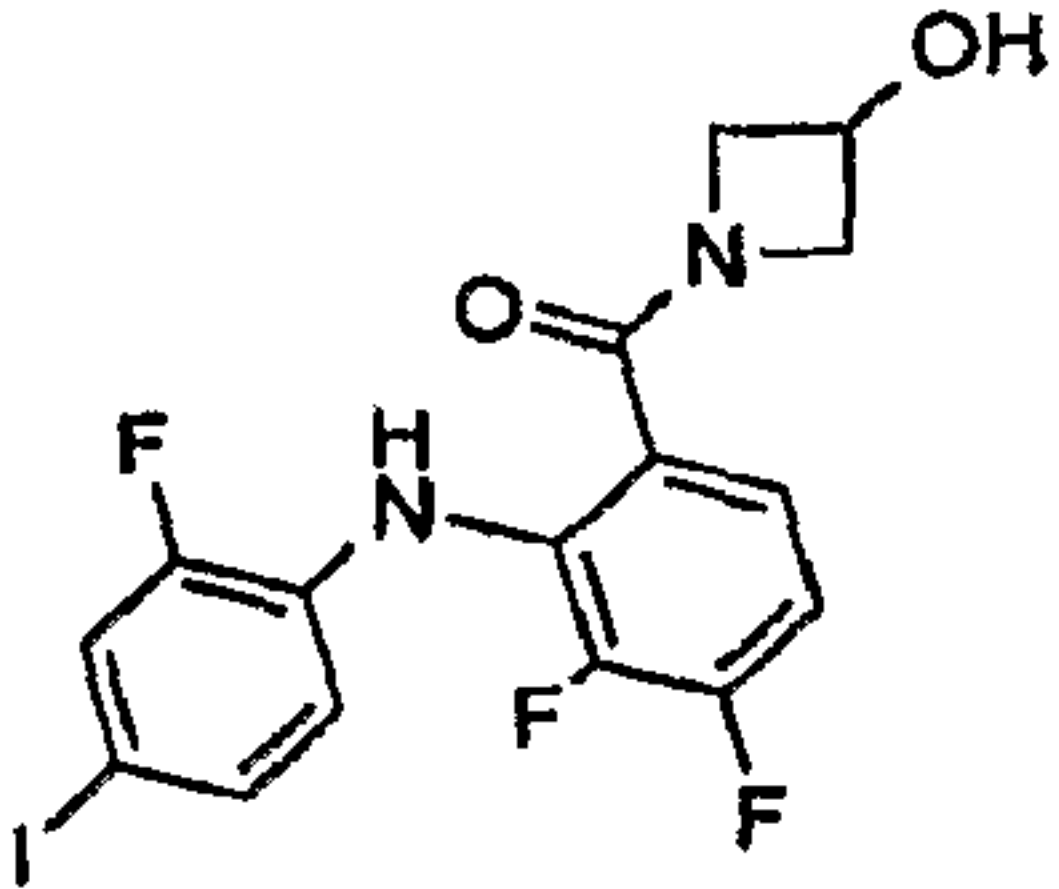
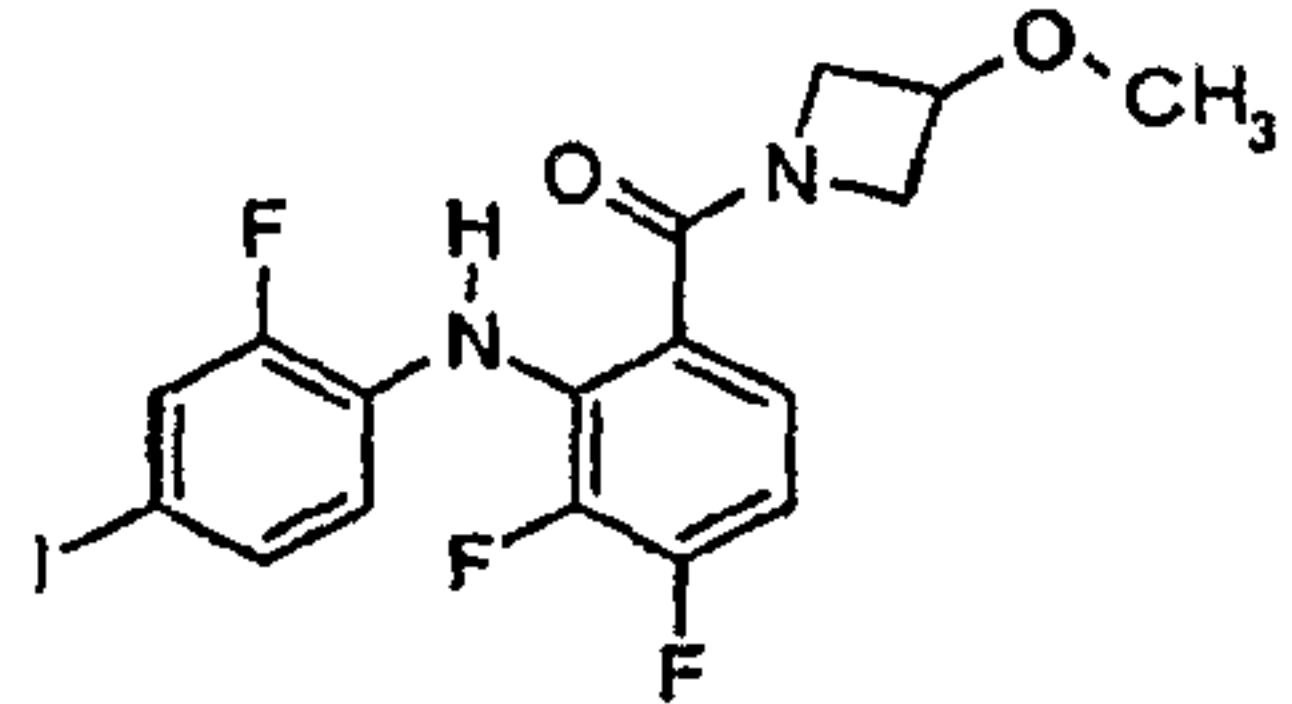
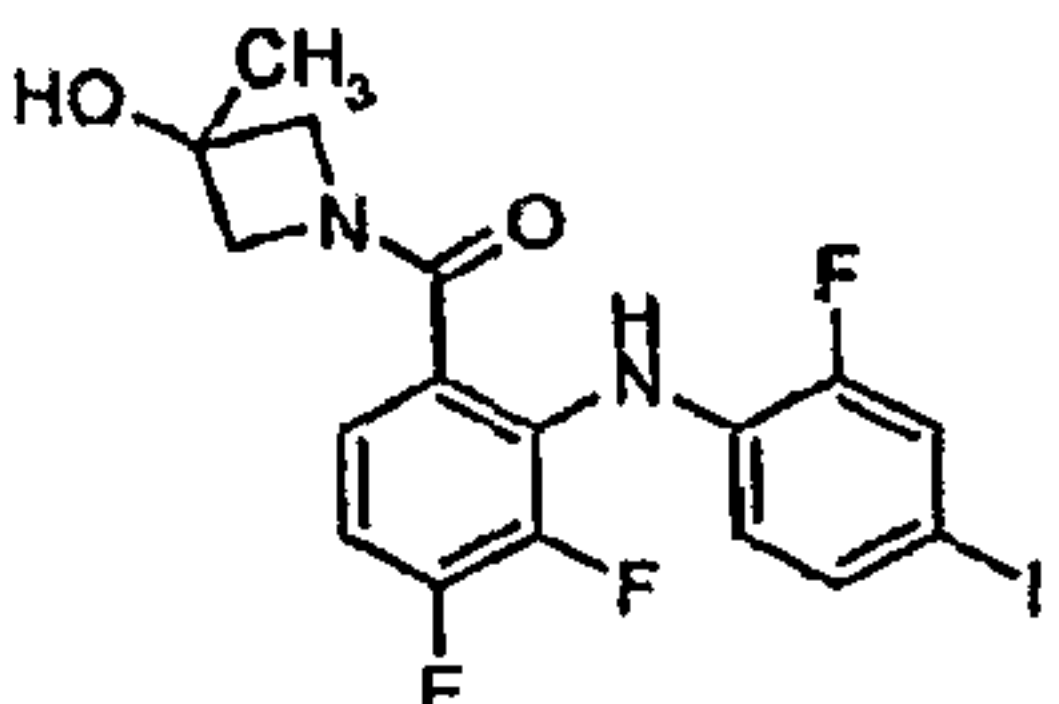
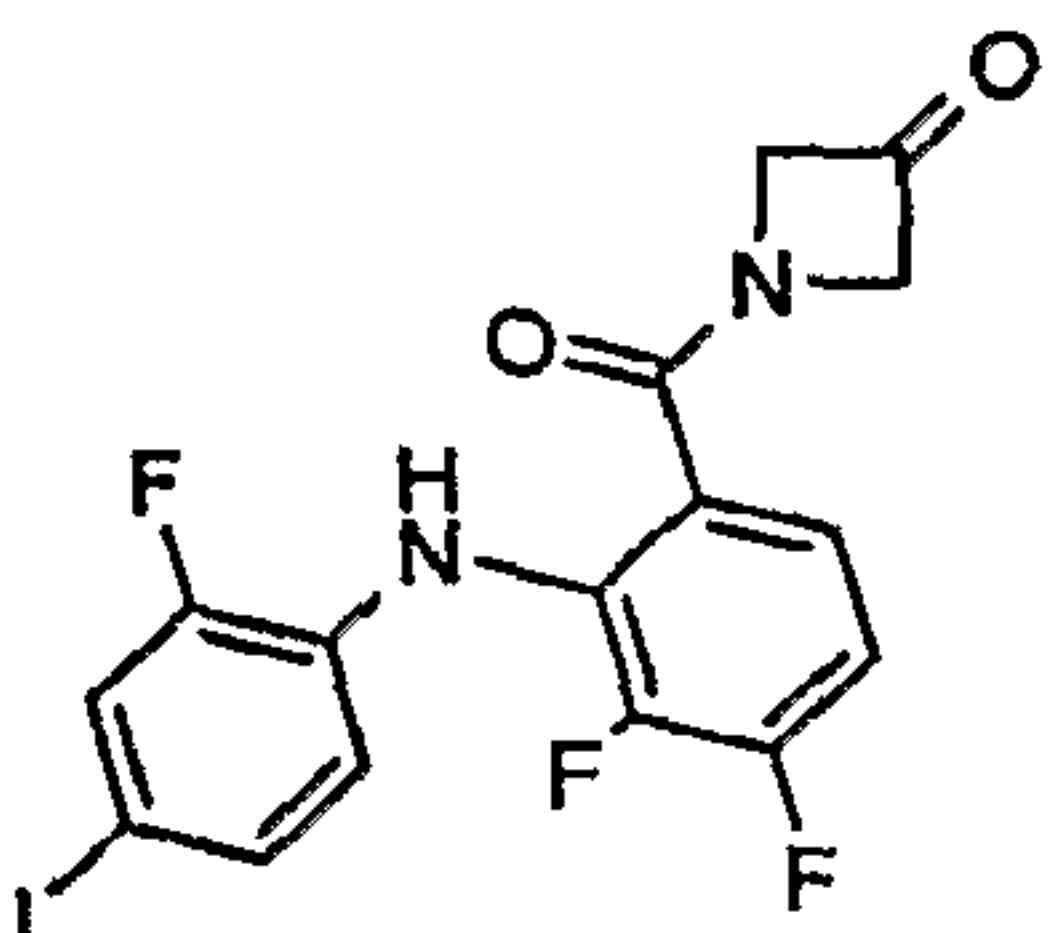
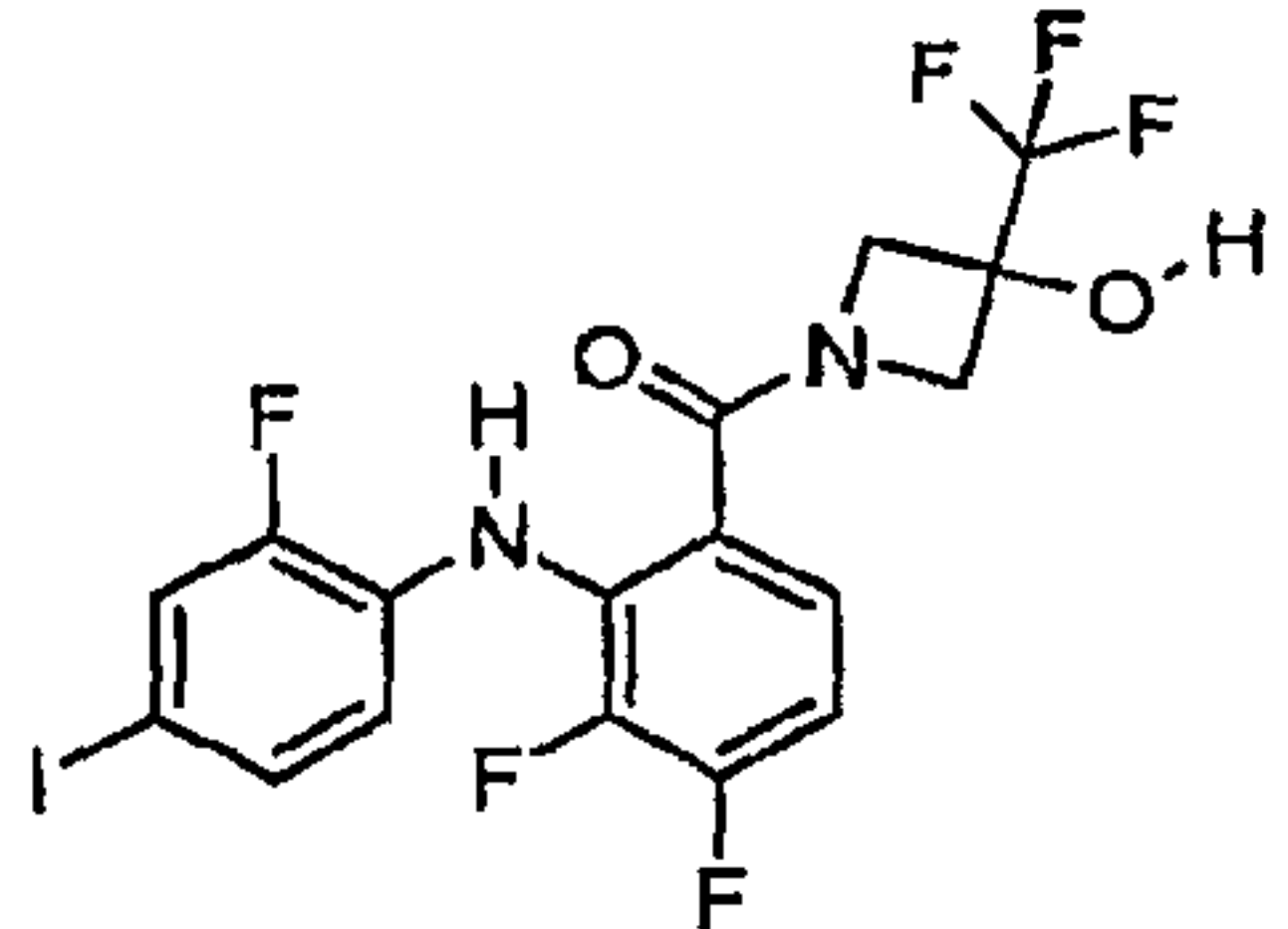
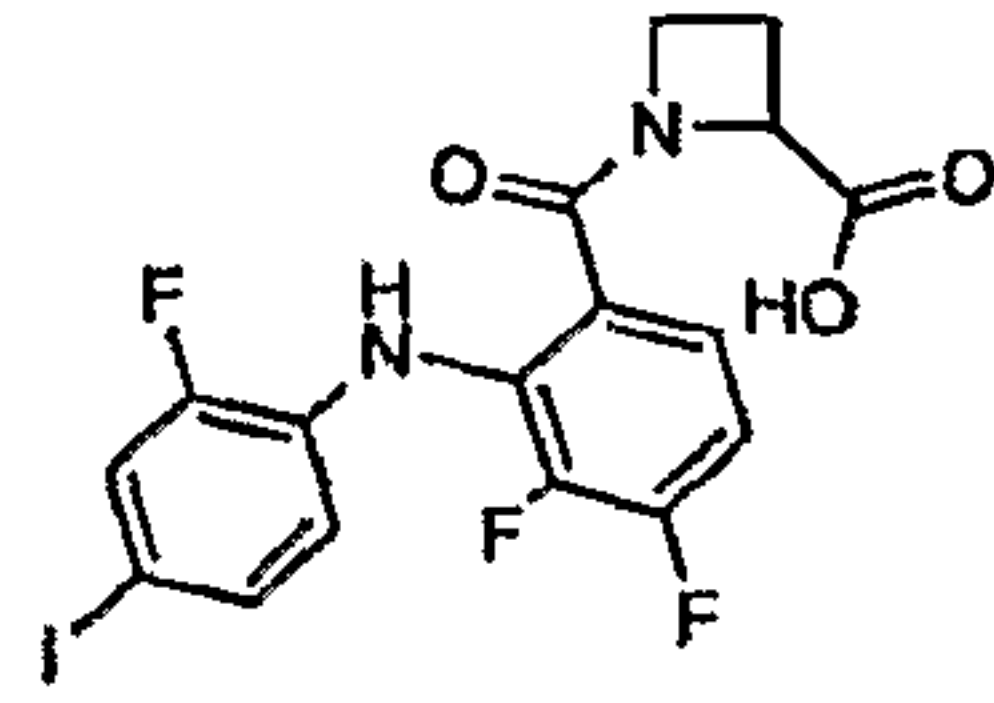
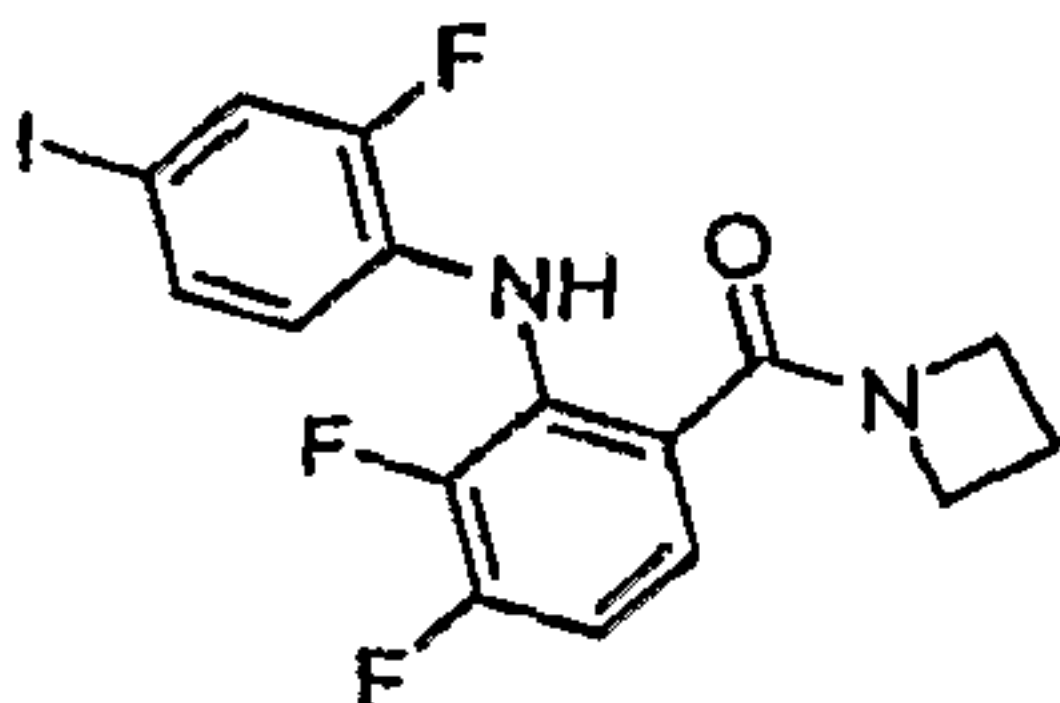
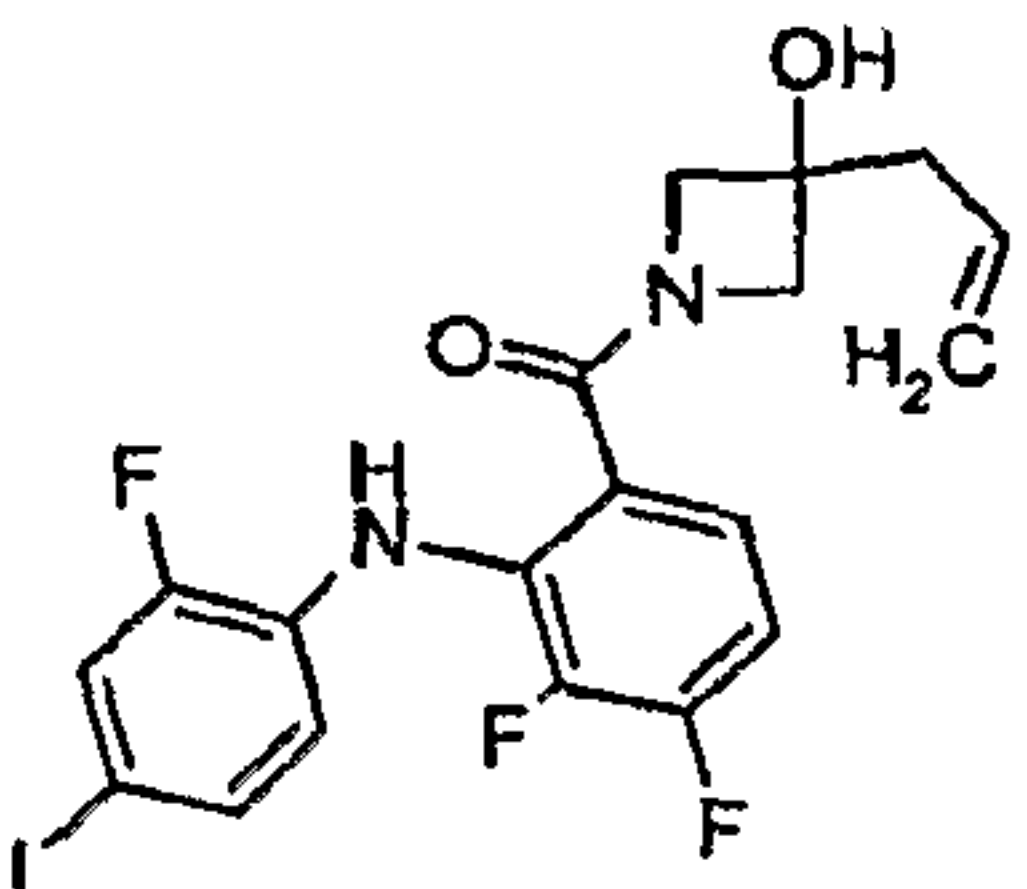
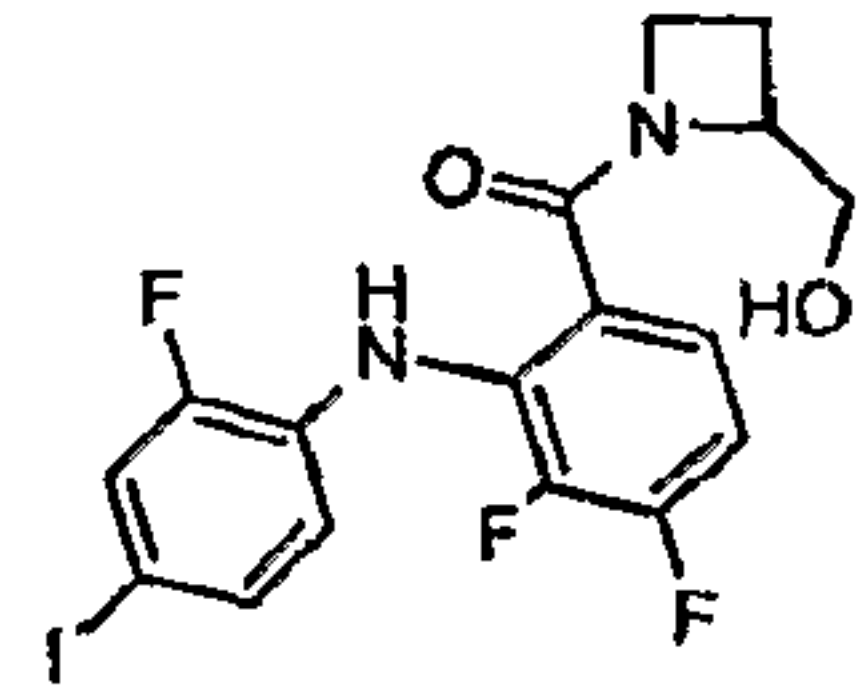
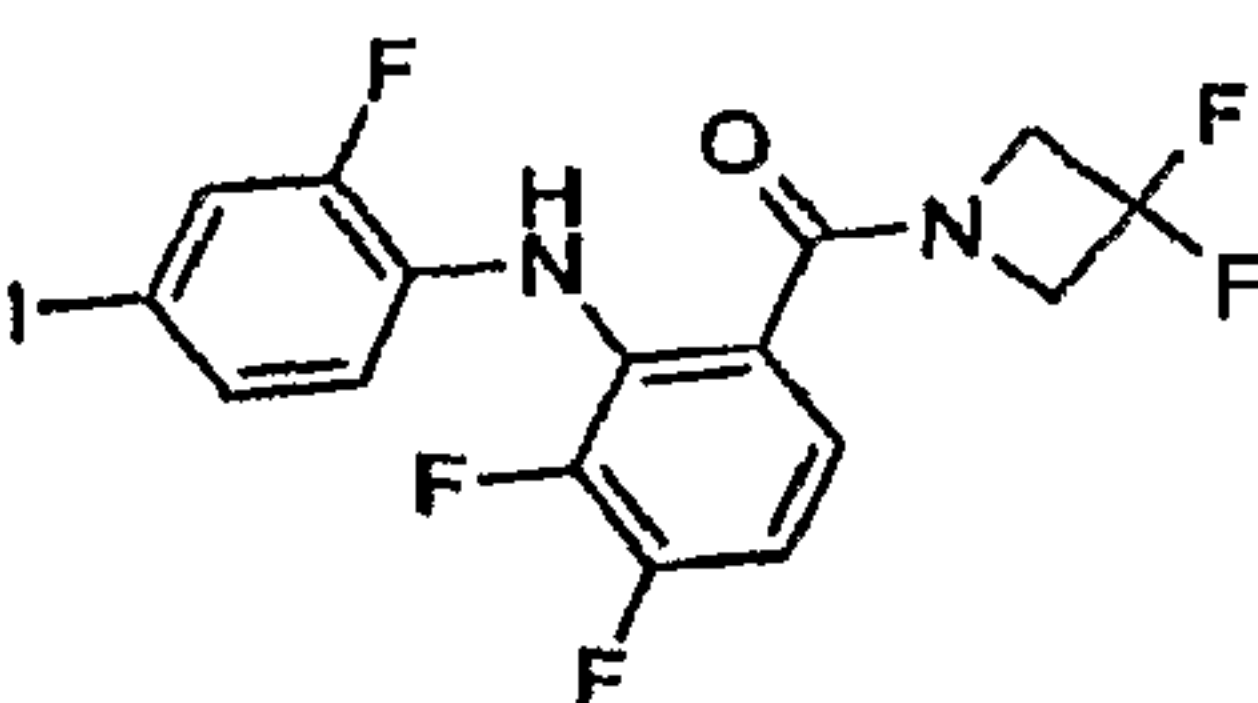
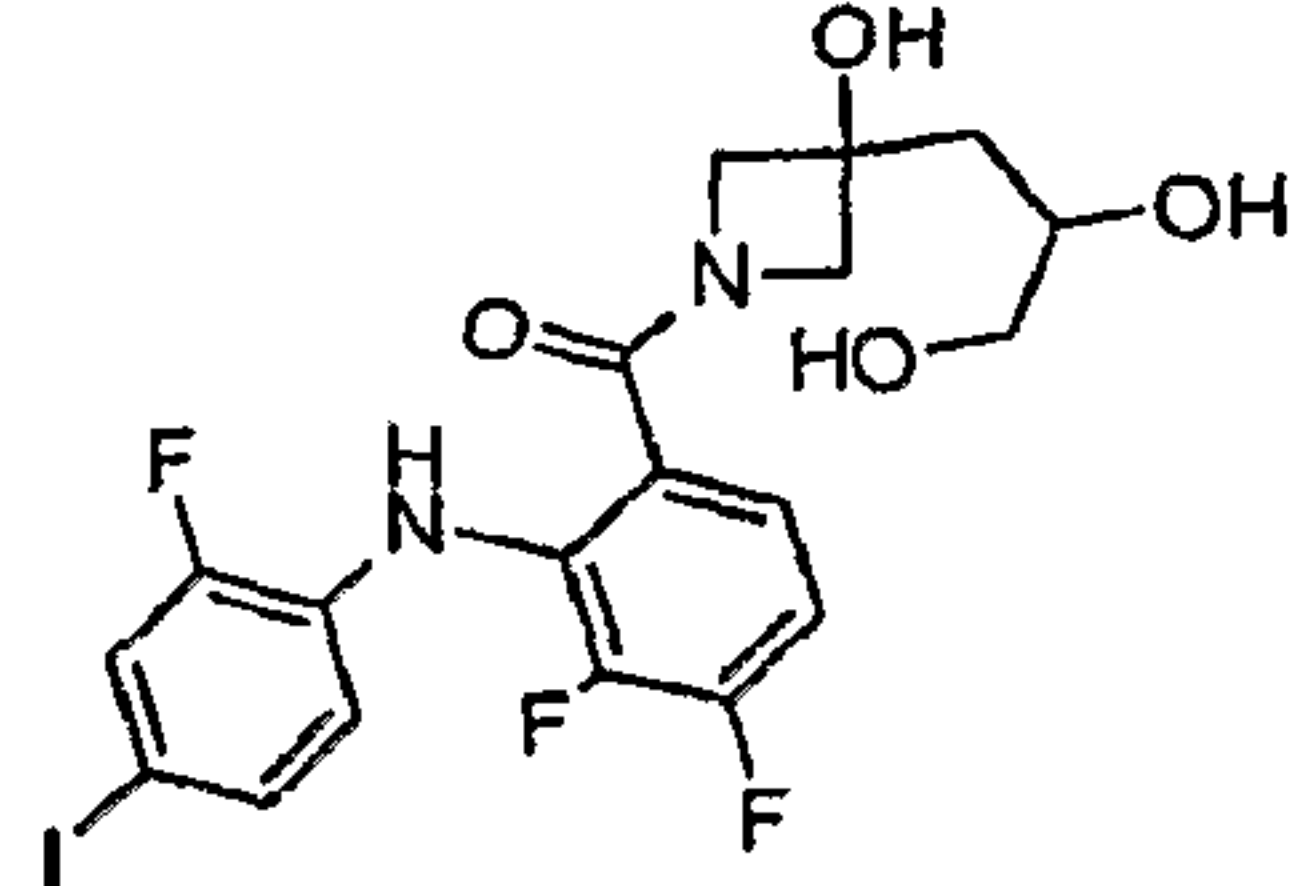
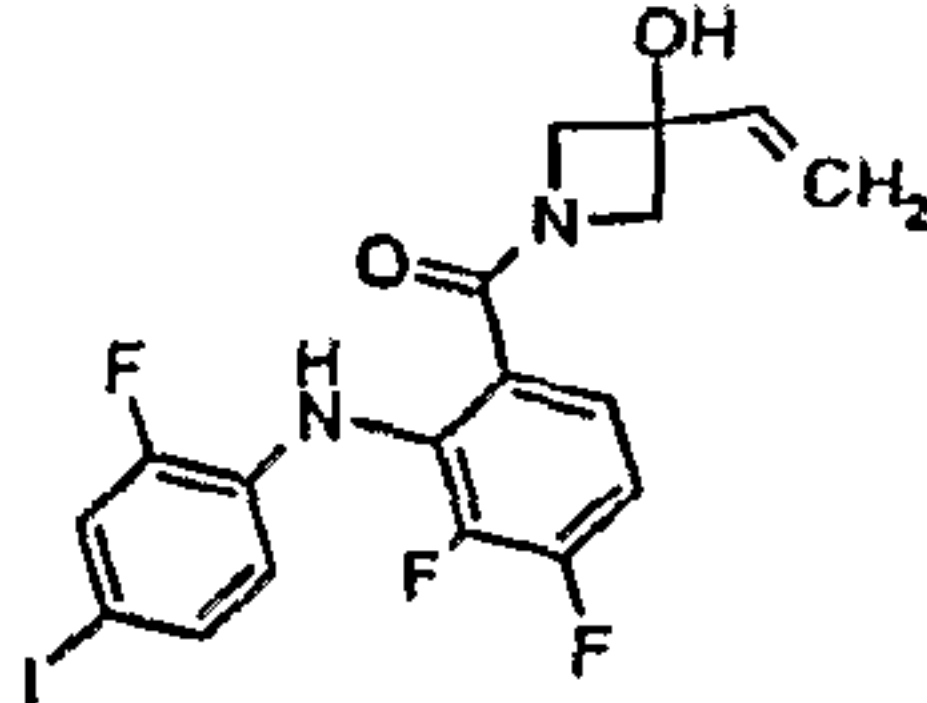
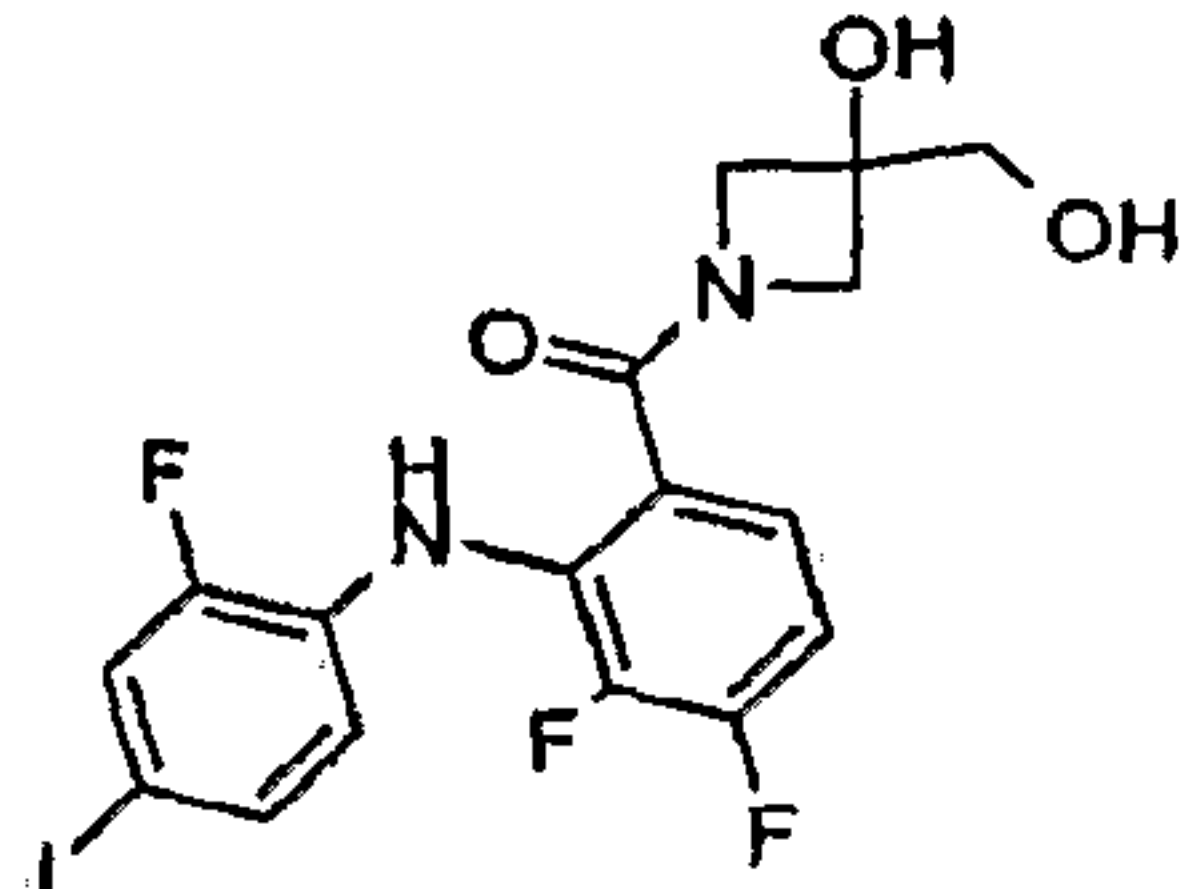
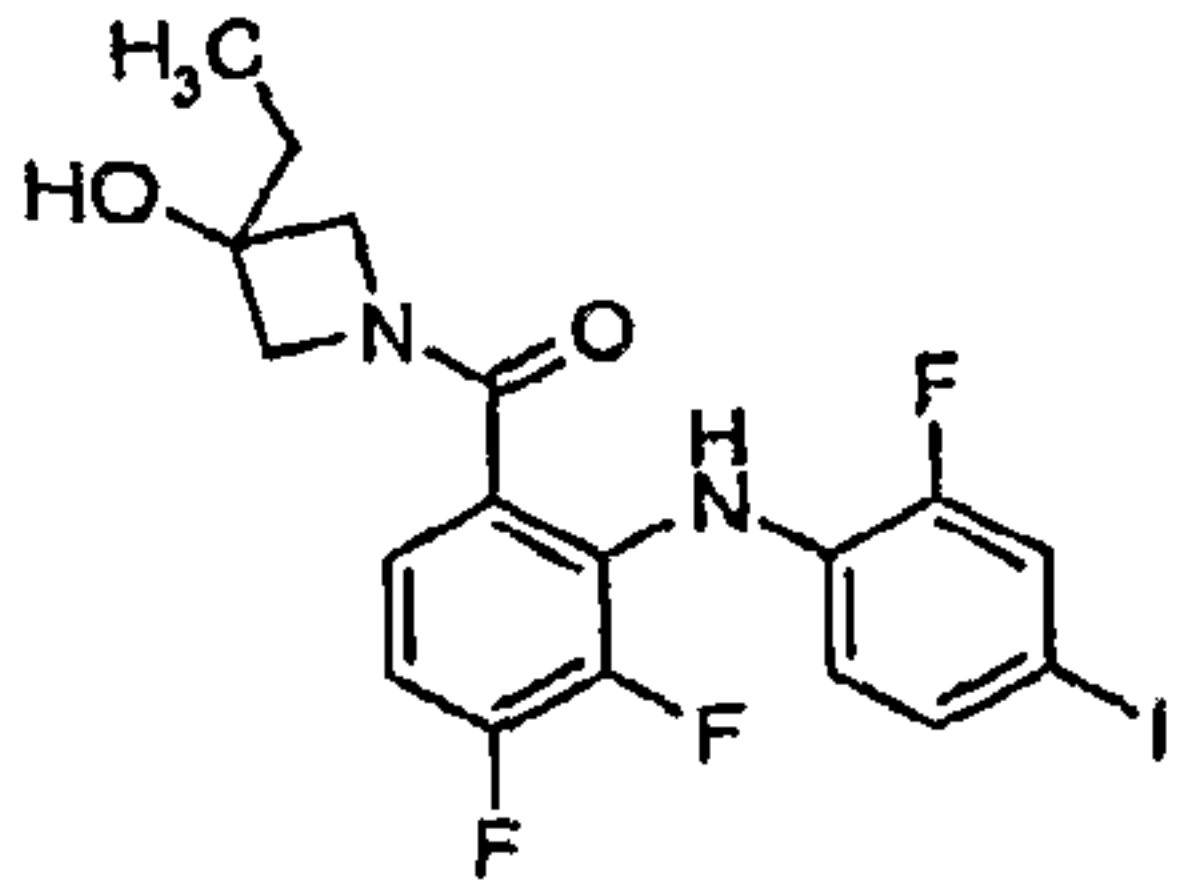
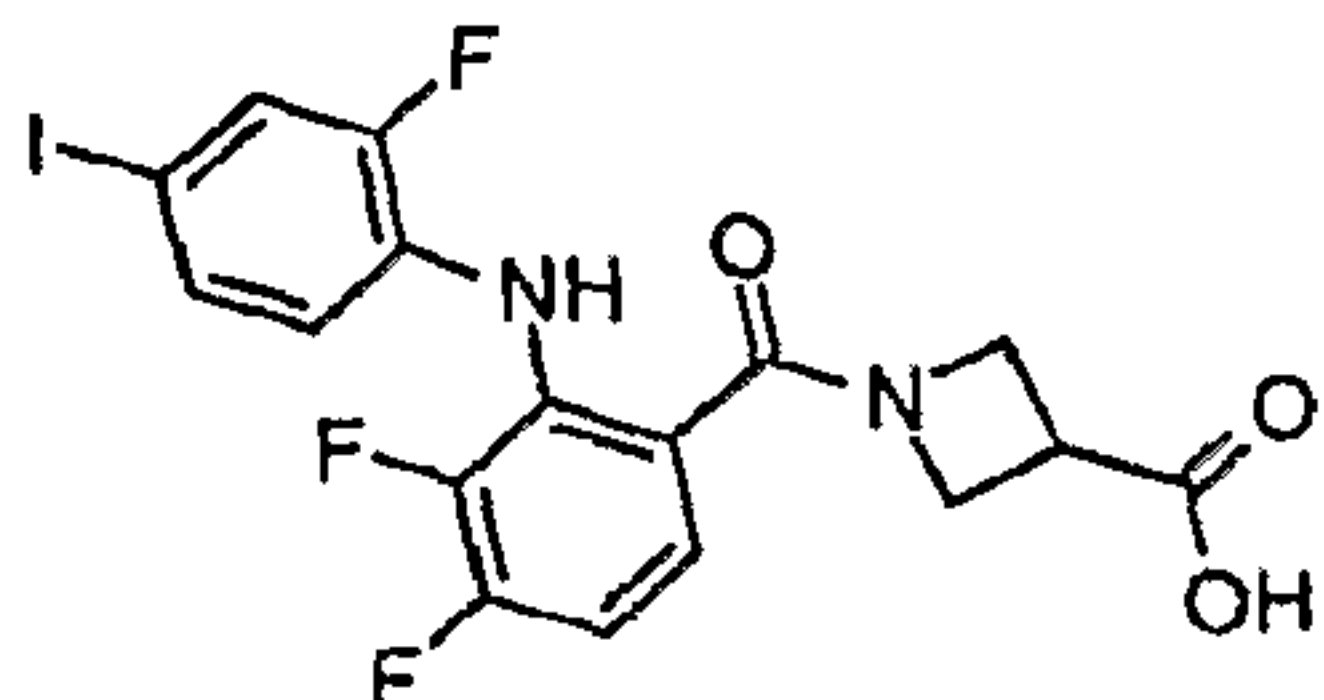
[00164] "Spiro", "Spirocyclyl" or "spiro ring" refers to a ring originating from a particular annular carbon of another ring. For example, as depicted below, a ring atom of a saturated bridged ring system (rings B and B'), but not a bridgehead atom, can be a shared atom between the saturated bridged ring system and a spirocyclyl (ring A) attached thereto. A spirocyclyl can be carbocyclic or heteroalicyclic.

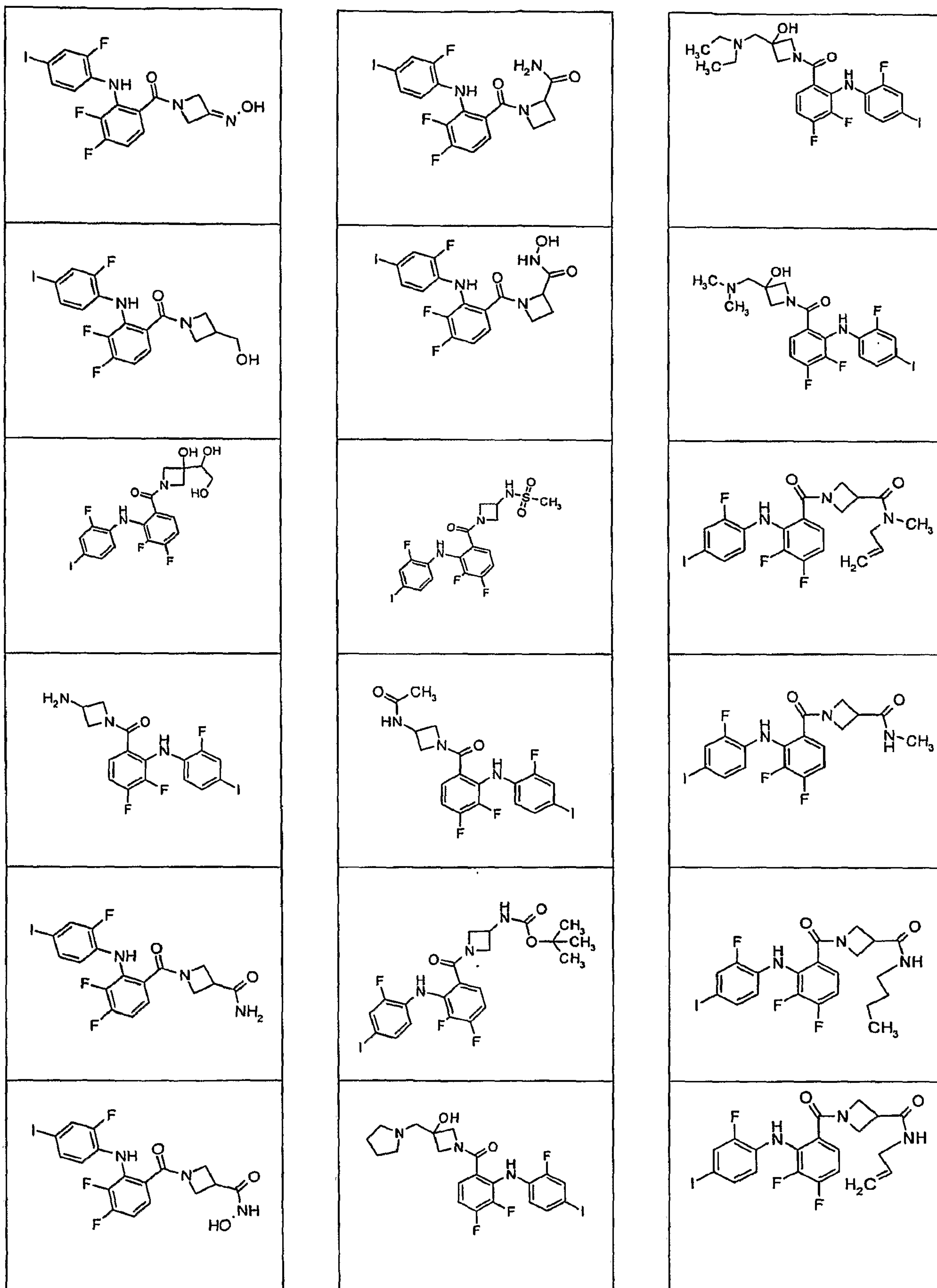
[00165] "Substituted" alkyl, alkylene, alkylidene, and alkylidyne refer respectively to alkyl, alkylene, alkylidene, and alkylidyne where one or more (for example up to about five, in another example, up to about three) hydrogen atoms are replaced by a substituent independently selected from halo, optionally substituted aryl, hydroxy, alkoxy, optionally substituted heterocyclyl, alkylenedioxy, amino, alkylamino, dialkylamino), amidino, aryloxy, arylalkyloxy, carboxy, carboxy ester, alkylcarbonyloxy, carbamyl, alkylaminocarbonyl, dialkylaminocarbonyl, benzyloxycarbonylamino (CBZ-amino), cyano, acyl, nitro, S(O)_{n1}R' (where n1 is 0, 1, or 2 and R' is alkyl, substituted alkyl, optionally substituted aryl, optionally

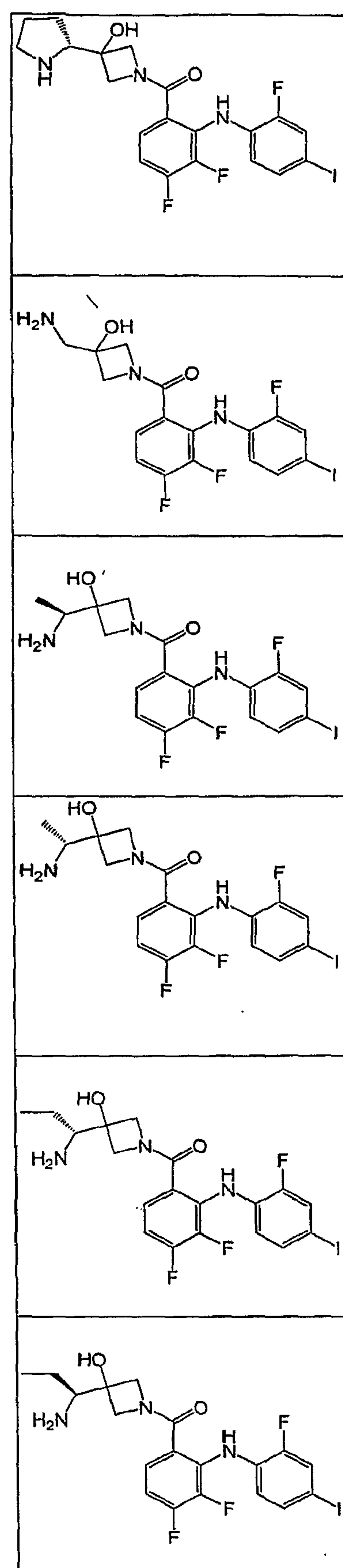
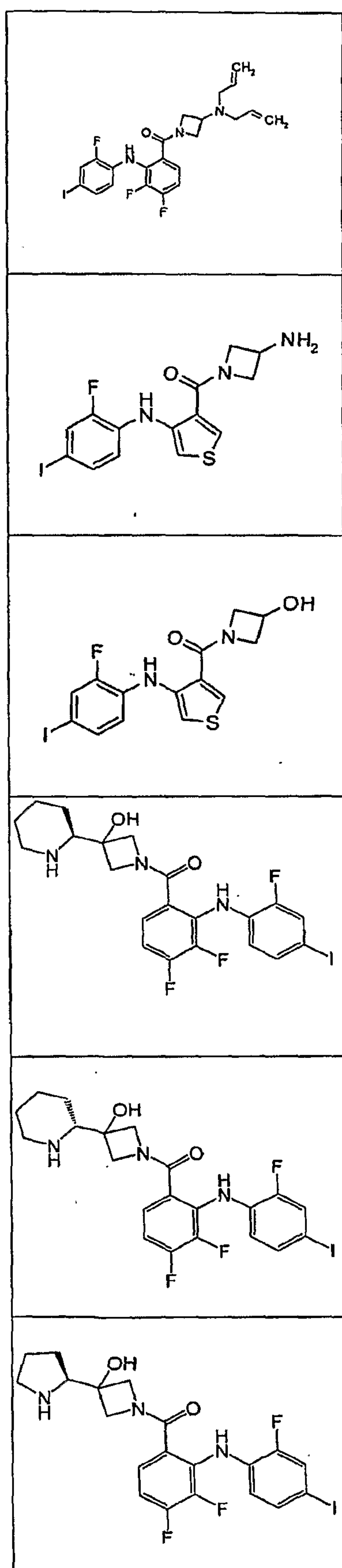
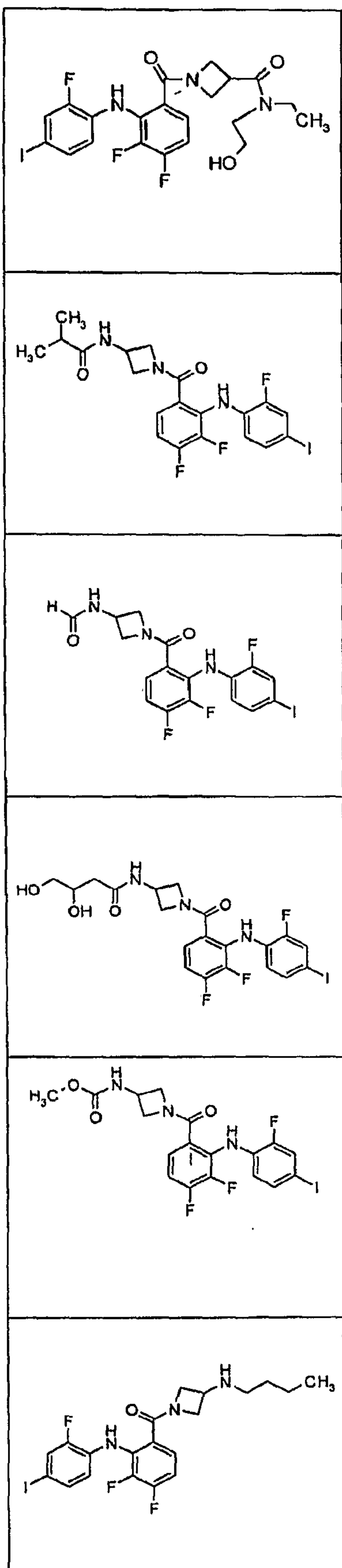
substituted heterocycloalkyl, or optionally substituted heteroaryl), oxo, acylamino, and sulfonamido.

[00166] Table 1 depicts a representative example of the compounds of Section I.

Table 1





[00167] As use in one embodiment of the invention, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 4 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 3 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 2 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 1.6 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 1 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 0.7 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 0.3 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 0.2 μ M or less. In another embodiment, the MEK inhibitor is selected from the compounds in Table I having a MEK-binding affinity of about 0.1 μ M or less.

Experimental

Preparation of Compounds

[00168] Generally, the compounds listed below were identified by LC-MS, and/or isolated, and characterized by ^1H -NMR (most typically 400 MHz). Liquid chromatography-mass spectral (LC-MS) analyses were performed using at least one of: a Hewlett-Packard Series 1100 MSD, an Agilent 1100 Series LC/MSD (available from Agilent Technologies Deutschland GmbH of Waldbronn Germany), or a Waters 8-Channel MUX System (available from Waters Corporation of Milford, Massachusetts). Compounds were identified according to either their observed mass $[\text{M}+1]$ or $[\text{M}+\text{Na}]$ ion (positive mode) or $[\text{M}-1]$ ion (negative mode). ^1H -NMR data for compounds was taken with a Varian AS400 Spectrometer (400MHz, available from Varian GmbH, Darmstadt, Germany).

[00169] Starting materials and intermediates used to prepare a compound of the invention are either commercially available or can be prepared by one of ordinary skill in the art.

EXAMPLE 1: *1-({3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol:*

[00170] 3,4-Difluoro-2-[(2-fluoro-4-iodophenyl)amino]benzoic acid (2.1 g, 5.3 mmol) was taken into DMF (10 mL) followed by addition of PyBOP (2.6 g, 5.3 mmol) and the mixture was allowed to stir at room temperature over 15 minutes. Azetidin-3-ol hydrochloride (870 mg, 8.0 mmol) and DIPEA (1.85 mL, 11.2 mmol) was then added and the mixture was allowed to stir an additional hour at room temperature. The mixture was then partitioned with ethyl acetate and 0.5 M aqueous sodium hydroxide solution. The organic layer was then washed with water (3x) then brine and dried over anhydrous sodium sulfate. Filtration and concentration followed by silica gel flash chromatography using ethyl acetate: hexanes (5:1) eluent afforded 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol (2.09 g, 87% yield) as a colorless amorphous solid. ¹H NMR (400 MHz, CDCl₃): 8.47 (s, 1H), 7.39 (dd, 1H), 7.32 (d, 1H), 7.13-7.09 (m, 1H), 6.84-6.78 (m, 1H), 6.63-6.57 (m, 1H), 4.74-4.67 (m, 1H), 4.43-4.39 (m, 2H), 4.20-3.96 (br d, 2H), 2.50 (d, 1H).

EXAMPLE 2: *4-(2-Fluoro-4-iodo-phenylamino)-thiophene-3-carboxylic acid:*

[00171] A solution of methyl-4-oxo-tetrahydro-thiophene-3-carboxylate (5.75 g, 35.9 mmol) and 2-fluoro-4-iodo-aniline (9.4 g, 40.9 mmol) were heated to reflux in a mixture of ethanol (25 mL) and acetic acid (0.3 mL) for 18 hours. The solution was cooled to room temperature, filtered and the solid product dried *in vacuo* to provide methyl-4-(2-fluoro-4-iodo-phenylamino)-2,3-dihydro-thiophene-3-carboxylate (5.70 g, 42% yield). MS (EI) for C₁₂H₁₁FINO₂S: 380 (MH⁺).

[00172] A mixture of methyl-4-(2-fluoro-4-iodo-phenylamino)-2,3-dihydro-thiophene-3-carboxylate (5.7 g, 15.0 mmol) and chloranil (5.7 g, 15.0 mmol) in toluene (50 mL) was heated to reflux for 2 hours. The solution was cooled to room temperature and the solvent was evaporated. The resulting dark brown solid was recrystallized from methanol to provide methyl 4-(2-fluoro-4-iodo-phenylamino)-thiophene-3-carboxylate (2.8 g, 49.5% yield). MS (EI) for C₁₂H₉FINO₂S: 378 (MH⁺).

[00173] Methyl 4-(2-Fluoro-4-iodo-phenylamino)-thiophene-3-carboxylate (270 mg, 0.72 mmol) was dissolved in a mixture of tetrahydrofuran:methanol (6:1, 3 mL) and a solution of lithium hydroxide (0.1 g, 4.2 mmol) in 1 mL of water was added. The solution was stirred at room temperature for 18 hours and the solvent was concentrated. The residue was dissolved in 5 mL of water and the solution was acidified to pH 1 with 1N HCl. The resulting solid

was filtered and dried *in vacuo* to provide 210 mg (79% yield) of 4-(2-fluoro-4-iodophenylamino)-thiophene-3-carboxylic acid. MS (EI) for $C_{11}H_7FINO_2S$: 364 (MH^+).

EXAMPLE 3

5 [00174] Using the same or analogous synthetic techniques described in examples 1 and 2 and substituting with alternative reagents, the following compounds of the invention were prepared:

- a) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{16}H_{12}F_3IN_2O_2$: 449 (MH^+).
- 10 b) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one: MS (EI) for $C_{16}H_{10}F_3IN_2O_2$: 447 (MH^+).
- c) 6-(azetidin-1-ylcarbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline: MS (EI) for $C_{16}H_{12}F_3IN_2O$: 433 (MH^+).
- 15 d) 6-[(3,3-difluoroazetidin-1-yl)carbonyl]-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline: MS (EI) for $C_{16}H_{10}F_5IN_2O$: 469 (MH^+).
- e) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol: MS (EI) for $C_{17}H_{14}F_3IN_2O_3$: 479 (MH^+).
- f) 2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-{[3-(methyloxy)azetidin-1-yl]carbonyl}aniline: MS (EI) for $C_{17}H_{14}F_3IN_2O_2$: 463 (MH^+).
- 20 g) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol: MS (EI) for $C_{17}H_{11}F_6IN_2O_2$: 517 (MH^+).
- h) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-prop-2-en-1-ylazetidin-3-ol: MS (EI) for $C_{19}H_{16}F_3IN_2O_2$: 489 (MH^+).
- 25 i) 3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]propane-1,2-diol: MS (EI) for $C_{19}H_{18}F_3IN_2O_4$: 523 (MH^+).
- j) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethylazetidin-3-ol: MS (EI) for $C_{18}H_{16}F_3IN_2O_2$: 477 (MH^+).
- k) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-methylazetidin-3-ol: MS (EI) for $C_{17}H_{14}F_3IN_2O_2$: 463 (MH^+).
- 30 l) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-2-carboxylic acid: MS (EI) for $C_{17}H_{12}F_3IN_2O_3$: 477 (MH^+).
- m) [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methanol: MS (EI) for $C_{17}H_{14}F_3IN_2O_2$: 463 (MH^+).

- n) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethenylazetidin-3-ol: MS (EI) for $C_{18}H_{14}F_3IN_2O_2$: 475 (MH^+).
- o) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxylic acid: MS (EI) for $C_{17}H_{12}F_3IN_2O_3$: 477 (MH^+).
- 5 p) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime: MS (EI) for $C_{16}H_{11}F_3IN_3O_2$: 462 (MH^+).
- q) [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol: MS (EI) for $C_{17}H_{14}F_3IN_2O_2$: 463 (MH^+).
- 10 r) 1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethane-1,2-diol: MS (EI) for $C_{18}H_{16}F_3IN_2O_4$: 509 (MH^+).
- s) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine: MS (EI) for $C_{16}H_{13}F_3IN_3O$: 448 (MH^+).
- 15 t) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide: MS (EI) for $C_{17}H_{13}F_3IN_3O_2$: 476 (MH^+).
- u) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-3-carboxamide: MS (EI) for $C_{17}H_{13}F_3IN_3O_3$: 492 (MH^+).
- v) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-2-carboxamide: MS (EI) for $C_{17}H_{13}F_3IN_3O_2$: 476 (MH^+).
- 20 w) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-2-carboxamide: MS (EI) for $C_{17}H_{13}F_3IN_3O_3$: 492 (MH^+).
- x) *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanesulfonamide: MS (EI) for $C_{17}H_{15}F_3IN_3O_3S$: 526 (MH^+).
- 25 y) *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]acetamide: MS (EI) for $C_{18}H_{15}F_3IN_3O_2$: 490 (MH^+).
- z) 1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate: MS (EI) for $C_{21}H_{21}F_3IN_3O_3$: 548 (MH^+).
- 30 aa) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(pyrrolidin-1-ylmethyl)azetidin-3-ol: MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).

- bb) 3-[(diethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{21}H_{23}F_3IN_3O_2$: 534 (MH^+).
- 5 cc) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(dimethylamino)methyl]azetidin-3-ol: MS (EI) for $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).
- dd) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methyl-*N*-prop-2-en-1-ylazetidine-3-carboxamide: MS (EI) for $C_{21}H_{19}F_3IN_3O_2$: 530 (MH^+).
- 10 ee) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methylazetidine-3-carboxamide: MS (EI) for $C_{18}H_{15}F_3IN_3O_2$: 490 (MH^+).
- ff) *N*-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide: MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).
- 15 gg) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-prop-2-en-1-ylazetidine-3-carboxamide: MS (EI) for $C_{20}H_{17}F_3IN_3O_2$: 516 (MH^+).
- hh) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethyl-*N*-(2-hydroxyethyl)azetidine-3-carboxamide: MS (EI) for $C_{21}H_{21}F_3IN_3O_3$: 548 (MH^+).
- 20 ii) *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-methylpropanamide: MS (EI) for $C_{20}H_{19}F_3IN_3O_2$: 518 (MH^+).
- jj) *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]formamide: MS (EI) for $C_{17}H_{13}F_3IN_3O_2$: 476 (MH^+).
- 25 kk) *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-3,4-dihydroxybutanamide: MS (EI) for $C_{20}H_{19}F_3IN_3O_4$: 550 (MH^+).
- ll) methyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate: MS (EI) for $C_{18}H_{15}F_3IN_3O_3$: 550 (MH^+).
- 30 mm) *N*-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine: MS (EI) for $C_{20}H_{21}F_3IN_3O$: 504 (MH^+).

- nn) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N,N*-diprop-2-en-1-ylazetidin-3-amine: MS (EI) for $C_{22}H_{21}F_3IN_3O$: 528 (MH^+).
- oo) 1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-amine: MS (EI) for $C_{14}H_{13}FIN_3OS$: 418 (MH^+).
- 5 pp) 1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{14}H_{12}FIN_2O_2S$: 419 (MH^+).
- qq) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol: MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).
- rr). 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*R*)-piperidin-2-yl]azetidin-3-ol: MS (EI) for $C_{21}H_{21}F_3IN_3O_2$: 532 (MH^+).
- 10 ss) 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[2-pyrrolidin-2-yl]azetidin-3-ol: MS (EI) for $C_{20}H_{19}F_3IN_3O_2$: 518 (MH^+).
- tt) 3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for
- 15 $C_{17}H_{15}F_3IN_3O_2$: 478 (MH^+).
- uu) 3-[1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for $C_{18}H_{17}F_3IN_3O_2$: 492 (MH^+).
- vv) 3-[1-aminopropyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol: MS (EI) for
- 20 $C_{19}H_{19}F_3IN_3O_2$: 506 (MH^+).

Assay

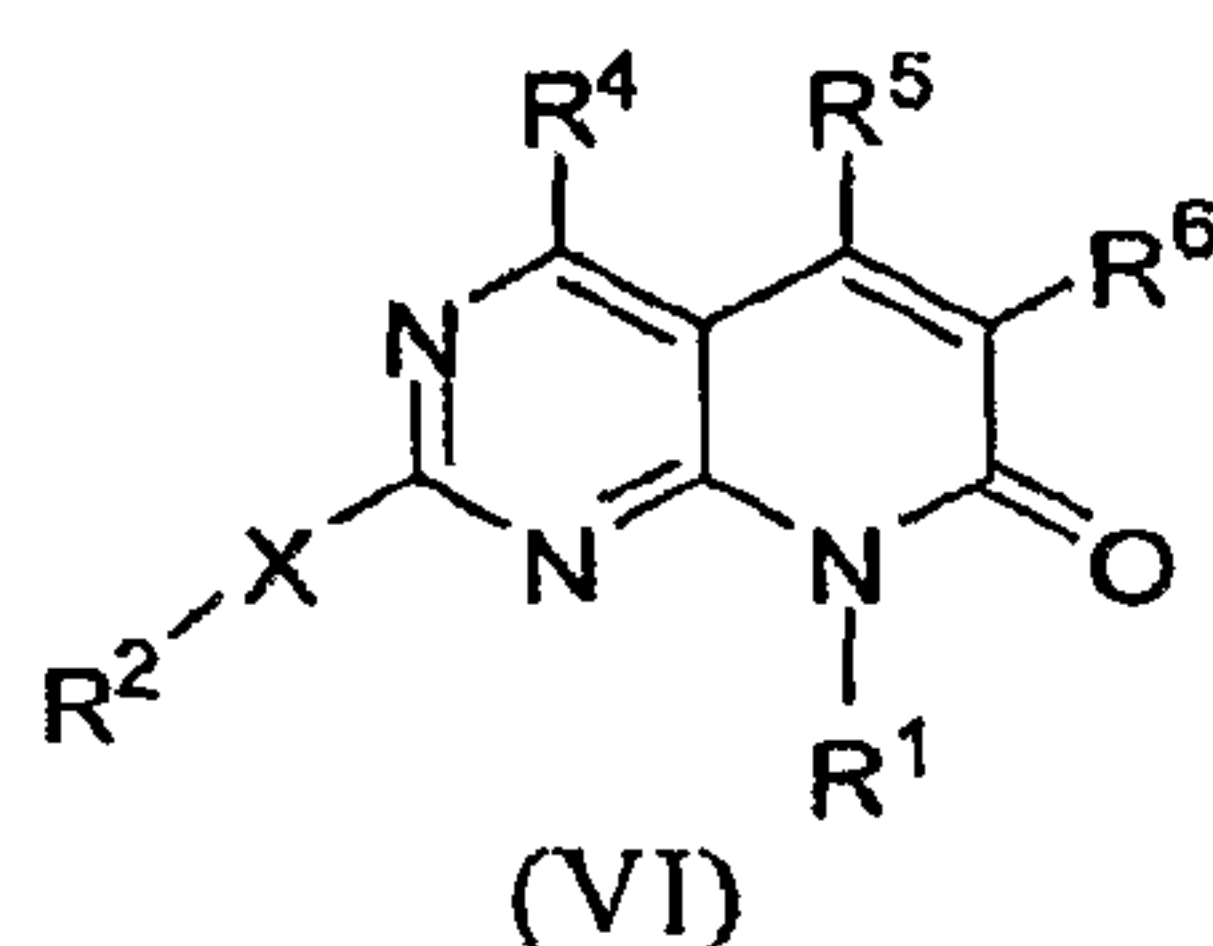
[00175] For a biochemical measurement of MEK1 inhibitory activity, compounds of the invention were screened in a triple coupled cRaf-MEK-ERK2 assay using ALPHASCREEN (Registered Trademark of Perkin Elmer) technology (Perkin Elmer). The compound of the invention, 0.5 μ L of 100% DMSO stock solution, is diluted into an assay buffer composed of 20 mM Tris (pH = 7.5), 10 mM magnesium chloride, 0.03% CHAPS and 1 mM DTT. Subsequently, 10 μ L of substrate mixture is added composed of inactive MEK1 (3 nM), ATP (50 μ M), inactive ERK2 (4 nM), biotinylated MBP peptide (b-FFKNIVTPRTPPPSQGK, 1 μ M) and antiphospho MBP peptide (0.5 nM). The mixture is then gently shaken for 30 minutes at room temperature followed by addition of active cRaf (5 μ L at 0.5 nM) to initiate reaction. The mixture is then shaken for 100 minutes at room temperature then quenched by addition of 10 μ L of a mixture of 5 μ g/mL streptavidin donor beads and 5 μ g/mL protein A

acceptor beads in detection buffer (75 mM Hepes pH = 7.5, 300 mM sodium chloride, 120 mM EDTA, 0.3% BSA and 0.03% Tween), followed by incubation overnight and signal detection on an ALPHAQuest® (Registered Trademark of Perkin Elmer) plate reader (Perkin Elmer).

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Section II

[00176] In one embodiment, in section II the invention provides compounds that are useful as inhibitors of PI3K that have the Formula VI:



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and optionally as a pharmaceutically acceptable salt or hydrate thereof, wherein

R^1 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

15

X is $-NR^3$ -;

R^2 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl- C_{1-6} alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, optionally substituted heterocyclyl-aryl- or optionally substituted heteroaryl; R^2 is optionally further substituted with 1, 2, 3, or 4 R^8 groups;

20

R^3 is hydrogen;

R_4 is hydrogen or optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

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R^5 is hydrogen or optionally substituted C_1 - C_6 alkyl;

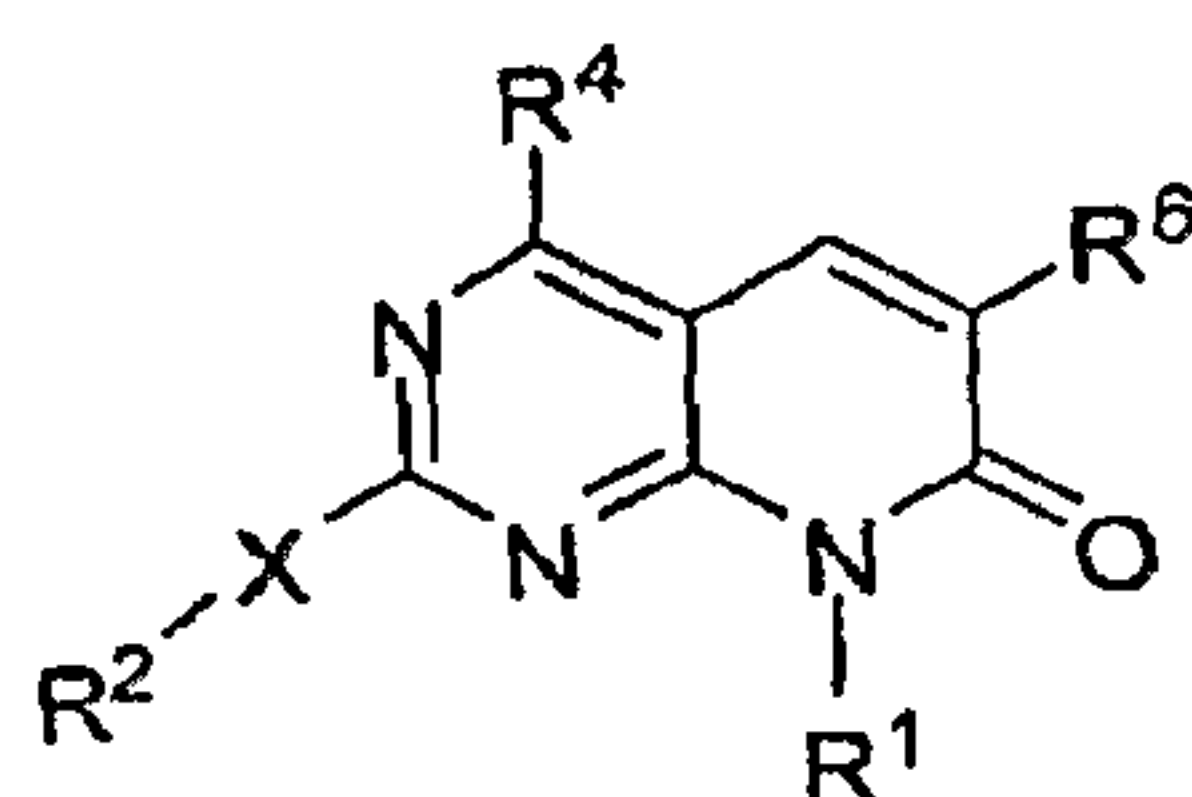
R^6 is hydrogen, halo, haloalkyl, haloalkoxy, $-NR^3$ -, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, acyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl- C_{1-6} alkyl, optionally substituted heterocyclyl, or optionally substituted heteroaryl; substitutable R^6 groups are optionally further substituted with 1, 2, 3, or 4 R^9 groups;

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R^8 at each occurrence is independently hydroxy, halo, haloalkyl, haloalkoxy, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, C_1 - C_6 alkoxyalkylaminoalkyl, C_1 - C_6 alkylcarboxyheterocyclyl, $-O$ - C_1 - C_6 alkylheterocyclyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl C_1 - C_6 alkyl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl; and

R^9 at each occurrence is independently halo, haloalkyl, haloalkoxy, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, C_1 - C_6 carboxyalkyl, alkoxy carbonyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl C_1 - C_6 alkyl, optionally substituted aryloxy, optionally substituted heterocyclyl, or optionally substituted heteroaryl.

[00177] In one embodiment, the invention provides a PI3K inhibitor of formula VIa:



(VIa)

and optionally as a pharmaceutically acceptable salt or hydrate thereof, wherein

R^1 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

X is $-NR^3$ -;

R^2 is hydrogen, optionally substituted C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, aryl, aryl- C_{1-6} alkyl, heteroalicyclic, heterocyclylalkyl, heterocyclyl-aryl- or heteroaryl; where the cycloalkyl, aryl, aryl- C_{1-6} alkyl, heteroalicyclic, heterocyclylalkyl, heterocyclyl-aryl-, and heteroaryl groups in R^2 are optionally substituted with 1, 2, 3, or 4 R^8 groups;

R^3 is hydrogen;

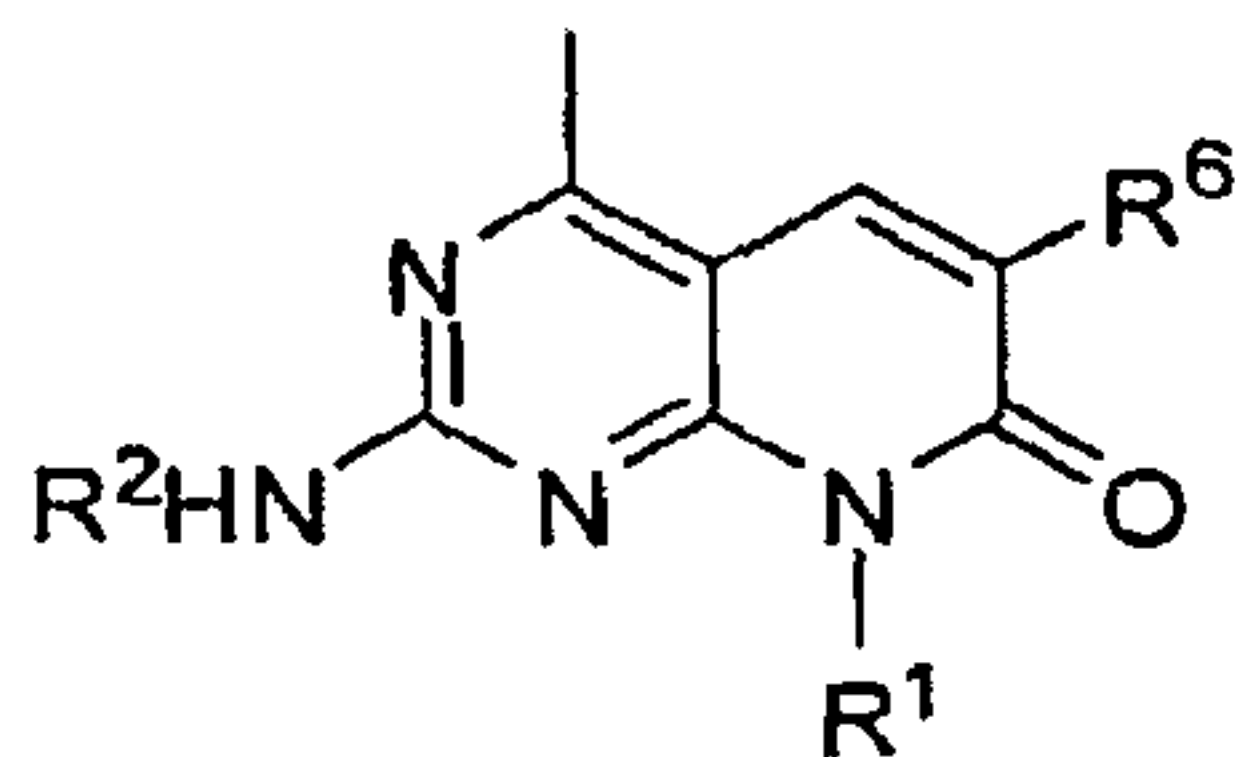
R^4 is optionally substituted C_1 - C_6 alkyl;

R^6 is hydrogen, acyl, phenyl, heteroalicyclic, or heteroaryl; where the phenyl, heteroalicyclic, and heteroaryl in R^6 are optionally substituted with 1, 2, 3, or 4 R^9 groups;

R^8 at each occurrence is independently hydroxy, halo, haloalkyl, C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, C_1 - C_6 alkoxyalkylaminoalkyl, C_1 - C_6 alkylcarboxyheterocyclyl, $-O-C_1$ - C_6 alkylheterocyclyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl C_1 - C_6 alkyl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl; and

R^9 at each occurrence is independently halo, haloalkyl, haloalkoxy, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, C_1 - C_6 carboxyalkyl, alkoxycarbonyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl C_1 - C_6 alkyl, optionally substituted aryloxy, optionally substituted heteroalicyclic, or optionally substituted heteroaryl.

[00178] In one embodiment, the invention provides a PI3K inhibitor of formula VIb:



(VIb)

and optionally a pharmaceutically acceptable salt or solvate thereof, wherein

R^1 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

R^6 is phenyl, acyl, or heteroaryl wherein the phenyl and heteroaryl are optionally substituted with 1, 2, 3, or 4 R^9 groups; and

R^9 at each occurrence is independently halo, haloalkyl, haloalkoxy, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, C_1 - C_6 carboxyalkyl, alkoxycarbonyl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl C_1 - C_6 alkyl, aryloxy, optionally substituted heteroalicyclic, or optionally substituted heteroaryl.

[00179] In another embodiment (A), the invention provides a compound of Formula VIa where R^1 is hydrogen, C_1 - C_6 optionally substituted alkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted

heteroaryl or optionally substituted heteroarylalkyl; and all other groups are as defined in Formula VIa. In another embodiment, R¹ is hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, or optionally substituted heteroalicyclicalkyl. In yet another embodiment, R¹ is hydrogen, alkyl, alkyl substituted with one or two hydroxy, alkyl substituted with alkoxy, alkyl substituted with aryl, C₃-C₇ cycloalkyl, or heteroalicyclicalkyl. In yet another embodiment, R¹ is hydrogen, methyl, ethyl, propyl, isopropyl, 2-hydroxypropyl, 3-hydroxypropyl, 2-ethoxyethyl, 3-methoxypropyl, 3-ethoxypropyl, 3-isopropoxypropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, benzyl, or 2-piperidin-1-ylethyl. In yet another embodiment, R¹ is ethyl, isopropyl, cyclopentyl, or cyclohexyl. In yet another embodiment, R¹ is ethyl.

[00180] In another embodiment (B), the invention provides a compound of Formula VIa where R² is hydrogen or optionally substituted C₁-C₆ alkyl; and all other groups are as defined in Formula VIa. In another embodiment, R² is hydrogen or alkyl where the alkyl is optionally substituted with one, two, or three amino, alkylamino, dialkylamino, or halo. In another embodiment, R² is hydrogen, methyl, ethyl, propyl, isopropyl, *tert*-butyl, 3-aminopropyl, 3-(*N*-methylamino)-propyl, or 3-(*N,N*-dimethylamino)-propyl. In another embodiment, R² is hydrogen or ethyl. In another embodiment, R² is hydrogen.

[00181] In another embodiment, the invention provides a compound of Formula VIa or VIb where R² is hydrogen and all other groups are as defined for Formula VIa or VIb, respectively.

[00182] In another embodiment, the invention provides a compound of Formula VIa or VIb where R² is optionally substituted C₁-C₆ alkyl; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment, R² is alkyl where the alkyl is optionally substituted with one, two, or three amino, alkylamino, dialkylamino, or halo. In another embodiment, R² is methyl, ethyl, propyl, isopropyl, *tert*-butyl, 3-aminopropyl, 3-(*N*-methylamino)-propyl, or 3-(*N,N*-dimethylamino)-propyl. In another embodiment, R² is ethyl.

[00183] In another embodiment (C), the invention is directed to a Compound of Formula VIa where R⁴ is optionally substituted C₁-C₆ alkyl; and all other groups are as defined in Formula VIa. In another embodiment, R⁴ is methyl or ethyl. In another embodiment, R⁴ is methyl.

[00184] Another embodiment (D), the invention is directed to a Compound of Formula VIa or VIb where R² is hydrogen or optionally substituted C₁-C₆ alkyl and R⁶ is acyl; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment, R⁶ is alkylcarbonyl. In another embodiment, R⁶ is acetyl.

[00185] Another embodiment (E), the invention is directed to a Compound of Formula VIa or VIb where R^2 is hydrogen or optionally substituted C_1 - C_6 alkyl and R^6 is phenyl optionally substituted with 1, 2, 3, or 4 R^9 groups; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment, R^6 is phenyl optionally substituted with one or two R^9 groups; and R^9 at each instance is independently selected from aryl, halo, alkoxy, aryloxy, alkoxycarbonyl, alkyl, and haloalkyl. In another embodiment, R^6 is phenyl optionally substituted with one or two R^9 groups; and each R^9 at each instance is independently selected from phenyl, fluoro, chloro, methoxy, phenyloxy, methyl, methoxycarbonyl, and trifluoromethyl. In another embodiment, R^6 is phenyl, phenyl substituted with phenyl, fluorophenyl, difluorophenyl, chlorophenyl, dichlorophenyl, phenyl substituted with chloro and fluoro, methoxyphenyl, dimethoxyphenyl, phenyloxyphenyl, or trifluoromethylphenyl. Yet even more specifically, R^6 is phenyl, 2-phenyl-phenyl, 3-phenyl-phenyl, 4-phenyl-phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 2,5-dichlorophenyl, 2,6-dichlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 3-chloro-4-fluoro-phenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2,3-dimethoxyphenyl, 2,4-dimethoxyphenyl, 2,5-dimethoxyphenyl, 2,6-dimethoxyphenyl, 3,4-dimethoxyphenyl, 3,5-dimethoxyphenyl, 4-phenyloxyphenyl, 2-trifluoromethylphenyl, or 3-trifluoromethylphenyl.

[00186] Another embodiment, the invention is directed to a Compound of Formula VIa or VIb where R^6 is phenyl substituted with 1, 2, 3, or 4 R^9 groups; and all other groups are as defined in Formula VIa or VIb, respectively.

[00187] Another embodiment, the invention is directed to a Compound of Formula VIa or VIb where R^6 is heteroaryl optionally substituted with 1, 2, 3, 4, or 5 R^9 groups; and all other groups are as defined in Formula VIa or VIb, respectively.

[00188] In another embodiment (G), the invention is directed to a Compound of Formula VIa or VIb where R^2 is hydrogen or optionally substituted C_1 - C_6 alkyl and R^6 is heteroaryl optionally substituted with 1, 2, 3, 4, or 5 R^9 groups; and all other groups are as defined in Formula VIa or VIb, respectively.

[00189] In another embodiment (G1), the invention is directed to a Compound of Formula VIa or VIb where R^2 is hydrogen or ethyl and R^6 is a 6-membered heteroaryl optionally substituted with one or two R^9 ; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment, R^6 is pyridinyl, pyrazinyl, pyrimidinyl, or pyridazinyl

each of which is optionally substituted with one R⁹ where R⁹ at each instance is halo. In another embodiment, R⁶ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, 3-fluoropyridin-4-yl, pyrazin-2-yl, pyrazin-3-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyridazin-3-yl, or pyridazin-4-yl, each of which is optionally substituted with one or two R⁹.

5 [00190] In another embodiment (G2), the invention is directed to a Compound of Formula VIa or VIb where R² is hydrogen or ethyl and R⁶ is pyrazinyl, pyrimidinyl, or pyridazinyl each of which is optionally substituted with one R⁹ where R⁹ at each instance is halo; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment, R⁶ is pyrazin-2-yl, pyrazin-3-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyridazin-3-yl,
10 or pyridazin-4-yl.

[00191] In another embodiment (G3), the invention is directed to a Compound of Formula VIa or VIb where R² is hydrogen or ethyl and R⁶ is 5-membered heteroaryl optionally substituted with one or two R⁹; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment R⁶ is pyrazolyl, imidazolyl, thienyl, thiazolyl, oxazolyl,
15 isoxazolyl, oxadiazolyl, furanyl, pyrrolyl, triazolyl, or tetrazolyl, each of which is optionally substituted with one R⁹ where R⁹ at each instance is alkyl, arylalkyl, cyano, aryl, alkoxycarbonyl, or halo. In another embodiment R⁶ is pyrazolyl, thienyl, thiazolyl, oxazolyl, furanyl, or pyrrolyl, each of which is optionally substituted with one R⁹ where R⁹ at each instance is alkyl, alkoxycarbonyl, or halo. In another embodiment, R⁶ is pyrazol-1-yl,
20 pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, furan-3-yl, pyrrol-1-yl, pyrrol-2-yl, or pyrrol-3-yl; each of which is optionally substituted with one R⁹ where R⁹ at each instance, is methyl, *N-tert*-butoxycarbonyl, or chloro. In another embodiment, R⁶ is pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl,
25 oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, furan-3-yl, pyrrol-2-yl, or pyrrol-3-yl; each of which is optionally substituted with one R⁹ where R⁹, when present, is methyl, *N-tert*-butoxycarbonyl, or chloro.

[00192] In another embodiment (G4), the invention is directed to a Compound of Formula VIa or VIb where R² is hydrogen or ethyl and R⁶ is thien-2-yl, thien-3-yl, pyrrol-2-yl, furan-2-yl, furan-3-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thiazol-2-yl, thiazol-5-yl, isoxazol-4-yl, imidazol-5-yl, triazol-5-yl, or tetrazol-5-yl, each of which is optionally substituted with one R⁹ where R⁹, when present, is methyl, *N-tert*-butoxycarbonyl, or chloro; and all other groups are as defined in Formula VIa or VIb, respectively.
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[00193] In another embodiment (G5), the invention is directed to a Compound of Formula VIa or VIb where R^2 is hydrogen or ethyl and R^6 is indolyl optionally substituted with 1, 2, 3, or 4 R^9 groups; and all other groups are as defined in Formula VIa or VIb, respectively. In another embodiment R^6 is indol-2-yl, indol-3-yl, indol-4-yl, indol-5-yl, indol-6-yl, or indol-7-yl; each of which is optionally substituted with 1, 2, 3, or 4 R^9 groups. In another embodiment, R^6 is indol-6-yl.

[00194] In another embodiment of the Invention (H), the invention is directed to a Compound of Formula VIa where R^1 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, or optionally substituted heteroalicyclicalkyl; R^2 is hydrogen or C_1 - C_6 alkyl optionally substituted with amino, alkylamino, dialkylamino, or halo; R^4 is alkyl; R^6 is phenyl or heteroaryl wherein the phenyl and heteroaryl are optionally substituted with one, two, or three R^9 groups; and each R^9 , when present, is independently alkyl, arylalkyl, cyano, aryl, alkoxycarbonyl, or halo.

[00195] In another embodiment of the Invention (J), the invention is directed to a Compound of Formula VIa where R^2 is hydrogen or ethyl, R^4 is methyl, and R^6 is pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, furan-3-yl, pyrrol-2-yl, or pyrrol-3-yl; each of which is optionally substituted with 1, 2, 3, 4, or 5 R^9 groups; and all other groups are as defined in Formula VIa.

[00196] In another embodiment of the Invention (K), the invention is directed to a Compound of Formula VIa where R^1 is alkyl or cycloalkyl; R^4 is methyl; and R^6 is heteroaryl optionally substituted with one or two R^9 groups; and all other groups are as defined in Formula VIa. In another embodiment, each R^9 , when present, is independently alkyl, alkoxycarbonyl, or halo. In another embodiment, R^6 is pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, furan-3-yl, pyrrol-2-yl, or pyrrol-3-yl; each of which is optionally substituted with one R^9 where R^9 , when present, is methyl or *N-tert*-butoxycarbonyl.

[00197] In another embodiment (K1) of embodiment K, the invention is directed to a Compound of Formula VIa where R^2 is hydrogen; and all other groups are as defined in Embodiment K.

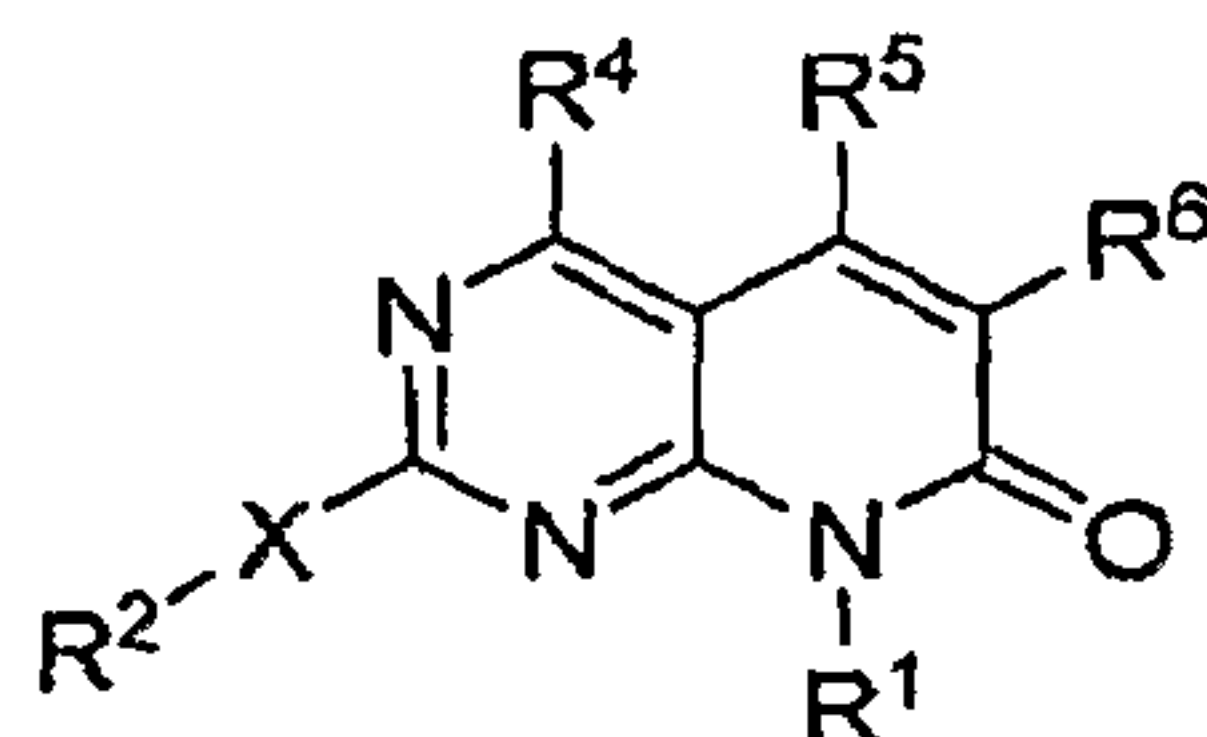
[00198] In another embodiment (K2) of embodiment K, the invention is directed to a Compound of Formula VIa where R^2 is methyl or ethyl; and all other groups are as defined in Embodiment K.

[00199] In another embodiment (L), the invention is directed to a Compound of Formula VIa where R^1 is alkyl or cycloalkyl; R^4 is methyl; and R^6 is phenyl optionally substituted with one or two R^9 groups; and all other groups are as defined in Formula VIa. In another embodiment, each R^9 , when present, is independently halo, alkoxy, or haloalkyl.

5 [00200] In another embodiment (M), the invention is directed to a Compound of Formula VIa where R^1 is alkyl or cycloalkyl; R^4 is methyl; and R^2 is hydrogen; and all other groups are as defined in Formula VIa.

[00201] In another embodiment (N), the invention is directed to a Compound of Formula VIa where R^1 is alkyl or cycloalkyl; R^4 is methyl; and R^2 is optionally substituted alkyl; and
10 all other groups are as defined in Formula VIa.

[00202] In another embodiment, the invention is directed to a Compound of Formula VII:



VII

R^1 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl,
15 optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

X is $-NR^3-$;

R^3 is hydrogen;

20 R^4 is optionally substituted C_1 - C_6 alkyl;

R^5 is hydrogen;

R^6 is acyl and R^2 is heterocycl-aryl- optionally substituted with 1, 2, 3, or 4 R^8 groups; or

R^6 is halo and R^2 is optionally substituted C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, phenyl, aryl- C_{1-6} alkyl, heteroalicyclicalkyl, or heterocycl-aryl-; where the C_3 - C_7 cycloalkyl, phenyl,
25 phenyl, aryl- C_{1-6} alkyl, heteroalicyclicalkyl, and heterocycl-aryl- groups in R^2 are optionally substituted with 1, 2, 3, or 4 R^8 groups; or

R^6 is phenyl optionally substituted with 1, 2, or 3 halo; and R^2 is phenyl or heterocycl-aryl-; where the phenyl and heterocycl-aryl- groups in R^2 are optionally substituted with 1, 2, 3, or 4 R^8 groups; or

30 R^6 is heteroaryl optionally substituted with 1, 2, or 3 halo; and R^2 is heterocycl-aryl- optionally substituted with 1, 2, 3, 4, or 5 R^8 groups;

each R⁸ at each instance is independently hydroxy, halo, C₁-C₆ alkyl, haloalkyl, optionally substituted C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, C₁-C₆ alkoxycarbonyl, C₁-C₆ alkoxyalkylaminoalkyl, -O-C₁-C₆alkylheterocyclyl, aminoalkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted aryl C₁-C₆ alkyl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl.

[00203] In another embodiment (A), the invention is directed to a Compound of Formula VII where R¹ is hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl; and all other groups are as defined in Formula VII. In another embodiment, R¹ is hydrogen, optionally substituted C₁-C₆ alkyl, or optionally substituted C₃-C₇ cycloalkyl. In another embodiment, R¹ is C₁-C₆ alkyl or C₃-C₇ cycloalkyl. In another embodiment, R¹ is methyl, ethyl, propyl, isopropyl, cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl. In another embodiment, R¹ is ethyl, isopropyl, or cyclopentyl.

[00204] In another embodiment (B), the invention is directed to a Compound of Formula VII where R⁴ is optionally substituted C₁-C₆ alkyl; and all other groups are as defined in Formula VII. In another embodiment, R⁴ is methyl or ethyl. In another embodiment, R⁴ is methyl.

[00205] In another embodiment (C), the invention is directed to a Compound of Formula VII where R⁶ is acyl and R² is heterocyclyl-aryl- optionally substituted with 1, 2, 3, or 4 R⁸ groups; and all other groups are as defined in Formula VII. In another embodiment, R⁶ is alkylcarbonyl. In another embodiment, R⁶ is acetyl.

[00206] In another embodiment of embodiment C, the invention is directed to a Compound of Formula VII where R⁶ is acyl and R² is heteroalicyclic-phenyl- optionally substituted with 1, 2, 3, or 4 R⁸ groups; and all other groups are as defined in Formula VII. In another embodiment, R⁸, when R⁸ is present, is C₁-C₆ alkyl, C₁-C₆ alkoxycarbonyl, or aryl C₁-C₆ alkyl. In another embodiment, R² is piperazinyl-phenyl- where the piperazinyl is optionally substituted with one R⁸ where R⁸, when present, is methyl, ethyl, isopropyl, *tert*-butoxycarbonyl, or benzyl. In another embodiment, R² is piperazinyl-phenyl- where the piperazinyl is optionally substituted with C₁-C₆ alkyl.

[00207] In another embodiment (E), the invention is directed to a Compound of Formula VII where R⁶ is phenyl optionally substituted with 1, 2, 3, or 4 R⁹ groups; and R² is phenyl or heterocyclyl-aryl-; where the phenyl and heterocyclyl-aryl- groups in R² are optionally

substituted with 1, 2, 3, or 4 R^8 groups; and all other groups are as defined in Formula VII. In another embodiment, R^6 is phenyl, phenyl substituted with one or two halo. In another embodiment, R^6 is phenyl, fluorophenyl, difluorophenyl, chlorophenyl, or dichlorophenyl. In another embodiment, R^6 is phenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl,
 5 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 3,4-difluorophenyl, or 3,5-difluorophenyl.

[00208] In another embodiment (E1) of Embodiment E, the invention is directed to a Compound of Formula VII where R^2 is phenyl or heteroalicyclic-phenyl-; where the phenyl and heteroalicyclic-phenyl- groups in R^2 are optionally substituted with 1, 2, 3, or 4 R^8
 10 groups; and all other groups are as defined in Embodiment E.

[00209] In another embodiment of embodiment E1, the invention is directed to a Compound of Formula VII where R^2 is phenyl or heteroalicyclic-phenyl-; where the phenyl and heteroalicyclic-phenyl- groups in R^2 are optionally substituted with one or two R^8 where each R^8 , when present, is independently hydroxy, C_1 - C_6 alkyl, optionally substituted C_1 - C_6
 15 alkoxy, alkoxycarbonyl, or $-O-C_1-C_6$ alkylheteroalicyclic; and all other groups are as defined in Embodiment E1.

[00210] In another embodiment of embodiment E1, R^2 is phenyl or phenyl substituted with one or two R^8 where each R^8 , when R^8 is present, is independently hydroxy, $-O-C_1-C_6$ alkylheteroalicyclic, or C_1 - C_6 alkoxy where the C_1 - C_6 alkoxy is optionally
 20 substituted with amino, alkylamino or dialkylamino; and all other groups are as defined in Embodiment E1. In another embodiment, R^2 is phenyl, hydroxyphenyl, [(2-aminoethyl)-oxy]-phenyl, [(2-alkylamino-ethyl)-oxy]-phenyl, [(2-dialkylamino-ethyl)-oxy]-phenyl, (morpholinylalkyloxy)-phenyl, (piperidinylalkyloxy)-phenyl, (piperazinylalkyloxy)-phenyl, (*N*-alkyl-piperazinylalkyloxy)-phenyl, or (*N*-benzylpiperazinylalkyloxy)-phenyl. In another
 25 embodiment, R^2 is hydroxyphenyl, [(2-aminoethyl)-oxy]-phenyl, [(2-alkylamino-ethyl)-oxy]-phenyl, [(2-dialkylamino-ethyl)-oxy]-phenyl, (morpholinylalkyloxy)-phenyl, (piperidinylalkyloxy)-phenyl, (piperazinylalkyloxy)-phenyl, (*N*-alkyl-piperazinylalkyloxy)-phenyl, or (*N*-benzylpiperazinylalkyloxy)-phenyl. In another embodiment, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 4-[(2-dimethylamino-ethyl)-oxy]-phenyl, 4-[2-
 30 (morpholin-4-yl)-ethyloxy]-phenyl, 4-[2-(piperidinyl)-ethyloxy]-phenyl, 4-[2-(piperazin-4-yl)-ethyloxy]-phenyl, 4-[2-(*N*-methyl-piperazin-4-yl)-ethyloxy]-phenyl, or 4-[2-(*N*-ethyl-piperazin-4-yl)-ethyloxy]-phenyl.

[00211] In another embodiment of embodiment E1, R^2 is piperazinyl-phenyl- where the piperazinyl is optionally substituted with one R^8 where R^8 , when present, is alkyl; and all

other groups are as defined in Embodiment E1. In another embodiment, R² is morpholinylphenyl, piperazinylphenyl, or (*N*-alkyl-piperazinyl)-phenyl. In another embodiment, R² is 4-morpholin-4-ylphenyl, 4-piperazin-4-ylphenyl, 4-(*N*-methyl-piperazin-4-yl)-phenyl, or 4-(*N*-ethyl-piperazin-4-yl)-phenyl.

5 **[00212]** In another embodiment (F), the invention is directed to a Compound of Formula VII where R⁶ is heteroaryl optionally substituted with 1, 2, or 3 halo; and R² is heterocyclaryl- optionally substituted with 1, 2, 3, 4, or 5 R⁸ groups.

[00213] In another embodiment (F1) of embodiment F, the invention is directed to a Compound of Formula VII where R⁶ is a 5-membered heteroaryl optionally substituted with one or two halo; R² is heteroalicyclic-phenyl- where the heteroalicyclic and phenyl portions of R² are independently optionally substituted with one R⁸ where R⁸, when R⁸ is present is C₁-C₆ alkyl or aryl C₁-C₆ alkyl; and all other groups are as defined in embodiment F.

[00214] In another embodiment (F2) of embodiment F, the invention is directed to a Compound of Formula VII where R⁶ is pyrazolyl, thienyl, thiazolyl, oxazolyl, furanyl, or pyrrolyl, each of which is optionally substituted with one or two halo. In another embodiment, R⁶ is pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, or furan-3-yl; each of which is optionally substituted with one chloro. In another embodiment, R⁶ is pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, or furan-3-yl.

[00215] In another embodiment (G), the invention is directed to a Compound of Formula VII where R⁶ is halo and R² is optionally substituted C₁-C₆ alkyl, C₃-C₇ cycloalkyl, phenyl, aryl-C₁₋₆ alkyl, heteroalicyclicalkyl, or heterocyclaryl-; where the C₃-C₇ cycloalkyl, phenyl, phenyl, aryl-C₁₋₆ alkyl, heteroalicyclicalkyl, and heterocyclaryl- groups in R² are optionally substituted with 1, 2, 3, or 4 R⁸ groups. In another embodiment, R⁶ is bromo and R² is C₃-C₇ cycloalkyl, C₁-C₆ alkyl optionally substituted with heteroalicyclic, dialkylamino, phenyl substituted with one or two halo, or heteroalicyclic-phenyl-; where the heteroalicyclic-phenyl- is optionally substituted with one or two R⁸ selected from C₁-C₆ alkyl and phenyl-C₁₋₆ alkyl. In another embodiment, R² is cyclopentyl, cyclohexyl, 2-(morpholinyl)-ethyl, 3-(morpholinyl)-propyl, 3-(dimethylamino)-propyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 4-[4-methyl-piperazinyl]-phenyl, 4-[4-ethyl-piperazinyl]-phenyl, 4-[4-benzyl-piperazinyl]-phenyl, or 4-(morpholinyl)-phenyl.

[00216] In another embodiment (H), the invention is directed to a Compound of Formula VII where R¹ is C₁-C₆ alkyl or C₃-C₇ cycloalkyl; R⁴ is methyl; and R⁶ is heteroaryl. In

another embodiment, R⁶ is pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, or furan-3-yl.

5 [00217] In another embodiment (J), the invention is directed to a Compound of Formula VII where R¹ is C₁-C₆ alkyl or C₃-C₇ cycloalkyl; R⁴ is methyl; R⁵ is hydrogen and R⁶ is phenyl optionally substituted with 1, 2, or 3 halo.

[00218] In another embodiment (M), the invention is directed to a Compound of Formula VII where R⁶ is pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thien-2-yl, thien-3-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, furan-2-yl, or furan-3-yl.

10 [00219] Another aspect of the invention is a pharmaceutical composition comprising a compound of formula VI, VIa, VIb or VII, or a pharmaceutically acceptable salt or solvate thereof, in combination with a compound of formula I, Ia, Ic, Id, II, III, IV, or V and a pharmaceutically acceptable carrier.

15 [00220] Another aspect of the invention is a method of inhibiting the *in vivo* activity of PI3K α , and MEK the method comprising administering to a subject an effective PI3K α -inhibiting amount of a compound of formula VI, VIa, VIb or VII, or a pharmaceutically acceptable salt or solvate thereof, in combination with a compound of formula I, Ia, Ic, Id, II, III, IV, or V or a pharmaceutical composition thereof.

20 [00221] Another aspect of the invention is a method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities effected directly or indirectly by PI3K α and MEK, the method comprising administering to a mammal (preferably human) in need thereof a therapeutically effective amount of a compound of any of formula VI, VIa, VIb or VII, or a pharmaceutically acceptable salt or solvate thereof, in combination with a compound of formula I, Ia, Ic, Id, II, III, IV, or V or a pharmaceutical composition thereof. In another embodiment, the MEK Compound is of Formula Ia and the PI3K Compound is of Formula VIa. In another embodiment, the MEK Compound is of Formula Ia and the PI3K Compound is of Formula VIb. In another embodiment, the MEK Compound is of Formula V and the PI3K Compound is of Formula VIa or VIb. In another embodiment, the MEK Compound is of Section I, Embodiment G and the PI3K Compound is of a compound from Section II, Formula VIa or VIb, Embodiment E. In another embodiment, the MEK Compound is of Section I, Embodiment G and the PI3K Compound is of a compound of Section II, Formula VIa or VIb, Embodiment G or G3. In another embodiment, the MEK Compound is of Formula Ia and the PI3K Compound is of Formula VII. In another

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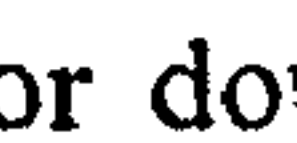
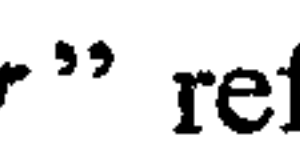
embodiment, the MEK Compound is of Formula V and the PI3K Compound is of Formula VII. In another embodiment, the MEK Compound is of Section I, Embodiment G and the PI3K Compound is of a compound from Section II, Formula VII, Embodiment E. In another embodiment, the MEK Compound is of Section I, Embodiment G and the PI3K Compound is of a compound of Section II, Formula VI, Embodiment F1 or F2. In another embodiment, the MEK Compound is of Section I, Table 1 and the PI3K Compound is of Formula VI, VIa, VIb or VII.

[00222] Another aspect of the invention is a method of inhibiting proliferative activity in a cell, the method comprising administering to a cell or a plurality of cells an effective amount of a compound of formula VI, VIa, VIb or VII, or a pharmaceutically acceptable salt or solvate thereof, in combination with a compound of formula I, Ia, Ic, Id, II, III, IV, or V or pharmaceutical composition thereof.

[00223] A further aspect of the invention is a method of treating malignancies such as melanoma, ovarian cancer, cervical cancer, breast cancer, colorectal cancer, and glioblastomas, among others, in a patient in need of such treatment, by administering a compound or salt of formula VI, VIa, VIb or VII, or a pharmaceutically acceptable salt or solvate thereof, in combination with a compound of formula I, Ia, Ic, Id, II, III, IV, or V or a pharmaceutical composition thereof.

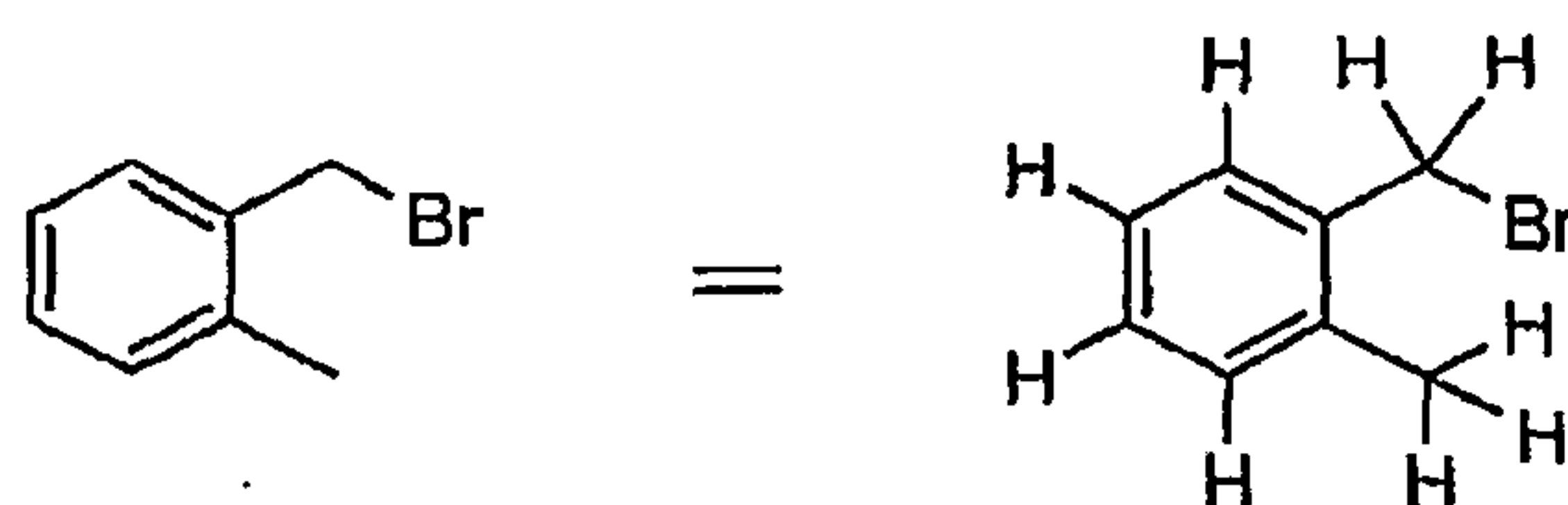
Section II Definitions

[00224] As used in the present specification, the following words and phrases are generally intended to have the meanings as set forth below, except to the extent that the context in which they are used indicates otherwise or they are expressly defined to mean something different.

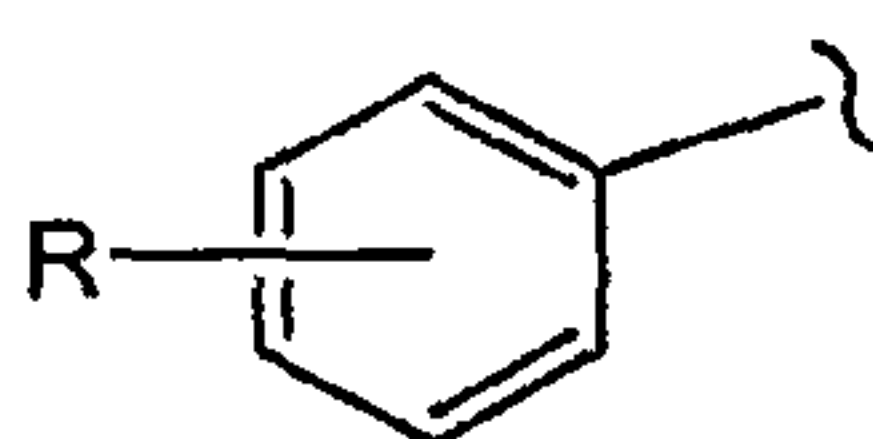
[00225] The symbol “-” means a single bond, “=” means a double bond, “≡” means a triple bond, “” means a single or double bond. The symbol “” refers to a group on a double-bond as occupying either position on the terminus of a double bond to which the symbol is attached; that is, the geometry, E- or Z-, of the double bond is ambiguous. When a group is depicted removed from its parent formula, the “” symbol will be used at the end of the bond which was theoretically cleaved in order to separate the group from its parent structural formula.

[00226] When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four. For example, in the structure on the left-hand side of the schematic below there are nine

hydrogens implied. The nine hydrogens are depicted in the right-hand structure. Sometimes a particular atom in a structure is described in textual formula as having a hydrogen or hydrogens as substitution (expressly defined hydrogen), for example, $-\text{CH}_2\text{CH}_2-$. It is understood by one of ordinary skill in the art that the aforementioned descriptive techniques are common in the chemical arts to provide brevity and simplicity to description of otherwise complex structures.

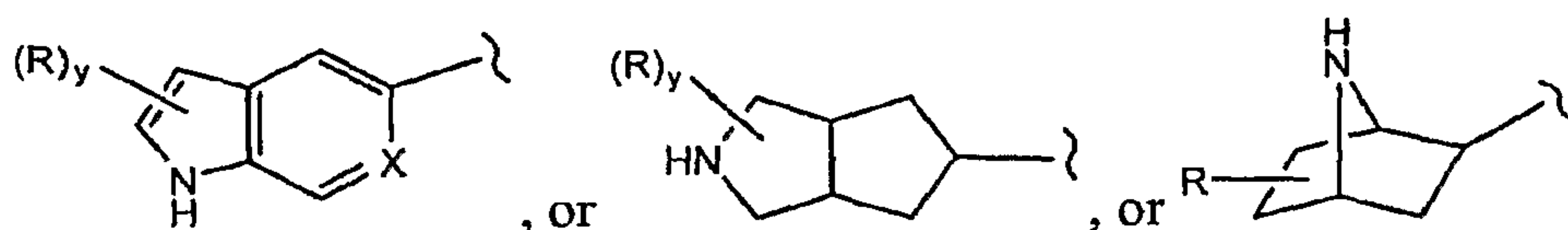


[00227] If a group “R” is depicted as “floating” on a ring system, as for example in the formula:



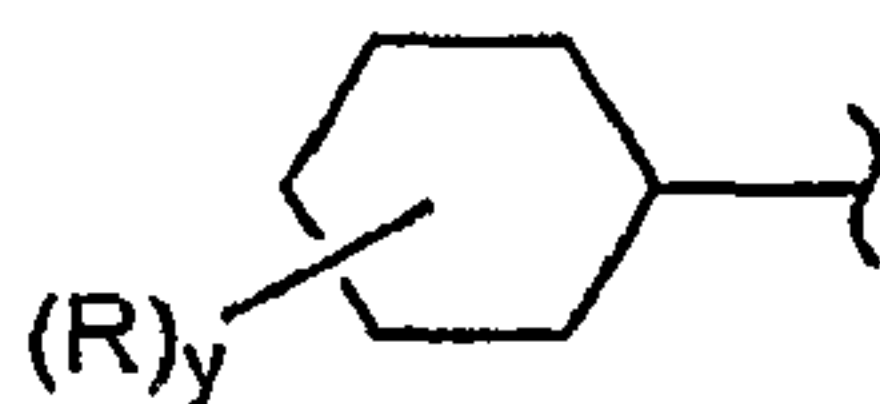
then, unless otherwise defined, a substituent “R” may reside on any atom of the ring system, assuming replacement of a depicted, implied, or expressly defined hydrogen from one of the ring atoms, so long as a stable structure is formed.

[00228] If a group “R” is depicted as floating on a fused ring system, as for example in the formulae:

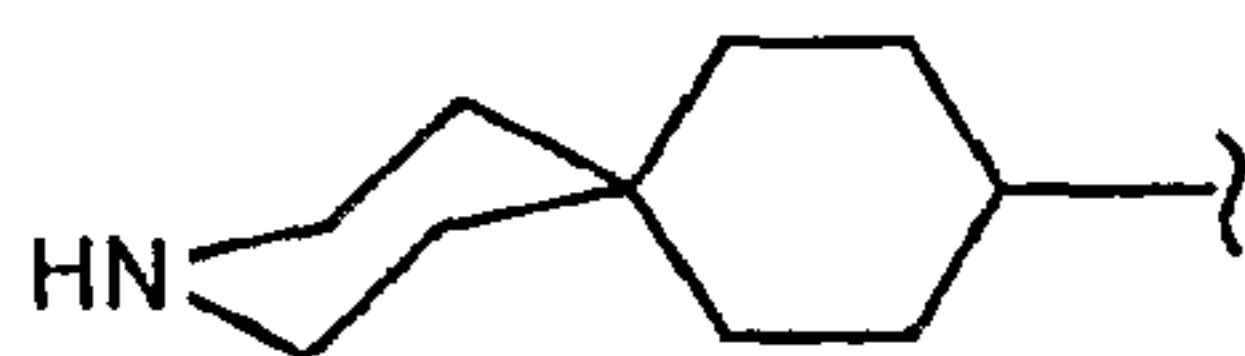


then, unless otherwise defined, a substituent “R” may reside on any atom of the fused ring system, assuming replacement of a depicted hydrogen (for example the $-\text{NH}-$ in the formula above), implied hydrogen (for example as in the formula above, where the hydrogens are not shown but understood to be present), or expressly defined hydrogen (for example where in the formula above, “X” equals $=\text{CH}-$) from one of the ring atoms, so long as a stable structure is formed. In the example depicted, the “R” group may reside on either the 5-membered or the 6-membered ring of the fused ring system. In the formula depicted above, when y is 2 for example, then the two “R’s” may reside on any two atoms of the ring system, again assuming each replaces a depicted, implied, or expressly defined hydrogen on the ring.

[00229] When a group “R” is depicted as existing on a ring system containing saturated carbons, as for example in the formula:



where, in this example, “y” can be more than one, assuming each replaces a currently depicted, implied, or expressly defined hydrogen on the ring; then, unless otherwise defined, where the resulting structure is stable, two “R’s” may reside on the same carbon. A simple example is when R is a methyl group; there can exist a geminal dimethyl on a carbon of the depicted ring (an “annular” carbon). In another example, two R’s on the same carbon, including that carbon, may form a ring, thus creating a spirocyclic ring (a “spirocyclyl” group) structure with the depicted ring as for example in the formula:



[00230] “Alkyl” is intended to include linear or branched hydrocarbon structures and combinations thereof, inclusively. For example, “C₈ alkyl” may refer to an *n*-octyl, *iso*-ctyl, and the like. Lower alkyl refers to alkyl groups of from one to six carbon atoms. Examples of lower alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, *s*-butyl, *t*-utyl, isobutyl, pentyl, and the like. Higher alkyl refers to alkyl groups containing more than eight carbon atoms. A “C₀” alkyl (as in “C₀-C₆ alkyl”) is a covalent bond. Exemplary alkyl groups are those of C₂₀ or below. In this application, alkyl refers to alkanyl, alkenyl, and alkynyl residues (and combinations thereof); it is intended to include vinyl, allyl, isoprenyl, and the like. Thus when an alkyl residue having a specific number of carbons is named, all geometric isomers having that number of carbons are intended to be encompassed; thus, for example, either “butyl” or “C₄ alkyl” is meant to include *n*-butyl, *sec*-butyl, isobutyl, *t*-butyl, isobutenyl and but-2-ynyl groups; and for example, “propyl” or “C₃ alkyl” each include *n*-propyl, propenyl, and isopropyl.

[00231] “Cycloalkyl” means a cyclic hydrocarbon groups of from three to thirteen carbon atoms. Examples of cycloalkyl groups include *c*-propyl, *c*-butyl, *c*-pentyl, norbornyl, adamantyl and the like.

[00232] “Alkoxy” or “alkoxyl” refers to the group -O-alkyl, for example including from one to eight carbon atoms of a straight, branched, cyclic configuration, unsaturated chains, and combinations thereof attached to the parent structure through an oxygen atom. Examples include methoxy, ethoxy, propoxy, isopropoxy, cyclopropyloxy, cyclohexyloxy and the like.

Lower-alkoxy refers to groups containing one to six carbons.

[00233] “Optionally substituted alkoxy” refers to the group -OR where R is optionally substituted alkyl, as defined herein. One exemplary substituted alkoxy group is “polyalkoxy” or -O-optionally substituted alkylene-optionally substituted alkoxy, and includes groups such as -OCH₂CH₂OCH₃, and glycol ethers such as polyethyleneglycol and -O(CH₂CH₂O)_xCH₃, where x is an integer of between about two and about twenty, in another example, between about two and about ten, and in a further example between about two and about five. Another exemplary substituted alkoxy group is hydroxyalkoxy or -OCH₂(CH₂)_yOH, where y is for example an integer of between about one and about ten, in another example y is an integer of between about one and about four.

[00234] “Acyl” refers to groups of from one to ten carbon atoms of a straight, branched, cyclic configuration, saturated, unsaturated and aromatic and combinations thereof, attached to the parent structure through a carbonyl functionality. One or more carbons in the acyl residue may be replaced by nitrogen, oxygen or sulfur as long as the point of attachment to the parent remains at the carbonyl. Examples include acetyl, benzoyl, propionyl, isobutyryl, *t*-butoxycarbonyl, benzyloxycarbonyl and the like. Lower-acyl refers to groups containing one to six carbons.

[00235] “Acyloxy” means an -OR group where R is acyl as defined herein.

[00236] “Acylamino” means an -NHR group where R is acyl as defined herein.

[00237] “Amino” refers to the group -NH₂. “Substituted amino,” refers to the group -N(H)R or -N(R)R where each R is independently selected from the group: optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heterocyclyl, acyl, carboxy, alkoxycarbonyl, sulfanyl, sulfinyl and sulfonyl, for example, diethylamino, methylsulfonylamino, and furanyl-oxy-sulfonamino.

[00238] “Aryl” refers to aromatic six- to fourteen-membered carbocyclic ring, for example, benzene, naphthalene, indane, tetralin, fluorene and the like, univalent substituents. As univalent substituents, the aforementioned ring examples are named, phenyl, naphthyl, indanyl, tetralinyl, and fluorenyl.

[00239] “Arylalkyl” refers to a residue in which an aryl moiety is attached to a parent structure via one of an alkylene, alkylidene, or alkylidyne group. Examples include benzyl, phenethyl, phenylvinyl, phenylallyl and the like. Both the aryl and the corresponding alkylene, alkylidene, or alkylidyne group portion of an arylalkyl group may be optionally substituted. “Lower arylalkyl” refers to an arylalkyl where the “alkyl” portion of the group has one to six carbons; this can also be referred to as C₁₋₆ arylalkyl.

[00240] In some examples, as appreciated by one of ordinary skill in the art, two adjacent groups on an aromatic system may be fused together to form a ring structure. The fused ring structure may contain heteroatoms and may be optionally substituted with one or more groups. It should additionally be noted that saturated carbons of such fused groups (*i.e.* saturated ring structures) can contain two substitution groups.

[00241] "Halogen" or "halo" refers to fluorine, chlorine, bromine or iodine.

[00242] "Haloalkyl" and "haloaryl" refer generically to alkyl and aryl groups that are substituted with one or more halogens, respectively. Thus, "dihaloaryl," "dihaloalkyl," "trihaloaryl" etc. refer to aryl and alkyl substituted with a plurality of halogens, but not necessarily a plurality of the same halogen; thus 4-chloro-3-fluorophenyl is within the scope of dihaloaryl. Haloalkyl includes, for instance, mono- to per-haloC₁-C₆ alkyl.

[00243] "Heteroatom" refers to O, S, N, or P.

[00244] "Heterocyclyl" refers to a stable three- to fifteen-membered ring substituent that consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, phosphorus, oxygen and sulfur. For purposes of this invention, the heterocyclyl substituent may be a monocyclic, bicyclic or tricyclic ring system, which may include fused or bridged ring systems as well as spirocyclic systems; and the nitrogen, phosphorus, carbon or sulfur atoms in the heterocyclyl group may be optionally oxidized to various oxidation states. In a specific example, the group -S(O)₀₋₂-, refers to -S- (sulfide), -S(O)- (sulfoxide), and -SO₂- (sulfone). For convenience, nitrogens, particularly but not exclusively, those defined as annular aromatic nitrogens, are meant to include their corresponding *N*-oxide form, although not explicitly defined as such in a particular example. Thus, for a compound of the invention having, for example, a pyridyl ring; the corresponding pyridyl-*N*-oxide is meant to be included as another compound of the invention. In addition, annular nitrogen atoms may be optionally quaternized; and the ring substituent may be partially or fully saturated or aromatic. Examples of heterocyclyl groups include, but are not limited to, azetidiny, acridiny, benzodioxoly, benzodioxany, benzofurany, carbazoy, cinnolin, dioxolany, indoliziny, naphthyridiny, perhydroazepiny, phenaziny, phenothiaziny, phenoxaziny, phthalaziny, pteridiny, puriny, quinazoliny, quinoxaliny, quinolin, isoquinolin, tetrazoy, tetrahydroisoquinoly, piperidiny, piperaziny, 2-oxopiperaziny, 2-oxopiperidiny, 2-oxopyrrolidiny, 2-oxoazepiny, azepiny, pyrroly, 4-piperidony, pyrrolidiny, pyrazoly, pyrazolidiny, imidazolyl, imidazoliny, imidazolidiny, dihydropyridiny, tetrahydropyridiny, pyridiny, pyraziny, pyrimidiny, pyridaziny, oxazolyl, oxazoliny, oxazolidiny, triazolyl, isoxazolyl, isoxazolidiny, morpholin,

thiazolyl, thiazolinyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, indolyl, isoindolyl, indolinyl, isoindolinyl, octahydroindolyl, octahydroisoindolyl, quinolyl, isoquinolyl, decahydroisoquinolyl, benzimidazolyl, thiadiazolyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, tetrahydrofuryl, tetrahydropyranyl, thienyl, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, dioxaphospholanyl, and oxadiazolyl.

[00245] "Heteroalicyclic" refers specifically to a non-aromatic heterocyclyl group. A heteroalicyclic may contain unsaturation, but is not aromatic.

[00246] "Heteroalicyclicalkyl" refers specifically to an alkyl group substituted with one or two non-aromatic heterocyclyl group. The heteroalicyclic ring portion of this group may contain unsaturation, but is not aromatic.

[00247] "Heteroaryl" refers specifically to an aromatic heterocyclyl group.

[00248] "Heterocyclylalkyl" refers to a residue in which a heterocyclyl is attached to a parent structure via one of an alkylene, alkylidene, or alkylidyne group. Examples include (4-methylpiperazin-1-yl) methyl, (morpholin-4-yl) methyl, (pyridine-4-yl) methyl, 2-(oxazolin-2-yl) ethyl, 4-(4-methylpiperazin-1-yl)-2-butenyl, and the like. Both the heterocyclyl and the corresponding alkylene, alkylidene, or alkylidyne portion of a heterocyclylalkyl group may be optionally substituted. "Lower heterocyclylalkyl" refers to a heterocyclylalkyl where the "alkyl" portion of the group has one to six carbons. "Heteroalicyclicalkyl" refers specifically to a heterocyclylalkyl where the heterocyclyl portion of the group is non-aromatic; and "heteroarylalkyl" refers specifically to a heterocyclylalkyl where the heterocyclyl portion of the group is aromatic. Such terms may be described in more than one way, for example, "lower heterocyclylalkyl" and "heterocyclyl C₁₋₆alkyl" are equivalent terms. Additionally, for simplicity, the number of annular atoms (including heteroatoms) in a heterocycle may be denoted as "C_x-C_y" (as in "C_x-C_y-heterocyclyl" and "C_x-C_y-heteroaryl" (and the like)), where x and y are integers. So, for example, C₅-C₁₄-heterocyclyl refers to a 5 to 14 membered ring system having at least one heteroatom and not a ring system containing 5 to 14 annular carbon atoms.

[00249] Preferred heterocyclyls and heteroaryls include, but are not limited to, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiophenyl, benzoxazolyl, benzthiazolyl, benztriazolyl, pyridotriazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, 4aH-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2H,6H-1,5,2-dithiazinyl, dihydrofuro[2,3-b]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1H-indazolyl, indolenyl, indolinyl, indoliziny, indolyl, 3H-indolyl,

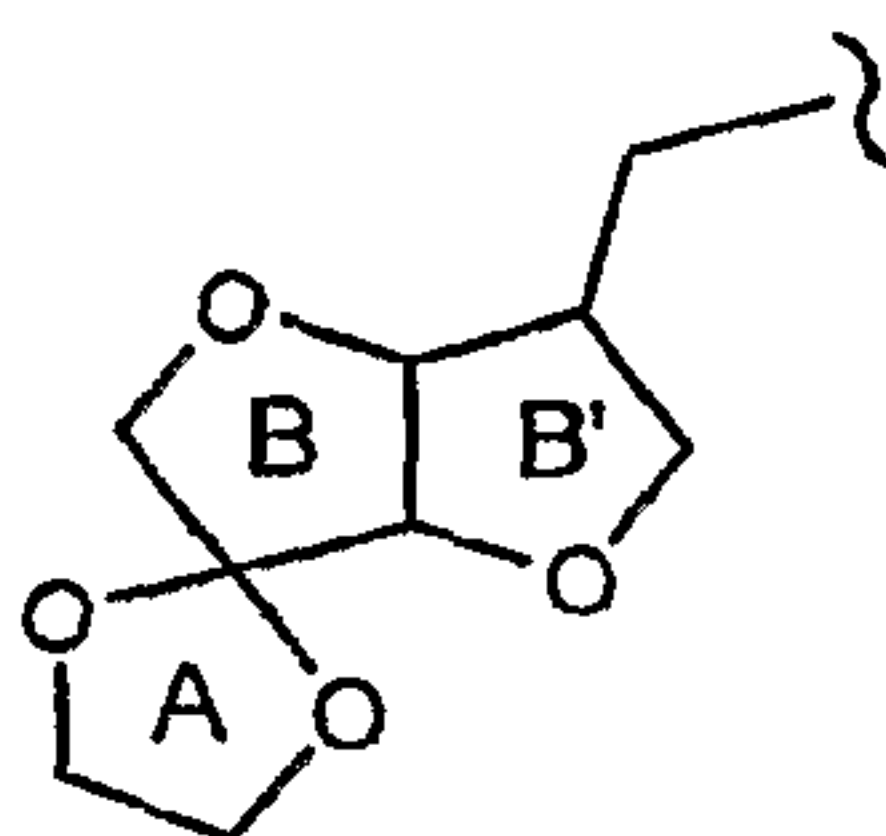
isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4H-quinoliziny, quinoxaliny, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,3,4-triazolyl, and xanthenyl.

[00250] “Heterocyclyl-aryl-” means an aryl group substituted with at least one, specifically 1 or 2 heterocyclyl, as defined herein. “Optionally substituted heterocyclyl-aryl-” means that either or both the aryl and the heterocyclyl can be substituted as defined in “substituted.”

[00251] “Optional” or “optionally” means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. One of ordinary skill in the art would understand that with respect to any molecule described as containing one or more optional substituents, only sterically practical and/or synthetically feasible compounds are meant to be included. “Optionally substituted” refers to all subsequent modifiers in a term. So, for example, in the term “optionally substituted arylC₁₋₈ alkyl,” optional substitution may occur on both the “C₁₋₈ alkyl” portion and the “aryl” portion of the molecule may or may not be substituted. A list of exemplary optional substitutions is presented below in the definition of “substituted.”

[00252] “Saturated bridged ring system” refers to a bicyclic or polycyclic ring system that is not aromatic. Such a system may contain isolated or conjugated unsaturation, but not aromatic or heteroaromatic rings in its core structure (but may have aromatic substitution thereon). For example, hexahydro-furo[3,2-b]furan, 2,3,3a,4,7,7a-hexahydro-1H-indene, 7-aza-bicyclo[2.2.1]heptane, and 1,2,3,4,4a,5,8,8a-octahydro-naphthalene are all included in the class “saturated bridged ring system.”

[00253] “Spirocyclyl” or “spirocyclic ring” refers to a ring originating from a particular annular carbon of another ring. For example, as depicted below, a ring atom of a saturated bridged ring system (rings B and B’), but not a bridgehead atom, can be a shared atom between the saturated bridged ring system and a spirocyclyl (ring A) attached thereto. A
5 spirocyclyl can be carbocyclic or heteroalicyclic.



[00254] “Substituted” alkyl, cycloalkyl, aryl, and heterocyclyl (including heteroalicyclic and heteroaryl), refer respectively to alkyl, aryl, and heterocyclyl, where one or more (for example up to about five, in another example, up to about three) hydrogen atoms are replaced
10 by a substituent. The substituent(s) on alkyl, aryl, heteroaryl, and heterocyclyl (including when any of these groups are part of another group, such as the alkyl portion of alkoxy, or the aryl portion of aryloxy) include, for instance, one or more groups selected from alkylenedioxy (for example methylenedioxy), aryloxy (for example, phenoxy), carboxy, acyloxy, acylamino, benzyloxycarbonylamino, acyl, carbamyl, oxo, hydroxy, halo, nitro,
15 cyano, -O-C₁-C₆ alkyl, haloalkyl, C₁-C₆ alkyl, cycloalkyl, -C(O)O-C₁-C₆ alkyl, -O-C₁-C₆ alkyl-aryl, -C₁-C₆ alkyl-aryl, -O-C₁-C₆ alkyl-O-C₁-C₆ alkyl, -N(R^a)(R^b), (R^a)(R^b)N-C₁-C₆ alkyl-, -O-C₁-C₆ alkyl-N(R^a)(R^b), -O-C₁-C₆ alkyl-heterocyclyl, C₀-C₆ alkyl-heterocyclyl, C₀-C₆ alkyl-aryl, C₀-C₆ alkyl-heteroaryl, -C(O)N(R^a)-C₁-C₆ -alkyl-N(R^a)(R^b), sulfanyl, sulfinyl, sulfonyl, aryl, heteroaryl, heterocyclyl, arylalkyl-, heteroarylalkyl-, and heterocyclylalkyl,
20 where R^a and R^b are independently hydrogen or alkyl, or R^a and R^b together with the nitrogen to which they are attached form a heterocyclyl group. Examples of heterocyclyl groups formed by R^a and R^b include morpholinyl and piperazinyl. Each substituent of a substituted group is optionally substituted, but these optional substituents themselves are not further substituted. Thus, an optionally substituted moiety is one that may or may not have one or
25 more substituents, and each of the substituents may or may not have one or more substituents. But, the substituents of the substituents may not be substituted.

[00255] “Sulfanyl” refers to the groups: -S-(optionally substituted alkyl), -S-(optionally substituted aryl), and -S-(optionally substituted heterocyclyl).

[00256] “Sulfinyl” refers to the groups: -S(O)-H, -S(O)-(optionally substituted alkyl), -S(O)-optionally substituted aryl, and -S(O)-(optionally substituted heterocyclyl).
30

[00257] "Sulfonyl" refers to the groups: -S(O₂)-H, -S(O₂)-(optionally substituted alkyl), -S(O₂)-optionally substituted aryl, -S(O₂)-(optionally substituted heterocyclyl), -S(O₂)-(optionally substituted alkoxy), -S(O₂)-optionally substituted aryloxy, and -S(O₂)-(optionally substituted heterocyclyloxy).

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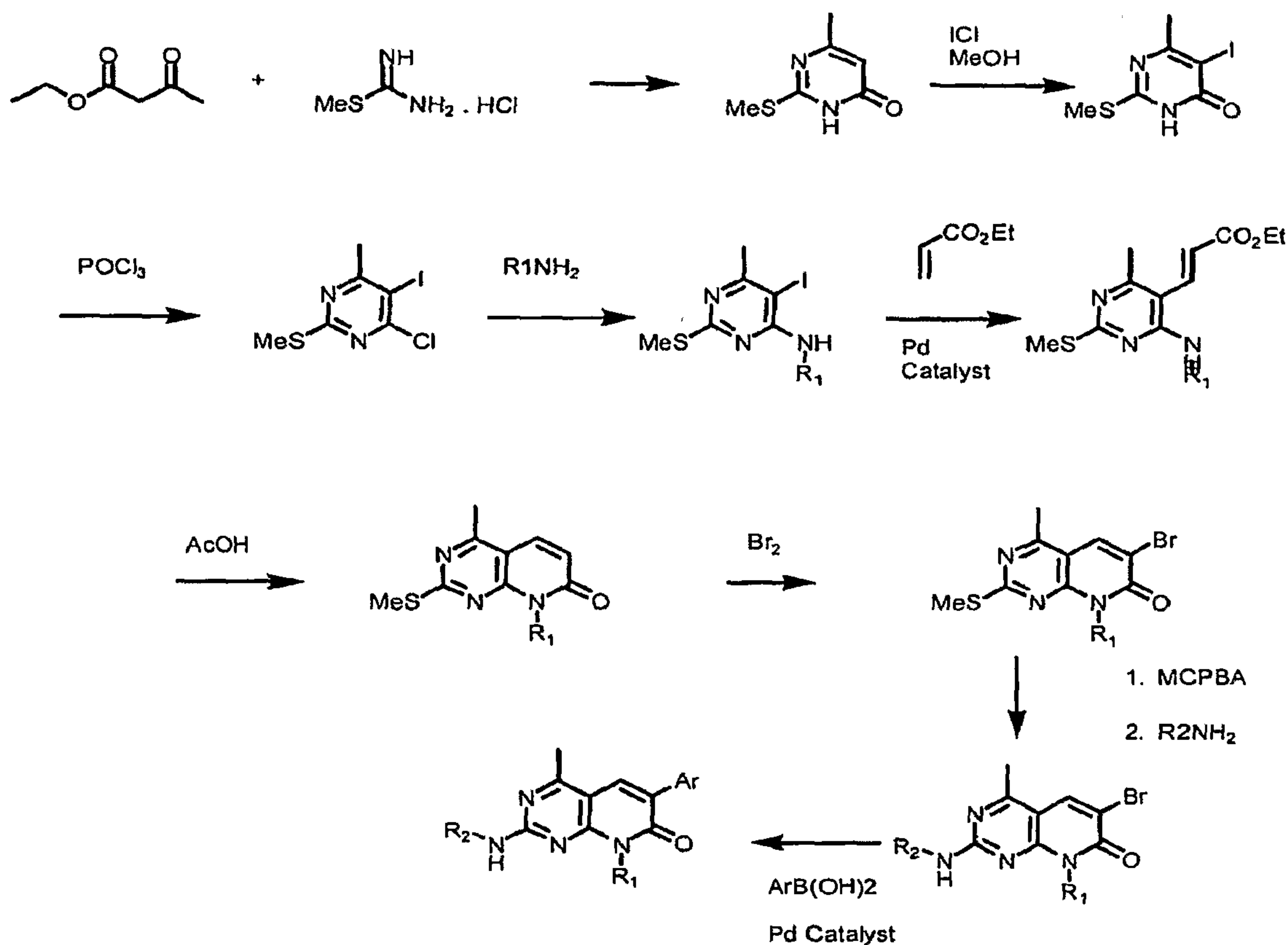
Preparation of Compounds

[00258] The compounds of the invention can be prepared by one skilled in the art based only on knowledge of the compound's chemical structure. The chemistry for the preparation of the compounds of this invention is known to those skilled in the art. In fact, there is more than one process to prepare the compounds of the invention. Specific examples of methods of preparation can be found in the art. For examples, see M. Barvian et al. J. Med. Chem. 2000, 43, 4606-4616; S. N. VanderWei et al. J. Med. Chem. 2005, 48, 2371-2387; P. L. Toogood et al. J. Med. Chem. 2005, 48, 2388-2406; J. Kaspavec et al. Tetrahedron Letters 2003, 44, 4567-4570; and references cited therein. See also U.S. Pre-grant publication US2004/0009993 A1 (M. Angiolini et al.), which is incorporated herein by reference, and references cited therein.

[00259] The following examples illustrate but do not limit the invention. All references cited herein are incorporated by reference in their entirety.

EXAMPLES

Experimental Scheme I



5

[00260] Using the same or analogous schemes described above and/or substituting with alternative reagents, the following compounds of the invention were prepared.

[00261] Illustrative compounds of Section II are shown in Table 1.

Table 1, Section II

Example	Structure	Name
1		6-bromo-8-ethyl-4-methyl-2-(methylamino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
2		6-bromo-8-ethyl-4-methyl-2-[(phenylmethyl)amino]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
3		6-bromo-8-ethyl-4-methyl-2-(phenylamino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
4		8-ethyl-2-(ethylamino)-4-methyl-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
5		6-bromo-8-ethyl-4-methyl-2-[(1-methylethyl)amino]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
6		6-bromo-2-[(1,1- <i>d</i> imethylethyl)amino]-8-ethyl-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
7		6-bromo-2-(cyclopentylamino)-8-ethyl-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
8		8-ethyl-4-methyl-6-phenyl-2-(phenylamino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
9		6-biphenyl-4-yl-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
10		6-(2,4-difluorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one
11		6-(3-chloro-4-fluorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one
12		8-ethyl-2-(ethylamino)-4-methyl-6-[4-(methoxy)phenyl]pyrido[2,3-d]pyrimidin-7(8H)-one
13		6-(2,4-dichlorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one
14		6-(3,4-difluorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one
15		8-ethyl-2-(ethylamino)-4-methyl-6-[2-(methoxy)phenyl]pyrido[2,3-d]pyrimidin-7(8H)-one
16		6-bromo-2-(cyclohexylamino)-8-ethyl-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one

Tabel 1, Section II

Example	Structure	Name
17		6-bromo-8-ethyl-4-methyl-2-[(2-morpholin-4-ylethyl)amino]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
18		6-bromo-8-ethyl-4-methyl-2-[(3-morpholin-4-ylpropyl)amino]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
19		6-bromo-2-[[3-(dimethylamino)propyl]amino]-8-ethyl-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
20		8-ethyl-2-(ethylamino)-4-methyl-6-[4-(phenyloxy)phenyl]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
21		6-[2,4-bis(methoxy)phenyl]-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
22		6-bromo-8-ethyl-2-[(2-fluorophenyl)amino]-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
23		8-ethyl-2-(ethylamino)-6-(3-fluorophenyl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
24		8-ethyl-2-(ethylamino)-6-(2-fluorophenyl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
25		8-ethyl-2-(ethylamino)-4-methyl-6-[3-(trifluoromethyl)phenyl]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
26		8-ethyl-2-(ethylamino)-6-(4-fluorophenyl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
27		8-ethyl-2-(ethylamino)-4-methyl-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
28		8-ethyl-2-(ethylamino)-4-methyl-6-[3-(methoxy)phenyl]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
29		6-(3-chlorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
30		6-bromo-8-ethyl-4-methyl-2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
31		6-(4-chlorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
32		8-ethyl-2-(ethylamino)-4-methyl-6-(3-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
33		8-ethyl-2-(ethylamino)-4-methyl-6-(4-methyl-2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
34		8-ethyl-2-(ethylamino)-4-methyl-6-(4-methyl-3-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
35		1,1- <i>d</i> imethylethyl 2-[8-ethyl-2-(ethylamino)-4-methyl-7-oxo-7,8- <i>d</i> ihydropyrido[2,3- <i>d</i>]pyrimidin-6-yl]-1 <i>H</i> -pyrrole-1-carboxylate
36		6-bromo-8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
37		6-bromo-8-ethyl-4-methyl-2-[(4-morpholin-4-yl)phenyl]amino]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
38		6-bromo-8-ethyl-4-methyl-2-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}amino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
39		8-ethyl-2-(ethylamino)-4-methyl-6-(1 <i>H</i> -pyrrol-2-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
40		6-(5-chloro-2-thienyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
41		8-ethyl-4-methyl-2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
42		8-ethyl-2-(ethylamino)-4-methyl-6-pyrimidin-5-ylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
43		8-ethyl-2-(ethylamino)-6-(3-fluoropyridin-4-yl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
44		8-ethyl-2-(ethylamino)-6-furan-3-yl-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
45		8-ethyl-2-(ethylamino)-4-methyl-6-[1-(phenylmethyl)-1 <i>H</i> -pyrazol-4-yl]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
46		6-(3,5- <i>d</i> imethylisoxazol-4-yl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
47		8-ethyl-4-methyl-2-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}amino)-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
48		6-bromo-2-(ethylamino)-4-methyl-8-(1-methylethyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
49		2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
50		8-ethyl-2-{{4-[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
51		8-ethyl-2-(ethylamino)-6-(1 <i>H</i> -indol-6-yl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
52		8-ethyl-2-(ethylamino)-4-methyl-6-(5-phenyl-2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
53		2-(ethylamino)-6-furan-3-yl-4-methyl-8-(1-methylethyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
54		6-bromo-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
55		8-ethyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
56		8-ethyl-2-(ethylamino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
57		8-ethyl-2-(ethylamino)-4-methyl-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
58		6-bromo-8-ethyl-2-(ethylamino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
59		8-ethyl-2-(ethylamino)-4-methyl-6-(1 <i>H</i> -pyrazol-5-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
60		8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-6-furan-3-yl-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
61		8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
62		2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
63		8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-6-(3-fluorophenyl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
64		2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
65		2-[(4-{[2-(diethylamino)ethyl]oxy}phenyl)amino]-8-ethyl-4-methyl-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
66		8-ethyl-2-[(4-hydroxyphenyl)amino]-4-methyl-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
67		8-cyclohexyl-2-(ethylamino)-4-methyl-6-(2-thienyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
68		8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1 <i>H</i> -pyrazol-5-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
69		6-(3,5- <i>d</i> ifluorophenyl)-8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
70		8-ethyl-4-methyl-6-phenyl-2-({4-[(2-piperidin-1-ylethyl)oxy]phenyl}amino)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
71		8-ethyl-4-methyl-2-({4-[(2-morpholin-4-ylethyl)oxy]phenyl}amino)-6-phenylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

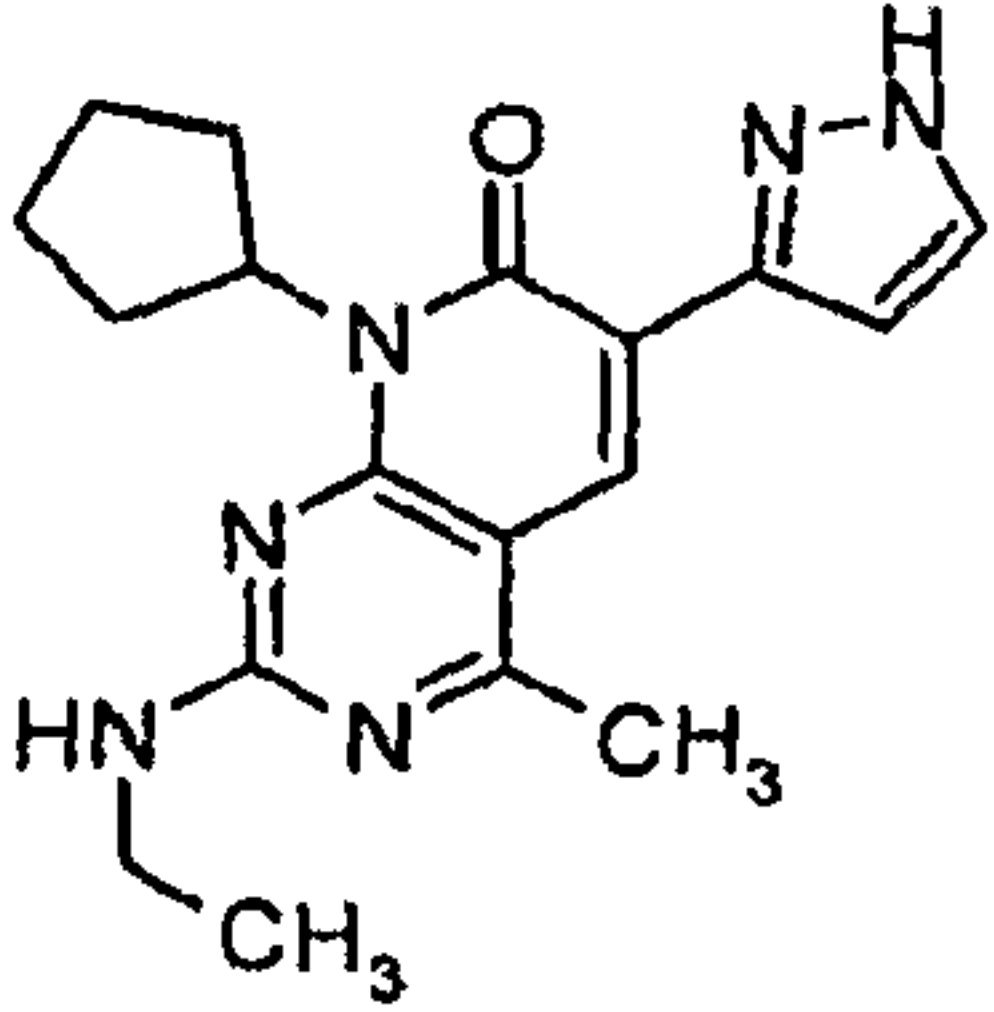
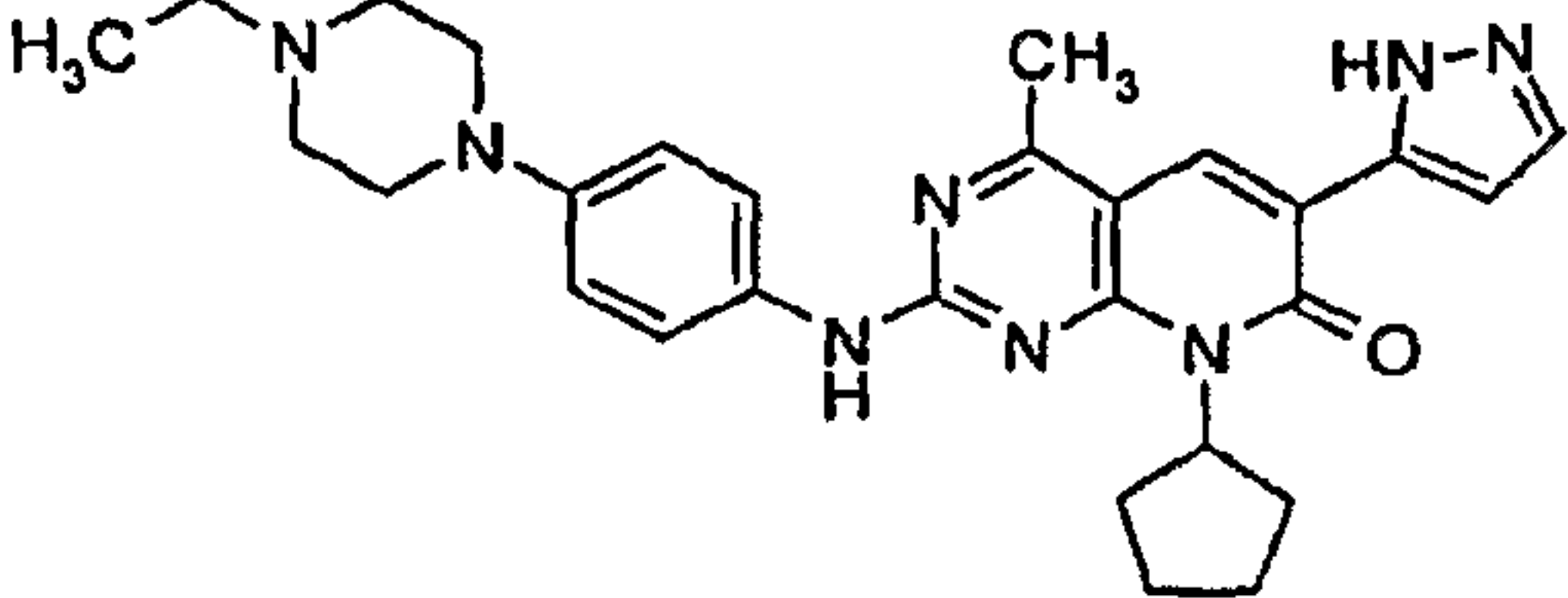
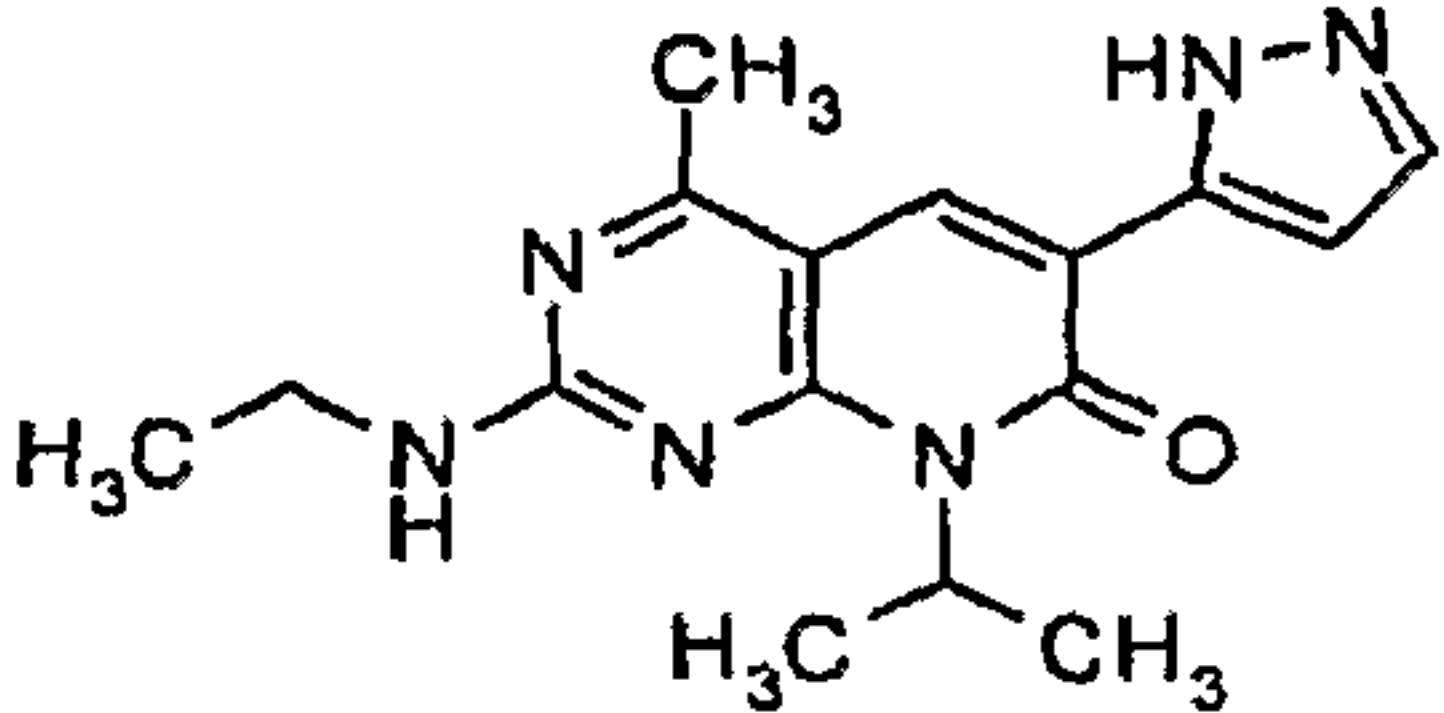
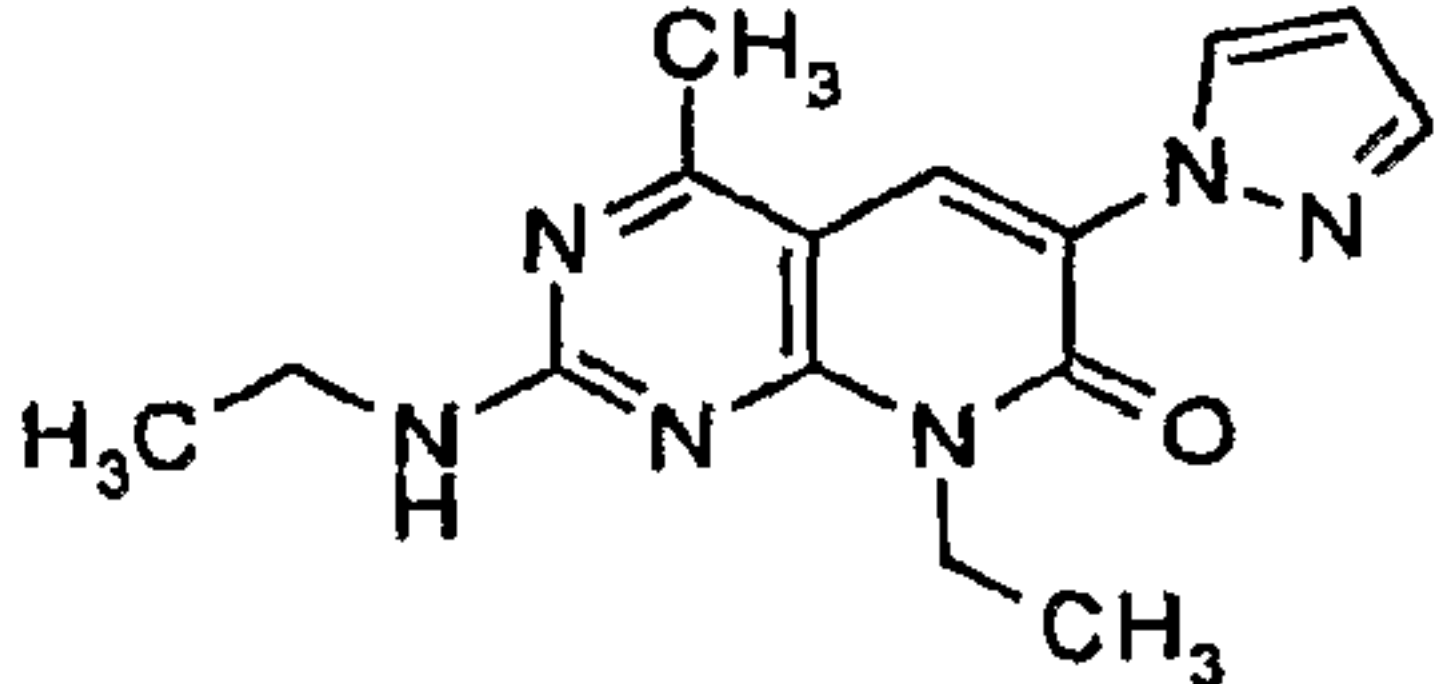
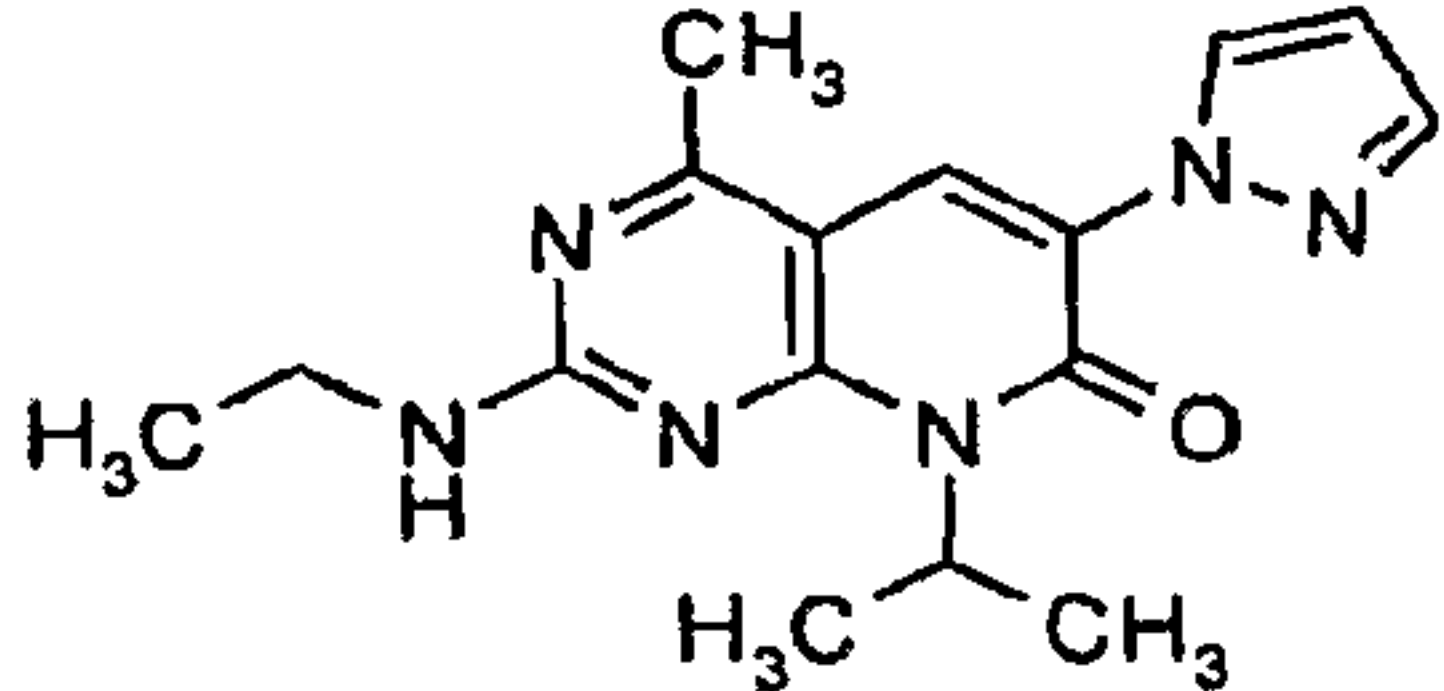
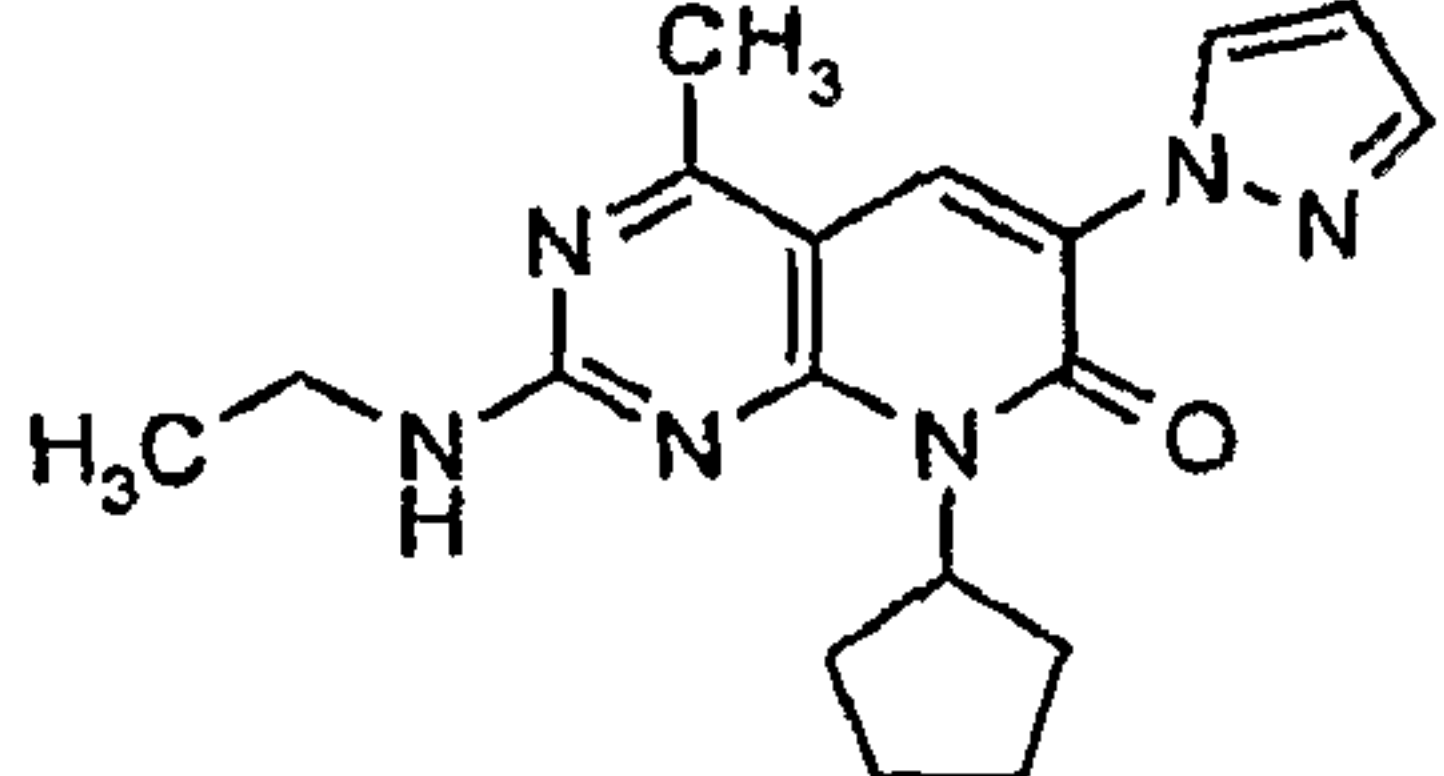
Tabel 1, Section II

Example	Structure	Name
72		6-bromo-2-(ethylamino)-4-methyl-8-[3-(methyloxy)propyl]pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
73		6-bromo-2-(ethylamino)-8-[2-(ethyloxy)ethyl]-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
74		6-bromo-2-(ethylamino)-4-methyl-8-(2-piperidin-1-ylethyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
75		6-bromo-2-(ethylamino)-8-[3-(ethyloxy)propyl]-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
76		6-bromo-2-(ethylamino)-4-methyl-8-{3-[(1-methylethyl)oxy]propyl}pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
77		6-bromo-2-(ethylamino)-8-(3-hydroxypropyl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
78		6-bromo-2-(ethylamino)-8-(2-hydroxyethyl)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
79		6-bromo-8-cyclopropyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
80		6-bromo-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
81		2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-(1 <i>H</i> -pyrazol-5-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
82		6-acetyl-8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
83		8-ethyl-2-(ethylamino)-4-methyl-6-(1,3-thiazol-2-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
84		6-bromo-8-cyclopentyl-2-(ethylamino)-4-methylpyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
85		8-cyclopentyl-2-(ethylamino)-4-methyl-6-(1 <i>H</i> -pyrazol-3-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
86		cyclopentyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1 <i>H</i> -pyrazol-5-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
87		2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(1 <i>H</i> -pyrazol-5-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
88		8-ethyl-2-(ethylamino)-4-methyl-6-(1 <i>H</i> -pyrazol-1-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
89		2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(1 <i>H</i> -pyrazol-1-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
90		8-cyclopentyl-2-(ethylamino)-4-methyl-6-(1 <i>H</i> -pyrazol-1-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

Tabel 1, Section II

Example	Structure	Name
91		8-ethyl-2-([4-(4-ethylpiperazin-1-yl)phenyl]amino)-4-methyl-6-(1 <i>H</i> -pyrazol-1-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
92		2-([4-(4-ethylpiperazin-1-yl)phenyl]amino)-4-methyl-8-(1-methylethyl)-6-(1 <i>H</i> -pyrazol-1-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one
93		8-cyclopentyl-2-([4-(4-ethylpiperazin-1-yl)phenyl]amino)-4-methyl-6-(1 <i>H</i> -pyrazol-1-yl)pyrido[2,3- <i>d</i>]pyrimidin-7(8 <i>H</i>)-one

[00262] In one embodiment of the invention, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 9 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 5 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 3 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 1.5 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 1 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.6 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.3 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.2 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.1 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.04 μ M or less. In another

embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.020 μ M or less.

In Vitro Enzymatic Assay Description for Sections II and III:

PI3Kalpha Luciferase-Coupled Chemiluminescence Assay Protocol

[00263] PI3Kalpha activity is measured as the percent of ATP consumed following the kinase reaction using luciferase-luciferin-coupled chemiluminescence. Reactions were conducted in 384-well white, medium binding microtiter plates (Greiner). Kinase reactions were initiated by combining test compounds, ATP, substrate (PIP2), and kinase in a 20 μ L volume. The standard assay concentrations for enzyme, ATP, and substrate are 1.1nm, 1 μ M, and 7.5 μ M, respectively. The reaction mixture was incubated at ambient temperature for 2 h. Following the kinase reaction, a 10 μ L aliquot of luciferase-luciferin mix (Promega Kinase-Glo) was added and the chemiluminescence signal measured using a Victor2 plate reader (Perkin Elmer). Total ATP consumption was limited to 40-60% and IC₅₀ values of control compounds correlate well with literature references. In this assay, preferred compounds of the invention exhibit an IC₅₀ of less than 50 micromolar. More preferred compounds of the invention exhibit an IC₅₀ of less than 1 micromolar. Even more preferred compounds of the invention exhibit an IC₅₀ of less than 500 nanomolar. Still more preferred compounds of the invention exhibit an IC₅₀ of less than 250 nanomolar.

Cell Assay Descriptions:

Phospho AKT assay

[00264] PC3 cells were seeded on 6-well plates at 150,000 cells/well. Cells were cultured for 3 days, then treated with compounds in serum-free medium for 3 hr. EGF (100 ng/ml) was added for the last 10 min. Cells were lysed in TENN buffer. Phospho T308 Akt and total Akt were quantified by ELISA performed according to the Biosource assay protocol. The readings of phospho Akt were normalized to total Akt readings.

Phospho S6 assay

[00265] PC3 cells were seeded on 96-well plates at 8,000 cells/well. For each experiment, cells were seeded and treated in duplicated plates: one plate for phospho S6 CellELISA, and one plate for total S6 CellELISA. Cells were cultured on the plates for 3 days, then treated with compounds in serum-free medium for 3 hr in triplicate. Cells were fixed with 4%

formaldehyde, quenched with 0.6% H₂O₂, blocked with 5% BSA, incubated with either phospho S6 antibody or total S6 antibody overnight, incubated with goat-anti-rabbit-IgG-HRP for 1 hr, and developed in chemiluminescent substrate.

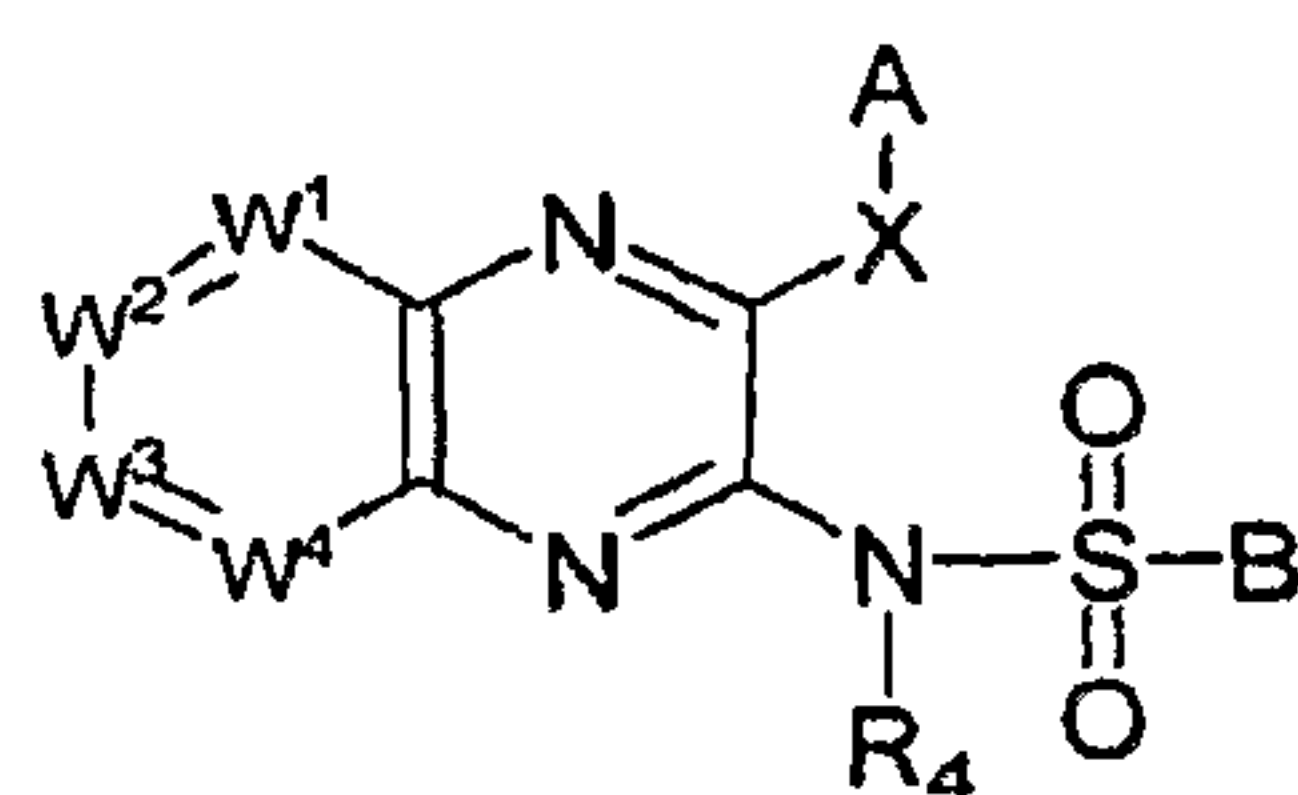
5 PIP3 assay

[00266] MCF-7 cells grown in 10-cm dishes were starved for 3 hours in DMEM, and then treated with compounds for 20 minutes. In the last 2 minutes of the incubation with the compounds, EGF (100 ng/ml) was added to stimulate the production of PIP3. The medium was aspirated and the cells were scraped with 10% trichloroacetic acid. The lipids were
10 extracted from the pellet after the cell lysates were centrifuged. PIP3 in the cellular lipid extraction was quantified with the AlphaScreen assay in which Grp1-PH is used as the PIP3 specific probe. The amount of cellular PIP3 was calculated from the standard curve of diC₈ PI (3,4,5) P3.

15

Section III

[00267] In one embodiment, in section III the invention provides a compound of Formula VIII:



VIII

20 or a pharmaceutically acceptable salt or solvate thereof, wherein

W¹, W², W³, and W⁴ are -C(R₁)- or one or two of W¹, W², W³, and W⁴ are independently -N- and the remaining are -C(R₁)-;

X is -N(R₅)-;

A is aryl, arylalkyl, -S(O)₂-aryl, heteroaryl, cycloalkyl, heterocycloalkyl, halo, haloalkyl,

25 haloalkoxy, C₁-C₆-alkyl, C₁-C₆-alkoxy, or -C₁-C₆-alkyl-N(R₇)R_{7a}, where each of the aryl, heteroaryl, cycloalkyl, heterocycloalkyl, and alkyl groups, each either alone or as part of another group within A, is independently optionally substituted with (R₂)_{n1};

B is aryl, heteroaryl, C₁-C₆-alkyl, -C₁-C₆-alkylaryl, or -C₁-C₆-alkylheteroaryl, wherein each of the aryl, heteroaryl and alkyl groups are independently optionally substituted with

30 (R₃)_{n2};

n1 and n2 are independently 0 or an integer from 1 to 5;

each R₁ is independently hydrogen, C₁-C₆-alkyl, haloalkyl, C₁-C₆-alkoxy, haloalkoxy, -NO₂, halo, hydroxy, hydroxyalkyl, -CN, cyanoalkyl, or -C₀-C₆ alkyl-N(R₁₀)R_{10a} where R₁₀ and R_{10a} are independently hydrogen, -C₁-C₆-alkyl, -OH, -O-C₁-C₆ alkyl, haloalkyl, or haloalkoxy;

each R₂ (when R₂ is present) is independently selected from -C₁-C₆-alkanyl, -C₁-C₆-alkenyl, -C₂-C₆-alkenyl-C(O)OR₆, -OR₆, -N(R₇)C(O)R₆, -N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -OC(O)-C₀-C₆-alkyl-N(R₇)R_{7a}, -N(R₇)C(O)-C₁-C₆-alkylC(O)OR₆, -C₀-C₆-alkyl-C(O)R₆, -S(O)₂N(R₇)R_{7a}, -C(O)OR₆, -CH(R₆)₂-C(O)OR₆, -S(O)₂R₆, cycloalkyl, heterocycloalkyl, heteroaryl, -C(O)N(R₇)-C₁-C₆-alkyl-OR₆, -C₀-C₆-alkyl-C(O)N(R₇)-C₁-C₆-alkyl-C(O)OR₆, -C₀-C₆-alkyl-C(O)N(R₇)R_{7a}, aryl, arylalkyl, -S-(C₁-C₆-alkyl), halo, oxo, -NO₂, -S-CN, -CN, and -C₀-C₆-alkyl-N(R₇)R_{7a}, wherein each of the alkyl, alkoxy, aryl, cycloalkyl, heterocycloalkyl, and heteroaryl groups, either alone or as part of another group within R₂, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkyl, halo, haloalkyl, haloalkoxy, oxo, -NO₂, -CN, -OH, -N(R₈)R_{8a}, C₁-C₆-alkoxy, and -C(O)OR₉;

each R₃ (when R₃ is present) is independently NO₂, halo, -CN, C₁-C₆-alkanyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkyl, C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})C(O)R_{7a}, -C₀-C₆ alkyl-C(O)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-C(O)N(R₇)-C₁-C₆alkylC(O)OR_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-(R_{7a}), -C₀-C₆-alkyl-N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})-C₀-C₆-alkyl-N(R_{7c})(R_{7a}), -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)-C₀-C₆-alkyl-C(=N(R_{7b})(R_{7a}))(NR_{7c}R_{7d}), -C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-heterocycloalkyl, -O-C₁-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-OR₆, -C₀-C₆ alkyl-C(O)OR₆, -C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)NR₇R_{7a}, -C₀-C₆-alkyl-C(O)-R₇, -SR₇, -S(O)₂R₇, -S(O)₃R₇, -S(O)R₇, -S(O)₂N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -S-heteroaryl, -S-aryl, -S-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)-aryl, -C₀-C₆-alkyl-N(R₇)-heteroaryl, -C₀-C₆-alkyl-N(R₇)-heterocycloalkyl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-N(R₇)C(O)-

C_0 - C_6 -alkyl-heteroaryl, $-C_0$ - C_6 -alkyl- $N(R_7)C(O)-C_0$ - C_6 -alkyl-heterocycloalkyl, $-C_0$ - C_6 -alkyl- $N(R_7)C(O)-C_0$ - C_6 -alkyl-heterocycloalkyl-aryl, $-N(R_7)C(O)OR_6$, or $-N(R_7)-C(O)-R_{7a}$, wherein each of the alkyl, alkanyl, alkenyl, cycloalkyl, aryl, alkoxy, heterocycloalkyl, and heteroaryl groups, either alone or as part of another group within

5 R_3 , is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C_1 - C_6 -alkanyl, C_1 - C_6 -alkenyl, $-C_0$ - C_6 -alkyl- OR_9 , cycloalkyl, halo, haloalkyl, haloalkoxy, $-C(O)R_9$, $-NO_2$, $-CN$, oxo, $-C_0$ - C_6 -alkyl- $N(R_8)R_{8a}$, $-C_0$ - C_6 -alkyl-heterocycloalkyl, $-C_0$ - C_6 -alkyl-aryl, $-C_0$ - C_6 -alkyl-heteroaryl, $-C(O)OR_9$, and hydroxyalkyl;

10 R_4 is hydrogen, aryl, $-C_0$ - C_6 -alkyl- $N(R_7)R_{7a}$, C_1 - C_6 -alkoxy, or C_1 - C_6 alkyl, wherein each of the alkyl and aryl groups, either alone or as part of another group in R_4 , is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C_1 - C_6 -alkyl, halo, haloalkyl, haloalkoxy, $-NO_2$, $-CN$, $-OH$, $-N(R_8)R_{8a}$, C_1 - C_6 -alkoxy, and $-C(O)OR_6$;

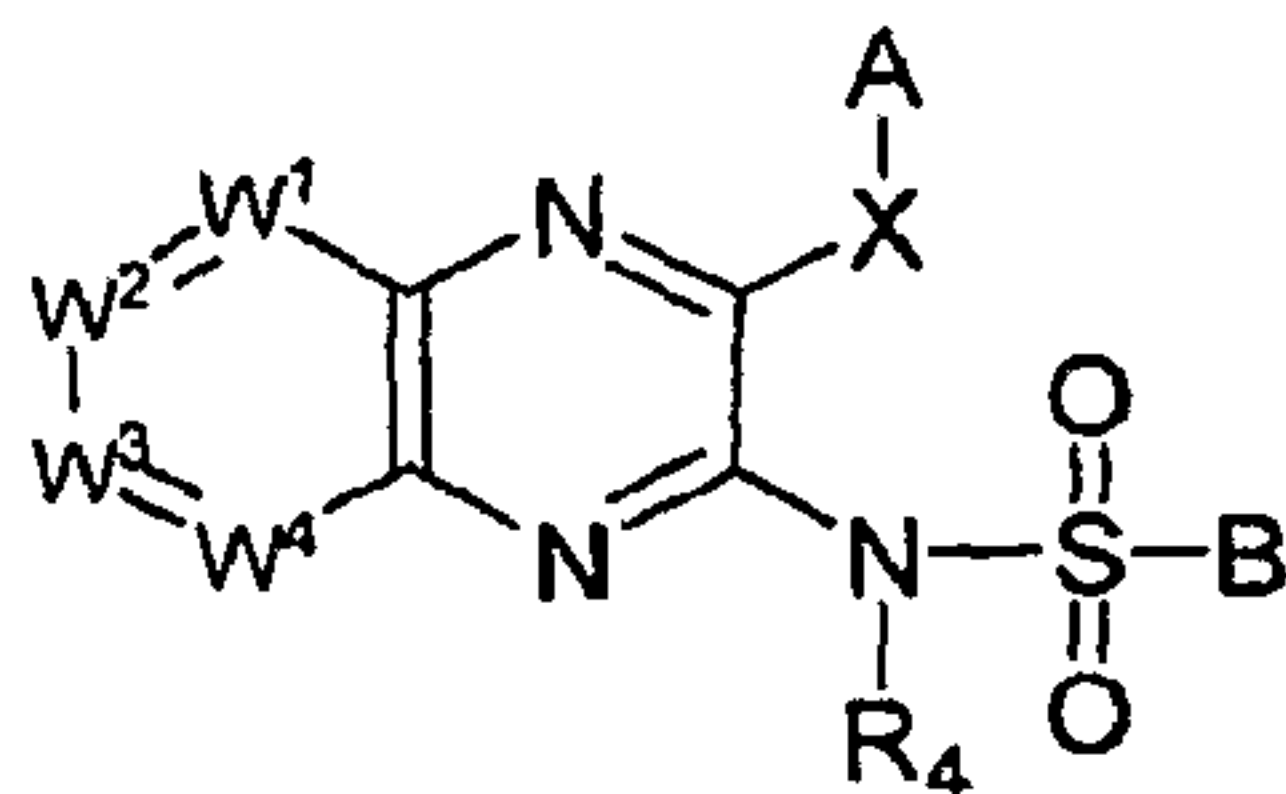
15 R_5 is hydrogen, $-C_1$ - C_6 -alkyl- $N(R_7)R_{7a}$, C_1 - C_6 -alkoxy, C_1 - C_6 -alkyl, or aryl, wherein each of the alkyl and aryl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from C_1 - C_6 -alkyl, halo, haloalkyl, haloalkoxy, $-NO_2$, $-CN$, $-OH$, $-N(R_8)R_{8a}$, C_1 - C_6 -alkoxy, or $-C(O)OR_6$; or

20 R_6 and R_9 are independently hydrogen, $-OH$, C_1 - C_6 -alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, or aryl, each C_1 - C_6 alkyl, aryl, cycloalkyl, heterocycloalkyl, and heteroaryl, either alone or as part of another group within R_6 and R_9 , is independently optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from $-NH_2$, $-OH$, C_1 - C_6 -alkoxy, C_1 - C_6 -alkyl, and halo; and

25 R_7 , R_{7a} , R_{7b} , R_{7c} , R_{7d} , R_8 , and R_{8a} are independently hydrogen, $-C_1$ - C_6 -alkanyl, $-C_1$ - C_6 -alkenyl, $-OH$, $-O-C_1$ - C_6 alkanyl, $-O-C_1$ - C_6 alkenyl, $-O-C_0$ - C_6 -alkyl-aryl, $-C_0$ - C_6 -alkyl- $C(O)OR_6$, $-C_0$ - C_6 -alkyl- $C(O)R_6$, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl, wherein each of the alkyl, aryl, heteroaryl, and heterocycloalkyl, either alone or part of another group within R_7 , R_{7a} , R_{7b} , R_{7c} , and R_{7d} , is independently optionally substituted with 1, 2, 3, 4, or 5 groups

30 selected from $-NH_2$, alkylamino, dialkylamino, $-S-C_1$ - C_6 -alkyl, $-CN$, $-OH$, $-NO_2$, oxo, C_1 - C_6 -alkoxy, C_1 - C_6 -alkyl, halo, aryl, and heteroaryl optionally substituted with one or two C_1 - C_6 -alkyl.

[00268] In one embodiment, in section III the invention provides a compound of Formula VIIIa:



VIIIa

- 5 or a pharmaceutically acceptable salt or solvate thereof, wherein
 W^1 , W^2 , W^3 , and W^4 are $-C(R_1)-$ or W^2 and W^3 are $-C(R_1)-$ and one of W^1 and W^4 is $-N-$ and
the other is $-C(R_1)-$;
X is $-N(R_5)-$;
A is aryl, heteroaryl, or heterocycloalkyl where the aryl, heteroaryl, and heterocycloalkyl are
10 optionally substituted with $(R_2)_{n1}$; or
B is aryl, $-C_1-C_6$ alkylaryl, heteroaryl, or heterocycloalkyl, where the aryl, C_1-C_6 -alkyl,
heteroaryl, and heterocycloalkyl are independently optionally substituted with $(R_3)_{n2}$;
 $n1$ is 0, 1, 2, or 3;
 $n2$ is or an integer from 1 to 5;
15 each R_1 is independently hydrogen, C_1-C_6 -alkyl, haloalkyl, C_1-C_6 -alkoxy, haloalkoxy, or $-NO_2$;
each R_2 (when R_2 is present) is independently $-C_1-C_6$ -alkanyl, $-C_1-C_6$ -alkenyl, $-OR_6$, $-N(R_7)-$
 $C(O)-R_6$, $-N(R_7)-C(O)-C_0-C_6$ alkyl- $N(R_{7b})R_{7a}$, $-OC(O)-C_0-C_6$ alkyl- $N(R_7)R_{7a}$,
 $-C_0-C_6$ alkyl- $C(O)R_6$, heterocycloalkyl, aryl, halo, $-NO_2$, or $-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$,
20 wherein each alkyl, aryl, and heterocycloalkyl groups, each either alone or as part of
another group within R_2 , is independently optionally substituted with one, two, three,
four, or five groups selected from C_1-C_6 -alkyl, C_1-C_6 -alkoxy, halo, haloalkyl, and
haloalkoxy;
each R_3 (when R_3 is present) is independently hydroxy, $-NO_2$, halo, $-CN$, C_1-C_6 -alkanyl,
25 C_2-C_6 -alkenyl, C_1-C_6 alkoxy, $-C_0-C_6$ alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})R_{7a}$, $-C_0-C_6$ -
alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})C(O)R_{7a}$, $-C_0-C_6$ alkyl- $C(O)N(R_7)-C_0-C_6$ -alkyl-
 $N(R_7)R_{7a}$, $-C_0-C_6$ -alkyl- $C(O)N(R_7)-C_1-C_6$ -alkyl- $C(O)OR_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)-C(O)-C_0$ -
 C_6 -alkyl- (R_7) , $-C_0-C_6$ -alkyl- $N(R_7)-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -
alkyl- $N(R_{7b})-C_0-C_6$ -alkyl- $N(R_{7c})R_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)O-C_0-C_6$ -alkyl- $N(R_{7b})R_{7a}$,
30 $-C_0-C_6$ -alkyl- $N(R_7)-C_0-C_6$ alkyl- $C(=N(R_{7b})(R_{7a}))(NR_{7c}R_{7d})$, $-C_0-C_6$ -alkyl-heteroaryl, $-C_0-$

C_6 -alkyl-OR₆, -C₀-C₆-alkyl-C(O)OR₆, -C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)-
 NR₇R_{7a}, -C₀-C₆-alkyl-C(O)-R₇, -S(O)₂R₇, -SO₂N(R₇)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-
 alkyl-C(O)-heterocycloalkyl (dupe of C(O)R₇), -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-
 heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-N(R₇)-
 C(O)-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-
 N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-
 heterocycloalkyl-aryl, or -N(R₇)C(O)R_{7a}, wherein each of the alkyl, alkanyl, alkenyl,
 cycloalkyl, aryl, alkoxy, heterocycloalkyl, and heteroaryl groups, either alone or as part
 of another group within R₃, is independently optionally substituted with 1, 2, 3, 4, or 5
 groups selected from C₁-C₆-alkanyl, C₁-C₆ alkenyl, cycloalkyl, halo, -C(O)-R₆, oxo,
 hydroxy, -C₀-C₆-alkyl-N(R₈)R_{8a}, -C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-aryl,
 -C₀-C₆-alkyl-heteroaryl, -C(O)OR₆, and hydroxyalkyl;

R₄ is hydrogen;

R₅ is hydrogen;

R₆ and R₉ are independently hydrogen, C₁-C₆-alkyl, aryl, arylalkyl, or cycloalkyl, where each
 of the -C₁-C₆-alkyl, aryl, arylalkyl, and cycloalkyl, is independently optionally
 substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkoxy, C₁-C₆-alkyl, and
 halo; and

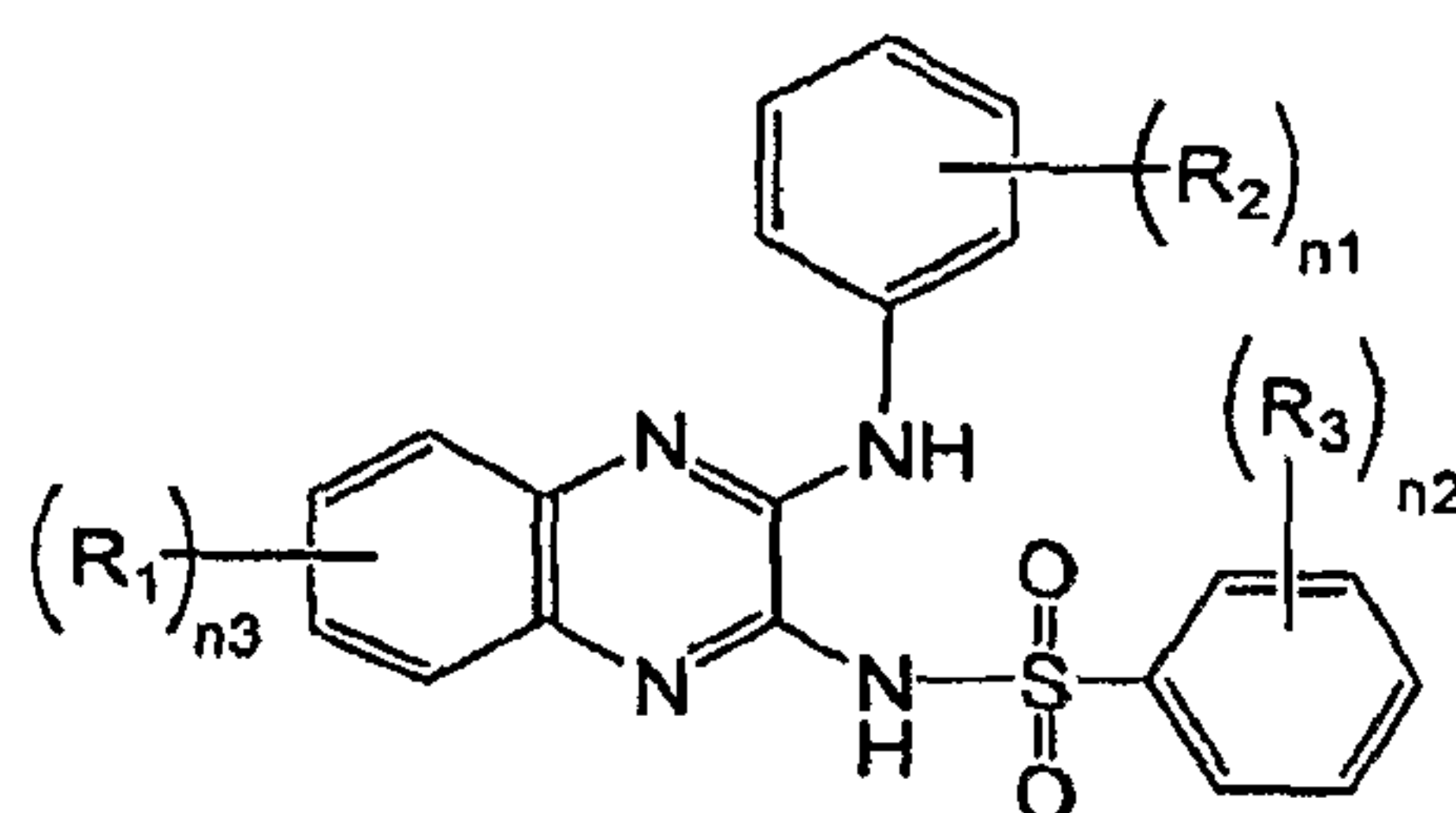
R₇, R_{7a}, R_{7b}, R_{7c}, and R_{7d} are independently hydrogen, -C₁-C₆-alkanyl, -C₁-C₆-alkenyl, -OH,
 -O-C₁-C₆ alkanyl, -O-C₁-C₆ alkenyl, -O-C₀-C₆-alkyl-aryl, aryl, arylalkyl, heteroaryl,
 heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl,
 wherein each of the alkyl, aryl, heteroaryl, and heterocycloalkyl, either alone or part of
 another group within R₇, R_{7a}, R_{7b}, R_{7c}, and R_{7d}, is independently optionally substituted
 with 1, 2, 3, 4, or 5 -NH₂, alkylamino, dialkylamino, -S-C₁-C₆-alkyl, -CN, hydroxy, oxo,
 C₁-C₆ alkoxy, C₁-C₆ alkyl, or halo.

[00269] In another embodiment (A1), the invention provides a compound of Formula VIIIa
 where X is -N(R₅)-, R₅ is hydrogen, and all other groups are as defined above for a
 compound of Formula VIIIa.

[00270] In another embodiment (A2), the invention provides a compound of Formula VIIIa
 where A is aryl or heteroaryl where the aryl and the heteroaryl are optionally substituted with
 (R₂)_{n1} where n1 is 1, 2, 3, 4, or 5; B is aryl or heteroaryl where the aryl and the heteroaryl are
 optionally substituted with (R₃)_{n2} where n2 is 1, 2, 3, 4, or 5; and all other groups are as
 defined above for a compound of Formula VIIIa.

[00271] In another embodiment (A3), the invention provides a compound of Formula VIIIa where W^1 , W^2 , W^3 , and W^4 are $-C(R_1)-$ where each R_1 is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, or nitro; and all other groups are as defined in the Summary of the Invention. In another embodiment, W^1 and W^4 are $-CH-$ and W^2 and W^3 are $-C(R_1)-$ where each R_1 is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, or nitro. In another embodiment, W^1 and W^4 are $-CH-$ and W^2 and W^3 are $-C(R_1)-$ where each R_1 is independently hydrogen, methyl, methoxy, or nitro. In another embodiment, W^1 , W^2 , W^3 , and W^4 are $-CH-$.

[00272] In another embodiment, the invention provides a compound of Formula VIIIb:



VIIIb

or a pharmaceutically acceptable salt or solvate thereof, wherein

n_1 is one or two; and n_2 is one or two; n_3 is 0, 1, or two;

each R_1 is independently hydrogen, C_1-C_6 -alkyl, haloalkyl, C_1-C_6 -alkoxy, haloalkoxy, $-NO_2$, halo, hydroxy, hydroxyalkyl, $-CN$, cyanoalkyl, or $-C_0-C_6$ alkyl- $N(R_{10})R_{10a}$ where R_{10} and R_{10a} are independently hydrogen, $-C_1-C_6$ -alkyl, $-OH$, $-O-C_1-C_6$ alkyl, haloalkyl, or haloalkoxy;

each R_2 (when R_2 is present) is independently C_1-C_6 -alkanyl, C_1-C_6 -alkenyl, $-OR_6$, $-N(R_7)-C(O)-R_6$, $-N(R_7)-C(O)-C_0-C_6$ alkyl- $N(R_{7b})R_{7a}$, $-OC(O)-C_0-C_6$ alkyl- $N(R_7)R_{7a}$, $-C_0-C_6$ alkyl- $C(O)R_6$, heterocycloalkyl, aryl, halo, $-NO_2$, or $-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$, wherein each alkyl, aryl, and heterocycloalkyl groups, each either alone or as part of another group within R_2 , is independently optionally substituted with one, two, three, four, or five groups selected from C_1-C_6 -alkyl, C_1-C_6 -alkoxy, halo, haloalkyl, and haloalkoxy;

each R_3 (when R_3 is present) is independently hydroxy, $-NO_2$, halo, $-CN$, C_1-C_6 -alkanyl, C_2-C_6 -alkenyl, C_1-C_6 alkoxy, $-C_0-C_6$ alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})R_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})C(O)R_{7a}$, $-C_0-C_6$ alkyl- $C(O)N(R_7)-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$, $-C_0-C_6$ -alkyl- $C(O)N(R_7)-C_1-C_6$ -alkyl- $C(O)OR_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)-C(O)-C_0-C_6$ -alkyl- (R_7) , $-C_0-C_6$ -alkyl- $N(R_7)-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -

- alkyl-N(R_{7b})-C₀-C₆-alkyl-N(R_{7c})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-N(R_{7b})R_{7a},
 -C₀-C₆-alkyl-N(R₇)-C₀-C₆ alkyl-C(=N(R_{7b})(R_{7a}))(NR_{7c}R_{7d}), -C₀-C₆-alkyl-heteroaryl, -C₀-
 C₆-alkyl-OR₆, -C₀-C₆-alkyl-C(O)OR₆, -C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)-
 NR₇R_{7a}, -C₀-C₆-alkyl-C(O)-R₇, -S(O)₂R₇, -SO₂N(R₇)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-
 5 alkyl-C(O)-heterocycloalkyl (dupe of C(O)R₇), -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-
 heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-N(R₇)-
 C(O)-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-
 N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-
 heterocycloalkyl-aryl, or -N(R₇)C(O)R_{7a}, wherein each of the alkyl, alkanyl, alkenyl,
 10 cycloalkyl, aryl, alkoxy, heterocycloalkyl, and heteroaryl groups, either alone or as part
 of another group within R₃, is independently optionally substituted with 1, 2, 3, 4, or 5
 groups selected from C₁-C₆-alkanyl, C₁-C₆ alkenyl, cycloalkyl, halo, -C(O)-R₆, oxo,
 hydroxy, -C₀-C₆-alkyl-N(R₈)R_{8a}, -C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-aryl,
 -C₀-C₆-alkyl-heteroaryl, -C(O)OR₆, and hydroxyalkyl;
- 15 R₄ is hydrogen;
 R₅ is hydrogen;
 R₆ is hydrogen, C₁-C₆-alkyl, aryl, arylalkyl, or cycloalkyl, where each of the -C₁-C₆-alkyl,
 aryl, arylalkyl, and cycloalkyl, is independently optionally substituted with 1, 2, 3, 4, or 5
 groups selected from C₁-C₆-alkoxy, C₁-C₆-alkyl, and halo; and
- 20 R₇, R_{7a} R_{7b}, R_{7c}, and R_{7d} are independently hydrogen, -C₁-C₆-alkanyl, -C₁-C₆-alkenyl, -OH,
 -O-C₁-C₆ alkanyl, -O-C₁-C₆ alkenyl, -O-C₀-C₆-alkyl-aryl, aryl, arylalkyl, heteroaryl,
 heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl,
 wherein each of the alkyl, aryl, heteroaryl, and heterocycloalkyl, either alone or part of
 another group within R₇, R_{7a} R_{7b}, R_{7c}, and R_{7d}, is independently optionally substituted
 25 with 1, 2, 3, 4, or 5 -NH₂, alkylamino, dialkylamino, -S-C₁-C₆-alkyl, -CN, hydroxy, oxo,
 C₁-C₆ alkoxy, C₁-C₆ alkyl, or halo.

[00273] In another embodiment (C), the invention provides a compound according to
 Embodiment B, wherein R₁ is hydrogen, -NO₂, C₁-C₄ alkoxy, or C₁-C₃ alkyl. In another
 embodiment, one or two R₁ are hydrogen, methoxy, or methyl and the remaining R₁ are
 30 hydrogen. In another embodiment, each R¹ is hydrogen.

[00274] In another embodiment (D), the invention provides a compound according to
 Embodiment B wherein n₁ is 1 or 2 and each R₂ is independently halo, -OR₆ (where R₆ is
 hydrogen or alkyl), -N(R₇)-C(O)-C₀-C₆ alkyl-N(R_{7b})R_{7a} (where R₇, R_{7a}, and R_{7b} are
 independently hydrogen or C₁-C₆-alkanyl), or -C₀-C₆alkyl-C(O)R₆ (where R₆ is C₁-C₆-

alkanyl). In another embodiment, each R_2 is independently chloro, bromo, fluoro, hydroxy, methoxy, $-N(H)C(O)-CH_2-N(CH_3)_2$, $-C(O)CH_3$, or methyl. In another embodiment, each R_2 is independently hydrogen, methoxy, or chloro.

- [00275] In another embodiment (E), the invention provides a compound according to Embodiment B wherein n_2 is 1 or 2 and each R_3 is independently C_1-C_6 -alkanyl, C_1-C_6 -alkenyl, halo, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})R_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})-C_0-C_6$ -alkyl- $N(R_{7c})(R_{7a})$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl- (R_{7a}) , $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl-heterocycloalkyl, $-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$, $-C_0-C_6$ -alkyl- $N(R_7)C(O)-C_0-C_6$ -alkyl-heteroaryl; where R_7 , R_{7a} , R_{7b} , and R_{7c} are independently hydrogen, C_1-C_6 -alkanyl, C_1-C_6 -alkoxy, cycloalkylalkyl, hydroxy, or heterocycloalkyl (optionally substituted with C_1-C_6 -alkyl); and where the alkyl and heterocycloalkyl, either alone or as part of another group within R_3 , are independently optionally substituted with 1, 2, or 3 groups, preferably 1 or 2, selected from hydroxy, halo, $-C_0-C_6$ -alkyl- $N(R_8)R_{8a}$ (where R_8 and R_{8a} are independently hydrogen or C_1-C_6 -alkanyl), and $-C_0-C_6$ -alkyl-heteroaryl.
- [00276] In another embodiment of embodiment E, n_2 is 1 and R_3 is C_1-C_6 -alkanyl, halo, $-N(R_7)C(O)-C_1-C_6$ -alkyl- $N(R_{7b})R_{7a}$, $-N(R_7)C(O)-C_0-C_6$ -alkyl- $N(R_{7b})-C_1-C_6$ -alkyl- $N(R_{7c})(R_{7a})$, $-N(R_7)C(O)-C_0-C_6$ -alkyl- (R_{7a}) , $-N(R_7)C(O)-C_0-C_6$ -alkyl-heterocycloalkyl, $-N(R_7)R_{7a}$, or $-N(R_7)C(O)-C_1-C_6$ -alkyl-heteroaryl; where R_7 , R_{7a} , R_{7b} , and R_{7c} are independently hydrogen, C_1-C_6 -alkanyl, C_1-C_6 -alkoxy, cycloalkylalkyl, hydroxy, or heterocycloalkyl (optionally substituted with C_1-C_6 -alkyl); and where the alkyl either alone or as part of another group within R_3 , is independently optionally substituted with 1, 2, or 3 groups, preferably 1 or 2, groups selected from hydroxy, halo, $-C_0-C_6$ -alkyl- $N(R_8)R_{8a}$ (where R_8 and R_{8a} are independently hydrogen or C_1-C_6 -alkanyl), and $-C_1-C_6$ -alkyl-heteroaryl.
- [00277] In another embodiment of embodiment E, n_2 is 1 and R_3 is methyl, chloro, $-NHC(O)CH_2NH(CH_3)$, $-NHC(O)CH_2NH(CH_2CH_3)$, $-NHC(O)CH(CH_3)NH_2$, $-NHC(O)C(CH_3)_2NH_2$, $-NHC(O)CH_2N(CH_3)_2$, $-NHC(O)CH_2N(CH_3)CH_2CH_2N(CH_3)_2$, $-NHC(O)CH(NH_2)CH_2CH_3$, $-NHC(O)CH_2N(CH_3)CH_2CH_2N(CH_3)_2$, $-NHC(O)CH(CH_3)NH(CH_3)$, $-NHC(O)CH_2NH_2$, $-NHC(O)CH_2NH(CH_3)$, $-NHC(O)CH_2N(CH_3)_2$, $-NHC(O)H$, $-NHC(O)CH_2$ (azetidin-1-yl), $-NHC(O)$ (pyrrolidin-2-yl), $-NHC(O)CH(NH_2)CH_2OH$, $-NHC(O)$ (azetidin-4-yl), $-NHC(O)C(CH_3)_2NH(CH_3)$, $-NH_2$, $-NHC(O)CH_2NH(CH_2CH_2CH_3)$, $-NHC(O)CH_2CH_2NH_2$, $-NHOH$, $-NHC(O)$ (piperidin-3-yl), $-NHC(O)$ (4-methyl-1,4-diazepan-1-yl), $-NHC(O)CH(NH_2)(CH_2CH_3)$, $-NHC(O)CH_2NH(CH_2CH(OH)(CH_3))$, $-NHC(O)CH_2NHCH_2CH_2F$, $-NHC(O)CH_2NH(OCH_2CH(CH_3)_2)$, $-NHC(O)$ (1-aminocycloprop-1-yl),

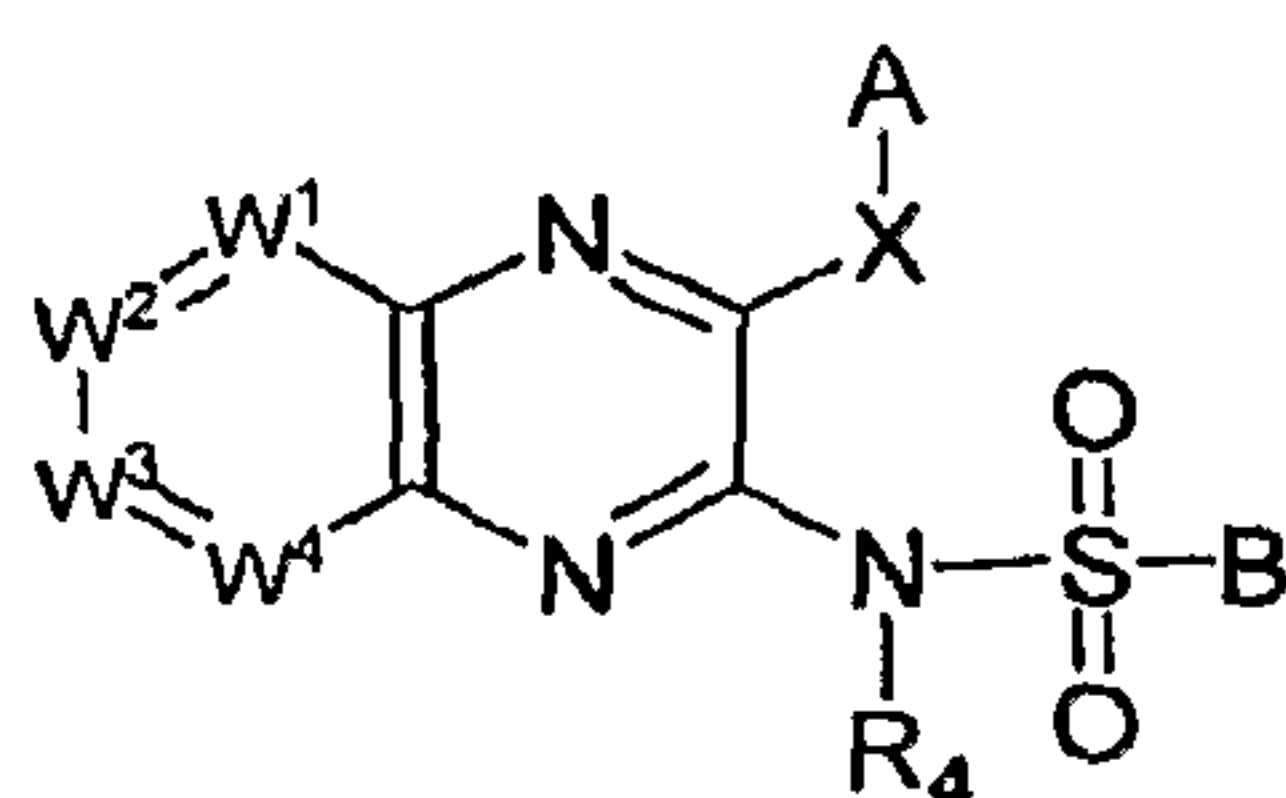
-NHC(O)CH₂NH(CH₂cyclopropyl), -NHC(O)CH₂(3-(dimethylamino)-azetidin-1-yl),
 -NHC(O)(piperidin-2-yl), -NHC(O)(morpholin-4-yl), -NHC(O)CH₂(pyrrolidin-1-yl),
 -NHC(O)CH(NH₂)CH₂CH₂CH₂CH₂N(CH₃)₂, -NHC(O)CH₂N(CH₃)(CH₂CH₃),
 -NHC(O)CH₂(imidazol-5-yl), -NHC(O)(1-aminocyclopent-1-yl),
 5 -NHC(O)CH₂NH(CH₂CH(CH₃)₂), -NHC(O)(N-(imidazol-4-ylmethyl)-azetidin-3-yl),
 -NHC(O)(N-ethyl-azetidin-3-yl), -NHCH₂N(CH₃)CH₂CH₂N(CH₃)₂, -NHC(O)CH₂N(CH₃)(N-
 methyl-pyrrolidin-3-yl), or -NHC(O)CH₂N(CH₃)(CH₂CH₂N(CH₃)₂).

[00278] In another embodiment of embodiment E, n₂ is 1 and R₃ is methyl,

-NHC(O)CH₂NH(CH₃), -NHC(O)CH(CH₃)NH₂, -NHC(O)C(CH₃)₂NH₂,
 10 -NHC(O)CH₂N(CH₃)₂, -NHC(O)CH₂N(CH₃)CH₂CH₂N(CH₃)₂, -NHC(O)CH(NH₂)CH₂CH₃,
 -NHC(O)CH₂N(CH₃)CH₂CH₂N(CH₃)₂, or -NHC(O)CH(CH₃)NH(CH₃).

[00279] In another embodiment (F), the invention provides a compound of Formula VIIIb
 where n₁ is two; R² is selected from -OR₆ (where R⁶ is C₁-C₆-alkyl) and halo; n₂ is 1; R³ is
 -C₀-C₆ alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a} (where R₇, R_{7a}, and R_{7b} are independently
 15 hydrogen or -C₁-C₆-alkanyl); and n₃ is 0.

[00280] In one embodiment, in section III the invention provides a compound of Formula IX:



IX

20 or a pharmaceutically acceptable salt thereof, wherein

W¹, W², W³, and W⁴ are -C(R₁)- or one or two of W¹, W², W³, and W⁴ are independently -N-
 and the remaining are -C(R₁)-;

X is a covalent bond, -N(R₅)-, -O-, -S-, or C₁-C₆ alkylene, wherein the alkylene is optionally
 substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆ alkoxy, halo, haloalkoxy, -
 25 NO₂, -CN, -OH, -N(R₇)R_{7a}, and -C(O)-OR₆;

A is aryl, -S(O)₂-aryl, heteroaryl, cycloalkyl, heterocycloalkyl, halo, haloalkyl, haloalkoxy,
 C₁-C₆-alkyl, C₁-C₆-alkoxy, or -C₁-C₆-alkyl-N(R₇)R_{7a}, where each of the aryl, heteroaryl,
 cycloalkyl, heterocycloalkyl, alkyl and alkoxy groups, each either alone or as part of
 another group within A, are independently optionally substituted with (R₂)_{n1};

B is aryl, heteroaryl, C₁-C₆-alkyl, -C₁-C₆-alkylaryl, or -C₁-C₆-alkylheteroaryl, wherein each of the aryl, heteroaryl and alkyl groups are independently optionally substituted with (R₃)_{n2};

n1 and n2 are independently 0 or an integer from 1 to 5;

- 5 each R₁ is independently selected from hydrogen, C₁-C₆-alkoxy, C₁-C₆-alkyl, -NO₂, halo, -CN, and -C₀-C₆-alkyl-N(R₇)R_{7a}, wherein each of the alkyl and alkoxy groups is optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkyl, C₁-C₆-alkoxy, halo, haloalkyl, haloalkoxy, -NO₂, -CN, hydroxy, -N(R₈)R_{8a}, and -C(O)OR₆;
- 10 each R₂ (when R₂ is present) is independently selected from C₁-C₆-alkanyl, C₁-C₆-alkenyl, C₂-C₆-alkenyl-C(O)OR₆, -OR₆, -N(R₇)C(O)R₆, -N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -OC(O)-C₀-C₆-alkyl-N(R₇)R_{7a}, -N(R₇)C(O)-C₁-C₆-alkylC(O)OR₆, C₀-C₆-alkyl-C(O)R₆, oxo, dioxo, -S(O)₂-N(R₇)R_{7a}, -C(O)OR₆, -CH(R₆)₂-C(O)-OR₆, -S(O)₂R₆, cycloalkyl, heterocycloalkyl, heteroaryl, -C(O)N(R₇)-C₁-C₆-alkyl-OR₆, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-C(O)OR₆, -C₀-C₆-alkyl-C(O)N(R₇)R_{7a}, aryl, arylalkyl, -S-(C₁-C₆-alkyl), halo,
- 15 oxo, -NO₂, -S-CN, -CN, and -C₀-C₆-alkyl-N(R₇)R_{7a}, wherein each of the alkyl (including, for example the alkyl within alkoxy), aryl, cycloalkyl, heterocycloalkyl, and heteroaryl groups, either alone or as part of another group within R₂, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkyl, halo, haloalkyl, haloalkoxy, oxo, -NO₂, -CN, -OH, -N(R₈)R_{8a}, C₁-C₆-alkoxy, and -C(O)OR₉;
- 20 each R₃ (when R₃ is present) is independently oxo, -NO₂, halo, -CN, C₁-C₆-alkanyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₃-C₆-cycloalkyl, -C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})C(O)R_{7a}, -C₀-C₆-alkyl-C(O)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-C(O)N(R₇)-C₁-C₆-alkylC(O)OR_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-(R_{7a}), -C₀-C₆-alkyl N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})-C₀-C₆-alkyl-N(R_{7c})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)-C₀-C₆-alkyl-C(=N(R_{7b})(R_{7a}))(NR_{7c}R_{7d}), -C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-heterocycloalkyl, -O-C₀-C₆-alkyl-N(R₇)R_{7a},
- 25 -C₀-C₆-alkyl-OR₆, -C₀-C₆-alkyl-C(O)OR₆, C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)NR₇R_{7a}, -C₀-C₆-alkyl-C(O)-R₇, -SR₇, -S(O)₂R₇, -S(O)₃R₇, -S(O)R₇, -SO₂N(R₇)R_{7a}, -SO₂N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -S-heteroaryl, -S-aryl, -S-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)-aryl, -C₀-C₆-alkyl-N(R₇)-heteroaryl, -C₀-C₆-alkyl-N(R₇)-heterocycloalkyl, -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-cycloalkyl, C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-
- 30

- aryl, C₀-C₆ alkyl-C(O)N(R₇)-C₀-C₆ alkyl-heteroaryl, C₀-C₆ alkyl-C(O)N(R₇)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-aryl, C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl, C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl-aryl, -N(R₇)C(O)OR₆, or -N(R₇)-C(O)-R_{7a}, wherein each of the alkyl, alkanyl, alkenyl, cycloalkyl, aryl, (including, for example the alkyl within alkoxy), heterocycloalkyl, and heteroaryl groups, either alone or as part of another group within R₃, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkanyl, C₁-C₆-alkenyl, -C₀-C₆-alkyl-OR₉, cycloalkyl, halo, haloalkyl, haloalkoxy, -C(O)R₉, -NO₂, -CN, oxo, -C₀-C₆-alkyl-N(R₈)R_{8a}, -C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-heteroaryl, -C(O)OR₉, and hydroxyalkyl;
- R₄ is hydrogen, aryl, -C₀-C₆-alkyl-N(R₇)R_{7a}, C₁-C₆-alkoxy, or C₁-C₆ alkyl, wherein each of the alkyl and aryl groups, either alone or as part of another group in R₄, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkyl, halo, haloalkyl, haloalkoxy, -NO₂, -CN, -OH, -N(R₈)R_{8a}, C₁-C₆-alkoxy, and -C(O)OR₆;
- R₅ is hydrogen, -C₁-C₆ alkyl-N(R₇)R_{7a}, C₁-C₆-alkoxy, C₁-C₆-alkyl, or aryl, wherein each of the alkyl and aryl is optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkyl, halo, haloalkyl, haloalkoxy, -NO₂, -CN, -OH, -N(R₈)R_{8a}, C₁-C₆ alkoxy, or -C(O)OR₆;
- R₆ and R₉ are independently hydrogen, -OH, C₁-C₆-alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, heteroaryl, heteroarylalkyl, or aryl, each C₁-C₆ alkyl, aryl, cycloalkyl, heterocycloalkyl, and heteroaryl, either alone or as part of another group within R₆ and R₉, is independently optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from -NH₂, -OH, C₁-C₆-alkoxy, C₁-C₆-alkyl, and halo; and
- R₇, R_{7a}, R_{7b}, R_{7c}, R_{7d}, R₈, and R_{8a} are independently hydrogen, -C₁-C₆-alkanyl, -C₁-C₆-alkenyl, -OH, -O-C₁-C₆ alkanyl, -O-C₁-C₆ alkenyl, -O-C₀-C₆ alkyl-aryl, -C₀-C₆ alkyl-C(O)OR₆, -C₀-C₆ alkyl-C(O)R₆, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl, wherein each of the alkyl, aryl, heteroaryl, and heterocycloalkyl, either alone or part of another group within R₇, R_{7a}, R_{7b}, R_{7c}, and R_{7d}, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from -NH₂, -S-C₁-C₆ alkyl, -CN, -OH, -NO₂, C₁-C₆ alkoxy, C₁-C₆ alkyl, halo, aryl, and heteroaryl optionally substituted with one or two C₁-C₆ alkyl.

[00281] In another embodiment, the invention comprises a pharmaceutical composition comprising a PI3K inhibitor of Formula VIII, VIIIa, VIIIb, or IX in combination with a compound of Formula I, Ia, Ic, Id, II, III, IV, or V and a pharmaceutically acceptable carrier, excipient, or diluent. In another embodiment, the compound is of Formula VIIIa or VIIIb.

[00282] In another embodiment, the invention provides a method of treating a disease or condition mediated by PI3K and MEK comprising administering to a patient a PI3K compound of Formula VIII, VIIIa, VIIIb, or IX in combination with a MEK compound of Formula I, Ia, Ic, Id, II, III, IV, or V. In another embodiment, the PI3K compound is of Formula VIIIa or VIIIb. In another embodiment, the MEK Compound is of Formula Ia and the PI3K Compound is of Formula VIIIa. In another embodiment, the MEK Compound is of Formula Ia and the PI3K Compound is of Formula VIIIb. In another embodiment, the MEK Compound is of Formula V and the PI3K Compound is of Formula VIIIb. In another embodiment, the MEK Compound is of Section I, Embodiment G and the PI3K Compound is of VIIIb. In another embodiment, the MEK Compound is of Section I, Table 1 and the PI3K compound is of Formula VIII, VIIIa, or VIIIb.

[00283] Another embodiment of the invention is directed to suitable x-ray quality crystals, and one of ordinary skill in the art would appreciate that they can be used as part of a method of identifying a candidate agent capable of binding to and modulating the activity of kinases.

Such methods may be characterized by the following embodiments: a) introducing into a suitable computer program, information defining a ligand binding domain of a kinase in a conformation (e.g. as defined by x-ray structure coordinates obtained from suitable x-ray quality crystals as described above) wherein the computer program creates a model of the three dimensional structures of the ligand binding domain, b) introducing a model of the three dimensional structure of a candidate agent in the computer program, c) superimposing the model of the candidate agent on the model of the ligand binding domain, and d) assessing whether the candidate agent model fits spatially into the ligand binding domain.

Embodiments a-d are not necessarily carried out in the aforementioned order. Such methods may further entail: performing rational drug design with the model of the three-dimensional structure, and selecting a potential candidate agent in conjunction with computer modeling.

[00284] Additionally, one skilled in the art would appreciate that such methods may further entail: employing a candidate agent, so-determined to fit spatially into the ligand binding domain, in a biological activity assay for kinase modulation, and determining whether said candidate agent modulates kinase activity in the assay. Such methods may also include

administering the candidate agent, determined to modulate kinase activity, to a mammal suffering from a condition treatable by kinase modulation, such as those described above.

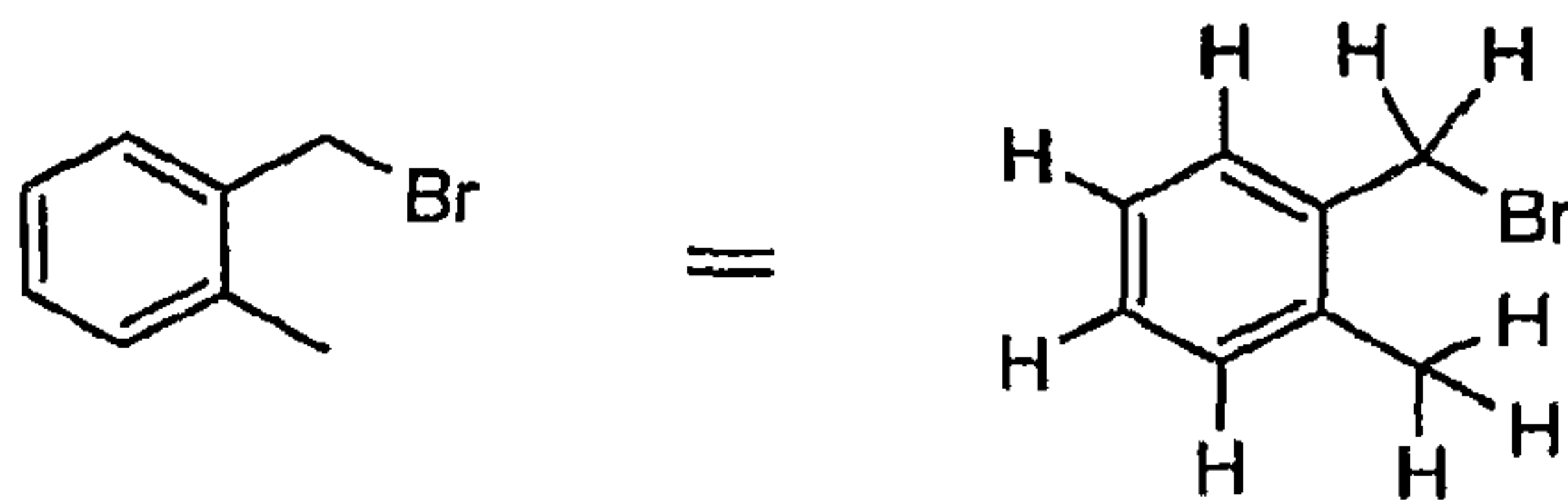
[00285] Also, one skilled in the art would appreciate that compounds of the invention can be used in a method of evaluating the ability of a test agent to associate with a molecule or molecular complex comprising a ligand binding domain of a kinase. Such a method may be characterized by the following embodiments: a) creating a computer model of a kinase binding pocket using structure coordinates obtained from suitable x-ray quality crystals of the kinase, b) employing computational algorithms to perform a fitting operation between the test agent and the computer model of the binding pocket, and c) analyzing the results of the fitting operation to quantify the association between the test agent and the computer model of the binding pocket.

Section III Definitions

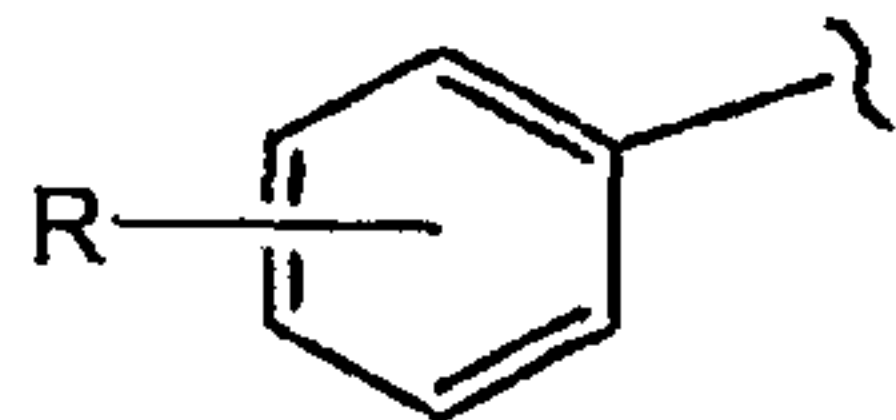
[00286] As used in the present specification, the following words and phrases are generally intended to have the meanings as set forth below, except to the extent that the context in which they are used indicates otherwise or they are expressly defined to mean something different.

[00287] The symbol “-” means a single bond, “=” means a double bond, “≡” means a triple bond, “====” means a single or double bond. When a group is depicted removed from its parent Formula, the “~” symbol will be used at the end of the bond which was theoretically cleaved in order to separate the group from its parent structural Formula.

[00288] When chemical structures are depicted or described, unless explicitly stated otherwise, all carbons are assumed to have hydrogen substitution to conform to a valence of four. For example, in the structure on the left-hand side of the schematic below there are nine hydrogens implied. The nine hydrogens are depicted in the right-hand structure. Sometimes a particular atom in a structure is described in textual Formula as having a hydrogen or hydrogens as substitution (expressly defined hydrogen), for example, -CH₂CH₂-. It is understood by one of ordinary skill in the art that the aforementioned descriptive techniques are common in the chemical arts to provide brevity and simplicity to description of otherwise complex structures.

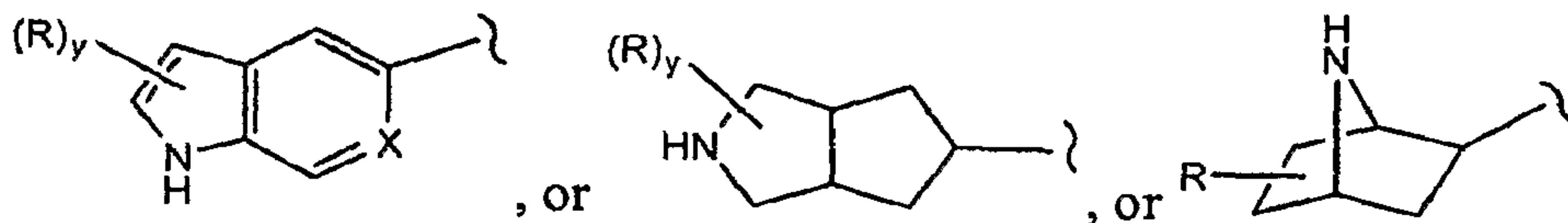


[00289] If a group “R” is depicted as “floating” on a ring system, as for example in the Formula:



then, unless otherwise defined, a substituent “R” may reside on any atom of the ring system, assuming replacement of a depicted, implied, or expressly defined hydrogen from one of the ring atoms, so long as a stable structure is formed.

[00290] If a group “R” is depicted as floating on a fused ring system, as for example in the Formulae:

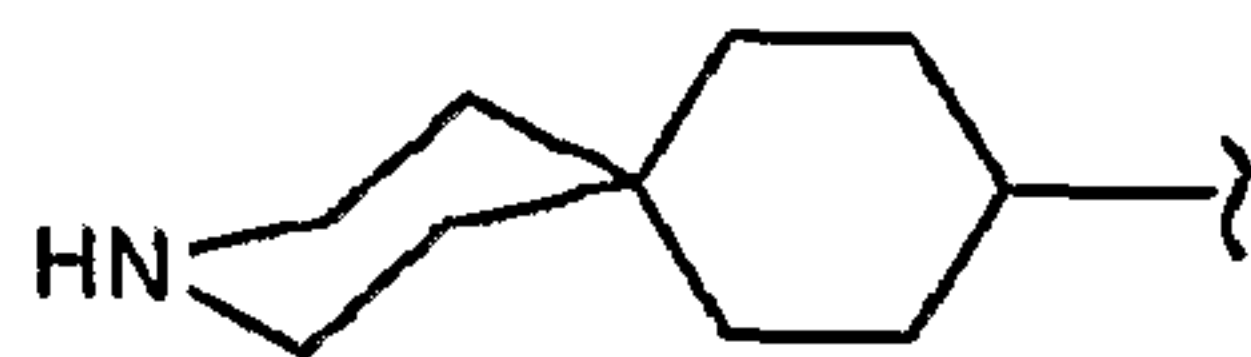


then, unless otherwise defined, a substituent “R” may reside on any atom of the fused ring system, assuming replacement of a depicted hydrogen (for example the -NH- in the Formula above), implied hydrogen (for example as in the Formula above, where the hydrogens are not shown but understood to be present), or expressly defined hydrogen (for example where in the Formula above, “X” equals =CH-) from one of the ring atoms, so long as a stable structure is formed. In the example depicted, the “R” group may reside on either the 5-membered or the 6-membered ring of the fused ring system. In the Formula depicted above, when y is 2 for example, then the two “R’s” may reside on any two atoms of the ring system, again assuming each replaces a depicted, implied, or expressly defined hydrogen on the ring.

[00291] When a group “R” is depicted as existing on a ring system containing saturated carbons, as for example in the Formula:



where, in this example, “y” can be more than one, assuming each replaces a currently depicted, implied, or expressly defined hydrogen on the ring; then, unless otherwise defined, where the resulting structure is stable, two “R’s” may reside on the same carbon. A simple example is when R is a methyl group; there can exist a geminal dimethyl on a carbon of the depicted ring (an “annular” carbon). In another example, two R’s on the same carbon, including that carbon, may form a ring, thus creating a spirocyclic ring (a “spirocyclyl” group) structure with the depicted ring as for example in the Formula:



[00292] "Acyl" means a $-C(O)R$ radical where R is alkyl (i.e., one to ten carbon atoms of a straight, branched, or cyclic configuration, and is saturated or unsaturated) or R is optionally substituted aryl or optionally substituted heteroaryl. One or more carbons in the R residue may be replaced by nitrogen, oxygen or sulfur. Examples include acetyl, benzoyl, propionyl, isobutyryl, *t*-butoxycarbonyl, benzyloxycarbonyl, and pyridinylcarbonyl, and the like. Lower-acyl refers to groups containing one to six carbons.

[00293] "Acylamino" means a $-NRR'$ group where R is acyl, as defined herein, and R' is hydrogen or alkyl.

[00294] "Alkyl" means a (C_1-C_{20}) linear, branched, or cyclic hydrocarbon group (and combinations thereof, inclusively) and may be saturated or unsaturated. For example, " C_6 alkyl" may refer to an *n*-hexyl, *iso*-hexyl, cyclobutylethyl, and the like. "Lower alkyl" means an alkyl group of from one to six carbon atoms. Examples of lower alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, *s*-butyl, *t*-butyl, isobutyl, pentyl, hexyl and the like. A " C_0 " alkyl (as in " C_0-C_6 -alkyl") is a covalent bond.

[00295] In this application, alkyl includes alkanyl, alkenyl, alkynyl, and cycloalkyl residues (and combinations thereof); it is intended to include cyclohexylmethyl, vinyl, allyl, isoprenyl, and the like. Thus when an alkyl residue having a specific number of carbons is named, all geometric isomers having that number of carbons are intended to be encompassed; thus, for example, " C_4 alkyl" is meant to include *n*-butyl, *sec*-butyl, isobutyl, *t*-butyl, cyclobutyl, isobutenyl and but-2-ynyl groups; and for example, " C_3 alkyl" each include *n*-propyl, propenyl, and isopropyl.

[00296] "Alkanyl" means a linear saturated monovalent hydrocarbon radical of one to twenty carbon atoms or a branched saturated monovalent hydrocarbon radical of three to 20 carbon atoms, e.g., methyl, ethyl, propyl, 2-propyl, butyl (including all isomeric forms), or pentyl (including all isomeric forms), and the like. "Lower alkanyl" means alkanyl having one to six carbons atoms.

[00297] "Cycloalkyl" means a monocyclic or polycyclic hydrocarbon radical having three to thirteen carbon atoms. The cycloalkyl can be saturated or partially unsaturated, but cannot contain an aromatic ring. Cycloalkyl includes fused, bridged, and spiro ring systems. Examples of such radicals include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. "Cycloalkylalkyl" means alkyl group substituted with one or two cycloalkyl group(s), as

defined herein. Representative examples include cyclopropylmethyl and 2-cyclobutyl-ethyl, and the like.

[00298] "Optionally substituted cycloalkyl" means a cycloalkyl radical, as defined herein, that is optionally substituted with one, two, three, or four groups independently selected from C₁-C₆ alkanyl, C₁-C₆ alkoxy, halo, haloalkyl, haloalkoxy, oxo, hydroxy, cyano, nitro, amino, mono(C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₆ haloalkyl, C₁-C₆ haloalkoxy, amino(C₁-C₆)alkyl, mono(C₁-C₆)alkylamino(C₁-C₆)alkyl di(C₁-C₆)alkylamino(C₁-C₆)alkyl, carboxy, carboxy ester, cycloalkyl, hydroxyalkyl, -C(O)NR'R" (where R' is hydrogen, alkyl, hydroxy, or alkoxy and R" is hydrogen, alkyl, aryl, or heterocyclyl), optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, or heterocyclyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heterocyclyl).

[00299] "Alkenyl" means a straight or branched hydrocarbon radical having from 2 to 20 carbon atoms and at least one double bond and includes ethenyl, propenyl, 1-but-3-enyl, 1-pent-3-enyl, 1-hex-5-enyl and the like. "Lower alkenyl" is alkenyl having 2-6 carbon atoms.

[00300] "Alkynyl" means a straight or branched hydrocarbon radical having from 2 to 20 carbon atoms and at least one triple bond and includes ethynyl, propynyl, butynyl, pentyn-2-yl and the like. "Lower alkynyl" is alkynyl having 2-6 carbon atoms.

[00301] "Alkylene" refers to straight or branched divalent hydrocarbon, containing no unsaturation and having from one to ten carbon atoms. Examples of alkylene include methylene (-CH₂-), ethylene (-CH₂CH₂-), propylene (-CH₂CH₂CH₂-), and dimethylpropylene (-CH₂C(CH₃)₂CH₂-), and the like.

[00302] "Alkylidyne" or "alkynylene" means a straight or branched divalent hydrocarbon having from two to ten carbon atoms, and containing at least one triple bond, for example, propylid-2-ynyl, *n*-butylid-1-ynyl, and the like.

[00303] "Alkoxy" or "alkoxyl" means -O-alkyl, where the alkyl group includes from one to eight carbon atoms of a straight, branched, cyclic configuration, unsaturated chains, and combinations thereof attached to the parent structure through an oxygen atom. Examples include methoxy, ethoxy, propoxy, isopropoxy, cyclopropyloxy, cyclohexyloxy and the like. Lower-alkoxy refers to groups containing one to six carbons.

[00304] "Alkylamino" means a -NHR radical where R is alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., methylamino, ethylamino, *n*-, *iso*-propylamino, *n*-, *iso*-, *tert*-butylamino, or methylamino-N-oxide, and the like.

[00305] "Alkylaminoalkyl" means an alkyl group substituted with one or two alkylamino groups, as defined herein.

[00306] "Aryl" means a monovalent six- to fourteen-membered, mono- or bi-carbocyclic ring, wherein the monocyclic ring is aromatic and at least one of the rings in the bicyclic ring is aromatic. Representative examples include phenyl, naphthyl, and indanyl, and the like.

[00307] "Optionally substituted aryl" means an aryl group, as defined herein, which is optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, -C(O)NR'R" (where R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, or heterocyclyl), -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, or heterocyclyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

[00308] "Arylalkyl" means a residue in which an aryl moiety is attached to a parent structure via one of an alkylene, alkylidene, or alkylidyne group. Examples include benzyl, phenethyl, phenylvinyl, phenylallyl and the like. "Lower arylalkyl" refers to an arylalkyl where the "alkyl" portion of the group has one to six carbons; this can also be referred to as C₁₋₆ arylalkyl. When a group is referred to as "C₁₋₆ alkyl-aryl" or "C₀₋₆ alkyl-aryl", an aryl moiety is attached to a parent structure via an alkylene group. Examples include benzyl, phenethyl, and the like.

[00309] "Arylalkyloxy" means an -OR group where R is arylalkyl, as defined herein.

[00310] "Carboxy ester" means a -C(O)OR group where R is lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, aryl or arylalkyl, each of which is defined herein. Representative examples include methoxycarbonyl, ethoxycarbonyl, and benzyloxycarbonyl, and the like.

[00311] "Dialkylamino" means a -NRR' radical where R and R' are independently alkyl as defined herein, or an N-oxide derivative, or a protected derivative thereof, e.g., dimethylamino, diethylamino, *N,N*-methylpropylamino or *N,N*-methylethylamino, and the like.

[00312] "Fused-polycyclic" or "fused ring system" refers to a polycyclic ring system that contains bridged or fused rings; that is, where two rings have more than one shared atom in their ring structures. In this application, fused-polycyclics and fused ring systems are not necessarily all aromatic ring systems. Typically, but not necessarily, fused-polycyclics share a vicinal set of atoms, for example naphthalene or 1,2,3,4-tetrahydro-naphthalene. A spiro

ring system is not a fused-polycyclic by this definition, but fused polycyclic ring systems of the invention may themselves have spiro rings attached thereto via a single ring atom of the fused-polycyclic. In some examples, as appreciated by one of ordinary skill in the art, two adjacent groups on an aromatic system may be fused together to form a ring structure. The fused ring structure may contain heteroatoms and may be optionally substituted with one or more groups. It should additionally be noted that saturated carbons of such fused groups (*i.e.* saturated ring structures) can contain two substitution groups.

[00313] "Haloaloxyl" means an -OR' group where R' is haloalkyl as defined herein, e.g., trifluoromethoxy or 2,2,2-trifluoroethoxy, and the like..

[00314] "Halogen" or "halo" means fluoro, chloro, bromo or iodo.

[00315] "Haloalkyl" and "haloaryl" mean an alkyl and an aryl group, respectively, that are substituted with one or more halogens, preferably one to five halo atoms. Thus, "dihaloaryl," "dihaloalkyl," and "trihaloaryl" etc. refer to aryl and alkyl substituted with a plurality of halogens, but not necessarily a plurality of the same halogen; thus 4-chloro-3-fluorophenyl is within the scope of dihaloaryl.

[00316] "Heteroatom" refers to O, S, N, or P.

[00317] "Heterocyclyl" refers to a stable three- to fifteen-membered ring substituent that consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, phosphorus, oxygen and sulfur. For purposes of this invention, the heterocyclyl substituent may be a monocyclic, bicyclic or tricyclic ring system, which may include fused or bridged ring systems as well as spirocyclic systems. The terms "heterocycloalkyl" and "heteroaryl" are groups that are encompassed by the broader term "heterocyclyl." The nitrogen, phosphorus, carbon or sulfur atoms in the heterocyclyl group may be optionally oxidized to various oxidation states. In a specific example, the group -S(O)₀₋₂-, refers to -S- (sulfide), -S(O)- (sulfoxide), and -SO₂- (sulfone). For convenience, nitrogens, particularly but not exclusively, those defined as annular aromatic nitrogens, are meant to include their corresponding *N*-oxide form, although not explicitly defined as such in a particular example. Thus, for a compound of the invention having, for example, a pyridyl ring; the corresponding pyridyl-*N*-oxide is meant to be included as another compound of the invention. In addition, annular nitrogen atoms may be optionally quaternized; and the ring substituent may be partially or fully saturated or aromatic. Examples of heterocyclyl groups include, but are not limited to, azetidiny, acridiny, benzodioxolyl, benzodioxanyl, benzofuranyl, carbazoyl, cinnolinyl, dioxolanyl, indoliziny, naphthyridiny, perhydroazepiny, phenaziny, phenothiaziny, phenoxaziny, phthalaziny, pteridiny, puriny, quinazolinyl, quinoxalinyl,

quinolinyl, isoquinolinyl, tetrazoyl, tetrahydroisoquinolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, imidazolyl, imidazolidinyl, dihydropyridinyl, tetrahydropyridinyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolyl, oxazolidinyl, triazolyl, isoxazolyl, isoxazolidinyl, morpholinyl, thiazolyl, thiazolyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, indolyl, isoindolyl, indolyl, isoindolyl, octahydroindolyl, octahydroisoindolyl, quinolyl, isoquinolyl, decahydroisoquinolyl, benzimidazolyl, thiadiazolyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, tetrahydrofuryl, tetrahydropyranyl, thienyl, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, dioxaphospholanyl, oxadiazolyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, and tetrahydroquinolinyl.

[00318] "Optionally substituted heterocyclyl" means a heterocyclyl group, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, oxo (valency rules permitting), lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, carboxy ester, $-C(O)NR'R''$ (where R' is hydrogen or alkyl and R'' is hydrogen, alkyl, aryl, or heterocyclyl), $-NR'C(O)R''$ (where R' is hydrogen or alkyl and R'' is alkyl, aryl, or heterocyclyl), amino, alkylamino, dialkylamino, and $-NHS(O)_2R'$ (where R' is alkyl, aryl, or heteroaryl).

[00319] "Heteroalicyclic" and "heterocycloalkyl" mean a non-aromatic heterocyclyl group, as defined herein. A "heteroalicyclic" or "heterocycloalkyl" may be fully saturated or may contain unsaturation, but is not aromatic. "Heteroalicyclic" or "heterocycloalkyl" may be monocyclic or bicyclic (including fused, bridged, and spiro ring systems).

[00320] "Optionally substituted heteroalicyclic" and "optionally substituted heterocycloalkyl" mean, respectively, a heteroalicyclic and heterocycloalkyl ring, each as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, hydroxy, oxo, lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, optionally substituted cycloalkyl, heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, alkylaminoalkyl, dialkylaminoalkyl, carboxy, carboxy ester, $-C(O)NR'R''$ (where R' is hydrogen or alkyl and R'' is hydrogen, alkyl, aryl, or heterocyclyl), $-NR'C(O)R''$ (where R' is hydrogen or alkyl and R'' is alkyl, aryl, or heterocyclyl), amino, alkylamino, dialkylamino, and $-NHS(O)_2R'$ (where R' is alkyl, aryl, or heteroaryl).

[00321] "Heteroaryl" means a 5- to 12-membered, monocyclic aromatic heterocyclyl (where heterocyclyl is defined herein) or bicyclic heterocyclyl ring system (where at least one of the rings in the bicyclic system is aromatic) where the monocyclic ring and at least one of the rings in the bicyclic ring system contains one, two, three, four, or five heteroatom(s) selected from nitrogen, oxygen, phosphorous, and sulfur. Representative examples include pyridinyl, imidazolyl, pyrimidinyl, pyrazolyl, triazolyl, pyrazinyl, tetrazolyl, furyl, thienyl, isoxazolyl, thiazolyl, oxazolyl, isothiazolyl, pyrrolyl, quinolinyl, isoquinolinyl, indolyl, benzimidazolyl, benzofuranyl, cinnolinyl, indazolyl, indoliziny, phthalazinyl, pyridazinyl, triazinyl, isoindolyl, pteridinyl, purinyl, oxadiazolyl, triazolyl, thiadiazolyl, thiadiazolyl, furazanyl, benzofurazanyl, benzothiophenyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, and furopyridinyl. Fused, bridged, and spiro moieties are also included within the scope of this definition.

[00322] "Optionally substituted heteroaryl" means a heteroaryl group, as defined herein, optionally substituted with one, two, three, four, or five groups selected from halo, haloalkyl, haloalkoxy, lower alkanyl, lower alkenyl, lower alkynyl, alkoxy, hydroxy, oxo (valency rules permitting), carboxy, carboxy ester, amino, alkylamino, dialkylamino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, heteroaryl, optionally substituted aryl, -C(O)NR'R" (where R' is hydrogen or alkyl and R" is hydrogen, alkyl, aryl, or heterocyclyl), -NR'C(O)R" (where R' is hydrogen or alkyl and R" is alkyl, aryl, or heterocyclyl), and -NHS(O)₂R' (where R' is alkyl, aryl, or heteroaryl).

[00323] "Optionally substituted heterocyclylalkyl" means an alkyl group substituted with an optionally substituted heterocyclyl group, as defined herein.. Examples include (4-methylpiperazin-1-yl) methyl, (morpholin-4-yl) methyl, (pyridin-4-yl) methyl, 2-(oxazolin-2-yl) ethyl, 4-(4-methylpiperazin-1-yl)-2-butenyl, and the like. In addition, the alkyl portion of a heterocyclylalkyl group may be substituted as described in the definition for "substituted". "Lower heterocyclylalkyl" means a heterocyclylalkyl where the "alkyl" portion of the group has one to six carbons. "Heteroalicyclylalkyl" or "lower heterocycloalkylalkyl" means a heterocyclylalkyl where the heterocyclyl portion of the group is non-aromatic; and "heteroarylalkyl" means a heterocyclylalkyl where the heterocyclyl portion of the group contains an aromatic ring. Such terms may be described in more than one way, for example, "lower heterocyclylalkyl" and "heterocyclyl C₁₋₆alkyl" are equivalent terms. Additionally, for simplicity, the number of annular atoms (including heteroatoms) in a heterocycle may be denoted as "C_x-C_y" (as in "C_x-C_y-heterocyclyl" and "C_x-C_y-

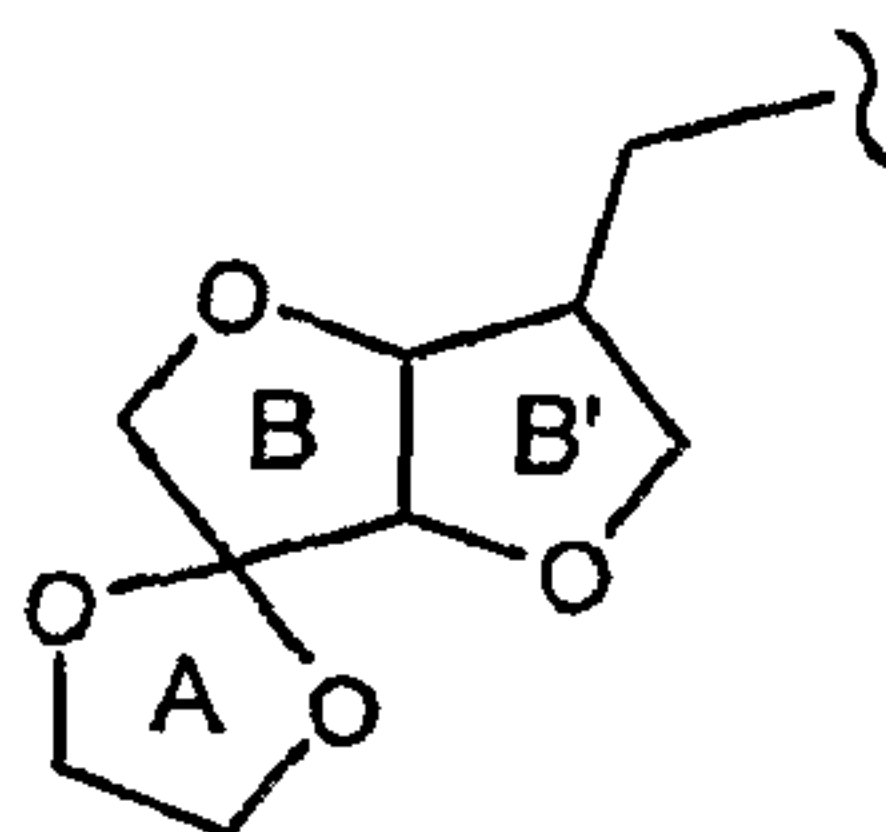
heteroaryl" (and the like)), where x and y are integers. So, for example, C₅-C₁₄-heterocyclyl refers to a 5 to 14 membered ring system having at least one heteroatom and not a ring system containing 5 to 14 annular carbon atoms.

[00324] "Hydroxyalkyl" means an alkanyl, alkenyl, or alkynyl radical, as defined herein, substituted with at least one, preferably one, two, or three, hydroxy group(s), provided that if two hydroxy groups are present they are not both on the same carbon atom. Representative examples include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 1-(hydroxymethyl)-2-hydroxyethyl, 2,3-dihydroxybutyl, 3,4-dihydroxybutyl and 2-(hydroxymethyl)-3-hydroxypropyl, preferably 2-hydroxyethyl, 2,3-dihydroxypropyl, or 1-(hydroxymethyl)-2-hydroxyethyl, and the like.

[00325] "Optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. One of ordinary skill in the art would understand that with respect to any molecule described as containing one or more optional substituents, only sterically practical and/or synthetically feasible compounds are meant to be included. "Optionally substituted" refers to all subsequent modifiers in a term. So, for example, in the term "optionally substituted arylC₁₋₈ alkyl," both the "C₁₋₈ alkyl" portion and the "aryl" portion of the molecule may or may not be substituted. A list of exemplary optional substitutions is presented below in the definition of "substituted."

[00326] "Saturated bridged ring system" refers to a bicyclic or polycyclic ring system that is not aromatic. Such a system may contain isolated or conjugated unsaturation, but not aromatic or heteroaromatic rings in its core structure (but may have aromatic substitution thereon). For example, hexahydro-furo[3,2-b]furan, 2,3,3a,4,7,7a-hexahydro-1H-indene, 7-aza-bicyclo[2.2.1]heptane, and 1,2,3,4,4a,5,8,8a-octahydro-naphthalene are all included in the class "saturated bridged ring system."

[00327] "Spirocyclyl" or "spirocyclic ring" refers to a ring originating from a particular annular carbon of another ring. For example, as depicted below, a ring atom of a saturated bridged ring system (rings B and B'), but not a bridgehead atom, can be a shared atom between the saturated bridged ring system and a spirocyclyl (ring A) attached thereto. A spirocyclyl can be carbocyclic or heteroalicyclic.



[00328] "Substituted" alkyl, alkylene, alkylidene, and alkylidyne refer respectively to alkyl, alkylene, alkylidene, and alkylidyne where one or more (for example up to about five, in another example, up to about three) hydrogen atoms are replaced by a substituent independently selected from halo, optionally substituted aryl, hydroxy, alkoxy, optionally substituted heterocyclyl, alkylendioxy, amino, alkylamino, dialkylamino), amidino, aryloxy, arylalkyloxy, carboxy, carboxy ester, alkylcarbonyloxy, carbamyl, alkylaminocarbonyl, dialkylaminocarbonyl, benzyloxycarbonylamino (CBZ-amino), cyano, acyl, nitro, $S(O)_{n1}R'$ (where $n1$ is 0, 1, or 2 and R' is alkyl, substituted alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), oxo, acylamino, and sulfonamido.

[00329] "Sulfonamido" means a $-NRSO_2R'$ or $-SO_2NRR''$ group where R is hydrogen or lower alkyl, R' is lower alkanyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl, and R'' is hydrogen or R' .

[00330] Representative compounds from Section III are depicted below. The examples are merely illustrative and do not limit the scope of the invention in any way. Compounds of the invention are named according to systematic application of the nomenclature rules agreed upon by the International Union of Pure and Applied Chemistry (IUPAC), International Union of Biochemistry and Molecular Biology (IUBMB), and the Chemical Abstracts Service (CAS).

Table 1		
Cpd. No.	Structure	IUPAC Name
1		<i>N</i> -(4-{[(3-{[4-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
2		4-bromo- <i>N</i> -[3-(phenylamino)quinoxalin-2-yl]benzene sulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
3		4-bromo- <i>N</i> -{3-[(2-methylphenyl)amino]quinoxalin-2-yl}benzene sulfonamide
4		<i>N</i> -(3-{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzene sulfonamide
5		4-bromo- <i>N</i> -(3-{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzene sulfonamide
6		4-chloro- <i>N</i> -[6-(methyloxy)-3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl]benzenesulfonamide
7		4-chloro- <i>N</i> -{3-[(4-chlorophenyl)amino]-6-(methyloxy)quinoxalin-2-yl}benzenesulfonamide
8		<i>N</i> -(4-{[3-{[(4-chlorophenyl)sulfonyl]amino}-7-(methyloxy)quinoxalin-2-yl]amino}phenyl)acetamide
9		4-chloro- <i>N</i> -{6-(methyloxy)-3-[(2-oxo-2,3-dihydro-1 <i>H</i> -benzimidazol-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide
10		<i>N</i> -{4-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide
11		<i>N</i> -(3-{[4-(ethyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzene sulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
12		<i>N</i> -{3-[(3,4-dimethylphenyl)amino]-6-methylquinoxalin-2-yl}-4-methylbenzene sulfonamide
13		<i>N</i> -(3-{[3-(dimethylamino)phenyl]amino}quinoxalin-2-yl)-4-methylbenzene sulfonamide
14		<i>N</i> -(3-{[4-(ethoxy)phenyl]amino}quinoxalin-2-yl)benzene sulfonamide
15		4-methyl- <i>N</i> -(3-{[4-(methoxy)phenyl]amino}quinoxalin-2-yl)benzene sulfonamide
16		4-methyl- <i>N</i> -{6-methyl-3-[(4-methylphenyl)amino]quinoxalin-2-yl}benzene sulfonamide
17		<i>N</i> -{3-[(4-hydroxyphenyl)amino]-6-methylquinoxalin-2-yl}-4-methylbenzene sulfonamide
18		4-methyl- <i>N</i> -(3-morpholin-4-ylquinoxalin-2-yl)benzenesulfonamide
19		<i>N</i> -{3-[(2,5-dimethylphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
20		4-chloro- <i>N</i> -[3-(naphthalen-2-ylamino)quinoxalin-2-yl]benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
21		<i>N</i> -{3-[(3-aminophenyl)amino]quinoxalin-2-yl}-4-chlorobenzenesulfonamide
22		<i>N</i> -(3-{[4-(aminosulfonyl)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
23		4-chloro- <i>N</i> -{3-[(4-chlorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
24		4-chloro- <i>N</i> -{3-[(4-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
25		4-chloro- <i>N</i> -{3-[(2-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
26		methyl 4-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoate
27		methyl 2-chloro-5-[(3-{[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoate
28		<i>N</i> -{4-[(7-methyl-3-{[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide
29		4-methyl- <i>N</i> -(6-methyl-3-{[2-(methoxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

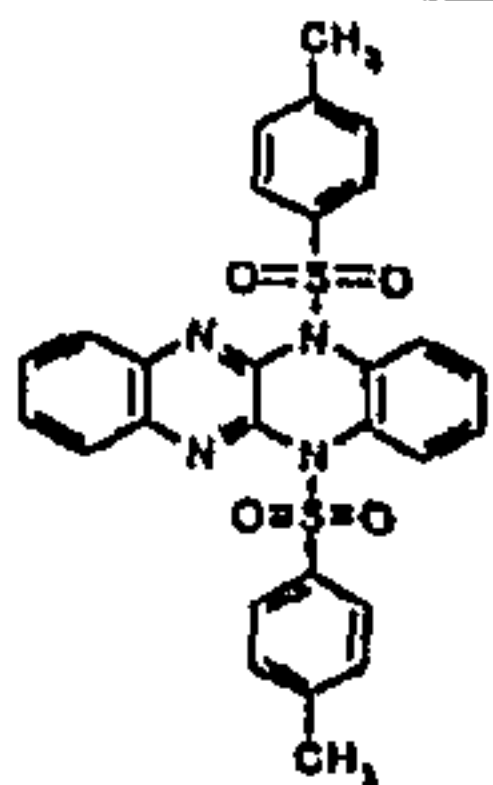
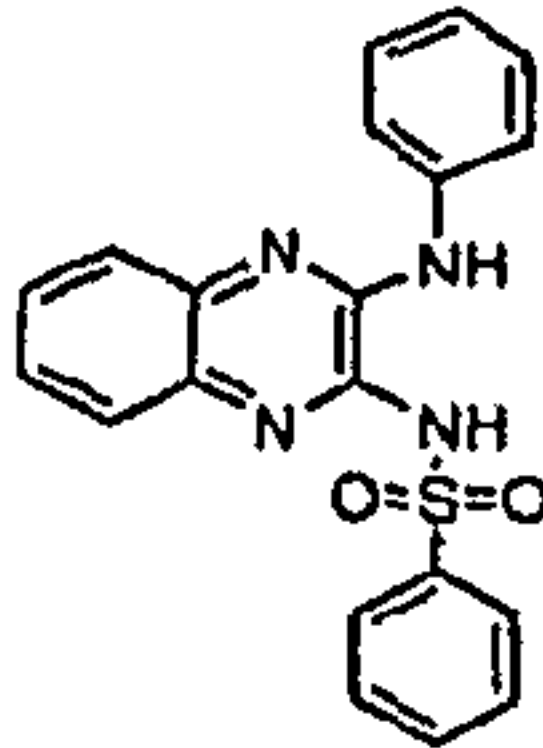
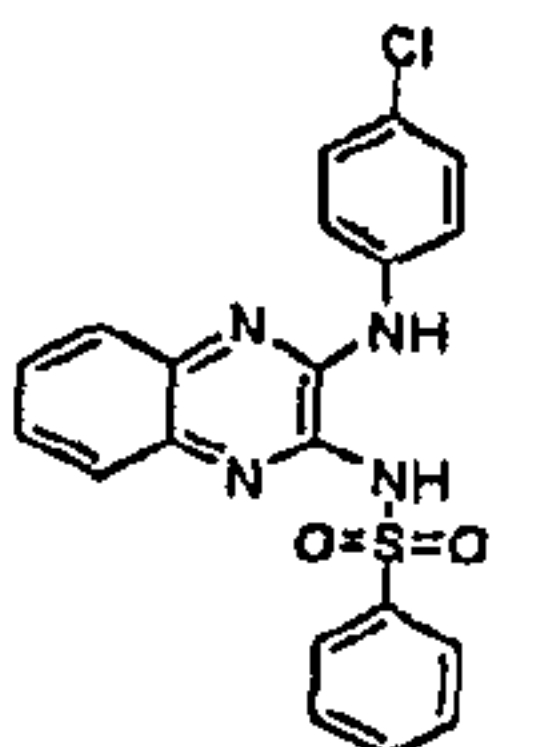
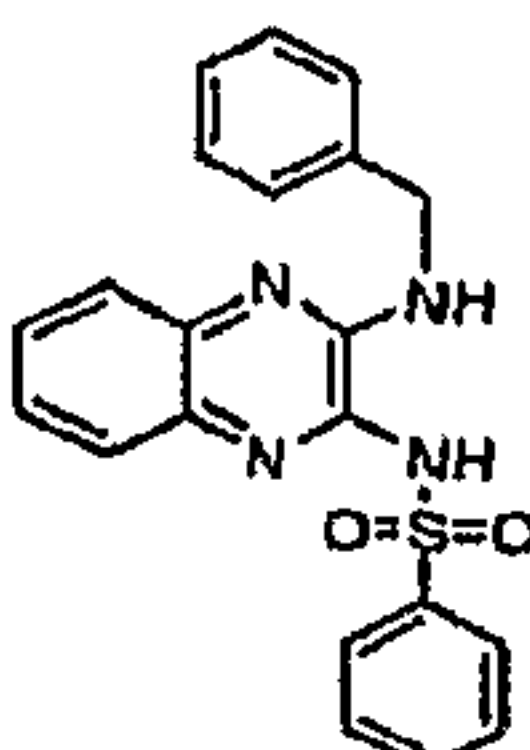
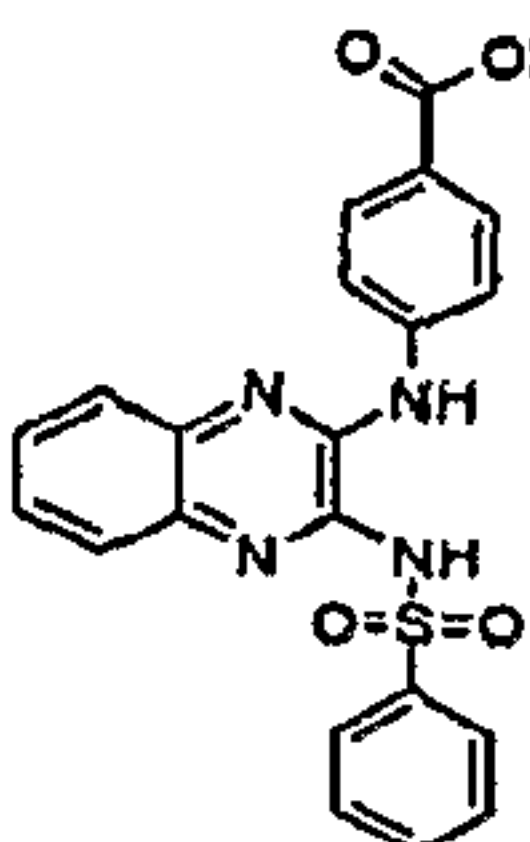
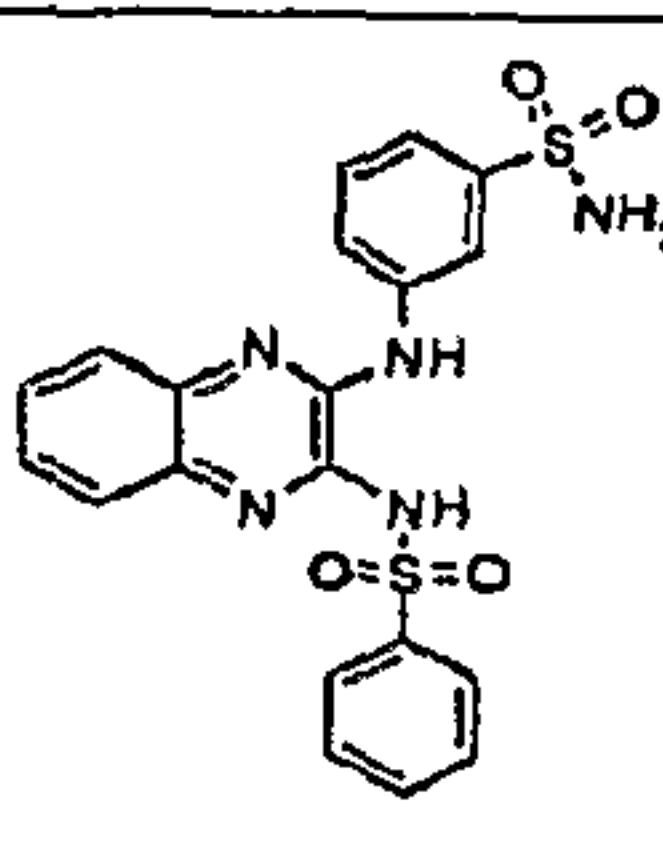
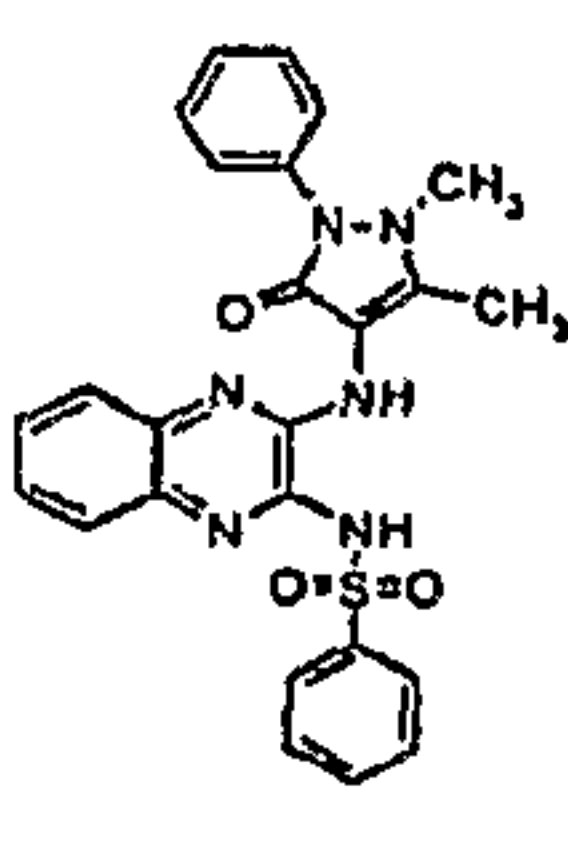
Table 1		
Cpd. No.	Structure	IUPAC Name
30		5,12-bis[(4-methylphenyl) sulfonyl] - 5,12-dihydroquinoxalino[2,3-b]quinoxaline
31		<i>N</i> -[3-(phenylamino)quinoxalin-2-yl]benzenesulfonamide
32		<i>N</i> -{3-[(4-chlorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
33		<i>N</i> -{3-[(phenylmethyl)amino]quinoxalin-2-yl}benzenesulfonamide
34		4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)benzoic acid
35		3-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)benzenesulfonamide
36		<i>N</i> -{3-[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1 <i>H</i> -pyrazol-4-yl)amino]quinoxalin-2-yl}benzenesulfonamide

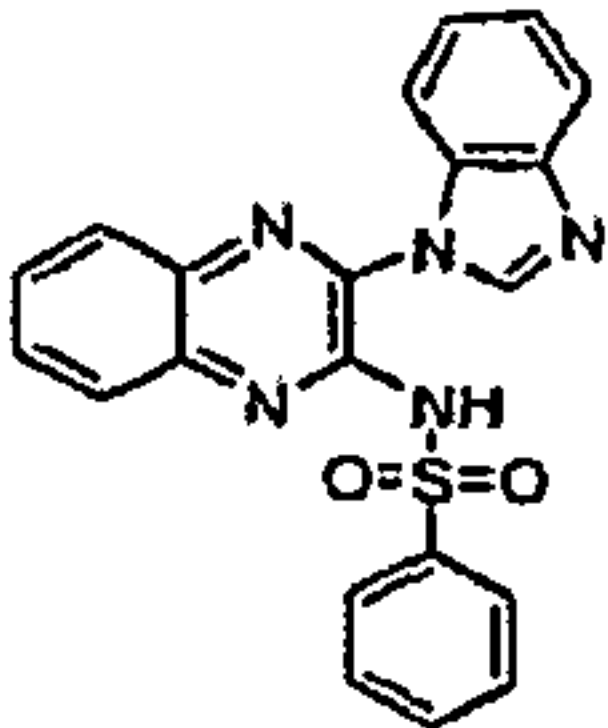
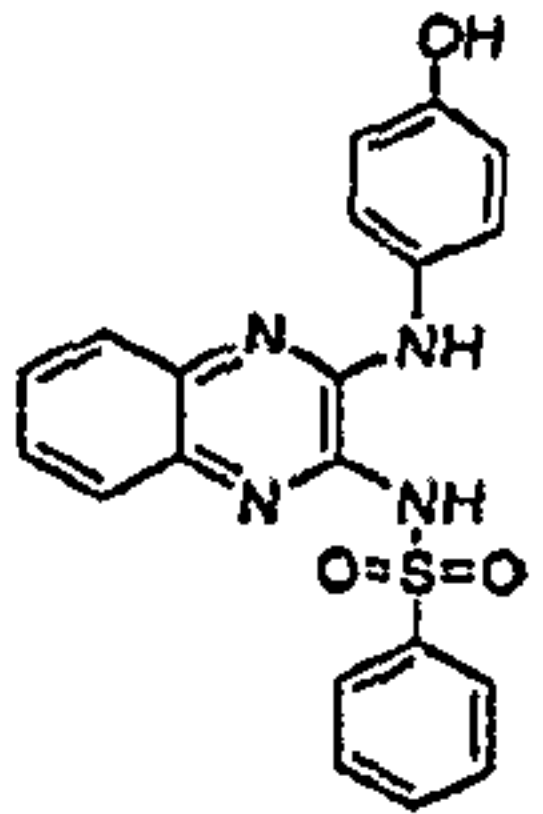
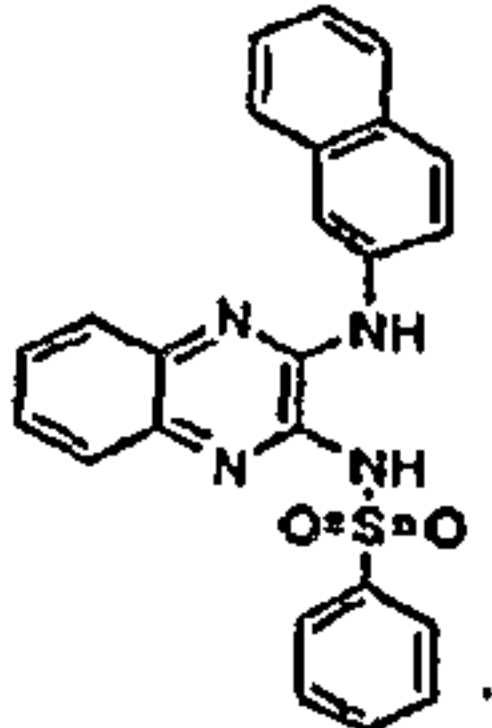
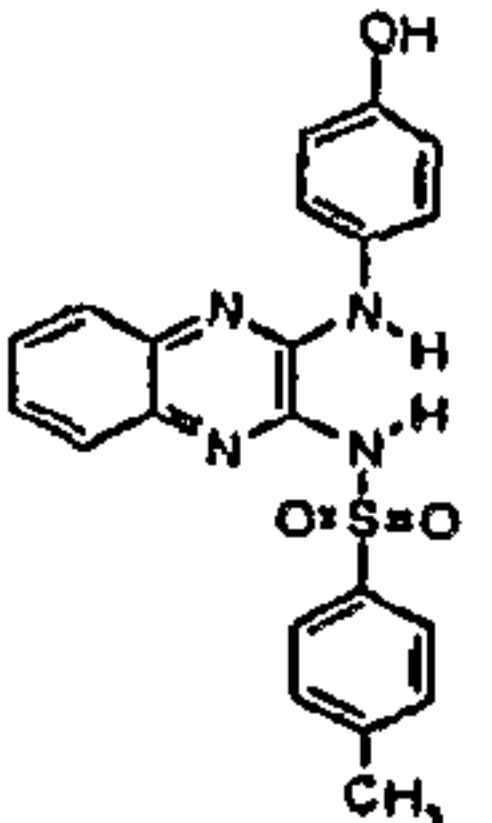
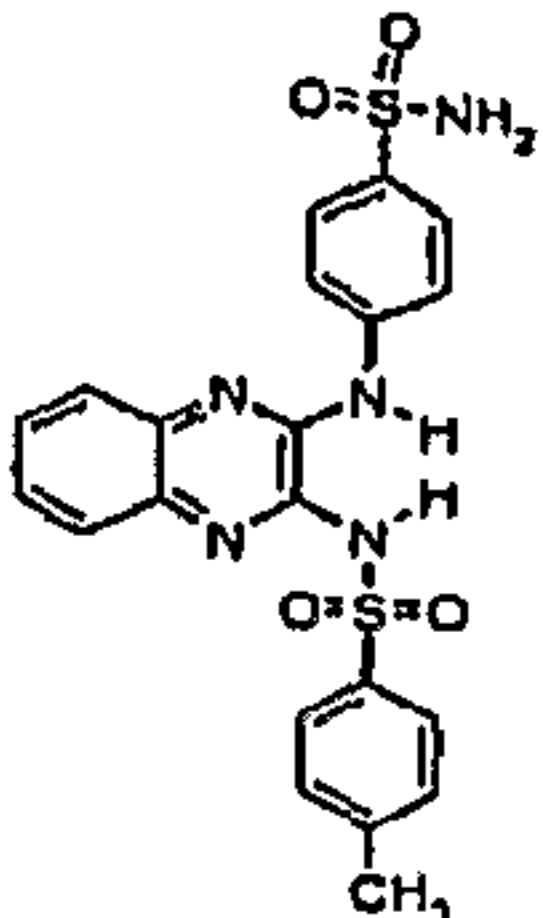
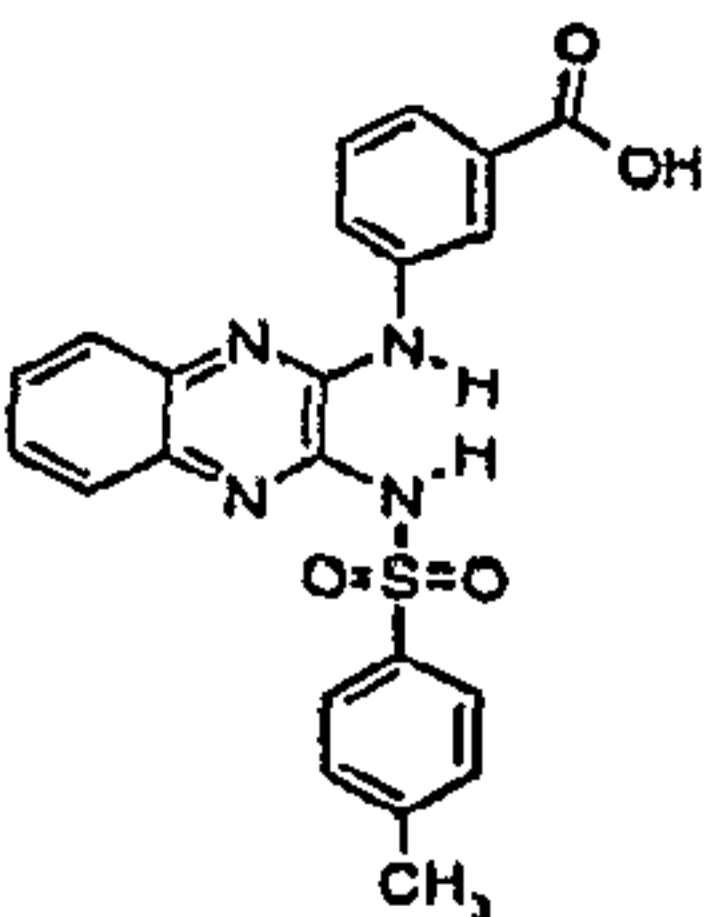
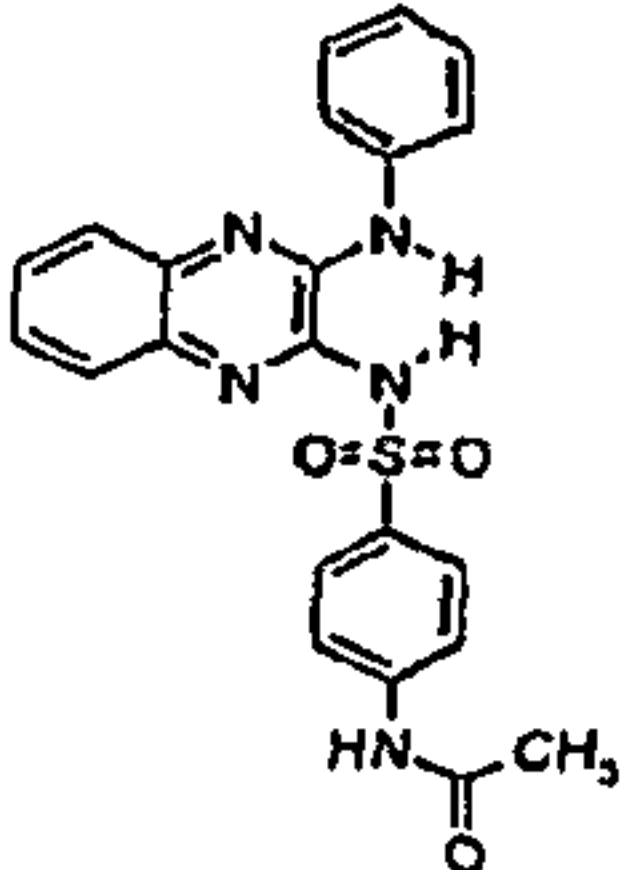
Table 1		
Cpd. No.	Structure	IUPAC Name
37		<i>N</i> -[3-(1 <i>H</i> -benzimidazol-1-yl)quinoxalin-2-yl]benzenesulfonamide
38		<i>N</i> -{3-[(4-hydroxyphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
39		<i>N</i> -[3-(naphthalen-2-ylamino)quinoxalin-2-yl]benzenesulfonamide
40		<i>N</i> -{3-[(4-hydroxyphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
41		<i>N</i> -(3-{[4-(aminosulfonyl)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide
42		3-[(3-{[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
43		<i>N</i> -[4-({[3-(phenylamino)quinoxalin-2-yl]amino}sulfonyl)phenyl]acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
44		<i>N</i> -(4-{{(3-([4-(aminosulfonyl)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
45		<i>N</i> -[4-({[3-(naphthalen-1-ylamino)quinoxalin-2-yl]amino]sulfonyl}phenyl)acetamide
46		<i>N</i> -{4-[(3-([4-(4-methylphenyl)sulfonyl]amino)quinoxalin-2-yl)amino]phenyl}acetamide
47		<i>N</i> -(3-{{[3-(aminosulfonyl)phenyl]amino}quinoxalin-2-yl)-4-bromobenzenesulfonamide
48		<i>N</i> -{3-[(3-hydroxyphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
49		<i>N</i> -{3-[(2-ethylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
50		4-chloro- <i>N</i> -(3-{{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
51		4-chloro- <i>N</i> -(3-{{[2-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

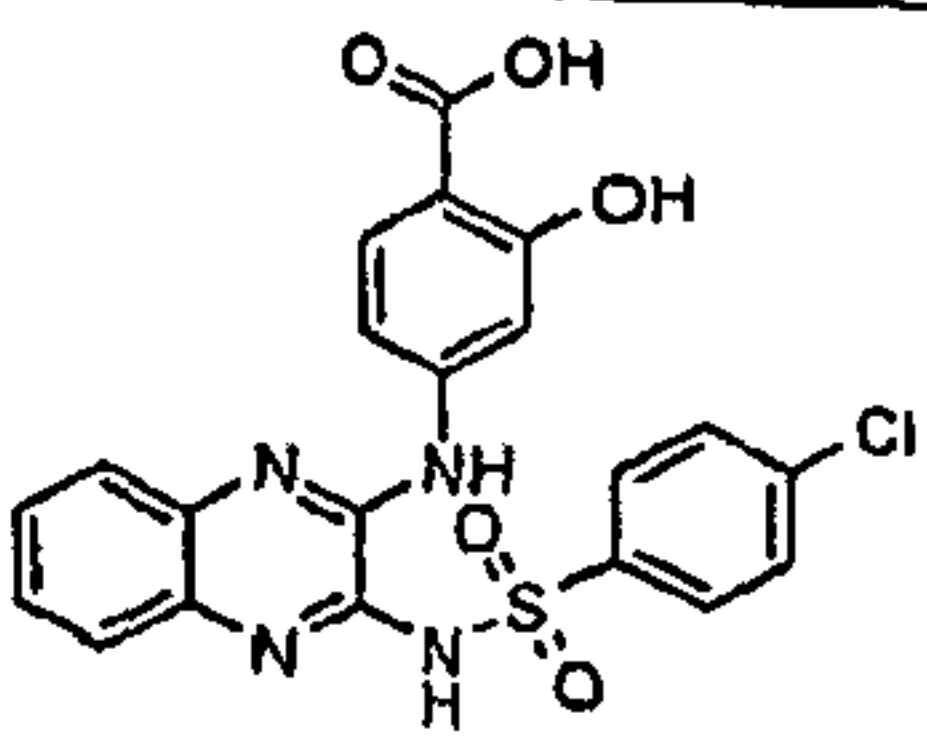
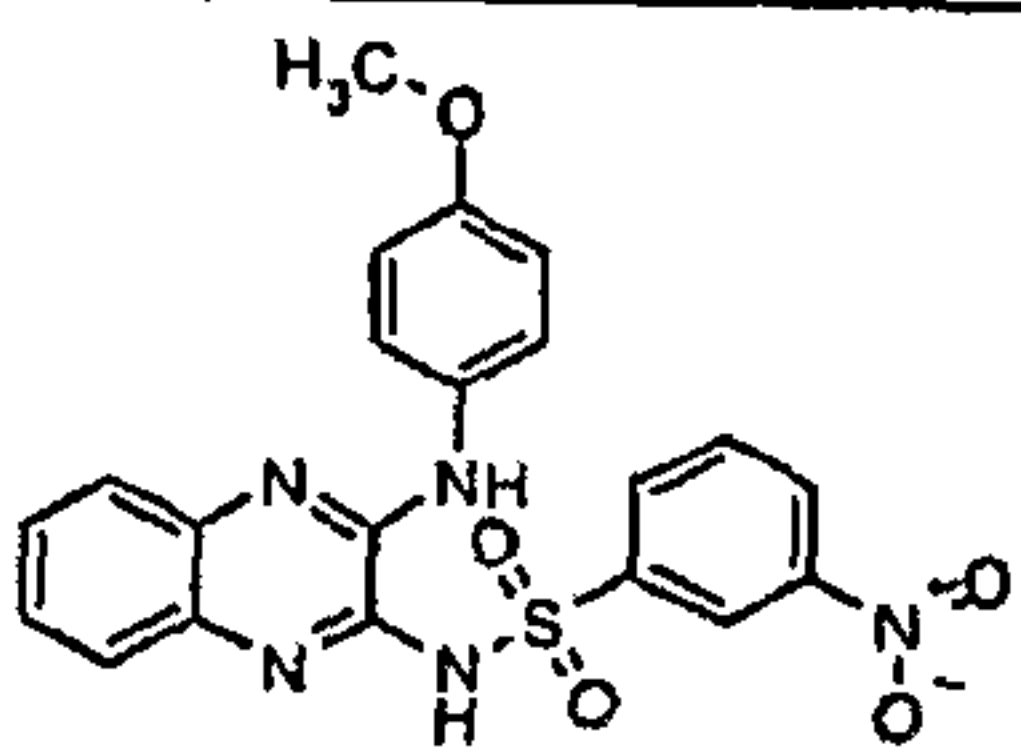
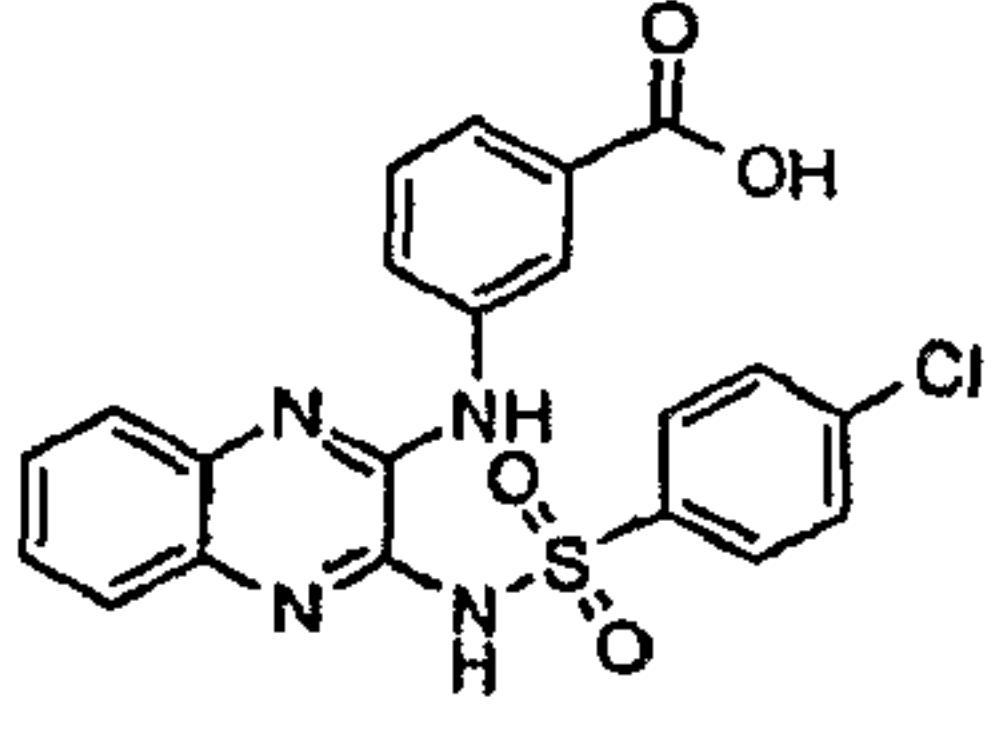
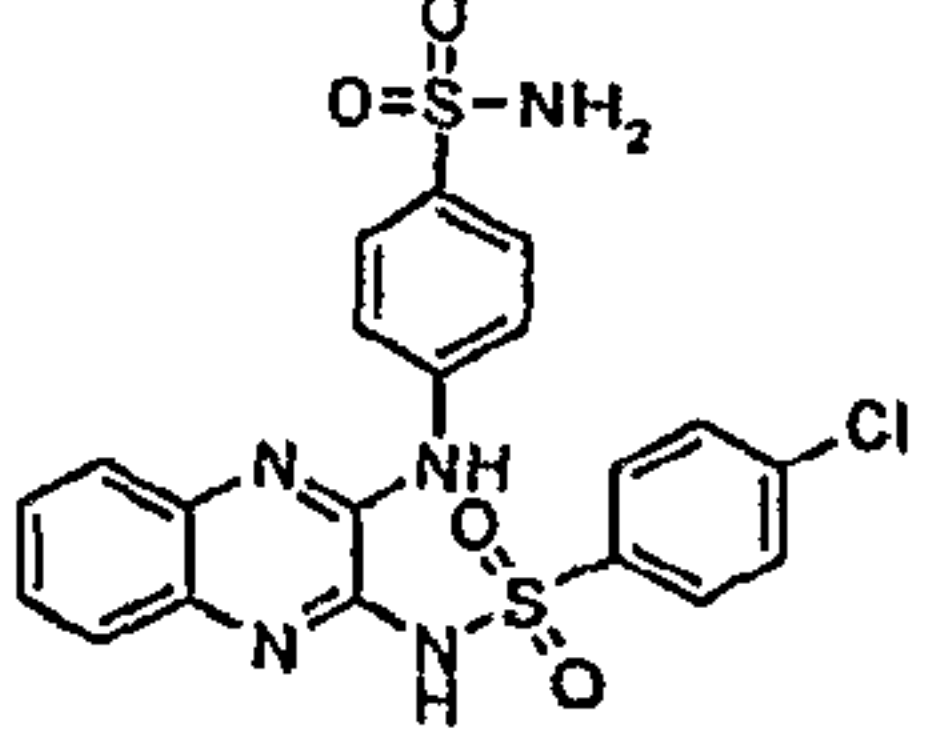
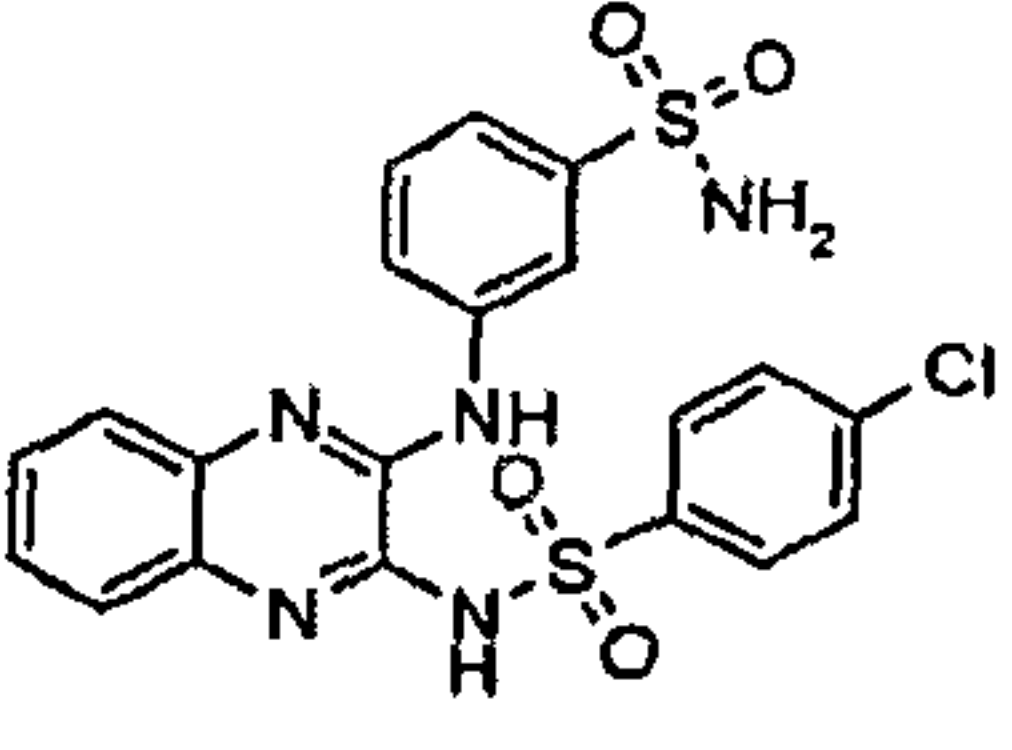
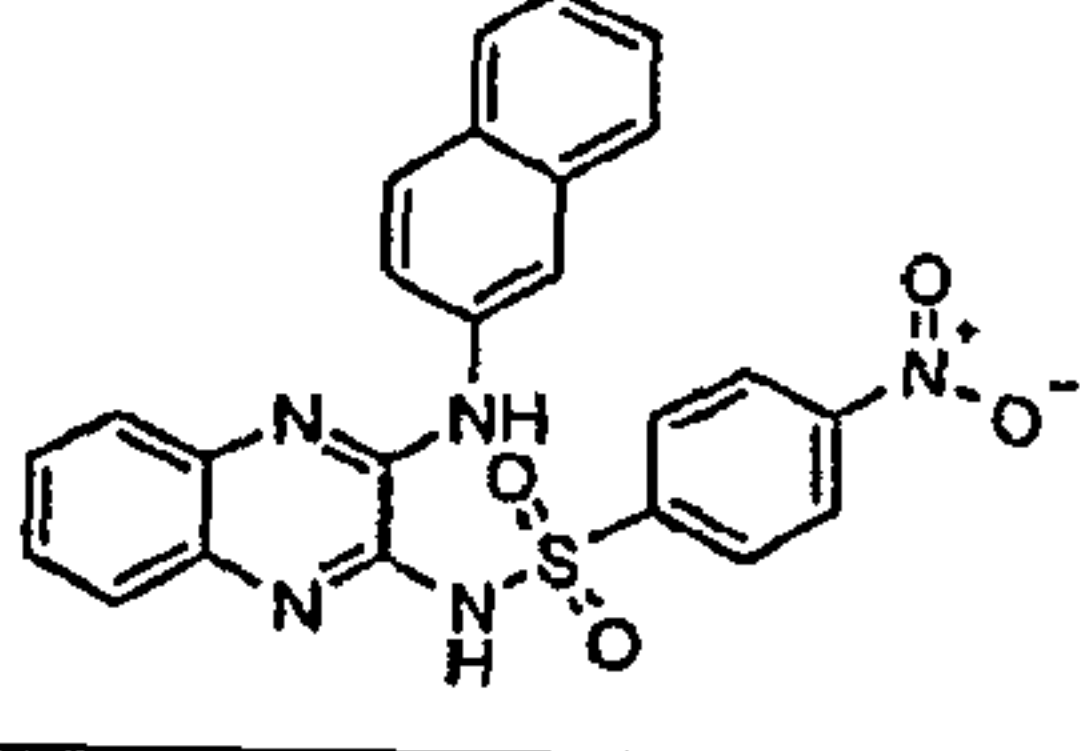
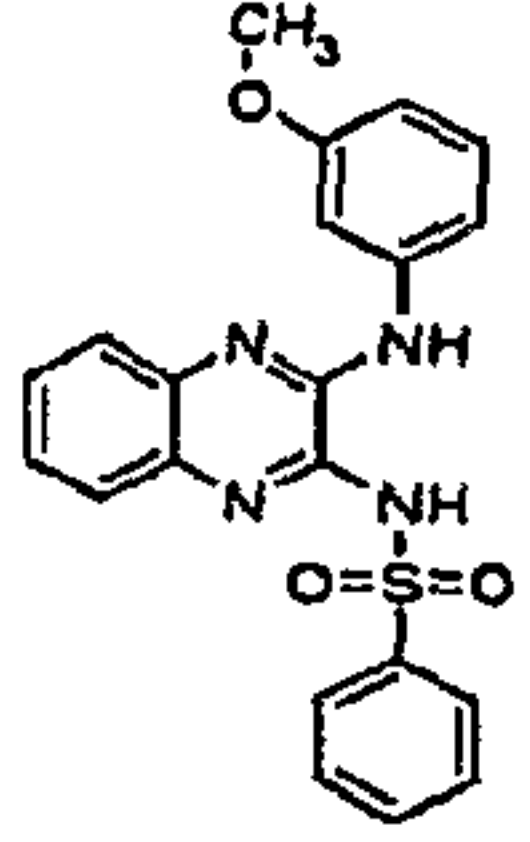
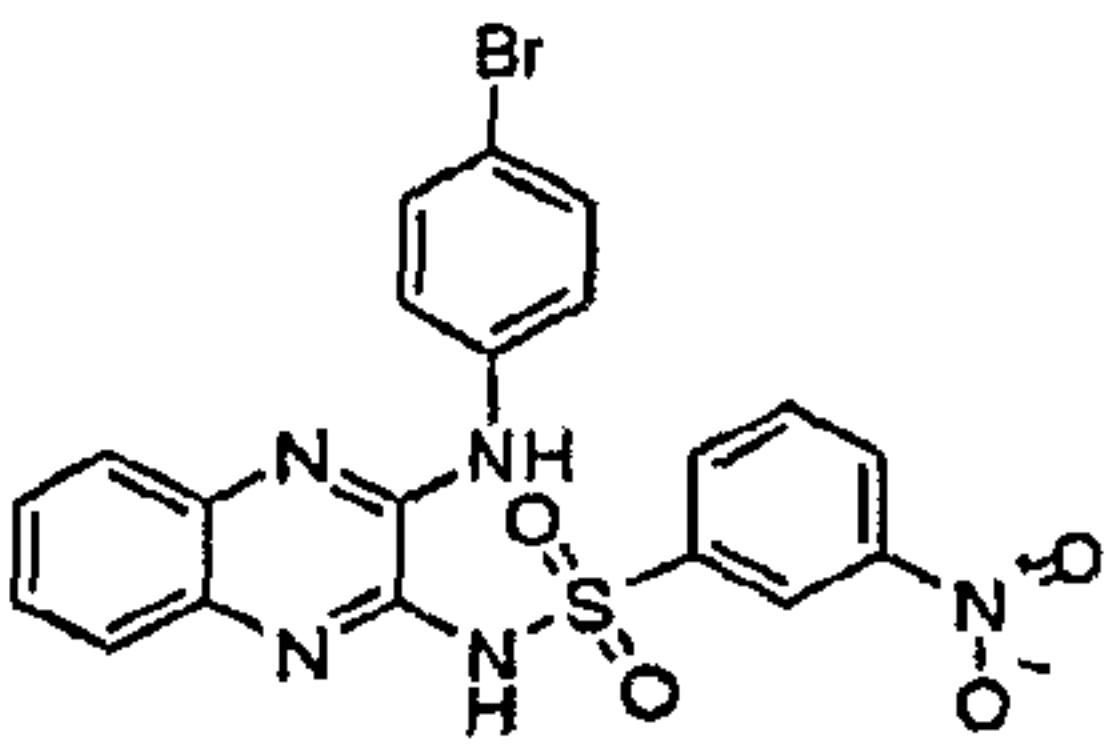
Table 1		
Cpd. No.	Structure	IUPAC Name
52		4-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-2-hydroxybenzoic acid
53		<i>N</i> -(3-{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
54		3-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
55		<i>N</i> -(3-{[4-(aminosulfonyl)phenyl]amino}quinoxalin-2-yl)-4-chlorobenzenesulfonamide
56		<i>N</i> -(3-{[3-(aminosulfonyl)phenyl]amino}quinoxalin-2-yl)-4-chlorobenzenesulfonamide
57		<i>N</i> -[3-(naphthalen-2-ylamino)quinoxalin-2-yl]-4-nitrobenzenesulfonamide
58		<i>N</i> -(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
59		<i>N</i> -{3-[(4-bromophenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
60		3-[(3-[(4-nitrophenyl)sulfonyl]amino)quinoxalin-2-yl]amino]benzoic acid
61		4-nitro-N-[3-(phenylamino)quinoxalin-2-yl]benzenesulfonamide
62		4-chloro-N-[3-(phenylamino)quinoxalin-2-yl]benzenesulfonamide
63		3-nitro-N-[3-(phenylamino)quinoxalin-2-yl]benzenesulfonamide
64		4-[(3-[(4-nitrophenyl)sulfonyl]amino)quinoxalin-2-yl]amino]benzoic acid
65		N-[3-(naphthalen-2-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
66		4-methyl-N-(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
67		N-(3-{[3-chloro-4-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
68		<i>N</i> -{3-[(3-chloro-4-fluorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
69		methyl 2-chloro-5-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl} amino)benzoate
70		4-chloro- <i>N</i> -{3-[(3-hydroxyphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
71		4-methyl- <i>N</i> -[6-methyl-3-(phenylamino)quinoxalin-2-yl] benzenesulfonamide
72		<i>N</i> -{4-[(3-[(4-methylphenyl)amino]quinoxalin-2-yl} amino)sulfonyl]phenyl} acetamide
73		1-methylethyl 4-[(3-[(4-chlorophenyl)sulfonyl]amino)-7-methylquinoxalin-2-yl]amino]benzoate
74		<i>N</i> -(3-{[2-(methyloxy)phenyl]amino} quinoxalin-2-yl) benzenesulfonamide

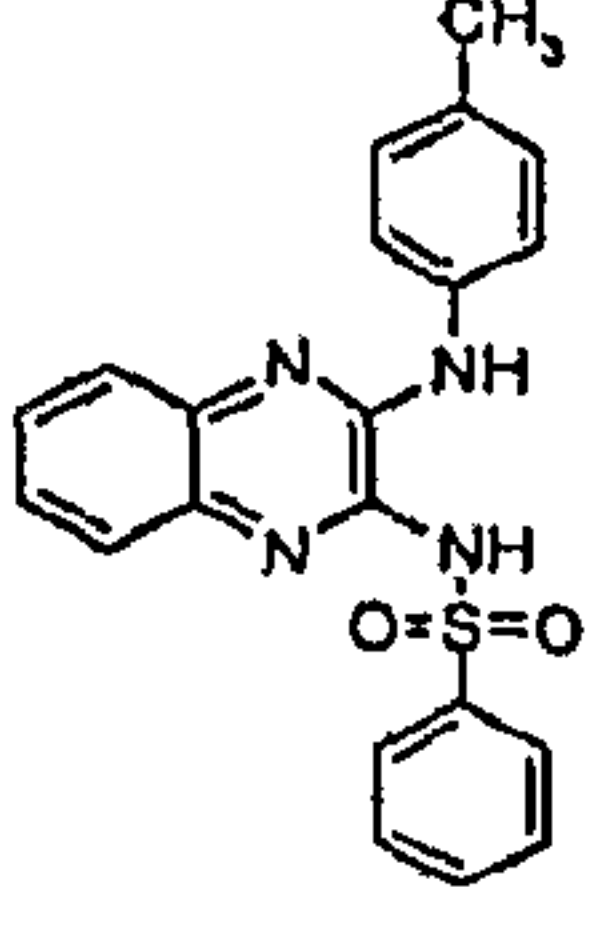
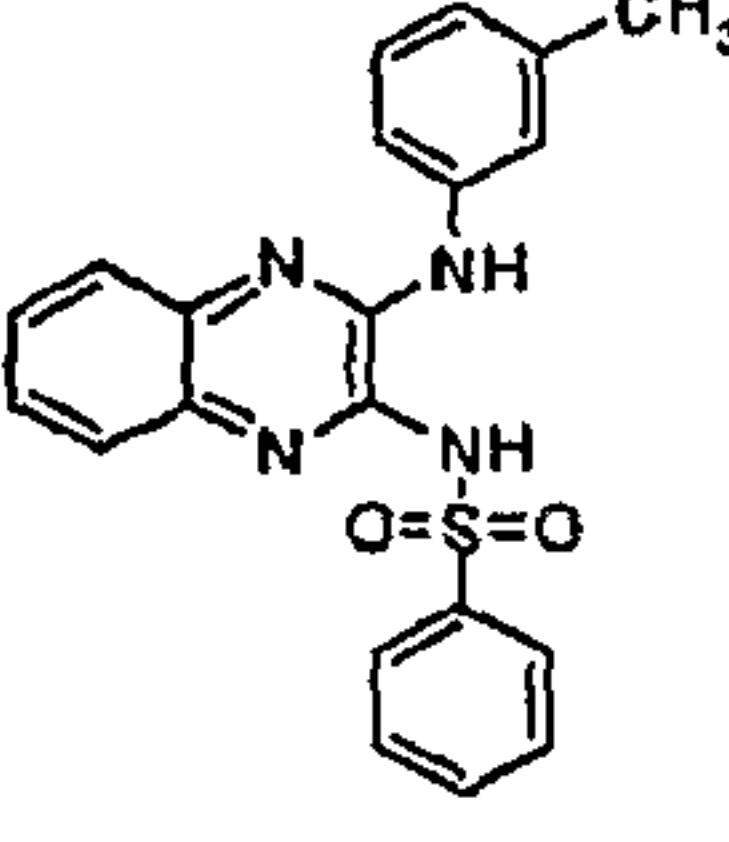
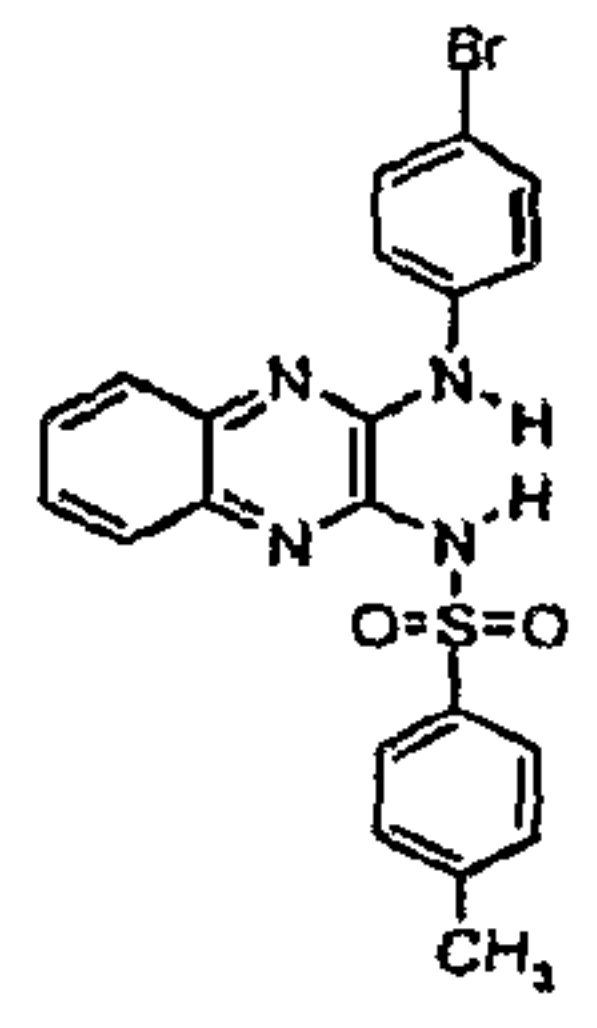
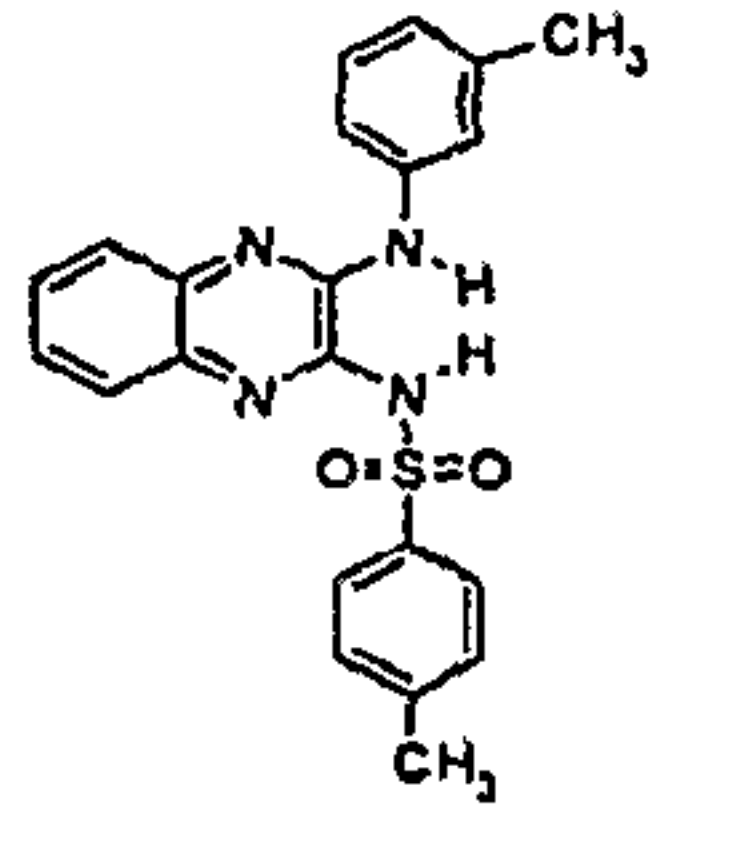
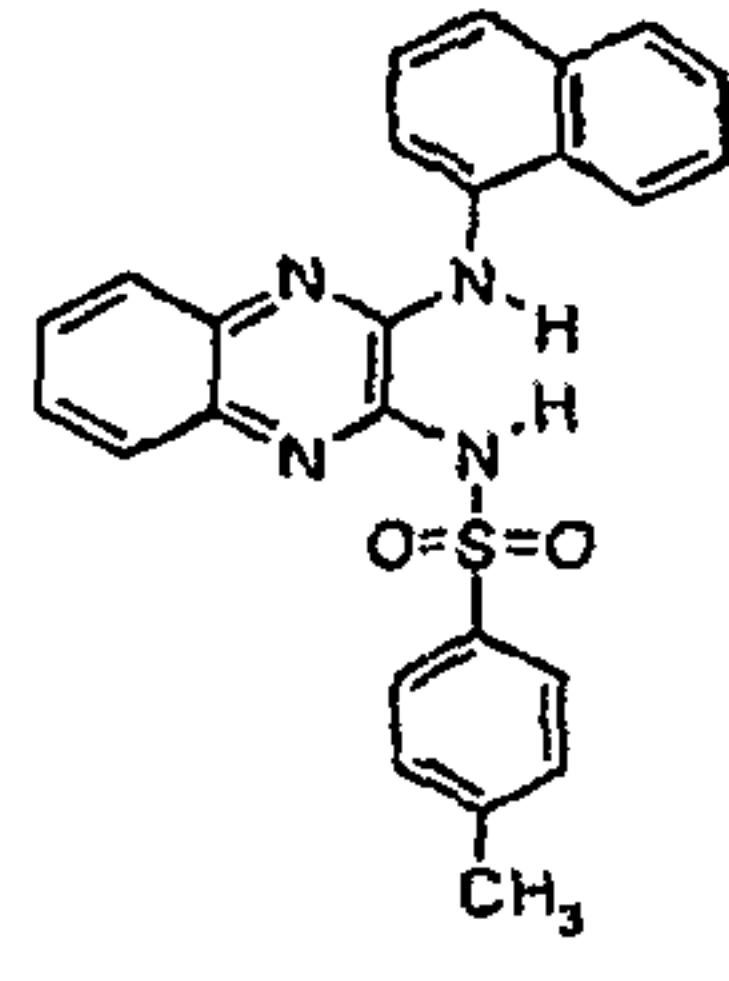
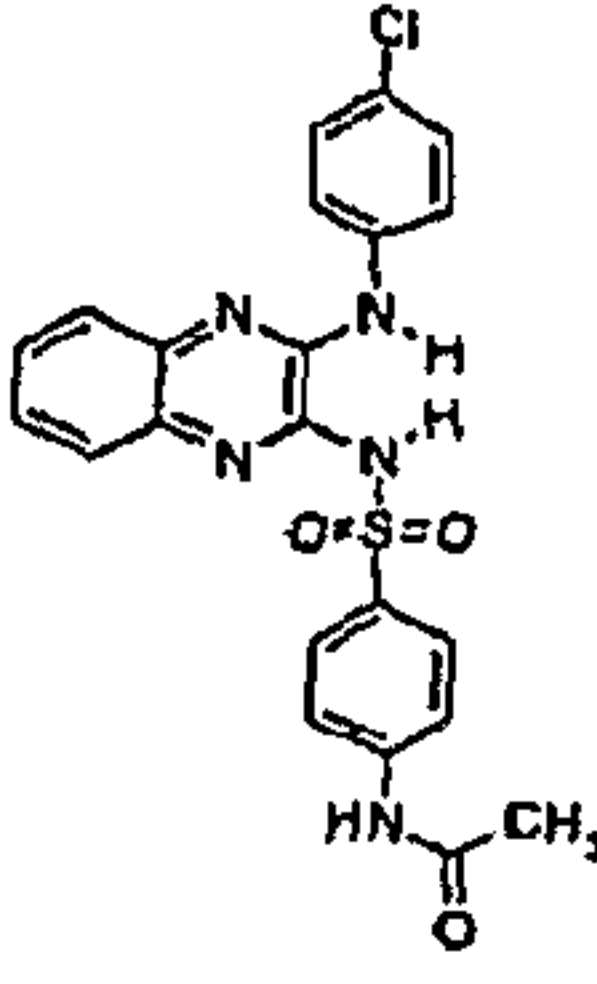
Table 1		
Cpd. No.	Structure	IUPAC Name
75		<i>N</i> -{3-[(4-methylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
76		<i>N</i> -{3-[(3-methylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
77		<i>N</i> -{3-[(4-bromophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
78		4-methyl- <i>N</i> -{3-[(3-methylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
79		4-methyl- <i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl] benzenesulfonamide
80		<i>N</i> -{4-[(3-[(4-chlorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl} acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
81		<i>N</i> -(4-{{(3-{{3-(aminosulfonyl)phenyl}amino}quinoxalin-2-yl)amino}sulfonyl}phenyl)acetamide
82		4-methyl- <i>N</i> -{3-[(phenylmethyl)amino]quinoxalin-2-yl}benzenesulfonamide
83		4-[(3-{{(4-bromophenyl)sulfonyl}amino}quinoxalin-2-yl)amino]-2-hydroxybenzoic acid
84		4-bromo- <i>N</i> -{3-[(4-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
85		4-bromo- <i>N</i> -{3-[(3-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
86		<i>N</i> -{4-[(3-[(2-hydroxyethyl)amino]quinoxalin-2-yl)amino)sulfonyl}phenyl}acetamide
87		4-bromo- <i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl]benzenesulfonamide
88		<i>N</i> -(3-{{3-(trifluoromethyl)phenyl}amino}quinoxalin-2-yl)benzenesulfonamide

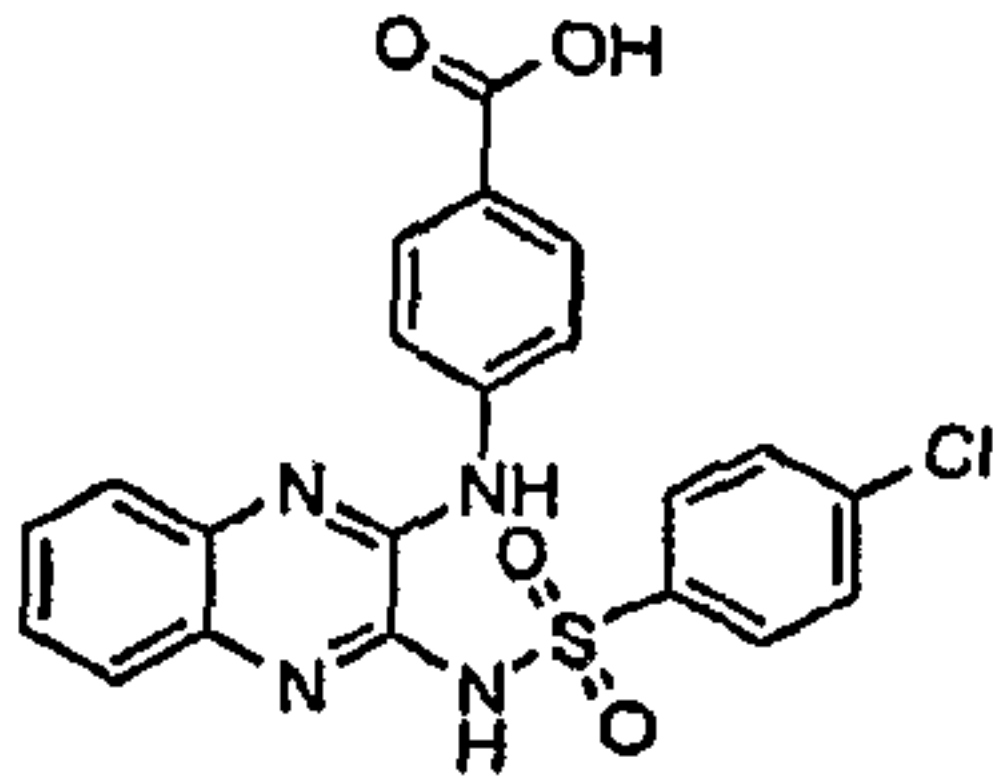
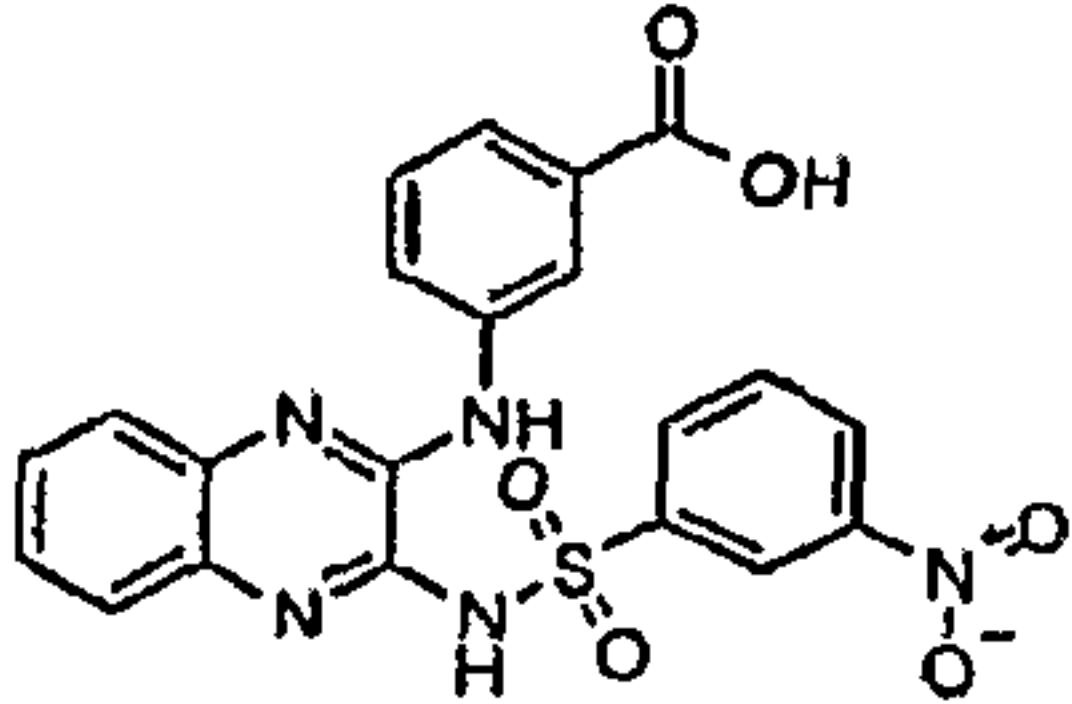
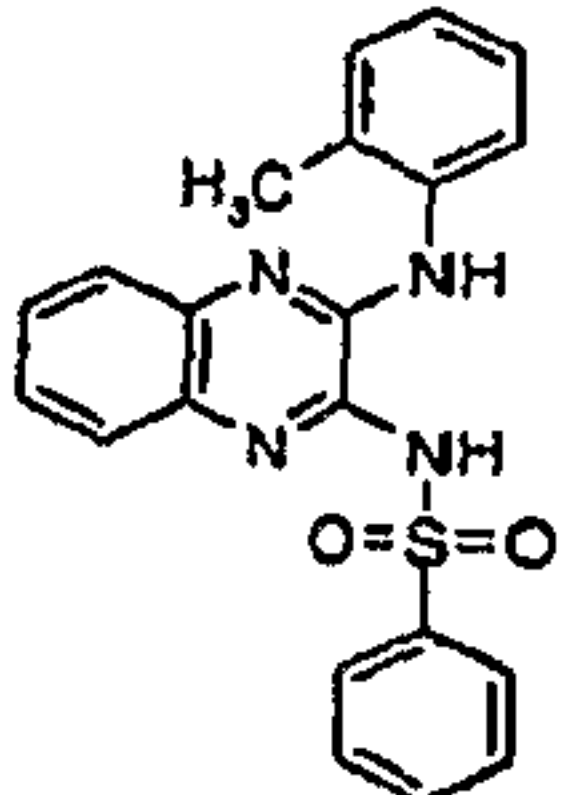
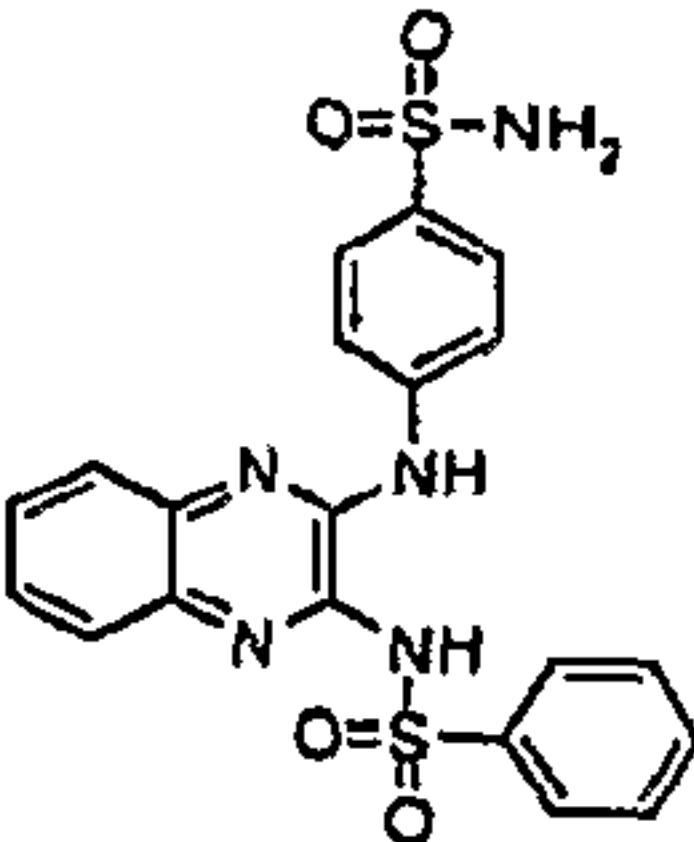
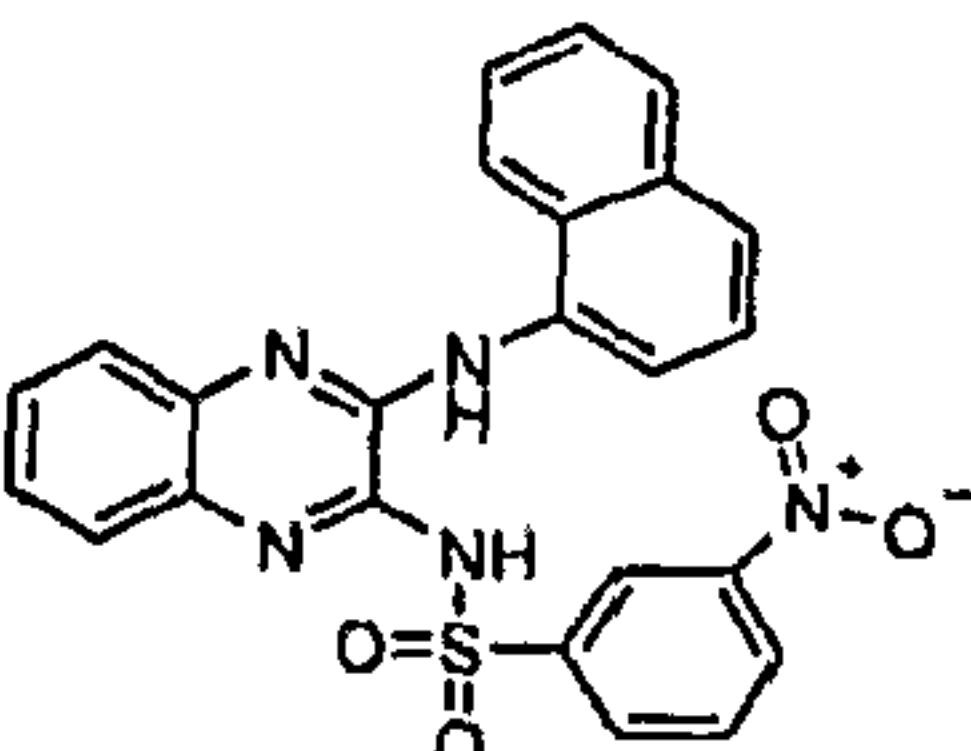
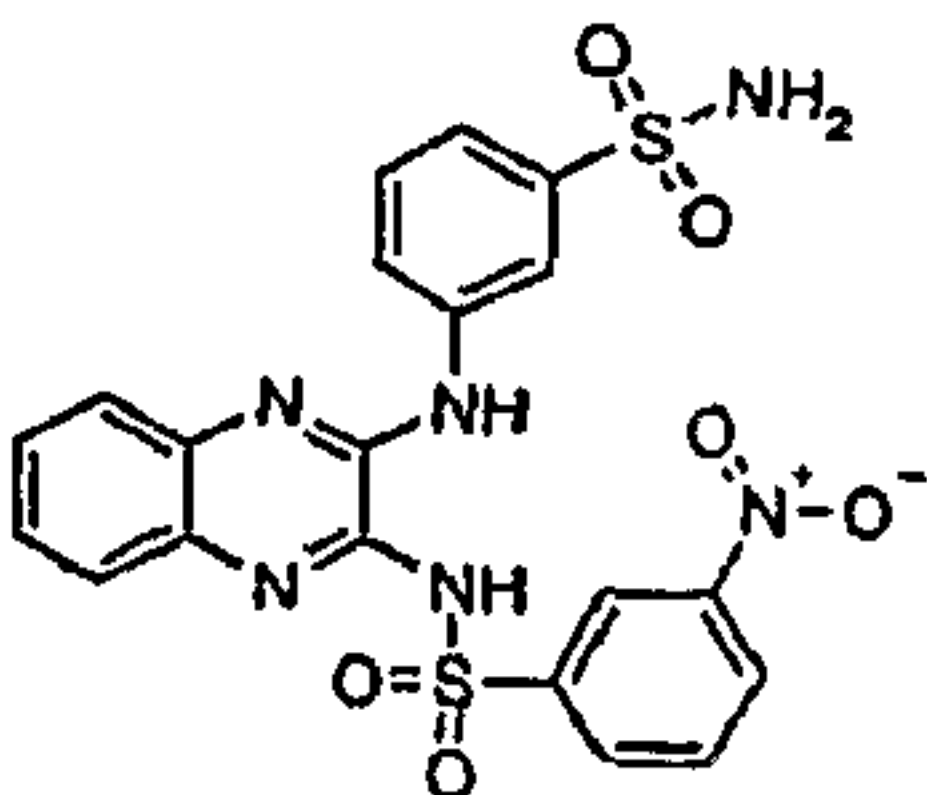
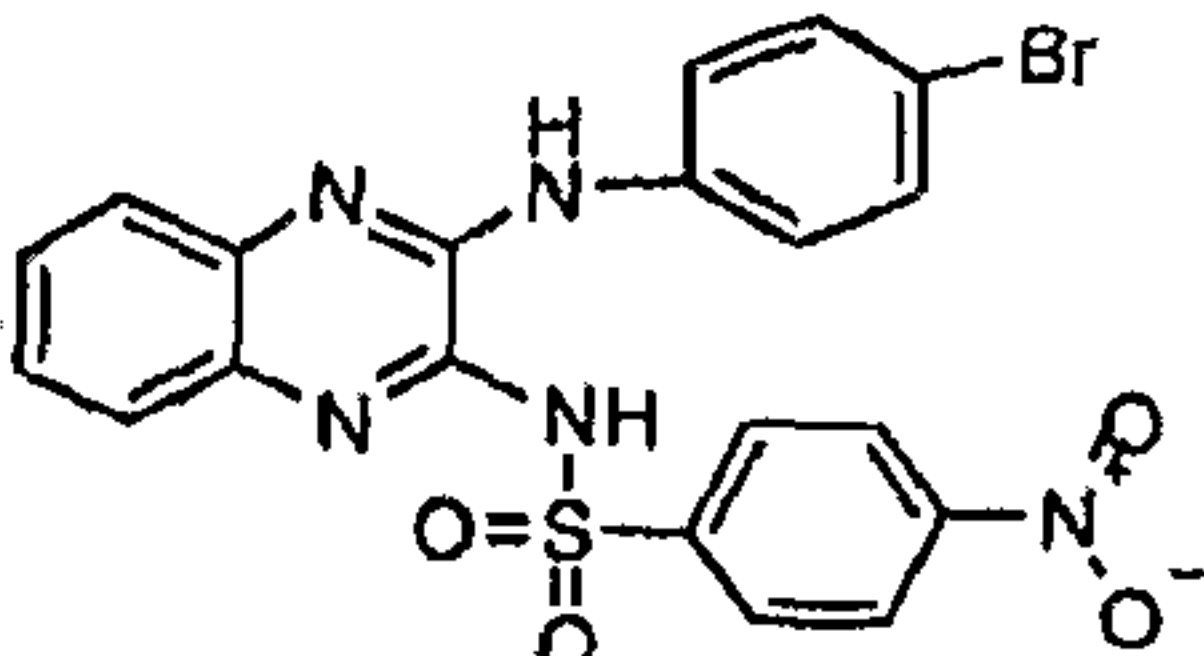
Table 1		
Cpd. No.	Structure	IUPAC Name
89		4-[(3-[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
90		3-[(3-[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
91		<i>N</i> -{3-[(2-methylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
92		4-[(3-[(phenylsulfonyl)amino]quinoxalin-2-yl)amino]benzenesulfonamide
93		<i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
94		<i>N</i> -(3-[(3-(aminosulfonyl)phenyl)amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
95		<i>N</i> -{3-[(4-bromophenyl)amino]quinoxalin-2-yl}-4-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
96		4-chloro- <i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl]benzenesulfonamide
97		<i>N</i> -{4-[(3-[(phenylmethyl)amino]quinoxalin-2-yl)amino]sulfonyl}phenyl}acetamide
98		<i>N</i> -[4-({3-(butylamino)quinoxalin-2-yl}amino)sulfonyl]phenyl}acetamide
99		<i>N</i> -[3-(butylamino)quinoxalin-2-yl]-4-methylbenzenesulfonamide
100		<i>N</i> -[3-(cyclohexylamino)quinoxalin-2-yl]benzenesulfonamide
101		1-(phenylsulfonyl)-3-[4-(pyrrolidin-1-ylsulfonyl)phenyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline

Table 1		
Cpd. No.	Structure	IUPAC Name
102		1-(phenylsulfonyl)-3-[4-(piperidin-1-ylsulfonyl)phenyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline
103		2,5-dichloro- <i>N</i> -[3-(3,4-dihydroquinolin-1(2 <i>H</i>)-yl)quinoxalin-2-yl]benzenesulfonamide
104		ethyl 2-[(3-[(4-methylphenyl)sulfonyl]amino)quinoxalin-2-yl]amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
105		2,5-dichloro- <i>N</i> -{3-[(2-morpholin-4-ylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
106		<i>N</i> -{4-[(3-[(3-methylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide
107		4-chloro- <i>N</i> -{3-[(3-chloro-4-piperidin-1-ylphenyl)amino]-6-methylquinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
108		3-nitro- <i>N</i> -[3-(quinolin-6-ylamino)quinoxalin-2-yl]benzenesulfonamide
109		butyl <i>N</i> -{{4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)phenyl}carbonyl}glycinate
110		4-nitro- <i>N</i> -(3-{[3-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
111		<i>N</i> -[4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)phenyl]acetamide
112		<i>N</i> -{3-[(3-{[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide
113		ethyl 3,3,3-trifluoro-2-hydroxy-2-{4-[(3-{[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}propanoate
114		<i>N</i> -{3-[(4-{[(2,6-dimethylpyrimidin-4-yl)amino]sulfonyl}phenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
115		4-chloro- <i>N</i> -{3-[(3,4-dimethylphenyl)amino]-6-methylquinoxalin-2-yl}benzenesulfonamide
116		4-chloro- <i>N</i> -(6-methyl-3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
117		butyl 4-[(3-{[(4-chlorophenyl)sulfonyl]amino}-7-methylquinoxalin-2-yl)amino]benzoate
118		4-chloro- <i>N</i> -{3-[(3-chloro-4-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
119		1-methylethyl 4-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoate
120		<i>N</i> -{3-[(2,5-dimethylphenyl)amino]-6-nitroquinoxalin-2-yl}-4-methylbenzenesulfonamide
121		<i>N</i> -[3-(cyclohexylamino)-6-nitroquinoxalin-2-yl]-4-methylbenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
122		<i>N</i> -{3-[(2,4-dimethylphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
123		<i>N</i> -(3-{[4-(ethyloxy)phenyl]amino}-6-methylquinoxalin-2-yl)-4-methylbenzenesulfonamide
124		3-({3-[(4-hydroxy(oxido)amino)phenyl]sulfonyl}amino)quinoxalin-2-yl)amino)benzoic acid
125		<i>N</i> -{[4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)phenyl]carbonyl}glycine
126		4-chloro- <i>N</i> -[3-({2-[(difluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide
127		<i>N</i> -{3-[(3-{[(4-chlorophenyl)sulfonyl]amino}-7-methylquinoxalin-2-yl)amino]phenyl}acetamide
128		4-chloro- <i>N</i> -{3-[(3,5-dimethyl-1 <i>H</i> -pyrazol-4-yl)amino]-6-methylquinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
129		4-bromo- <i>N</i> -{3-[(4'-nitrobiphenyl-3-yl)amino]quinoxalin-2-yl} benzenesulfonamide
130		4-bromo- <i>N</i> -{3-[(2-chlorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
131		<i>N</i> -{3-[(4-butylphenyl)amino]-6-methylquinoxalin-2-yl}-4-chlorobenzenesulfonamide
132		<i>N</i> -{4-[(3-{[(4-chlorophenyl)sulfonyl]amino}-7-methylquinoxalin-2-yl)amino]phenyl}acetamide
133		4-chloro- <i>N</i> -{6-methyl-3-[(2-oxo-2,3-dihydro-1 <i>H</i> -benzimidazol-5-yl)amino]quinoxalin-2-yl} benzenesulfonamide
134		propyl 4-[(3-{[(4-chlorophenyl)sulfonyl]amino}-7-methylquinoxalin-2-yl)amino]benzoate
135		4-chloro- <i>N</i> -{3-[(4-fluorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
136		<i>N</i> -[4-({[3-(naphthalen-2-ylamino)quinoxalin-2-yl]amino}sulfonyl)phenyl]acetamide
137		4-bromo- <i>N</i> -(3-{[4-(phenylamino)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
138		2-hydroxy-4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)benzoic acid
139		<i>N</i> -(3-{[3-(aminosulfonyl)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide
140		4-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
141		<i>N</i> -(3-{[3-(butyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide
142		<i>N</i> -{3-[(4-fluorophenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
143		4-{{[3-({[4-(acetylamino)phenyl]sulfonyl}amino)quinoxalin-2-yl]amino}-2-hydroxybenzoic acid
144		<i>N</i> -(3-{{[4-(butyloxy)phenyl]amino}quinoxalin-2-yl]-4-chlorobenzenesulfonamide
145		<i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl]-4-nitrobenzenesulfonamide
146		4-[(3-{{[4-bromophenyl]sulfonyl}amino}quinoxalin-2-yl)amino]benzoic acid
147		<i>N</i> -{4-[(3-{{[3-hydroxyphenyl]amino}quinoxalin-2-yl}amino)sulfonyl]phenyl}acetamide
148		3-[(3-{{[4-bromophenyl]sulfonyl}amino}quinoxalin-2-yl)amino]benzoic acid
149		4-bromo- <i>N</i> -(3-{{[3-(butyloxy)phenyl]amino}quinoxalin-2-yl]benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
150		4-bromo- <i>N</i> -(3-{[3-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
151		4-methyl- <i>N</i> -{3-[(4'-nitrobiphenyl-3-yl)amino]quinoxalin-2-yl}benzenesulfonamide
152		4-chloro- <i>N</i> -{3-[(3-fluorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
153		<i>N</i> -{3-[(2-chlorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
154		4-bromo- <i>N</i> -[3-(quinolin-5-ylamino)quinoxalin-2-yl]benzenesulfonamide
155		<i>N</i> -{3-[(3-fluorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide

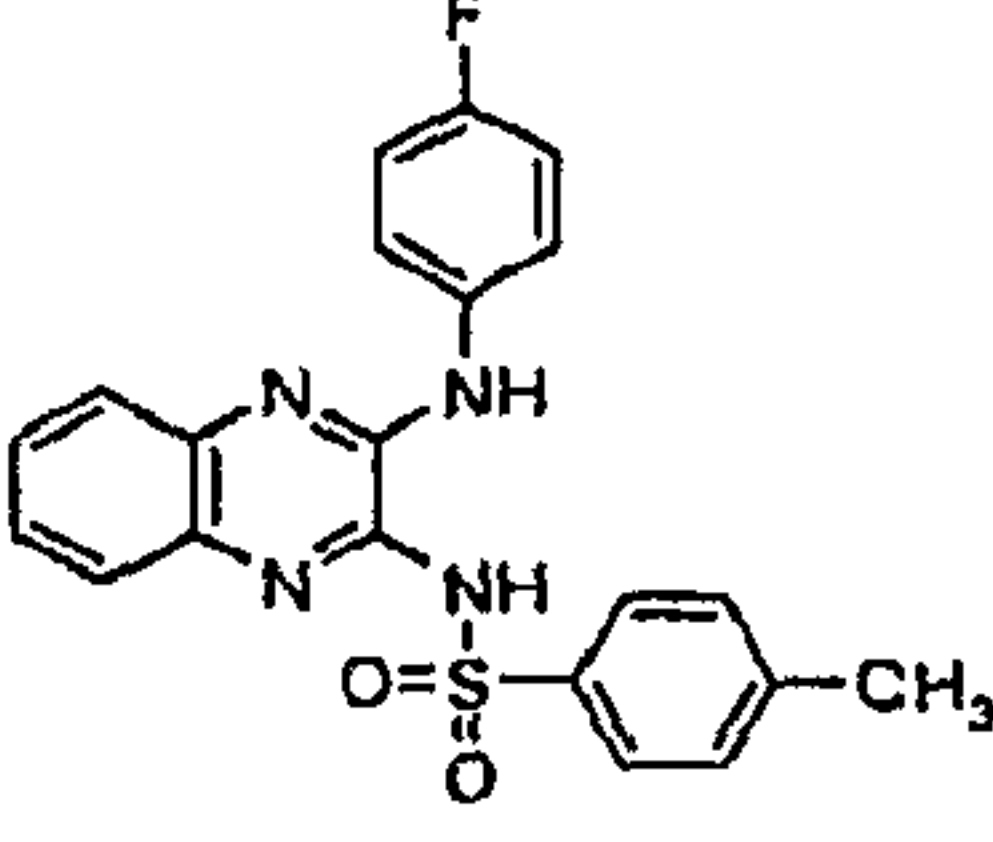
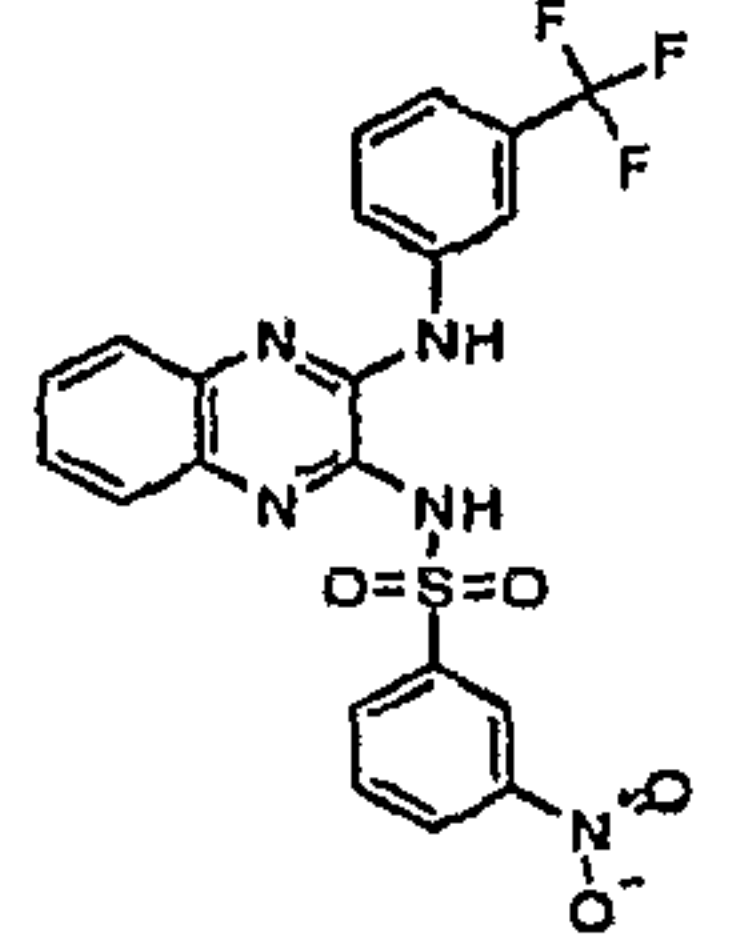
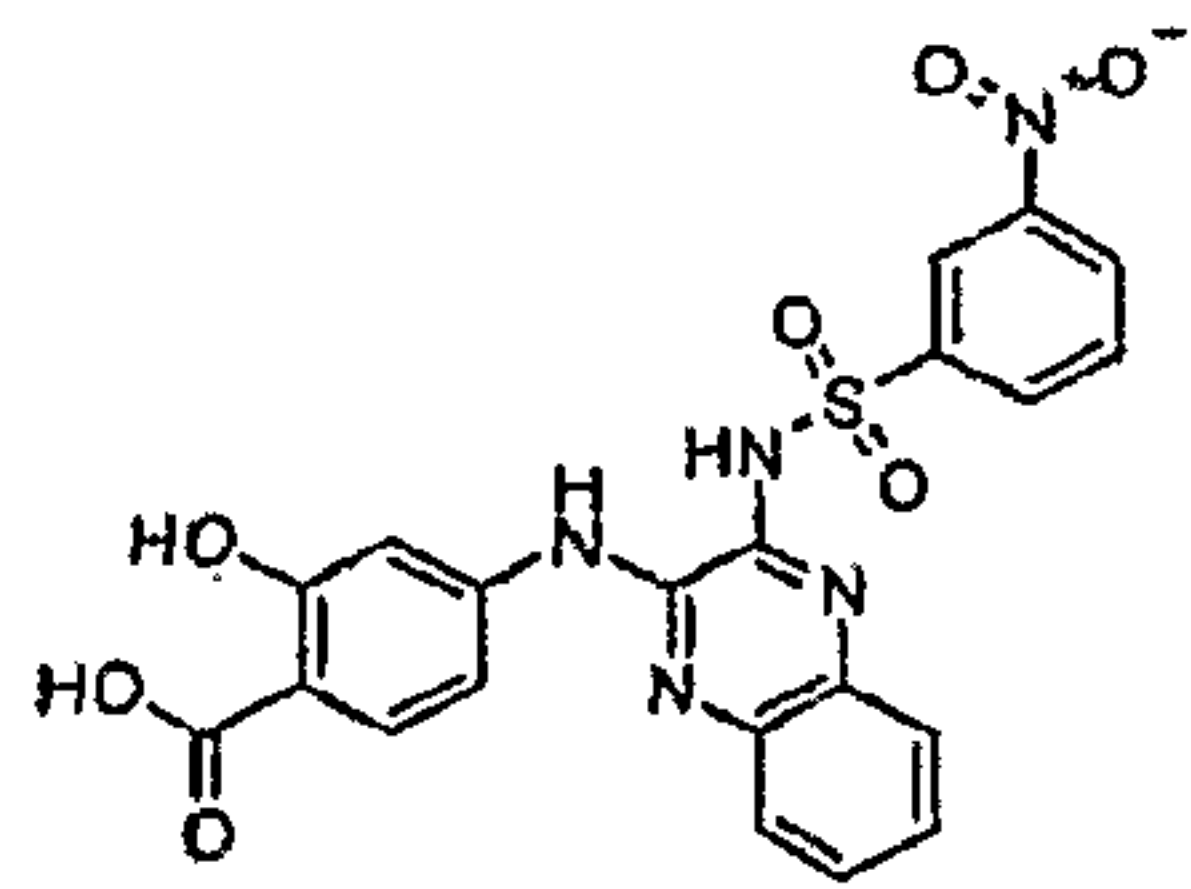
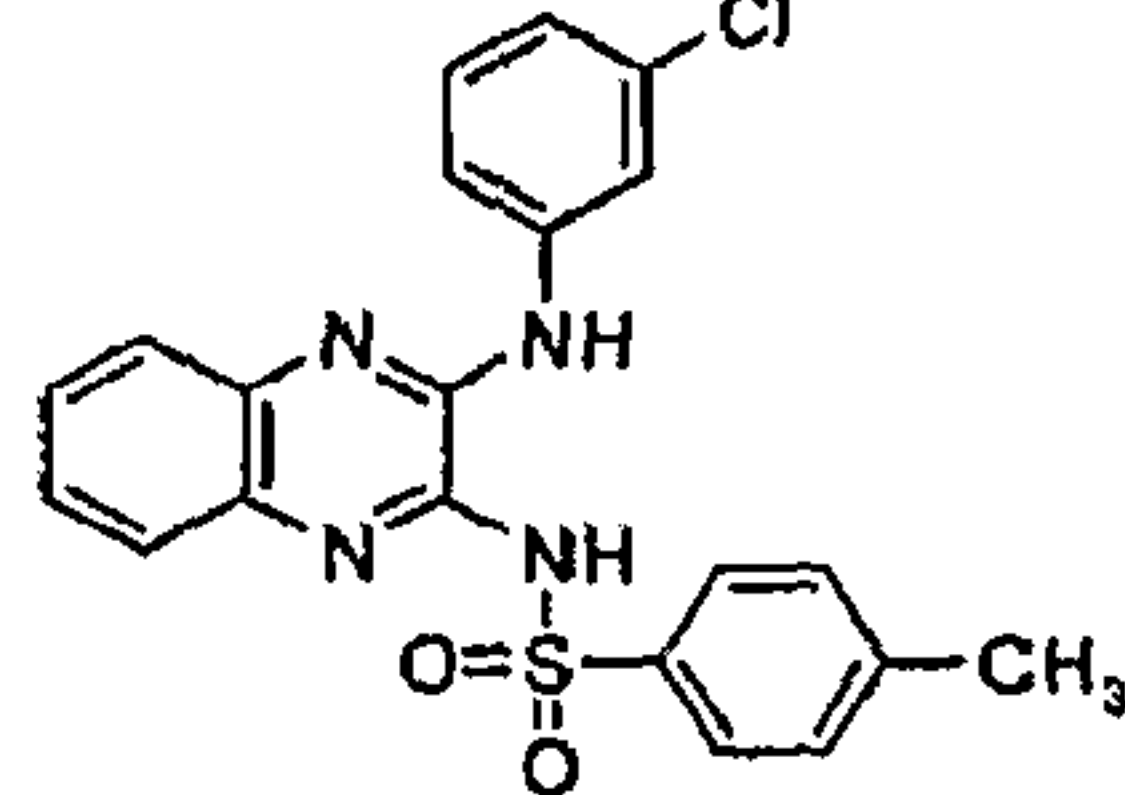
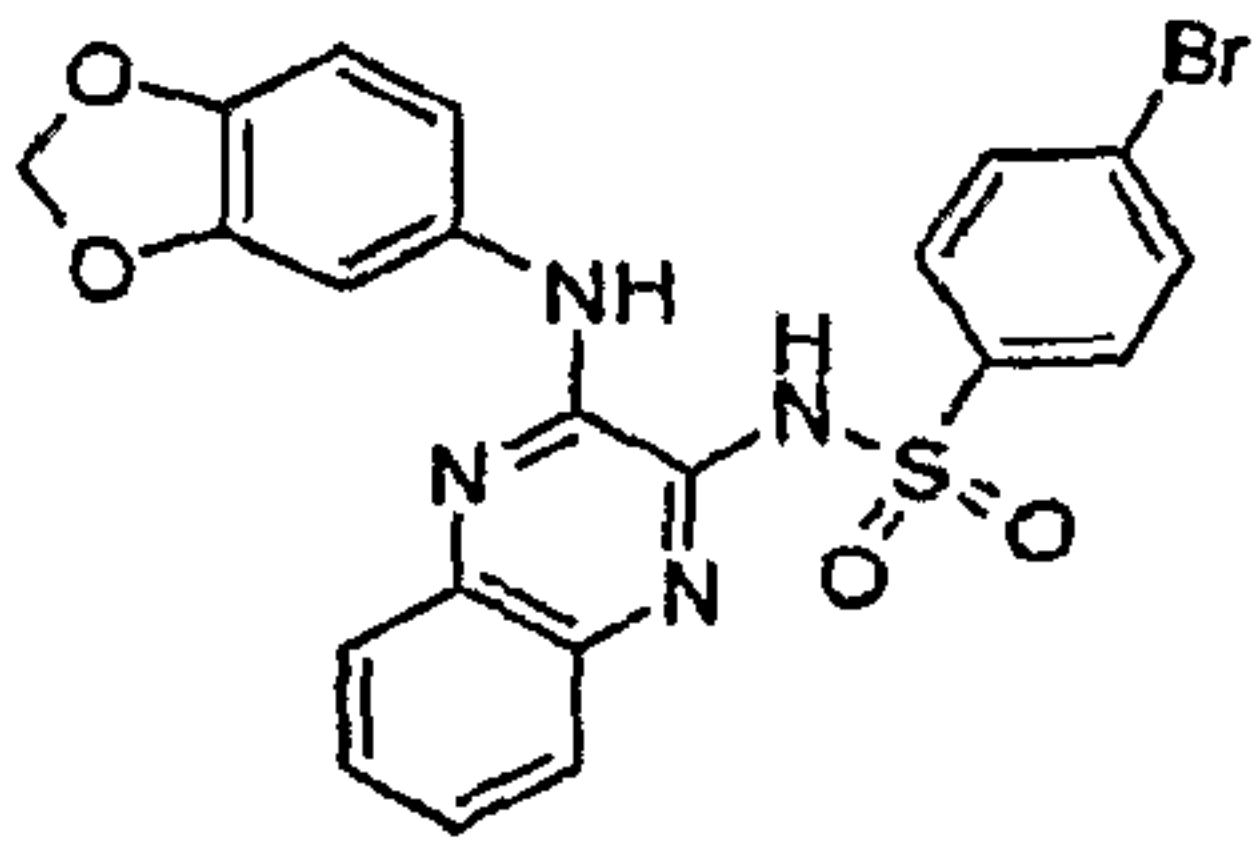
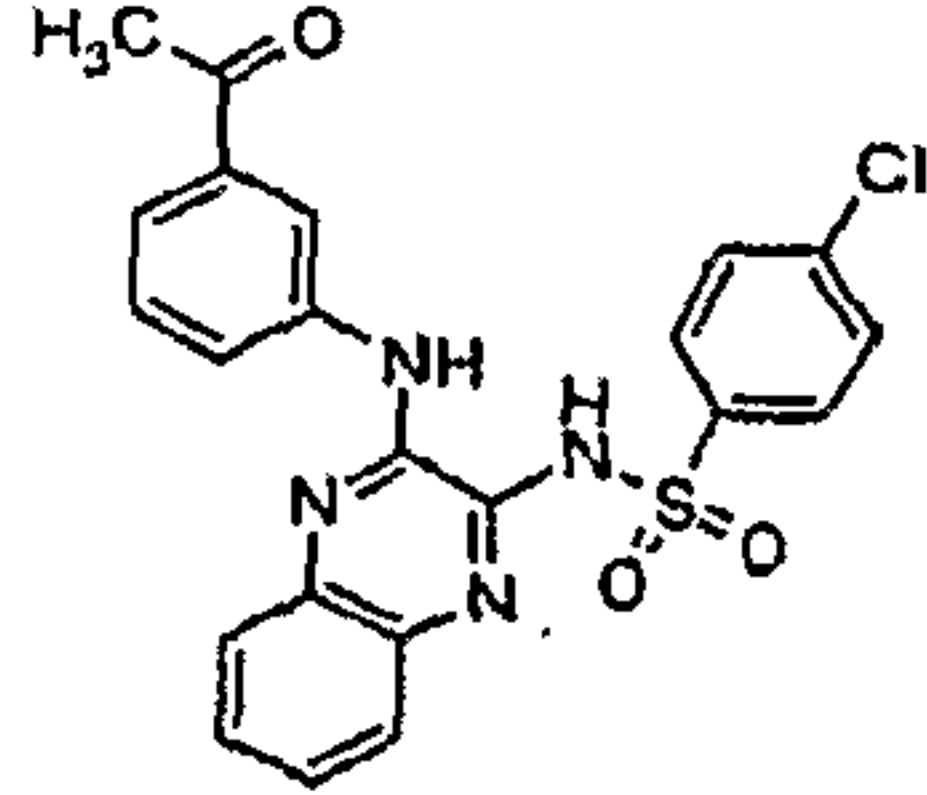
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Cpd. No.	Structure	IUPAC Name
156		<i>N</i> -{3-[(4-fluorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
157		3-nitro- <i>N</i> -(3-{[3-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
158		2-hydroxy-4-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
159		<i>N</i> -{3-[(3-chlorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
160		<i>N</i> -[3-(1,3-benzodioxol-5-ylamino)quinoxalin-2-yl]-4-bromobenzenesulfonamide
161		<i>N</i> -{3-[(3-acetylphenyl)amino]quinoxalin-2-yl}-4-chlorobenzenesulfonamide

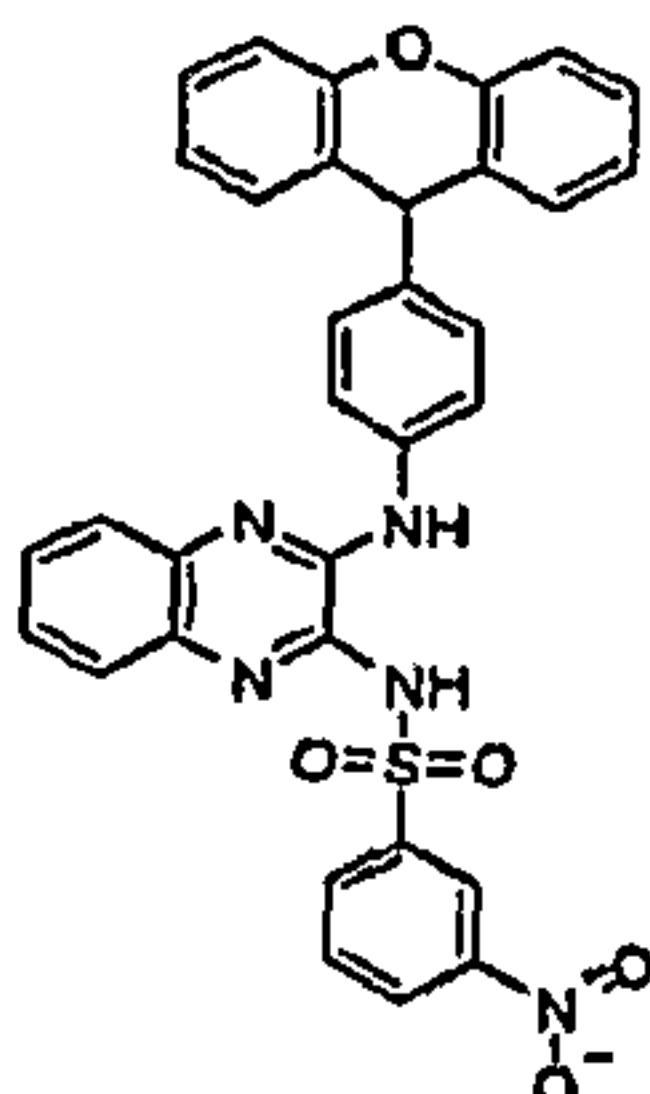
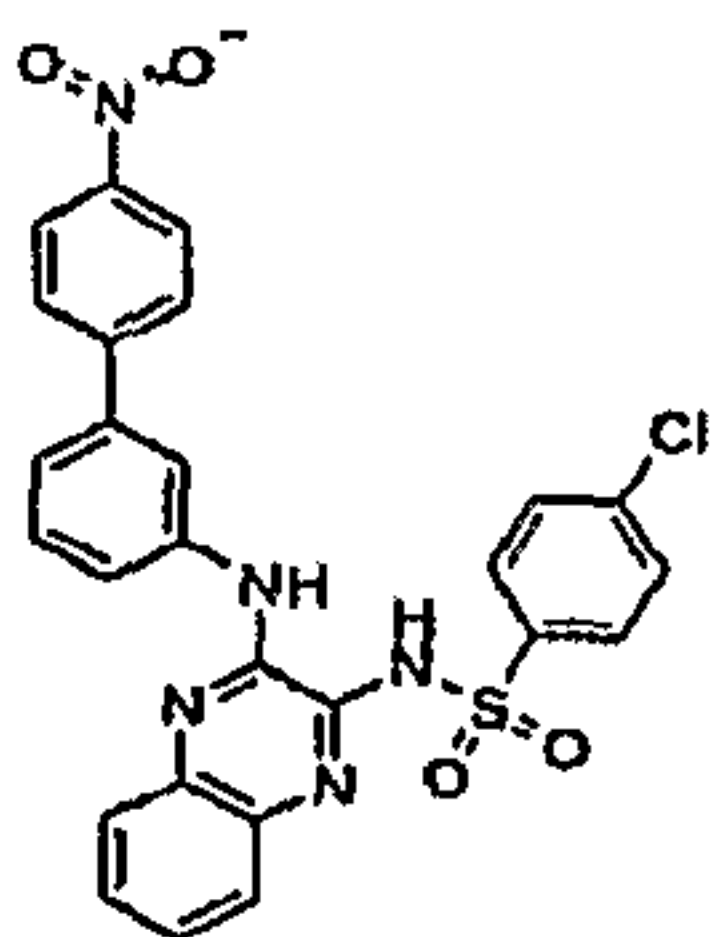
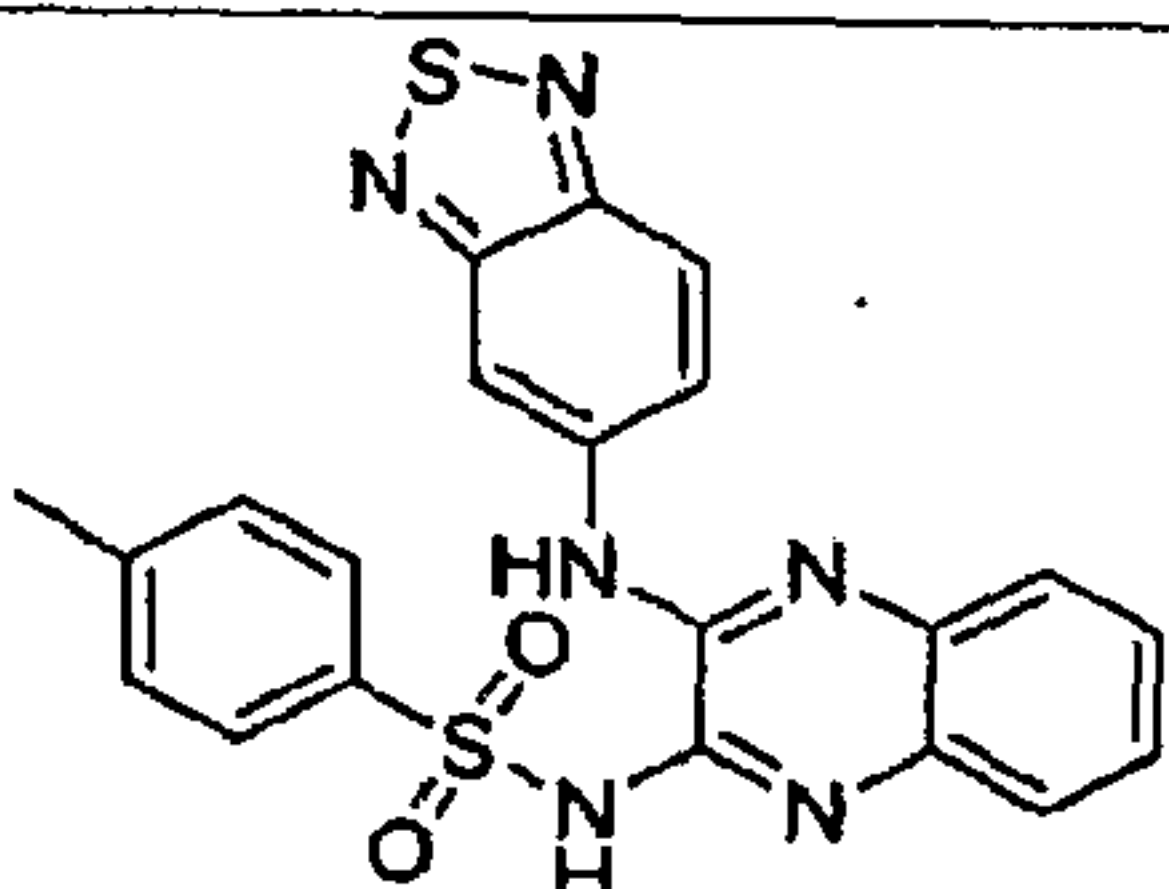
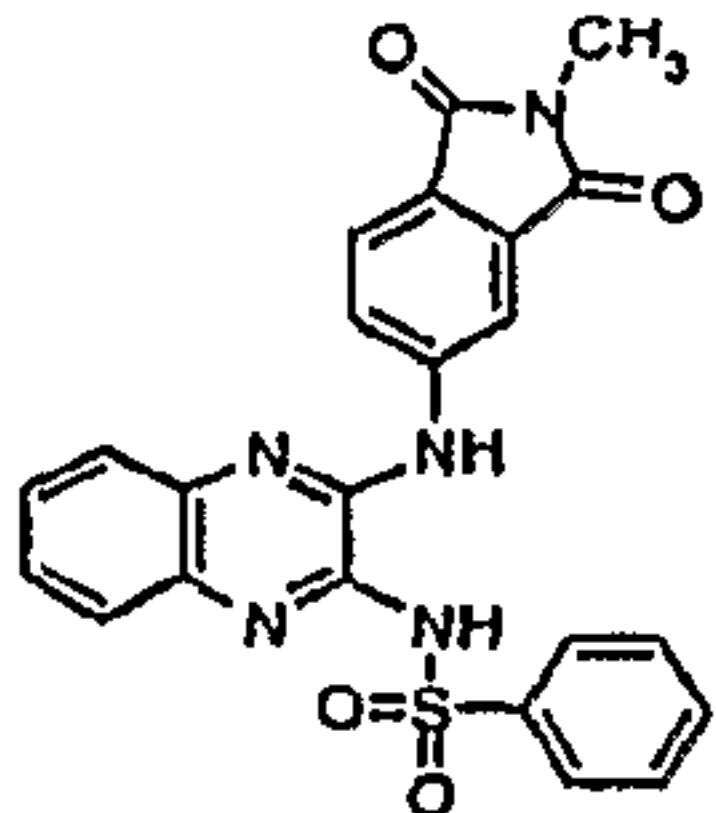
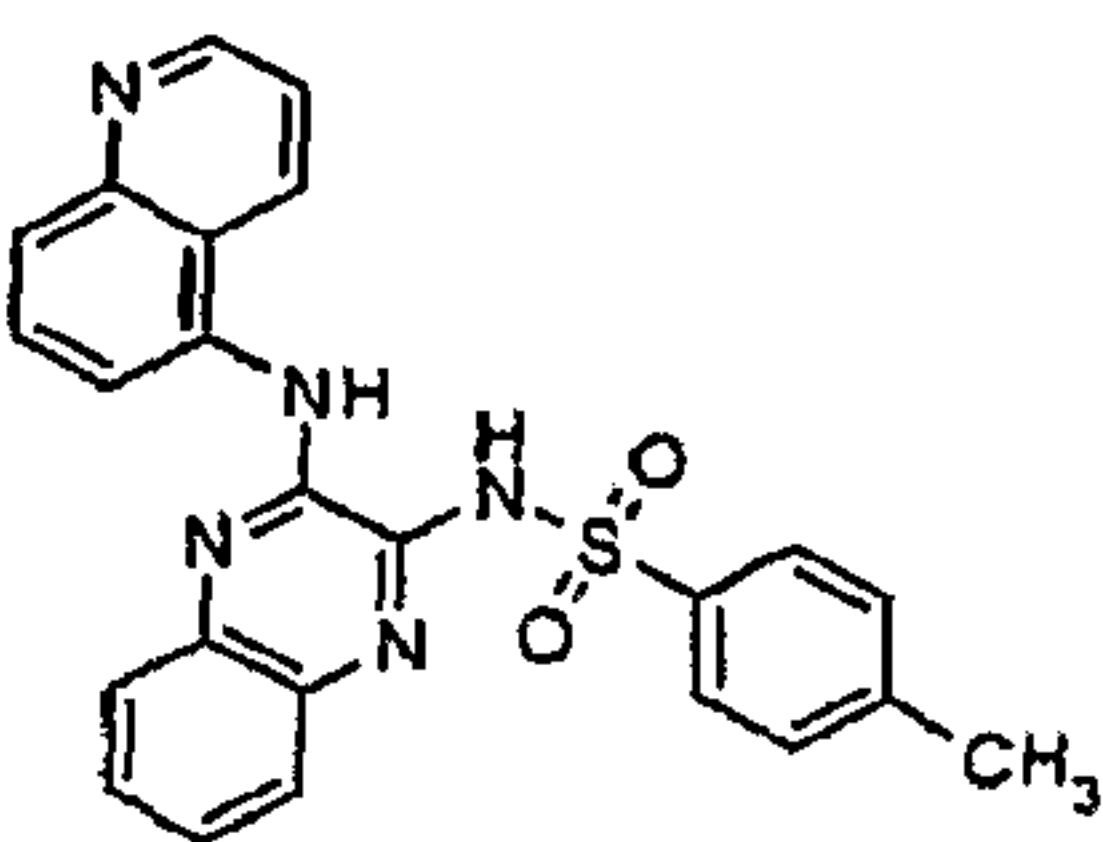
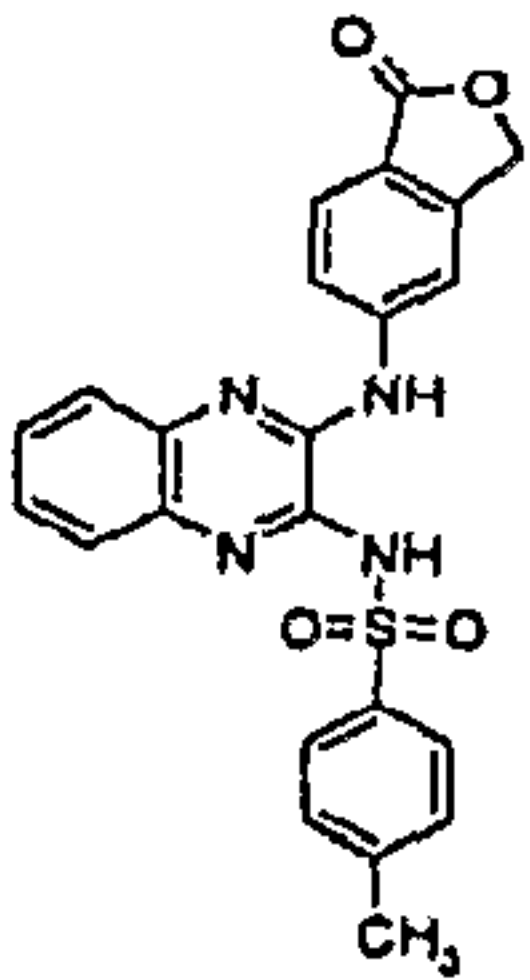
Table 1		
Cpd. No.	Structure	IUPAC Name
162		3-nitro- <i>N</i> -(3-{[4-(9 <i>H</i> -xanthen-9-yl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
163		4-chloro- <i>N</i> -{3-[(4'-nitrobiphenyl-3-yl)amino]quinoxalin-2-yl}benzenesulfonamide
164		<i>N</i> -[3-(2,1,3-benzothiadiazol-5-ylamino)quinoxalin-2-yl]-4-tolylsulfonamide
165		<i>N</i> -{3-[(2-methyl-1,3-dioxo-2,3-dihydro-1 <i>H</i> -isoindol-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide
166		4-methyl- <i>N</i> -[3-(quinolin-5-ylamino)quinoxalin-2-yl]benzenesulfonamide
167		4-methyl- <i>N</i> -{3-[(1-oxo-1,3-dihydro-2-benzofuran-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide

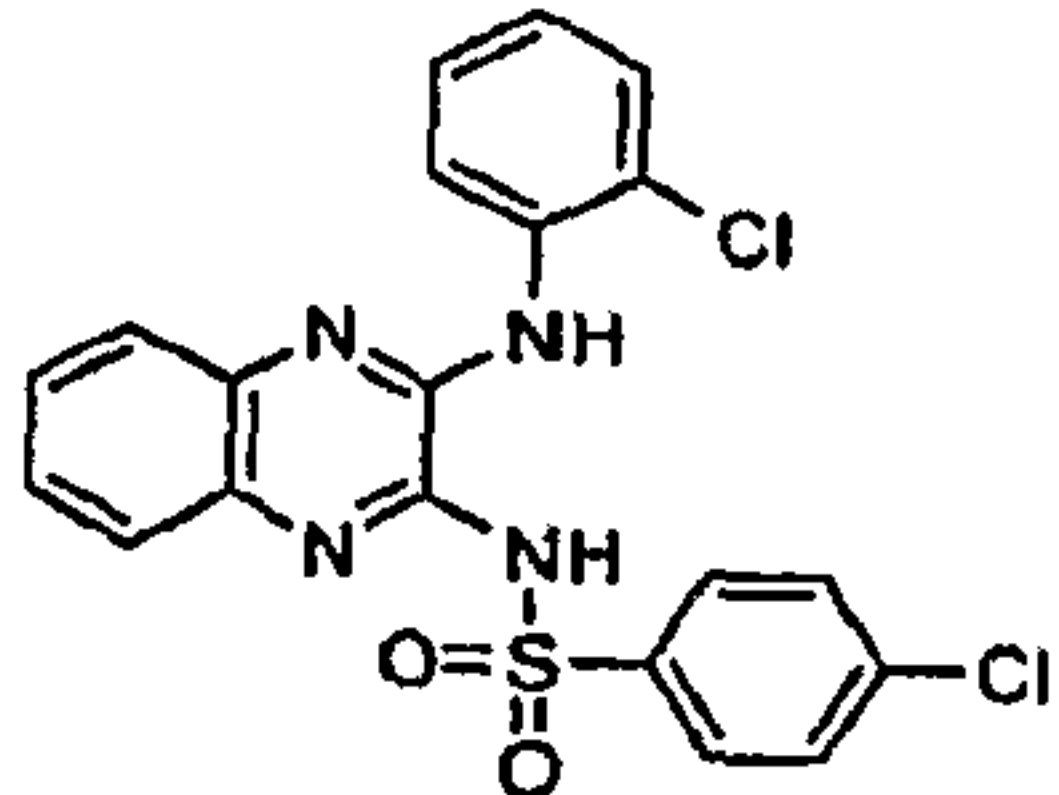
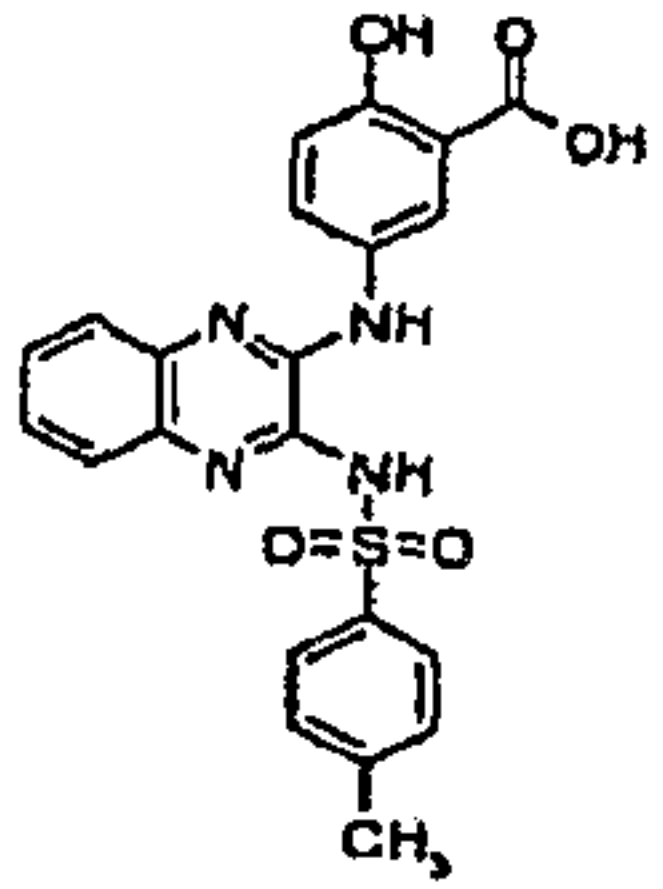
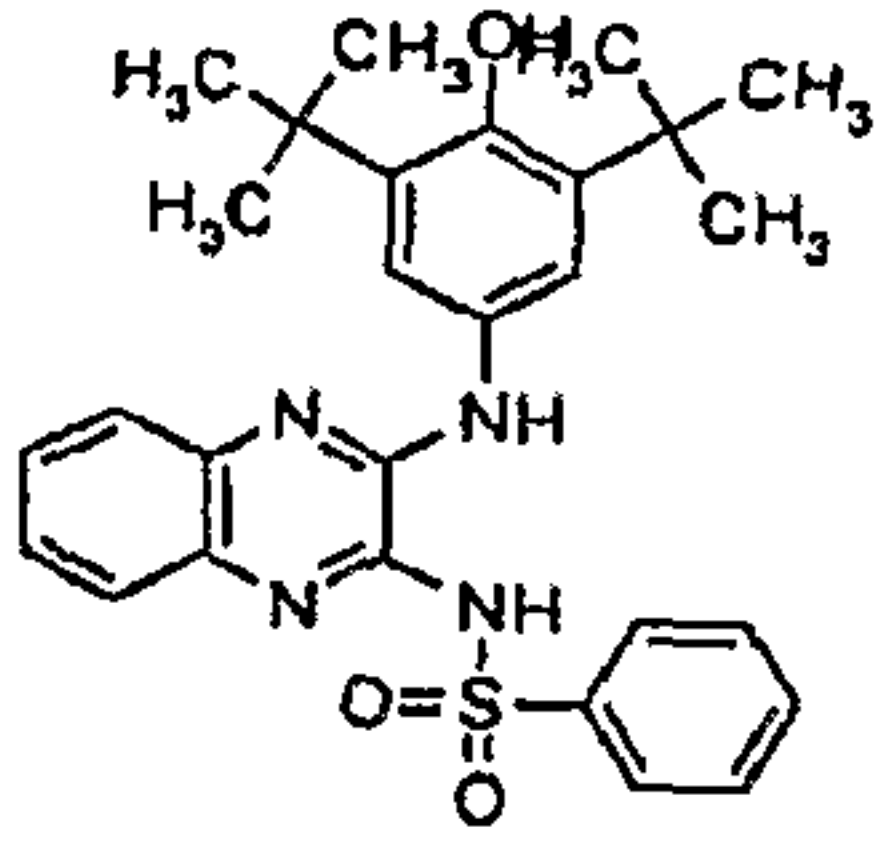
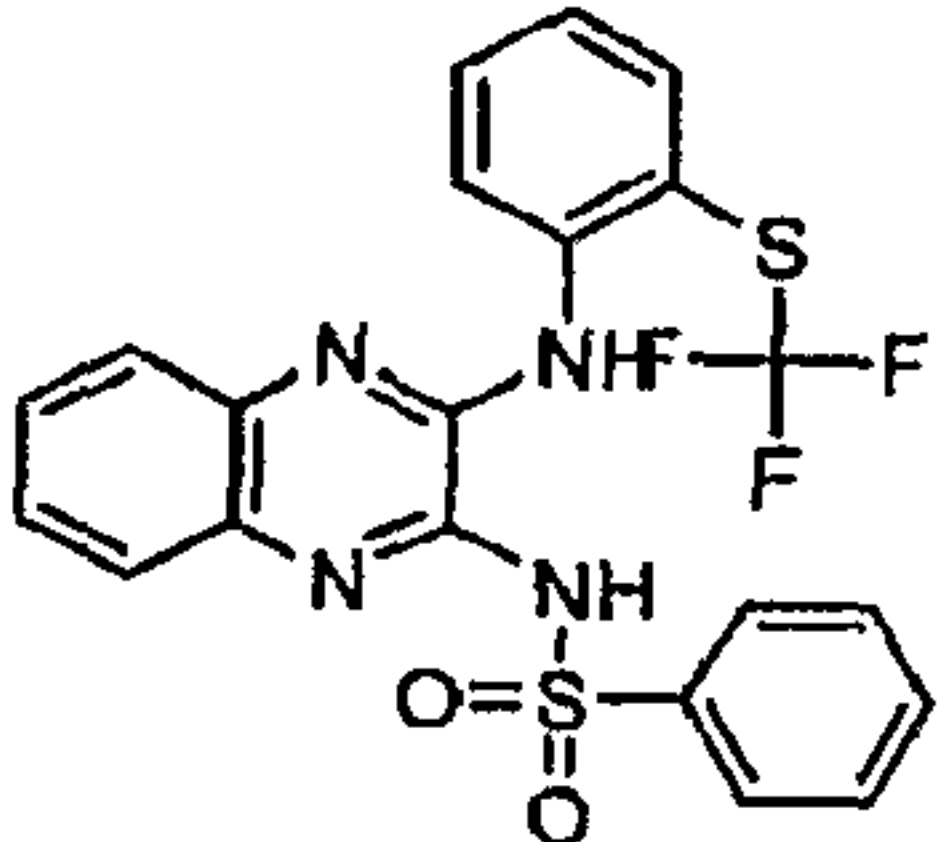
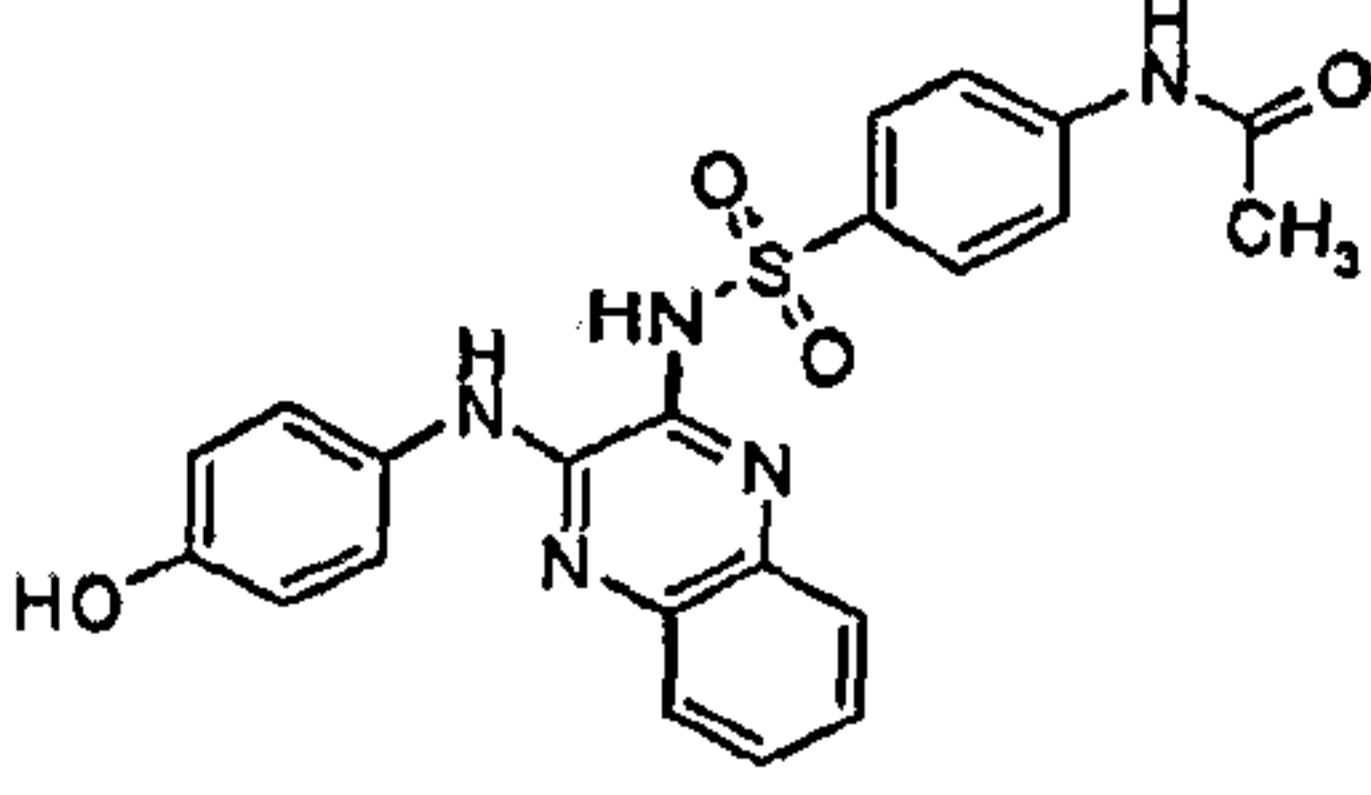
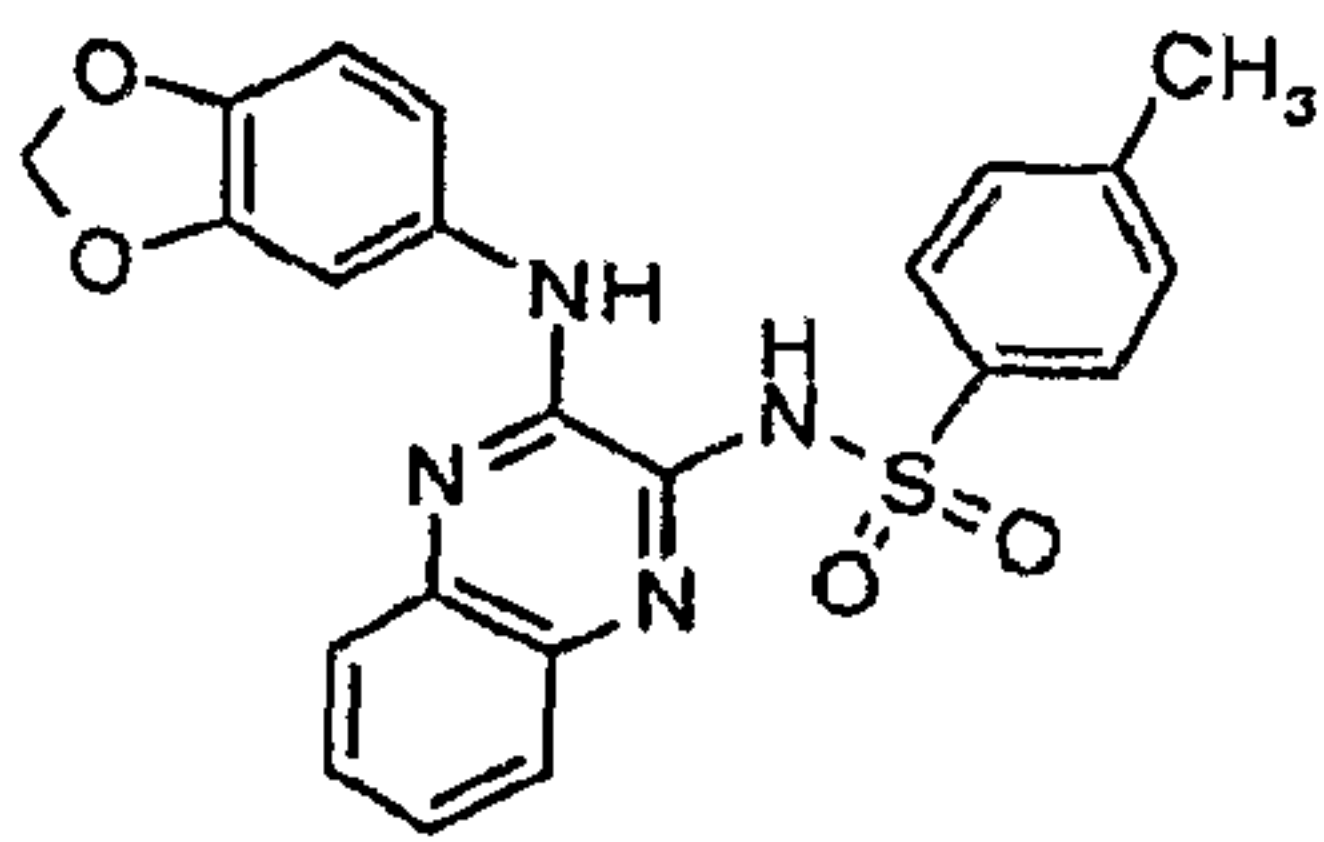
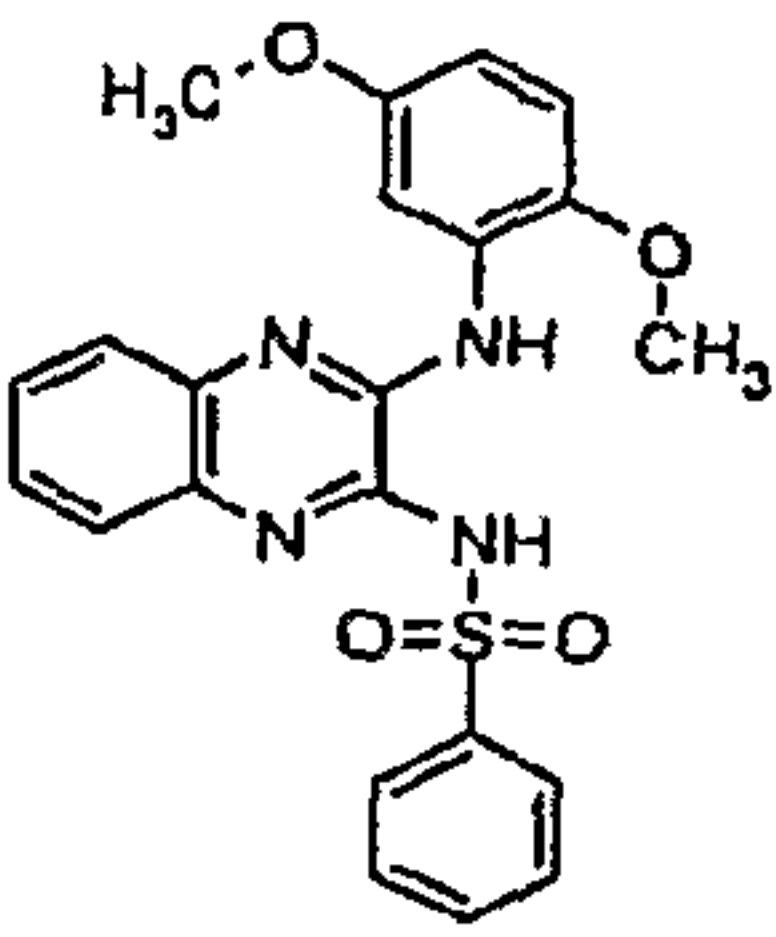
Table 1		
Cpd. No.	Structure	IUPAC Name
168		4-chloro- <i>N</i> -{3-[(2-chlorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
169		2-hydroxy-5-[(3-[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
170		<i>N</i> -(3-{[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]amino}quinoxalin-2-yl)benzenesulfonamide
171		<i>N</i> -[3-({2-[(trifluoromethyl)thio]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide
172		<i>N</i> -{4-[(3-[(4-hydroxyphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide
173		<i>N</i> -[3-(1,3-benzodioxol-5-ylamino)quinoxalin-2-yl]-4-methylbenzenesulfonamide
174		<i>N</i> -(3-{[2,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

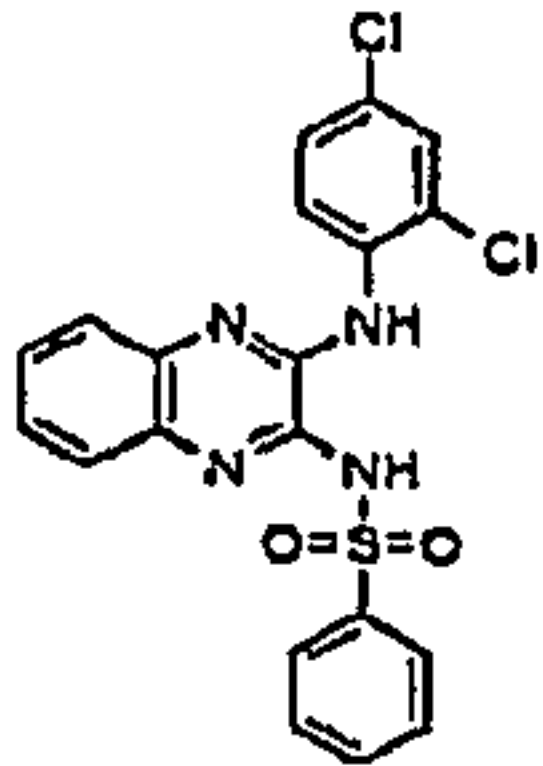
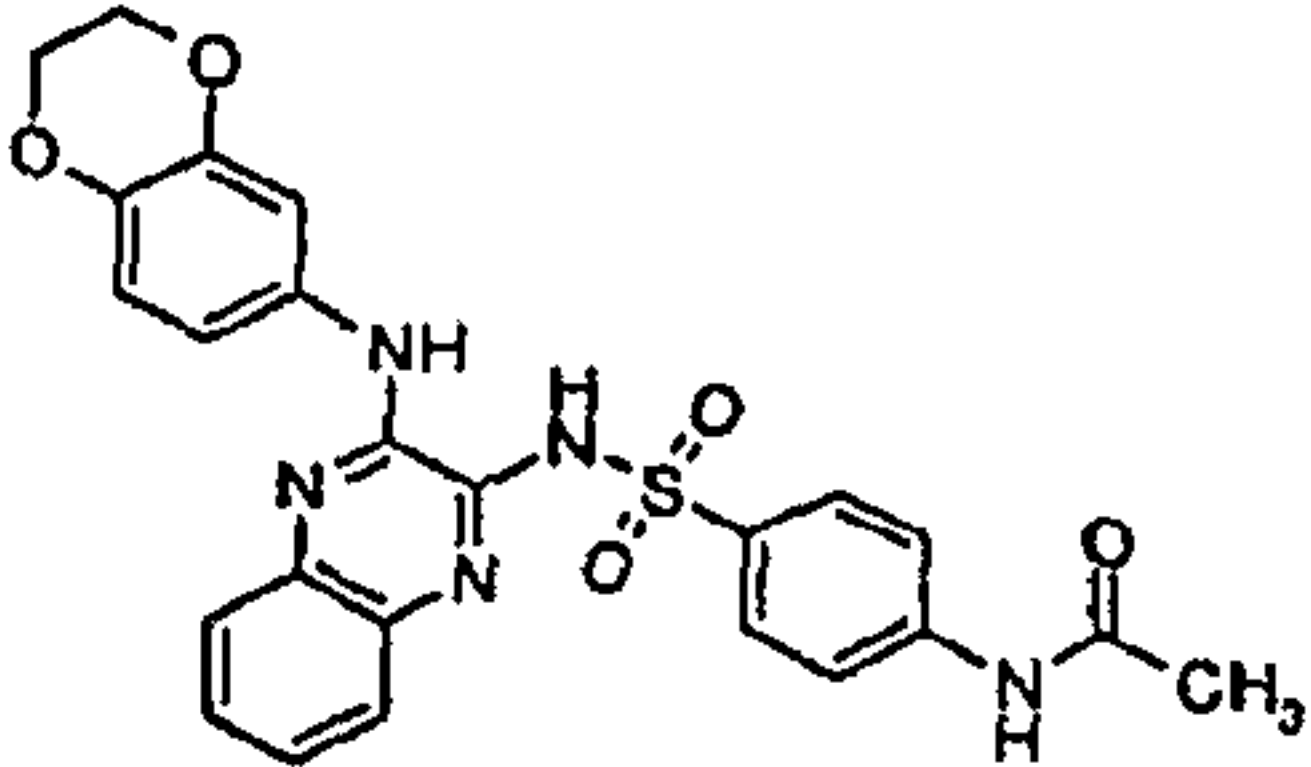
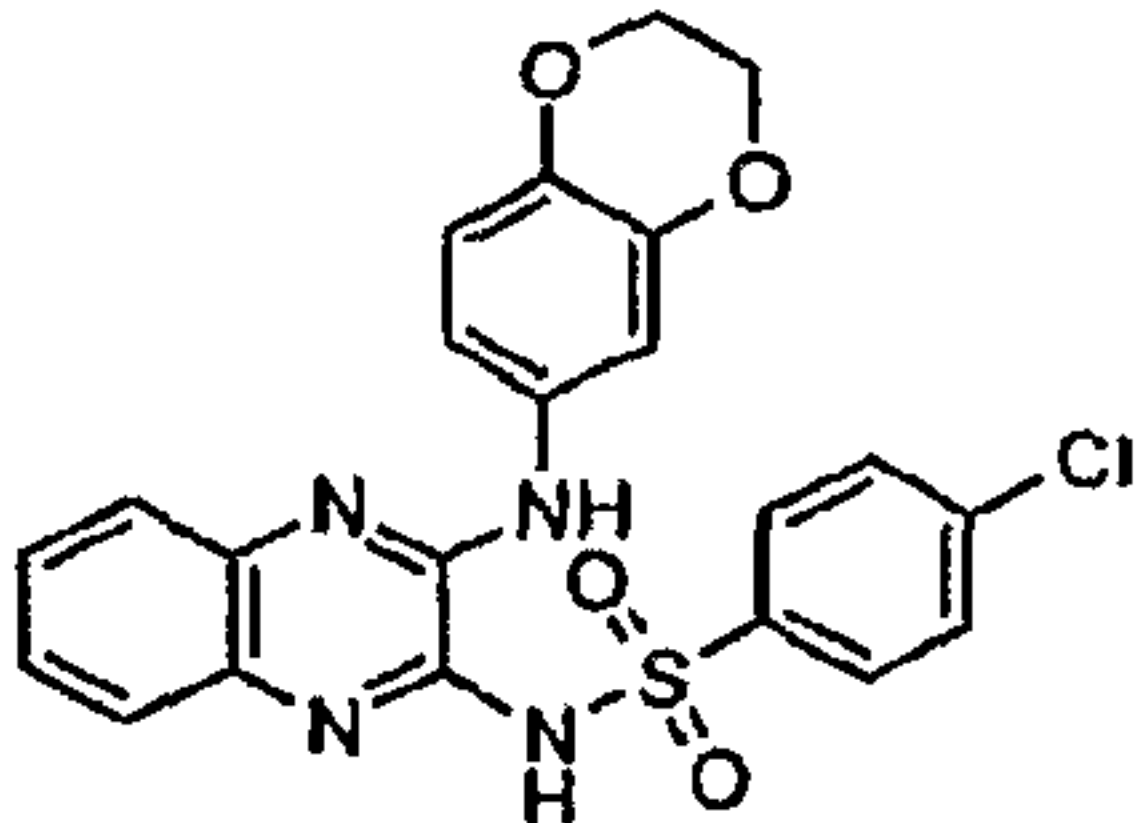
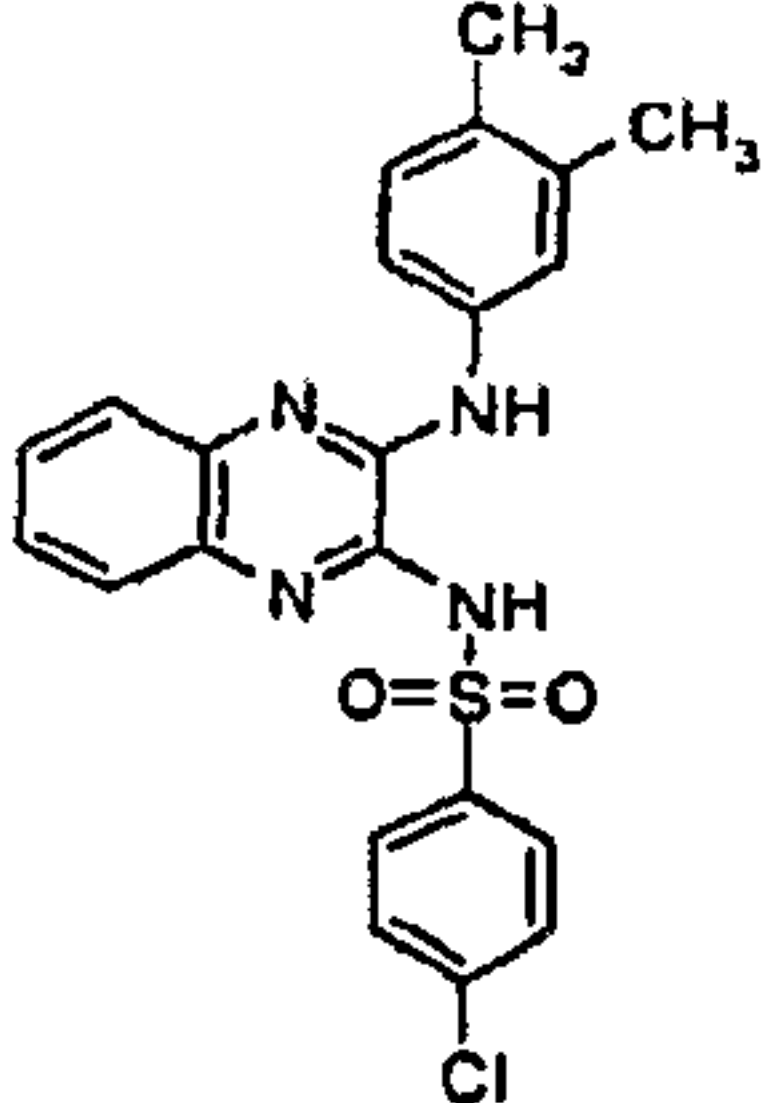
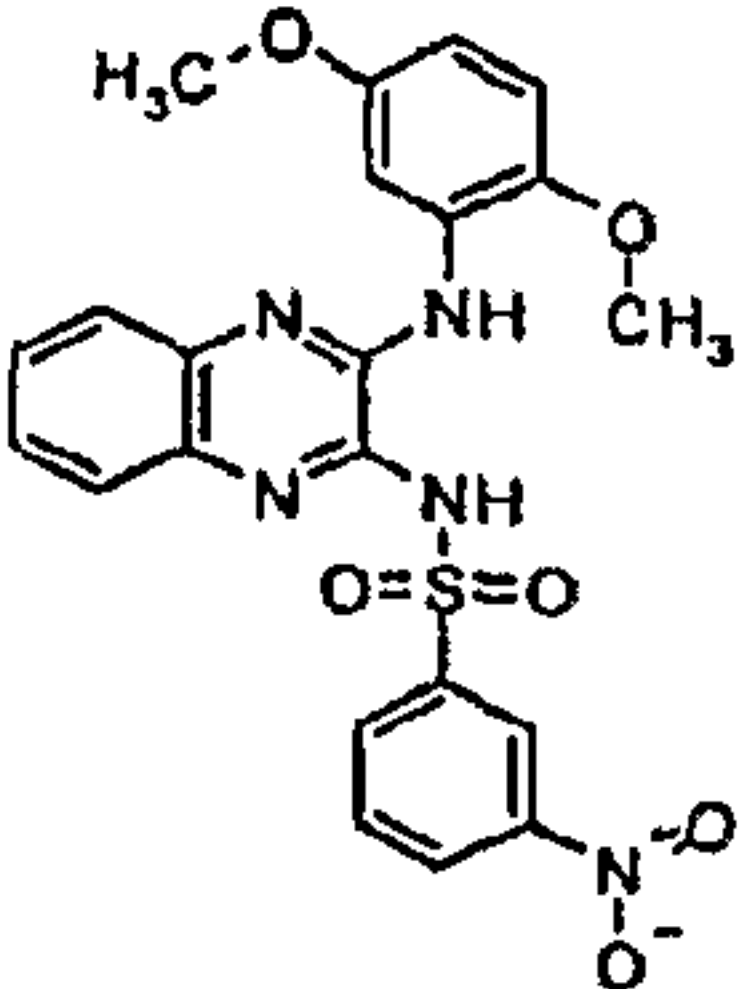
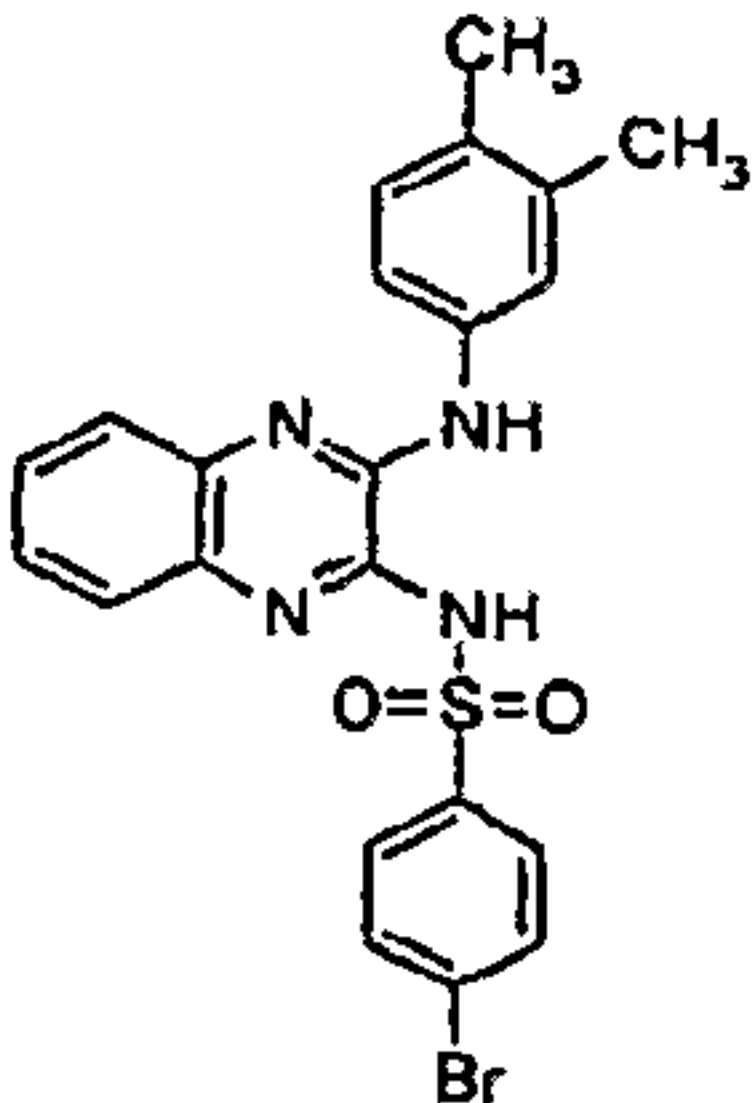
Table 1		
Cpd. No.	Structure	IUPAC Name
175		<i>N</i> -{3-[(2,4-dichlorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
176		<i>N</i> -[4-({[3-(2,3-dihydro-1,4-benzodioxin-6-ylamino)quinoxalin-2-yl]amino} sulfonyl)phenyl]acetamide
177		4-chloro- <i>N</i> -[3-(2,3-dihydro-1,4-benzodioxin-6-ylamino)quinoxalin-2-yl] benzenesulfonamide
178		4-chloro- <i>N</i> -{3-[(3,4-dimethylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
179		<i>N</i> -(3-{[2,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
180		4-bromo- <i>N</i> -{3-[(3,4-dimethylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide

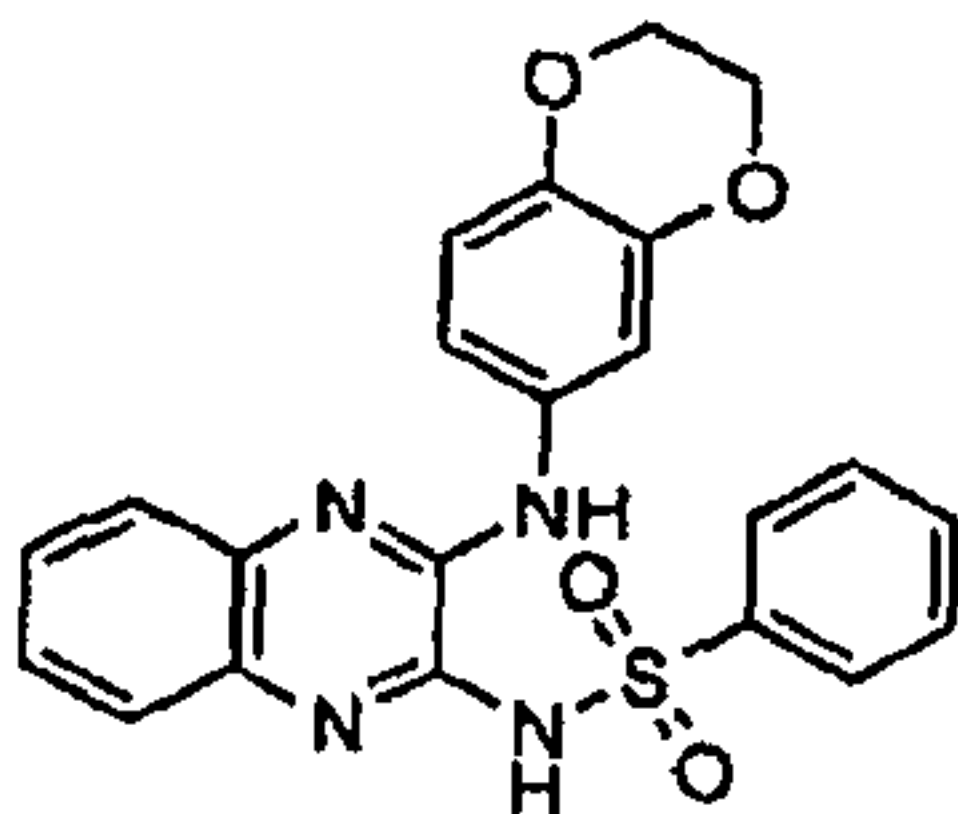
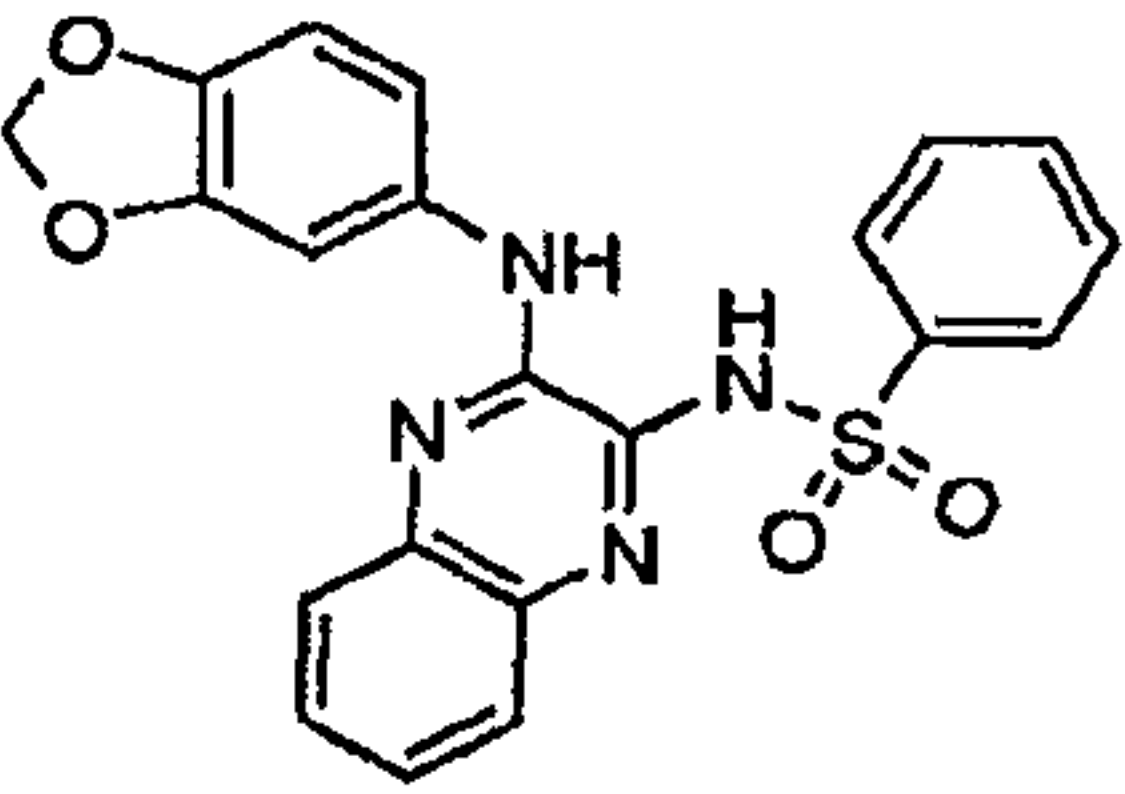
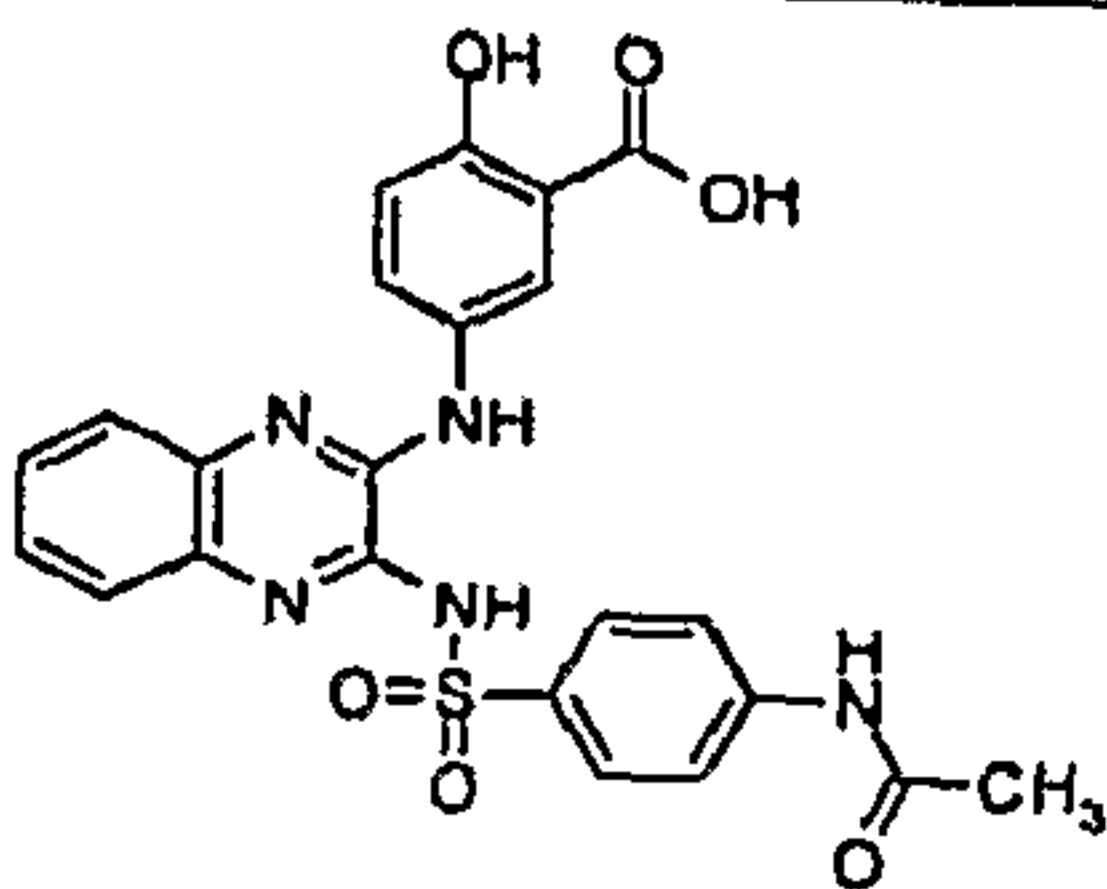
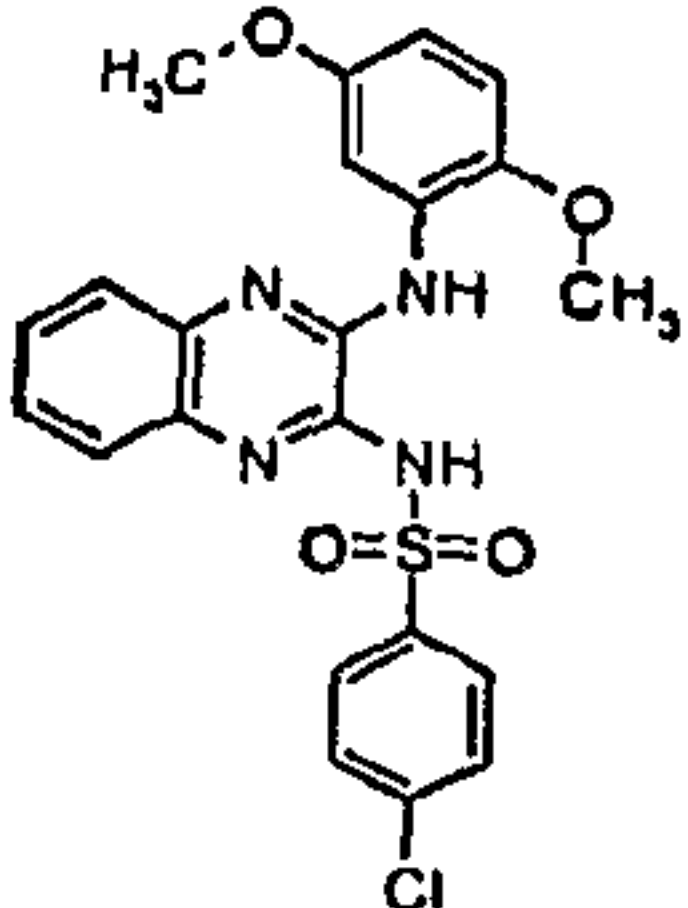
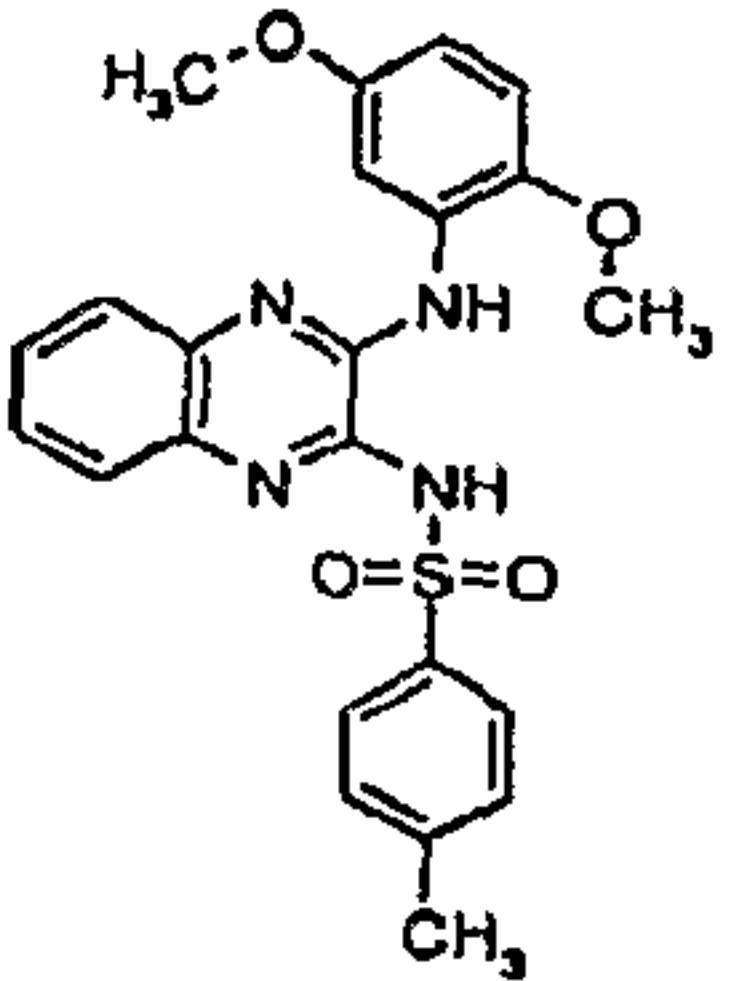
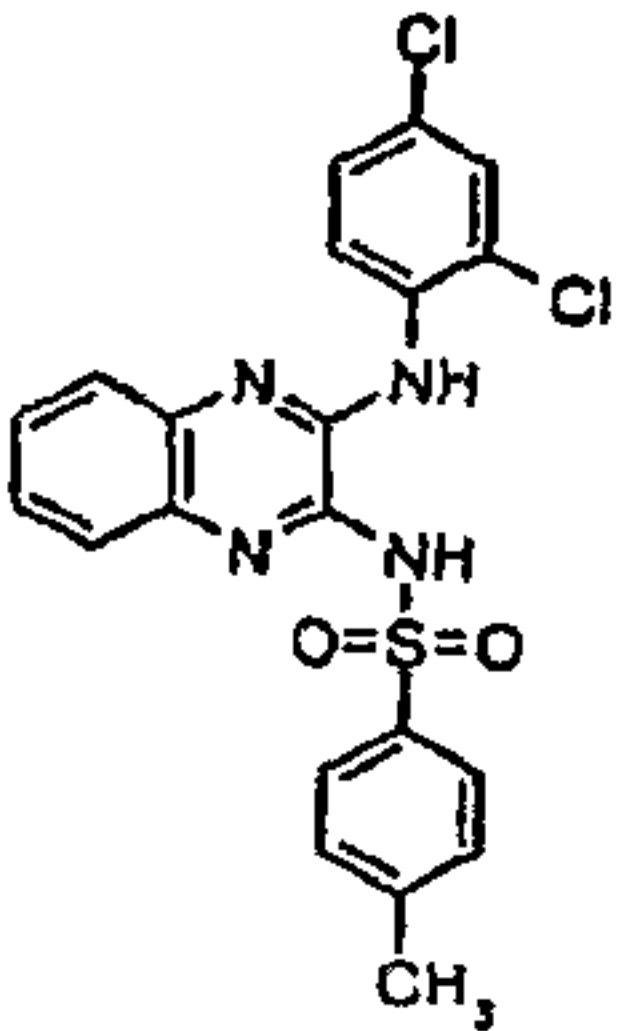
Table 1		
Cpd. No.	Structure	IUPAC Name
181		<i>N</i> -[3-(2,3-dihydro-1,4-benzodioxin-6-ylamino)quinoxalin-2-yl]benzenesulfonamide
182		<i>N</i> -[3-(1,3-benzodioxol-5-ylamino)quinoxalin-2-yl]benzenesulfonamide
183		5-{{3-([4-(acetylamino)phenyl]sulfonyl)amino}quinoxalin-2-yl}amino}-2-hydroxybenzoic acid
184		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-chlorobenzenesulfonamide
185		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide
186		<i>N</i> -{3-[(2,4-dichlorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
187		<i>N</i> -{3-[(2,4-difluorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
188		4-bromo- <i>N</i> -{3-[(3-fluorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
189		4-{[3-({[4-(acetamino)phenyl]sulfonyl}amino)quinoxalin-2-yl]amino} benzoic acid
190		<i>N</i> -{3-[(2-fluorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
191		<i>N</i> -[3-(2,3-dihydro-1,4-benzodioxin-6-ylamino)quinoxalin-2-yl]-4-methylbenzenesulfonamide
192		<i>N</i> -{3-[(3,4-dimethylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
193		4-methyl- <i>N</i> -(3-{[3-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl) benzenesulfonamide

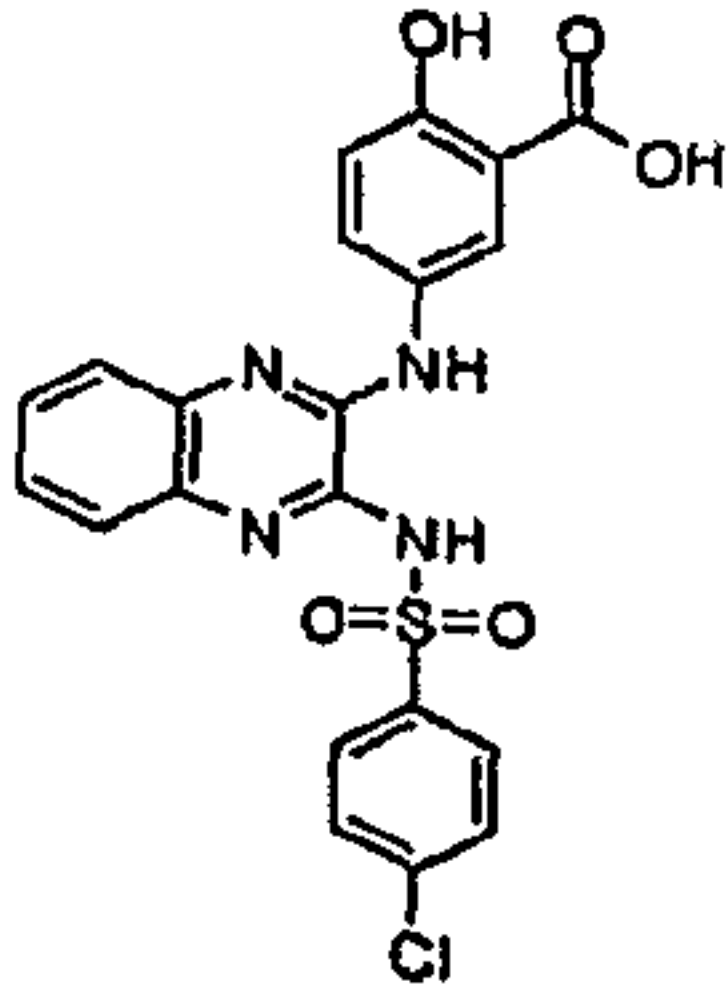
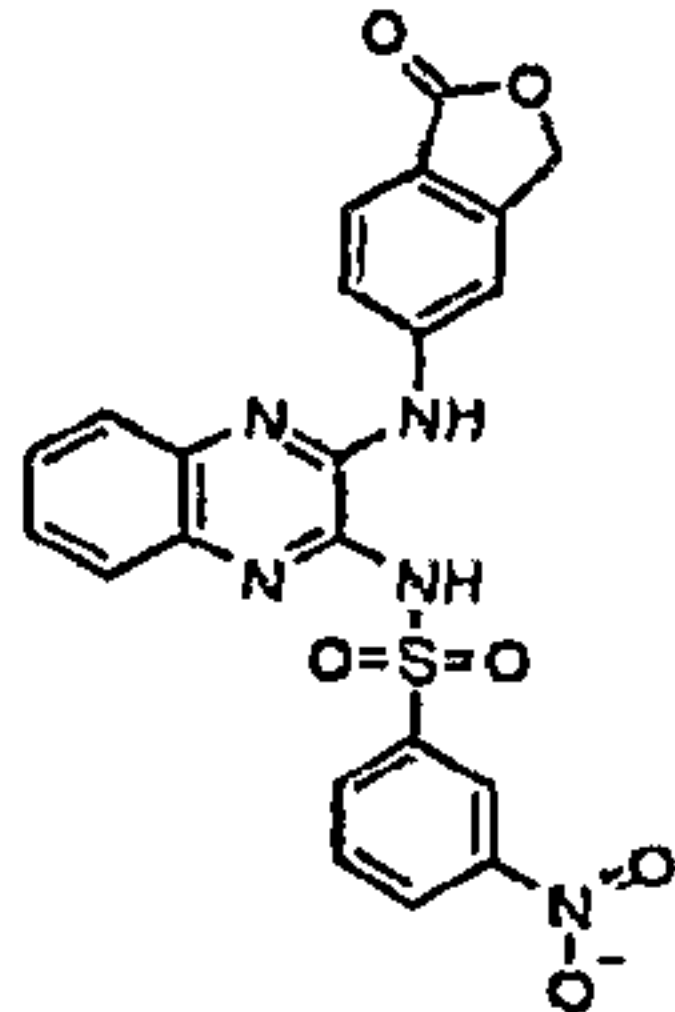
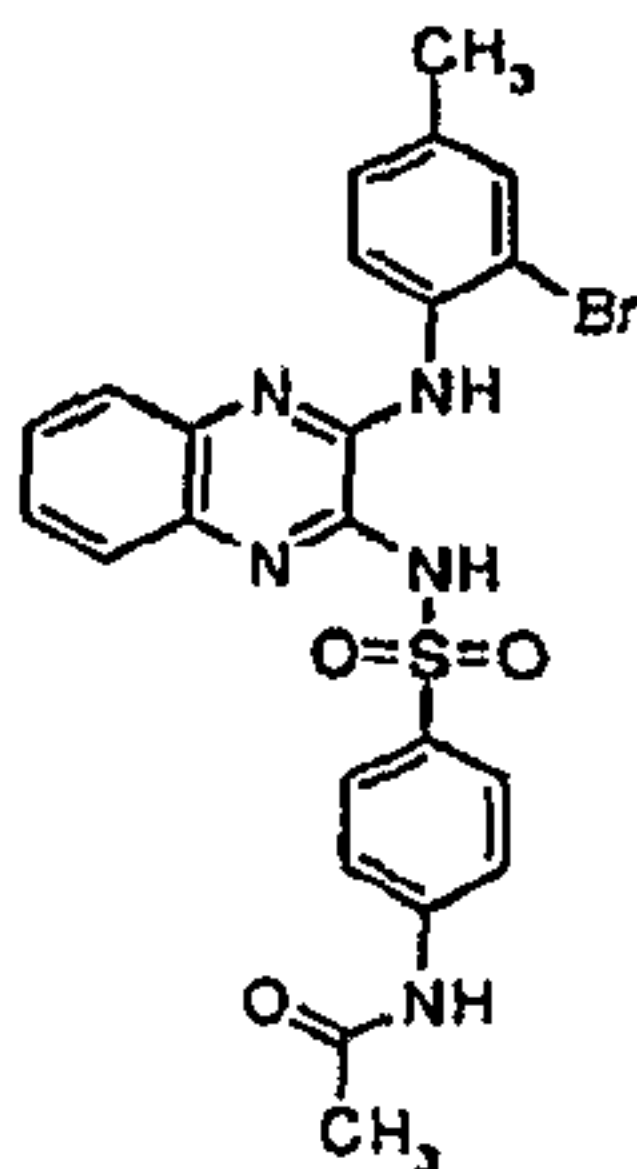
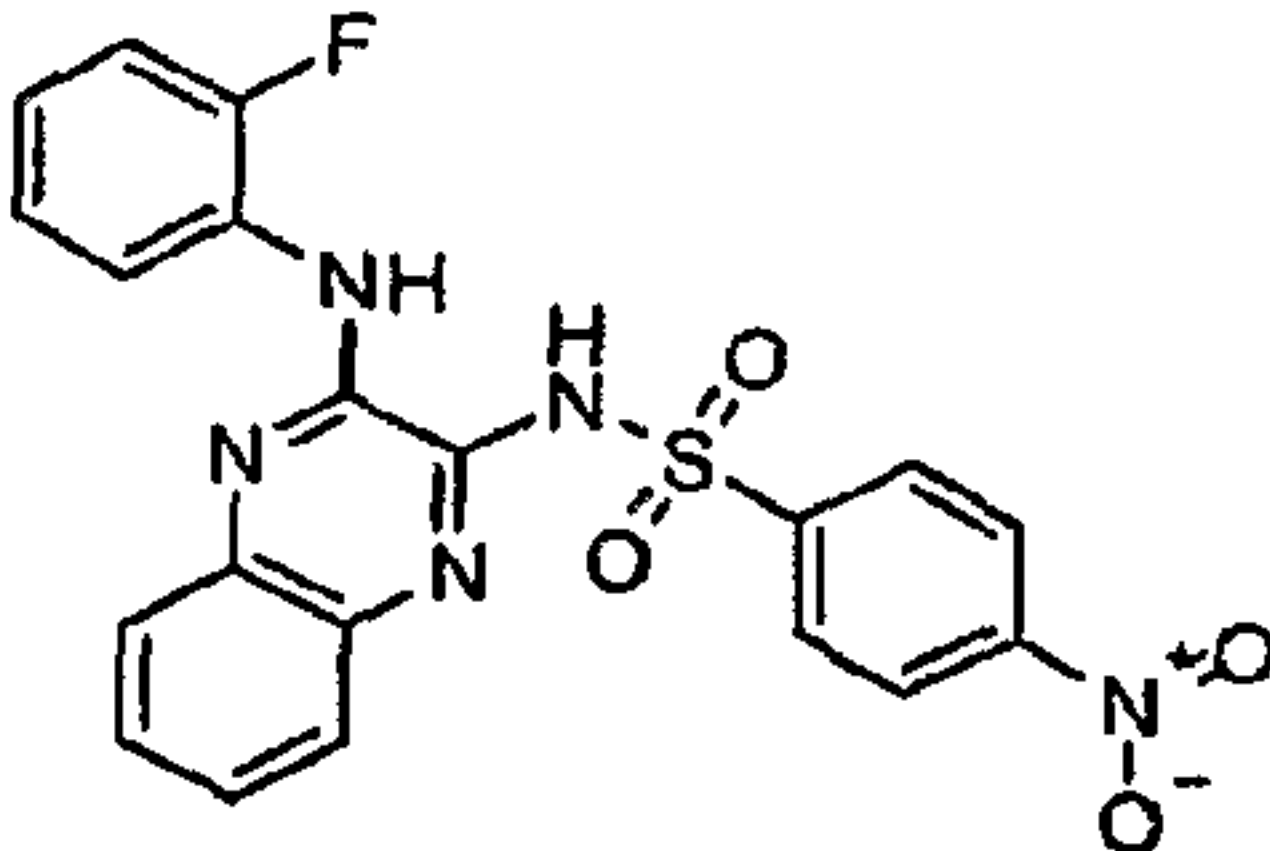
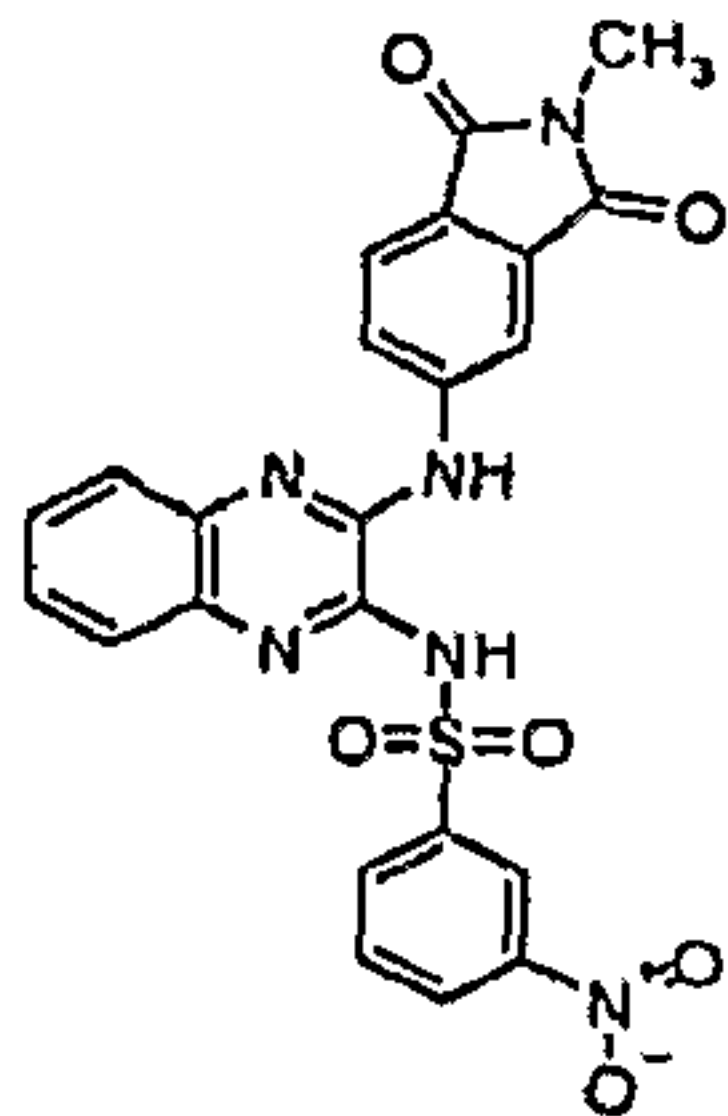
Table 1		
Cpd. No.	Structure	IUPAC Name
194		5-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-2-hydroxybenzoic acid
195		3-nitro-N-{3-[(1-oxo-1,3-dihydro-2-benzofuran-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide
196		N-{4-[(3-[(2-bromo-4-methylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide
197		N-{3-[(2-fluorophenyl)amino]quinoxalin-2-yl}-4-nitrobenzenesulfonamide
198		N-{3-[(2-methyl-1,3-dioxo-2,3-dihydro-1H-indol-5-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
199		4-chloro- <i>N</i> -{3-[(1-oxo-1,3-dihydro-2-benzofuran-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide
200		<i>N</i> -{3-[(1-oxo-1,3-dihydro-2-benzofuran-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide
201		<i>N</i> -{3-[(2-fluorophenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
202		<i>N</i> -[2-(butyloxy)-2-hydroxyethyl]-4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)benzamide
203		3-nitro- <i>N</i> -(3-{[4-(phenylamino)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

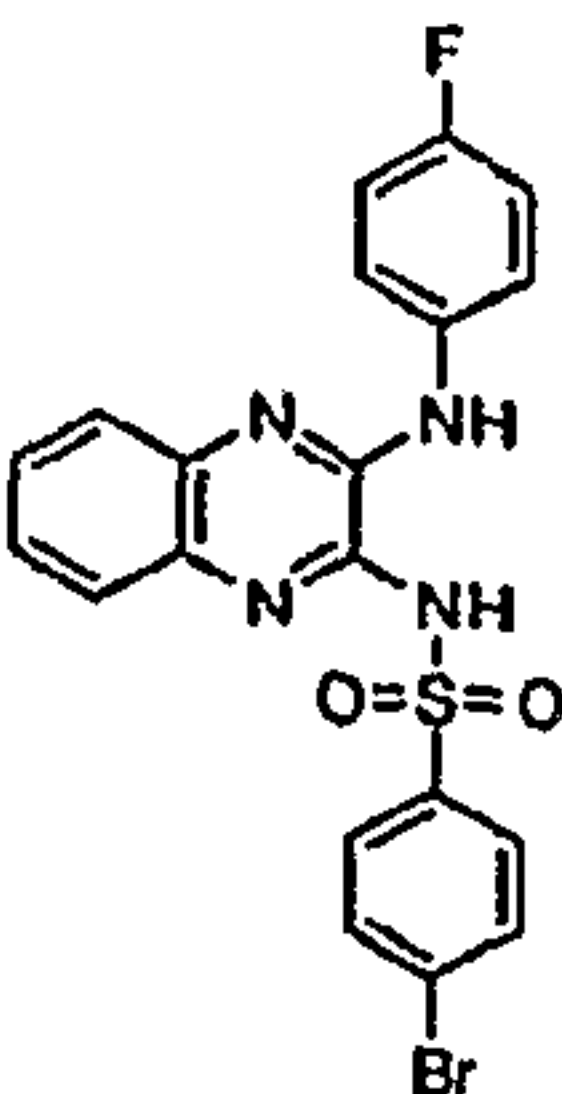
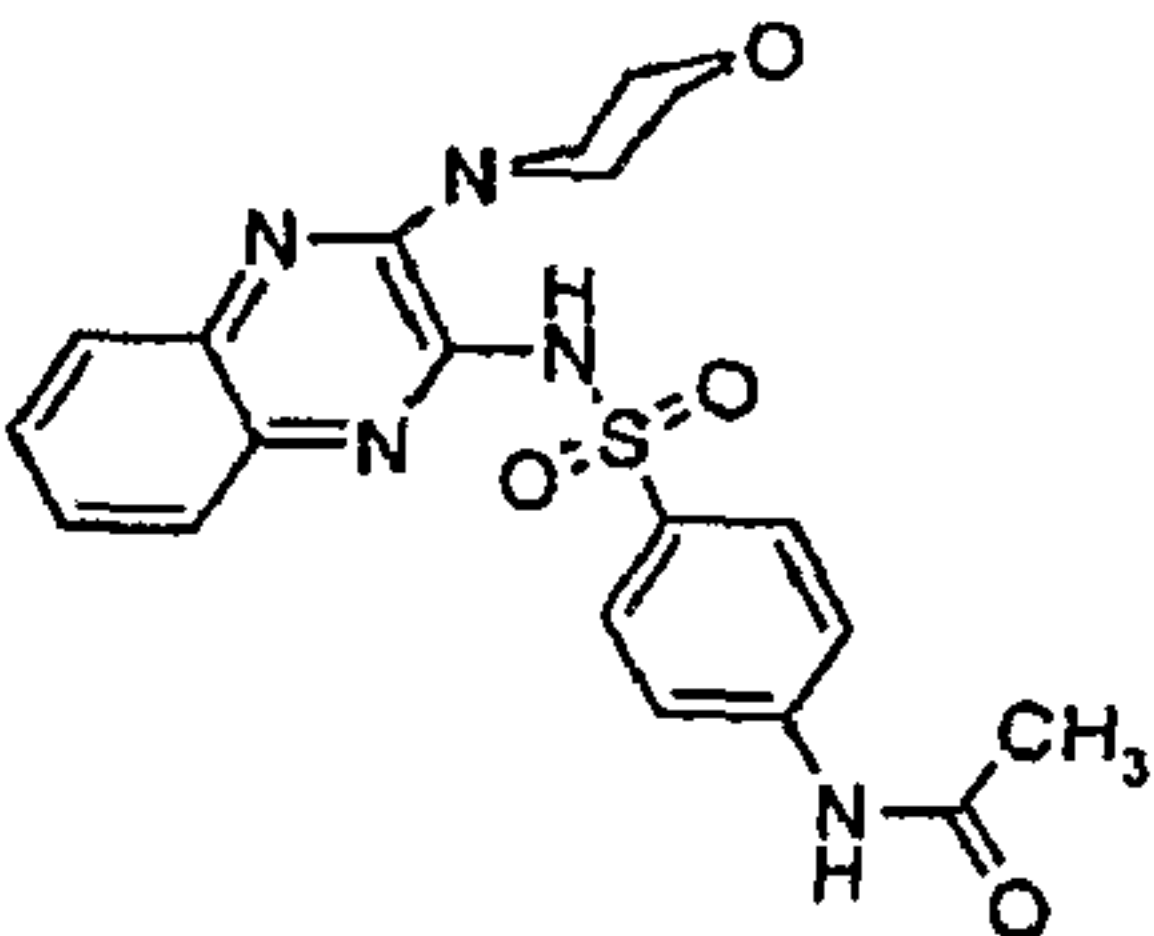
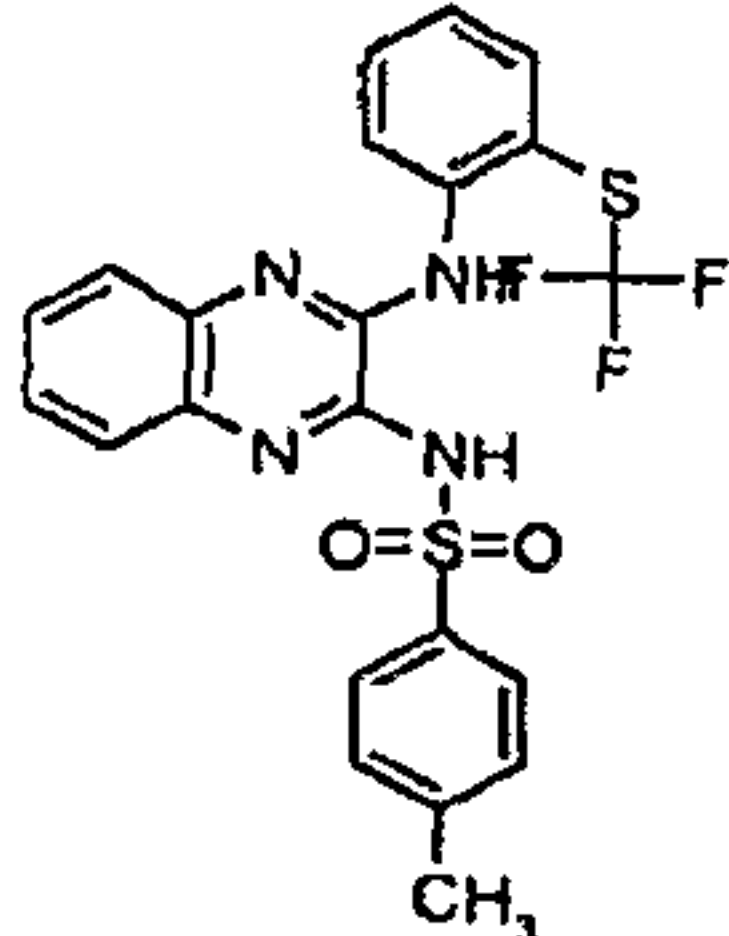
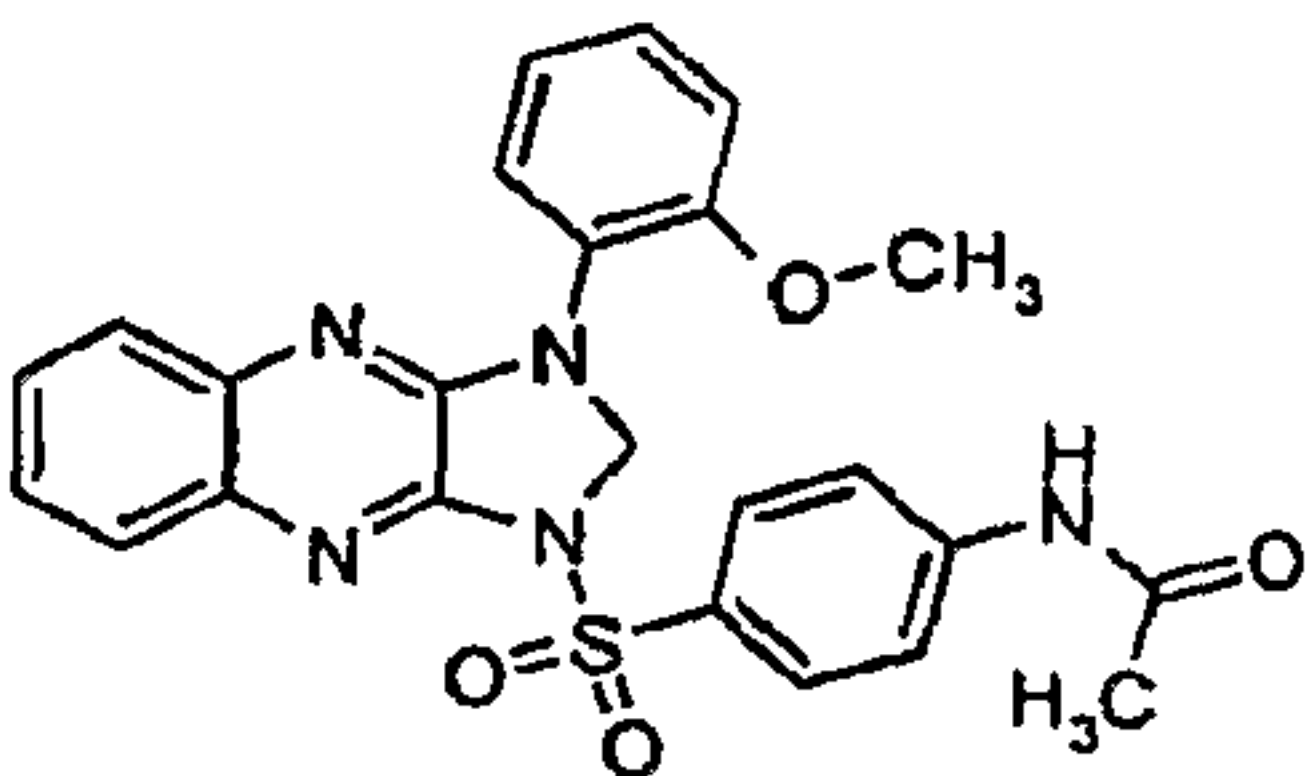
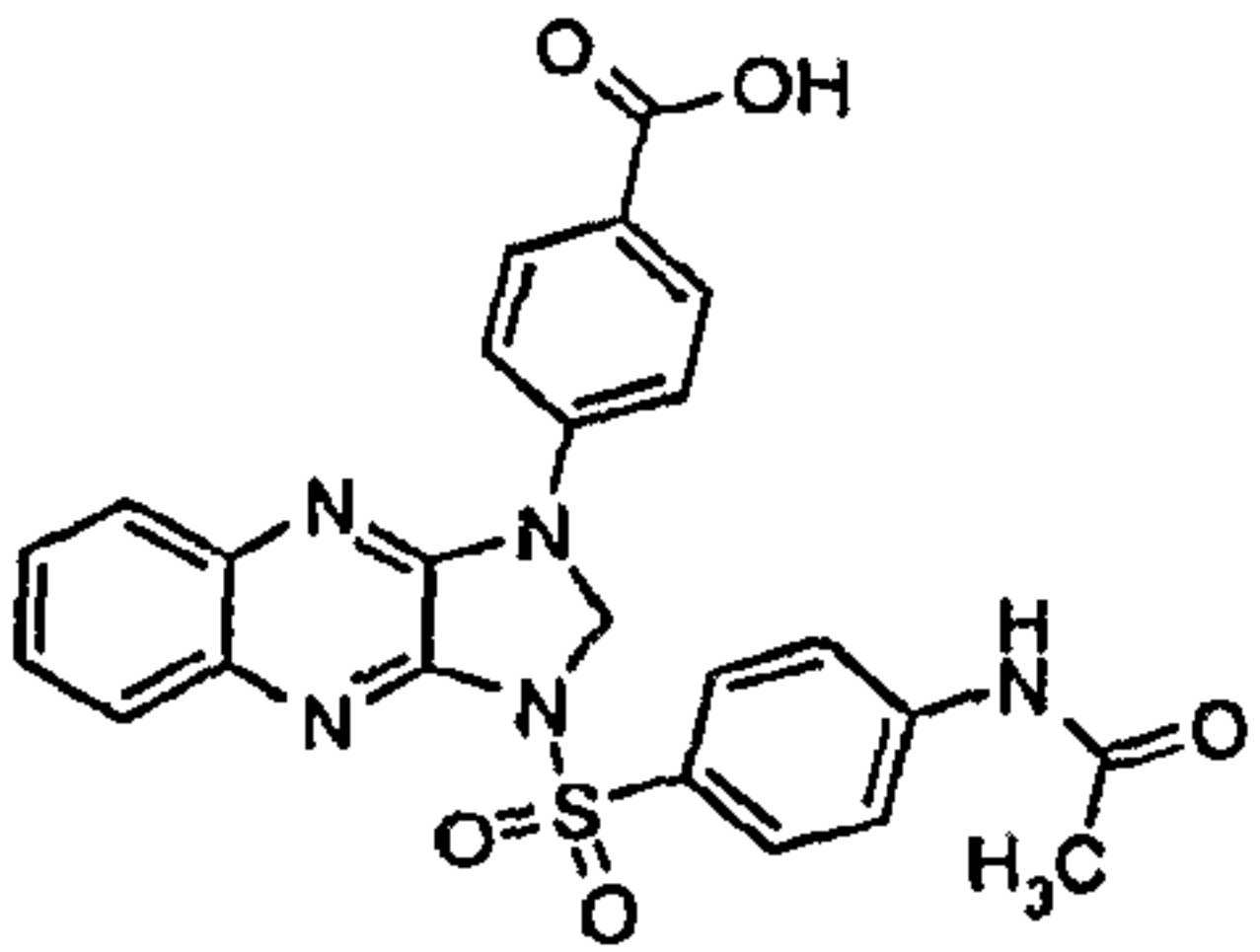
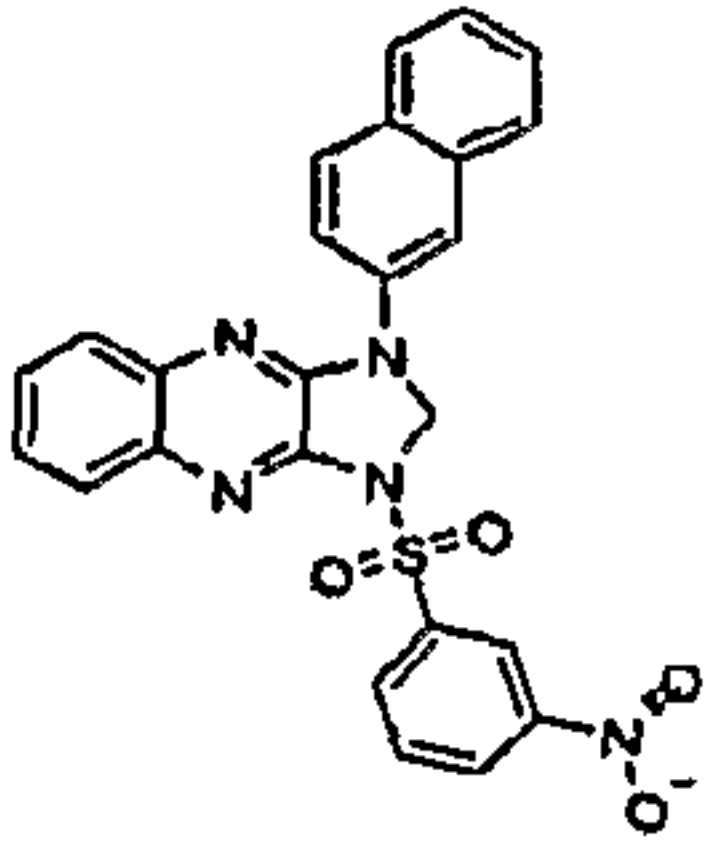
Table 1		
Cpd. No.	Structure	IUPAC Name
204		4-bromo- <i>N</i> -{3-[(4-fluorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
205		<i>N</i> -(4-[[[(3-morpholin-4-yl)quinoxalin-2-yl]amino]sulfonyl]phenyl)acetamide
206		4-methyl- <i>N</i> -[3-({2-[(trifluoromethyl)thio]phenyl}amino)quinoxalin-2-yl] benzenesulfonamide
207		<i>N</i> -[4-({3-[2-(methoxyloxy)phenyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl} sulfonyl)phenyl]acetamide
208		4-(3-{[4-(acetylamino)phenyl]sulfonyl}-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl) benzoic acid
209		1-naphthalen-2-yl-3-[(3-nitrophenyl)sulfonyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline

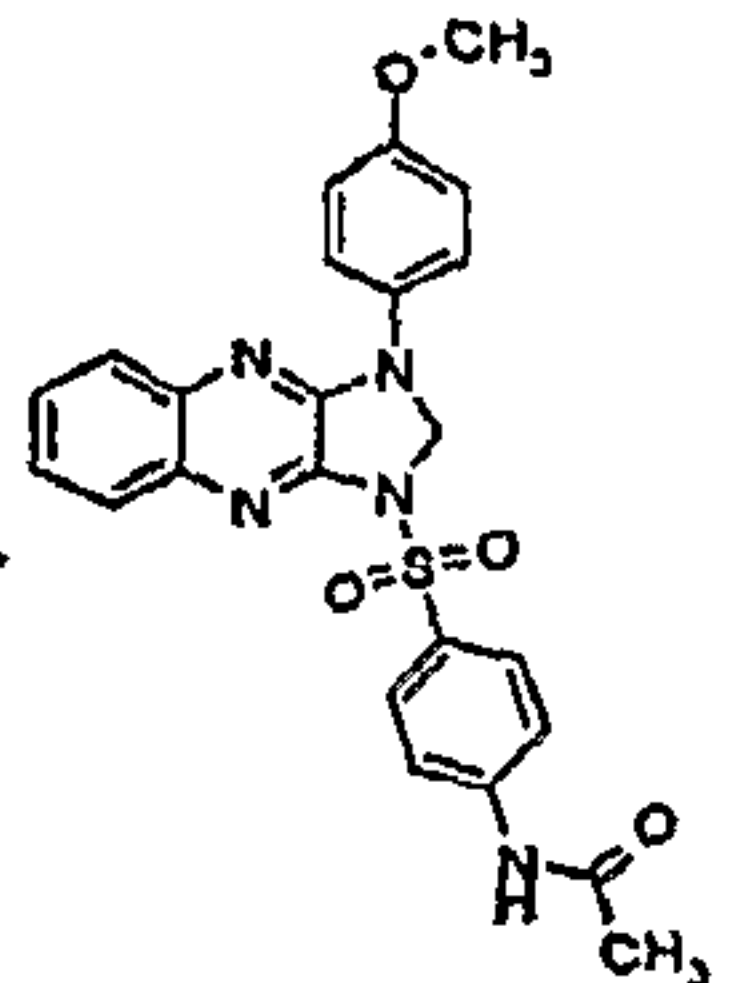
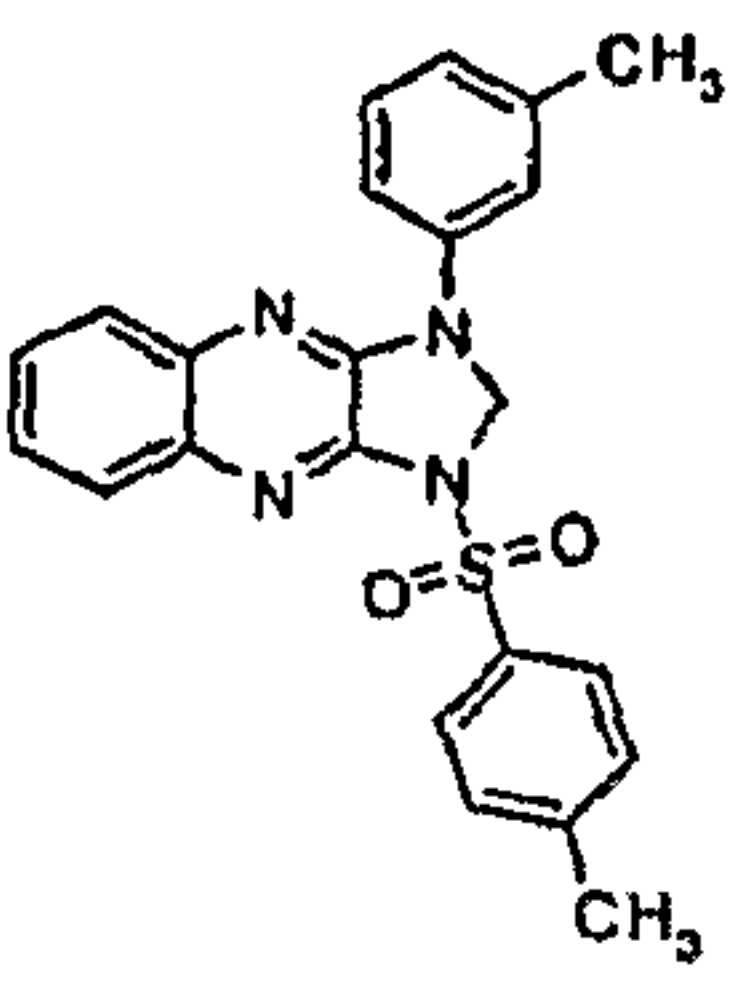
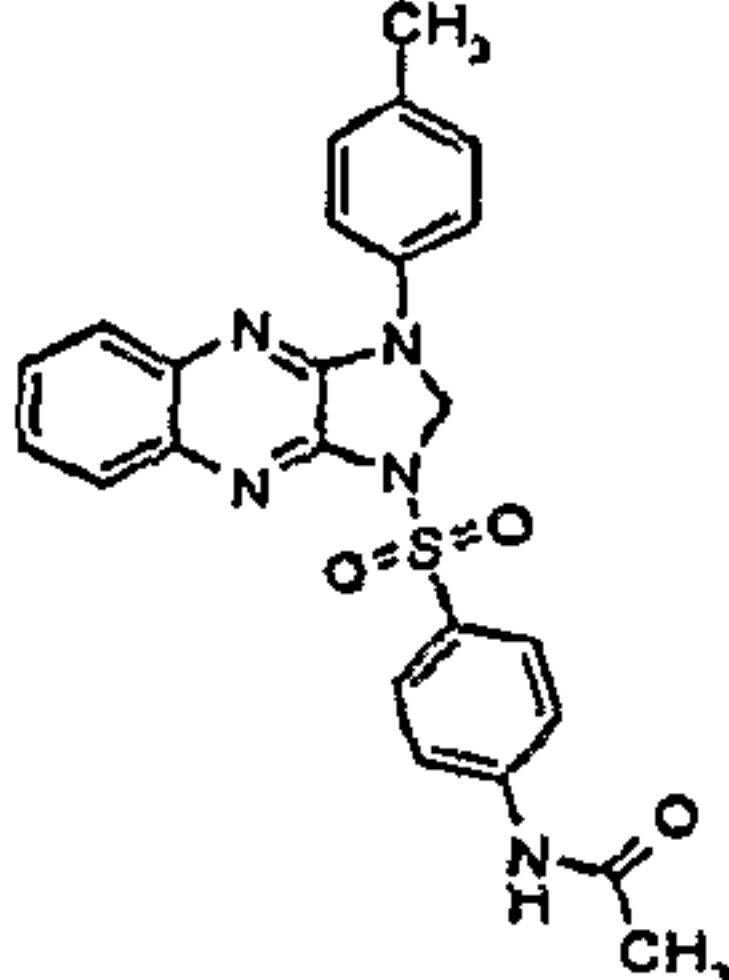
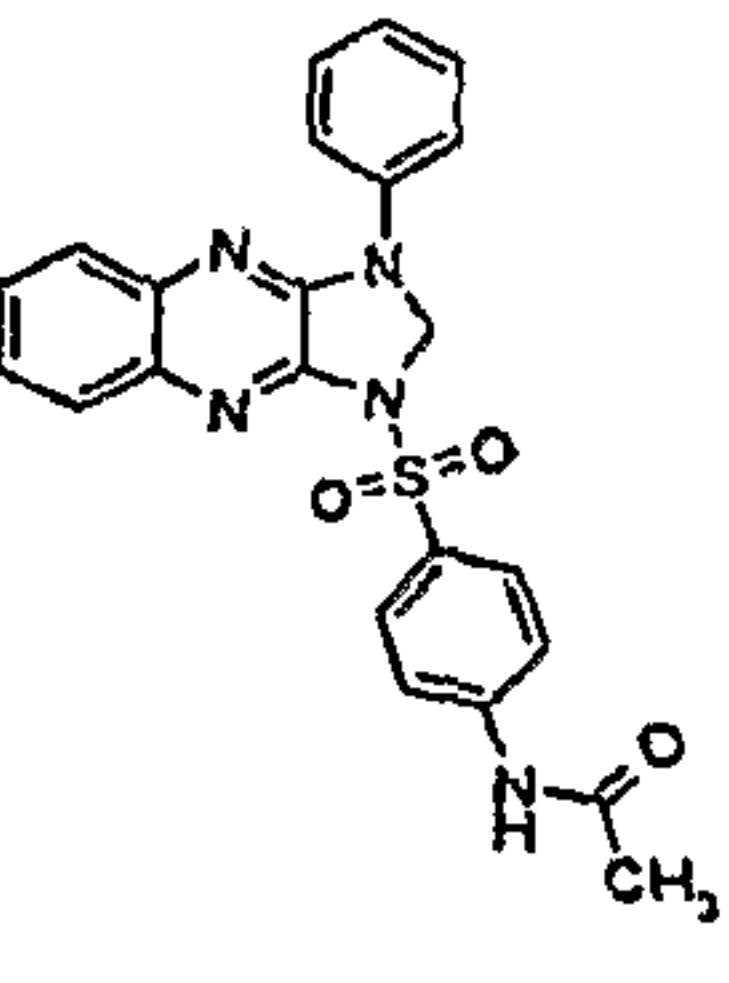
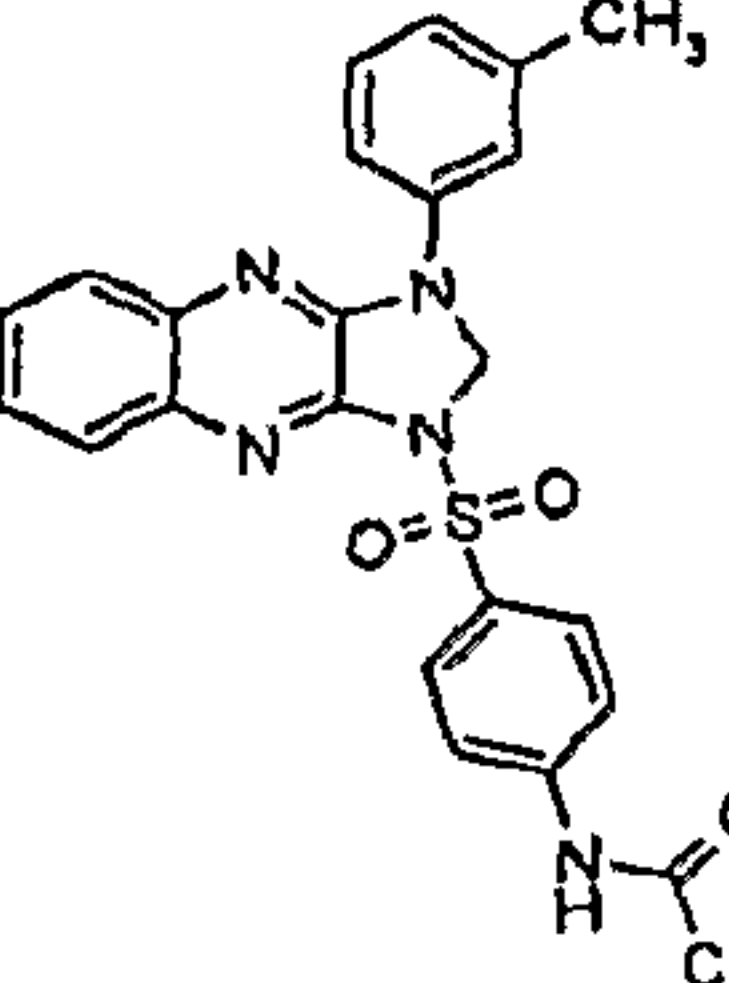
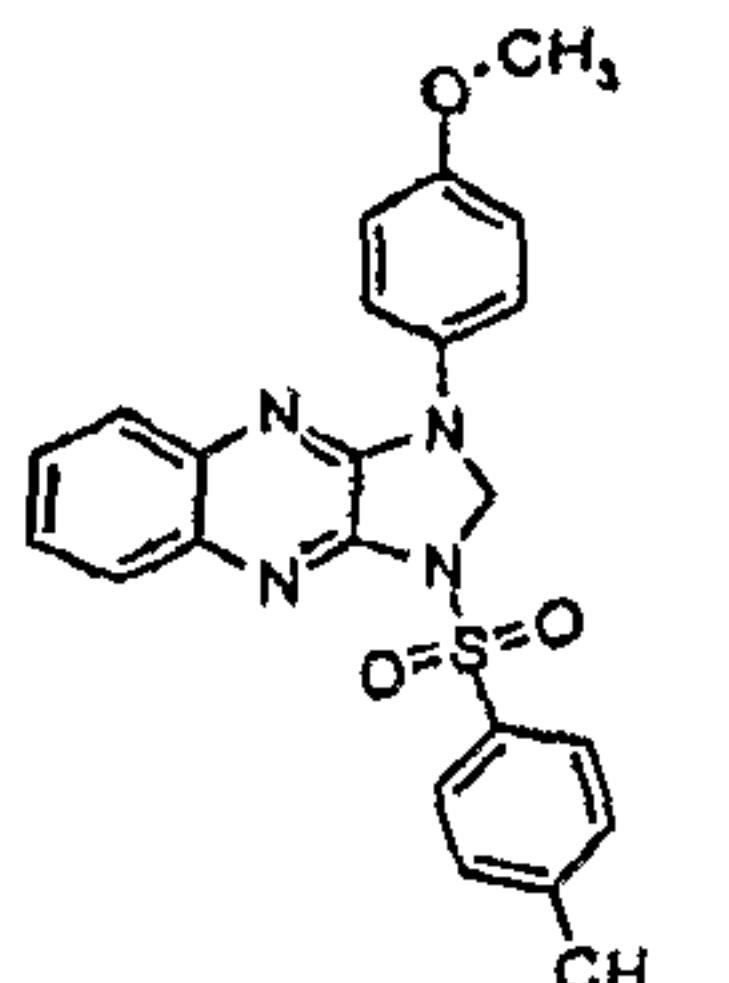
Table 1		
Cpd. No.	Structure	IUPAC Name
210		<i>N</i> -[4-({3-[4-(methyloxy)phenyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl}sulfonyl)phenyl]acetamide
211		1-(3-methylphenyl)-3-[(4-methylphenyl)sulfonyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline
212		<i>N</i> -(4-{[3-(4-methylphenyl)-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl]sulfonyl}phenyl)acetamide
213		<i>N</i> -{4-[(3-phenyl-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl)sulfonyl]phenyl}acetamide
214		<i>N</i> -(4-{[3-(3-methylphenyl)-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl]sulfonyl}phenyl)acetamide
215		1-[4-(methyloxy)phenyl]-3-[(4-methylphenyl)sulfonyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline

Table 1		
Cpd. No.	Structure	IUPAC Name
216		<i>N</i> -(4-([3-(2-methylphenyl)-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxalin-1-yl]sulfonyl)phenyl)acetamide
217		1-(3-methylphenyl)-3-[(3-nitrophenyl)sulfonyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline
218		1-(4-methylphenyl)-3-[(3-nitrophenyl)sulfonyl]-2,3-dihydro-1 <i>H</i> -imidazo[4,5- <i>b</i>]quinoxaline
219		<i>N</i> -{3-[(4-methylphenyl)amino]quinoxalin-2-yl}-3-(1 <i>H</i> -tetrazol-1-yl)benzenesulfonamide
220		<i>N</i> -(3-{[2-(ethyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide
221		<i>N</i> -{4-[(3-[(4-ethylphenyl)amino]quinoxalin-2-yl)amino]sulfonyl}phenyl}acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
222		4-bromo-N-(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
223		N-(4-{[(3-{[4-(ethyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
224		N-{4-[(3-{[2-ethylphenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl}acetamide
225		N-(4-{[(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
226		N-(4-{[(3-{[2-(ethyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
227		N-{3-[(4-nitrophenyl)amino]quinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
228		4-(ethyloxy)- <i>N</i> -(3-{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
229		<i>N</i> -(4-{[(3-piperidin-1-yl)quinoxalin-2-yl]amino}sulfonyl)phenyl)acetamide
230		<i>N</i> -cyano- <i>N</i> -(3-piperidin-1-yl)quinoxalin-2-yl)benzenesulfonamide
231		methyl <i>N</i> -acetyl- <i>N</i> -[4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)phenyl]-beta-alaninate
232		methyl <i>N</i> -acetyl- <i>N</i> -{4-[(3-{[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}-beta-alaninate
233		<i>N</i> -{3-[(3-chloro-5-methylphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
234		<i>N</i> -{3-[(3-acetylphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
235		<i>N</i> -[4-(methyloxy)phenyl]-4-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)benzamide
236		4-{{3-}([4-(acetylamino)phenyl]sulfonyl}amino)quinoxalin-2-yl}amino}- <i>N</i> -[4-(methyloxy)phenyl]benzamide
237		2-hydroxy-5-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)benzoic acid
238		<i>N</i> -[3-(2,3-dihydro-1,4-benzodioxin-6-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
239		<i>N</i> -[4-(methyloxy)phenyl]-4-[(3-{{(4-nitrophenyl)sulfonyl}amino}quinoxalin-2-yl)amino]benzamide
240		4-chloro- <i>N</i> -{3-[(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)amino]quinoxalin-2-yl}benzenesulfonamide

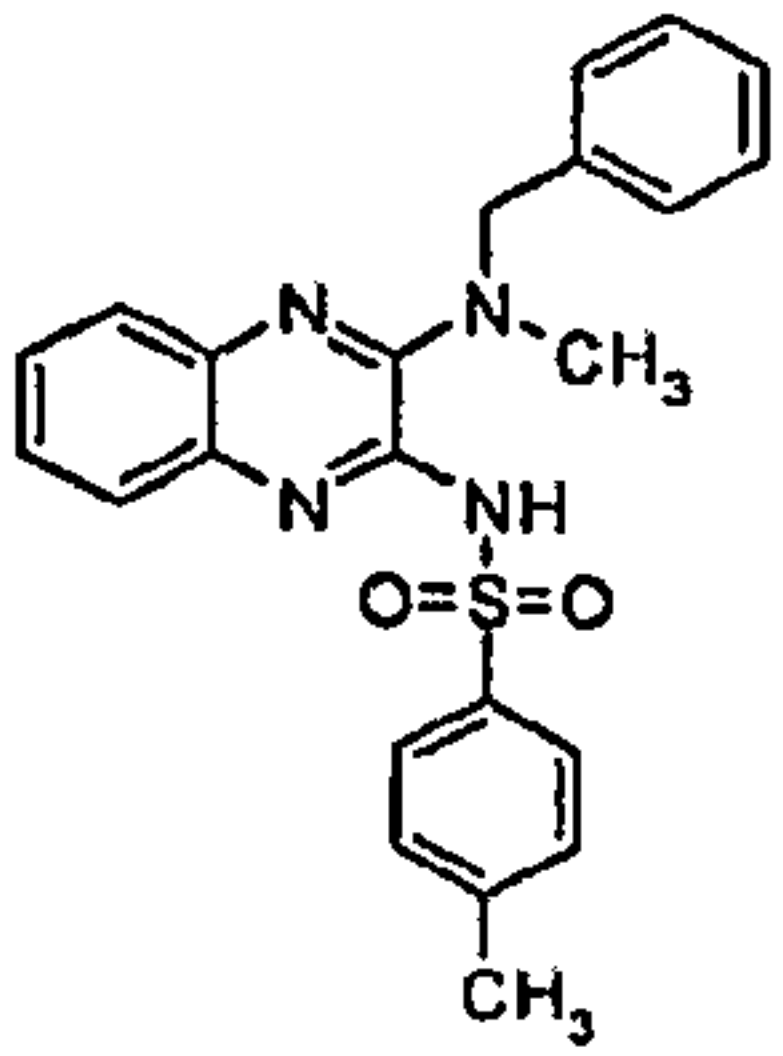
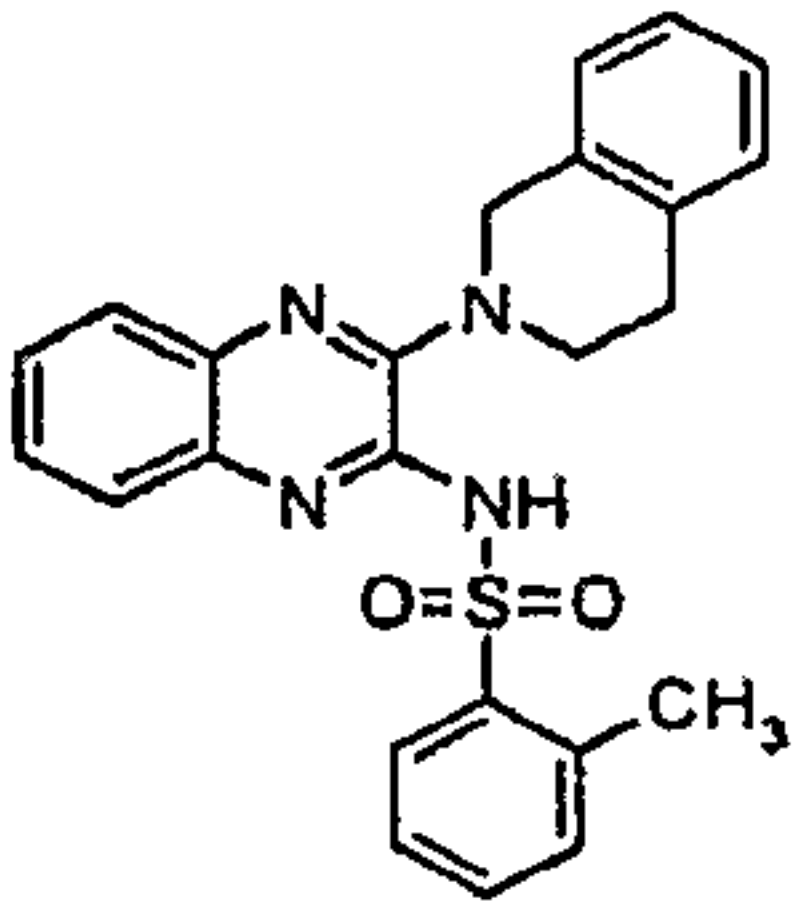
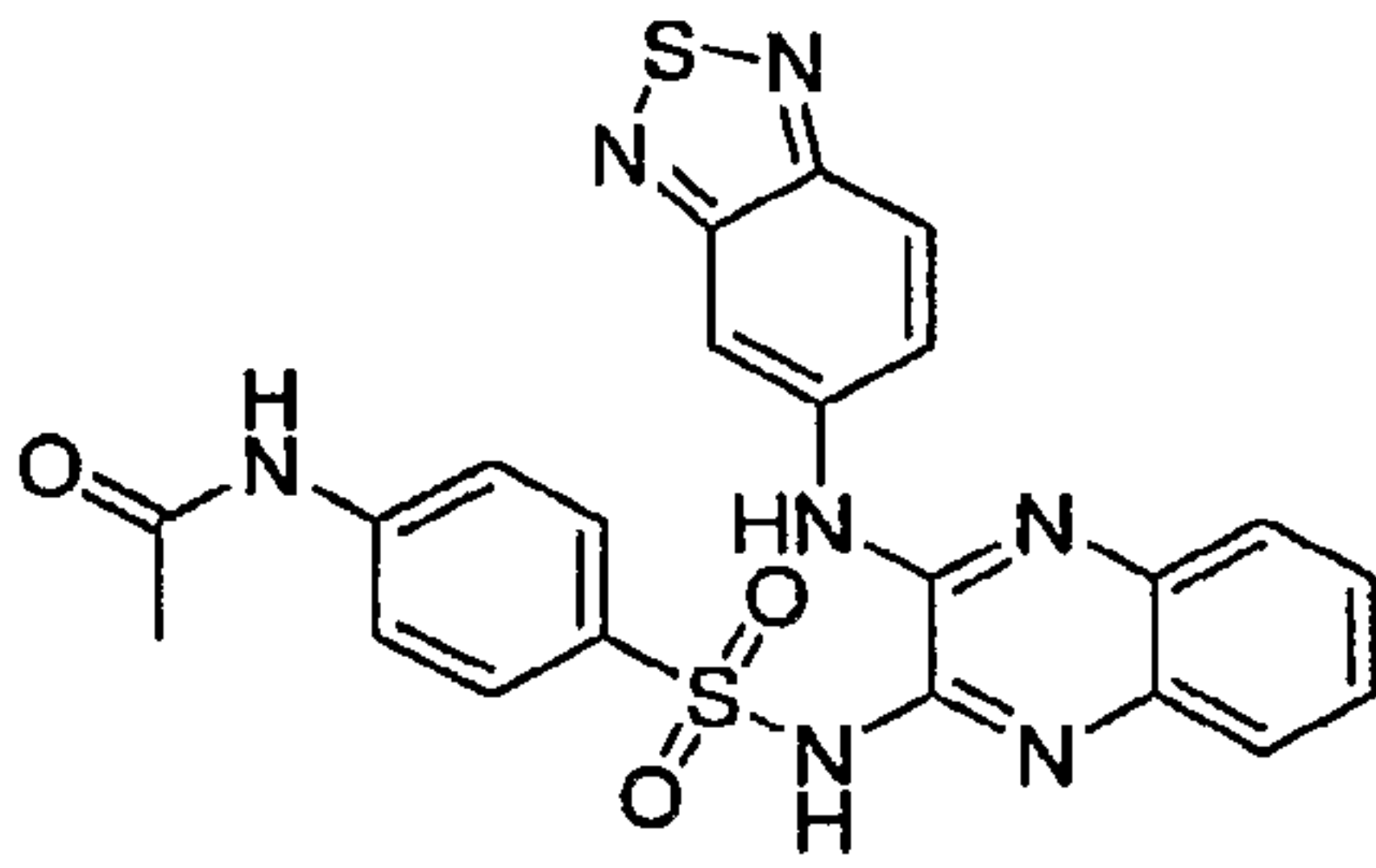
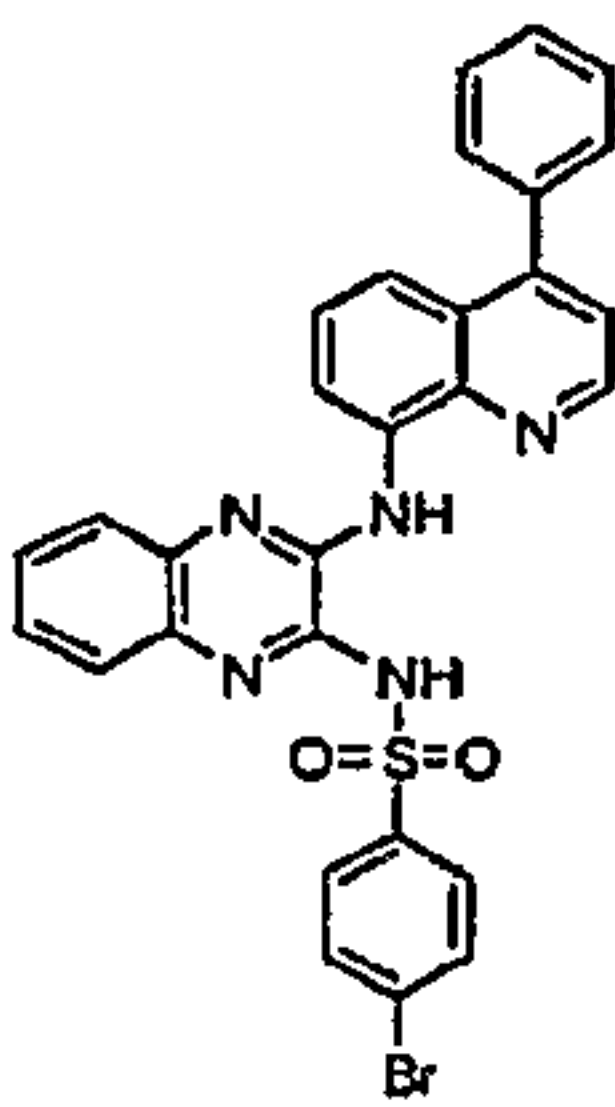
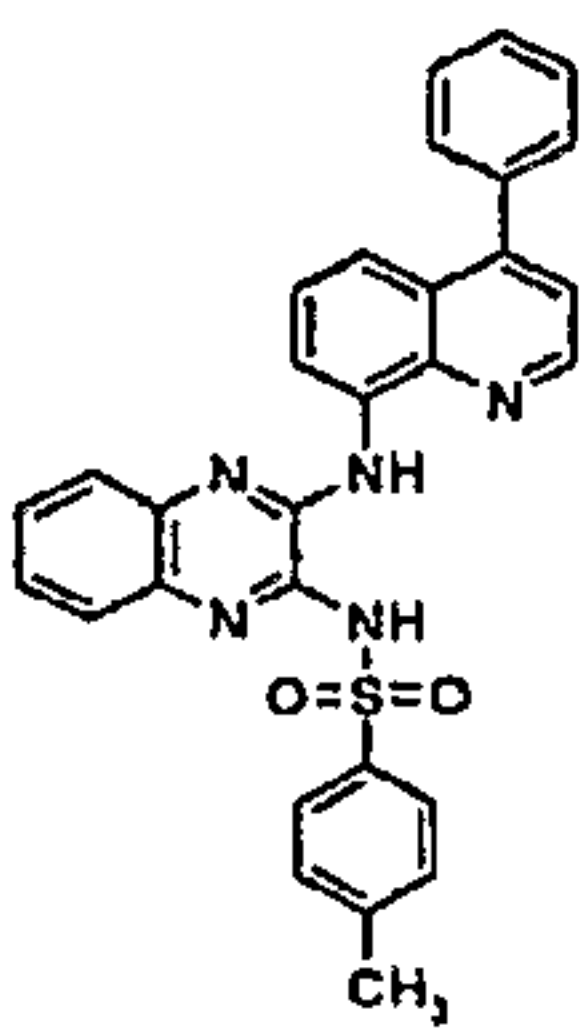
Table 1		
Cpd. No.	Structure	IUPAC Name
241		4-methyl- <i>N</i> -{3-[methyl(phenylmethyl)amino]quinoxalin-2-yl}benzenesulfonamide
242		<i>N</i> -[3-(3,4-dihydroisoquinolin-2(1 <i>H</i>)-yl)quinoxalin-2-yl]-2-methylbenzenesulfonamide
243		<i>N</i> -[4-({[3-(2,1,3-benzothiadiazol-5-ylamino)quinoxalin-2-yl]amino}sulfonyl)phenyl]acetamide
244		4-bromo- <i>N</i> -{3-[(4-phenylquinolin-8-yl)amino]quinoxalin-2-yl}benzenesulfonamide
245		4-methyl- <i>N</i> -{3-[(4-phenylquinolin-8-yl)amino]quinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
246		1-[(4-chlorophenyl)sulfonyl]-3-[4-(pyrrolidin-1-ylsulfonyl)phenyl]-2,3-dihydro-1H-imidazo[4,5-b]quinoxaline
247		1-(4-morpholin-4-ylphenyl)-3-(phenylsulfonyl)-2,3-dihydro-1H-imidazo[4,5-b]quinoxaline
248		methyl 4,5-dimethyl-2-({3-[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)thiophene-3-carboxylate
249		ethyl 6-methyl-2-[(3-{[(2-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
250		ethyl 2-{{3-({[4-(acetamido)phenyl]sulfonyl}amino)quinoxalin-2-yl}amino}-6-phenyl-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
251		ethyl 6-methyl-2-[(3-{[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate

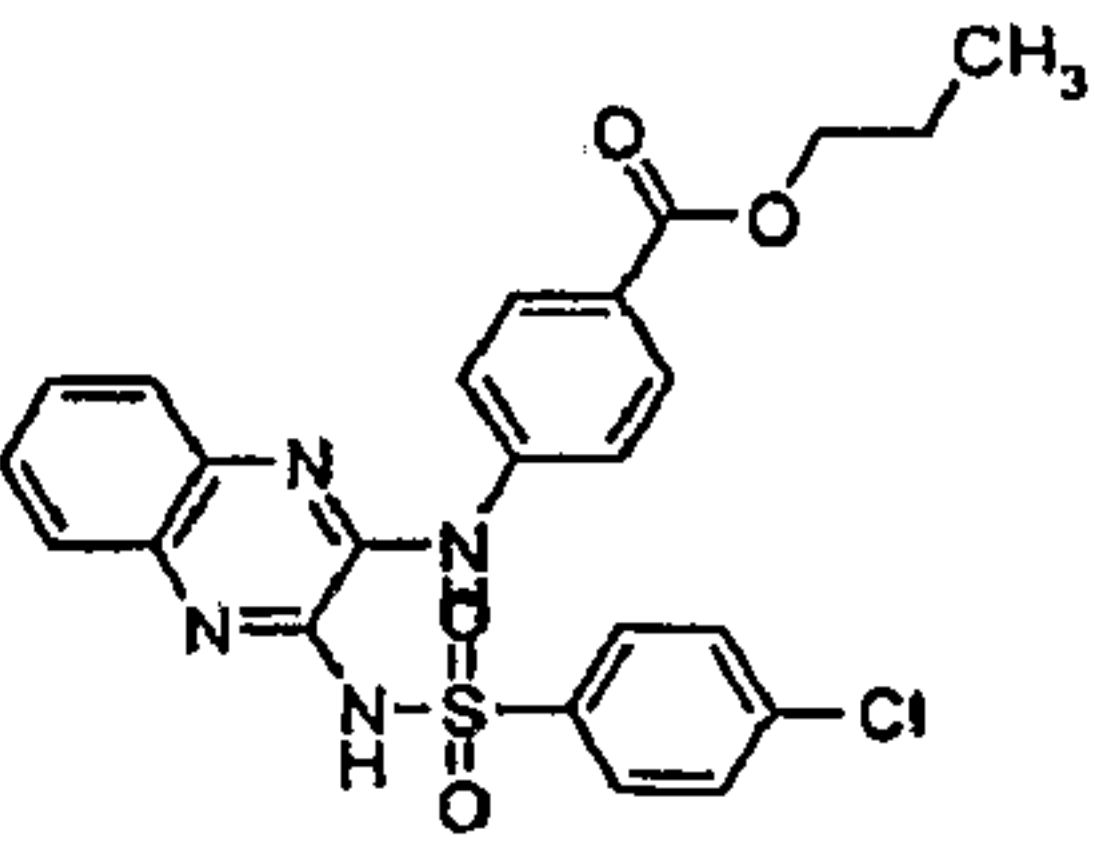
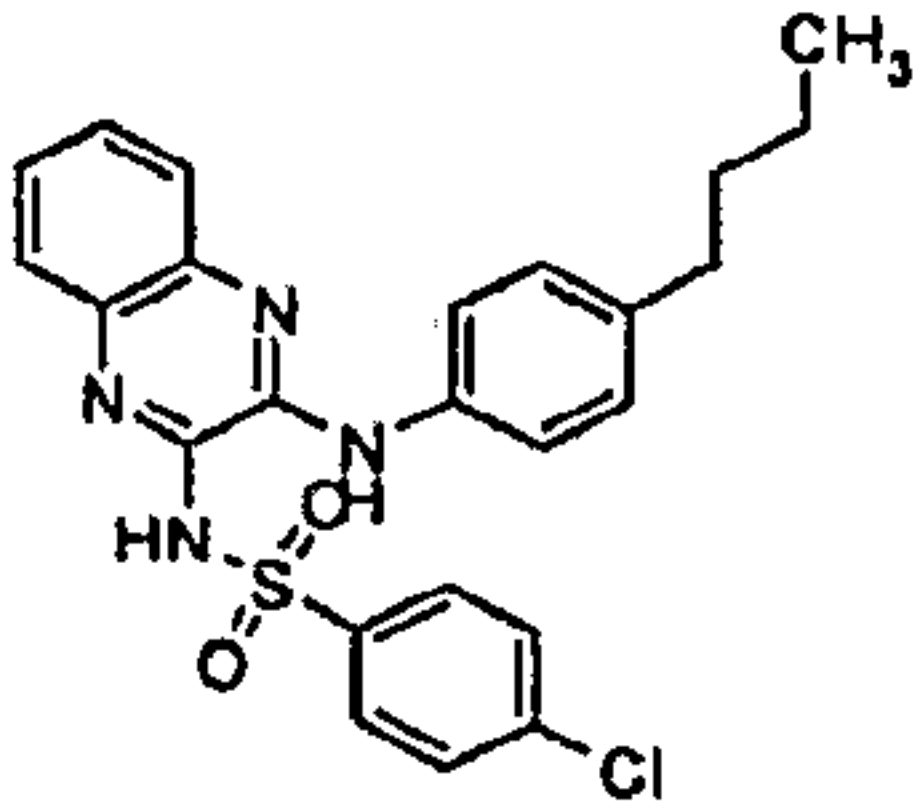
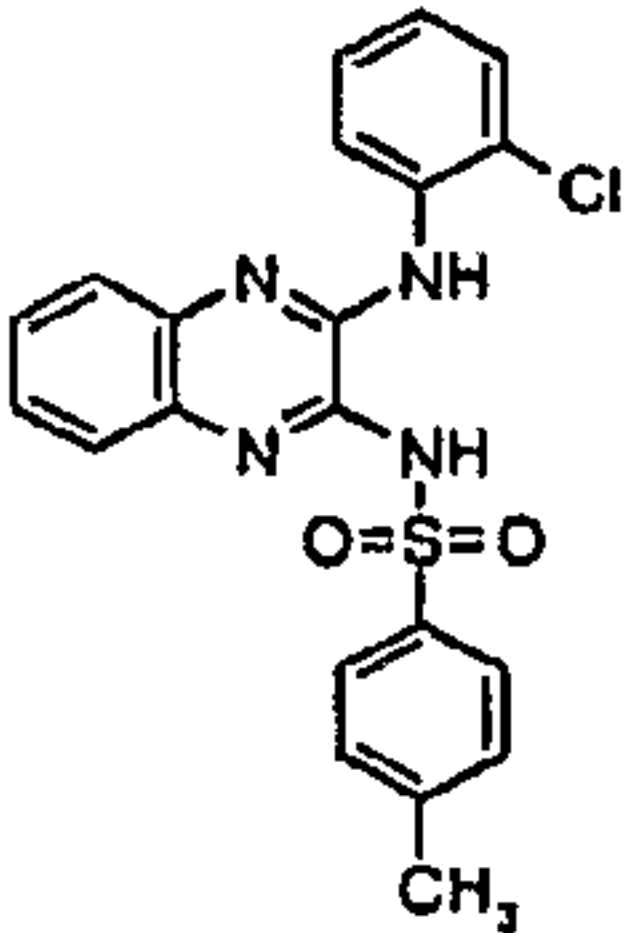
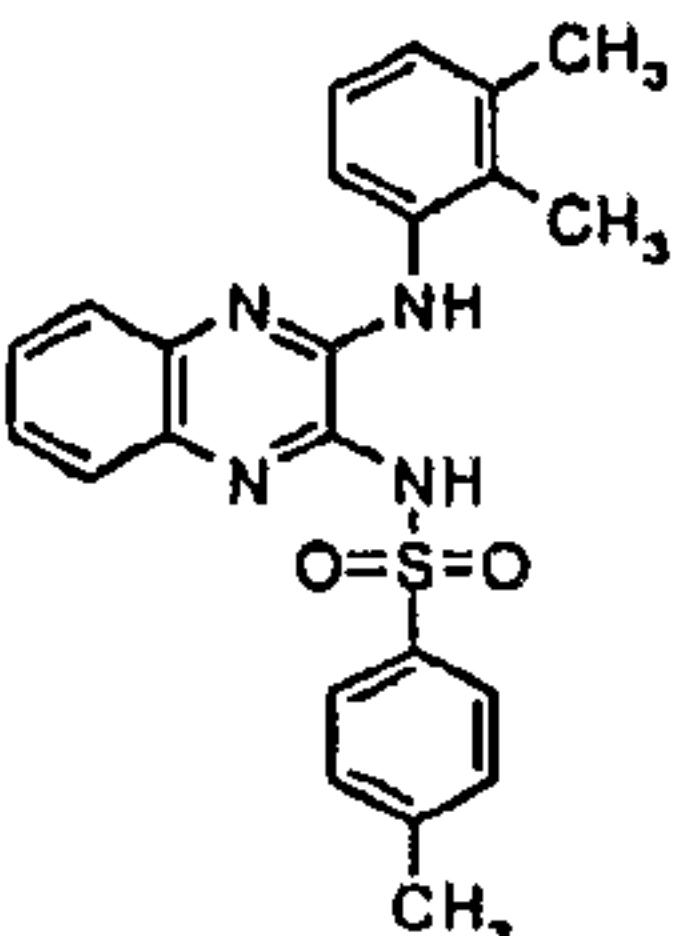
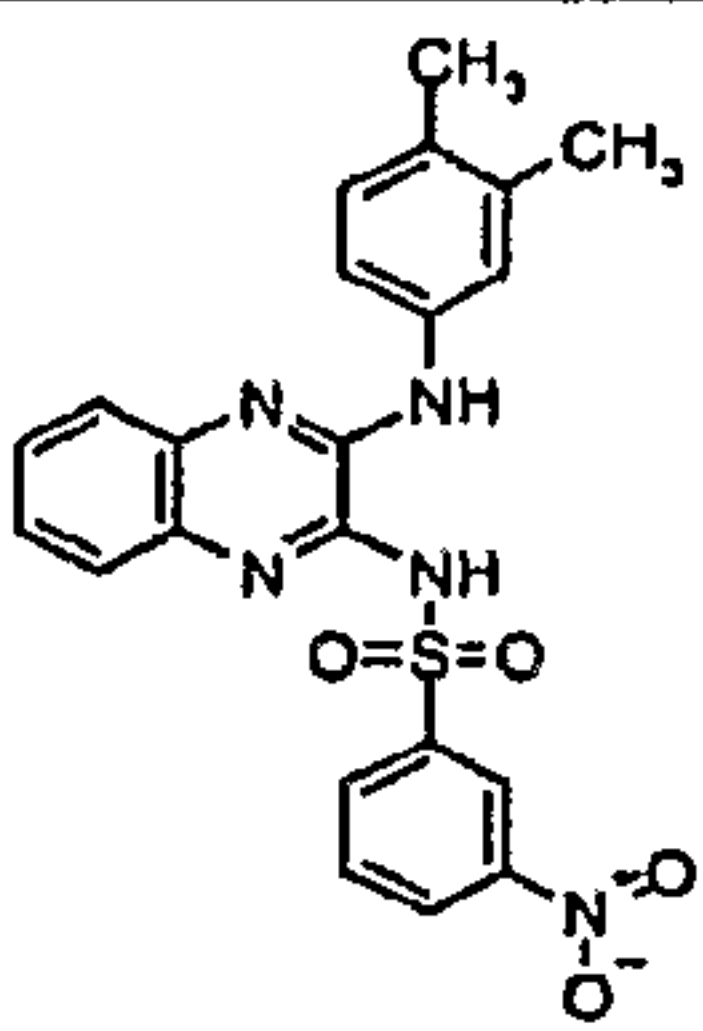
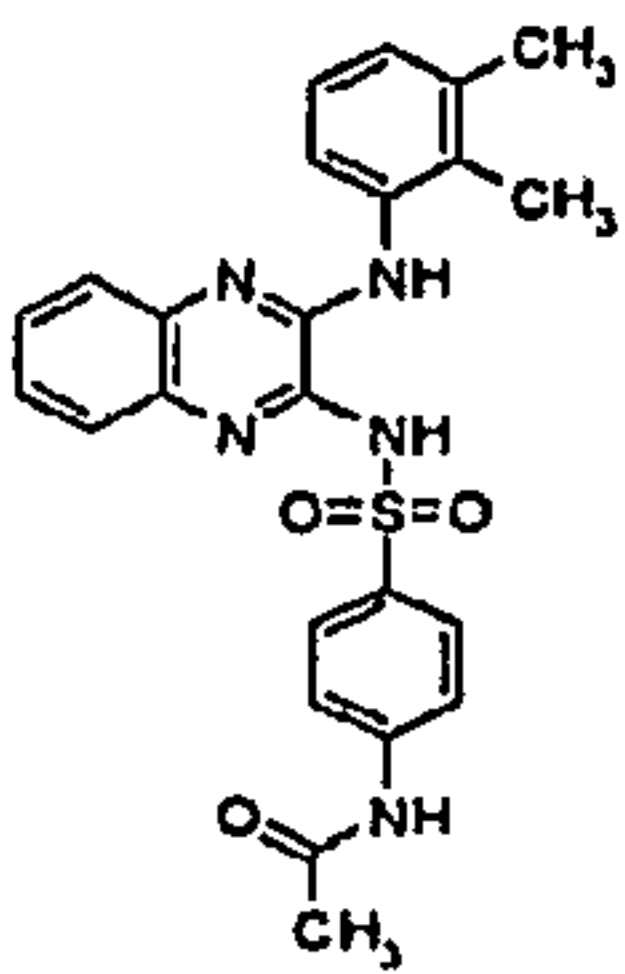
Table 1		
Cpd. No.	Structure	IUPAC Name
252		propyl 4-[(3-[(4-chlorophenyl)sulfonyl]amino)quinoxalin-2-yl]amino]benzoate
253		<i>N</i> -{3-[(4-butylphenyl)amino]quinoxalin-2-yl}-4-chlorobenzenesulfonamide
254		<i>N</i> -{3-[(2-chlorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
255		<i>N</i> -{3-[(2,3-dimethylphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
256		<i>N</i> -{3-[(3,4-dimethylphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
257		<i>N</i> -{4-[(3-[(2,3-dimethylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
258		4-chloro- <i>N</i> -{3-[(2,3-dimethylphenyl)amino]quinoxalin-2-yl} benzenesulfonamide
259		3-nitro- <i>N</i> -(3-{[3,4,5-tris(methyloxy)phenyl]amino}quinoxalin-2-yl) benzenesulfonamide
260		4-chloro- <i>N</i> -{3-[(2,4-dichlorophenyl)amino]quinoxalin-2-yl} benzenesulfonamide
261		<i>N</i> -{3-[(2,3-dimethylphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
262		<i>N</i> -{4-[(3-[(3,4-dimethylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide
263		ethyl 2-[(3-[(4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-5,6-dihydro-4 <i>H</i> -cyclopenta[b]thiophene-3-carboxylate

Table 1		
Cpd. No.	Structure	IUPAC Name
264		4-chloro- <i>N</i> -(3-{[4-chloro-3-(morpholin-4-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
265		ethyl 2-[(3-{[(2-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
266		4-bromo- <i>N</i> -{3-[(2,4-dichlorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
267		ethyl 5-ethyl-2-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]thiophene-3-carboxylate
268		<i>N</i> -(3-{[3-(morpholin-4-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
269		ethyl 2-[(3-{[(4-bromophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
270		4-methyl- <i>N</i> -(3-{[3-(piperidin-1-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
271		4-chloro- <i>N</i> -(3-{[4-(morpholin-4-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
272		4-chloro- <i>N</i> -(3-{[3-(morpholin-4-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
273		4-methyl- <i>N</i> -[3-(quinolin-6-ylamino)quinoxalin-2-yl]benzenesulfonamide
274		<i>N</i> -(3-{[3-(piperidin-1-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
275		<i>N</i> -(3-{[4-(phenylamino)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
276		<i>N</i> -(3-{[2,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-4-bromobenzenesulfonamide
277		ethyl 2-[(3-([(3-nitrophenyl)sulfonyl]amino)quinoxalin-2-yl)amino]-5,6-dihydro-4 <i>H</i> -cyclopenta[b]thiophene-3-carboxylate

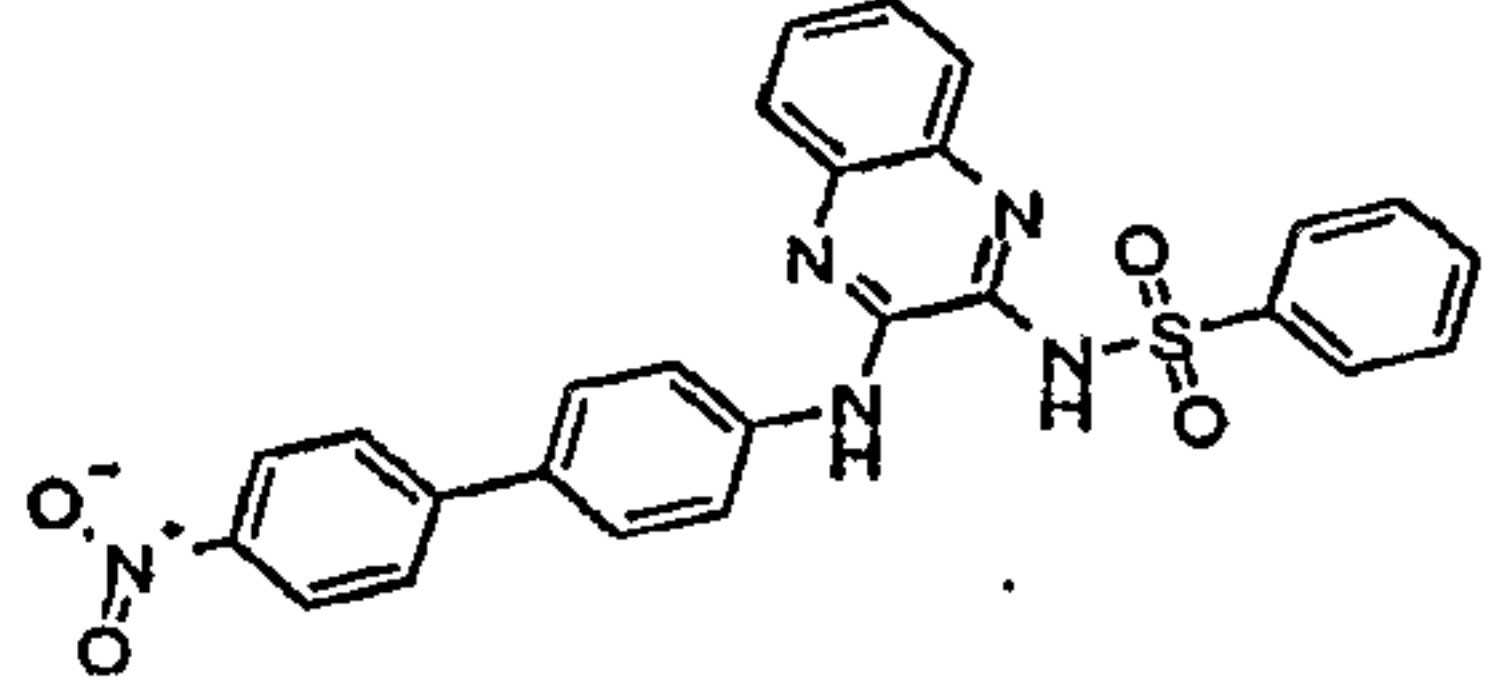
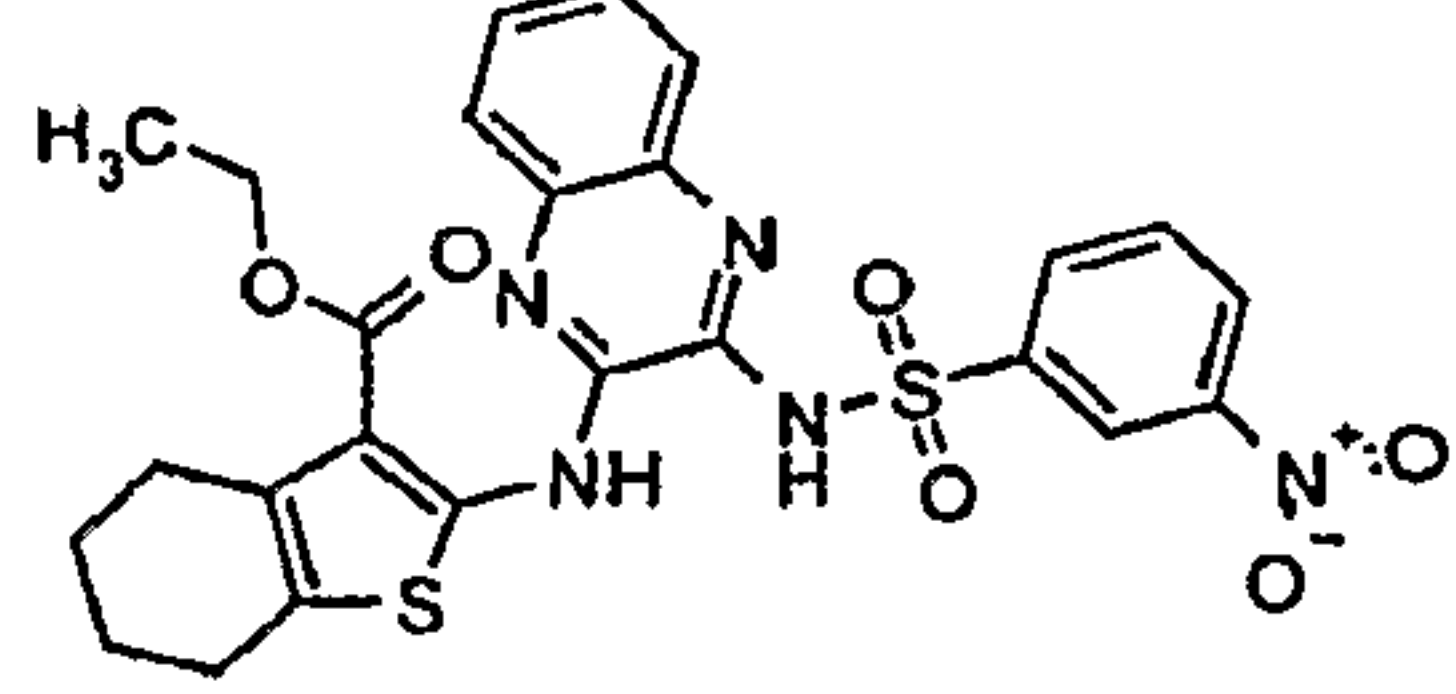
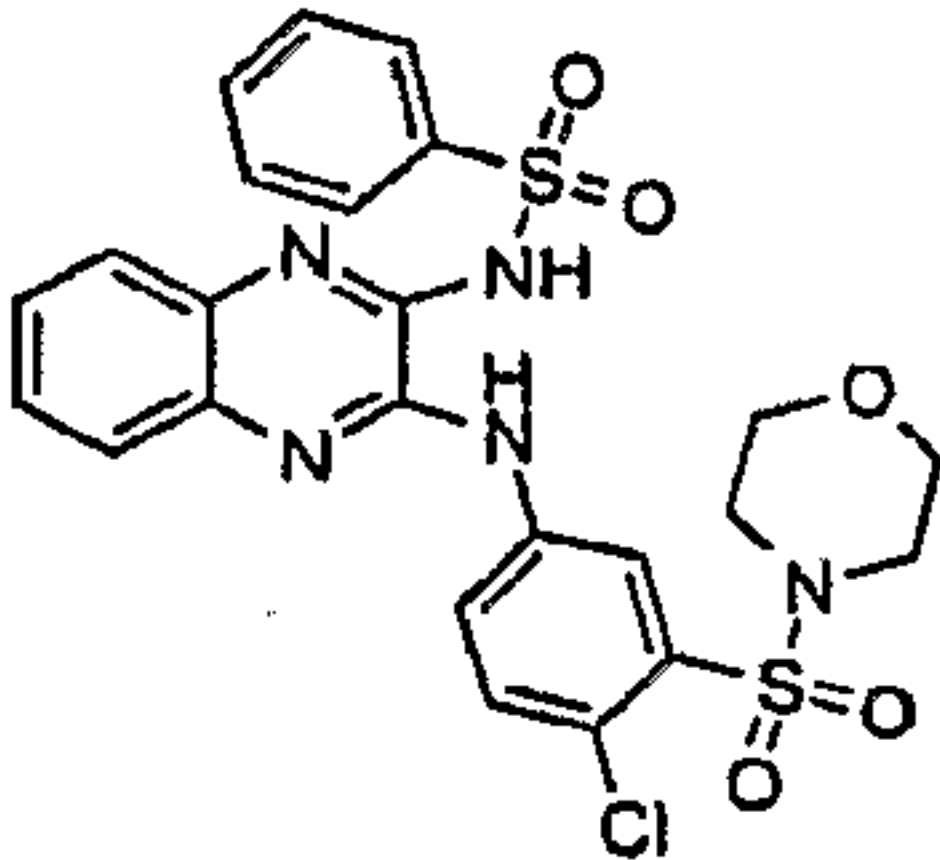
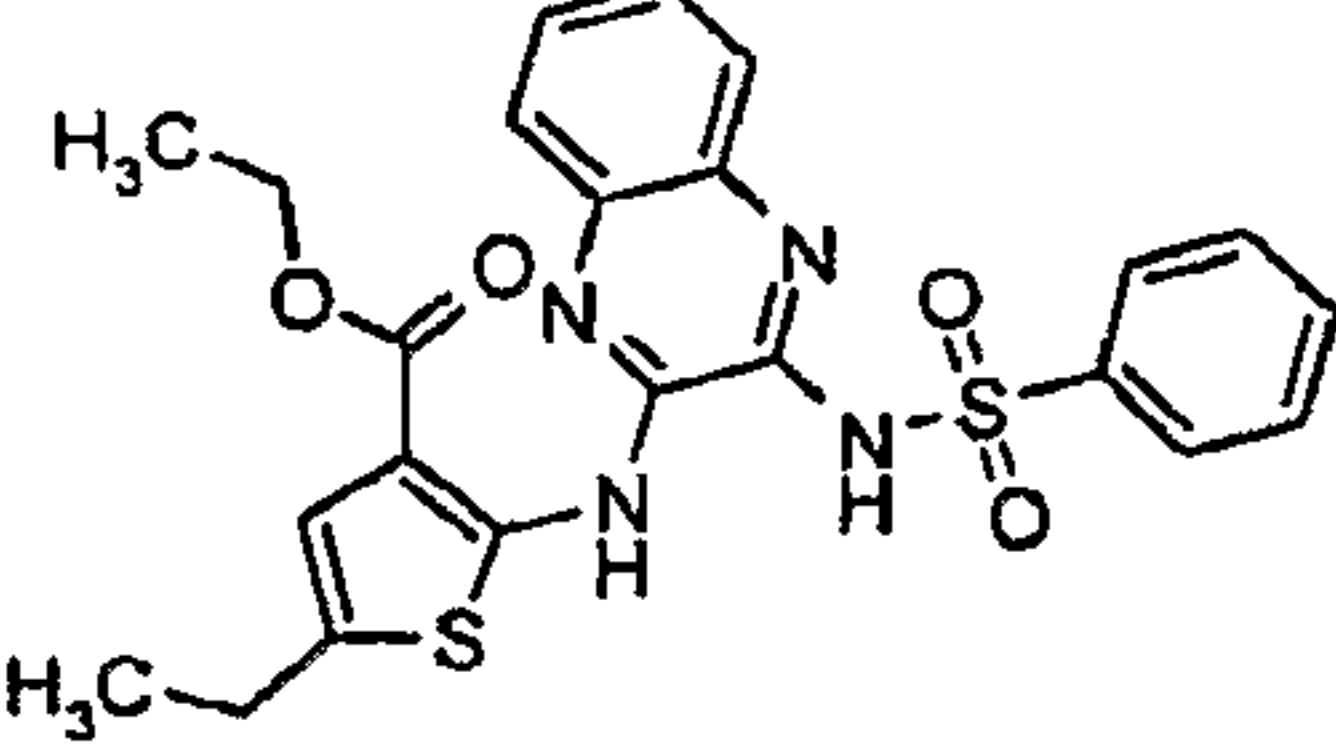
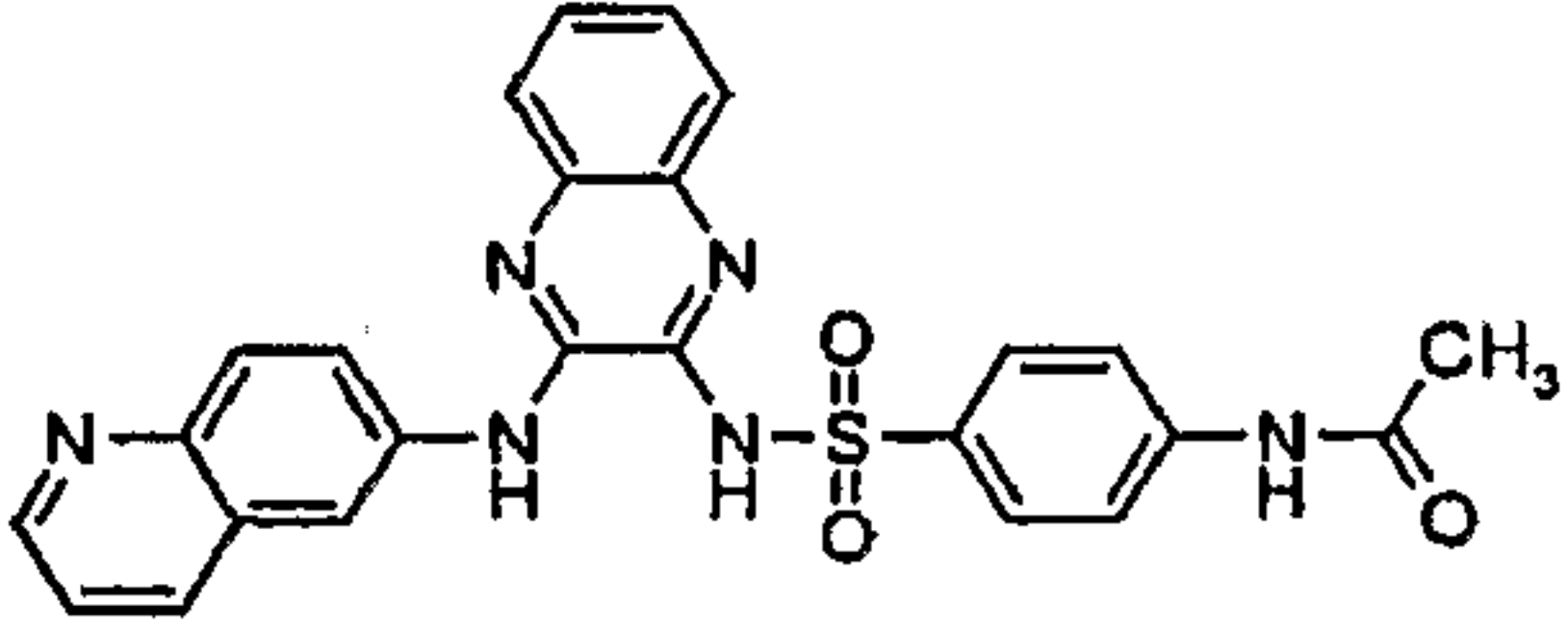
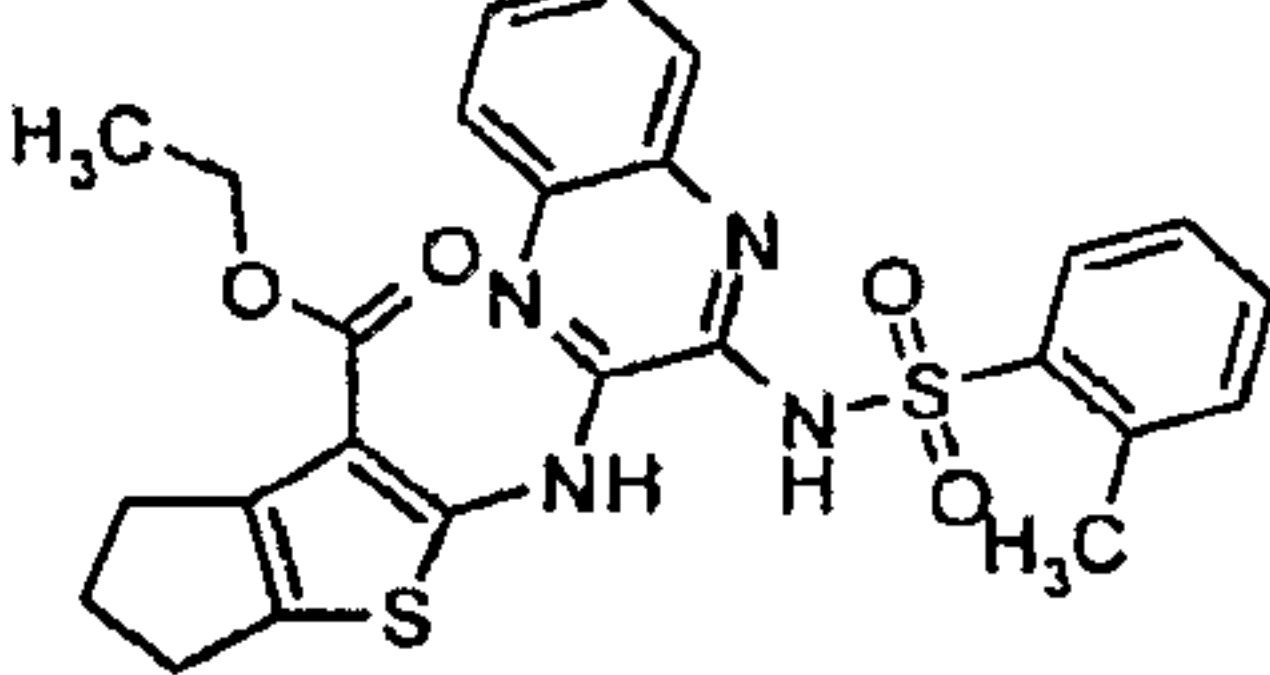
Table 1		
Cpd. No.	Structure	IUPAC Name
278		<i>N</i> -{3-[(4'-nitrobiphenyl-4-yl)amino]quinoxalin-2-yl}benzenesulfonamide
279		ethyl 2-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
280		<i>N</i> -(3-{[4-chloro-3-(morpholin-4-ylsulfonyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
281		ethyl 5-ethyl-2-[(3-{[(phenylsulfonyl)amino]quinoxalin-2-yl}amino)thiophene-3-carboxylate
282		<i>N</i> -[4-({[3-(quinolin-6-ylamino)quinoxalin-2-yl]amino}sulfonyl)phenyl]acetamide
283		ethyl 2-[(3-{[(2-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]-5,6-dihydro-4 <i>H</i> -cyclopenta[b]thiophene-3-carboxylate

Table 1		
Cpd. No.	Structure	IUPAC Name
284		3,4-dichloro- <i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl]benzenesulfonamide
285		ethyl 2-[[3-([4-(acetylamino)-3,5-dibromophenyl]sulfonyl)amino]quinoxalin-2-yl]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
286		ethyl 2-[(3-[(2-chloro-5-nitrophenyl)sulfonyl]amino)quinoxalin-2-yl]amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
287		<i>N</i> -{3-[(3-fluorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
288		<i>N</i> -(3-[[4-(morpholin-4-ylsulfonyl)phenyl]amino]quinoxalin-2-yl)benzenesulfonamide
289		ethyl 2-[[3-([4-(acetylamino)phenyl]sulfonyl)amino]quinoxalin-2-yl]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
290		ethyl 2-[(3-[[4-(4-chlorophenyl)sulfonyl]amino]quinoxalin-2-yl]amino]-5-ethylthiophene-3-carboxylate

Table 1		
Cpd. No.	Structure	IUPAC Name
291		<i>N,N</i> -diethyl-4-[(3-[[4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzenesulfonamide
292		ethyl 2-[[3-((4-(acetylamino)phenyl)sulfonyl)amino}quinoxalin-2-yl]amino]-5-ethylthiophene-3-carboxylate
293		<i>N</i> -[3-(1,3-benzodioxol-5-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
294		ethyl 2-[(3-[[4-chlorophenyl)sulfonyl]amino}quinoxalin-2-yl]amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
295		ethyl 2-[(3-[(phenylsulfonyl)amino]quinoxalin-2-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate
296		<i>N</i> -[4-(methoxy)phenyl]-4-[(3-[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzamide
297		<i>N</i> -[3-((4-[(4-aminophenyl)oxy]phenyl)amino)quinoxalin-2-yl]-4-chlorobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
298		<i>N</i> -[4-({[3-({4-[(4-aminophenyl)oxy]phenyl}amino)quinoxalin-2-yl]amino}sulfonyl)phenyl]acetamide
299		(2E)-3-{3-[(3-{{(4-methylphenyl)sulfonyl}amino}quinoxalin-2-yl)amino]phenyl}prop-2-enoic acid
300		<i>N</i> -{3-[(9-ethyl-9 <i>H</i> -carbazol-3-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
301		<i>N</i> -[3-({4-[(4-aminophenyl)oxy]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide
302		4-[(3-{{(4-chlorophenyl)sulfonyl}amino}quinoxalin-2-yl)amino]- <i>N</i> -[4-(methyloxy)phenyl]benzamide
303		4-bromo- <i>N</i> -{3-[(9-ethyl-9 <i>H</i> -carbazol-3-yl)amino]quinoxalin-2-yl}benzenesulfonamide
304		<i>N</i> -{3-[(9-ethyl-9 <i>H</i> -carbazol-3-yl)amino]quinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
305		<i>N</i> -{3-[(2-iodophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
306		<i>N</i> -{3-[(1-phenylethyl)amino]quinoxalin-2-yl}benzenesulfonamide
307		4-bromo- <i>N</i> -{3-[(4-bromophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
308		4-bromo- <i>N</i> -{3-[(4-chlorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
309		4-bromo- <i>N</i> -[3-(naphthalen-2-ylamino)quinoxalin-2-yl]benzenesulfonamide
310		<i>N</i> -{3-[(2,3-dimethylphenyl)amino]-6-methylquinoxalin-2-yl}-4-methylbenzenesulfonamide
311		4-chloro- <i>N</i> -{3-[(2-iodophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
312		<i>N</i> -(3-{[4-(octyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

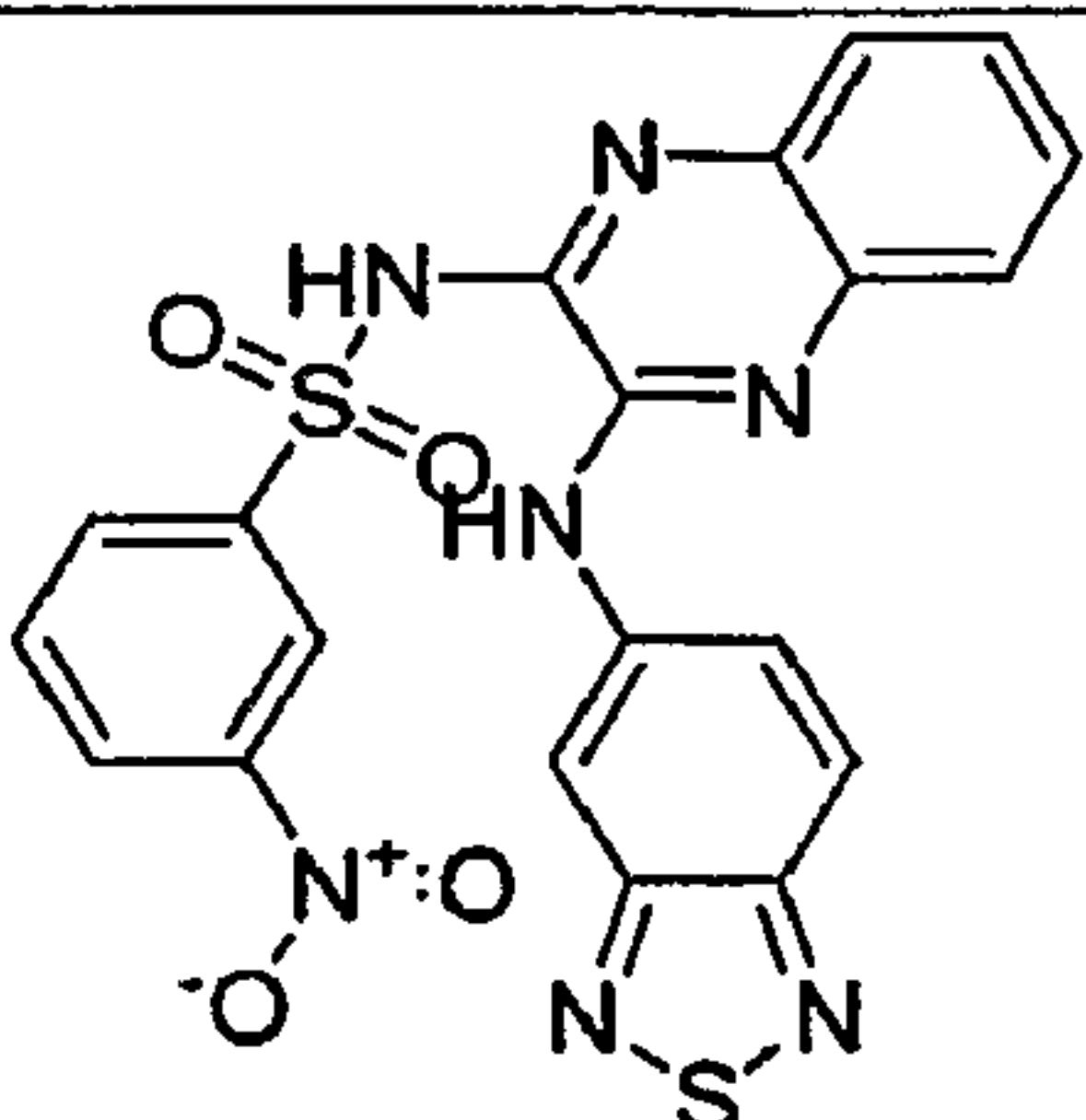
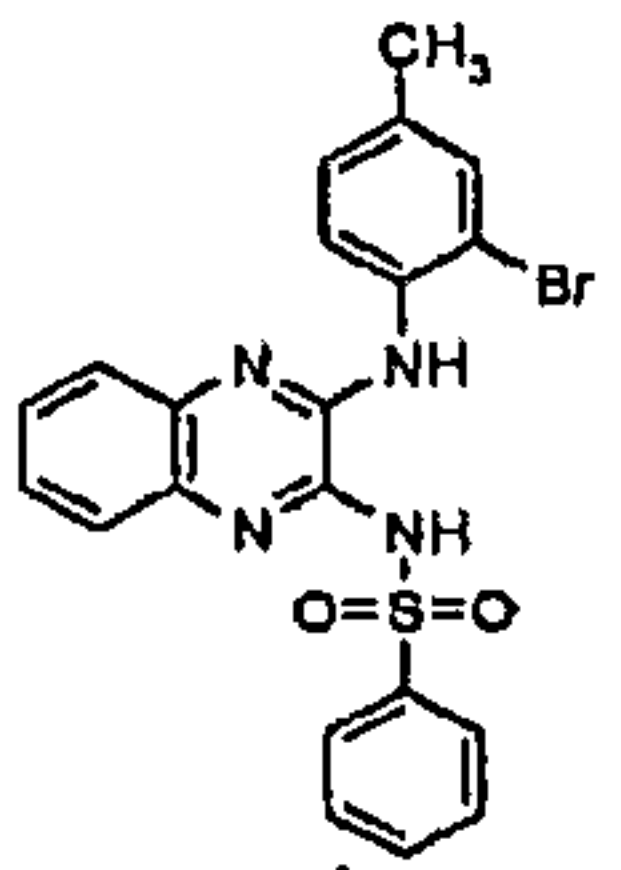
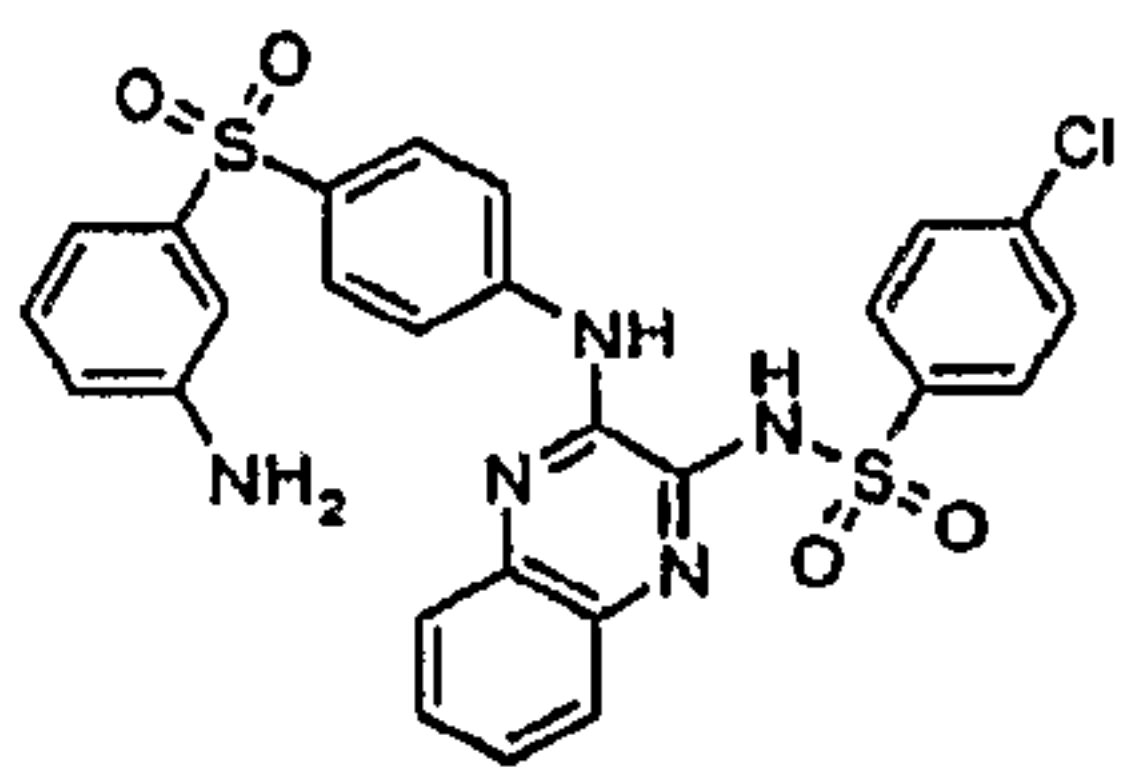
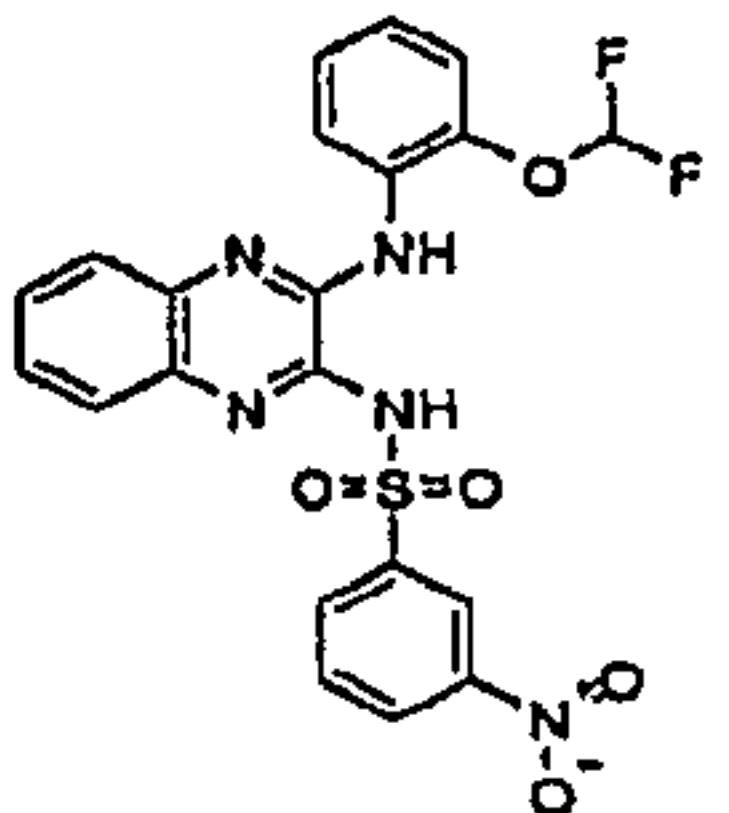
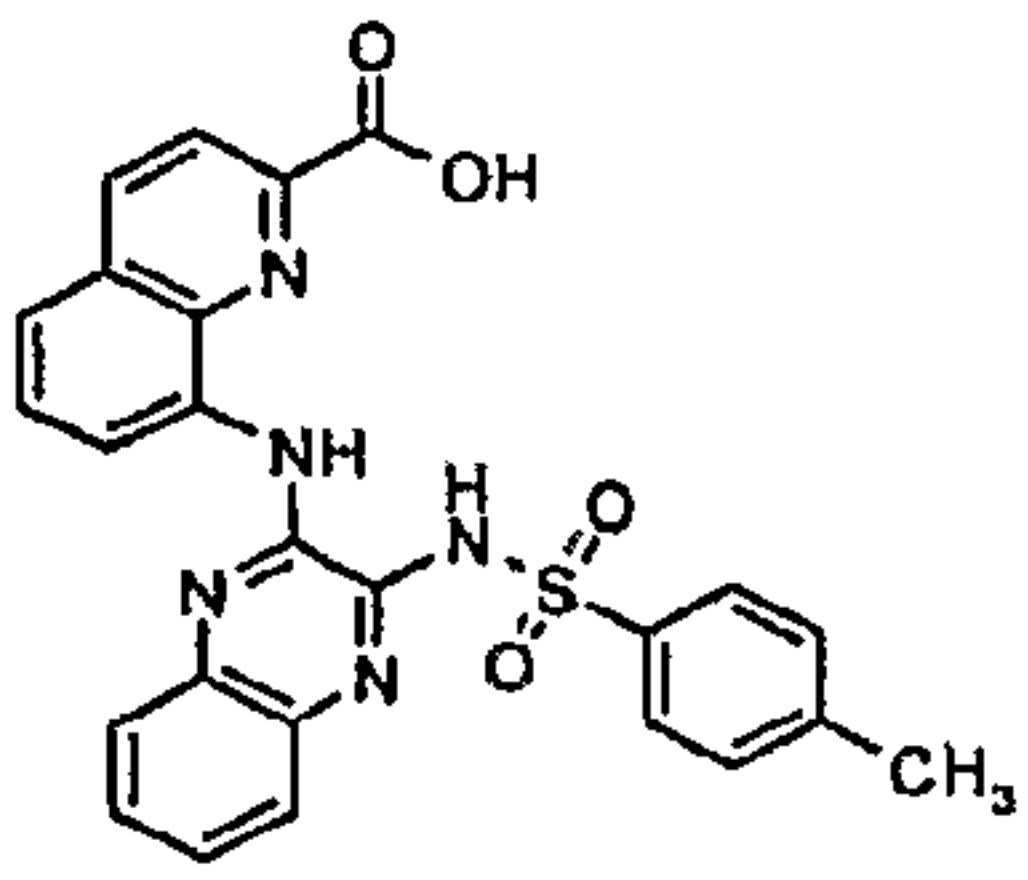
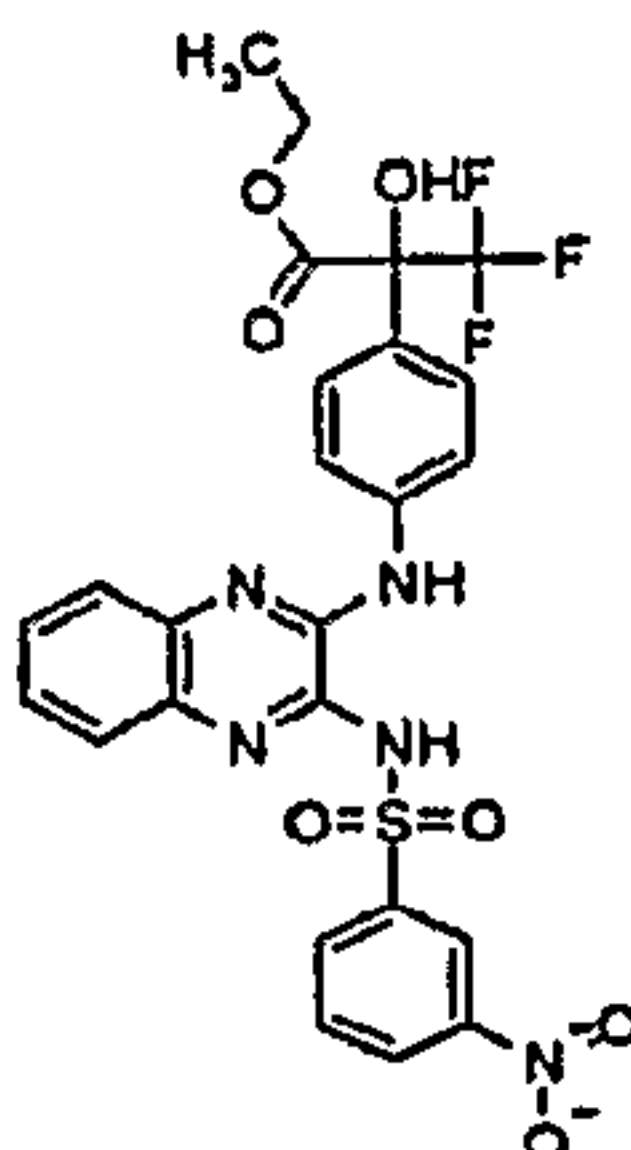
Table 1		
Cpd. No.	Structure	IUPAC Name
313		<i>N</i> -[3-(2,1,3-benzothiadiazol-5-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
314		<i>N</i> -{3-[(2-bromo-4-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
315		<i>N</i> -[3-({4-[(3-aminophenyl)sulfonyl]phenyl}amino)quinoxalin-2-yl]-4-chlorobenzenesulfonamide
316		<i>N</i> -[3-({2-[(difluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
317		8-[(3-{{4-methylphenyl}sulfonyl}amino}quinoxalin-2-yl)amino]quinoline-2-carboxylic acid
318		ethyl 3,3,3-trifluoro-2-hydroxy-2-{4-[(3-{{3-nitrophenyl}sulfonyl}amino}quinoxalin-2-yl)amino]phenyl}propanoate

Table 1		
Cpd. No.	Structure	IUPAC Name
319		<i>N</i> -[3-(quinolin-6-ylamino)quinoxalin-2-yl]benzenesulfonamide
320		4-{[3-({[4-(acetylamino)phenyl]sulfonyl}amino)quinoxalin-2-yl]amino}phenyl thiocyanate
321		1-[3-({[4-(acetylamino)phenyl]sulfonyl}amino)quinoxalin-2-yl]-4-methylpyridinium
322		<i>N</i> -{3-[(2-chlorophenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
323		4-methyl- <i>N</i> -[3-(phenylamino)quinoxalin-2-yl]benzenesulfonamide
324		4-methyl- <i>N</i> -{3-[(2-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
325		4-methyl- <i>N</i> -{3-[(4-methylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
326		<i>N</i> -{3-[(4-chlorophenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
327		4-methyl- <i>N</i> -[3-(naphthalen-2-ylamino)quinoxalin-2-yl]benzenesulfonamide
328		<i>N</i> -{4-[(3-[(4-bromophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide
329		<i>N</i> -{4-[(3-[(2-methylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}acetamide
330		<i>N</i> -{3-[bis(phenylmethyl)amino]quinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
331		<i>N</i> -(3-piperidin-1-ylquinoxalin-2-yl)benzenesulfonamide
332		4-[(3-[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
333		2-hydroxy-4-[(3-[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)amino]benzoic acid
334		4-bromo- <i>N</i> -(3-{[2-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
335		4-methyl- <i>N</i> -(3-piperidin-1-ylquinoxalin-2-yl)benzenesulfonamide
336		<i>N</i> -{3-[(3-hydroxyphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
337		<i>N</i> -[3-(naphthalen-1-ylamino)quinoxalin-2-yl]benzenesulfonamide
338		3-methyl-1-(3-[(4-methylphenyl)sulfonyl]amino}quinoxalin-2-yl)pyridinium

Table 1		
Cpd. No.	Structure	IUPAC Name
339		<i>N</i> -(3-{{3-[(4-methoxyphenyl)sulfonyl]amino}-7-(methoxy)quinoxalin-2-yl}amino)phenyl)acetamide
340		<i>N</i> -{3-[(3-[(4-chlorophenyl)sulfonyl]amino)quinoxalin-2-yl]amino}phenyl)acetamide
341		<i>N</i> -{3-[(4-bromophenyl)amino]quinoxalin-2-yl}-4-chlorobenzenesulfonamide
342		<i>N</i> -{3-[(2,4-dimethylphenyl)amino]-6-methylquinoxalin-2-yl}-4-methylbenzenesulfonamide
343		<i>N</i> -{3-[(3,4-dimethylphenyl)amino]quinoxalin-2-yl}-4-methylbenzenesulfonamide
344		<i>N</i> -{3-[(2,5-dimethylphenyl)amino]-6-methylquinoxalin-2-yl}-4-methylbenzenesulfonamide
345		ethyl 4-[(3-[(4-chlorophenyl)sulfonyl]amino)quinoxalin-2-yl]amino]benzoate
346		4-chloro- <i>N</i> -{3-[(4-ethylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
347		4-chloro- <i>N</i> -(6-methyl-3-{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
348		4-chloro- <i>N</i> -{3-[(4-chlorophenyl)amino]-6-methylquinoxalin-2-yl}benzenesulfonamide
349		<i>N</i> -(3-{[4-chloro-2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
350		<i>N</i> -[3-({2-[2,5-bis(methyloxy)phenyl]ethyl}amino)quinoxalin-2-yl]benzenesulfonamide
351		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
352		<i>N</i> -(3-{[3,4,5-tris(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
353		<i>N</i> -[3-({3-[(phenylmethyl)oxy]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide

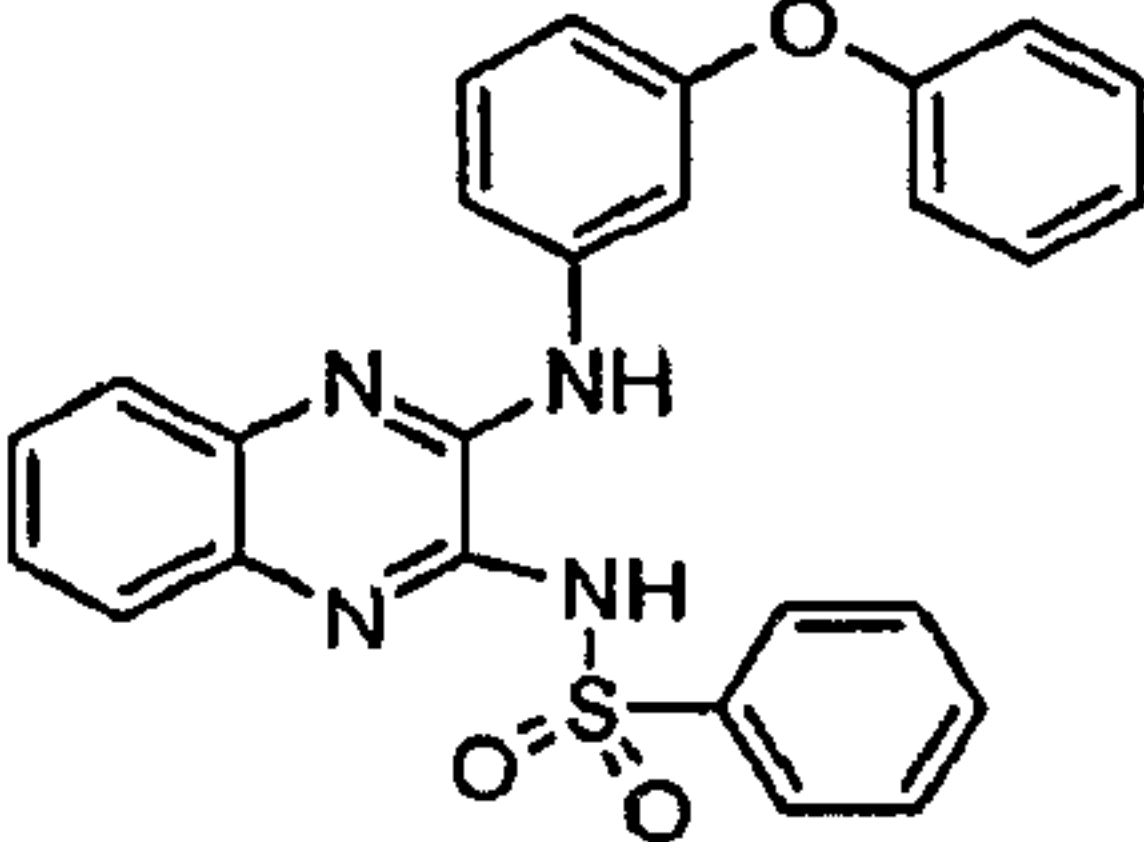
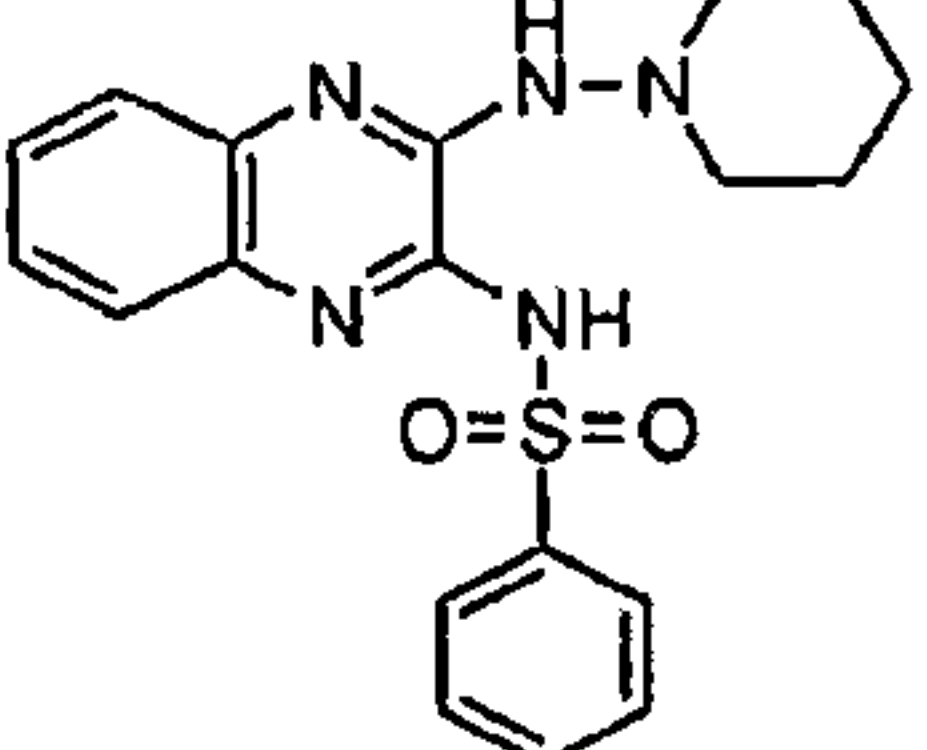
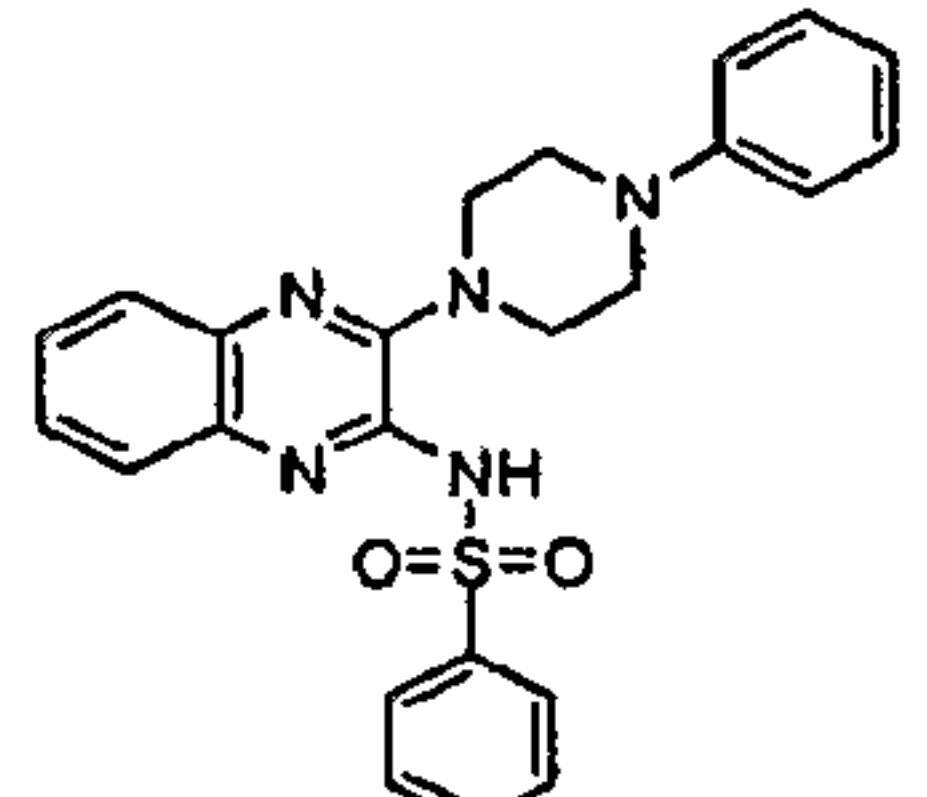
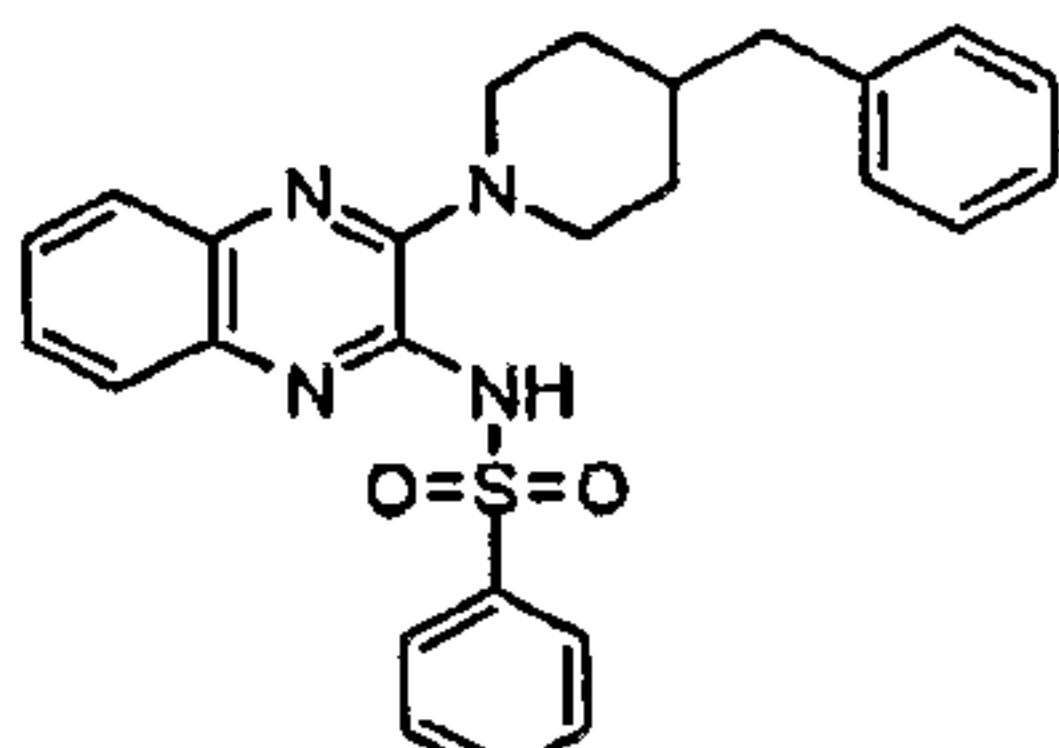
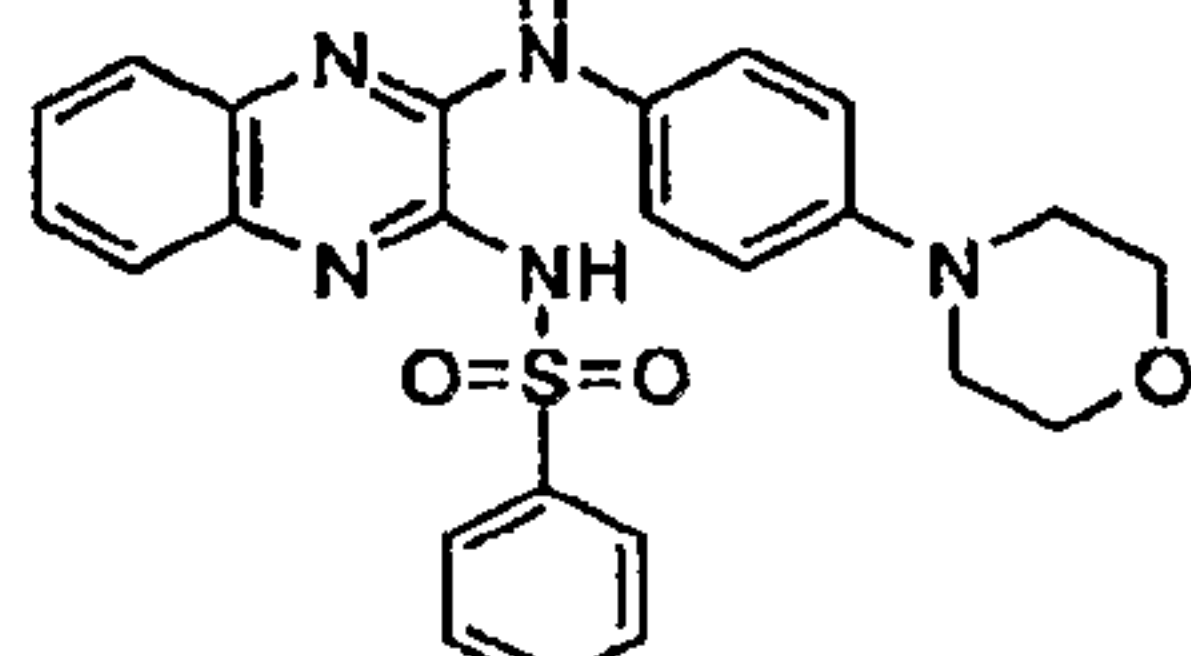
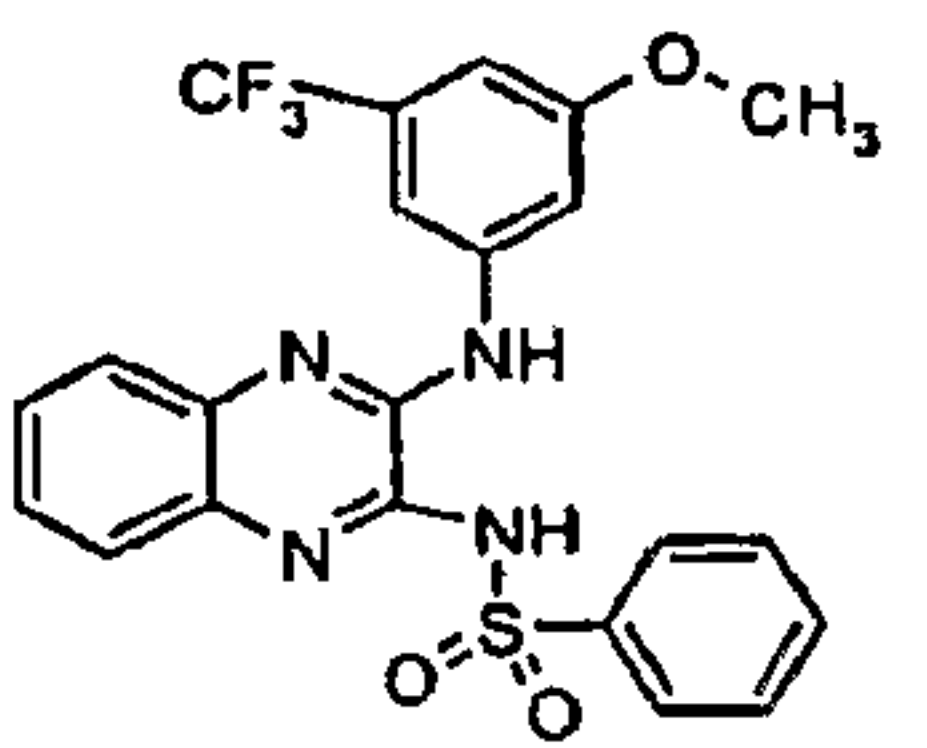
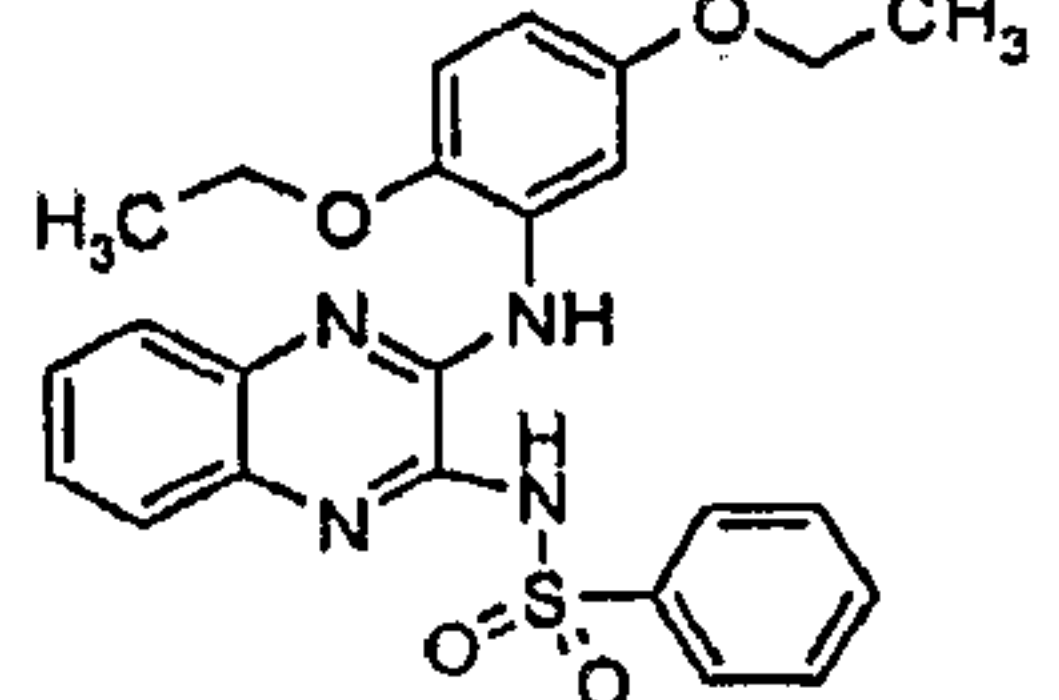
Table 1		
Cpd. No.	Structure	IUPAC Name
354		<i>N</i> -(3-{[3-(phenyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
355		<i>N</i> -[3-(piperidin-1-ylamino)quinoxalin-2-yl]benzenesulfonamide
356		<i>N</i> -[3-(4-phenylpiperazin-1-yl)quinoxalin-2-yl]benzenesulfonamide
357		<i>N</i> -{3-[4-(phenylmethyl)piperidin-1-yl]quinoxalin-2-yl}benzenesulfonamide
358		<i>N</i> -{3-[(4-morpholin-4-yl)phenyl]amino}quinoxalin-2-yl}benzenesulfonamide
359		<i>N</i> -(3-{[3-(methoxy)-5-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
360		<i>N</i> -(3-{[2,5-bis(ethoxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

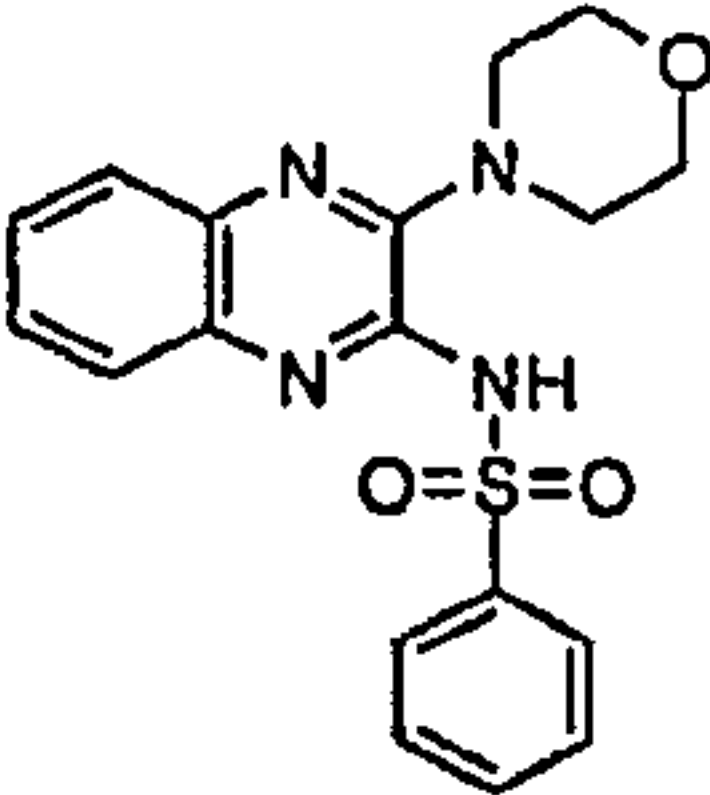
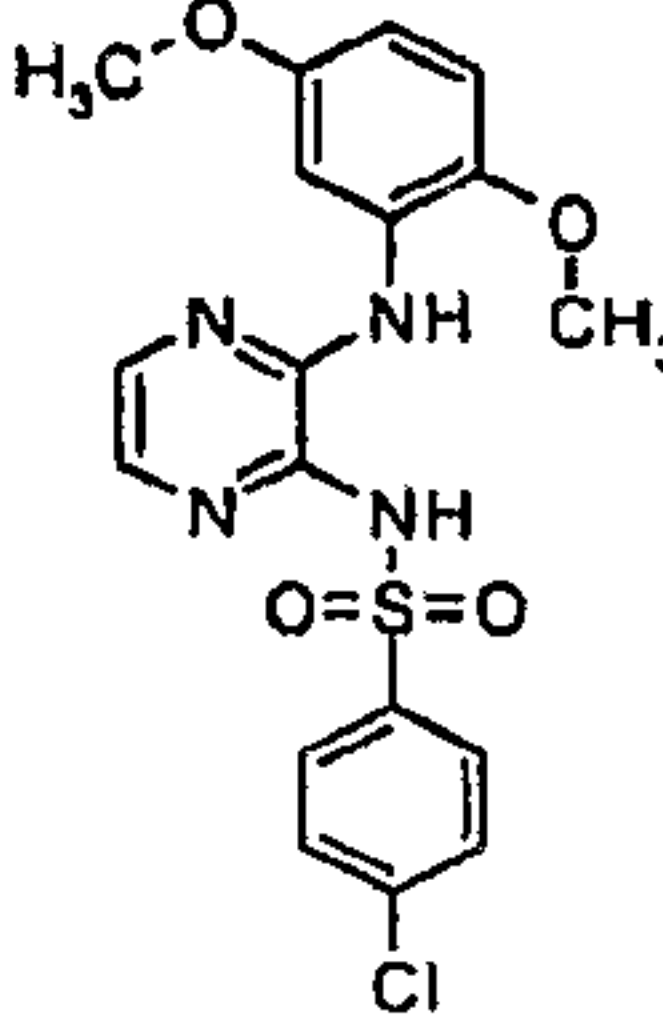
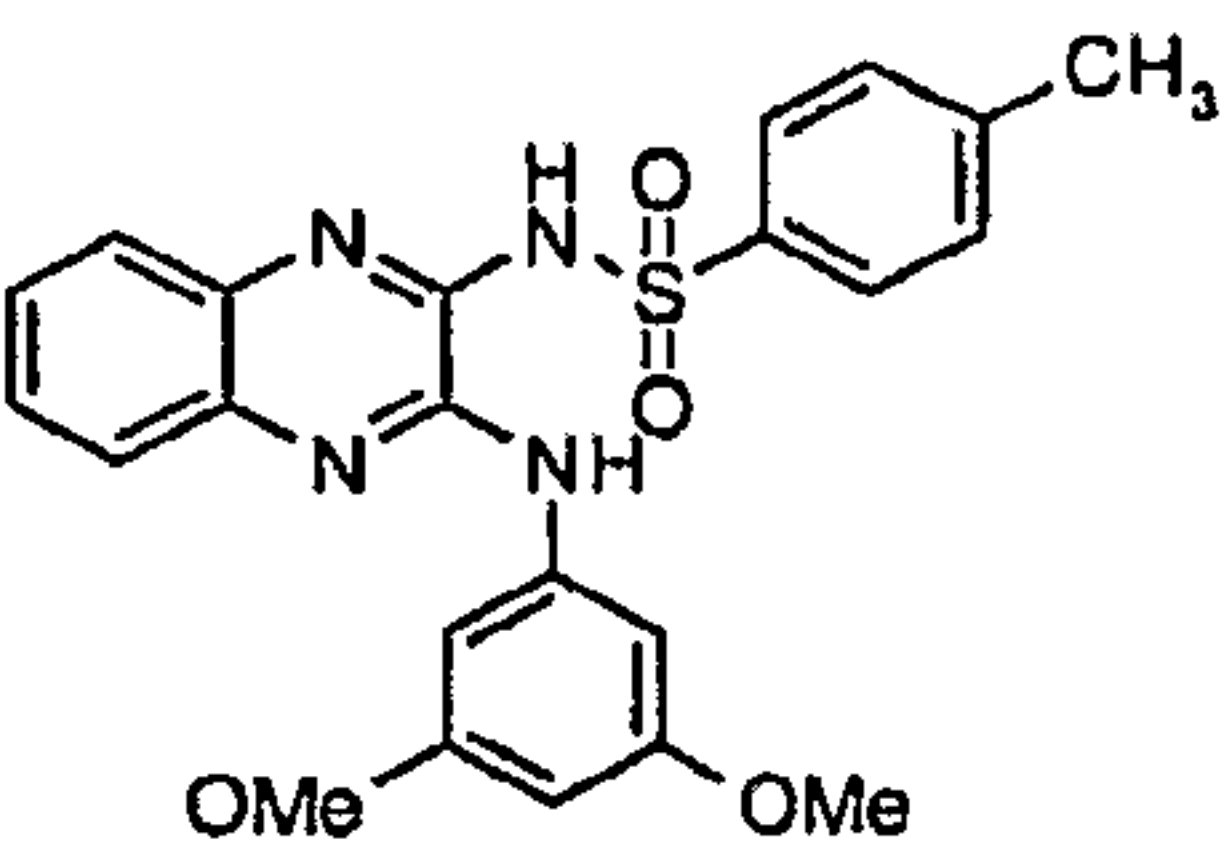
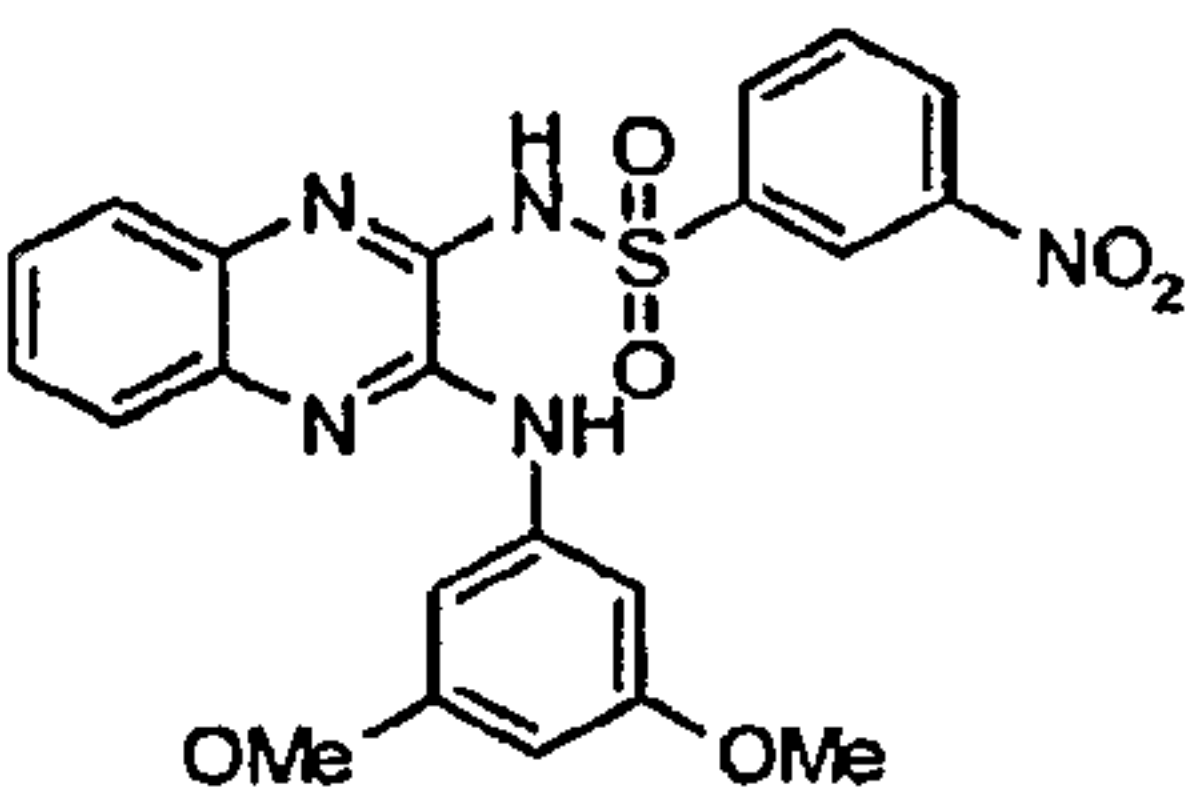
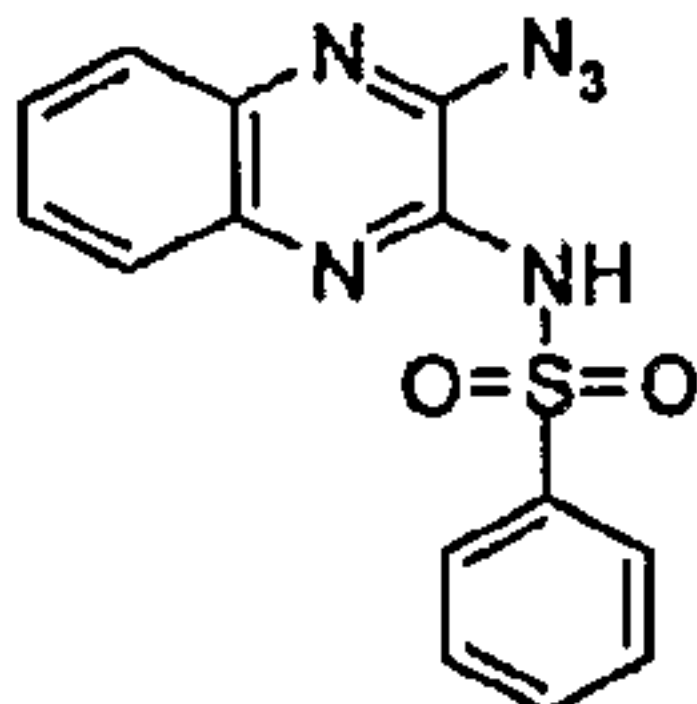
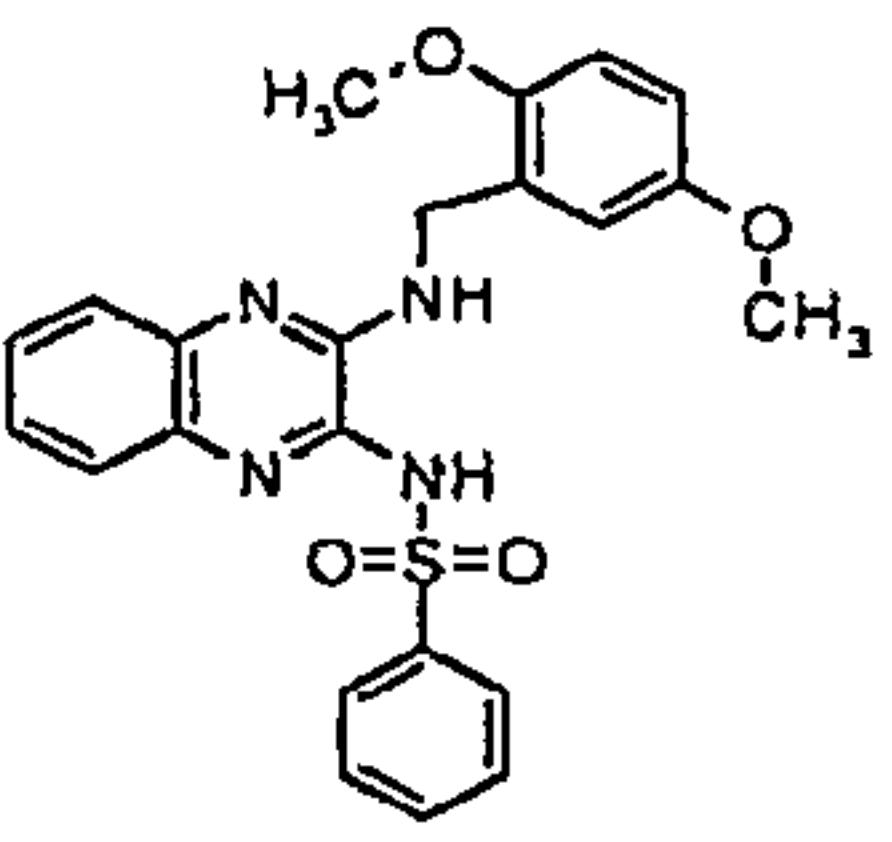
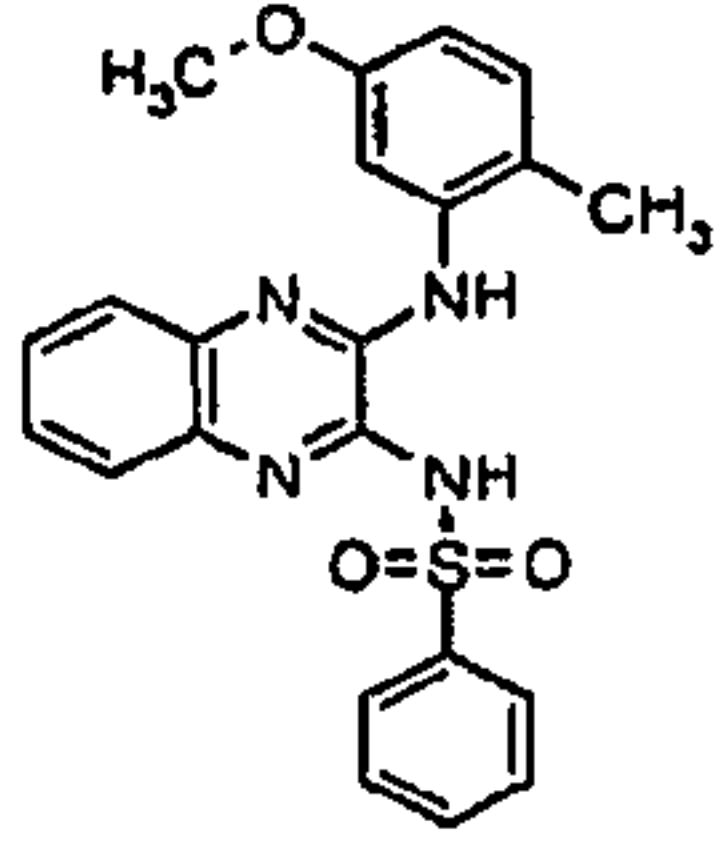
Table 1		
Cpd. No.	Structure	IUPAC Name
361		<i>N</i> -(3-morpholin-4-ylquinoxalin-2-yl)benzenesulfonamide
362		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}pyrazin-2-yl)-4-chlorobenzenesulfonamide
363		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide
364		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
365		<i>N</i> -(3-azidoquinoxalin-2-yl)benzenesulfonamide
366		<i>N</i> -[3-({[2,5-bis(methyloxy)phenyl]methyl}amino)quinoxalin-2-yl]benzenesulfonamide
367		<i>N</i> -(3-{[2-methyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

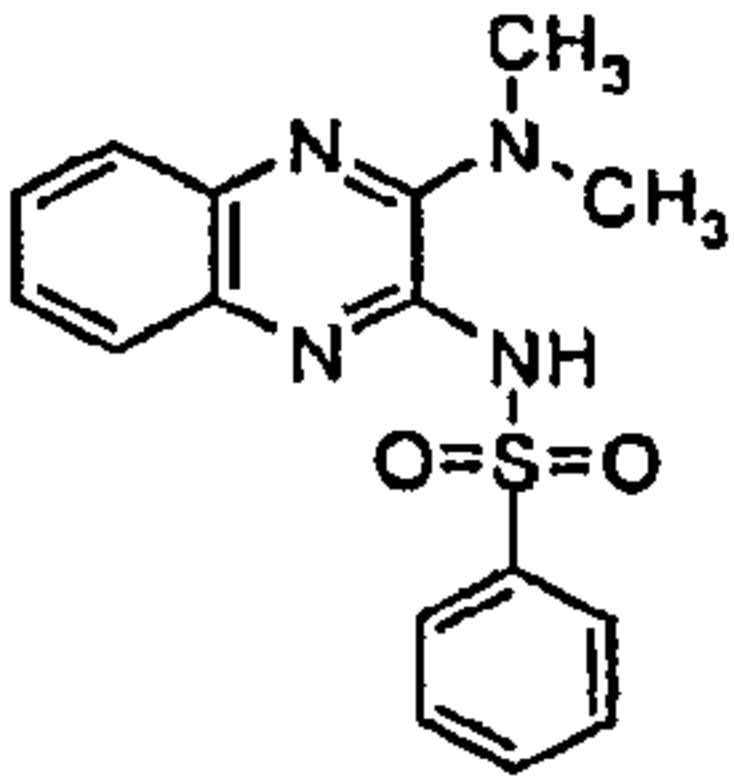
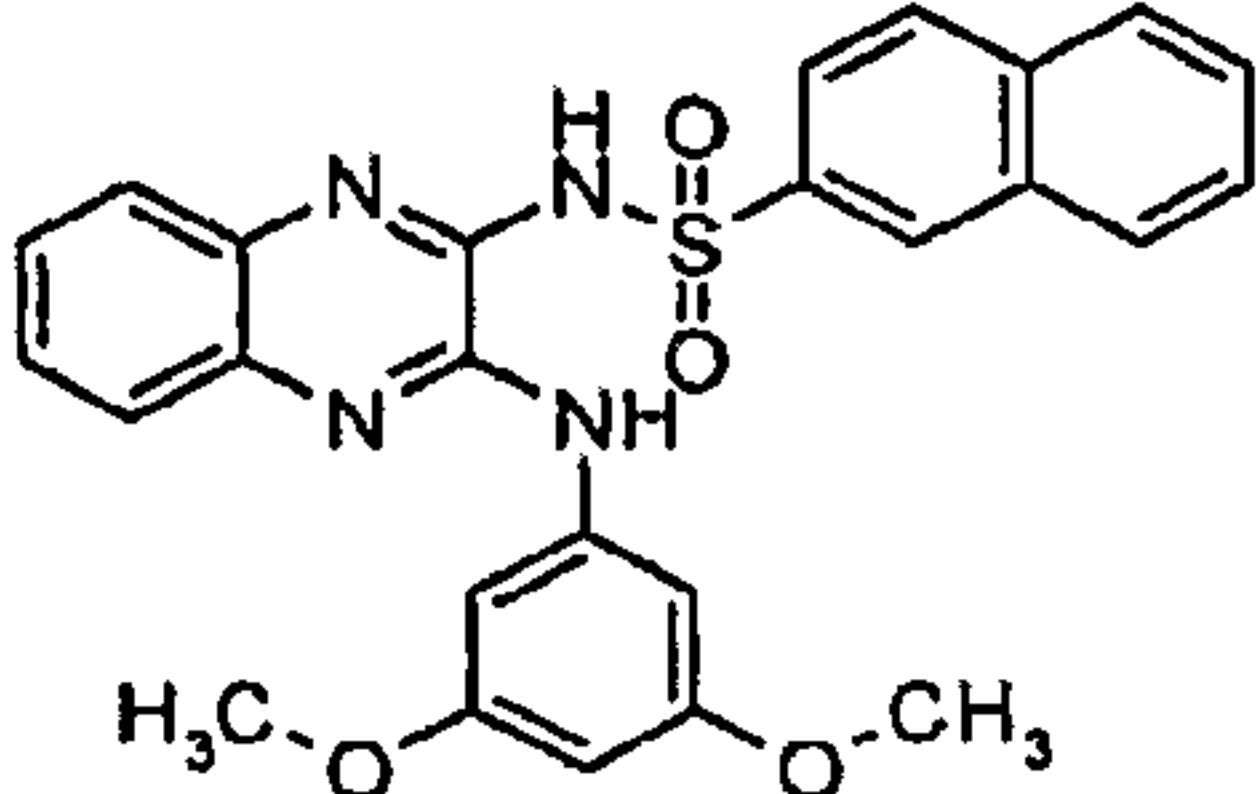
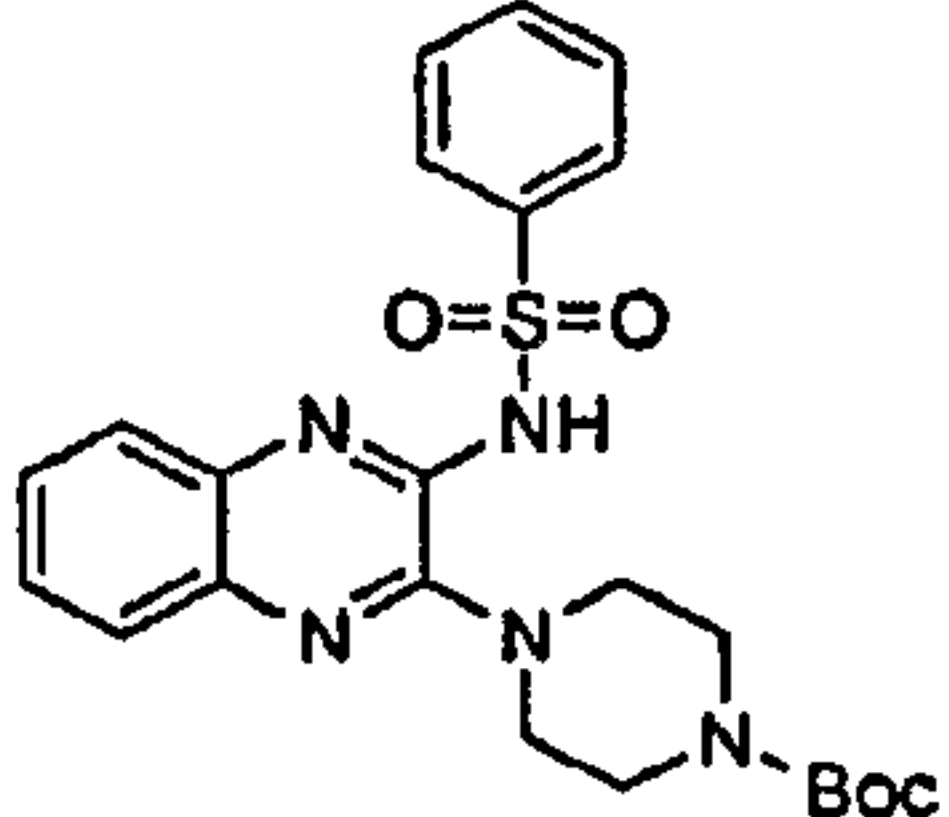
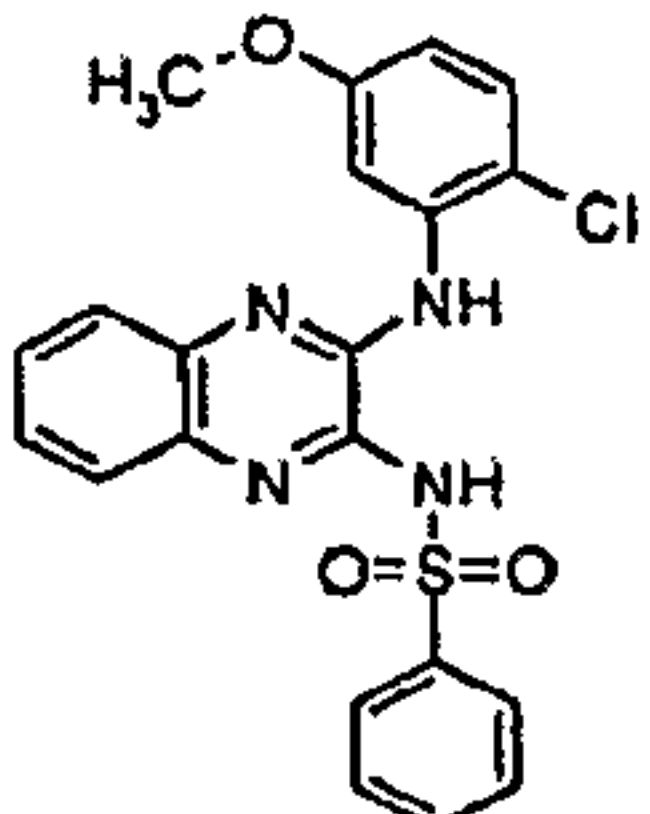
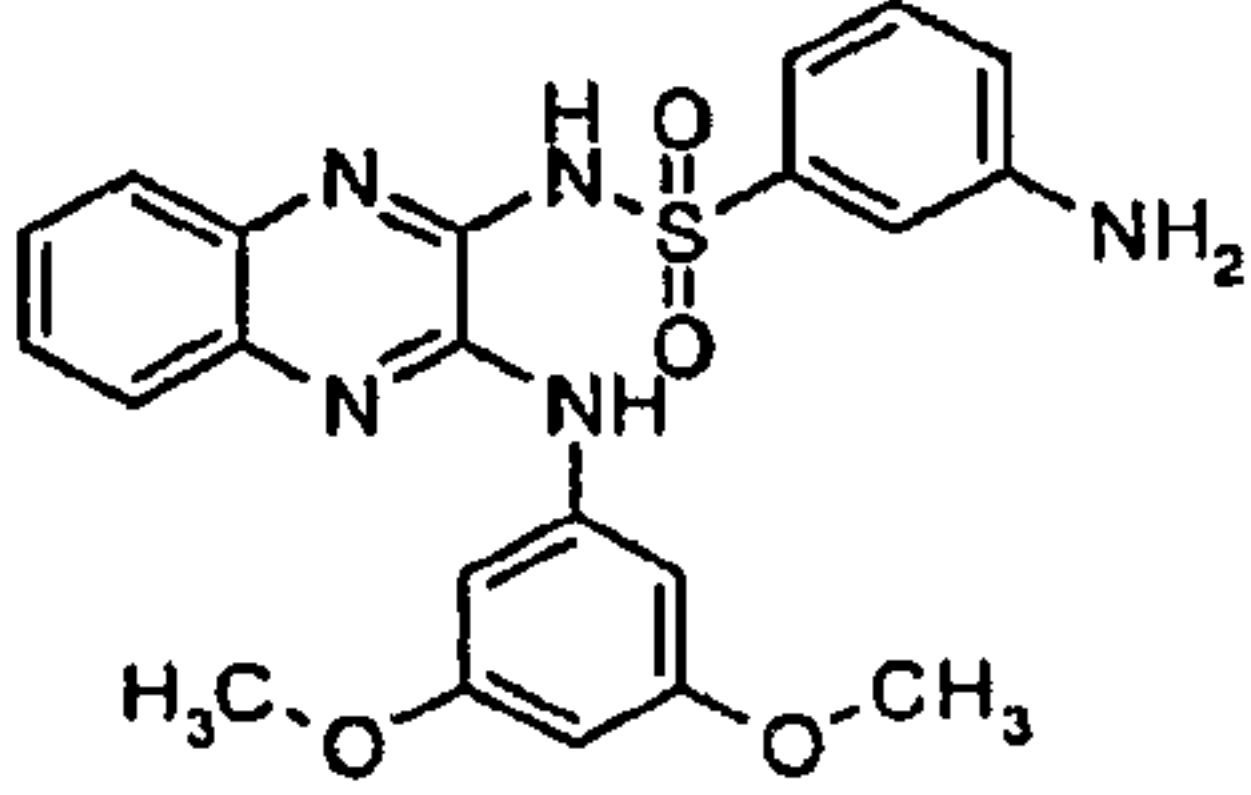
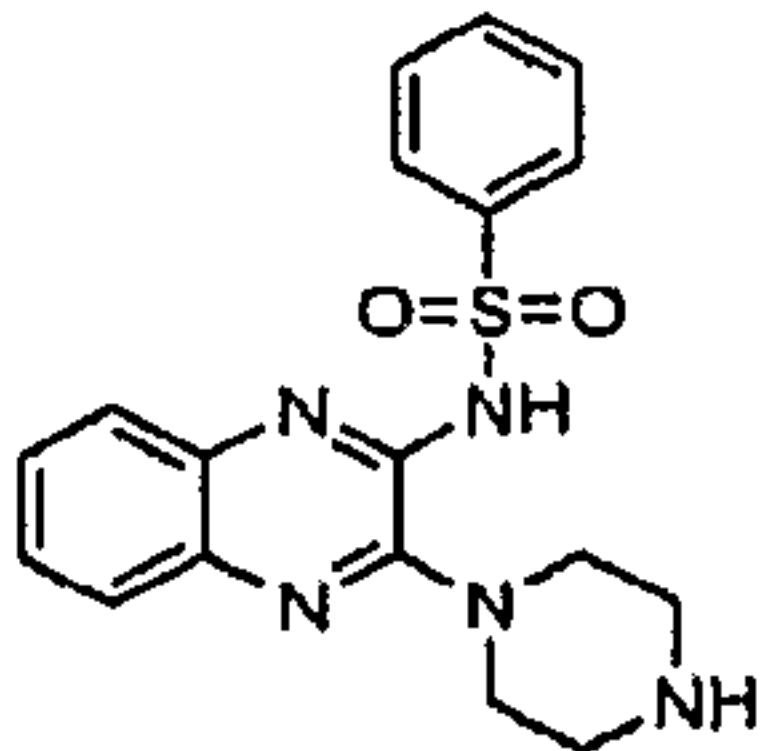
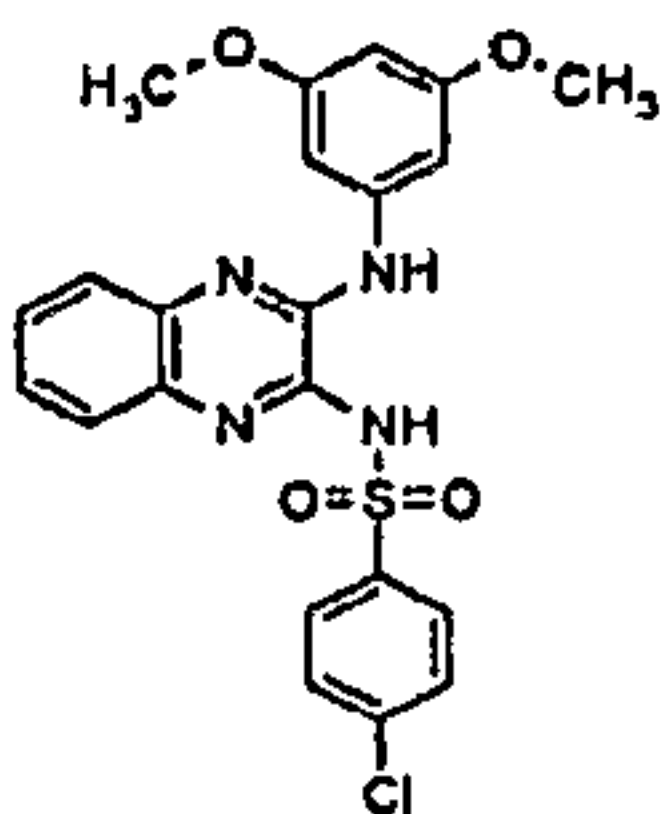
Table 1		
Cpd. No.	Structure	IUPAC Name
368		<i>N</i> -[3-(dimethylamino)quinoxalin-2-yl]benzenesulfonamide
369		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)naphthalene-2-sulfonamide
370		4-(3-Benzensulfonylamino-quinoxalin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester
371		<i>N</i> -[3-(2-Chloro-5-methoxyphenylamino)-quinoxalin-2-yl]-benzenesulfonamide
372		3-amino- <i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
373		<i>N</i> -(3-piperazin-1-ylquinoxalin-2-yl)benzenesulfonamide
374		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-4-chlorobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
375		<i>N</i> -(3-{4-[(9-oxo-9 <i>H</i> -fluoren-1-yl)carbonyl]piperazin-1-yl}quinoxalin-2-yl)benzenesulfonamide
376		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
377		<i>N</i> -(3-{[4-chloro-3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
378		<i>N</i> -(3-{[4-fluoro-3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
379		<i>N</i> -(3-{[2'-(methyloxy)biphenyl-4-yl]amino}quinoxalin-2-yl)benzenesulfonamide
380		<i>N</i> -(3-{[5-methyl-2-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
381		3-amino- <i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
382		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}-6,7-dimethylquinoxalin-2-yl)benzenesulfonamide
383		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-bromobenzenesulfonamide
384		<i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
385		<i>N</i> -(3-{[5-chloro-2-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
386		<i>N</i> -(3-{[2-(methyloxy)-5-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
387		<i>N</i> -(3-{[2-(methyloxy)biphenyl-4-yl]amino}quinoxalin-2-yl)benzenesulfonamide
388		3-amino- <i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
389		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
390		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}-7-methylquinoxalin-2-yl)benzenesulfonamide
391		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-(methyloxy)benzenesulfonamide
392		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-bromobenzenesulfonamide
393		<i>N</i> -(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-fluorobenzenesulfonamide
394		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-fluorobenzenesulfonamide
395		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-(methyloxy)benzenesulfonamide
396		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-bromobenzenesulfonamide
397		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-methylpiperidine-4-carboxamide

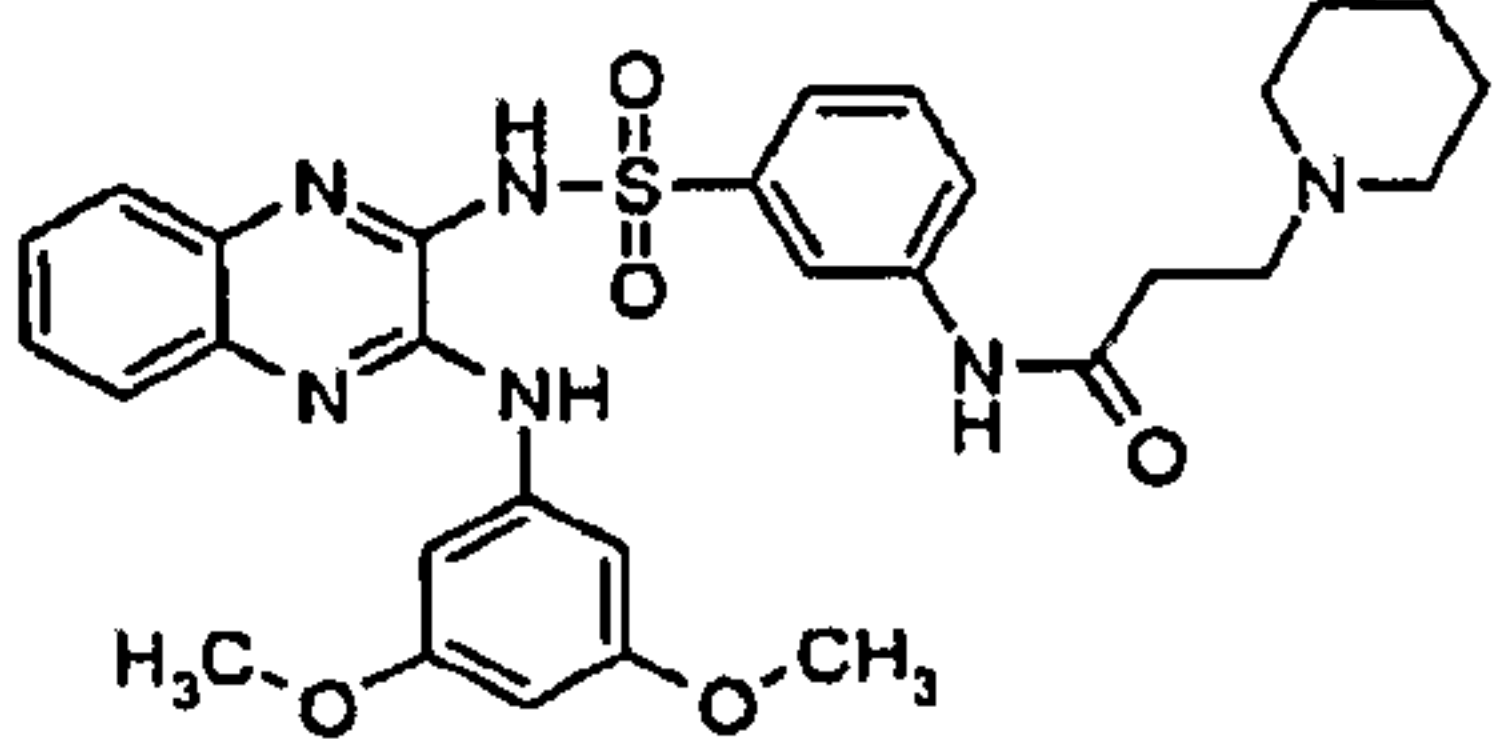
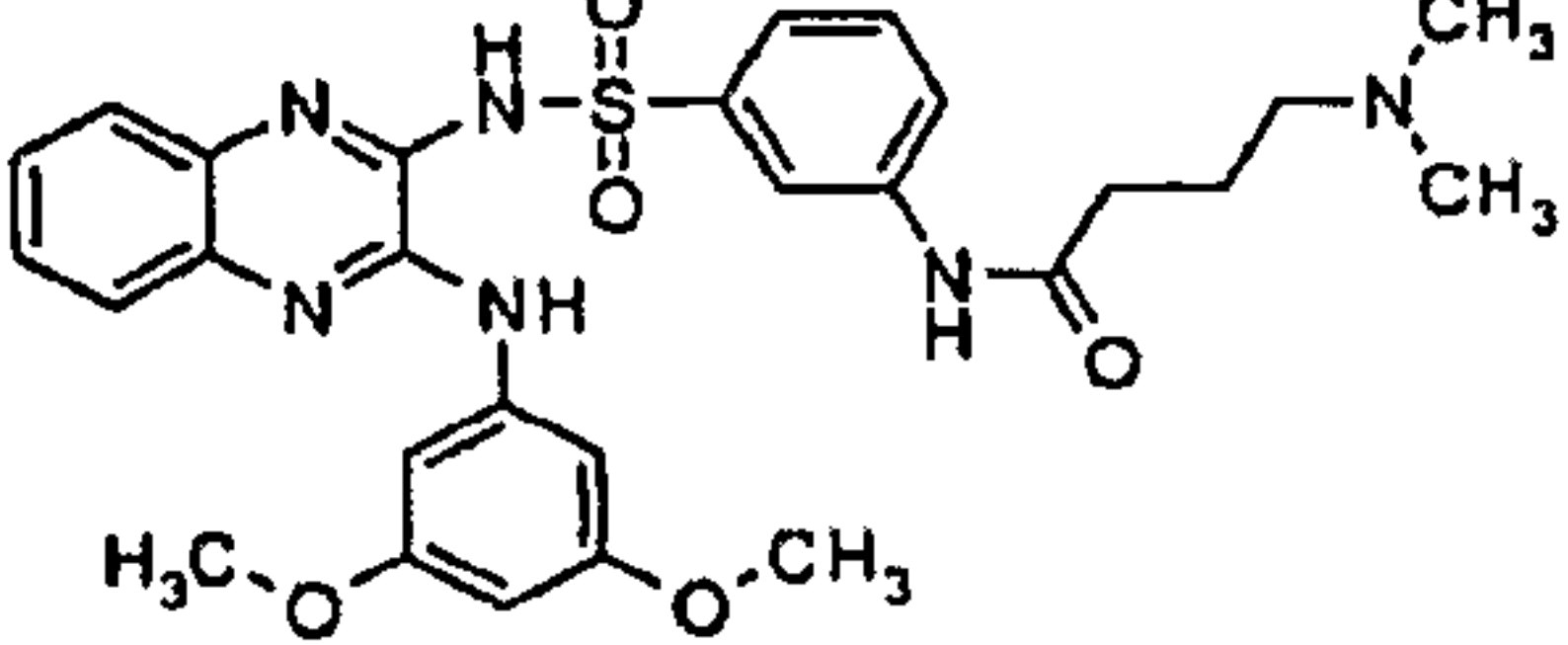
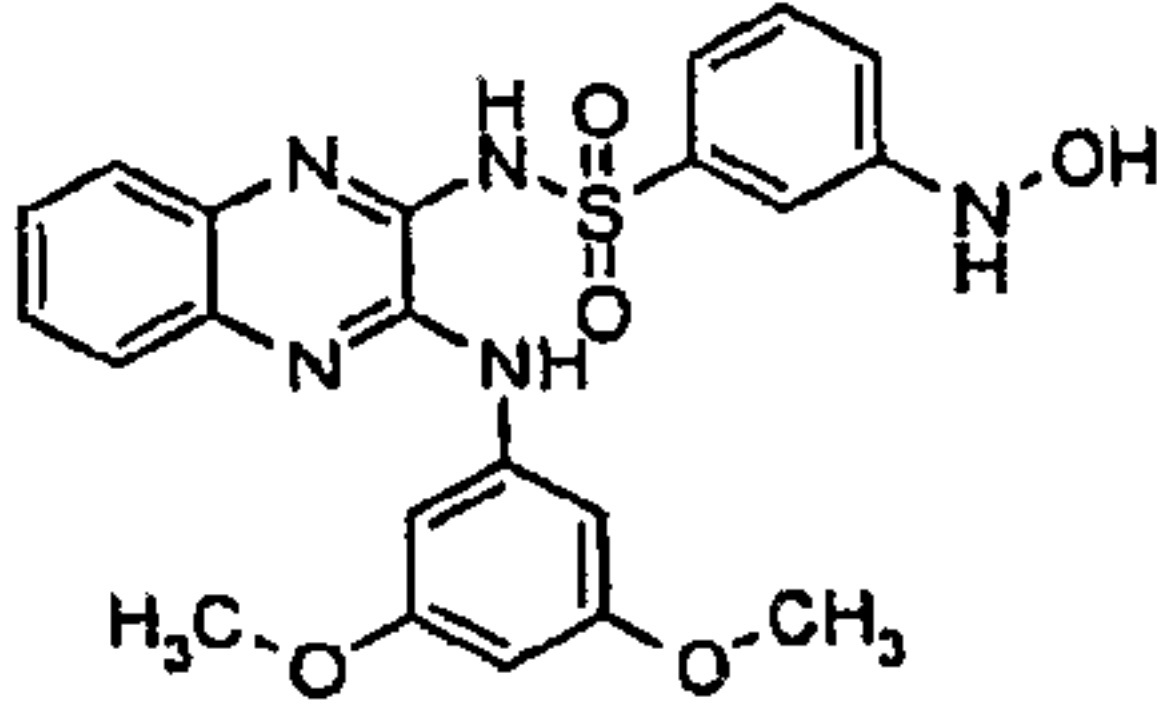
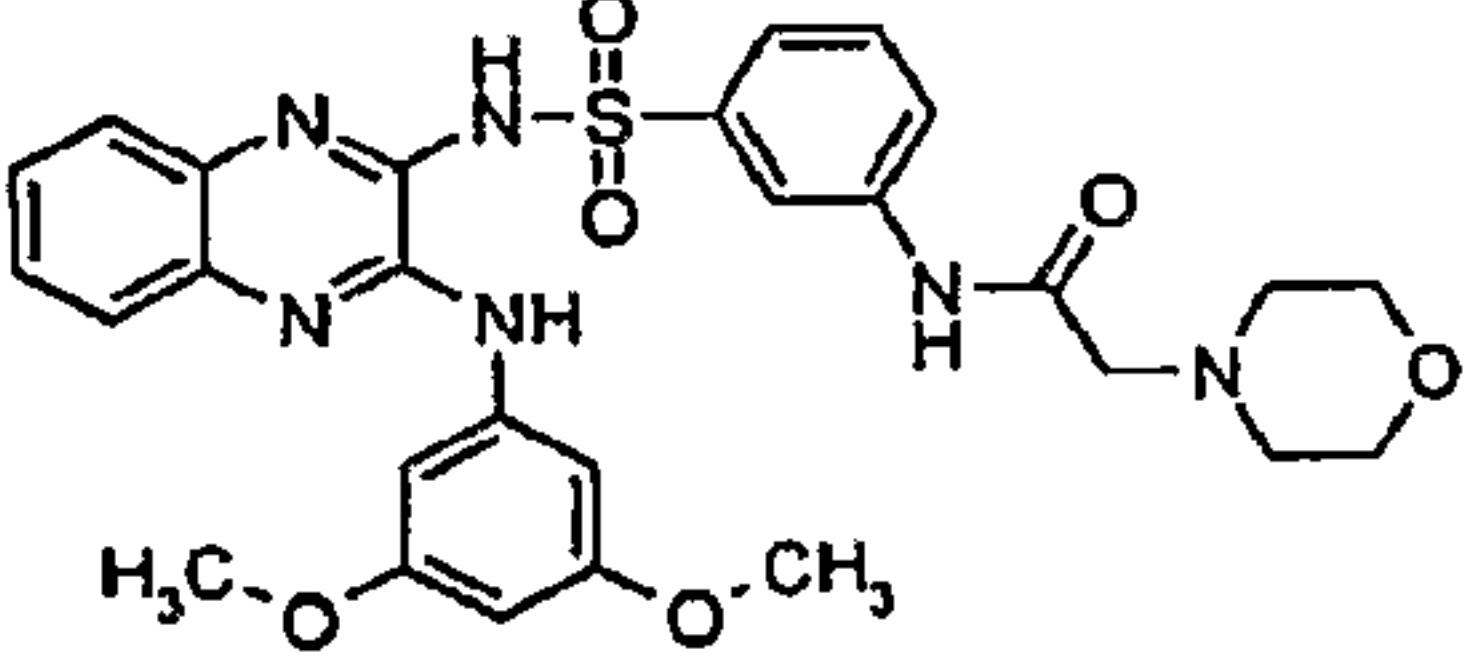
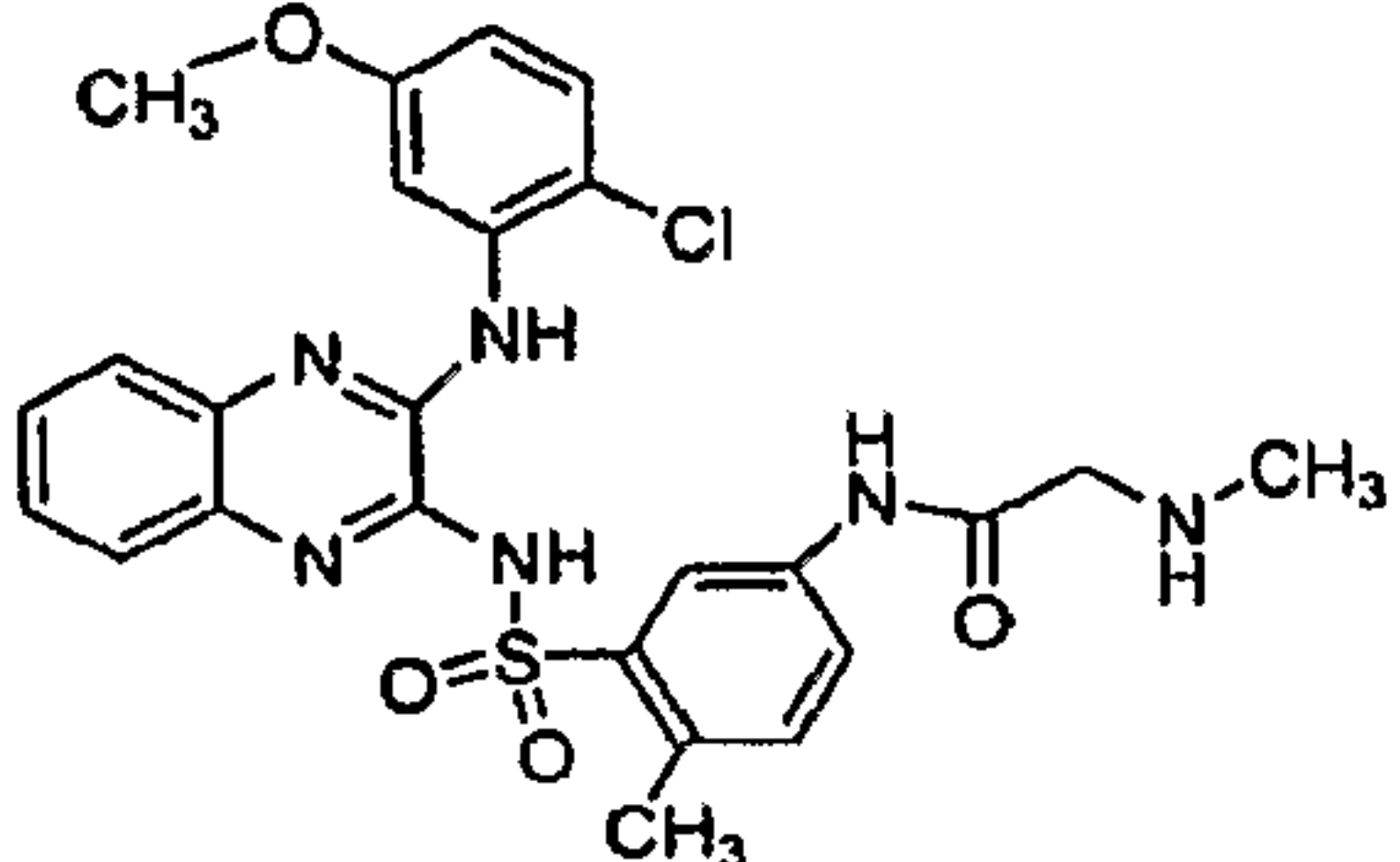
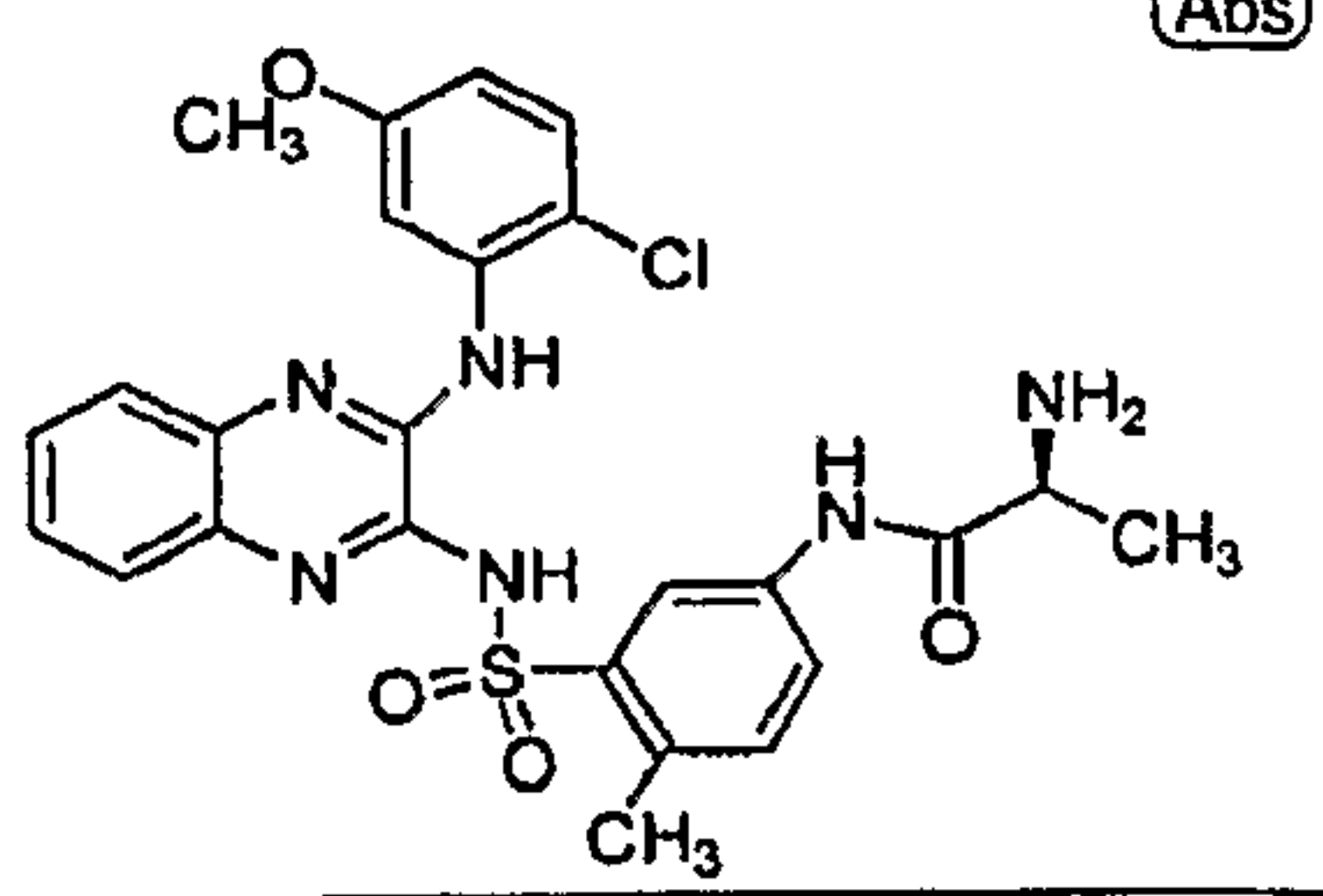
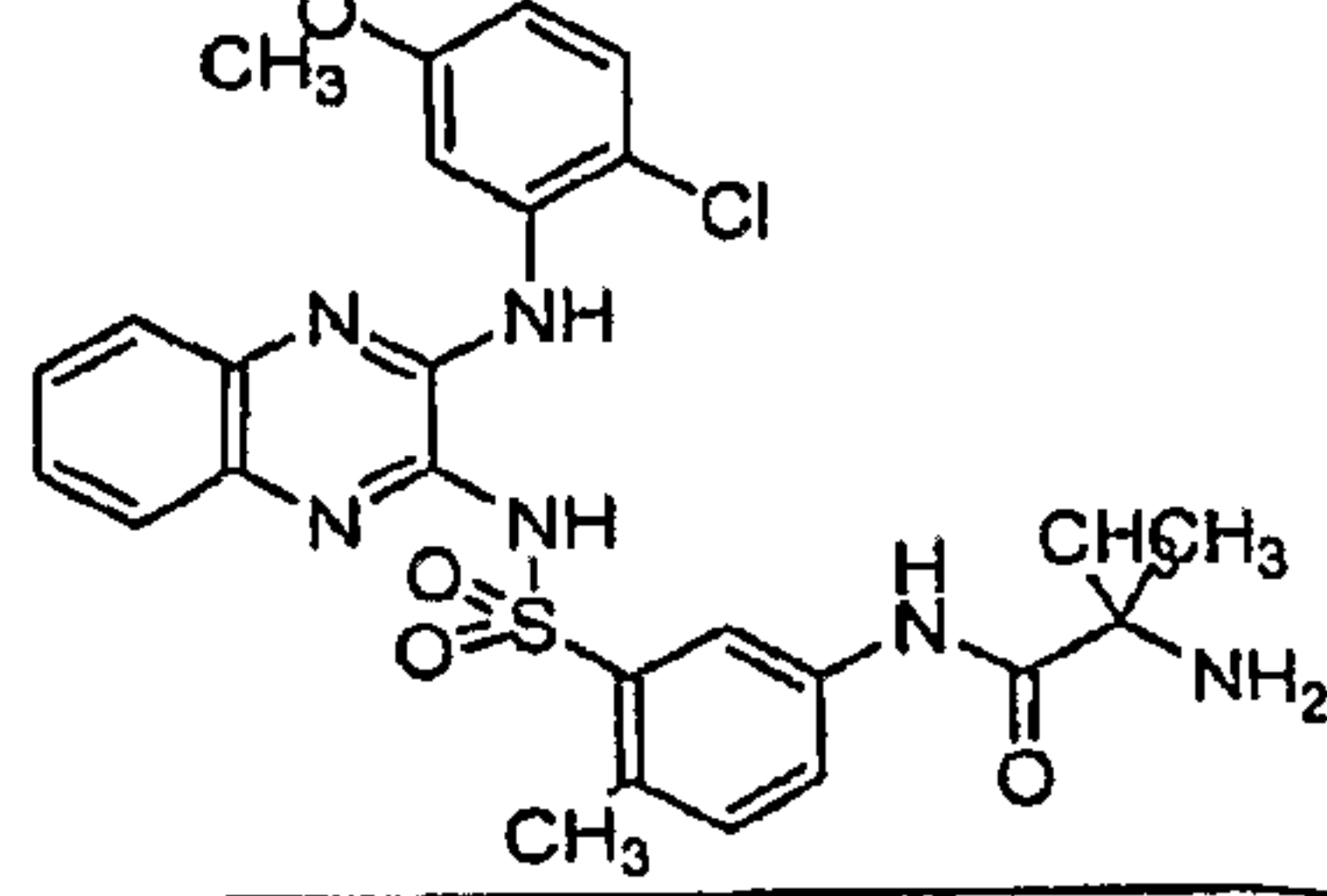
Table 1		
Cpd. No.	Structure	IUPAC Name
398		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-piperidin-1-ylpropanamide
399		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-(dimethylamino)butanamide
400		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-3-(hydroxyamino)benzenesulfonamide
401		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-morpholin-4-ylacetamide
402		<i>N</i> -(3-{[(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)- <i>N</i> -2-methylglycinamide
403		<i>N</i> -(3-{[(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-L-alaninamide
404		<i>N</i> -(3-{[(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-2-methylalaninamide

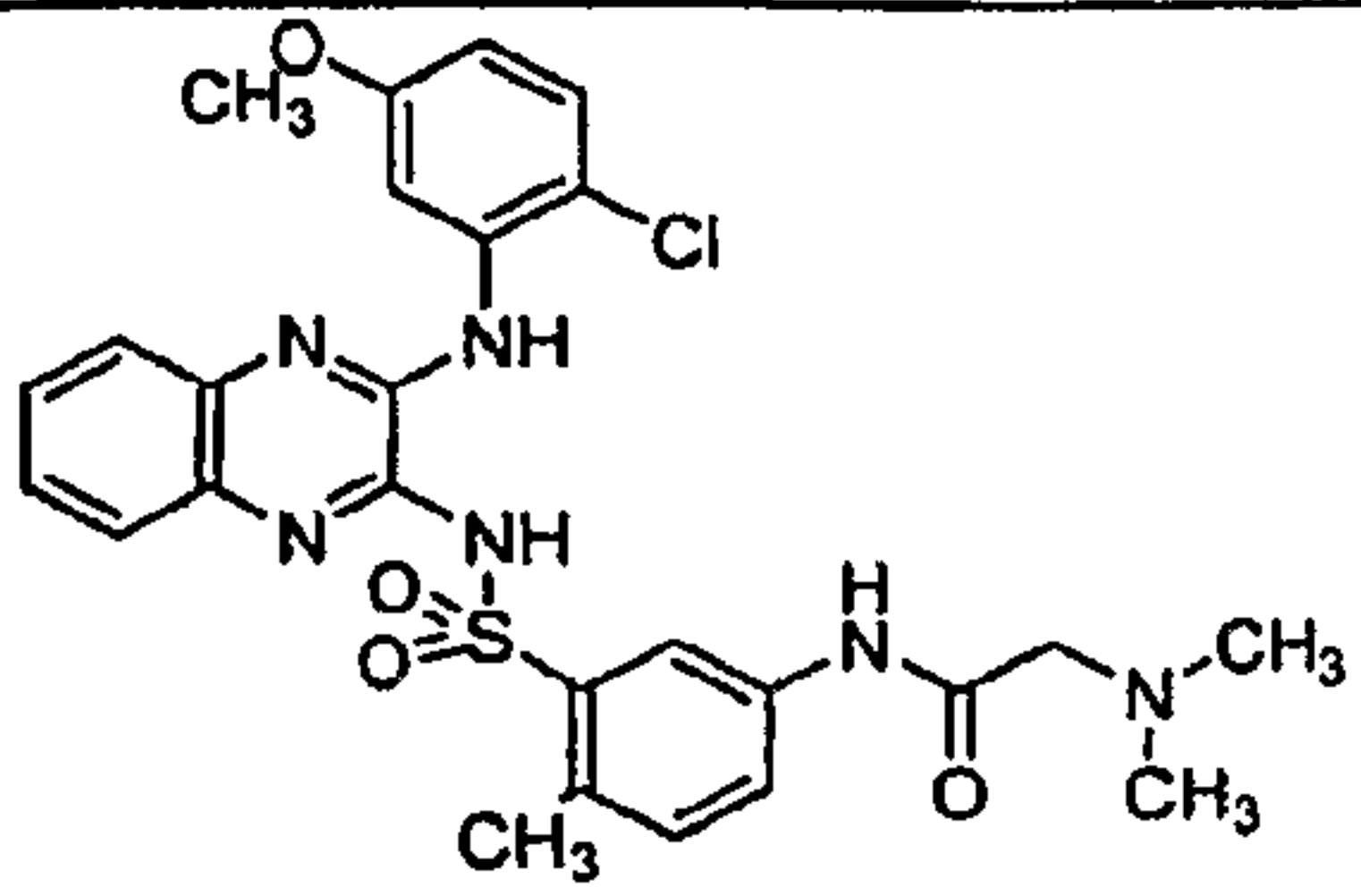
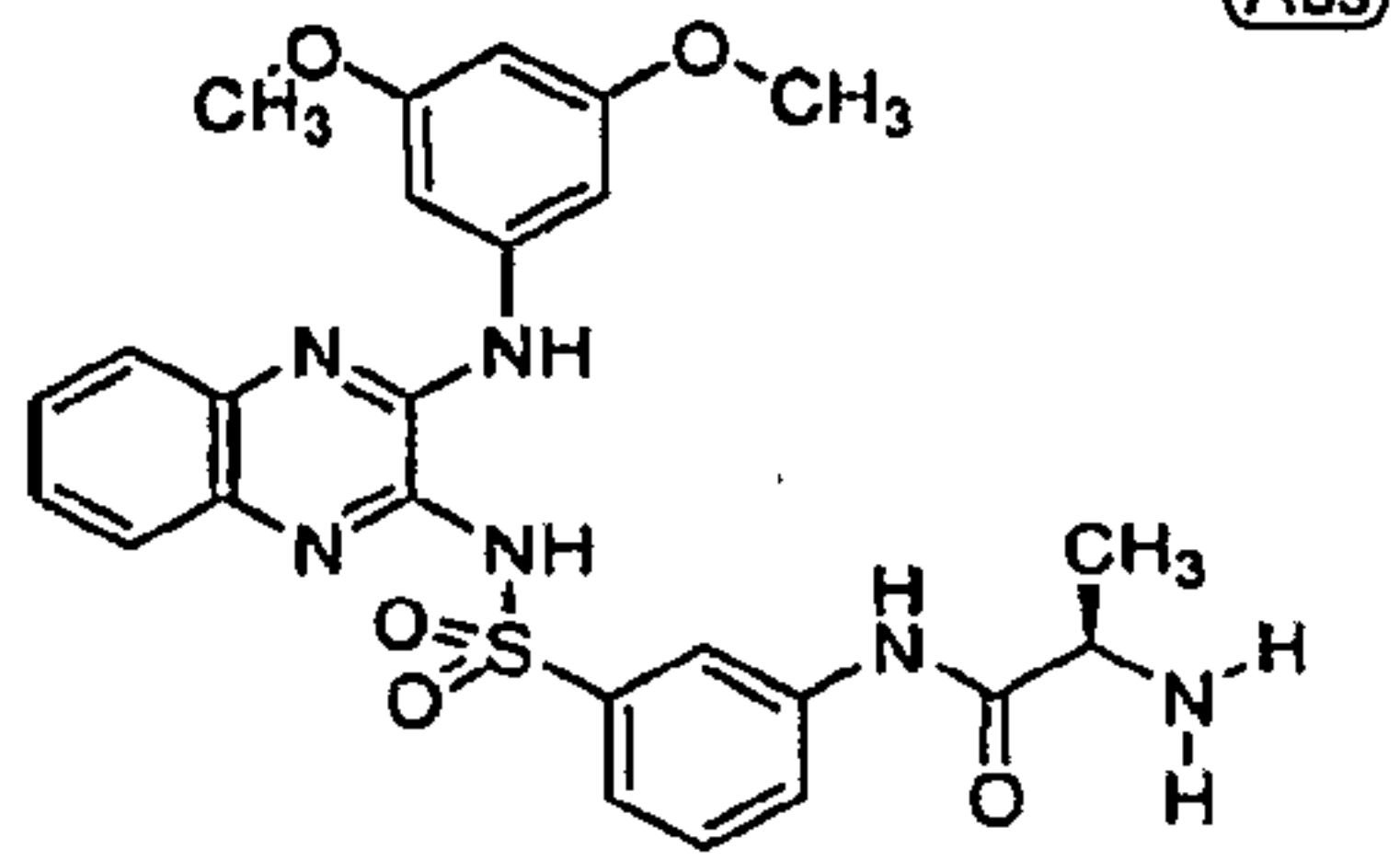
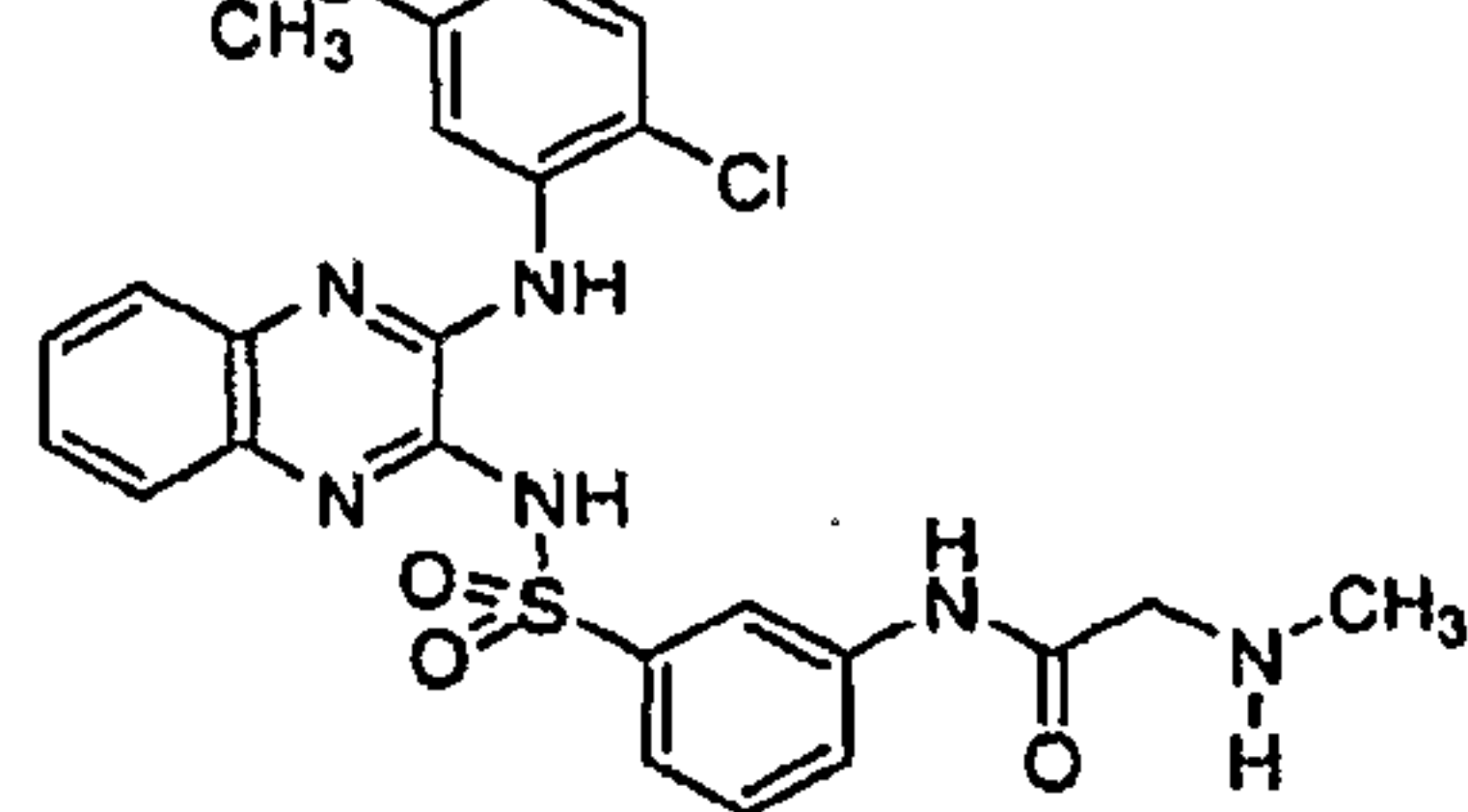
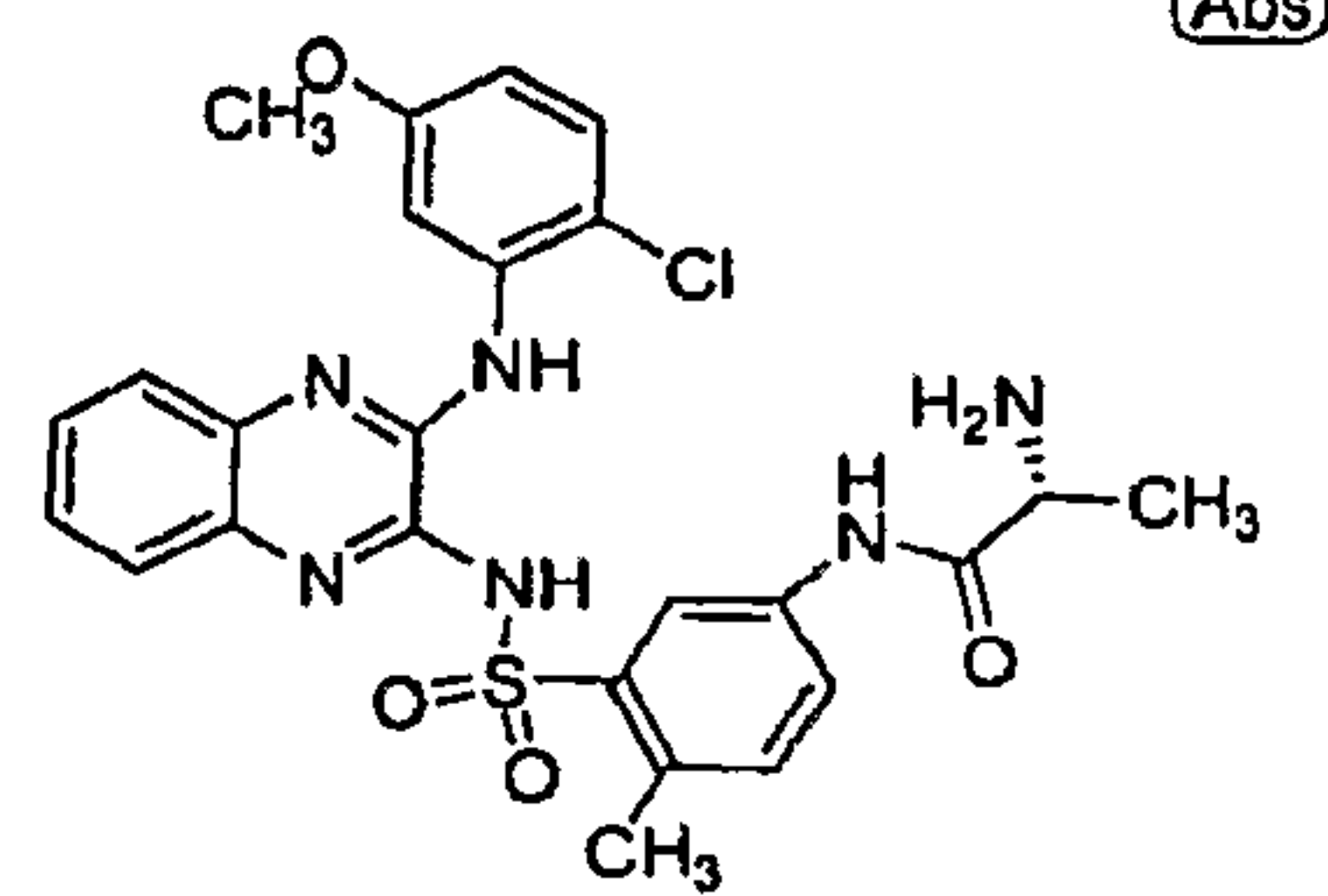
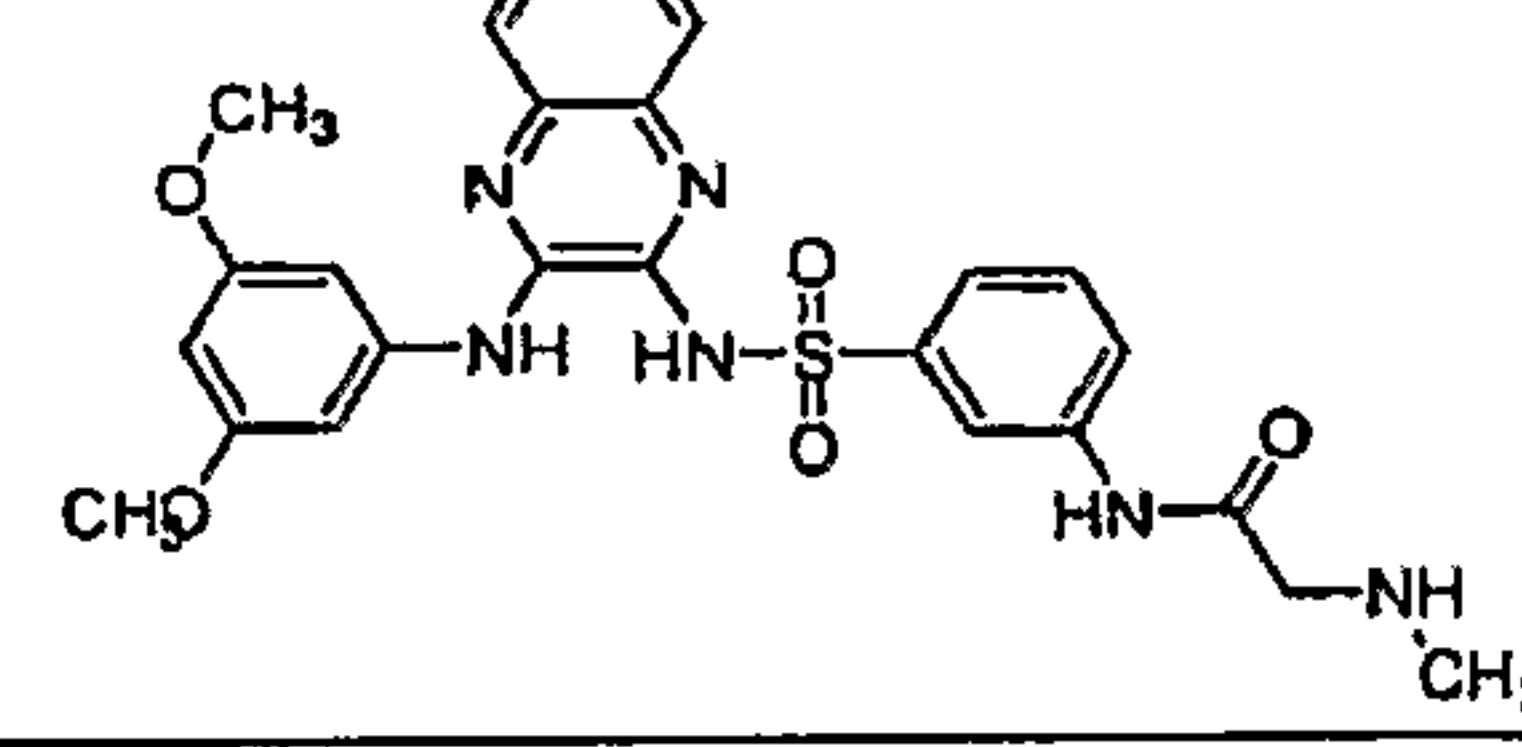
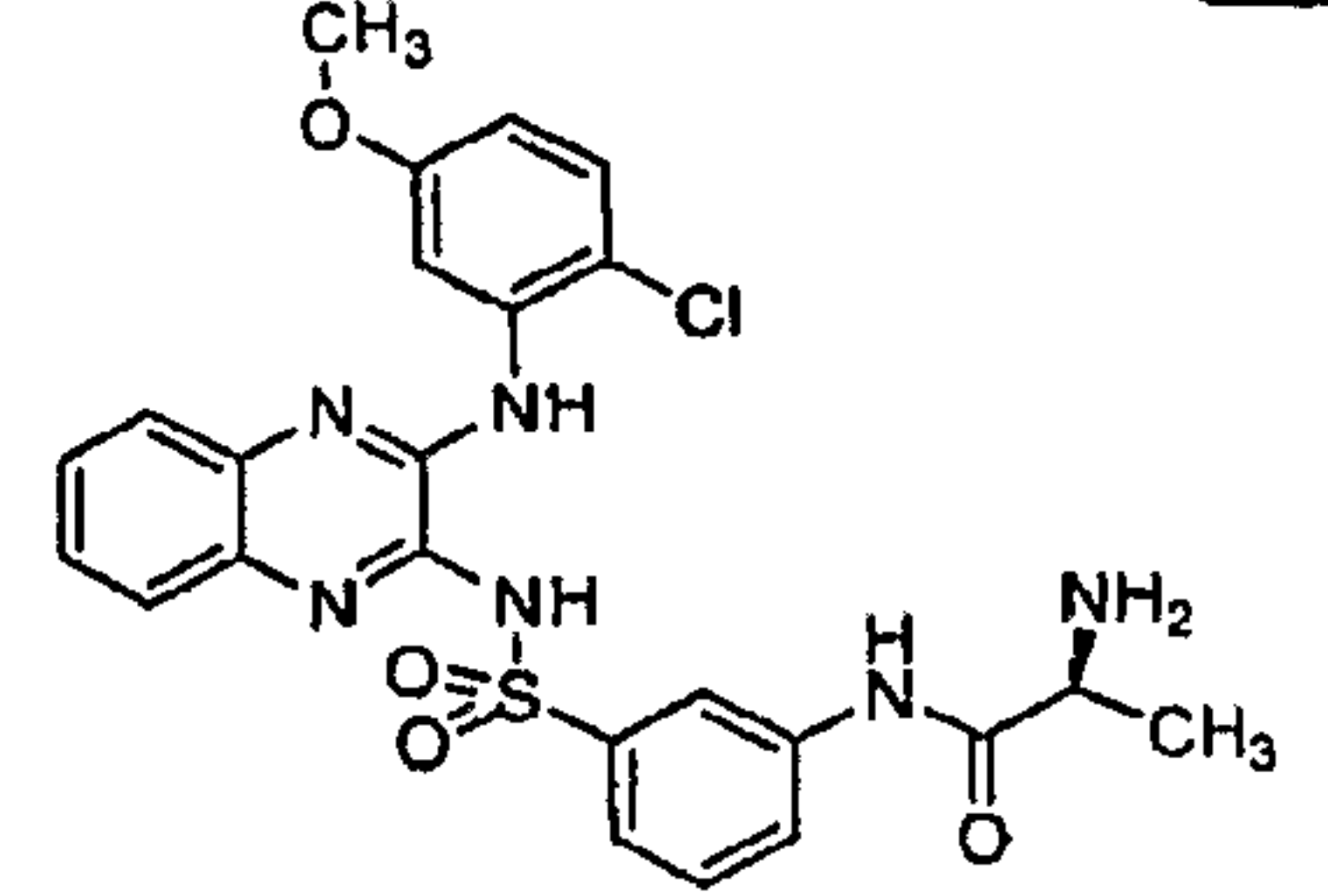
Table 1		
Cpd. No.	Structure	IUPAC Name
405		<i>N</i> -(3-([(3-([2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl)-4-methylphenyl)- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
406		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl)phenyl)- <i>D</i> -alaninamide
407		<i>N</i> -(3-([(3-([2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl)phenyl)- <i>N</i> -2-methylglycinamide
408		<i>N</i> -(3-([(3-([2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl)-4-methylphenyl)- <i>D</i> -alaninamide
409		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl)phenyl)- <i>N</i> -2-methylglycinamide
410		<i>N</i> -(3-([(3-([2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl)phenyl)- <i>L</i> -alaninamide

Table 1		
Cpd. No.	Structure	IUPAC Name
411	 (Abs)	<i>N</i> -(3-(((3-([2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-D-alaninamide
412		<i>N</i> -(3-(((3-([2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylalaninamide
413		<i>N</i> -(3-(((3-([3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylalaninamide
414		<i>N</i> -(3-(((3-([3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl)-4-methylphenyl)- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide
415		<i>N</i> -(3-(((3-([2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[2-(dimethylamino)ethyl]- <i>N</i> -2-methylglycinamide
416		(2 <i>S</i>)-2-amino- <i>N</i> -(3-(((3-([2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)butanamide
417		<i>N</i> -(3-(((3-([3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[2-(dimethylamino)ethyl]- <i>N</i> -2-methylglycinamide

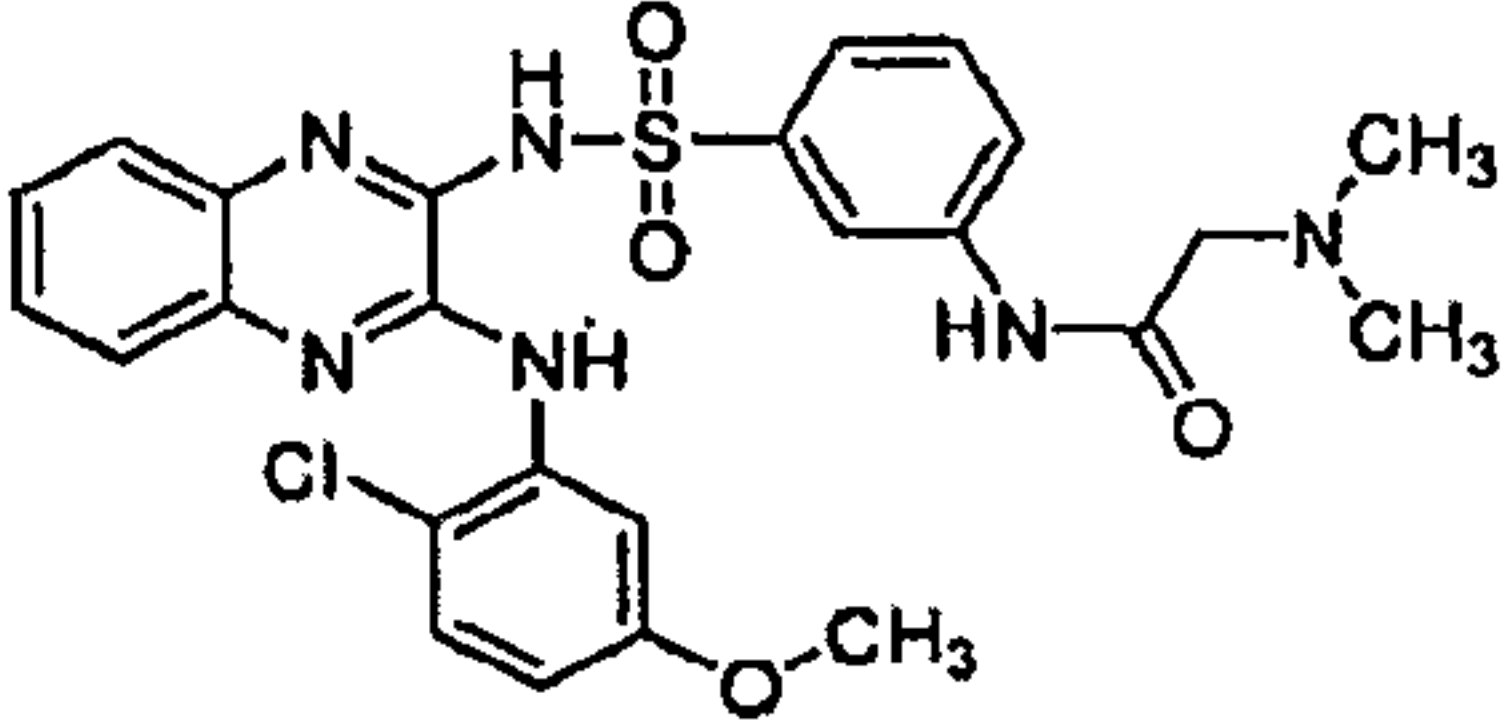
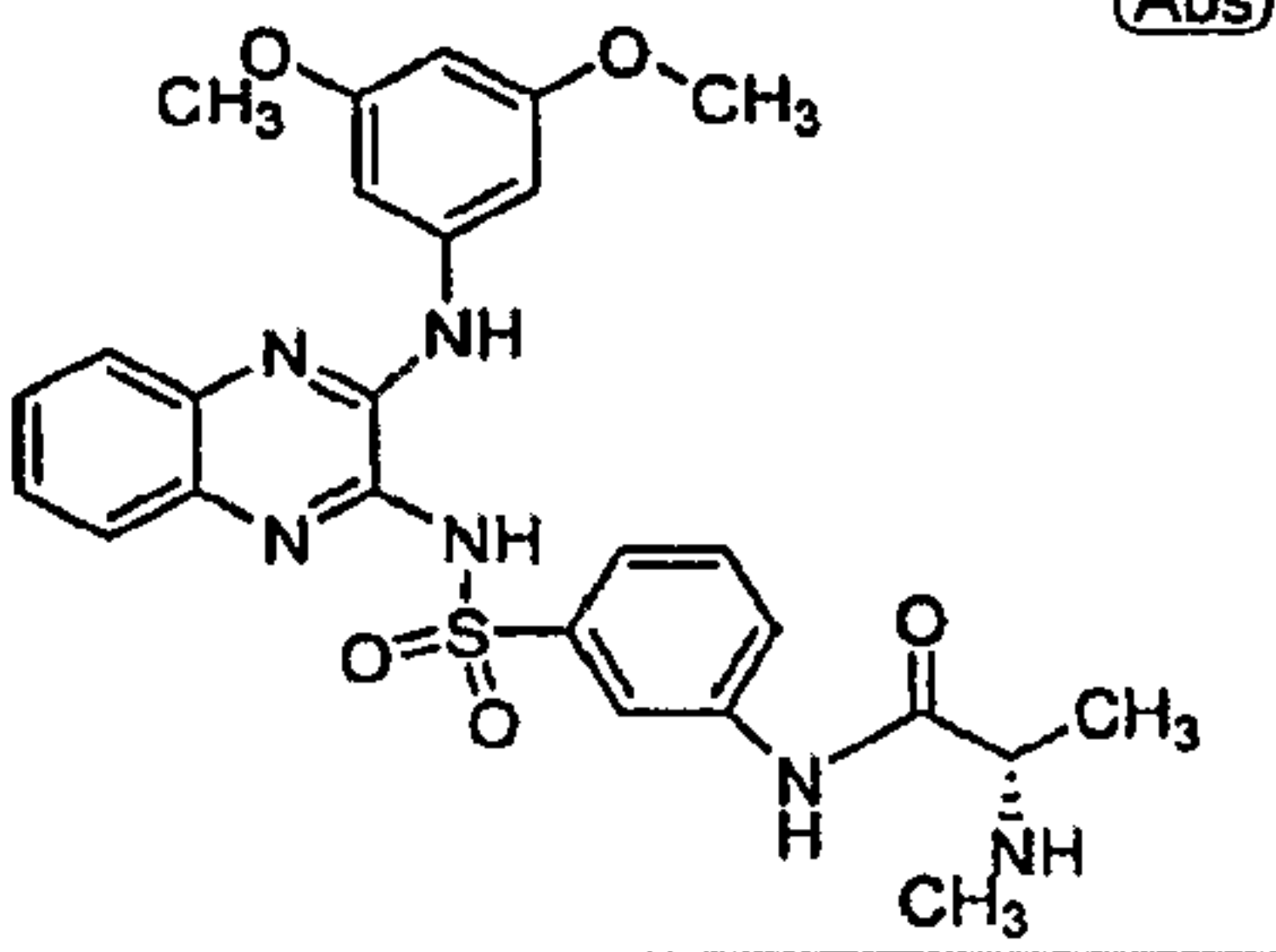
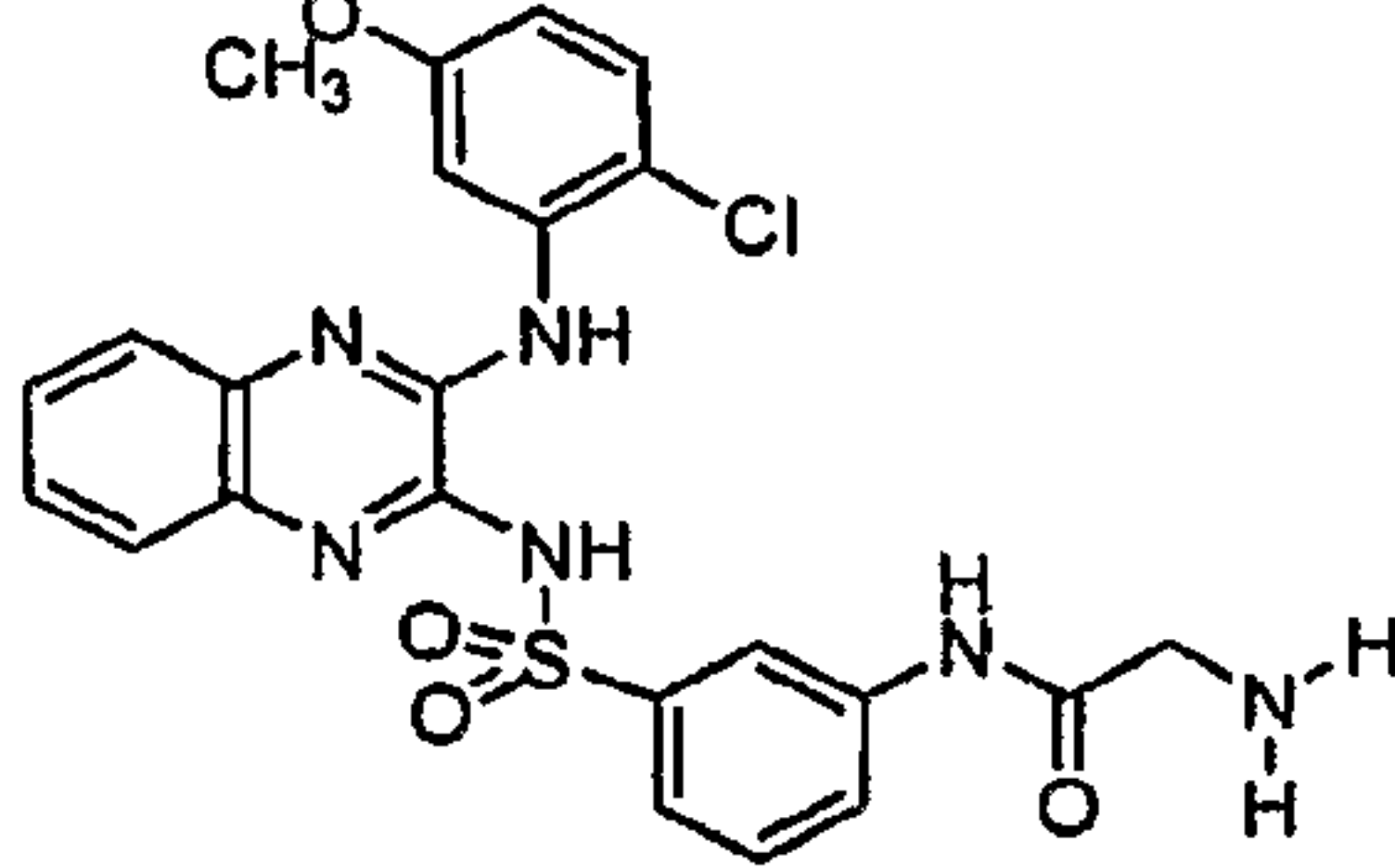
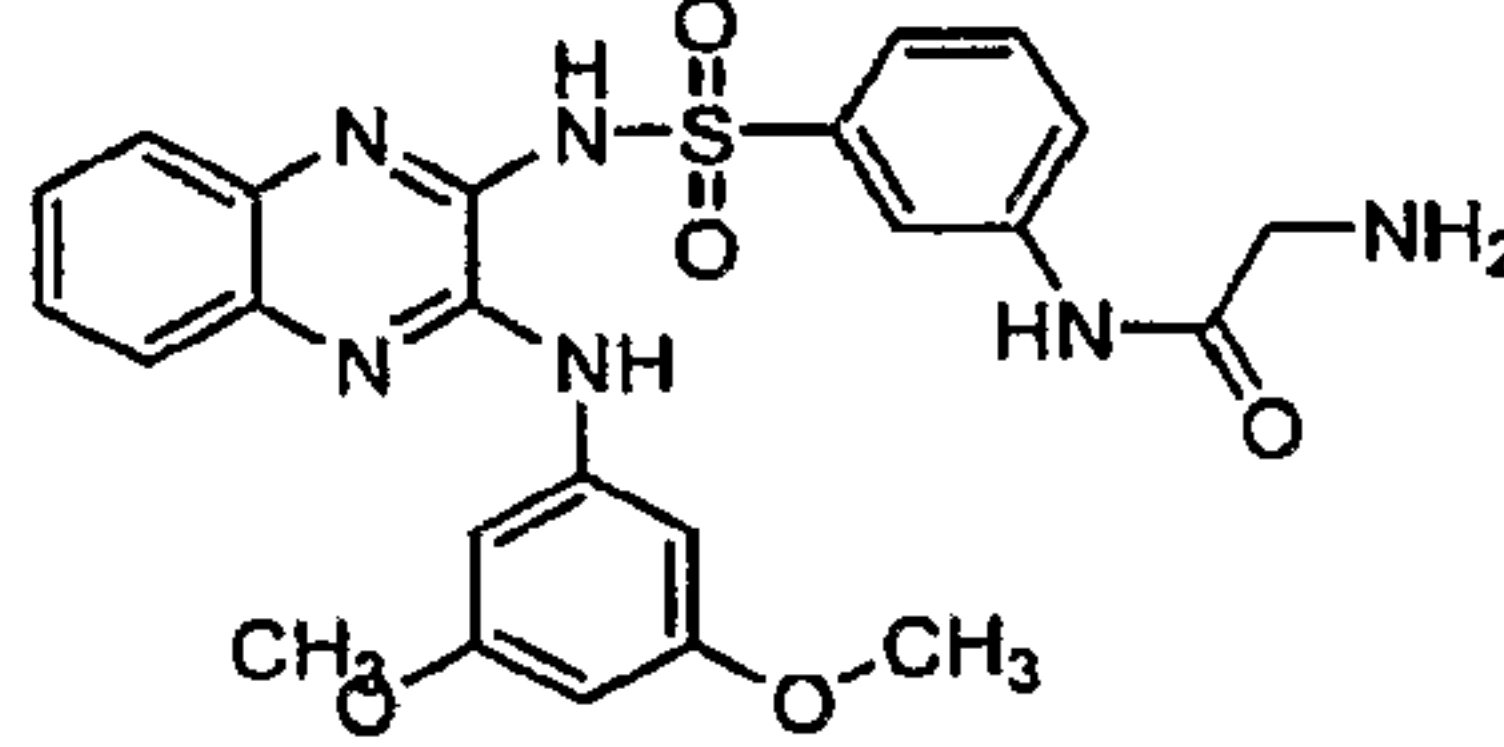
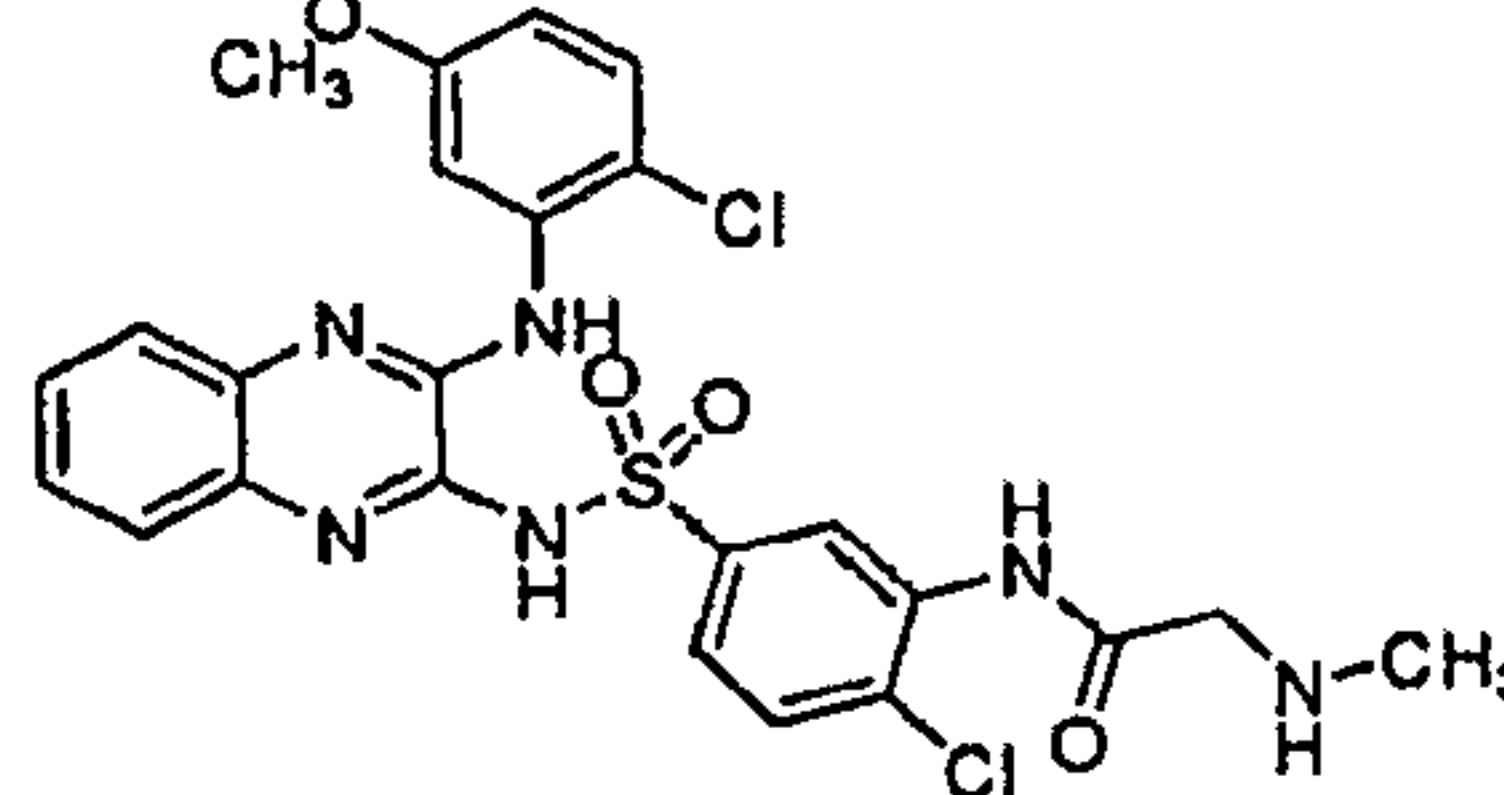
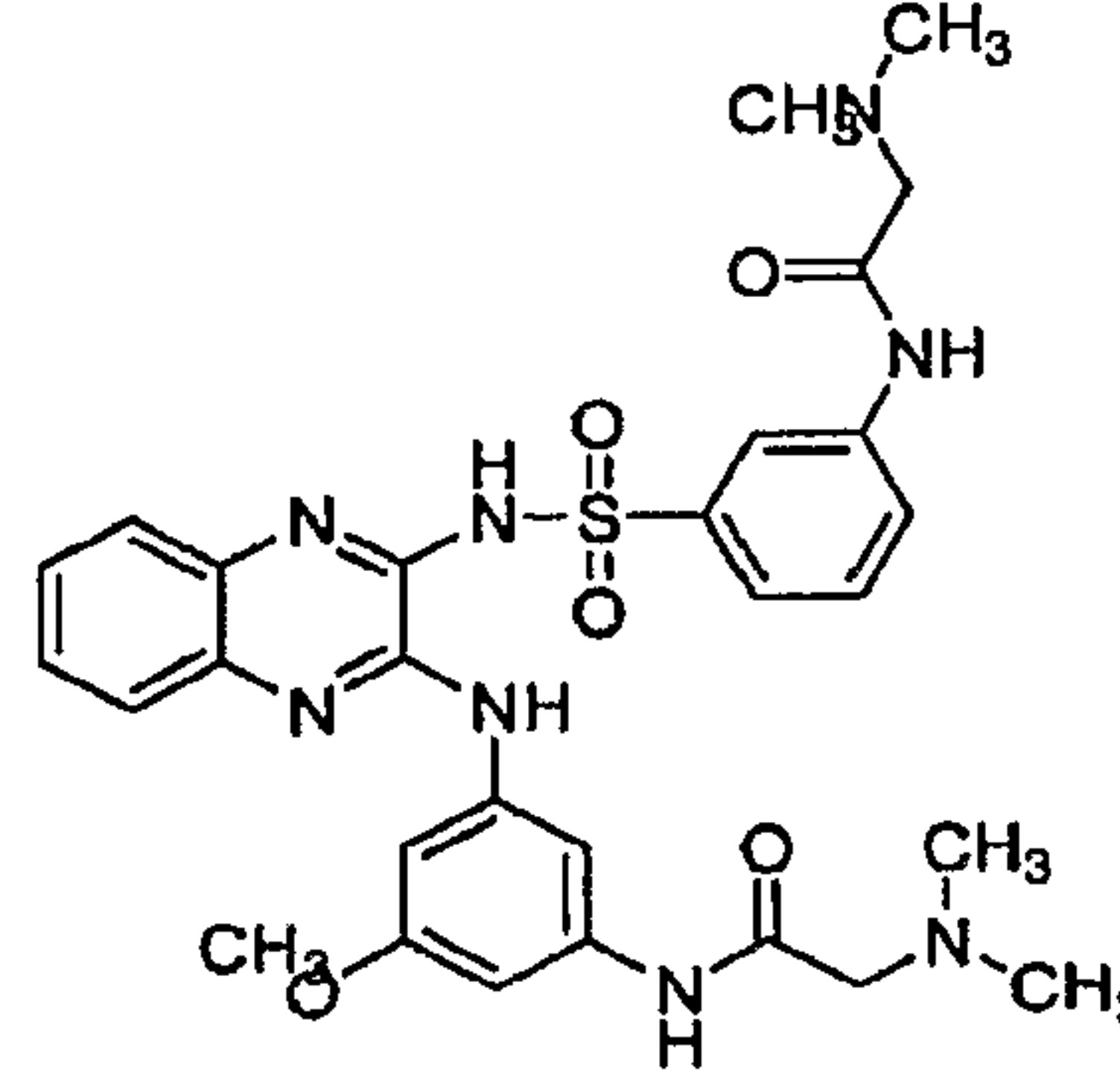
Table 1		
Cpd. No.	Structure	IUPAC Name
418		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
419		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methyl-L-alaninamide
420		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide
421		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide
422		<i>N</i> -(2-chloro-5-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methylglycinamide
423		2-(dimethylamino)- <i>N</i> -(3-(<i>N</i> -(3-(3-(2-(dimethylamino)acetamido)-5-methoxyphenylamino)quinoxalin-2-yl)sulfonyl)phenyl)acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
424		<i>N</i> -(3-{[(3-{[2-acetyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
425		<i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(formylamino)benzenesulfonamide
426		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-ethylglycinamide
427		<i>N</i> -(5-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-2-methylphenyl)glycinamide
428		2-azetidin-1-yl- <i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
429		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>L</i> -prolinamide
430		<i>N</i> -(3-{[(3-{[2-bromo-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methylglycinamide

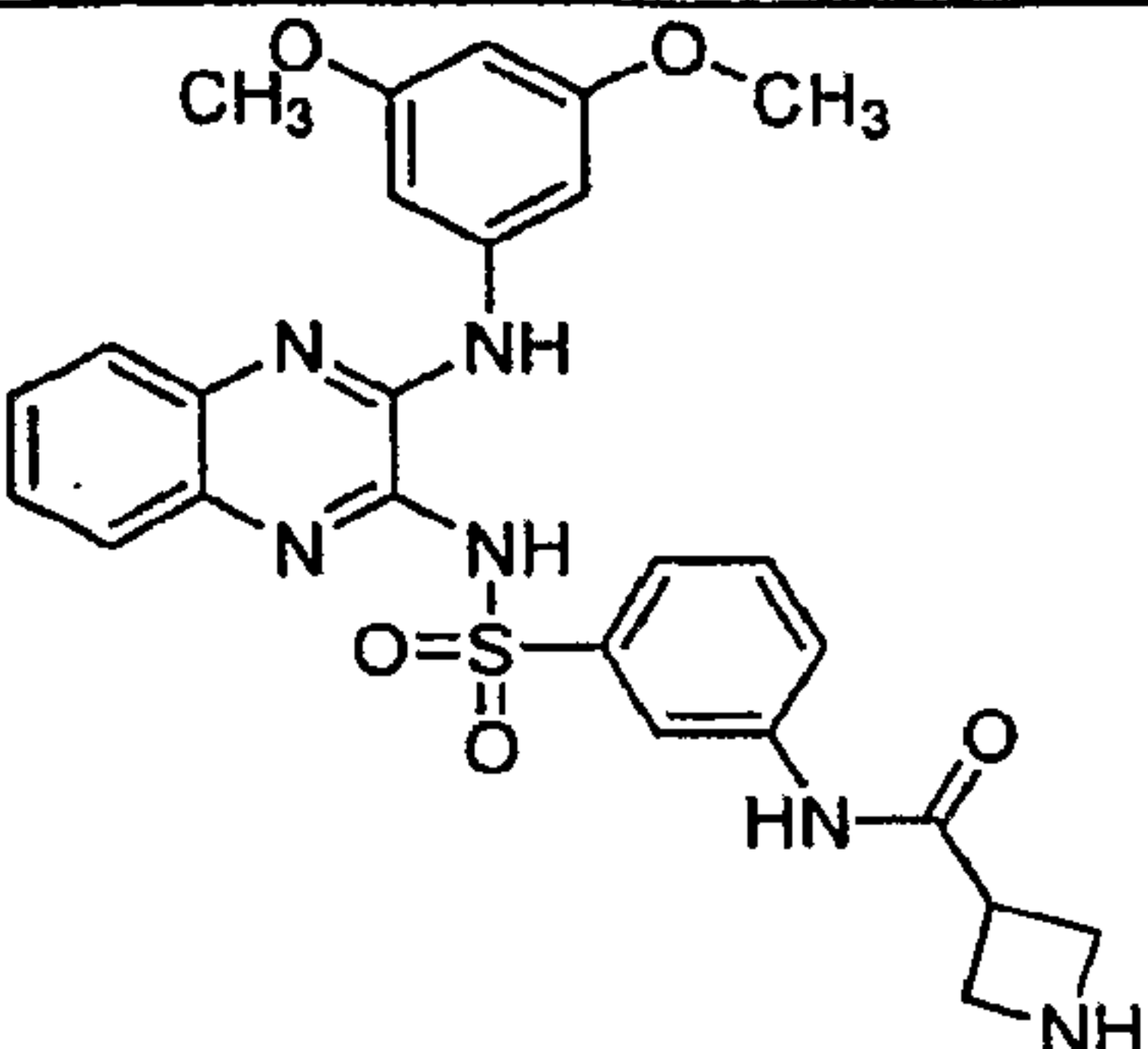
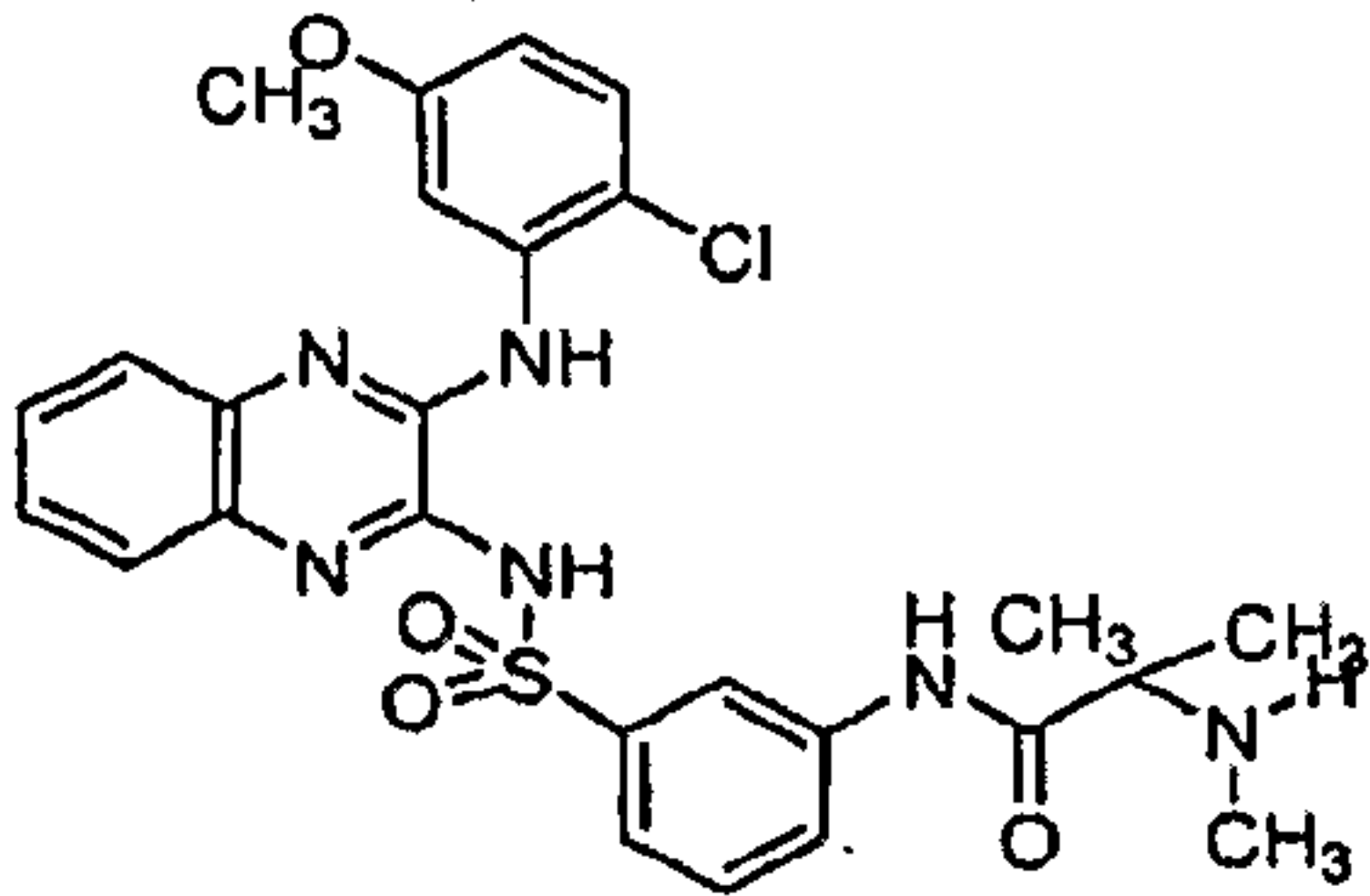
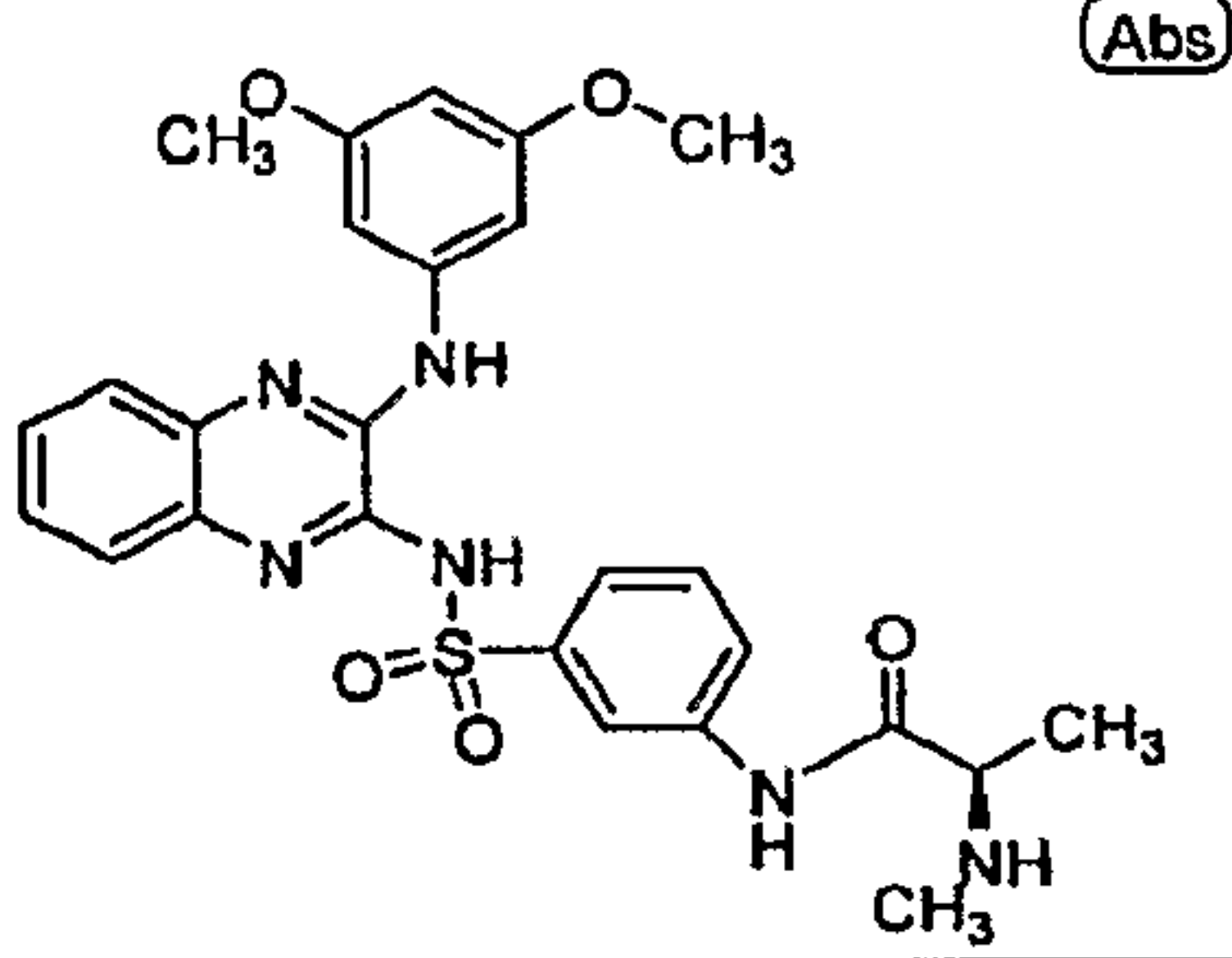
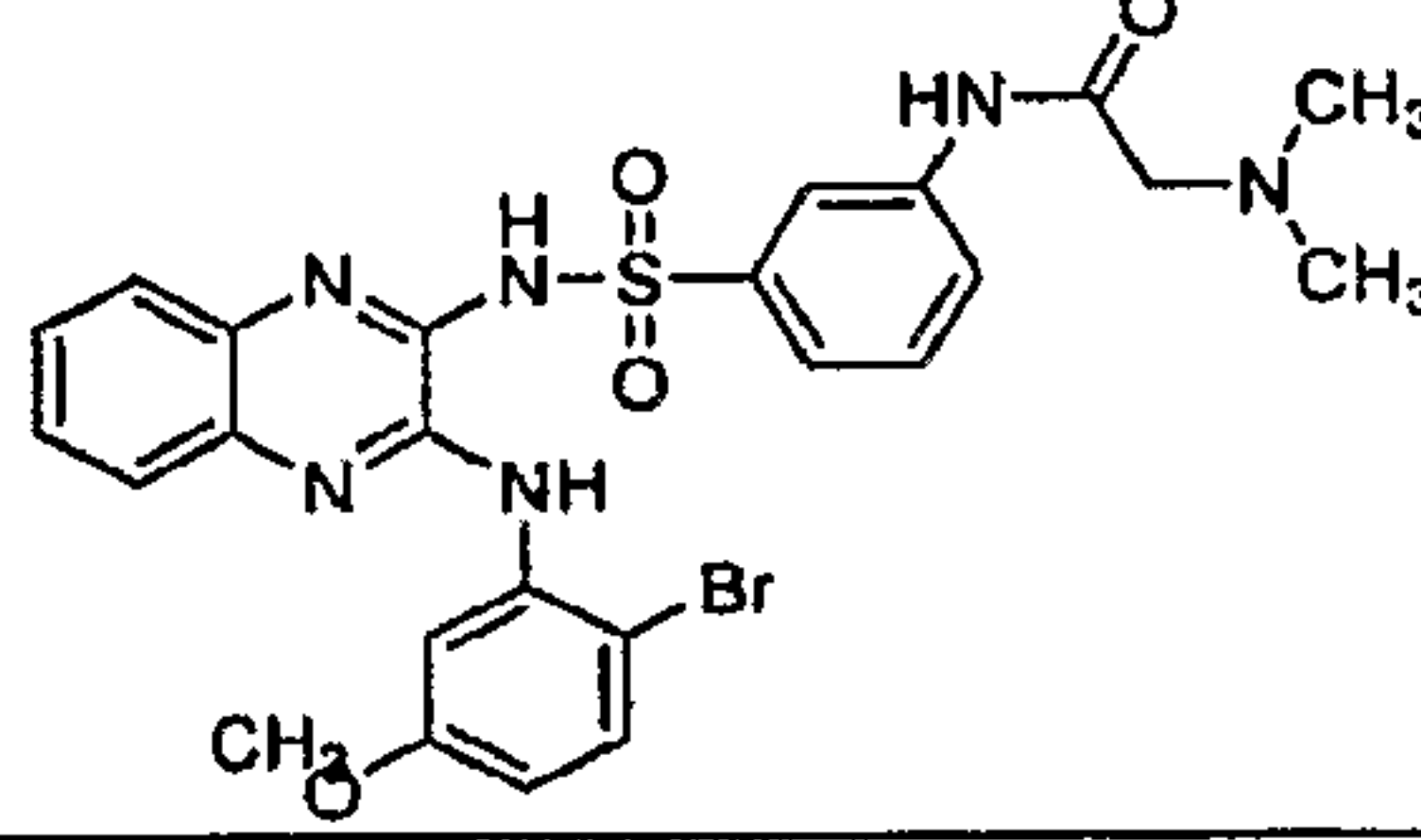
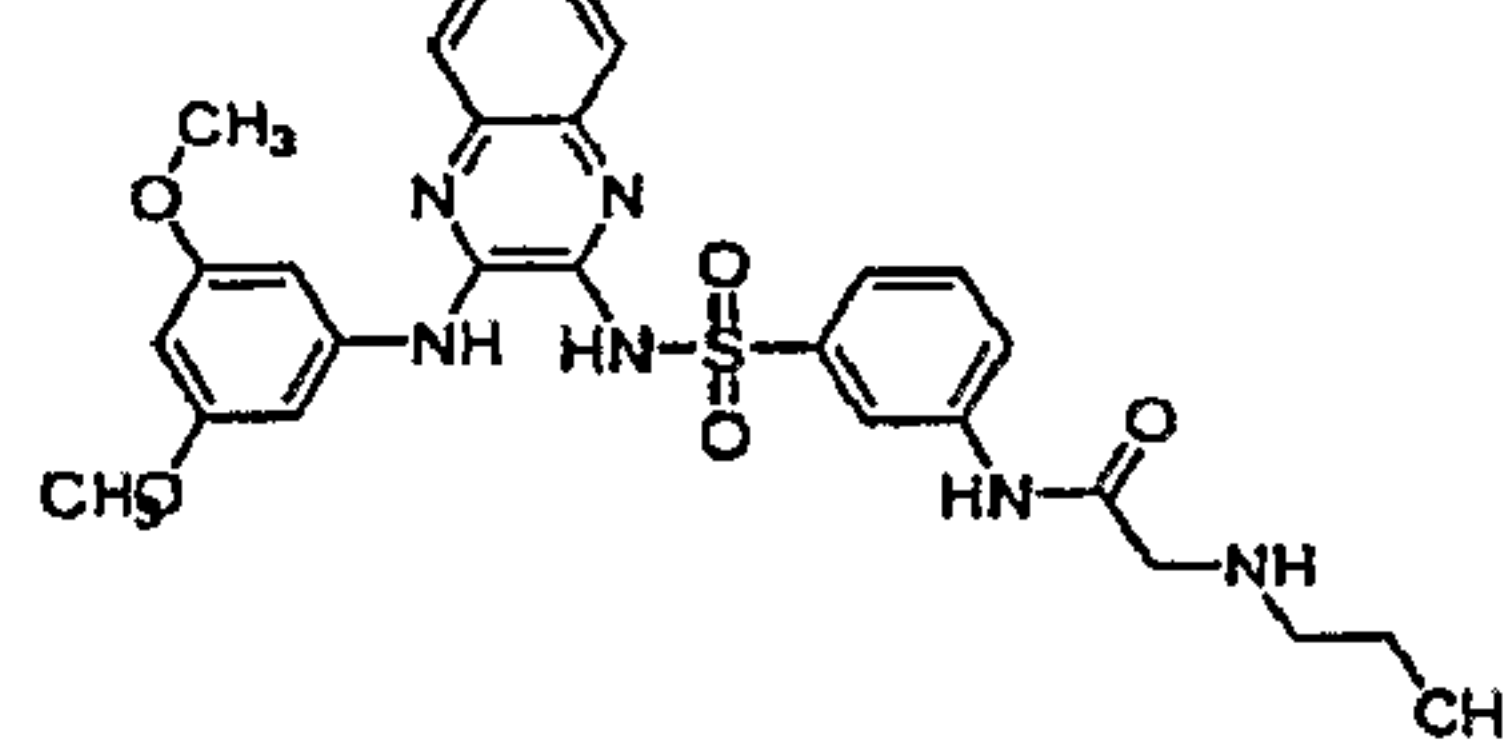
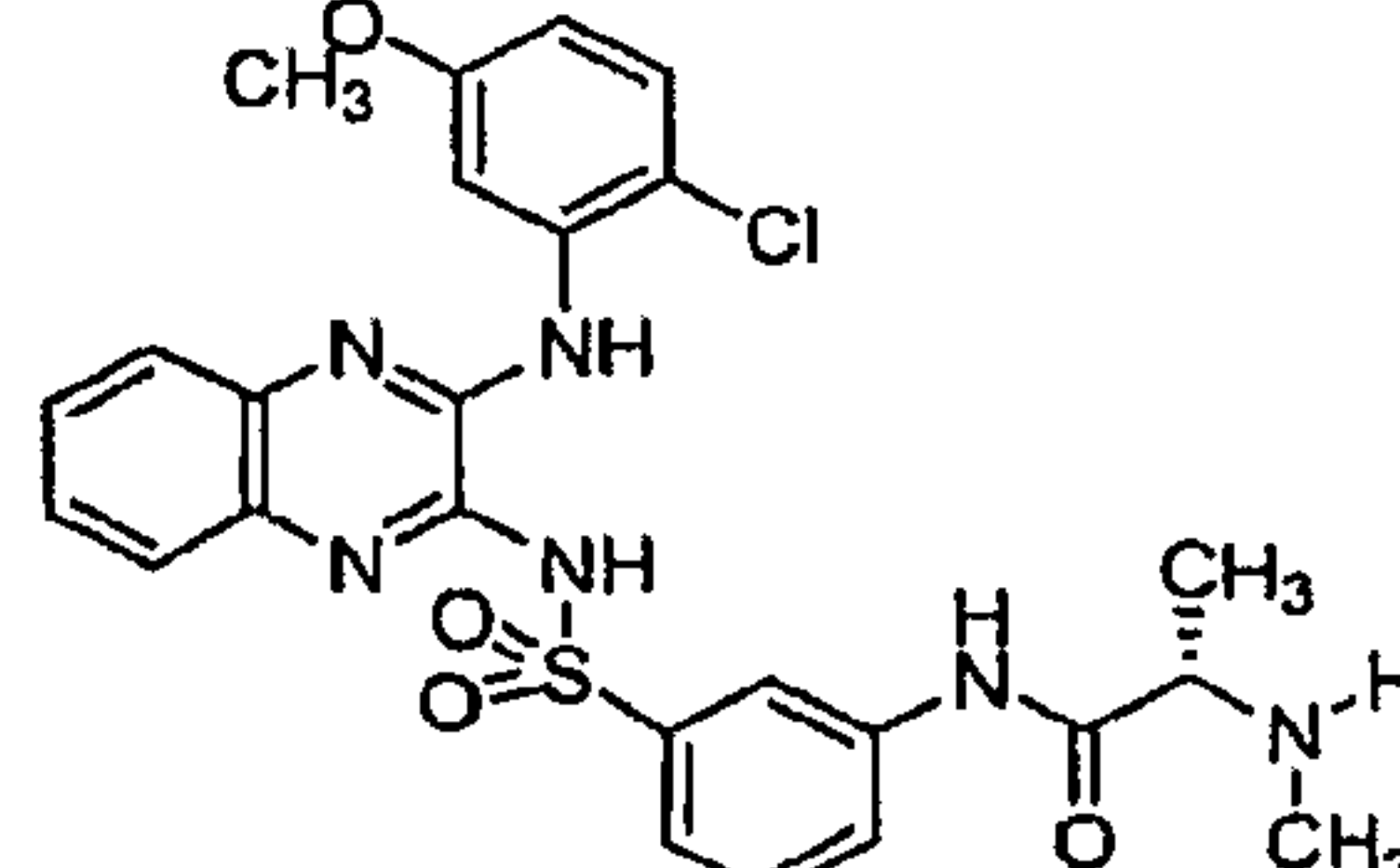
Table 1		
Cpd. No.	Structure	IUPAC Name
436		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)azetidine-3-carboxamide
437		<i>N</i> -(3-{[(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2,2-dimethylalaninamide
438		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methyl-D-alaninamide
439		<i>N</i> -(3-{[(3-{[2-bromo-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2,2-dimethylglycinamide
440		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-propylglycinamide
441		<i>N</i> -(3-{[(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methyl-L-alaninamide

Table 1		
Cpd. No.	Structure	IUPAC Name
442		<i>N</i> -(5-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}-2-methylphenyl)-beta-alaninamide
443		<i>N</i> -(3-([(3-([2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)piperidine-3-carboxamide
444		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-methyl-1,4-diazepan-1-yl)acetamide
445		(2 <i>S</i>)-2-amino- <i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)butanamide
446		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2-hydroxypropyl)glycinamide
447		<i>N</i> -(3-([(3-([2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2-fluoroethyl)glycinamide
448		3-amino- <i>N</i> -(2-([3,5-bis(methoxy)phenyl]amino)pyrido[2,3-b]pyrazin-3-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
449		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(2-methylpropyl)oxy]glycinamide
450		1-amino- <i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopropanecarboxamide
451		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(formylamino)benzenesulfonamide
452		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(cyclopropylmethyl)glycinamide
453		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>D</i> -prolinamide
454		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(dimethylamino)azetidin-1-yl]acetamide
455		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>D</i> -prolinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
456		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)piperidine-2-carboxamide
457		<i>N</i> -(3-(((3-((2-chloro-5-(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)morpholine-4-carboxamide
458		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-pyrrolidin-1-ylacetamide
459		<i>N</i> -(3-(((3-((2-chloro-5-(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -6, <i>N</i> -6-dimethyl-L-lysineamide
460		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-ethyl- <i>N</i> -2-methylglycinamide
461		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(1 <i>H</i> -imidazol-4-yl)acetamide
462		1-amino- <i>N</i> -(3-(((3-((2-chloro-5-(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)cyclopentanecarboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
463		<i>N</i> -(3-[[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl]- <i>N</i> -2-(2-methylpropyl)glycinamide
464		<i>N</i> -(3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]sulfonyl}phenyl]- <i>N</i> -2-ethyl- <i>N</i> -2-methylglycinamide
465		<i>N</i> -(3-[[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl]-1-(1 <i>H</i> -imidazol-4-ylmethyl)azetidine-3-carboxamide
466		<i>N</i> -(5-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]sulfonyl}-2-methylphenyl]- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide
467		<i>N</i> -(3-[[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl]-1-ethylazetidine-3-carboxamide
468		<i>N</i> -(3-[[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl]- <i>N</i> -2-methyl- <i>N</i> -2-(1-methylpyrrolidin-3-yl)glycinamide
469		<i>N</i> -(3-[[[2-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl]- <i>N</i> -2-[2-(dimethylamino)ethyl]- <i>N</i> -2-methylglycinamide

Table 1

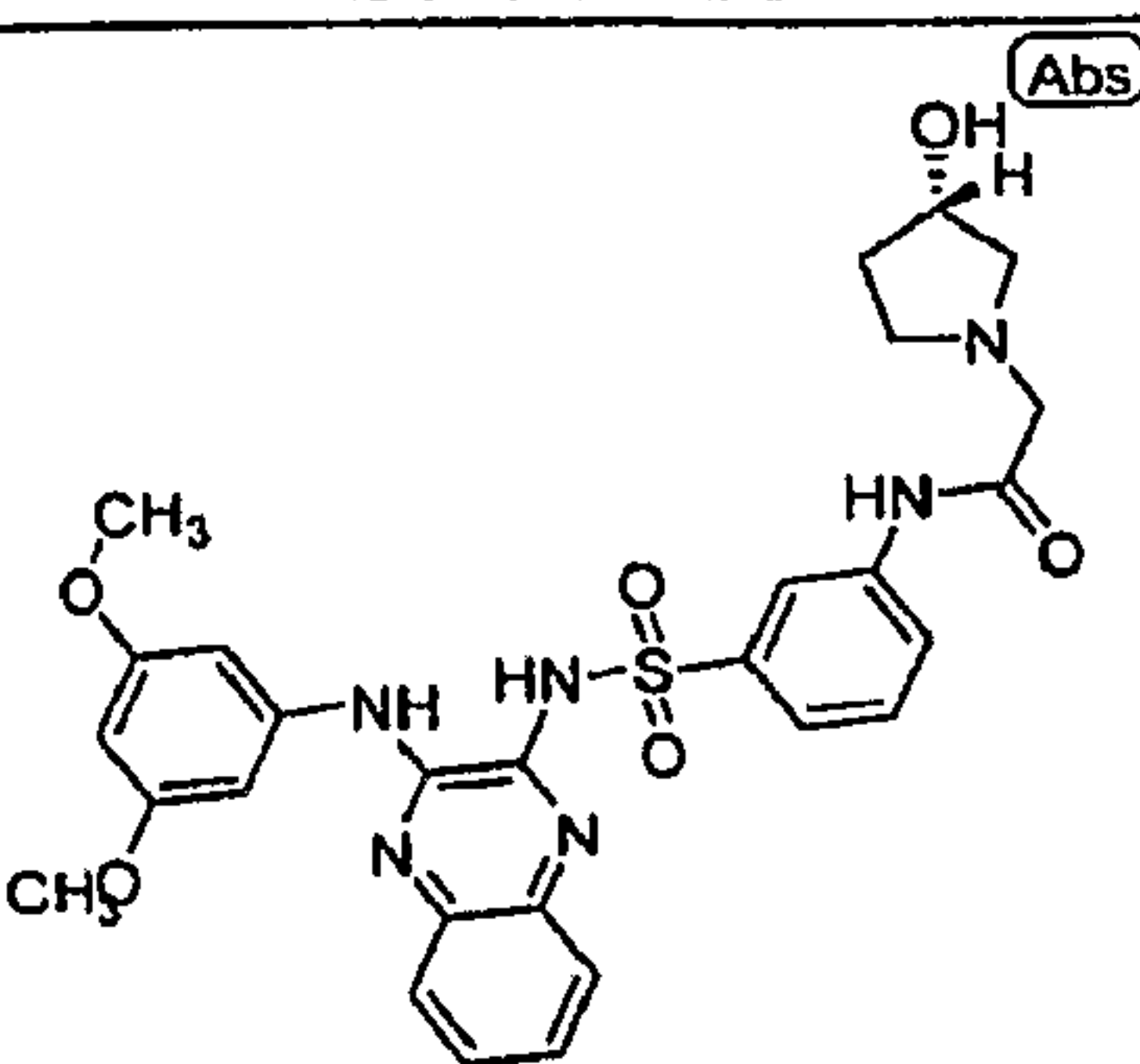
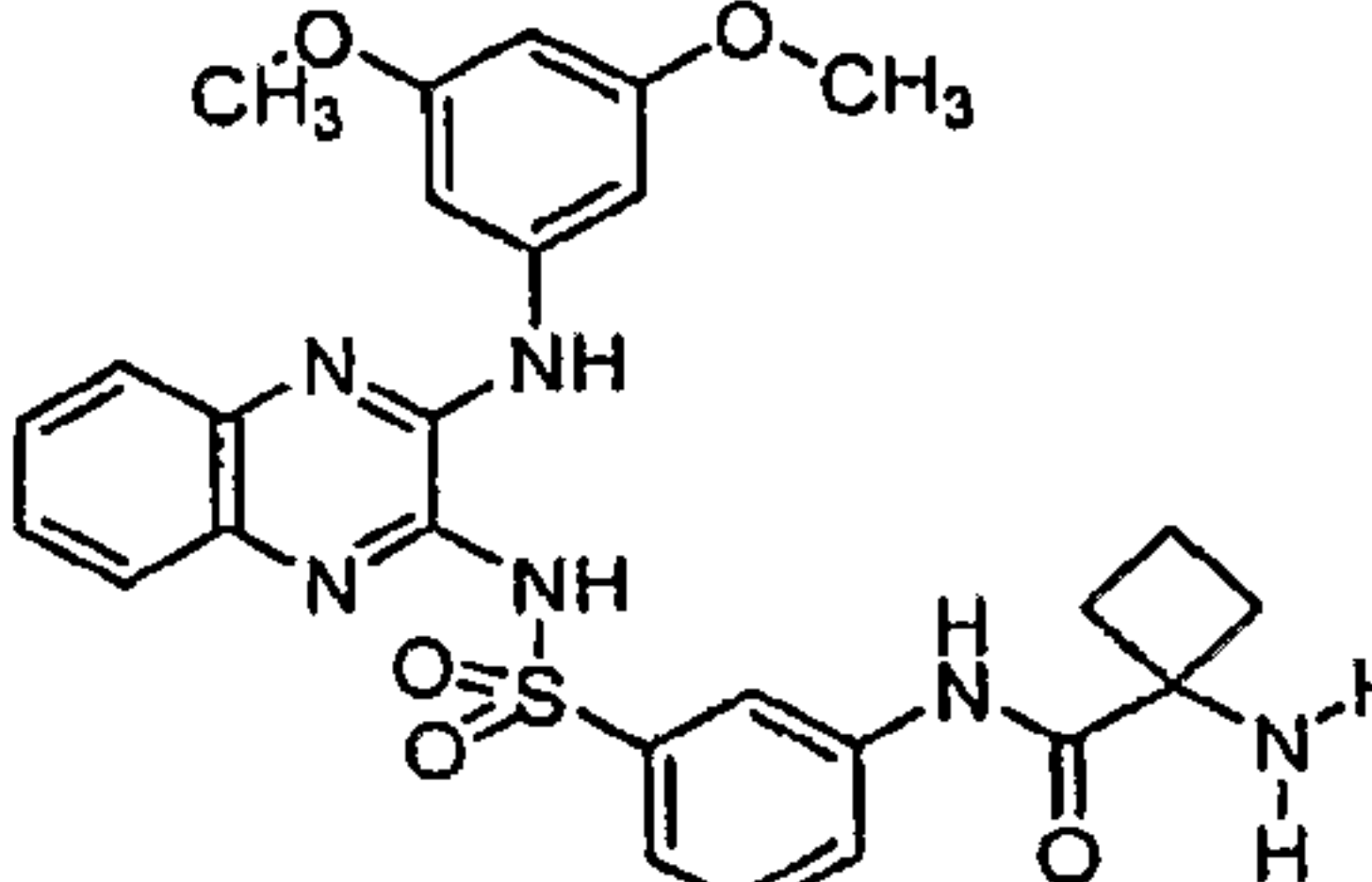
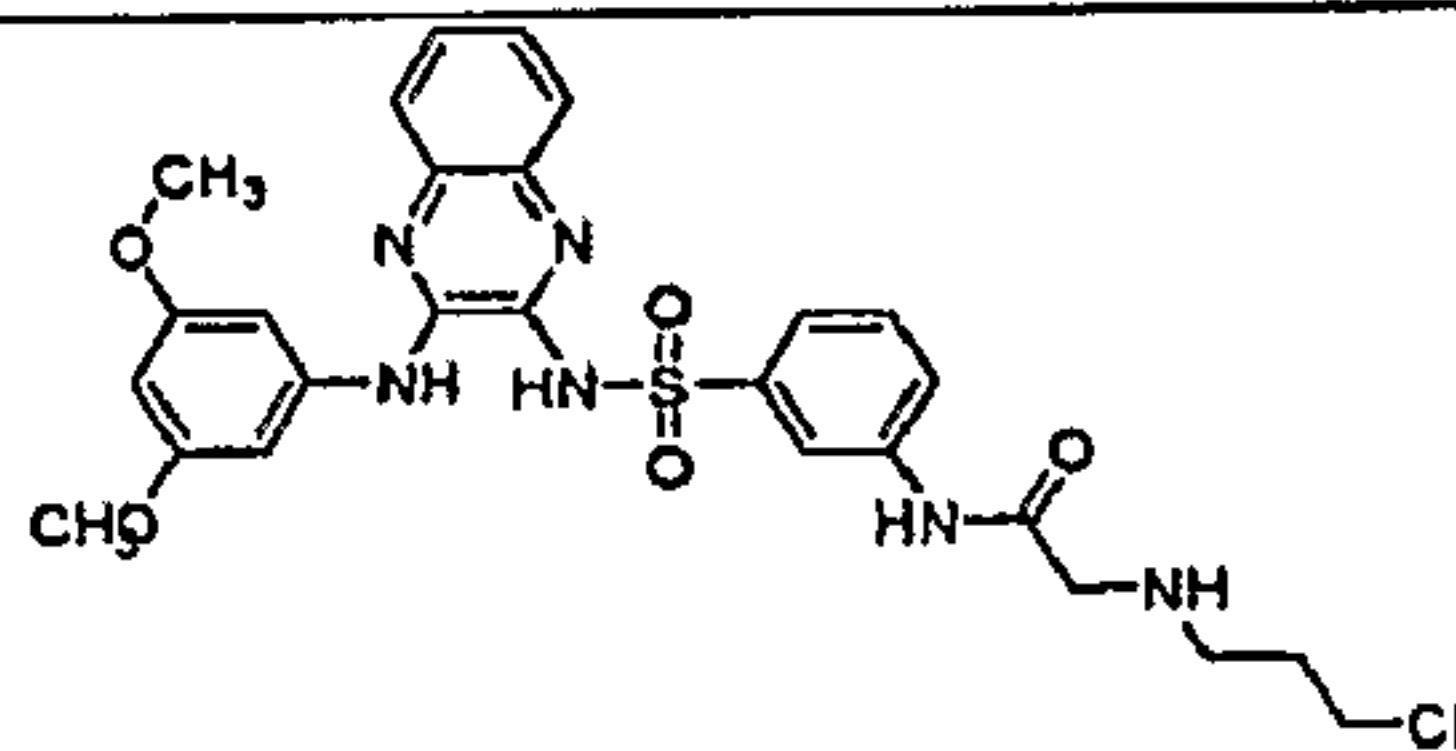
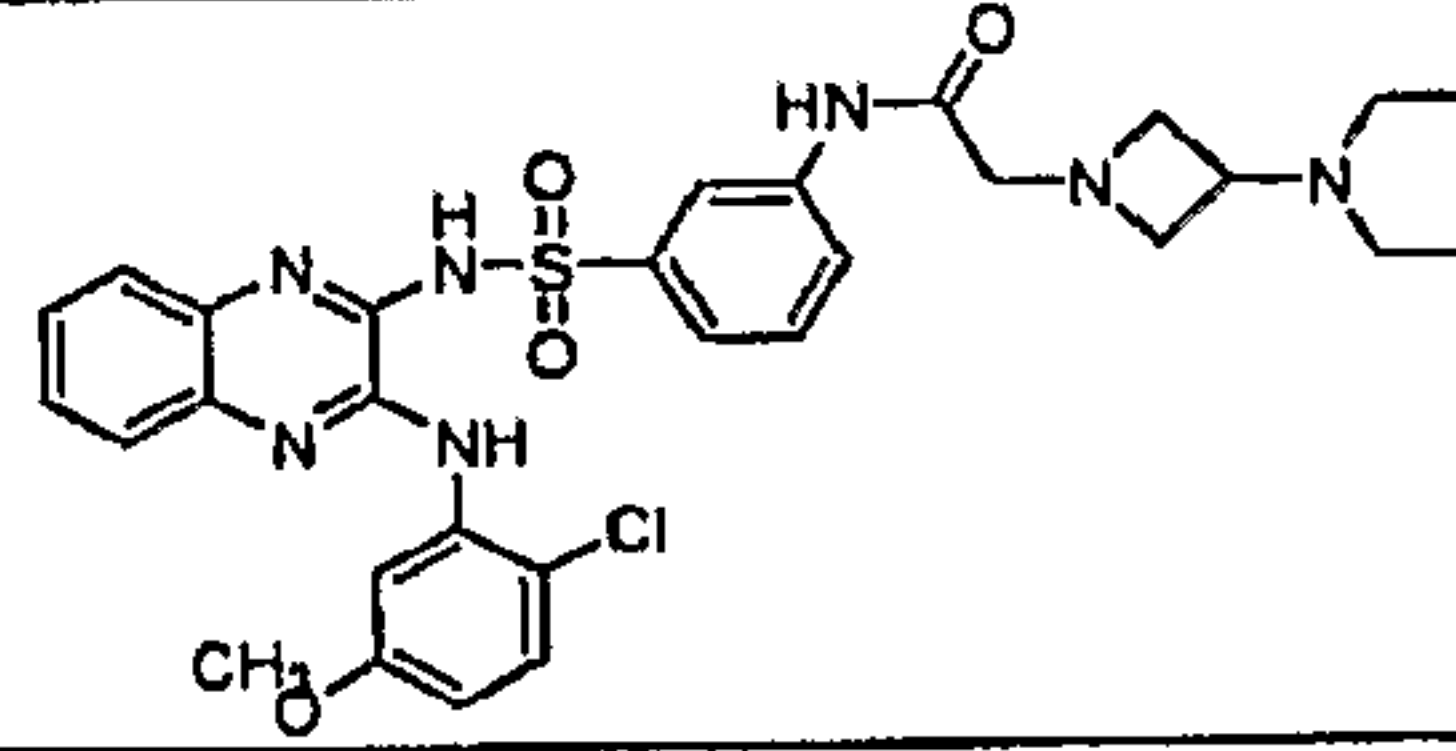
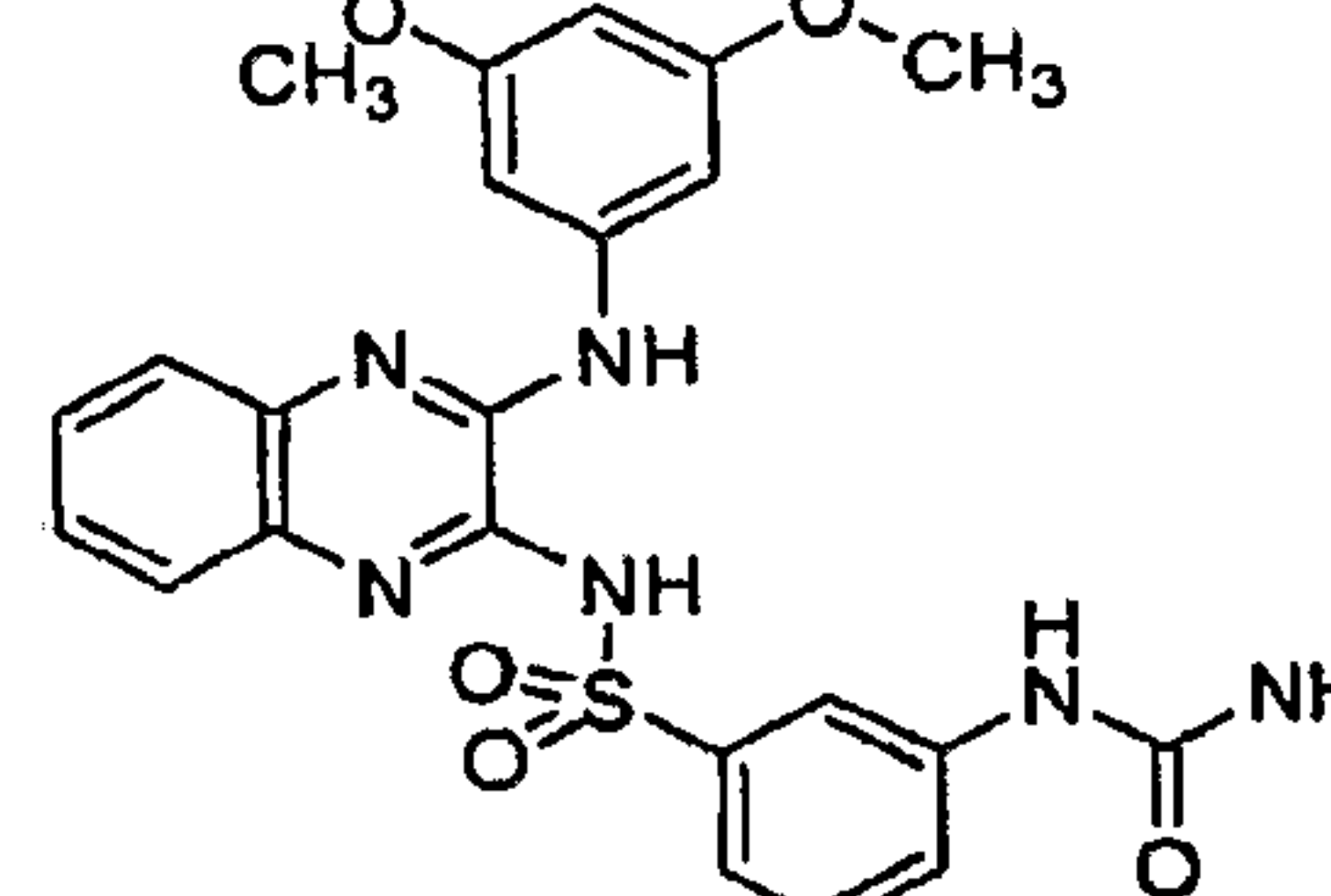
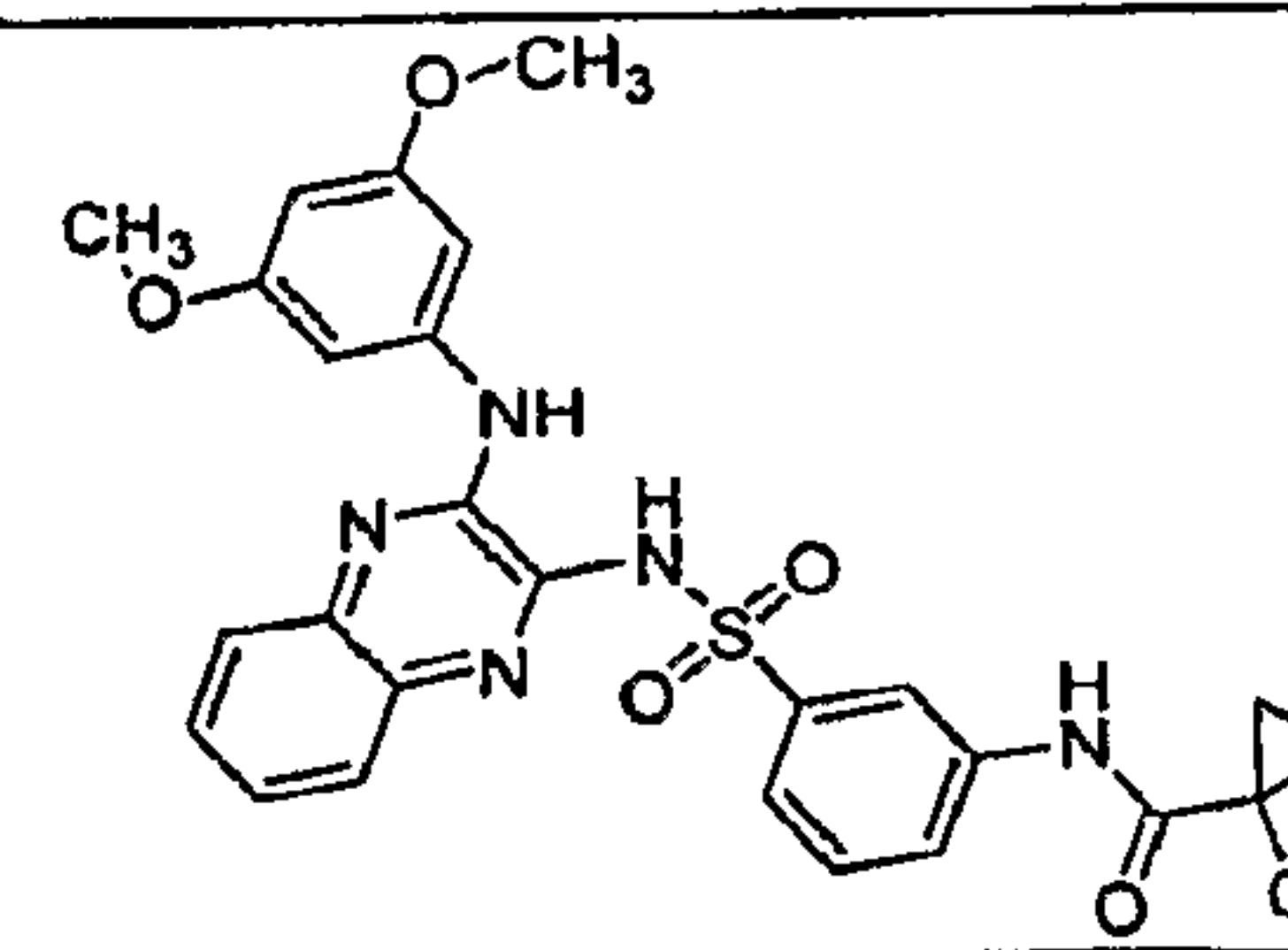
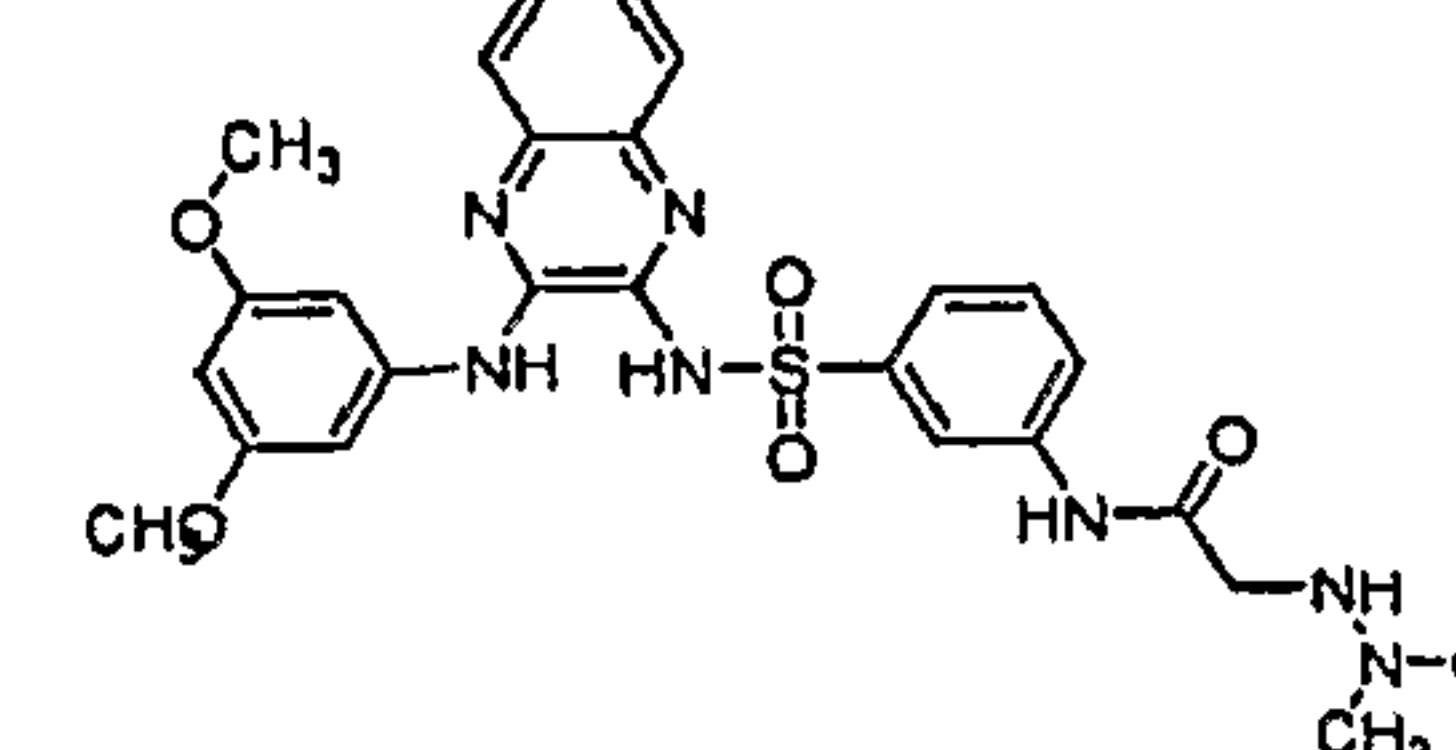
Cpd. No.	Structure	IUPAC Name
470		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(3 <i>S</i>)-3-hydroxypyrrolidin-1-yl]acetamide
471		1-amino- <i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclobutane-1-carboxamide
472		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-butylglycinamide
473		<i>N</i> -(3-{[(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3-piperidin-1-ylazetidin-1-yl)acetamide
474		3-[(aminocarbonyl)amino]- <i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
475		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-hydroxycyclopropanecarboxamide
476		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2,2-dimethylhydrazino)acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
477		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-[(2-(dimethylamino)ethyl)amino]benzenesulfonamide
478		<i>N</i> -(3-{[(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methylglycinamide
479		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-hydroxyacetamide
480		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyridazine-4-carboxamide
481		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(1-methylethyl)glycinamide
482		1-amino- <i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopentanecarboxamide
483		1-amino- <i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopropanecarboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
484		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(dimethylamino)pyrrolidin-1-yl]acetamide
485		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[2-(dimethylamino)ethyl]glycinamide
486		2-(dimethylamino)ethyl(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)carbamate
487		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(cyclopropylmethyl)azetidine-3-carboxamide
488		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(1,1-dimethylethyl)glycinamide
489		<i>N</i> -2-methyl- <i>N</i> -(3-([(3-([3-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide
490		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-1 <i>H</i> -imidazole-2-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
491		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)isoxazole-5-carboxamide
492		<i>N</i> -(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2,2,2-trifluoroethyl)glycinamide
493		3-amino- <i>N</i> -(3-{[2-methyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
494		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-oxocyclopentanecarboxamide
495		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-6-hydroxypyridine-2-carboxamide
496		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(3-fluoro-4-hydroxyphenyl)glycinamide
497		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(furan-2-ylmethyl)azetidine-3-carboxamide
498		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyrimidine-5-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
499		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-1 <i>H</i> -pyrrole-2-carboxamide
500		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-methyl- <i>N</i> -2-(1-methylethyl)glycinamide
501		<i>N</i> -(3-(((3-((3-fluoro-5-(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
502		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-1 <i>H</i> -imidazole-4-carboxamide
503		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2, <i>N</i> -2-diethylglycinamide
504		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(3-methylisoxazol-5-yl)acetamide
505		<i>N</i> -2, <i>N</i> -2-dimethyl- <i>N</i> -(3-(((3-((2-methyl-5-(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)glycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
506		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(3-hydroxyphenyl)methyl]glycinamide
507		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-methyl-1 <i>H</i> -pyrrole-2-carboxamide
508		4-amino- <i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)tetrahydro-2 <i>H</i> -pyran-4-carboxamide
509		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(methylamino)piperidin-1-yl]acetamide
510		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-piperidin-1-ylacetamide
511		<i>N</i> -(4-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide

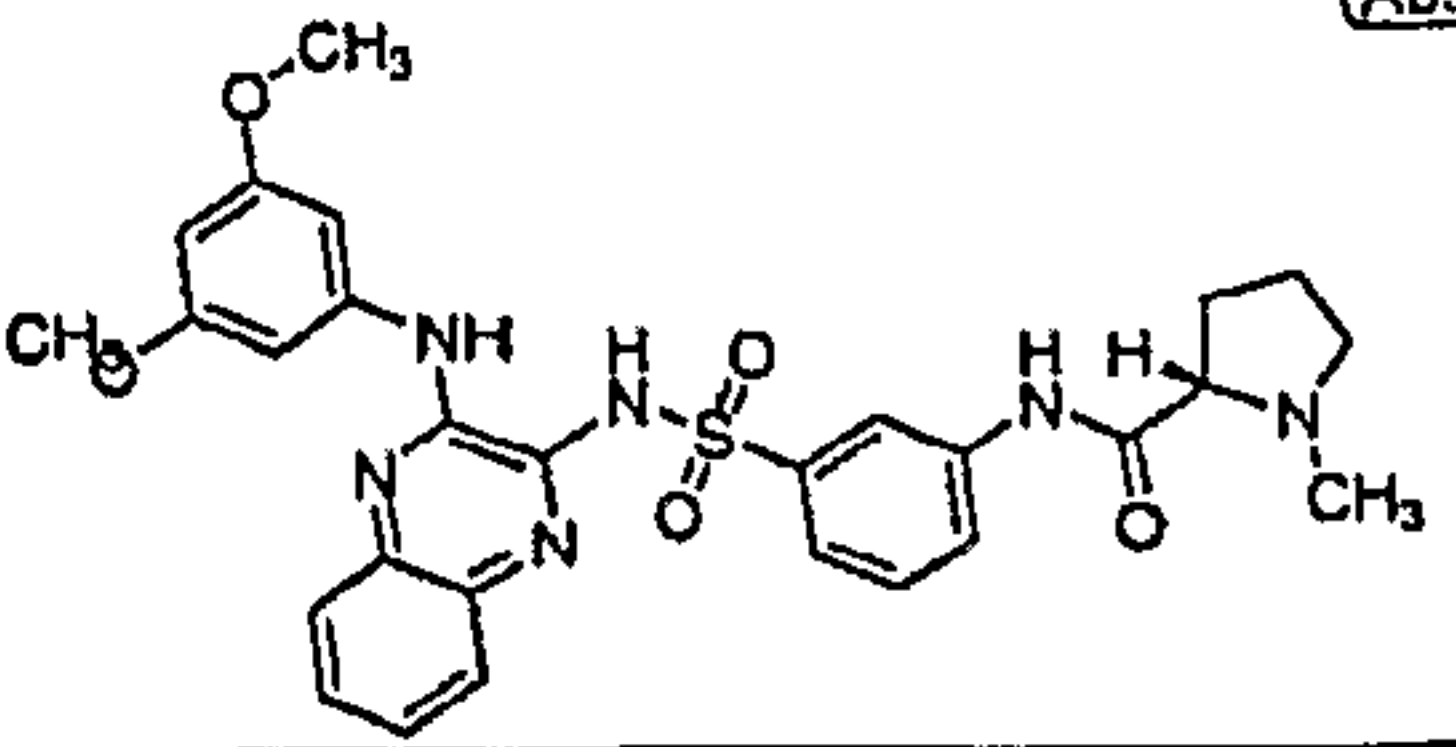
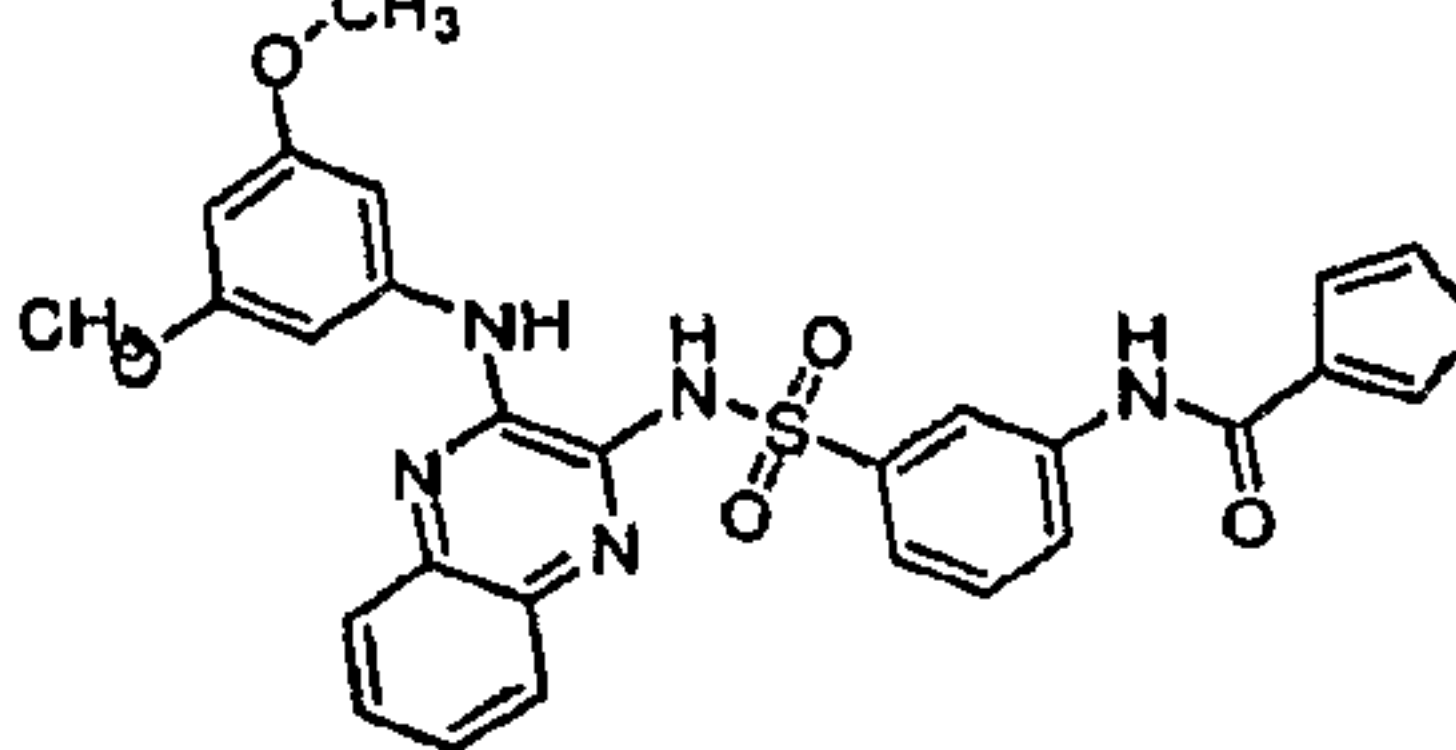
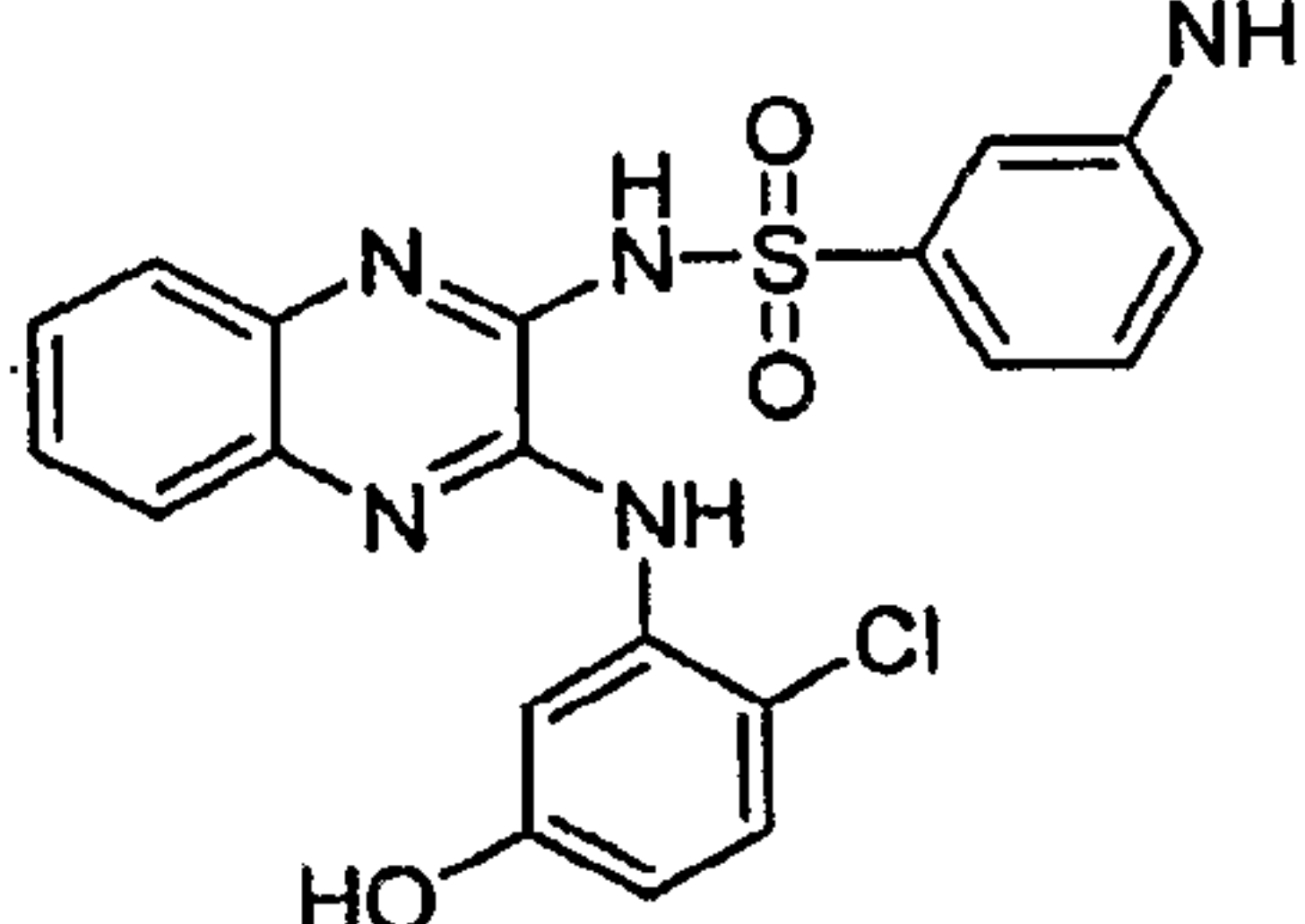
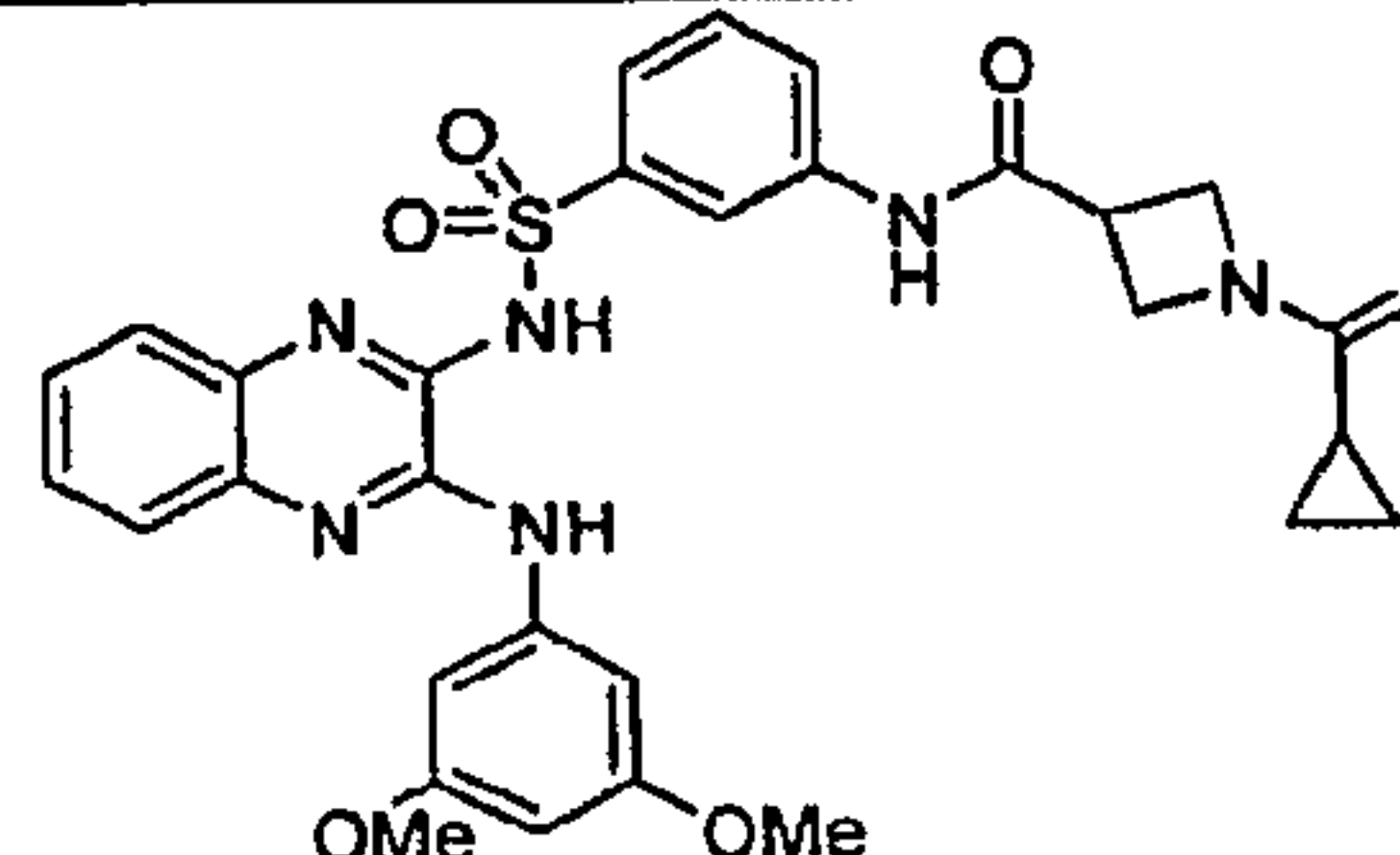
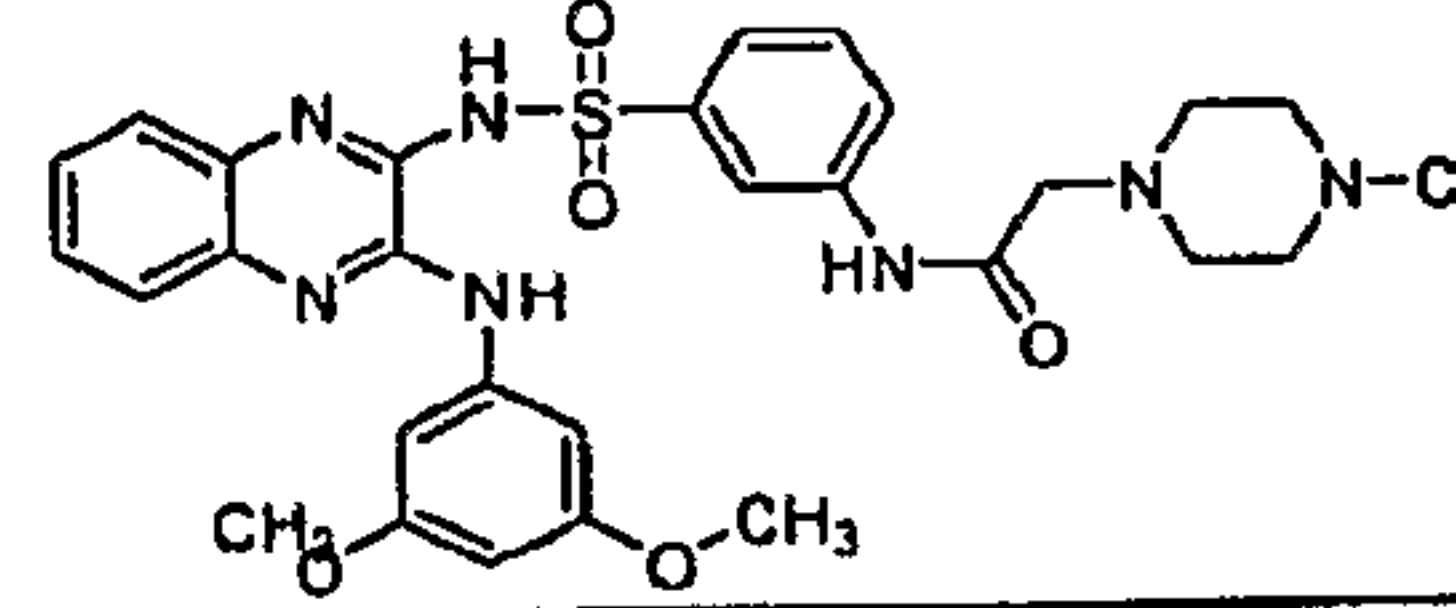
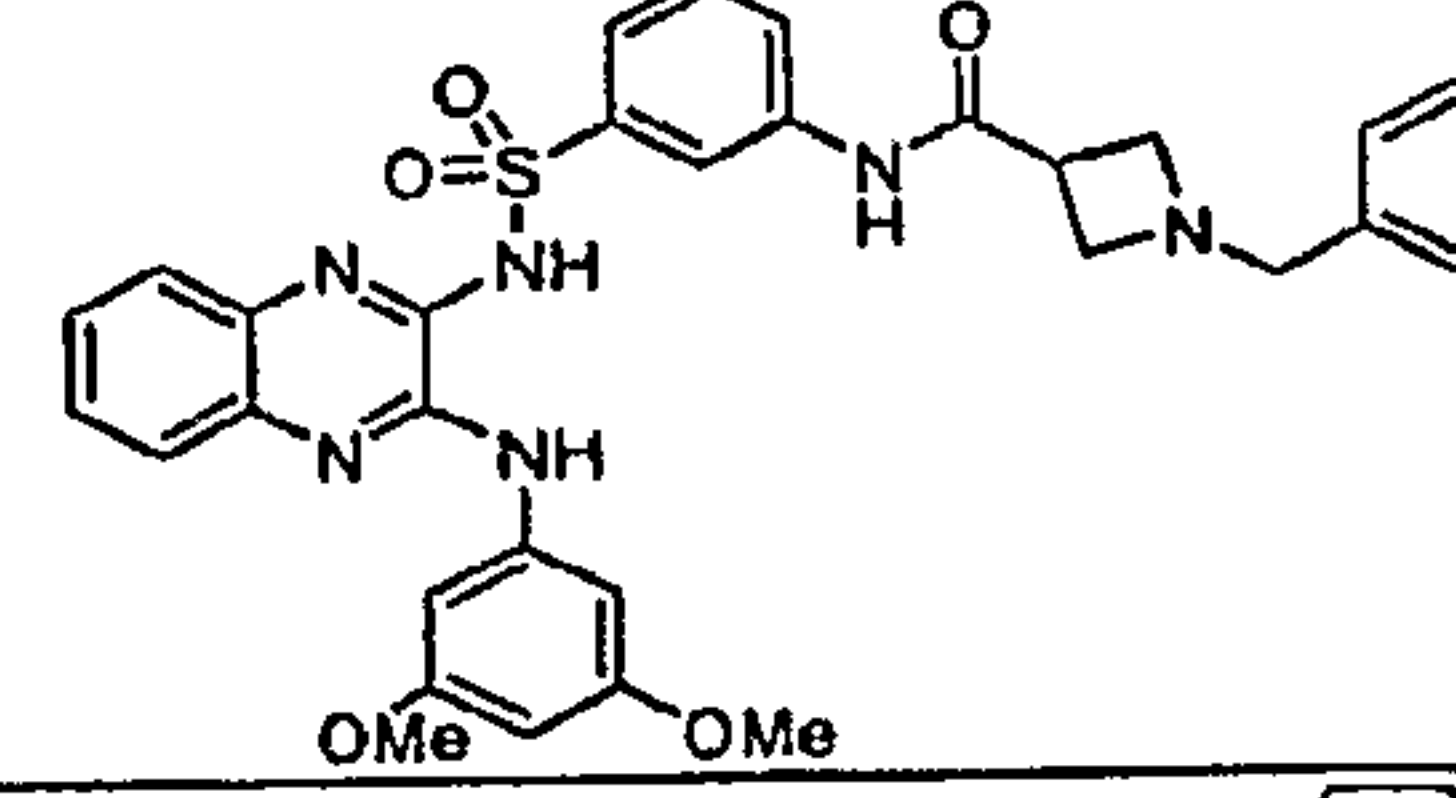
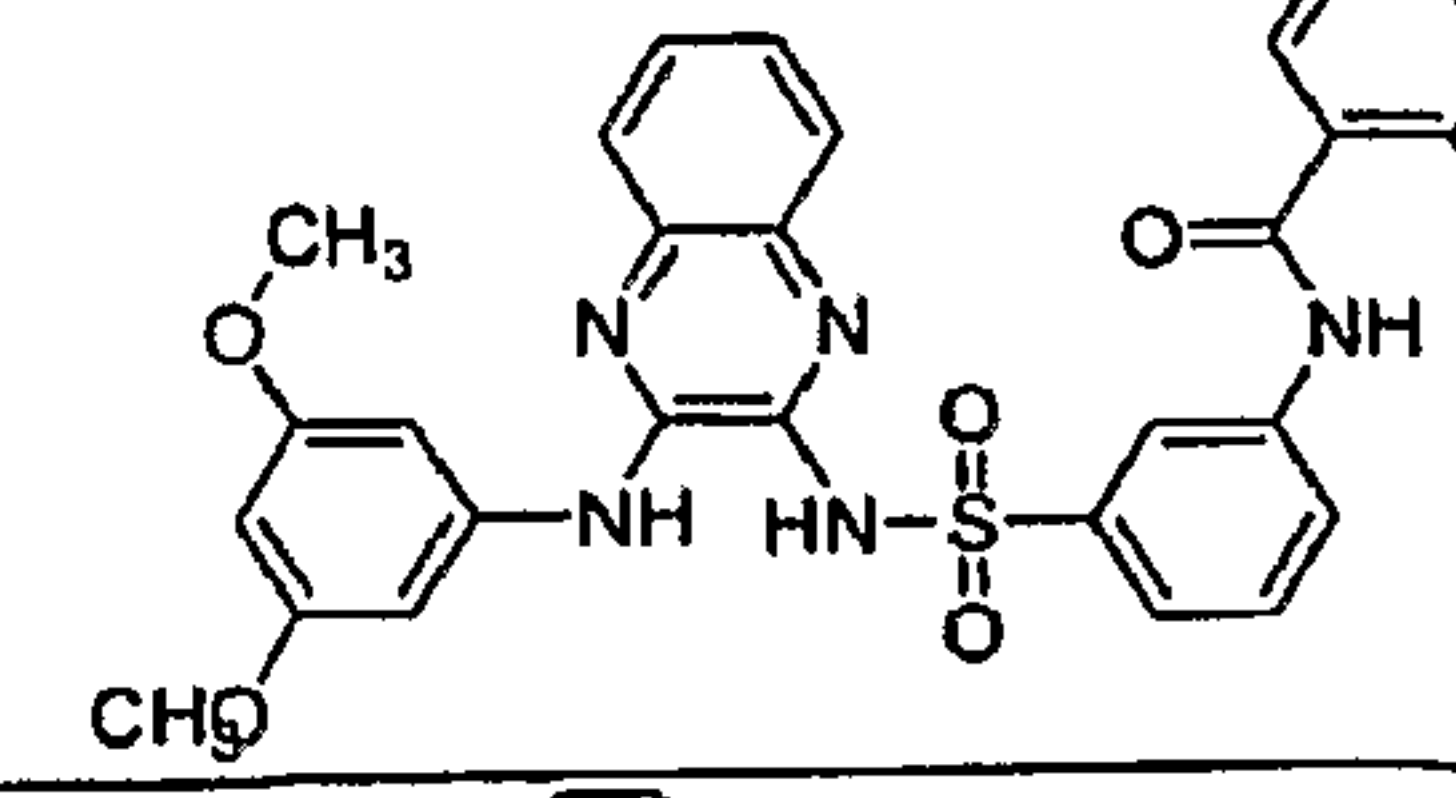
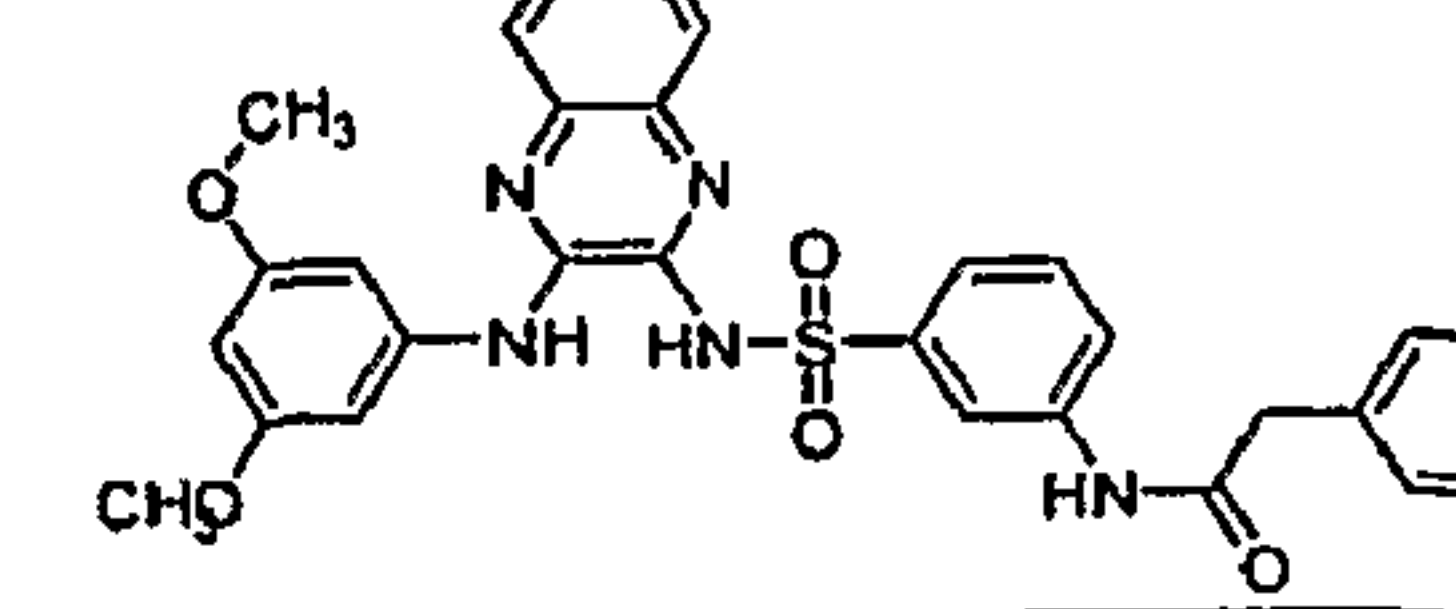
Table 1		
Cpd. No.	Structure	IUPAC Name
512		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-methyl-L-prolinamide
513		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)thiophene-3-carboxamide
514		3-amino- <i>N</i> -{3-[(2-chloro-5-hydroxyphenyl)amino]quinoxalin-2-yl}benzenesulfonamide
515		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(cyclopropylcarbonyl)azetidine-3-carboxamide
516		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-methylpiperazin-1-yl)acetamide
517		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(phenylmethyl)azetidine-3-carboxamide
518		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-chloropyridine-3-carboxamide
519		<i>N</i> -(3-{{(3-{{3,5-bis(methoxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyridin-4-ylacetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
520		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-methyl- <i>N</i> -2-prop-2-en-1-ylglycinamide
521		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-(phenylmethyl)glycinamide
522		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(methoxy)acetamide
523		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-1-propanoylazetidine-3-carboxamide
524		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)pyridine-3-carboxamide
525		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-[2-(methoxy)ethyl]glycinamide
526		1-acetyl- <i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)piperidine-4-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
527		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-methylpyrrolidin-1-yl)acetamide
528		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)furan-3-carboxamide
529		<i>N</i> -2-, <i>N</i> -2-dimethyl- <i>N</i> -(3-{[(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide
530		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-6-chloropyridine-3-carboxamide
531		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-chlorobenzamide
532		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyridin-2-ylacetamide
533		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(dimethylamino)azetidin-1-yl]acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
534		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyridin-3-ylacetamide
535		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-chlorophenyl)acetamide
536		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[3-(dimethylamino)propyl]- <i>N</i> -2-methylglycinamide
537		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-ethyl- <i>N</i> -2-(2-hydroxyethyl)glycinamide
538		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[2-(phenylmethyl)pyrrolidin-1-yl]acetamide
539		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)propanamide
540		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)furan-2-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
541		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-chloropyridine-4-carboxamide
542		<i>N</i> -2-acetyl- <i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide
543		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)butanamide
544		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-chlorobenzamide
545		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-methylbenzamide
546		1,1-dimethylethyl 2-([(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)amino]-2-oxoethyl}carbamate
547		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-1,3-benzodioxole-5-carboxamide
548		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-([2-(methyloxy)phenyl]methyl}oxy)glycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
549		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)pyridine-4-carboxamide
550		<i>N</i> -(3-([(3-([4-fluoro-3-(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
551		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(3,4-dichlorophenyl)piperazin-1-yl]acetamide
552		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-pyridin-3-ylpropanamide
553		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)tetrahydrofuran-3-carboxamide
554		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(2-methylphenyl)methyl]glycinamide
555		<i>N</i> -(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylbutanamide

Table 1		
Cpd. No.	Structure	IUPAC Name
556		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(3-fluorophenyl)acetamide
557		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-(1-methyl-1-phenylethyl)glycinamide
558		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-methylcyclopropanecarboxamide
559		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-methyl-4-(methoxy)benzamide
560		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-methylpyridine-3-carboxamide
561		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-4-(methoxy)benzamide
562		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(4-ethylpiperazin-1-yl)acetamide
563		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)thiophene-2-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
564		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-3-fluoro-2-methylbenzamide
565		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-bromothiophene-3-carboxamide
566		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-4-fluorobenzamide
567		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(3-methylpiperidin-1-yl)acetamide
568		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-methylpropanamide
569		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)pentanamide
570		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(ethyloxy)acetamide
571		<i>N</i> -(3-(((3-((3,5-bis(methyloxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-(2-fluorophenyl)glycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
572		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-(dimethylamino)benzamide
573		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-methylpiperidin-1-yl)acetamide
574		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2-propylphenyl)glycinamide
575		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)benzamide
576		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyrazine-2-carboxamide
577		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluoro-4-(methoxy)benzamide
578		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,2-dimethylbutanamide
579		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(4-fluorophenyl)oxy]acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
580		1-acetyl-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)azetidine-3-carboxamide
581		N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(4-methylphenyl)glycinamide
582		N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-phenylglycinamide
583		N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-prop-2-en-1-yl)piperazin-1-yl)acetamide
584		N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylbenzamide
585		N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-(methyloxy)propanamide
586		N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-methylfuran-2-carboxamide

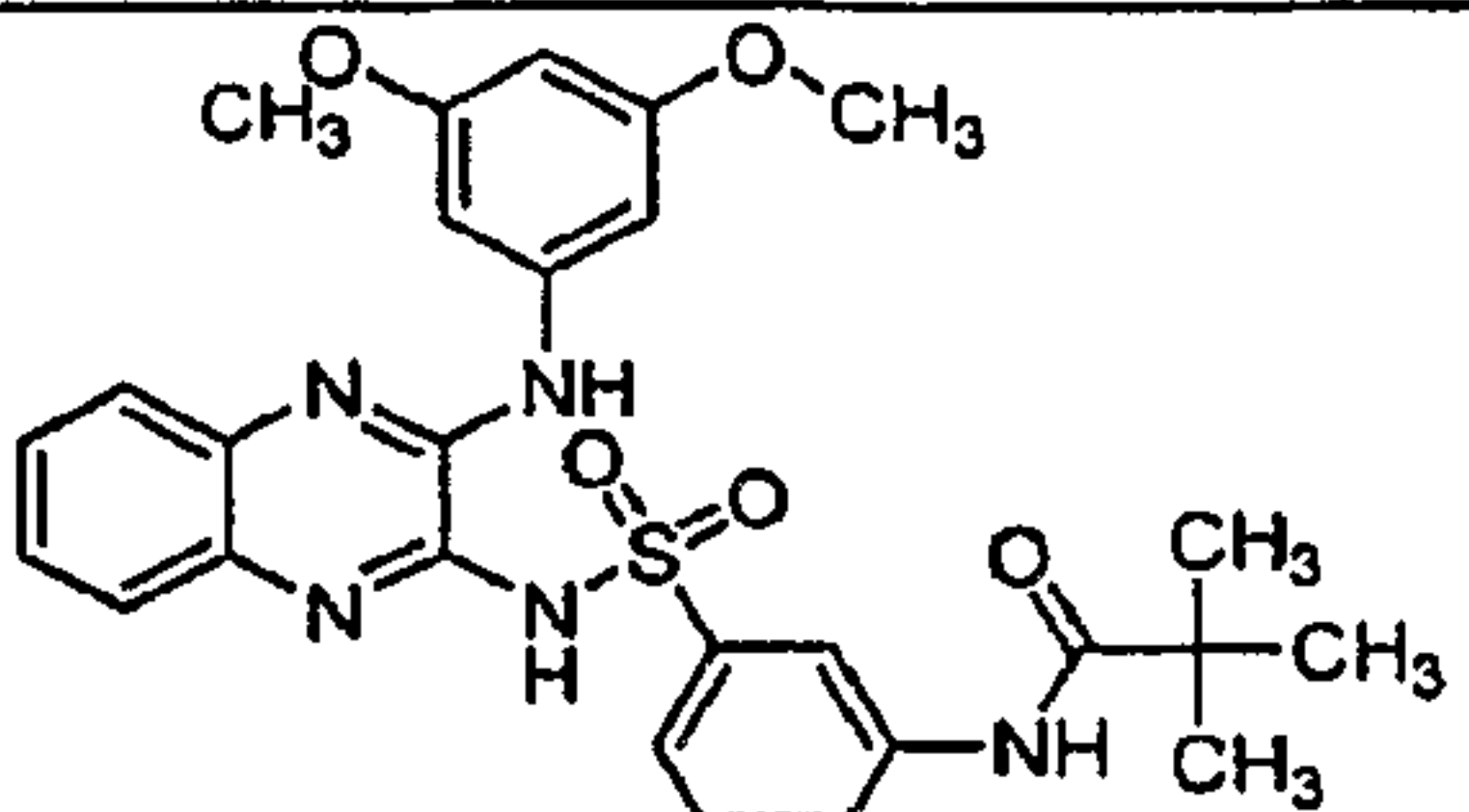
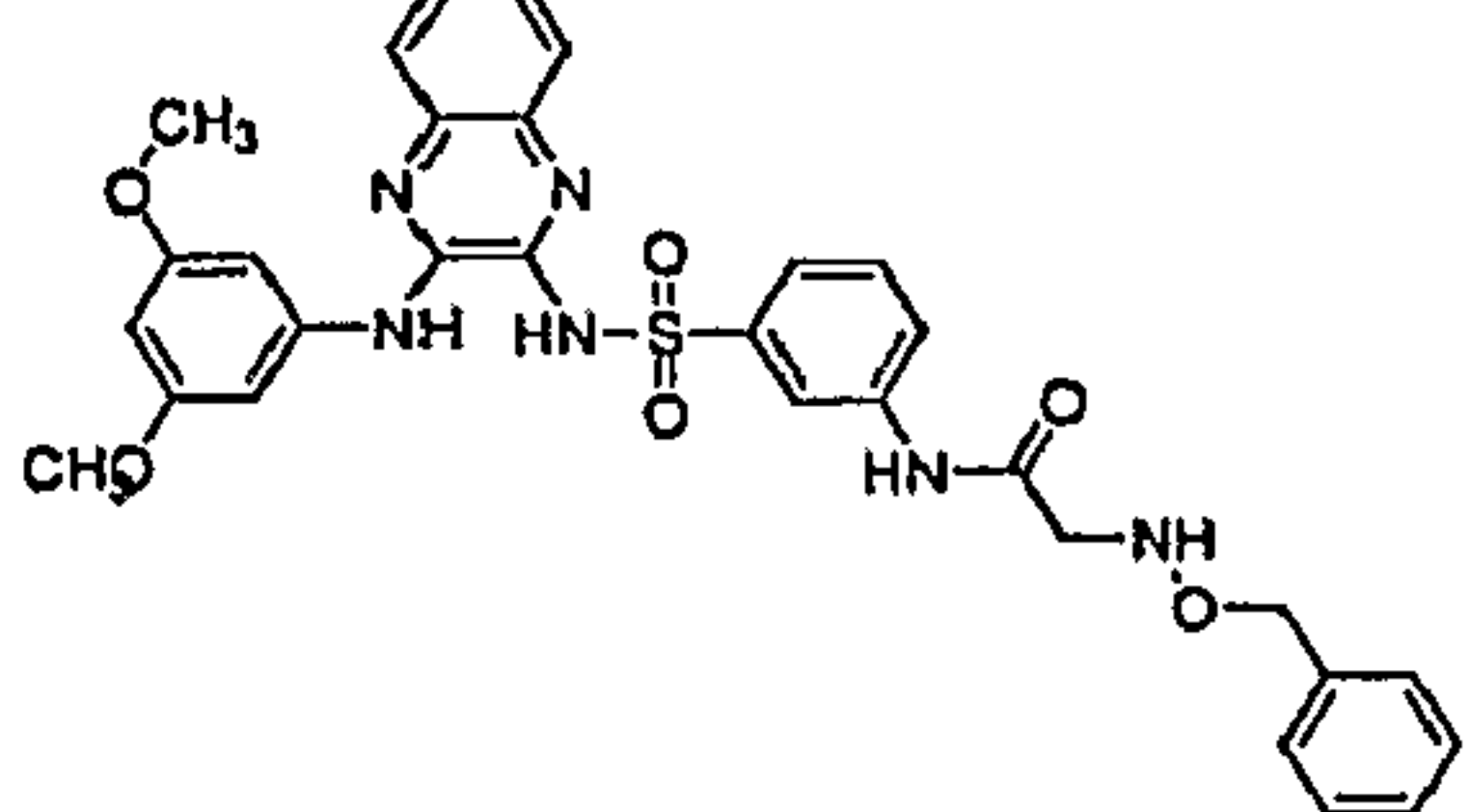
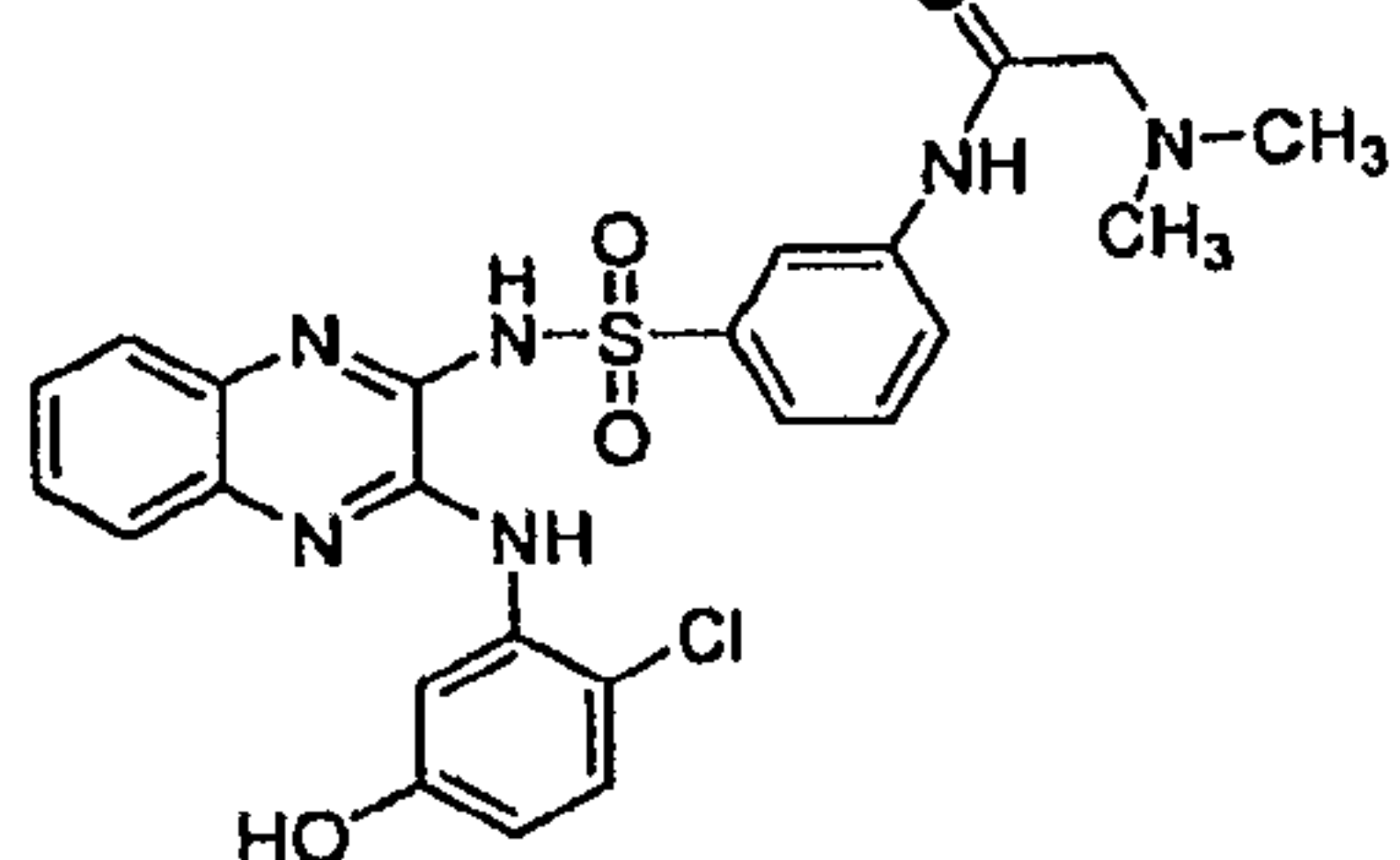
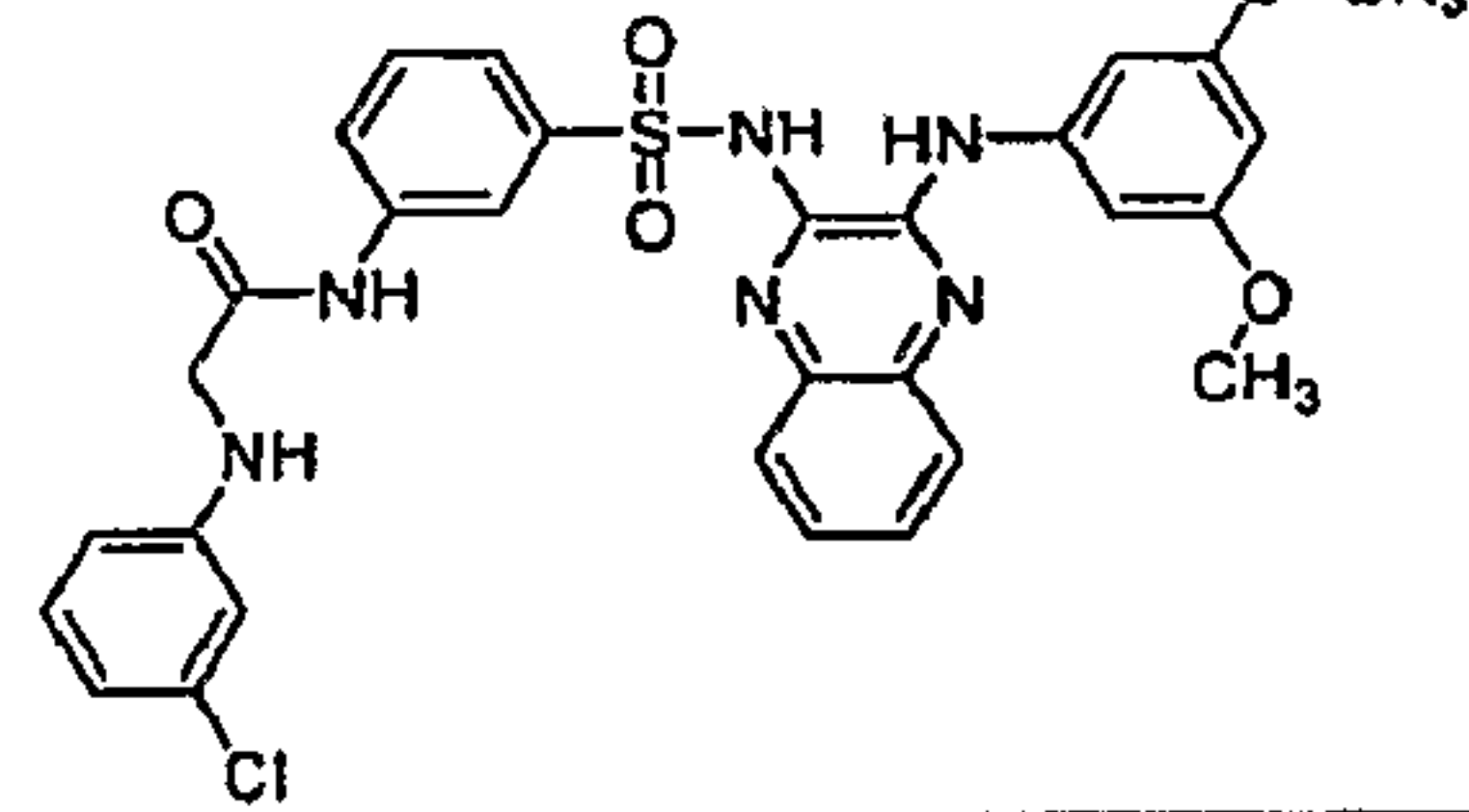
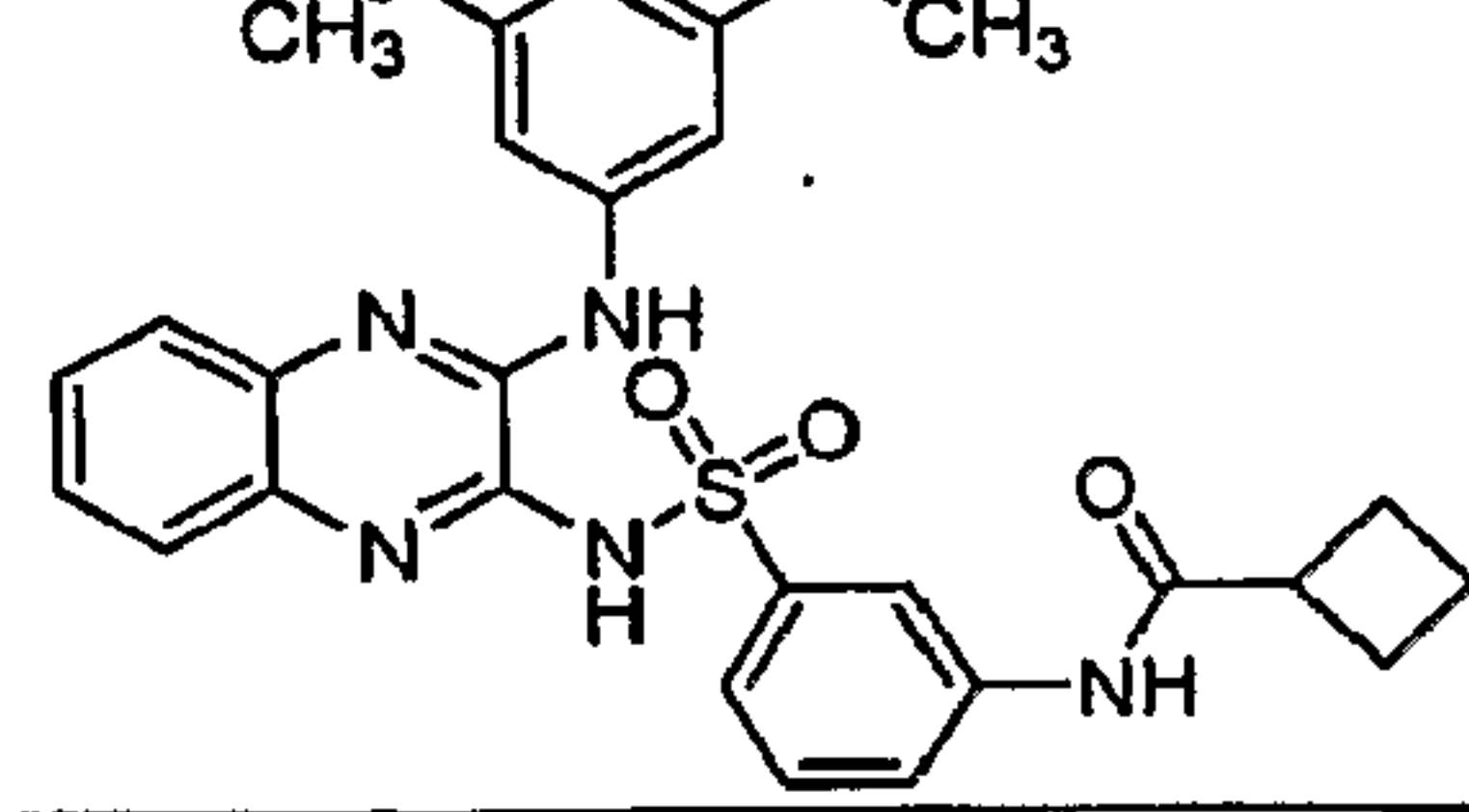
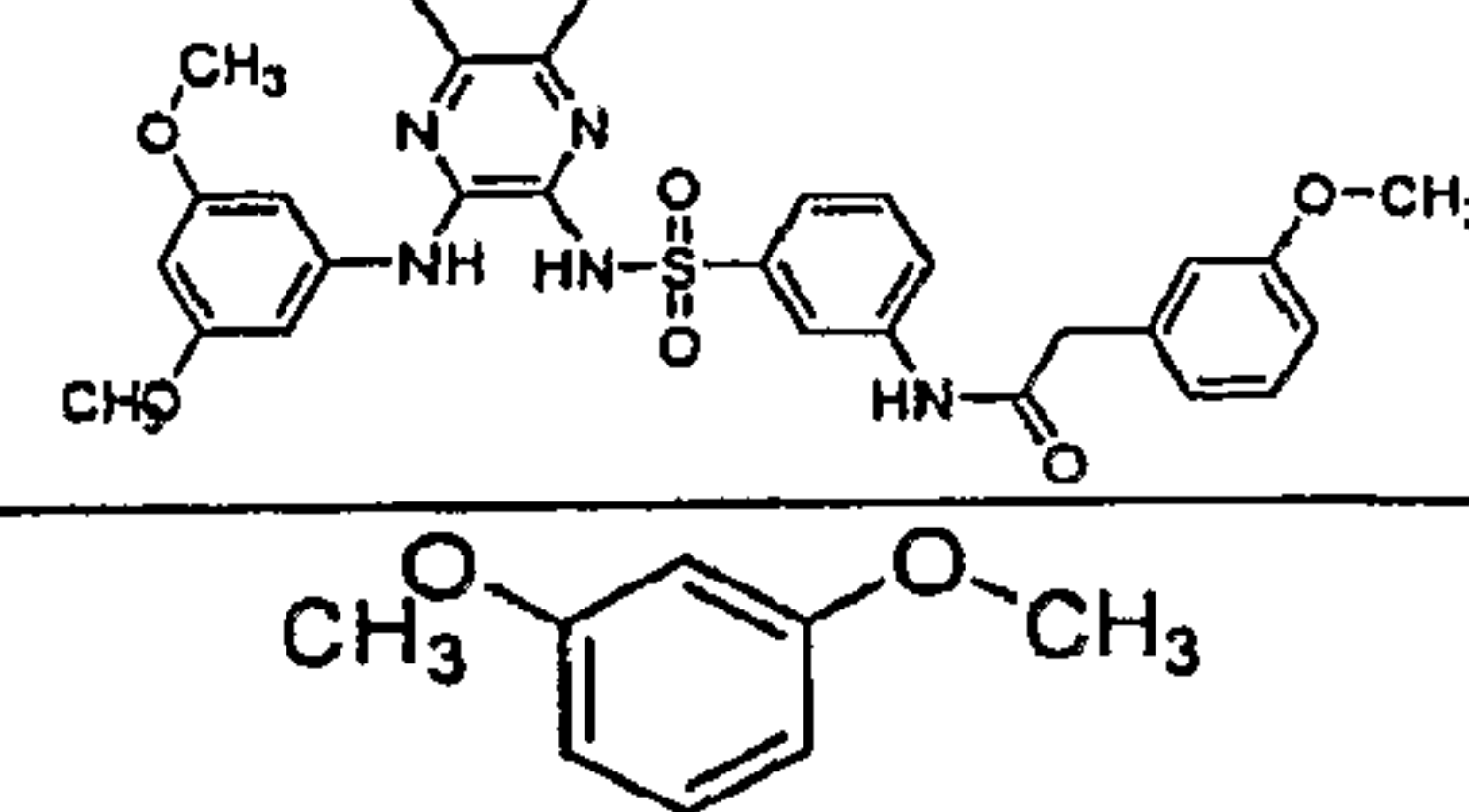
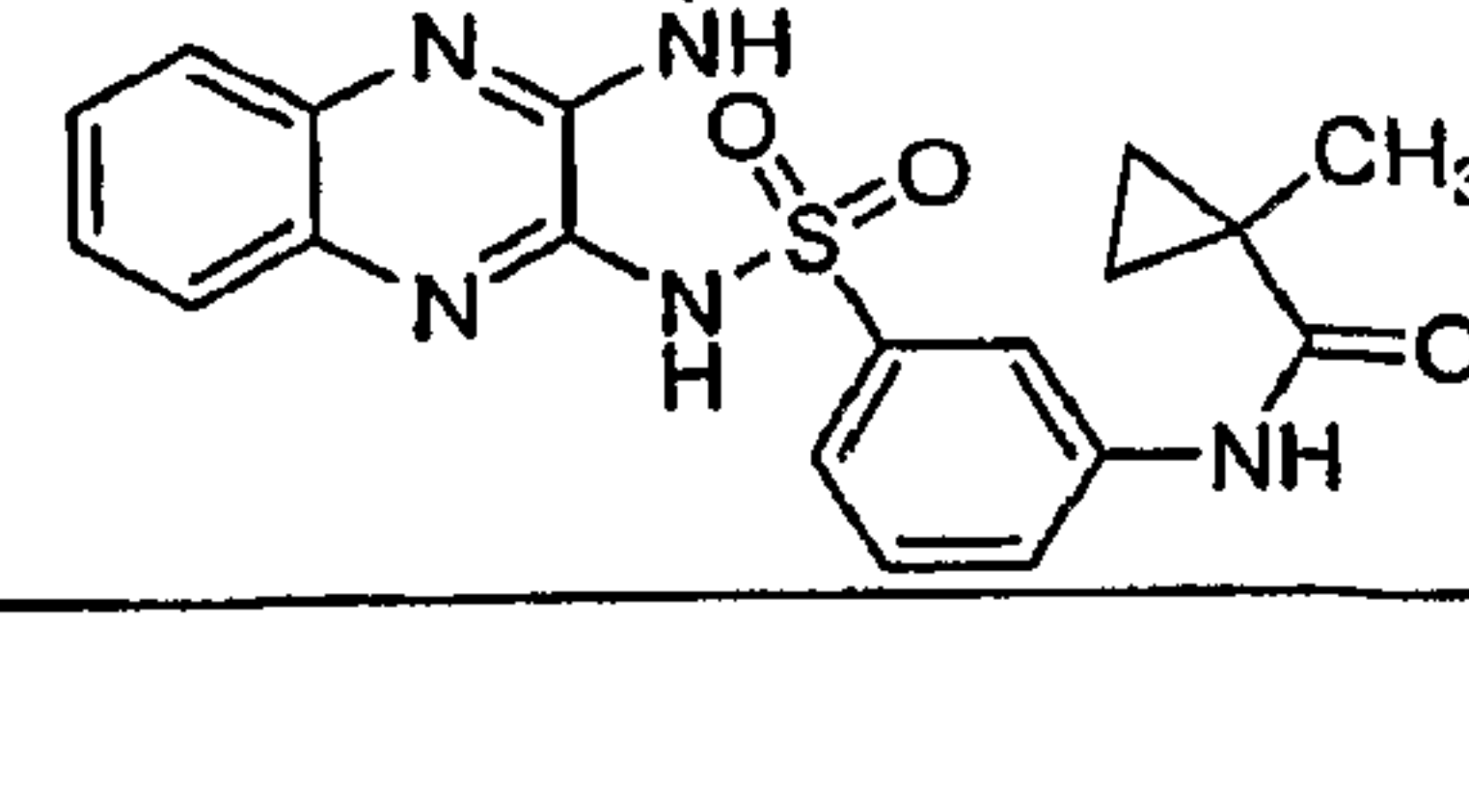
Table 1		
Cpd. No.	Structure	IUPAC Name
587		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,2-dimethylpropanamide
588		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(phenylmethyl)oxy]glycinamide
589		<i>N</i> -{3-[(3-[(2-chloro-5-hydroxyphenyl)amino]quinoxalin-2-yl)amino]sulfonyl}phenyl}- <i>N</i> -2,2-dimethylglycinamide
590		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(3-chlorophenyl)glycinamide
591		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclobutanecarboxamide
592		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(methoxy)phenyl]acetamide
593		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-methylcyclopropanecarboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
594		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluorobenzamide
595		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-(dimethylamino)benzamide
596		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3,4-dichlorobenzamide
597		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-{[2-(methylthio)phenyl]methyl}glycinamide
598		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-fluorophenyl)acetamide
599		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-ethyl- <i>N</i> -2-(1-methylethyl)glycinamide
600		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1,3-thiazole-4-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
601		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-methyl- <i>N</i> -2-(phenylmethyl)glycinamide
602		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-(2-thienylmethyl)glycinamide
603		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-(pyridin-2-ylmethyl)glycinamide
604		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-3-(methoxy)benzamide
605		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-((3-chloro-4-methylphenyl)methyl)glycinamide
606		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-methylpentanamide
607		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(4-chlorophenyl)acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
608		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluoro-4-methylbenzamide
609		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(2-methylphenyl)oxy]acetamide
610		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-cyclohexylacetamide
611		(1R,2R)- <i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-phenylcyclopropanecarboxamide
612		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-chlorobenzamide
613		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[2-(methyloxy)phenyl]acetamide
614		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-[3-(methyloxy)phenyl]propanamide
615		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2-fluoro-4-methylphenyl)glycinamide

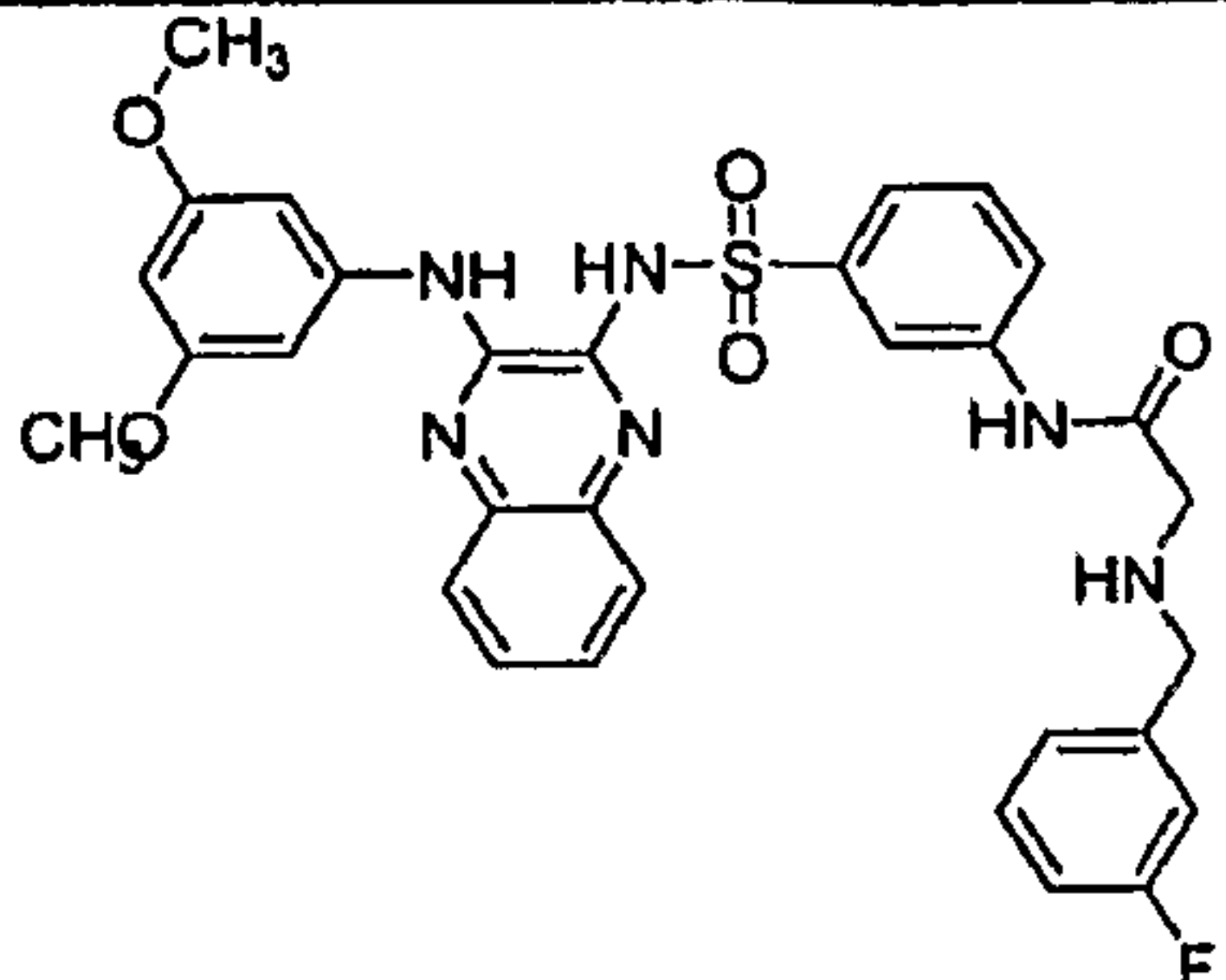
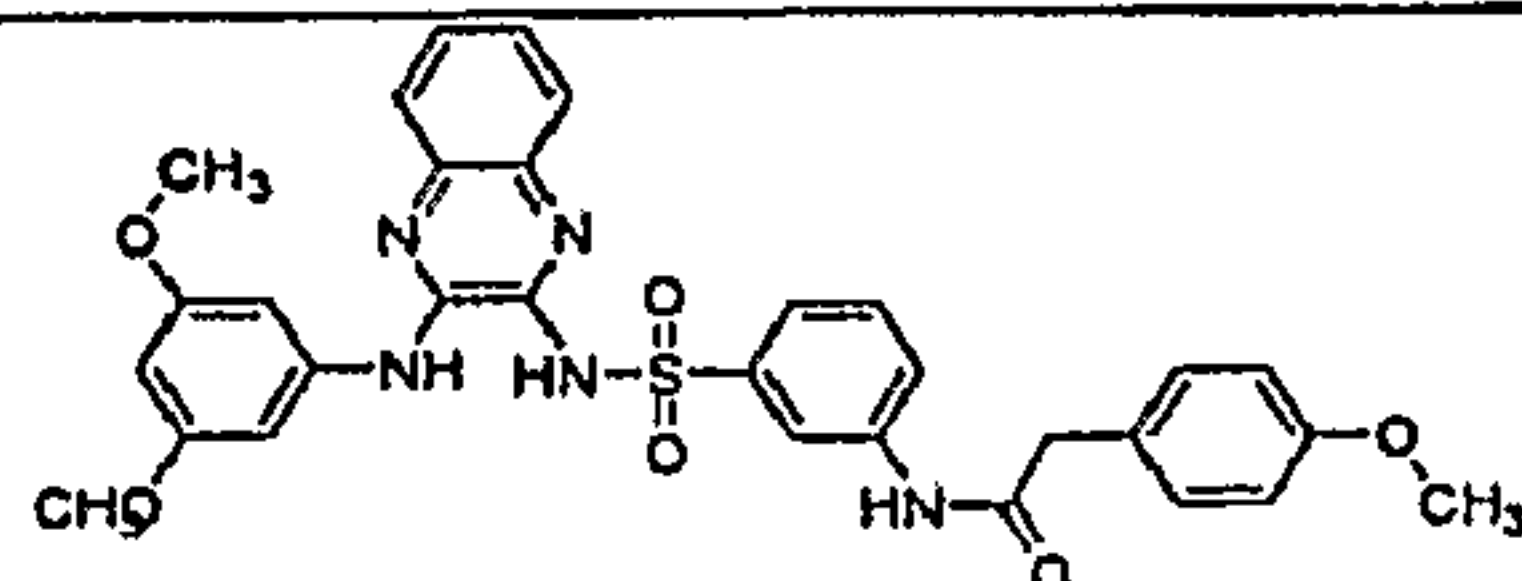
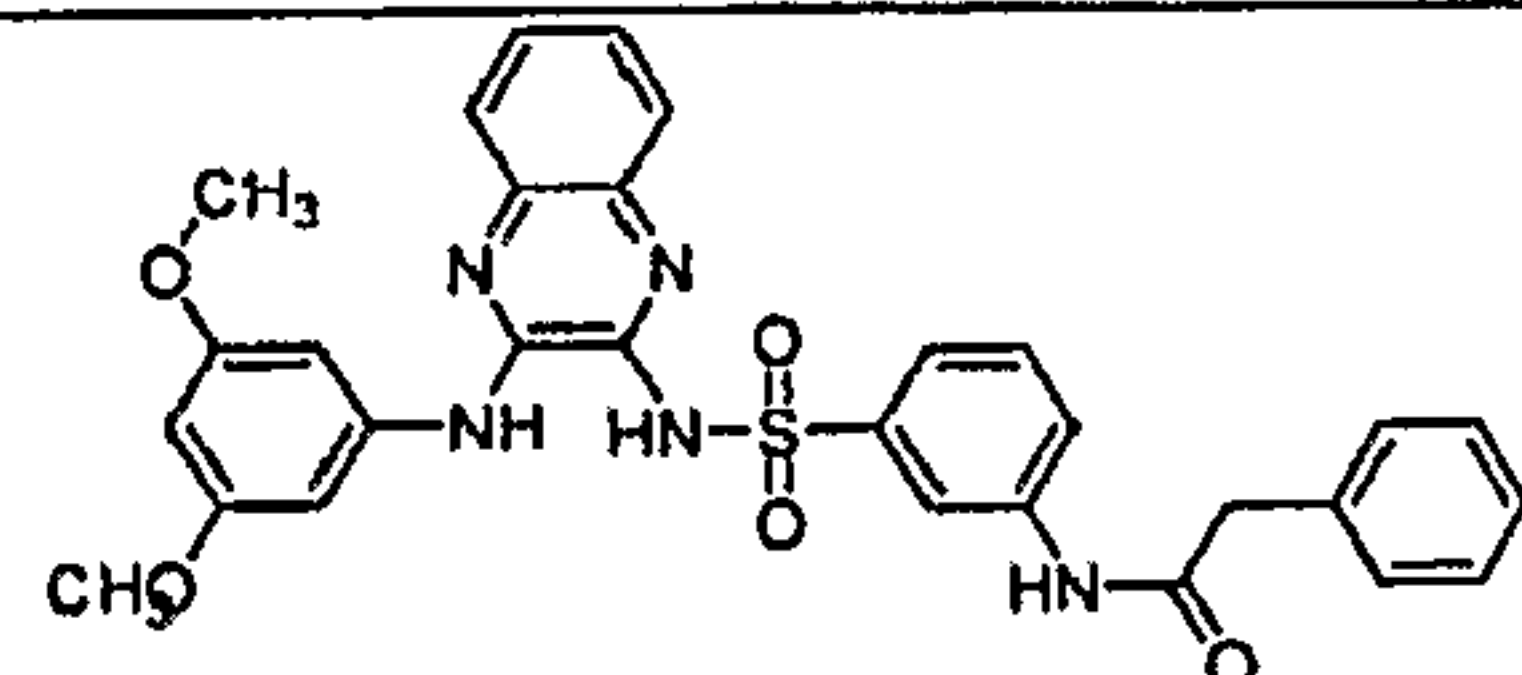
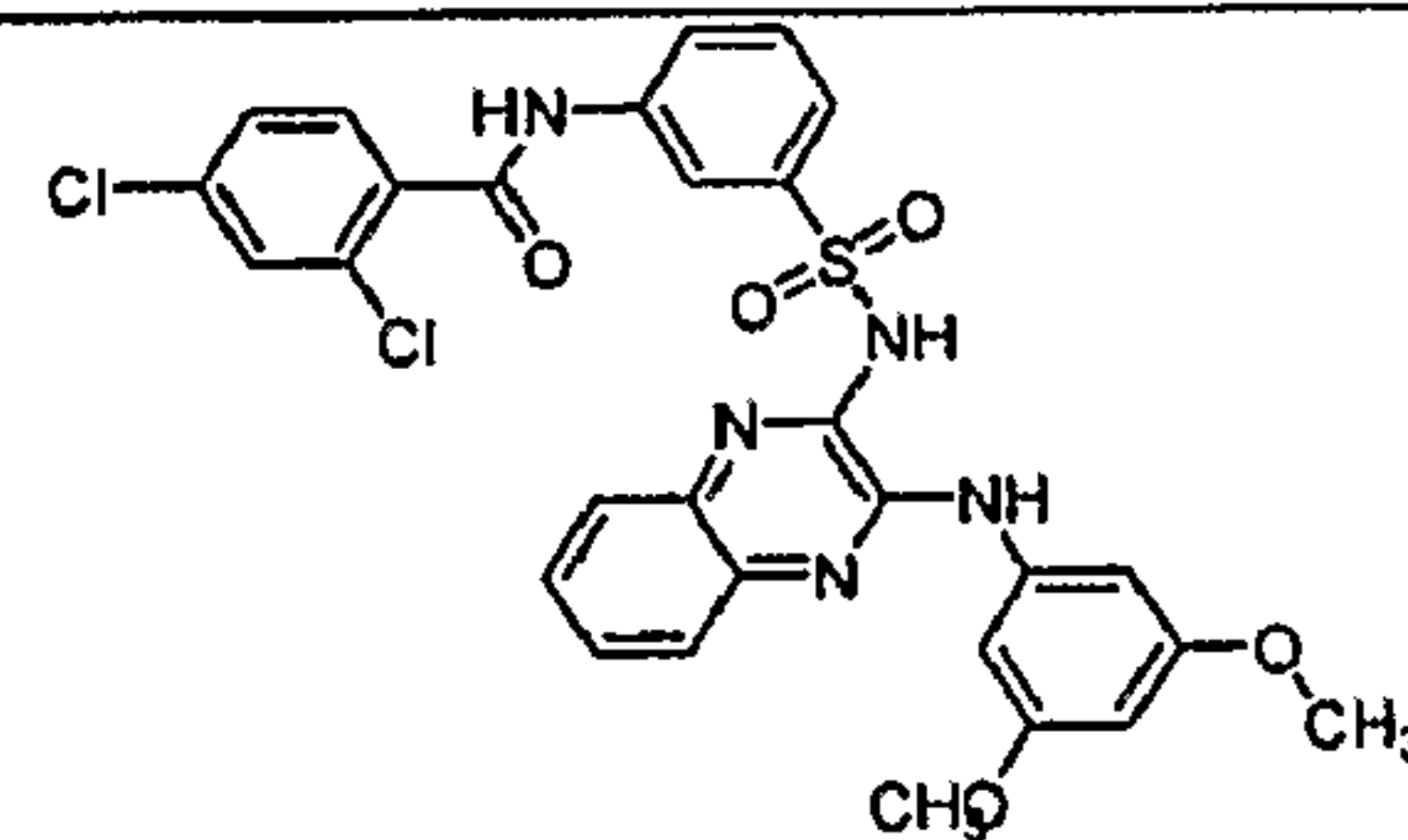
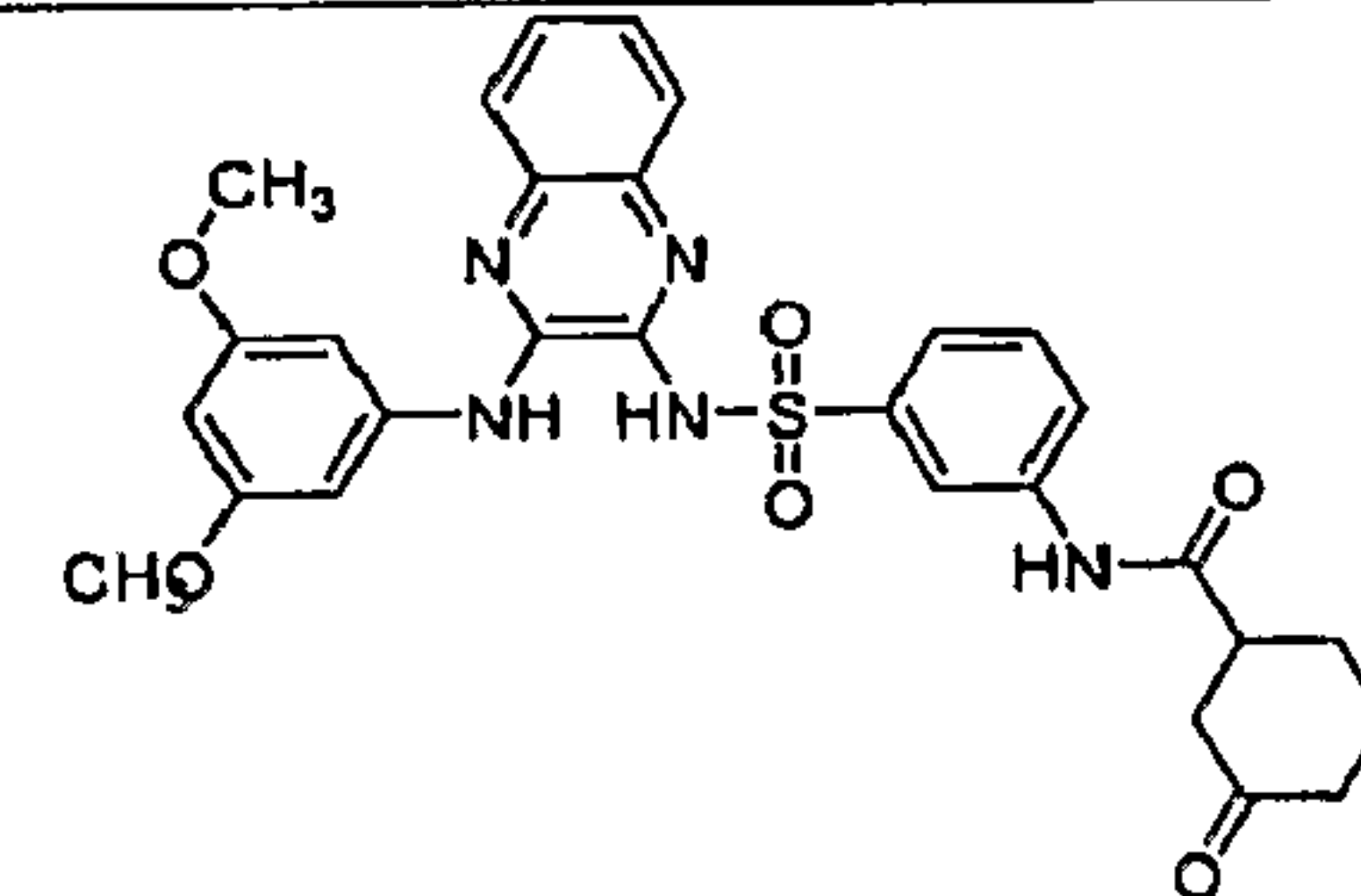
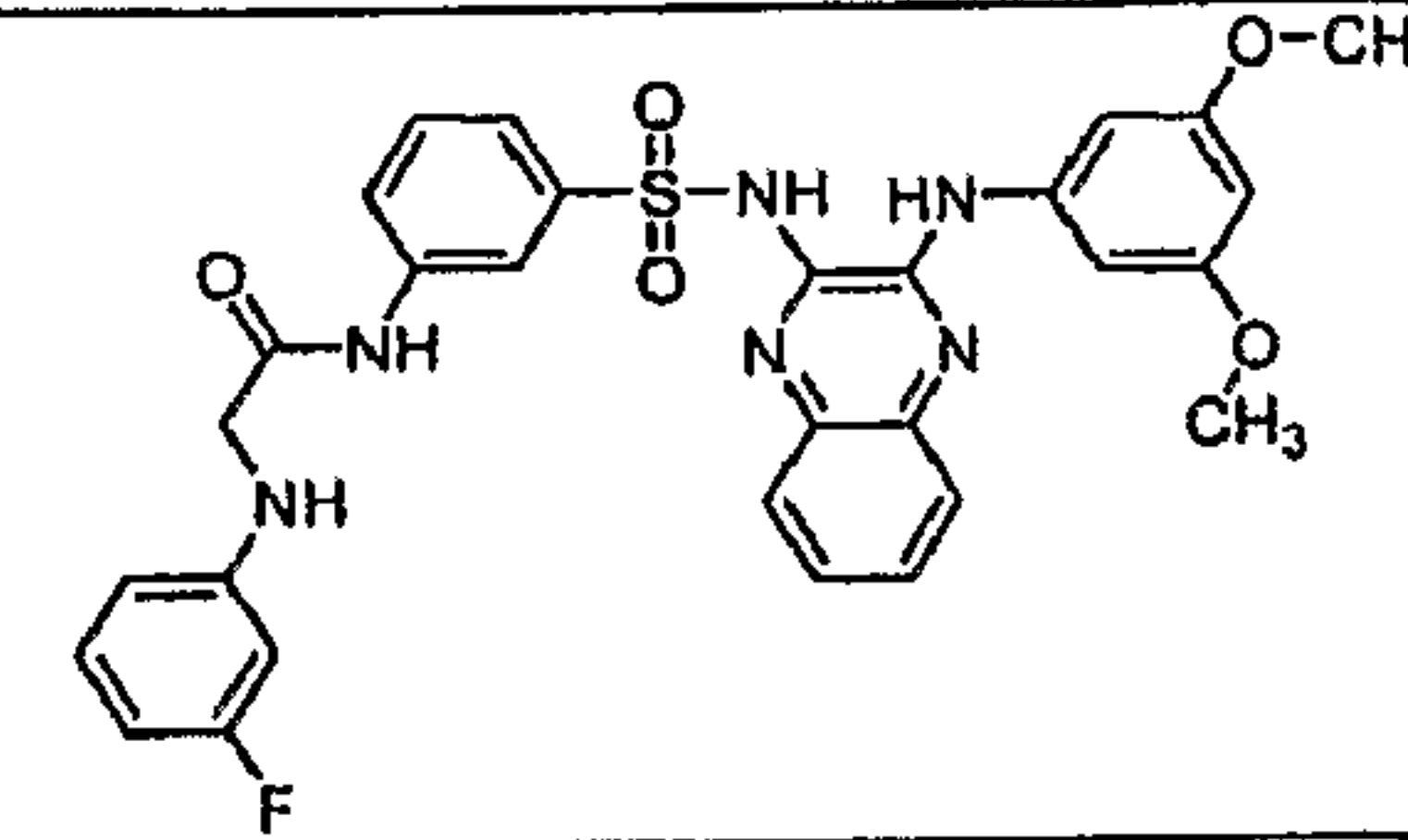
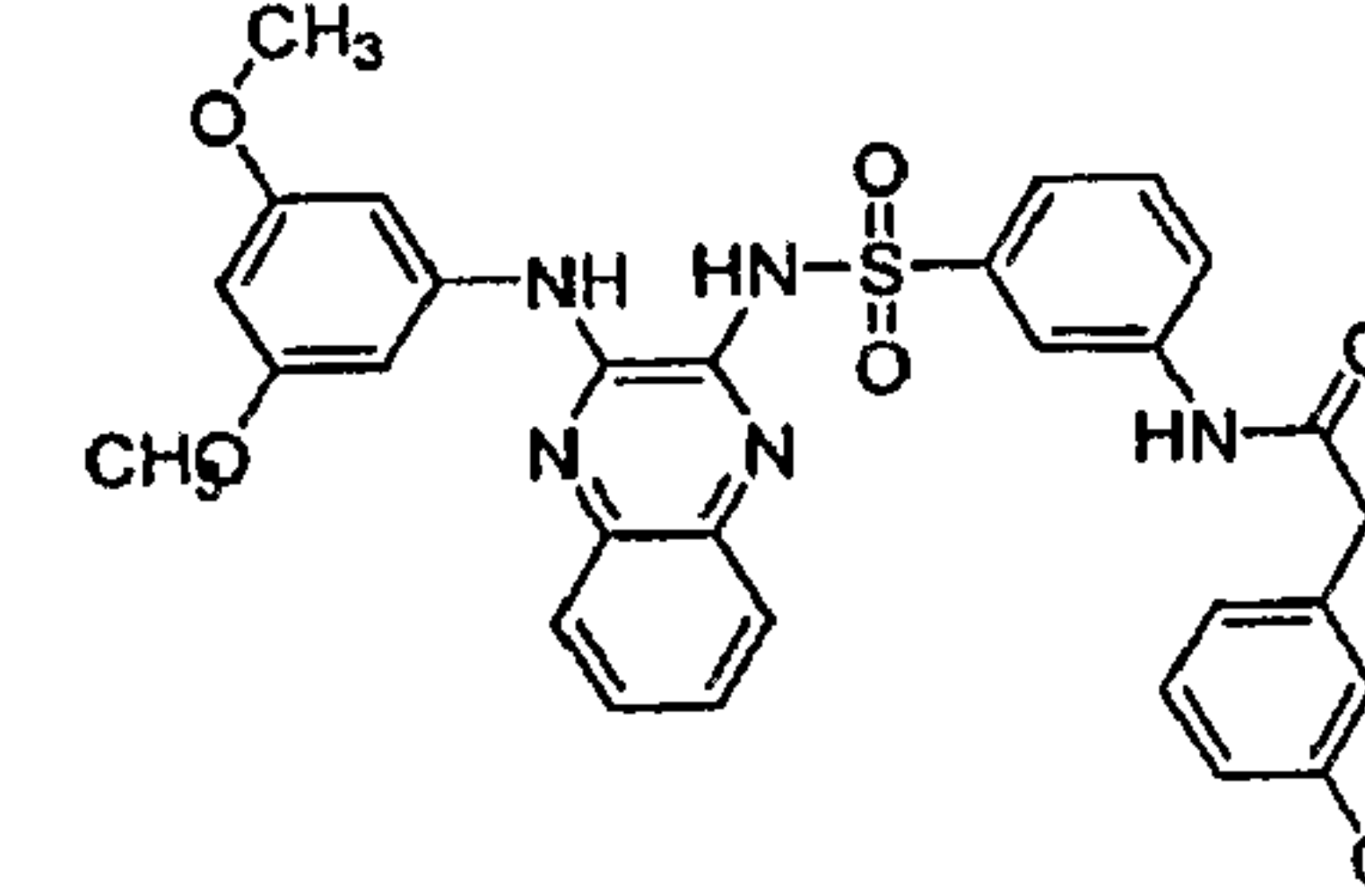
Table 1		
Cpd. No.	Structure	IUPAC Name
616		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(3-fluorophenyl)methyl]glycinamide
617		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(methoxy)phenyl]acetamide
618		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-phenylacetamide
619		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,4-dichlorobenzamide
620		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-oxocyclohexanecarboxamide
621		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(3-fluorophenyl)glycinamide
622		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3-chlorophenyl)acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
623		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2-phenylpropyl)glycinamide
624		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(2,4-dimethylphenyl)methyl]glycinamide
625		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-methylpiperidin-1-yl)acetamide
626		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[2-(methyloxy)phenyl]glycinamide
627		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3,4-dihydroisoquinolin-2(1 <i>H</i>)-yl)acetamide
628		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pent-4-enamide
629		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(2-methylphenyl)glycinamide
630		<i>N</i> -(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-oxopiperidin-1-yl)acetamide

Table 1

Cpd. No.	Structure	IUPAC Name
631		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-fluorobenzamide
632		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(1-phenylethyl)glycinamide
633		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-fluoro-6-(methyloxy)benzamide
634		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[2-(1-methylethyl)phenyl]glycinamide
635		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-[2-(methyloxy)phenyl]propanamide
636		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-methylpentanamide
637		<i>N</i> -(3-([(3-([3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-phenylmorpholin-4-yl)acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
638		<i>N</i> -(3-[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl)-3-[4-(methoxy)phenyl]propanamide
639		<i>N</i> -(3-[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl)- <i>N</i> -2-cyclopentyl- <i>N</i> -2-prop-2-en-1-ylglycinamide
640		<i>N</i> -(3-[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl)- <i>N</i> -2-methyl- <i>N</i> -2-[2-(methoxy)ethyl]glycinamide
641		<i>N</i> -(3-[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl)-4-cyclopropyl-4-oxobutanamide
642		<i>N</i> -(3-[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl)- <i>N</i> -2-[3-(1,1-dimethylethyl)phenyl]glycinamide
643		<i>N</i> -(3-[[3-[[3,5-bis(methoxy)phenyl]amino]sulfonyl}phenyl)- <i>N</i> -2-(cyclopropylmethyl)- <i>N</i> -2-propylglycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
644		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-oxocyclopentyl)acetamide
645		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-(4-chlorophenyl)glycinamide
646		2-(1,4'-bipiperidin-1'-yl)- <i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
647		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-cyclopentylpiperazin-1-yl)acetamide
648		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-methylphenyl)acetamide
649		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-[(5-fluoro-2-methylphenyl)methyl]glycinamide
650		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3,3-dimethylbutanamide

Table 1		
Cpd. No.	Structure	IUPAC Name
651		2-(2-chlorophenylamino)-N-(3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide
652		N-(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-5-fluoro-2-methylbenzamide
653		N-(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-fluoro-3-methylbenzamide
654		N-(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,3-dichlorobenzamide
655		N-(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(phenyloxy)acetamide
656		N-(3-([(3-([3,5-bis(methoxy)phenyl]amino)quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2,3-dimethylphenyl)glycinamide
657		3-amino-N-(3-([3,5-bis(methoxy)phenyl]amino)pyrido[2,3-b]pyrazin-2-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
658		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-fluoro-5-methylbenzamide
659		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)- <i>N</i> -2-((4-methylphenyl)methyl)oxy}glycinamide
660		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-[4-(1-methylethyl)piperazin-1-yl]acetamide
661		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(4-fluorophenyl)acetamide
662		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-3-methylbutanamide
663		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-4-methyl-2-(methoxy)benzamide
664		<i>N</i> -(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(4-propylpiperidin-1-yl)acetamide

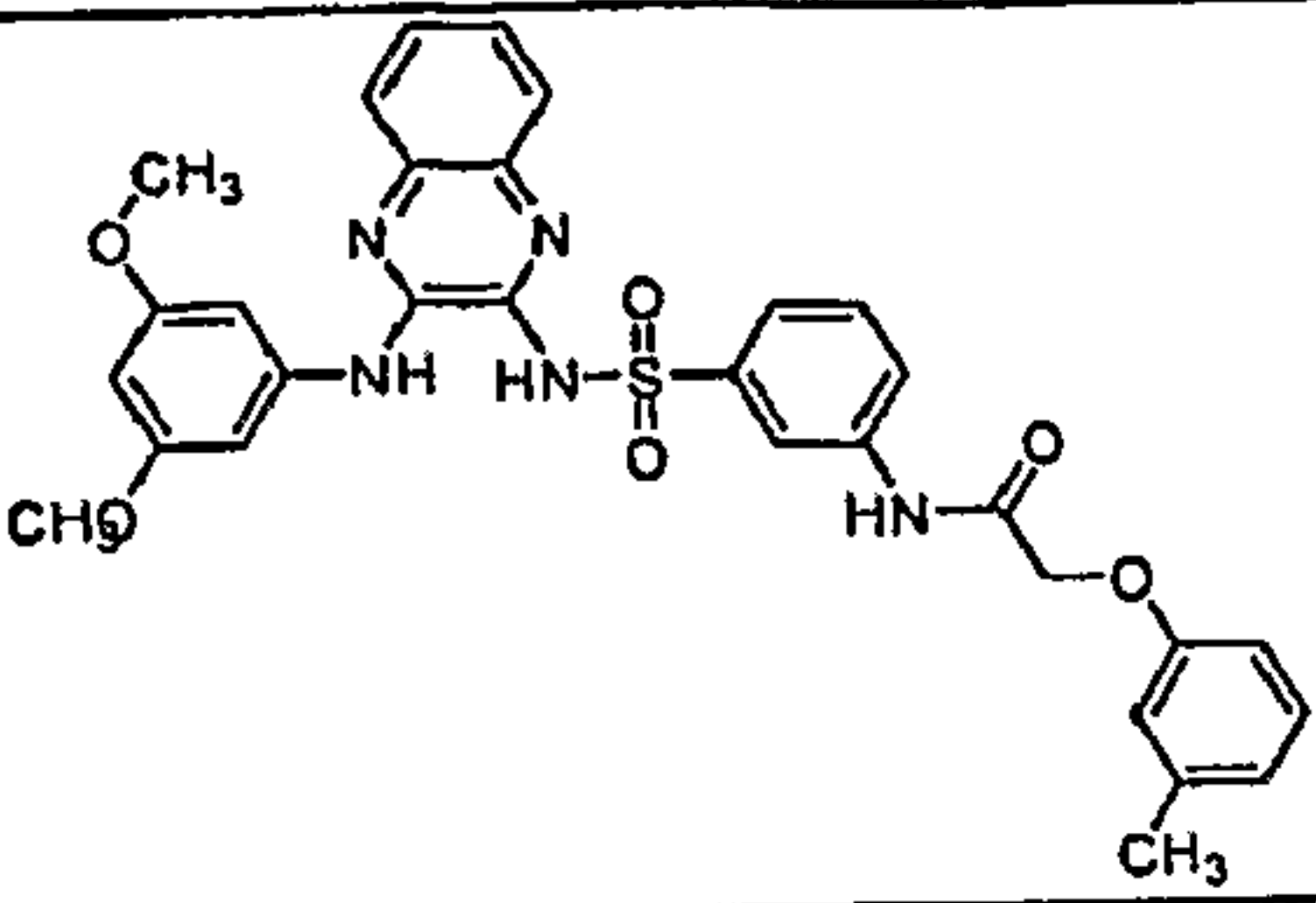
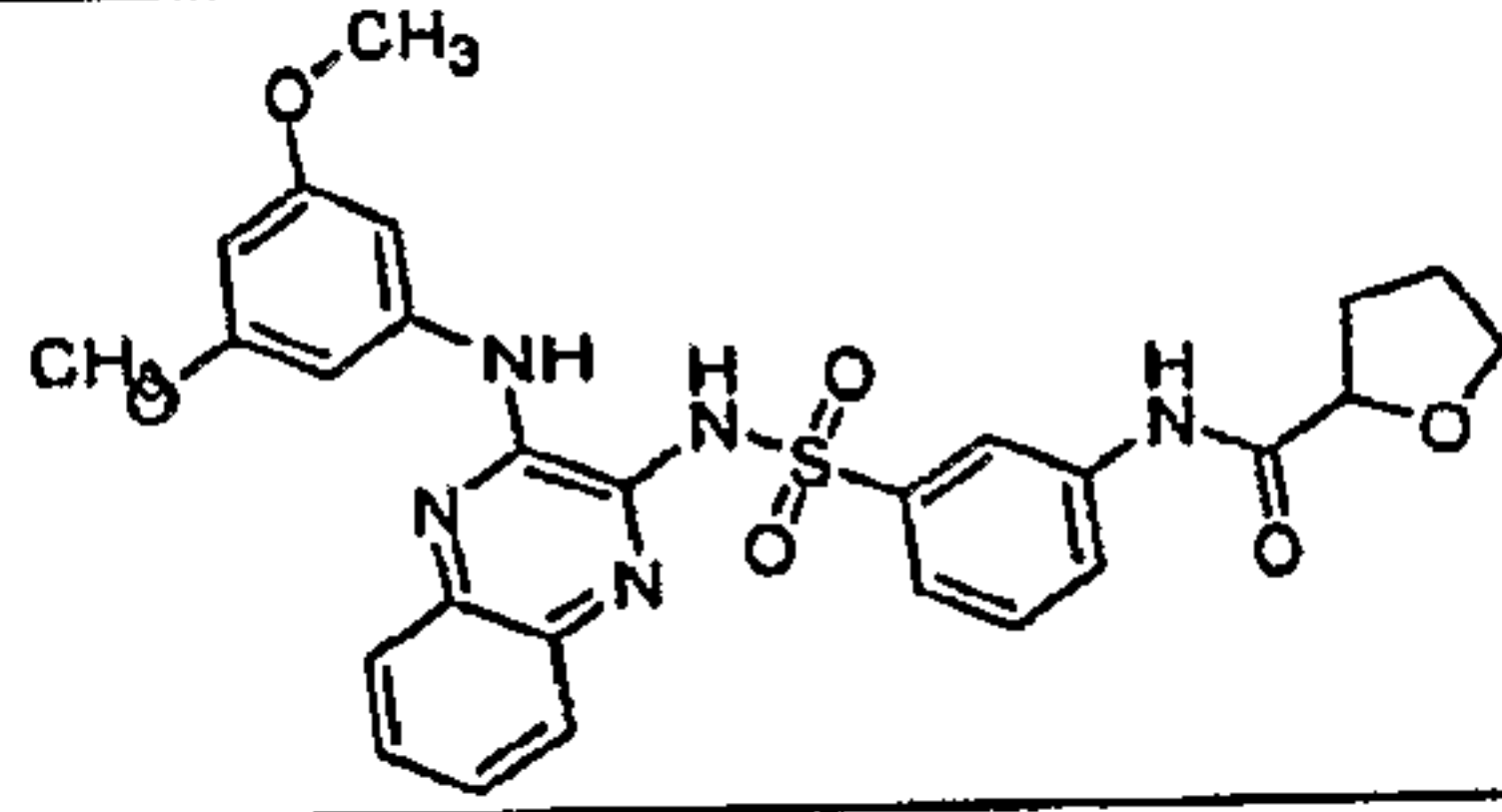
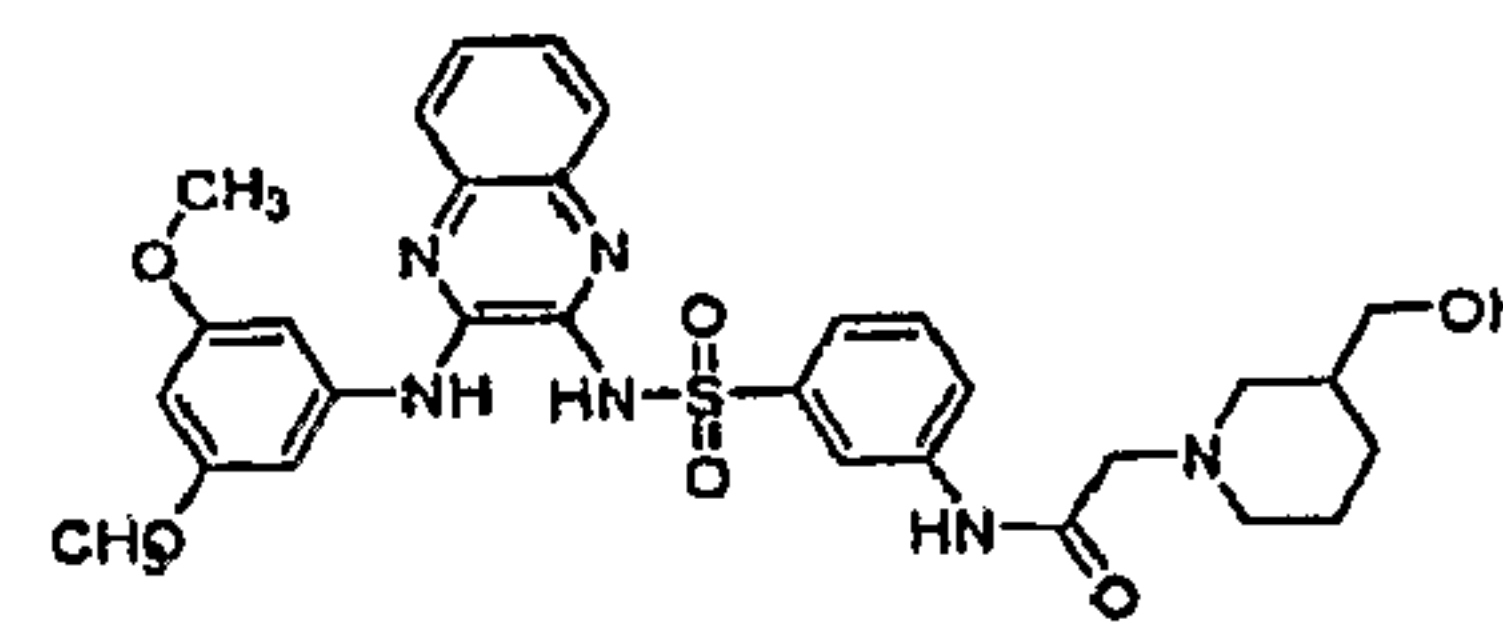
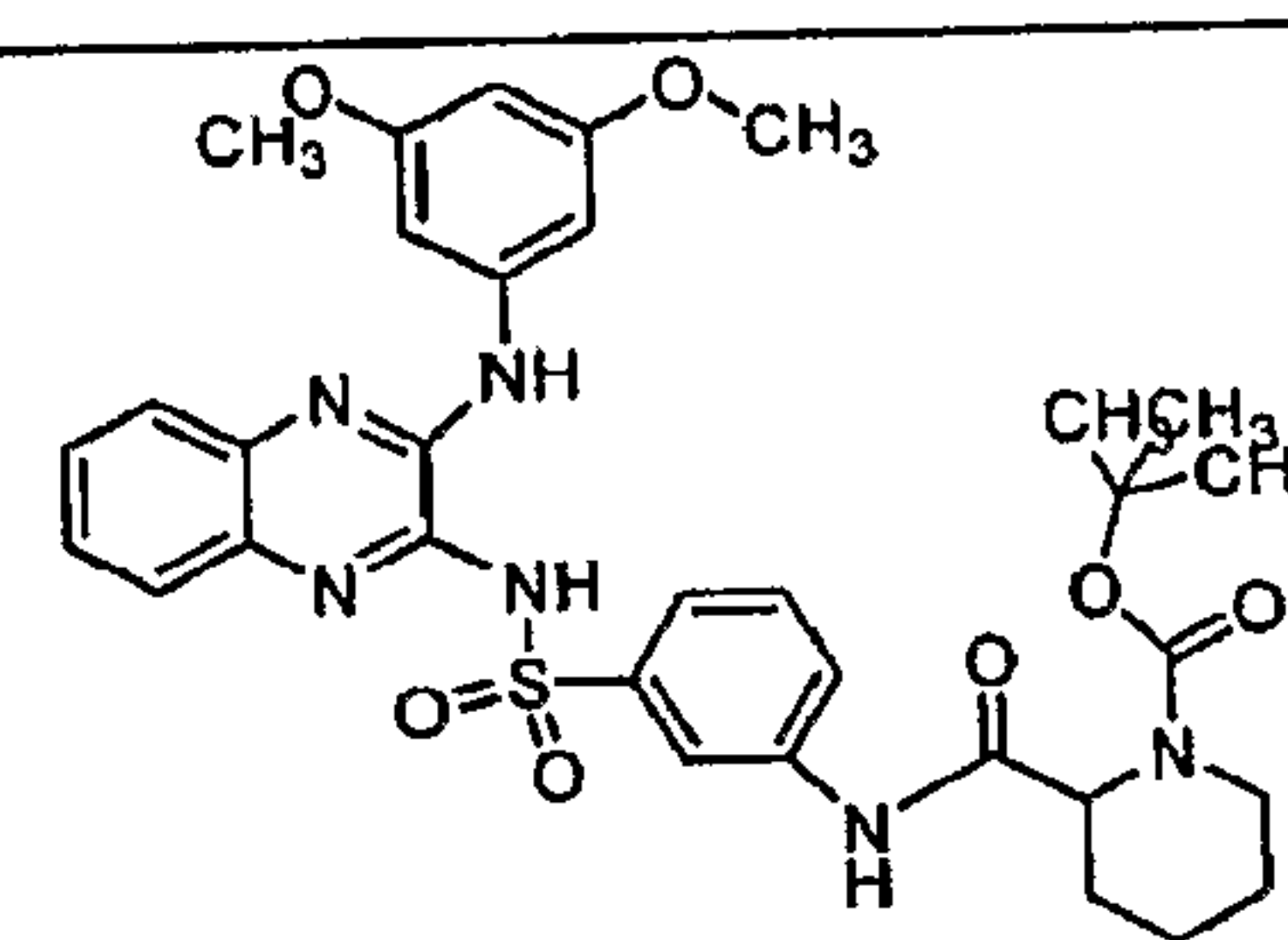
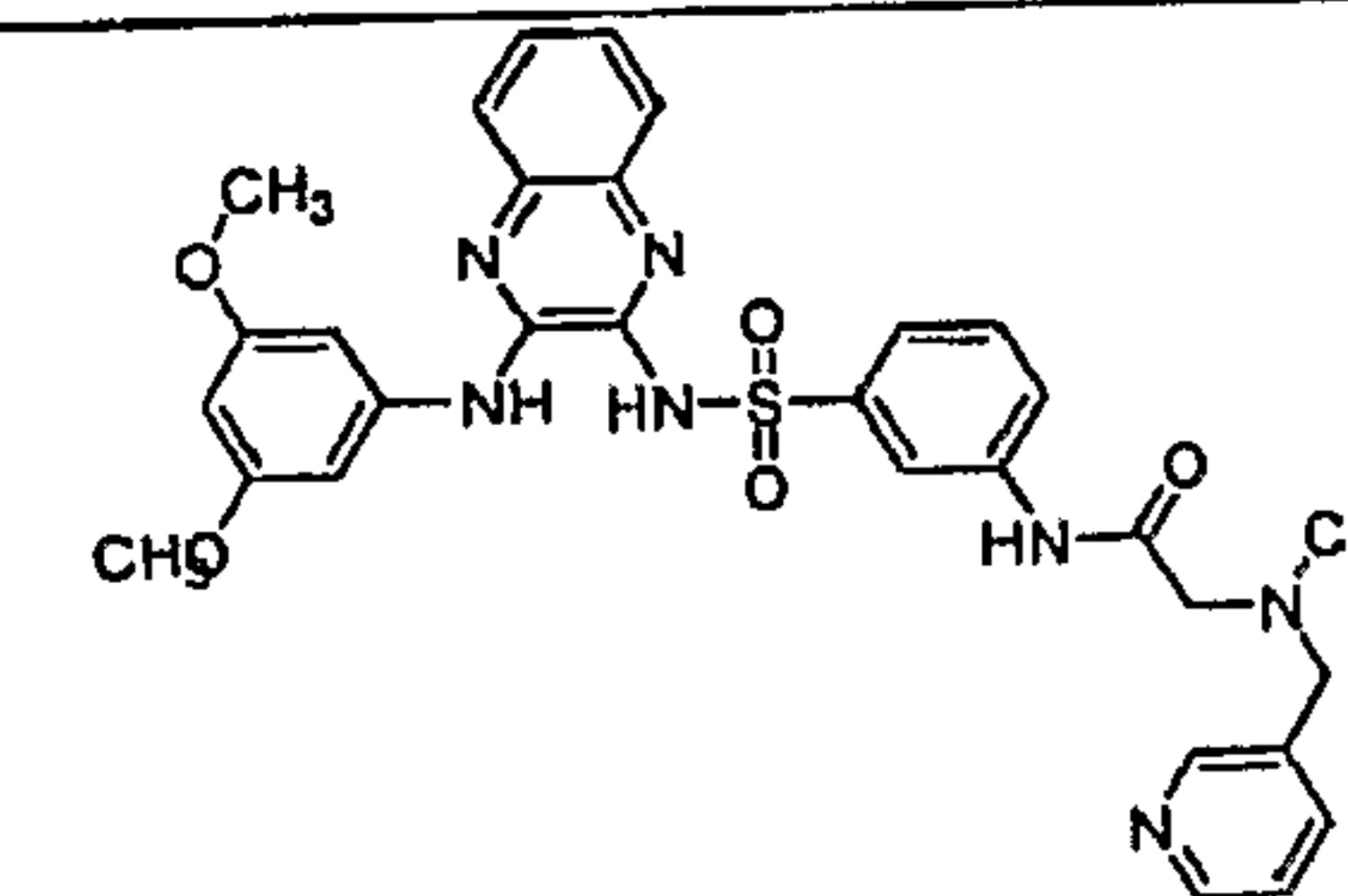
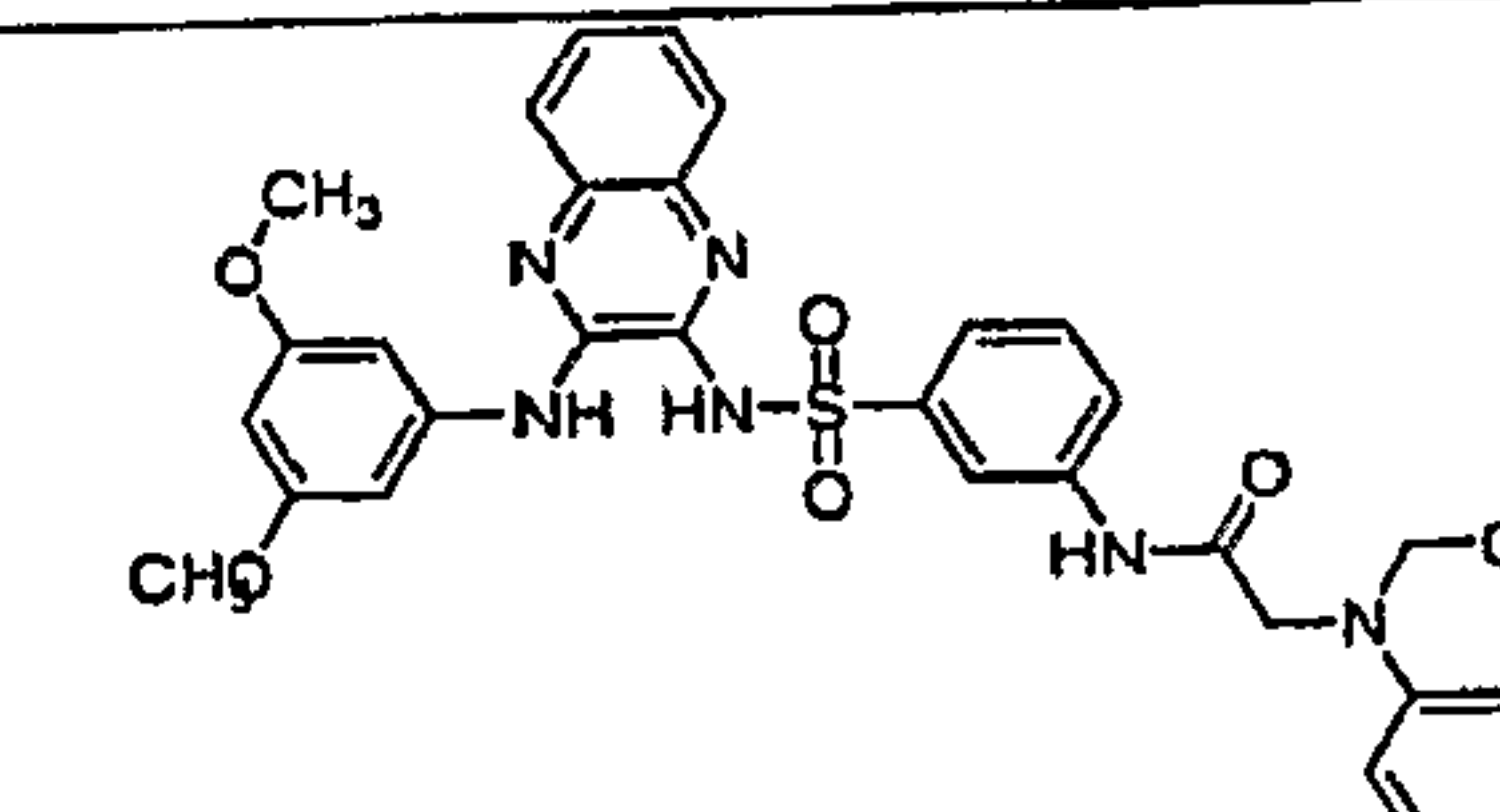
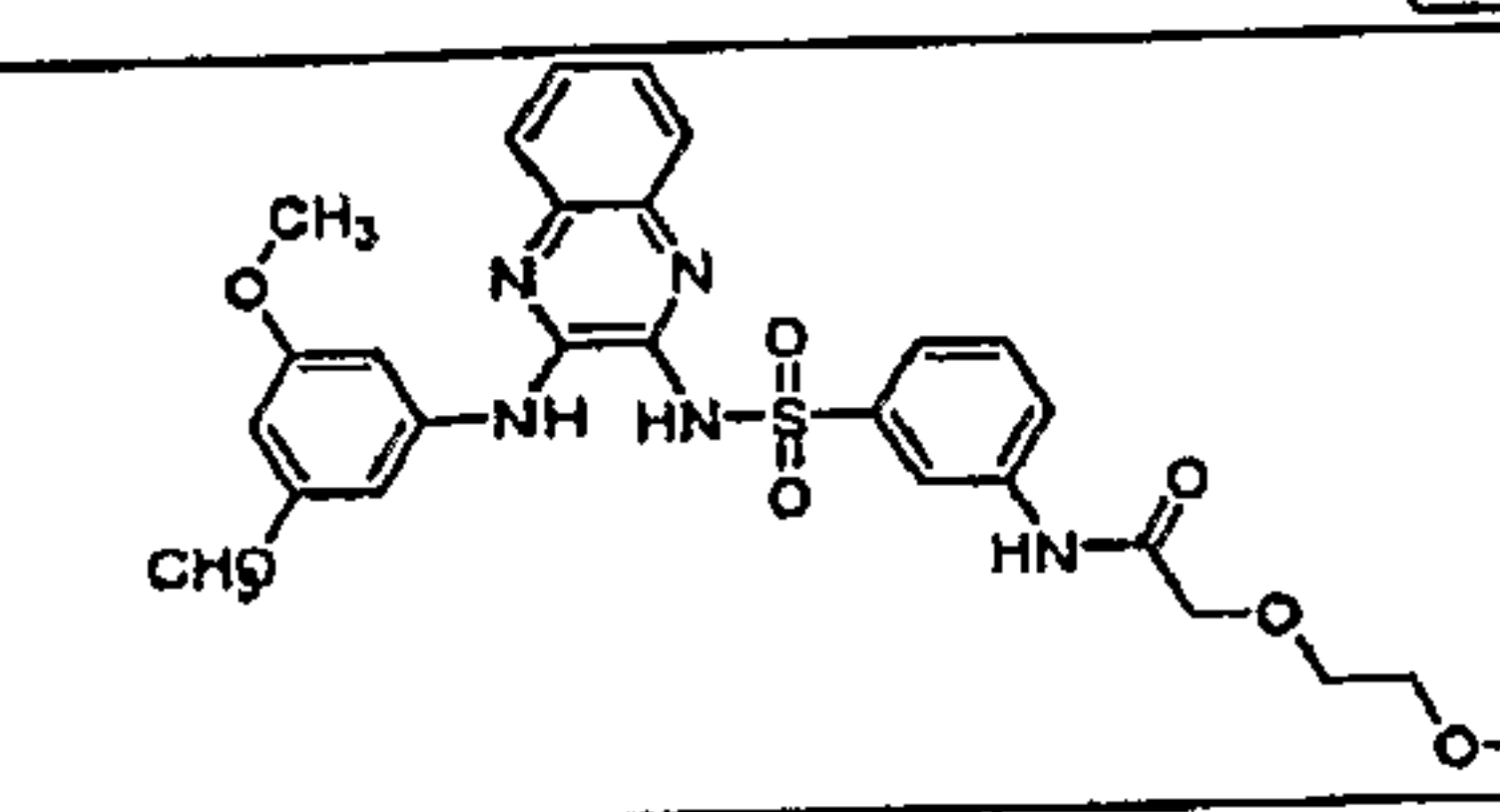
Table 1		
Cpd. No.	Structure	IUPAC Name
665		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(3-methylphenyl)oxy]acetamide
666		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)tetrahydrofuran-2-carboxamide
667		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(hydroxymethyl)piperidin-1-yl]acetamide
668		1,1-dimethylethyl 2-{[(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)amino]carbonyl}piperidine-1-carboxylate
669		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methyl- <i>N</i> -2-(pyridin-3-ylmethyl)glycinamide
670		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-ethyl- <i>N</i> -2-phenylglycinamide
671		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-{[2-(methoxy)ethyl]oxy}acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
672		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-cyclopentylpropanamide
673		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,5-dichlorobenzamide
674		2-(4-acetypiperazin-1-yl)- <i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
675		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-5-fluoro-2-(methoxy)benzamide
676		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-cyclohexyl- <i>N</i> -2-ethylglycinamide
677		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-5-methylisoxazole-3-carboxamide
678		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-methylpyridine-2-carboxamide
679		<i>N</i> -(3-{[(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(methoxy)pyridine-3-carboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
680		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3,5-dichlorobenzamide
681		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(1,3-thiazolidin-3-yl)acetamide
682		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-formylpiperazin-1-yl)acetamide
683		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-pyridin-4-ylpiperidin-1-yl)acetamide
684		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(methyloxy)benzamide
685		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-methyl- <i>N</i> -2-(2-methylpropyl)glycinamide
686		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-formyl-1,4-diazepan-1-yl)acetamide
687		<i>N</i> -(3-{{(3-{{3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-phenylcyclopropanecarboxamide

Table 1		
Cpd. No.	Structure	IUPAC Name
688		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl)phenyl)-2-(2,6-dimethylmorpholin-4-yl)acetamide
689		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl)phenyl)-2-(2-phenylpyrrolidin-1-yl)acetamide
690		<i>N</i> -(3-(((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl)phenyl)-2-(2,6-dimethylpiperidin-1-yl)acetamide
691		<i>N</i> -{3-[(3-[(4-chlorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
692		<i>N</i> -{3-[(3-[(3-fluorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide
693		<i>N</i> -{3-[(3-[(3-chlorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}- <i>N</i> -2, <i>N</i> -2-dimethylglycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
694		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl]-N-[2-(dimethylamino)-1-methylethyl]benzamide
695		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl]-N-[2-(dimethylamino)ethyl]benzamide
696		5-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl]-N-[2-(dimethylamino)ethyl]-2-fluorobenzamide
697		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl]-N-pyrrolidin-3-ylbenzamide
698		3-[[[(3-[[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl]-N-[2-(dimethylamino)ethyl]benzamide
699		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl]-N-(2-pyrrolidin-1-ylethyl)benzamide

Table 1		
Cpd. No.	Structure	IUPAC Name
700		<i>N</i> -(2-aminoethyl)-3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide
701		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}- <i>N</i> -[2-(dimethylamino)ethyl]- <i>N</i> -methylbenzamide
702		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}- <i>N</i> -(piperidin-2-ylmethyl)benzamide
703		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}- <i>N</i> -(1-methylazetidin-3-yl)benzamide
704		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}- <i>N</i> -(2-piperidin-1-ylethyl)benzamide

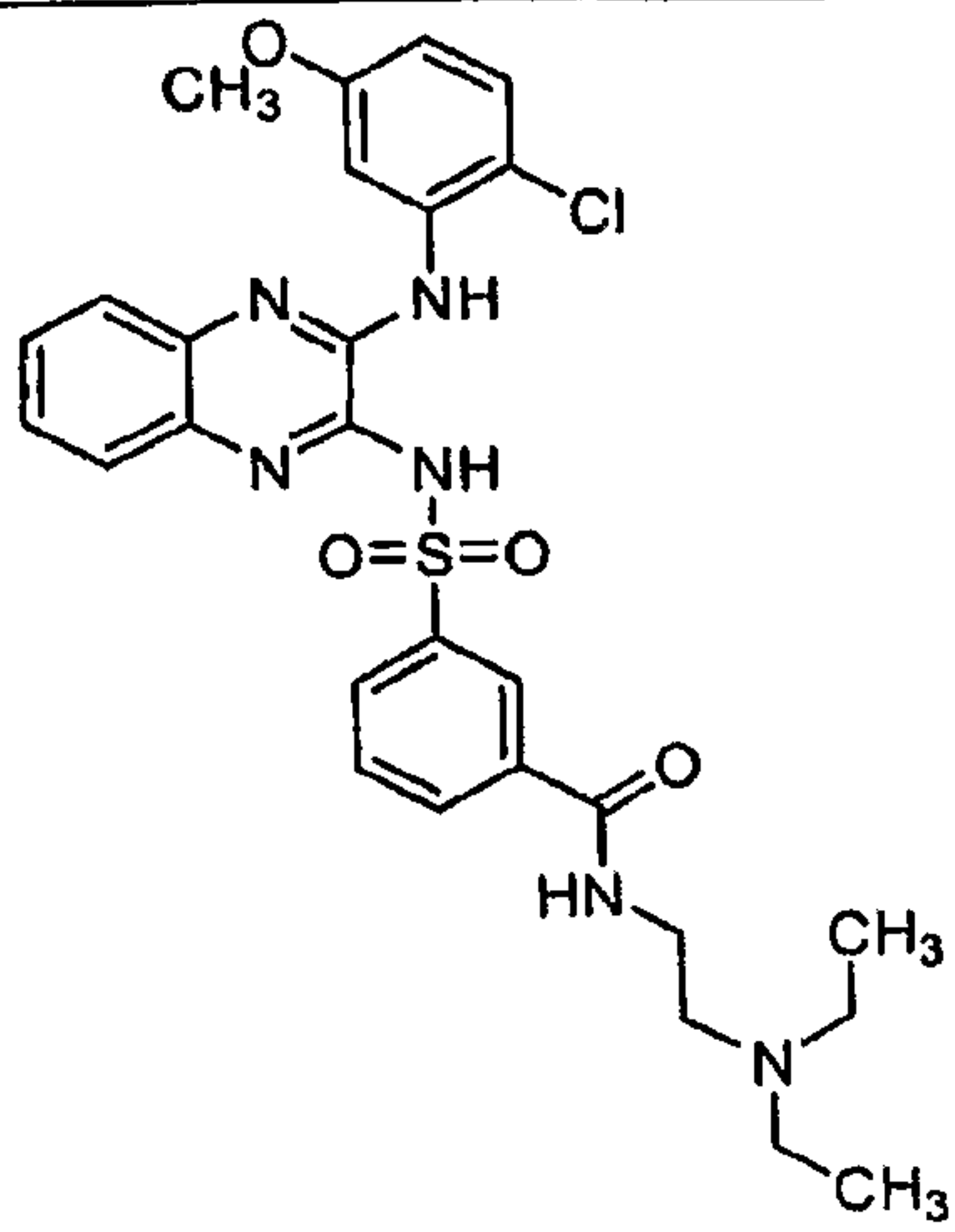
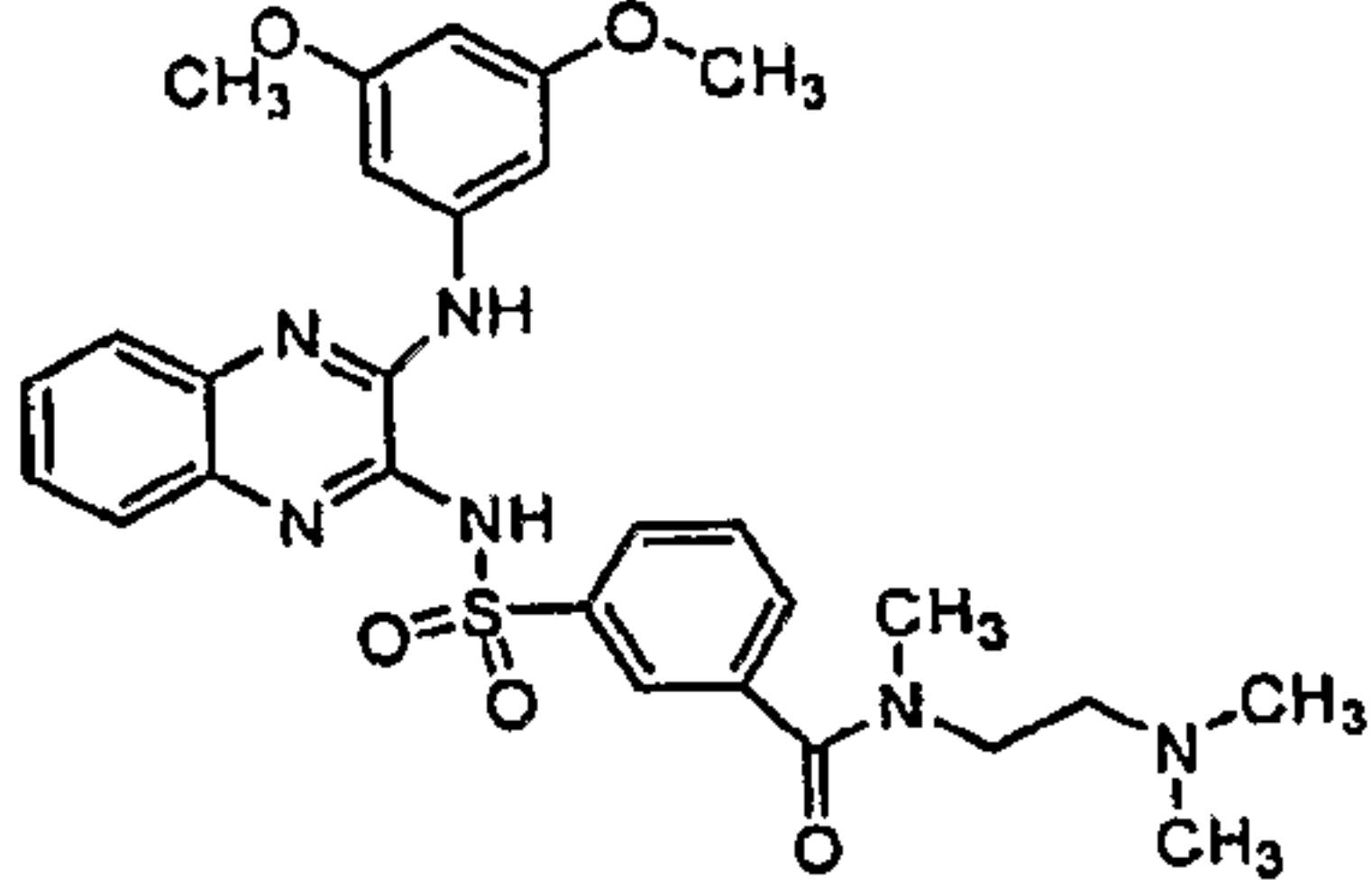
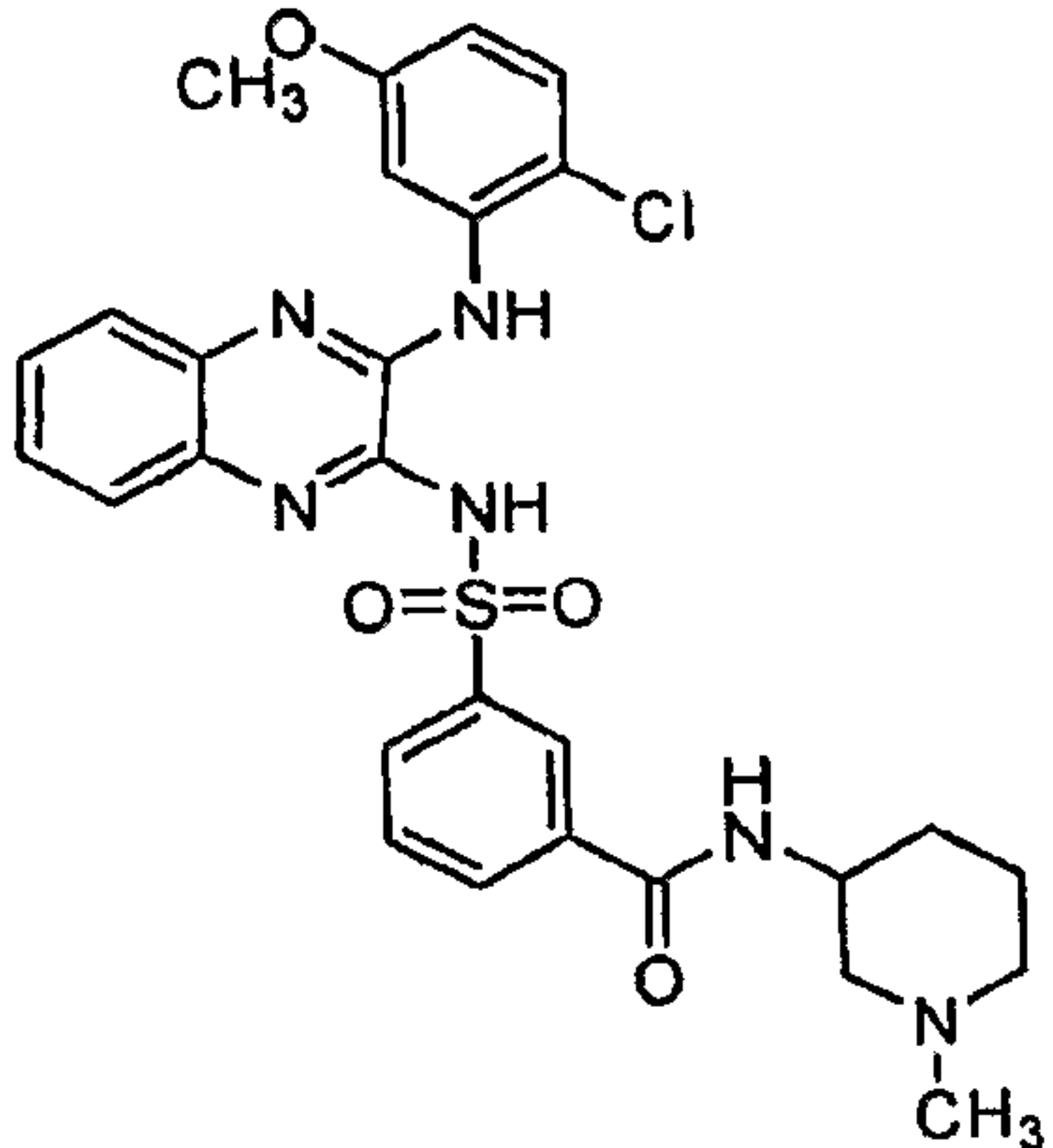
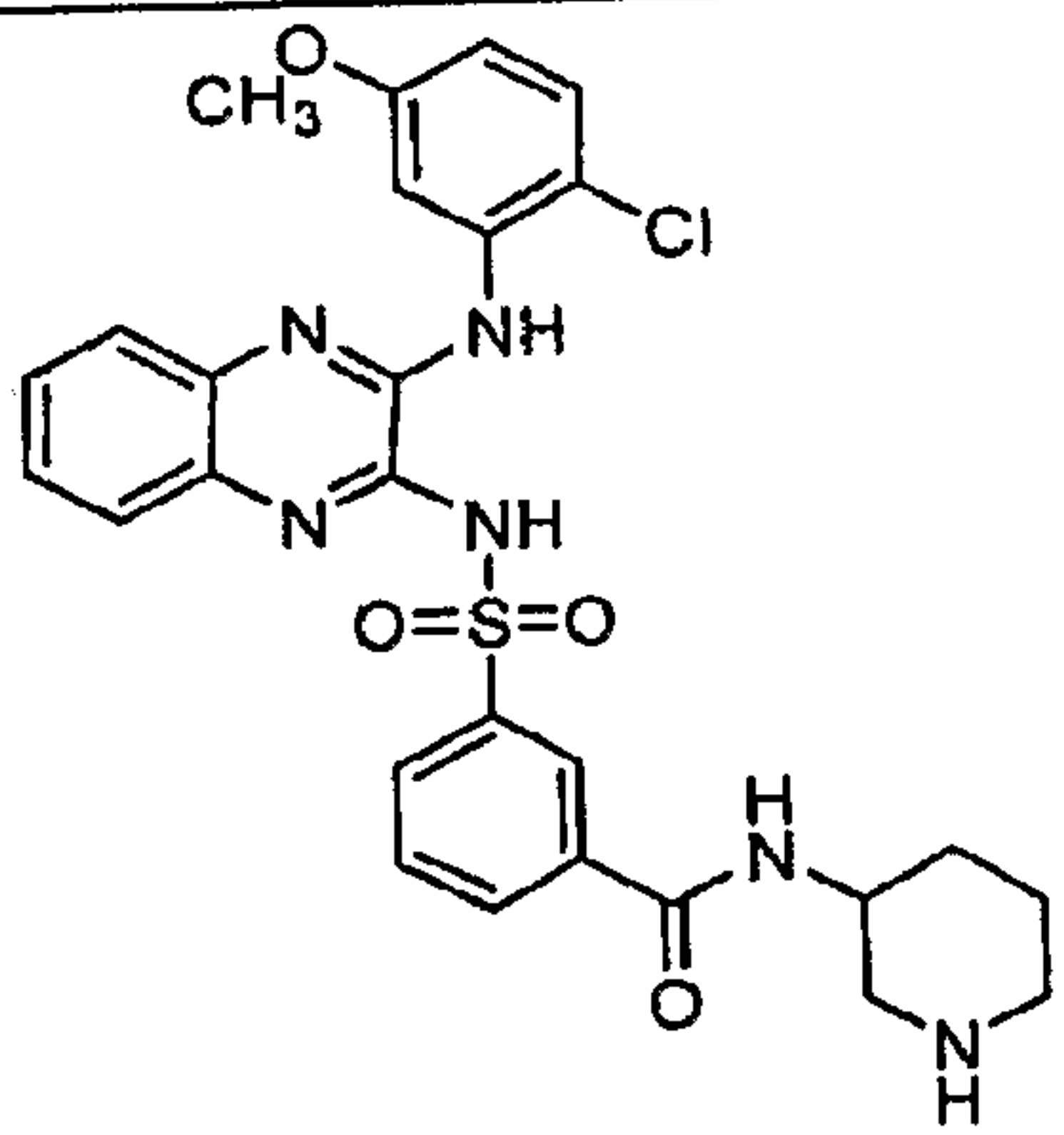
Table 1		
Cpd. No.	Structure	IUPAC Name
705		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(diethylamino)ethyl]benzamide
706		3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(dimethylamino)ethyl]-N-methylbenzamide
707		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1-methylpiperidin-3-yl)benzamide
708		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-piperidin-3-ylbenzamide

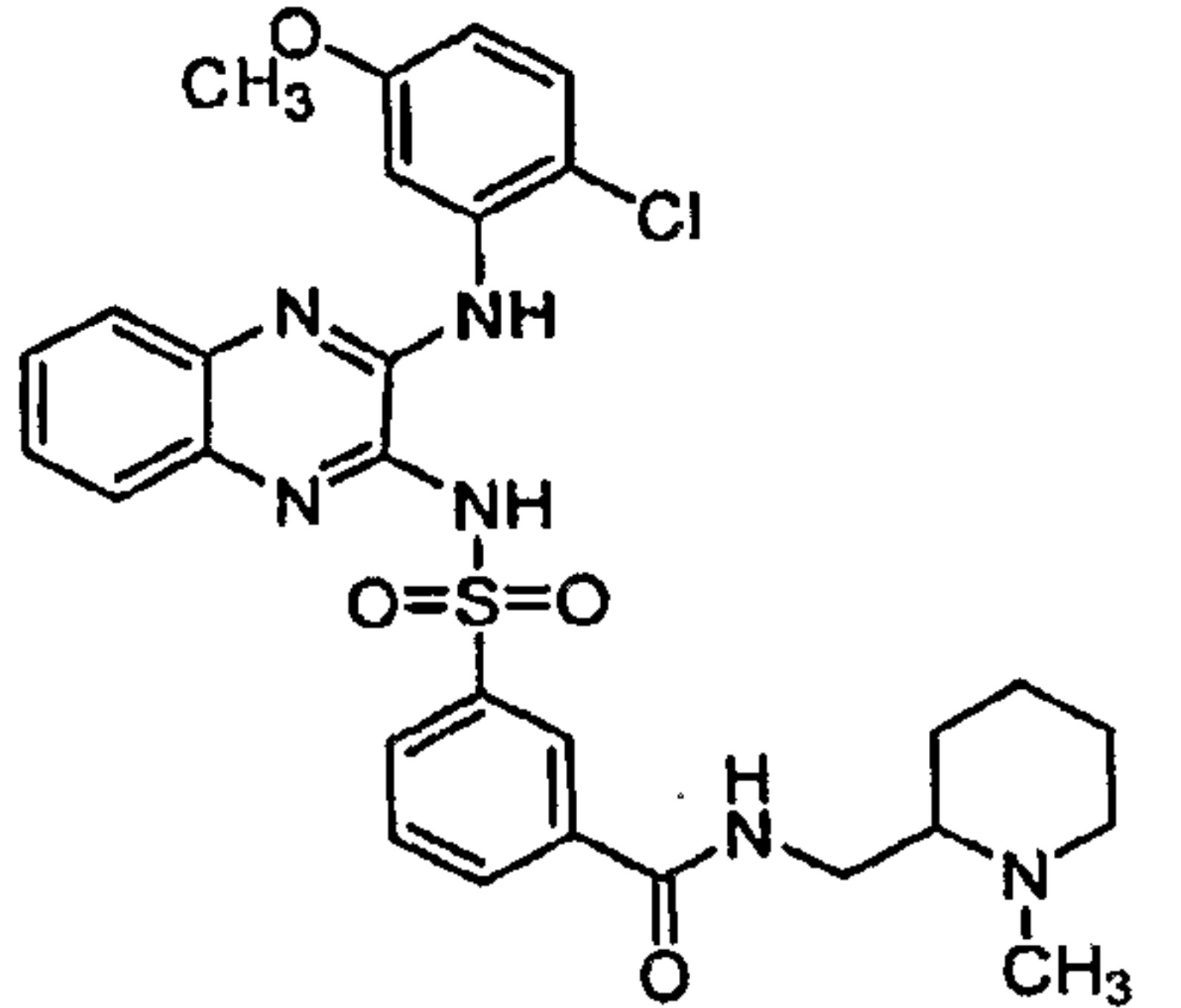
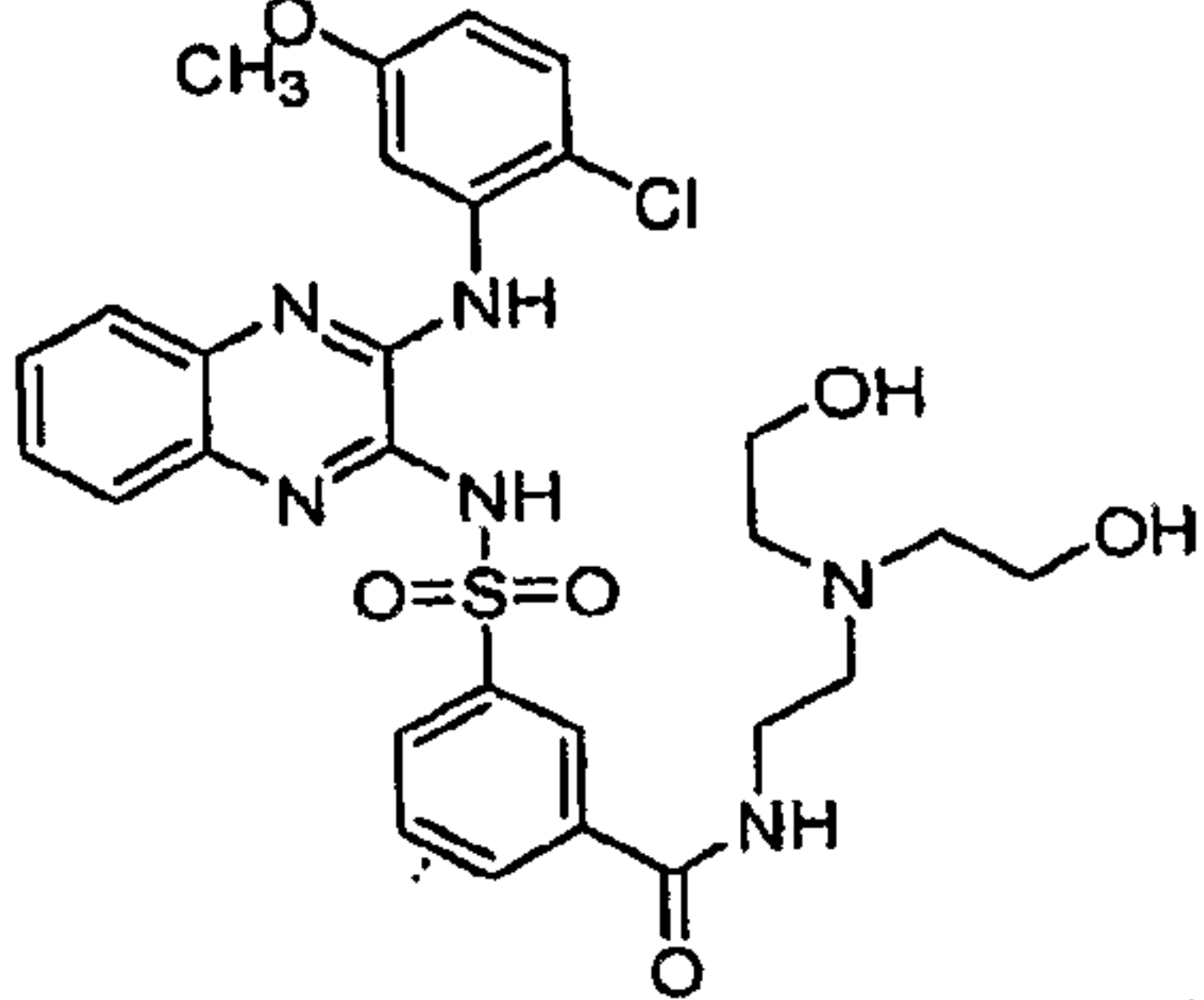
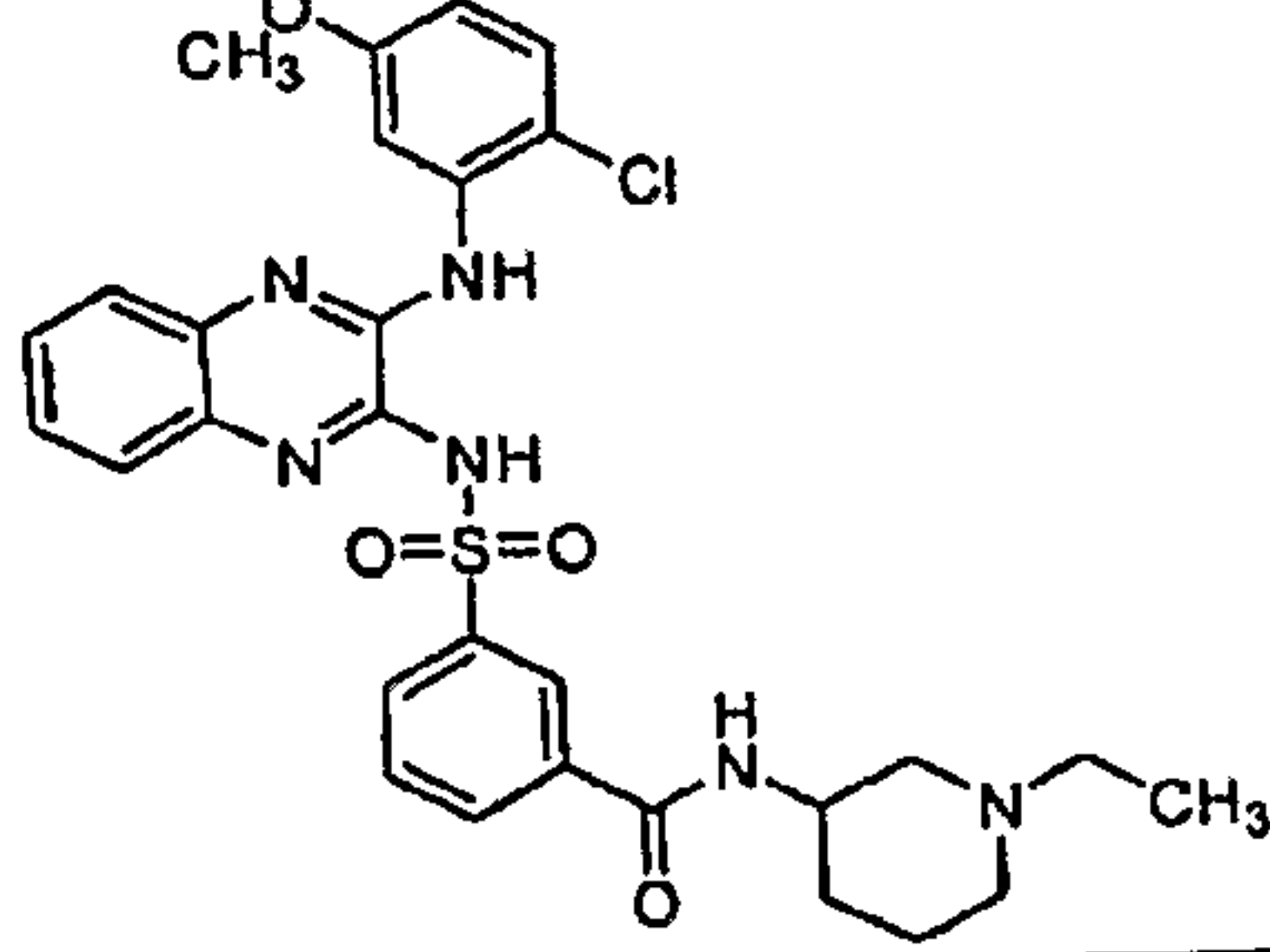
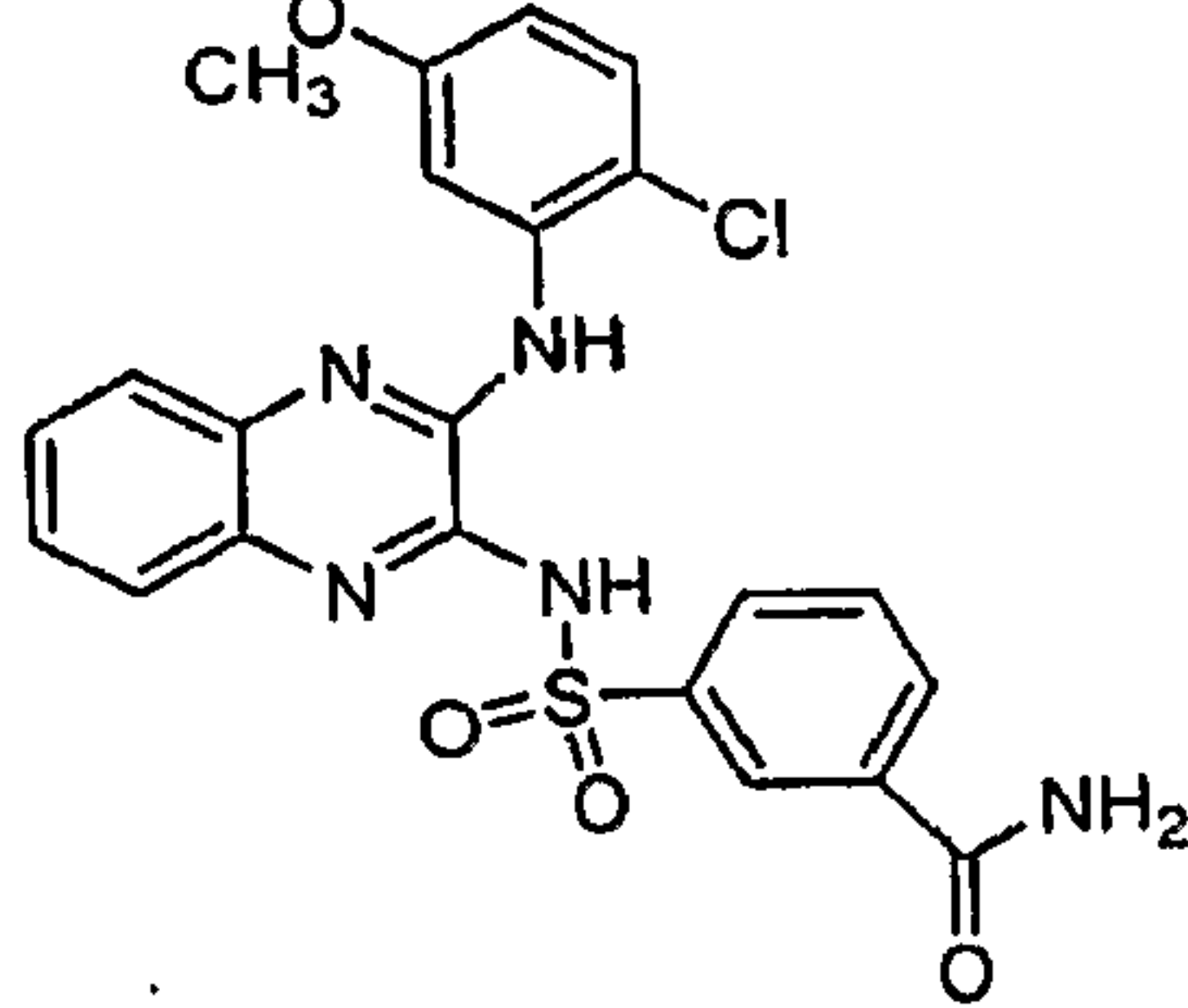
Table 1		
Cpd. No.	Structure	IUPAC Name
709		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[(1-methylpiperidin-2-yl)methyl]benzamide
710		N-{2-[bis(2-hydroxyethyl)amino]ethyl}-3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide
711		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1-ethylpiperidin-3-yl)benzamide
712		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide

Table 1		
Cpd. No.	Structure	IUPAC Name
713		3-[(3-aminopyrrolidin-1-yl)carbonyl]-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
714		5-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(dimethylamino)ethyl]-2-(methyloxy)benzamide
715		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[3-(methylamino)pyrrolidin-1-yl]carbonyl}benzenesulfonamide
716		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzoic acid
717		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-morpholin-4-ylethyl)benzamide

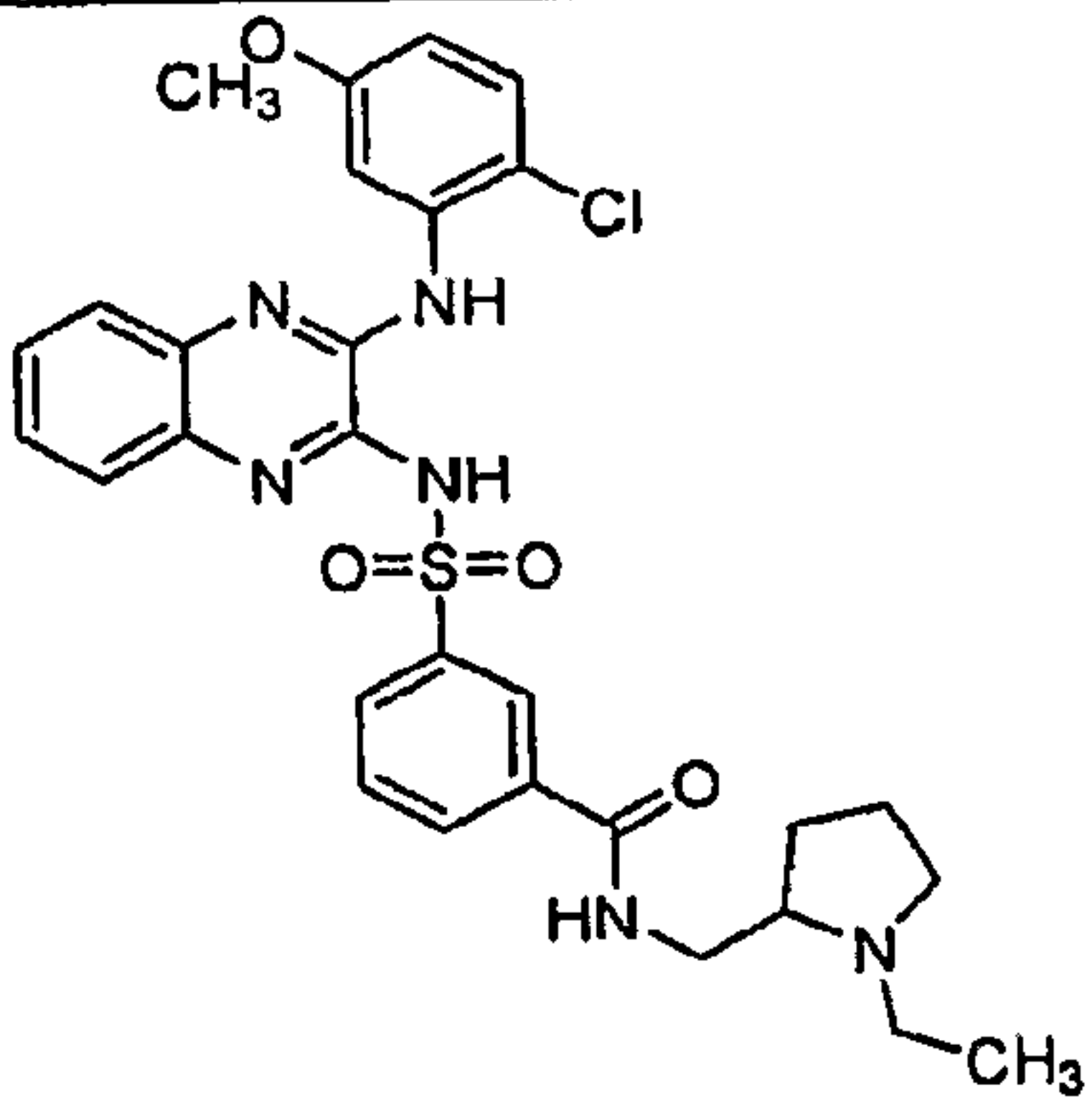
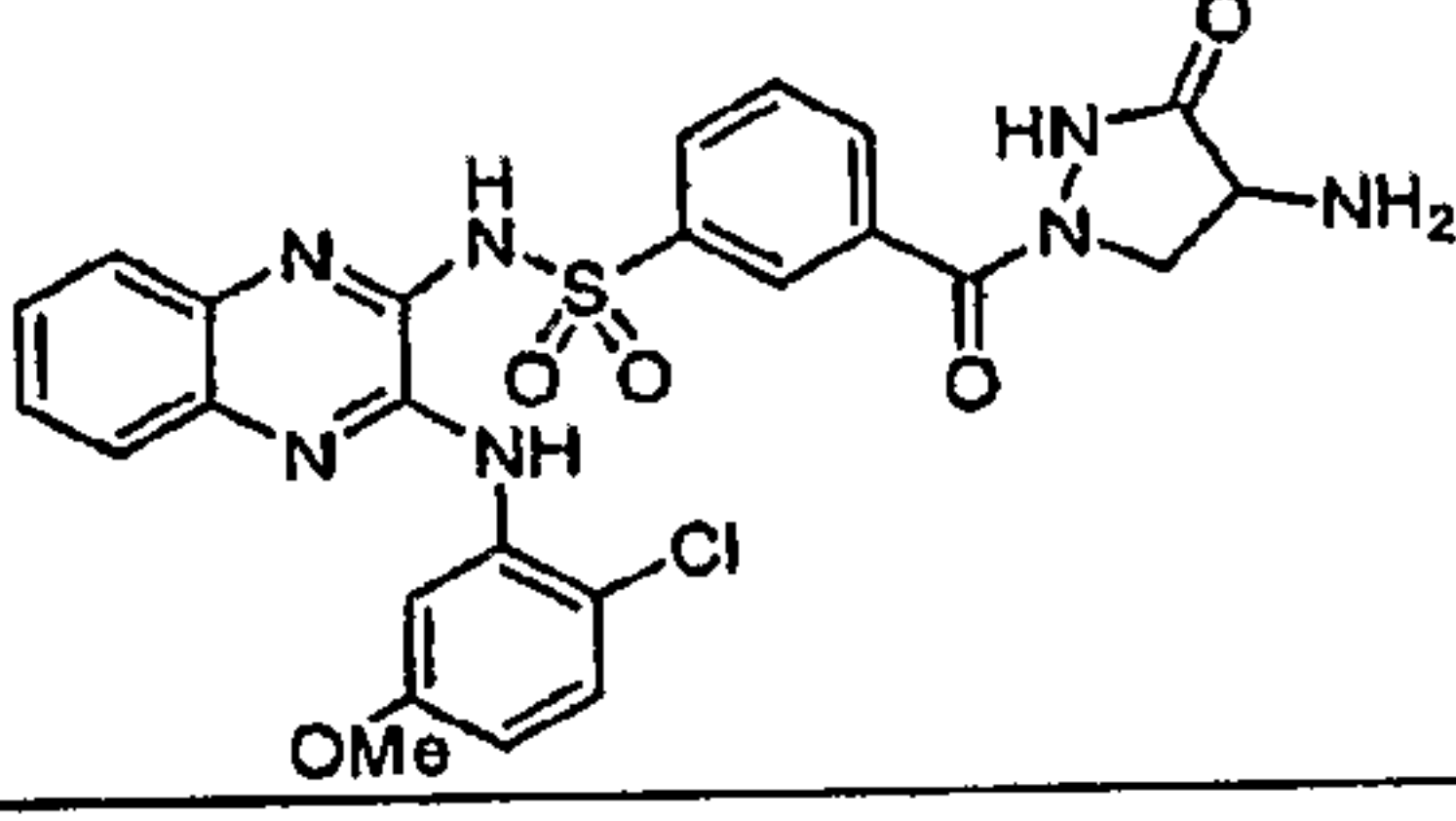
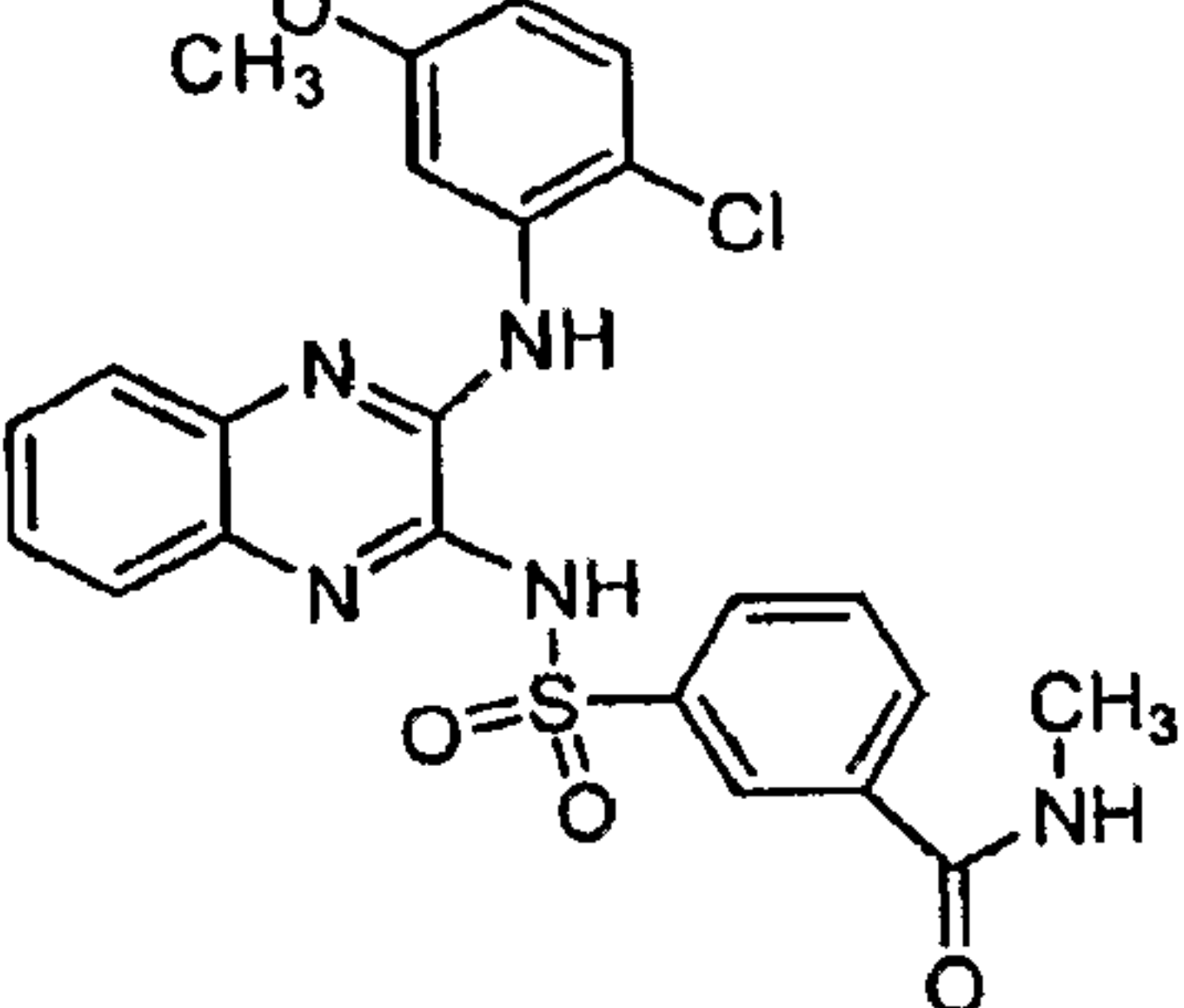
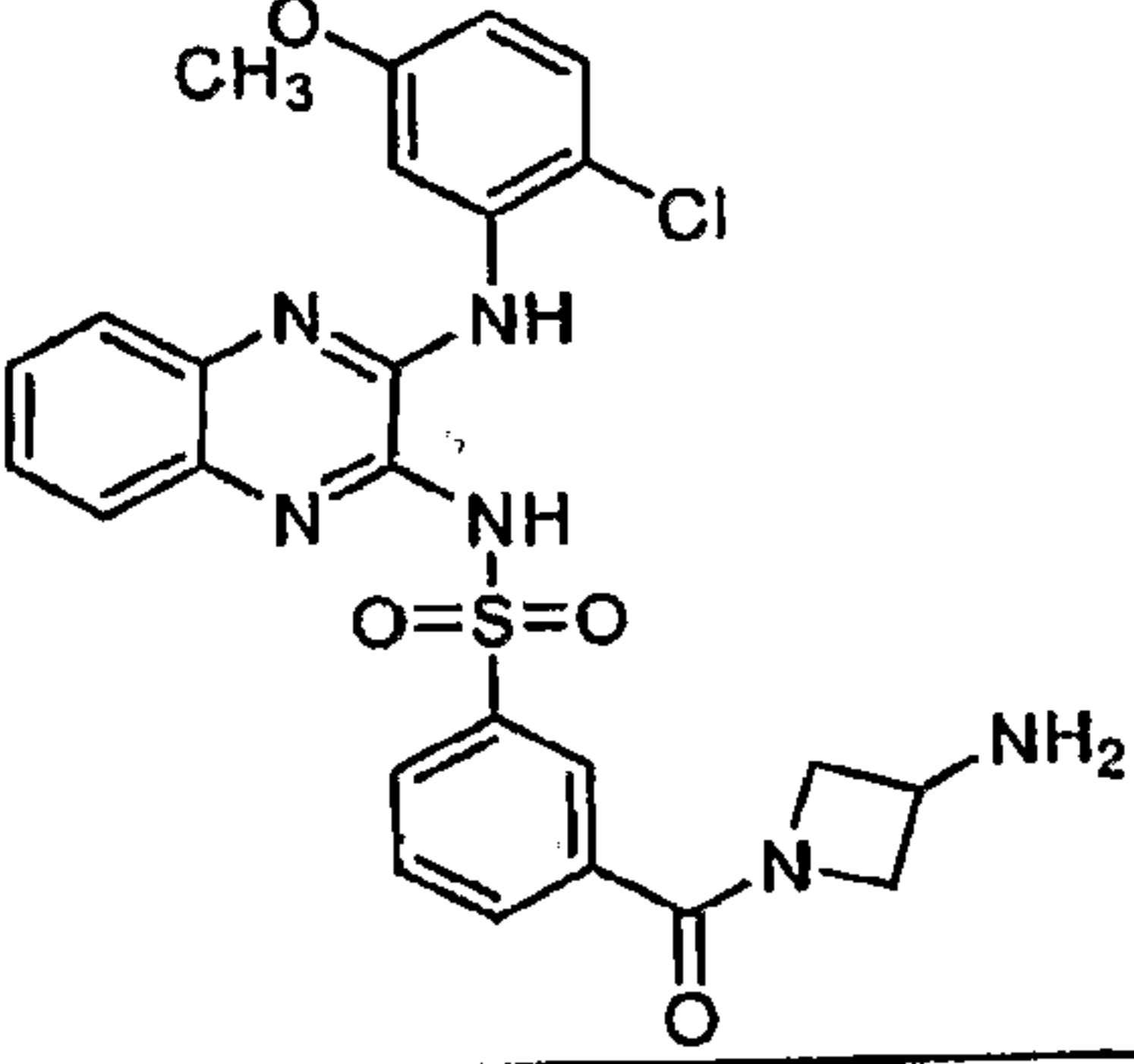
Table 1		
Cpd. No.	Structure	IUPAC Name
718		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl]-N-[(1-ethylpyrrolidin-2-yl)methyl]benzamide
719		3-[(4-amino-3-oxopyrazolidin-1-yl)carbonyl]-N-(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
720		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl]-N-methylbenzamide
721		3-[(3-aminoazetidin-1-yl)carbonyl]-N-(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide

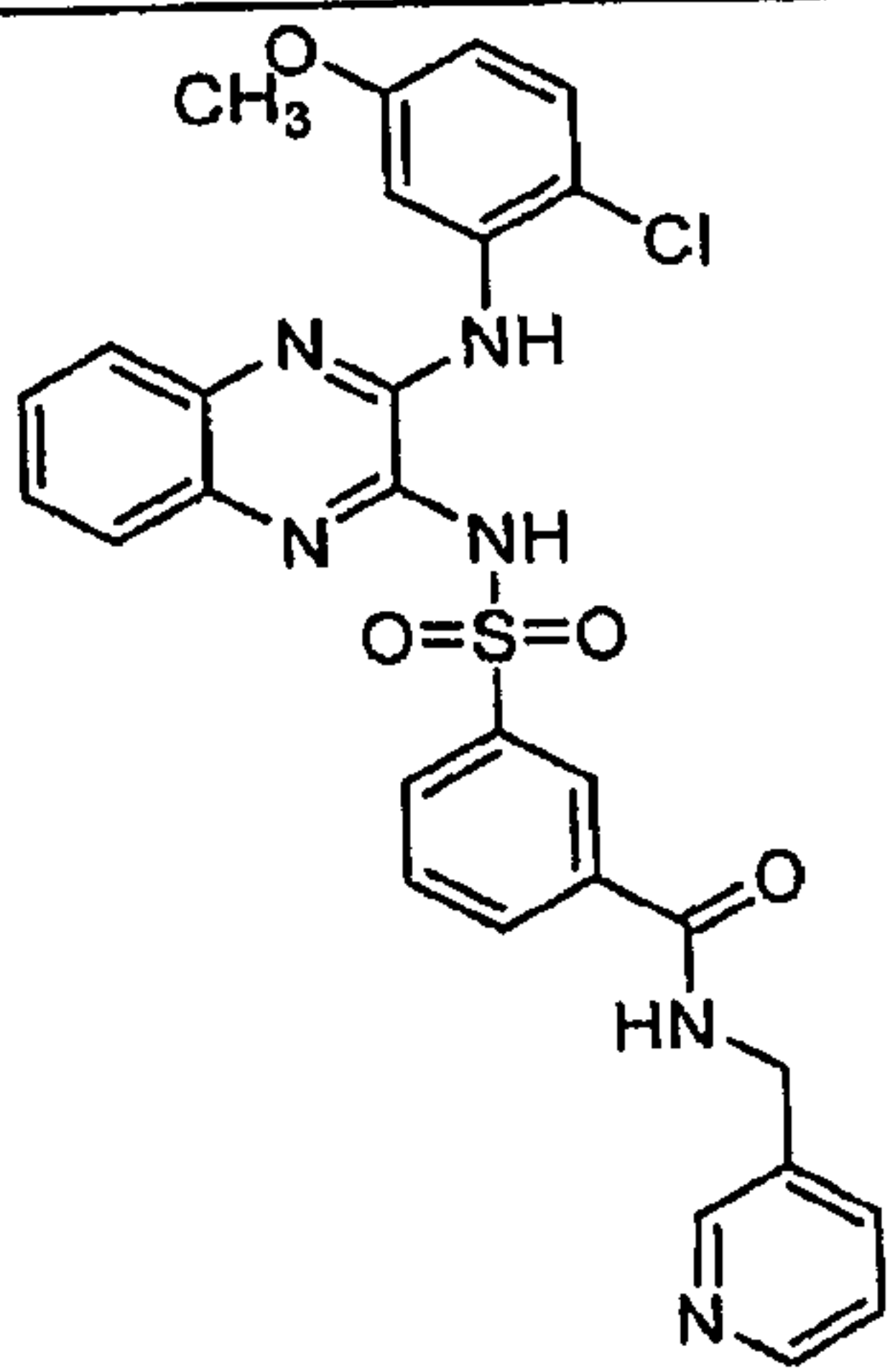
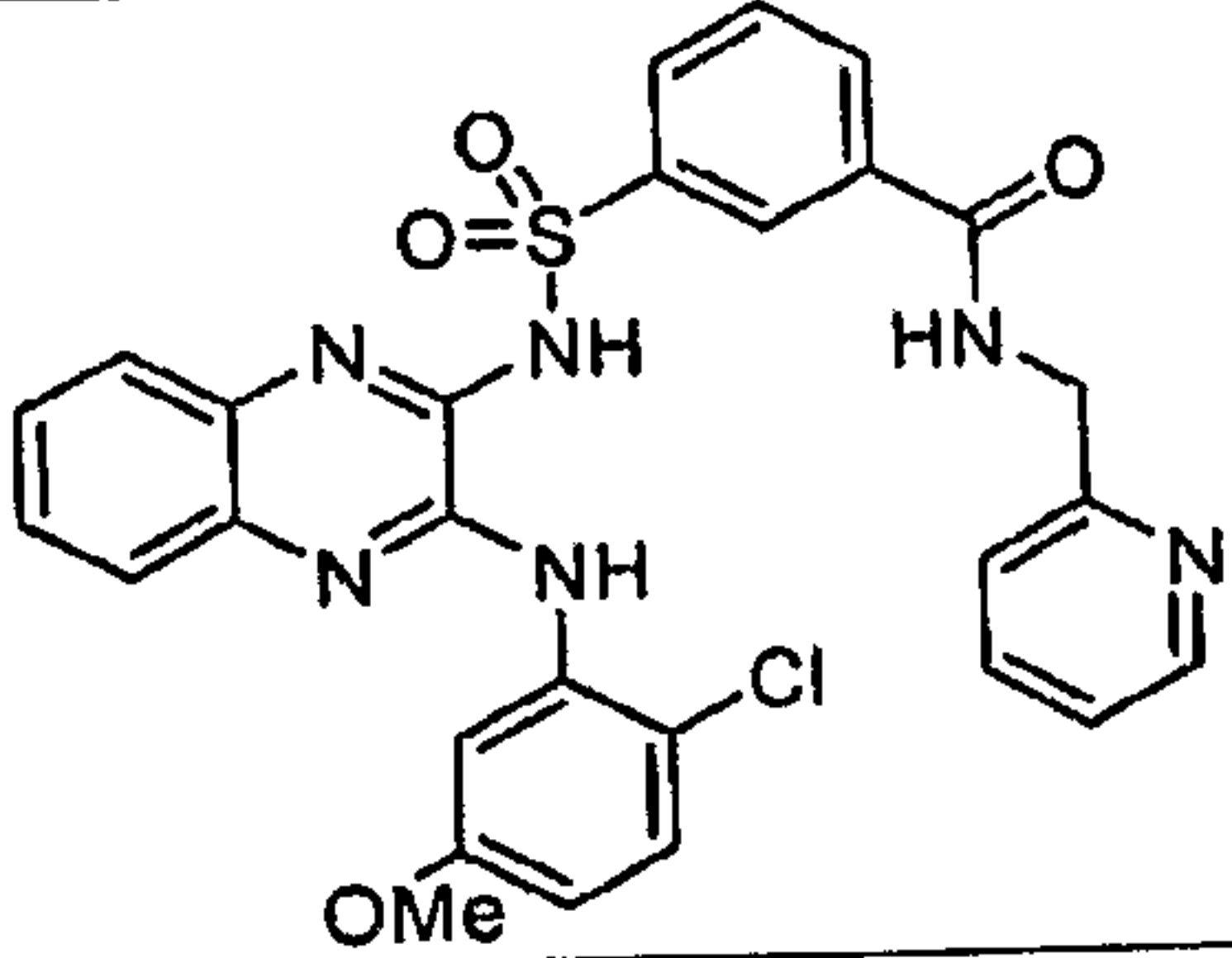
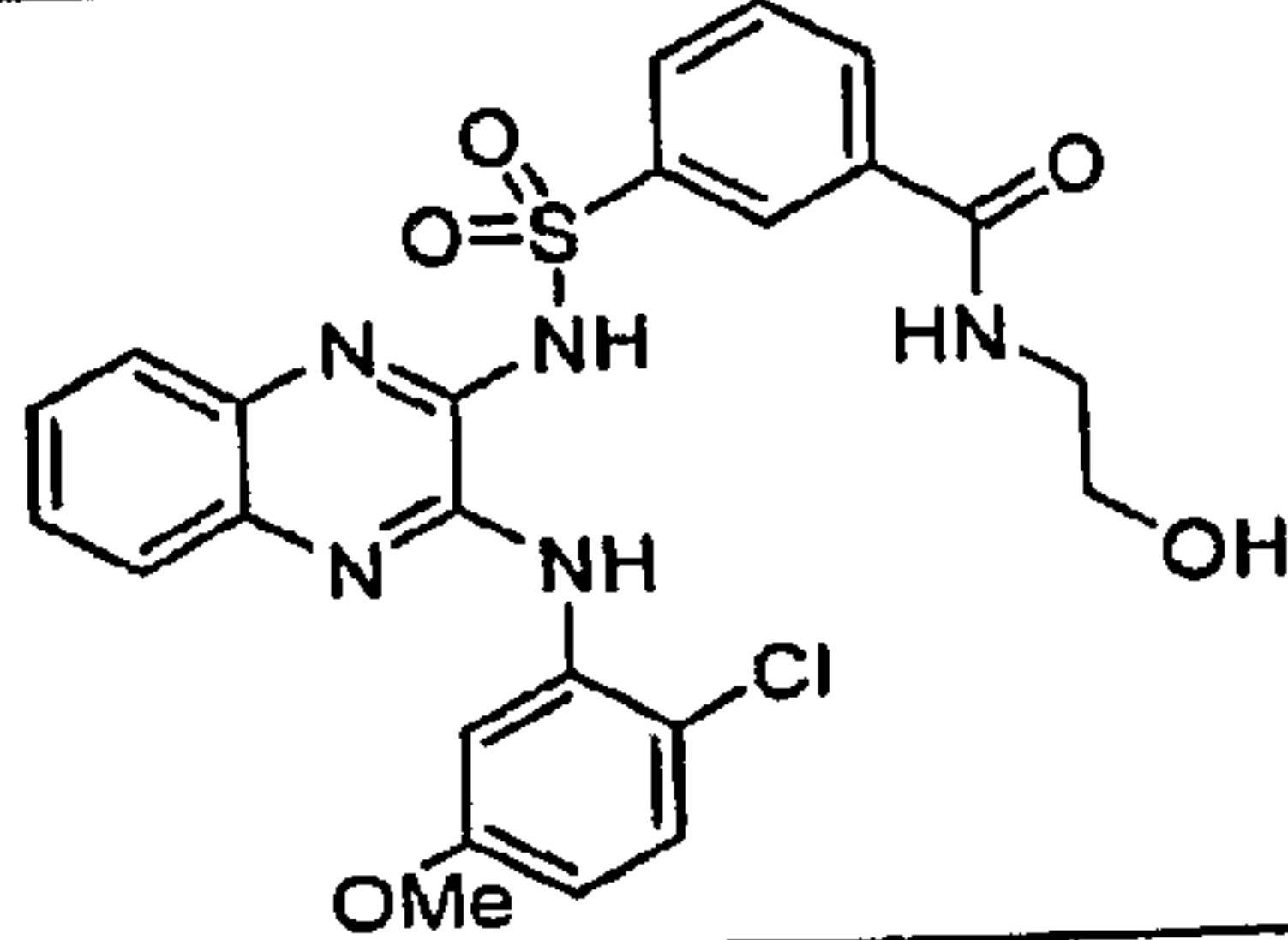
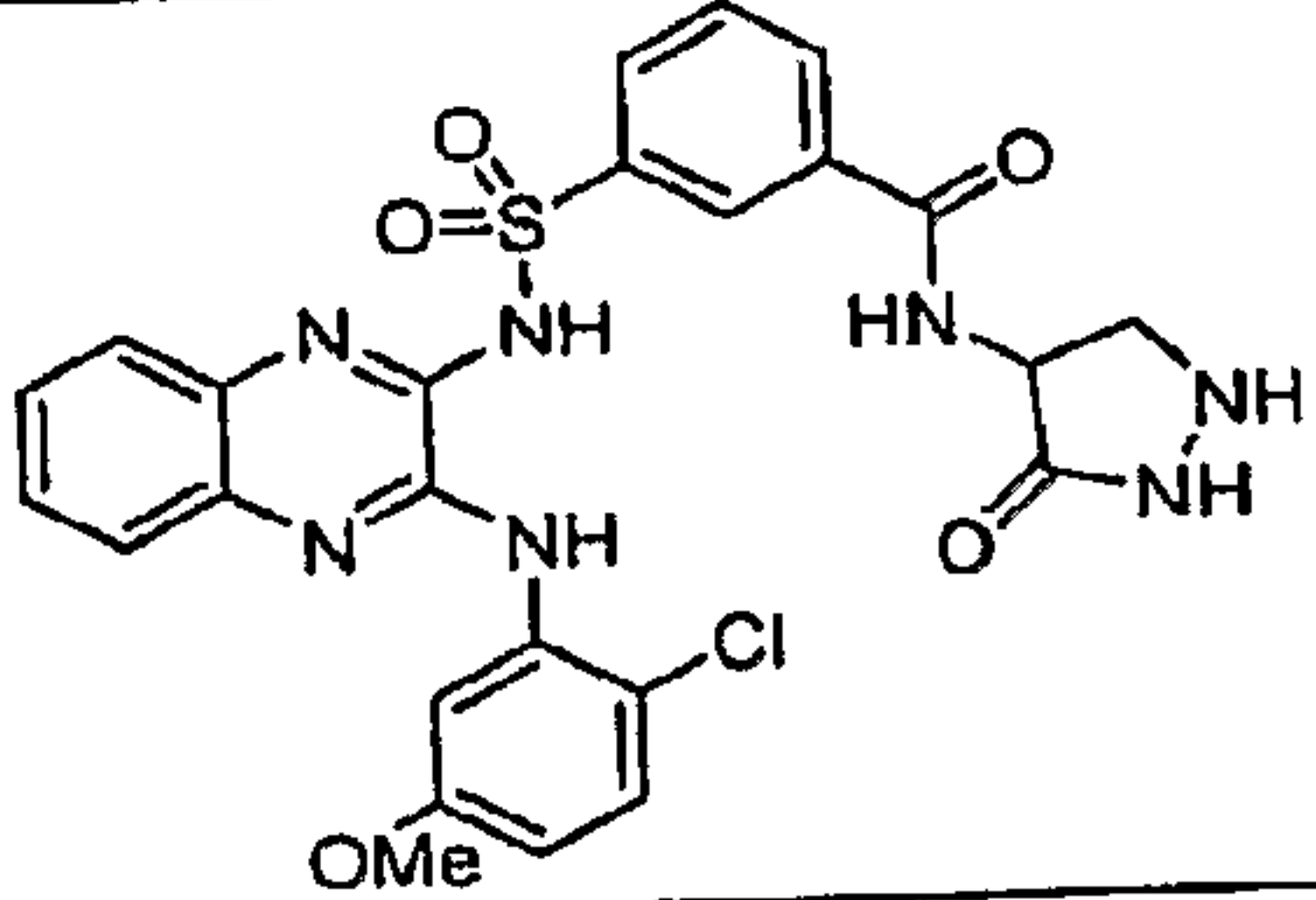
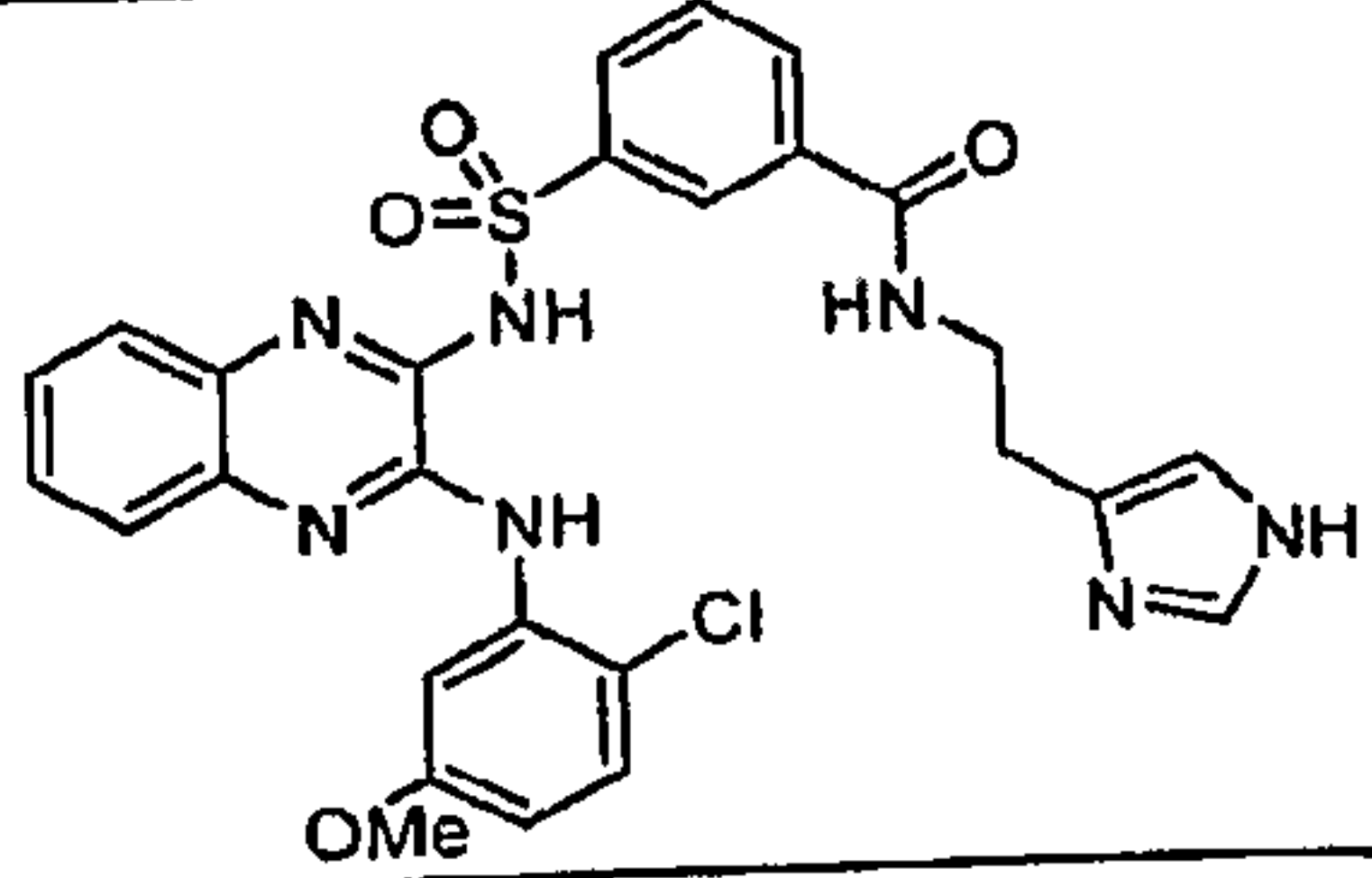
Table 1		
Cpd. No.	Structure	IUPAC Name
722		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-(pyridin-3-ylmethyl)benzamide
723		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-(pyridin-2-ylmethyl)benzamide
724		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-(2-hydroxyethyl)benzamide
725		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-(3-oxopyrazolidin-4-yl)benzamide
726		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-[2-(1H-imidazol-4-yl)ethyl]benzamide

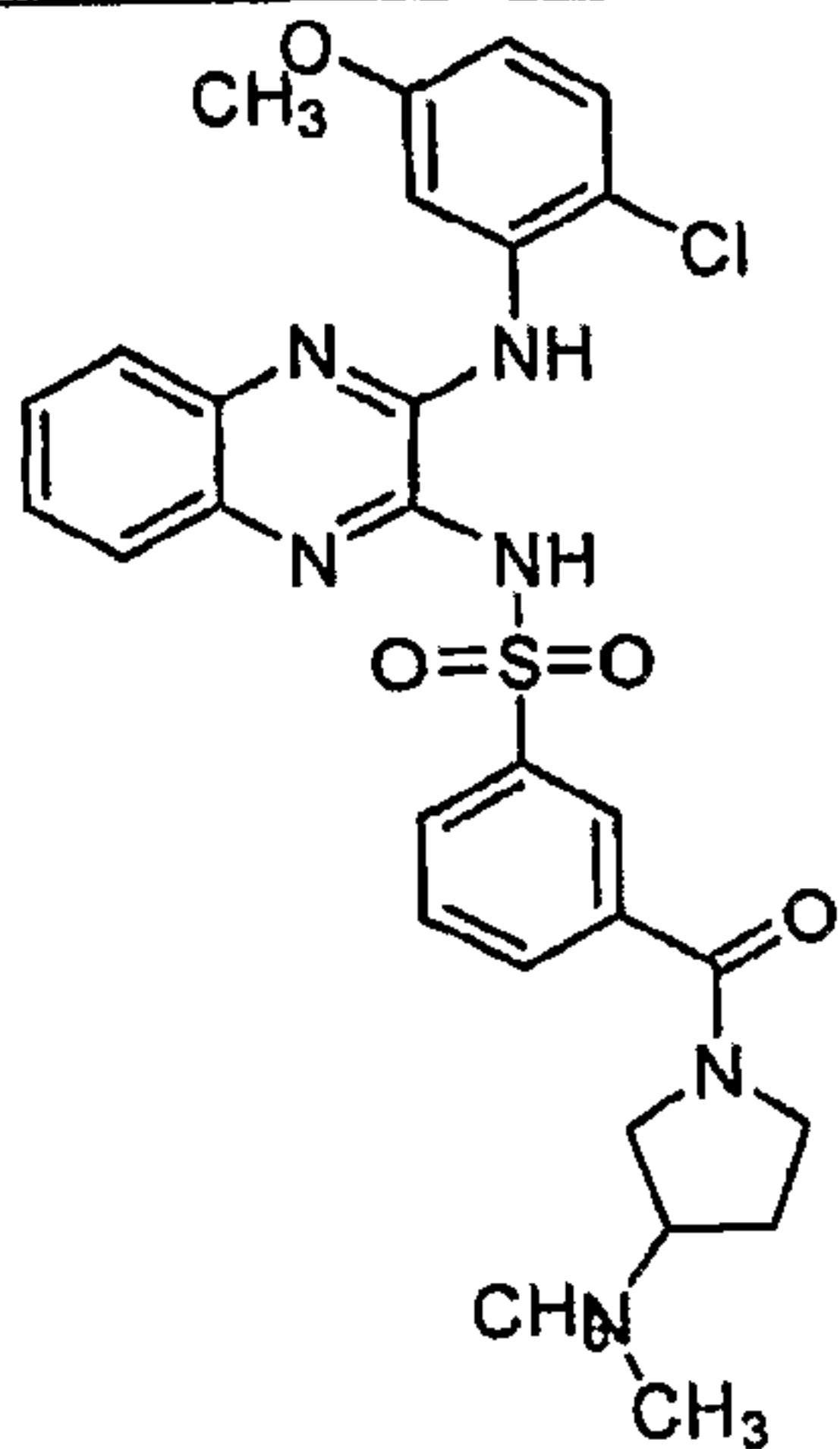
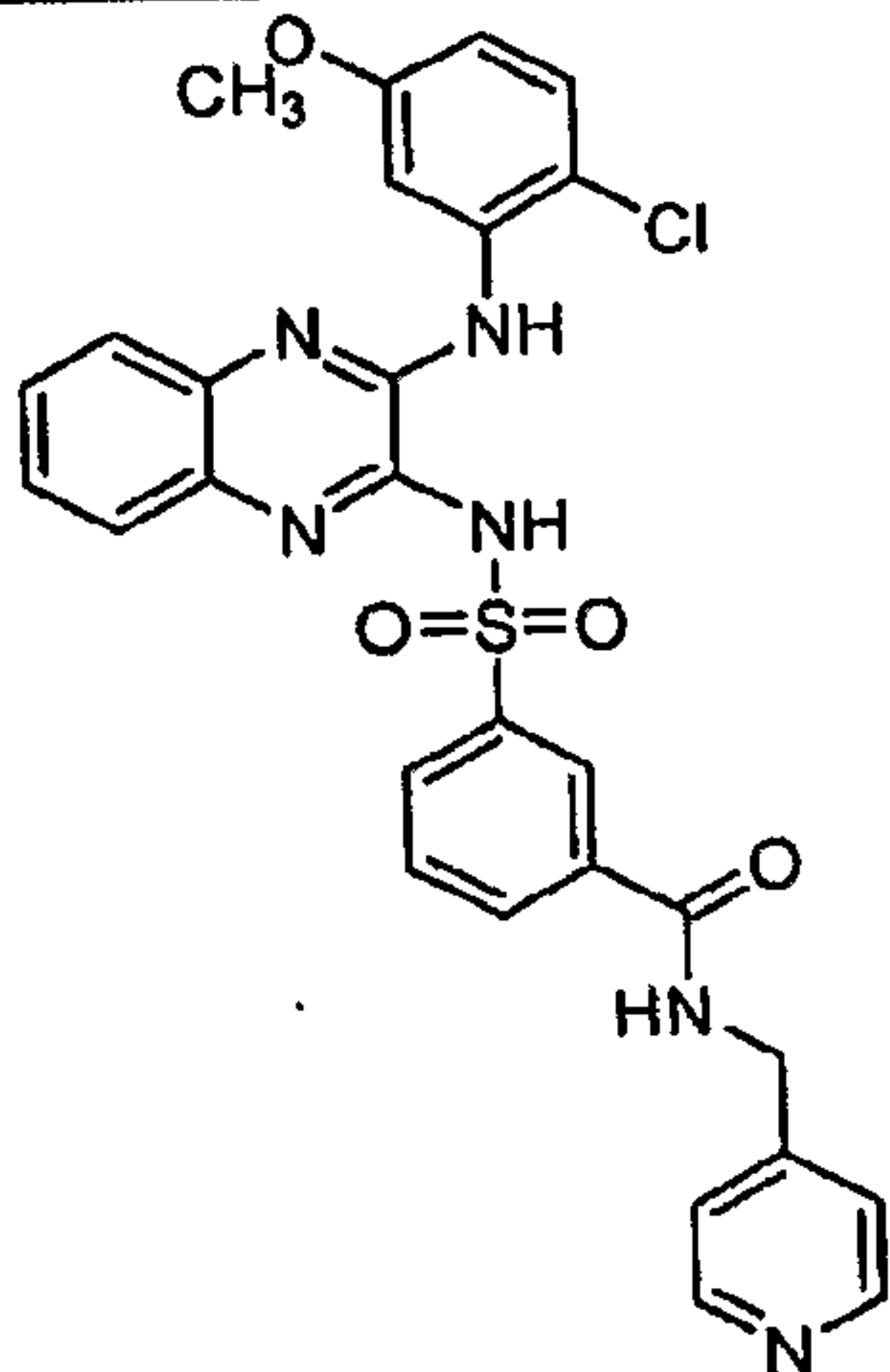
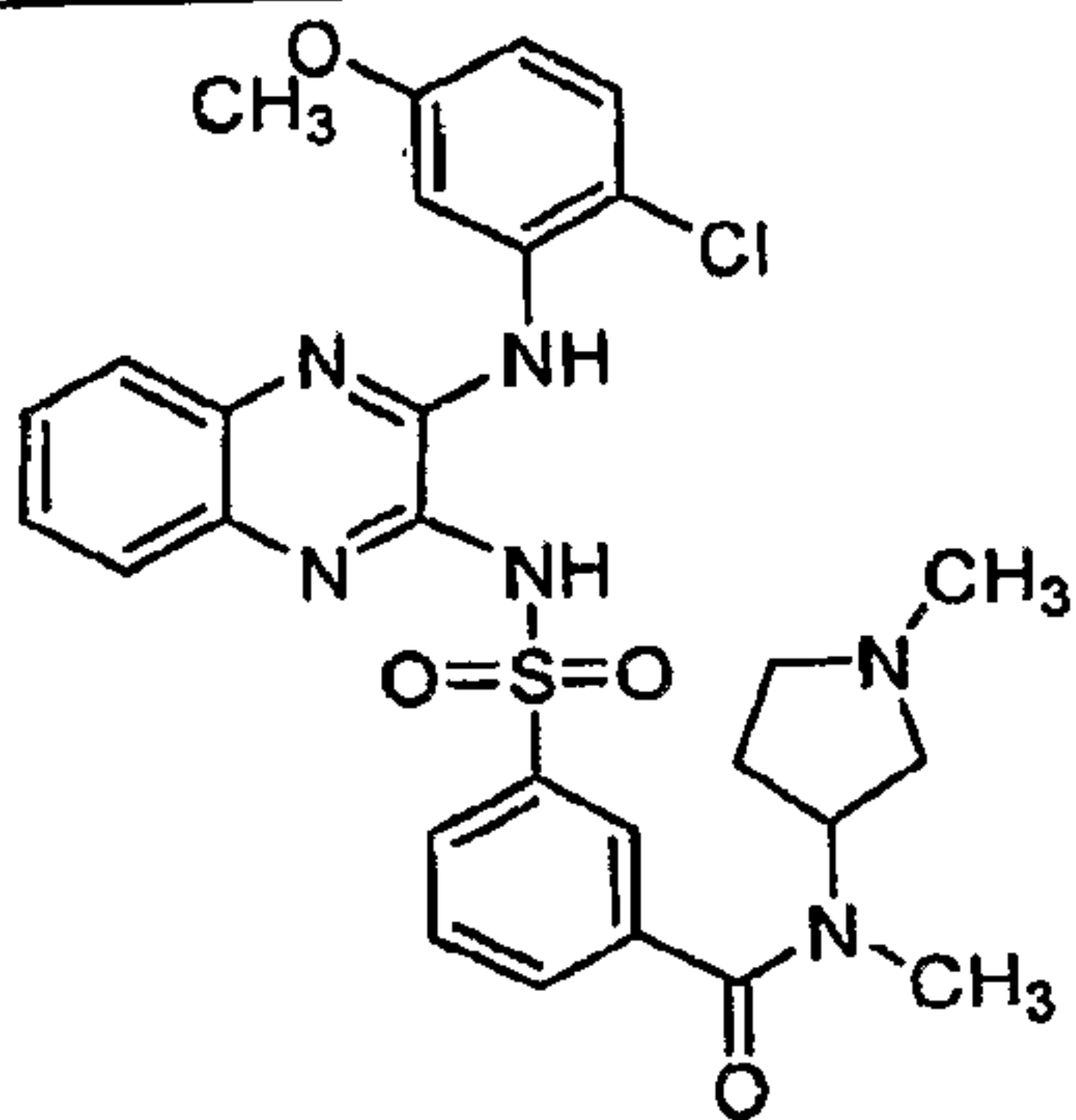
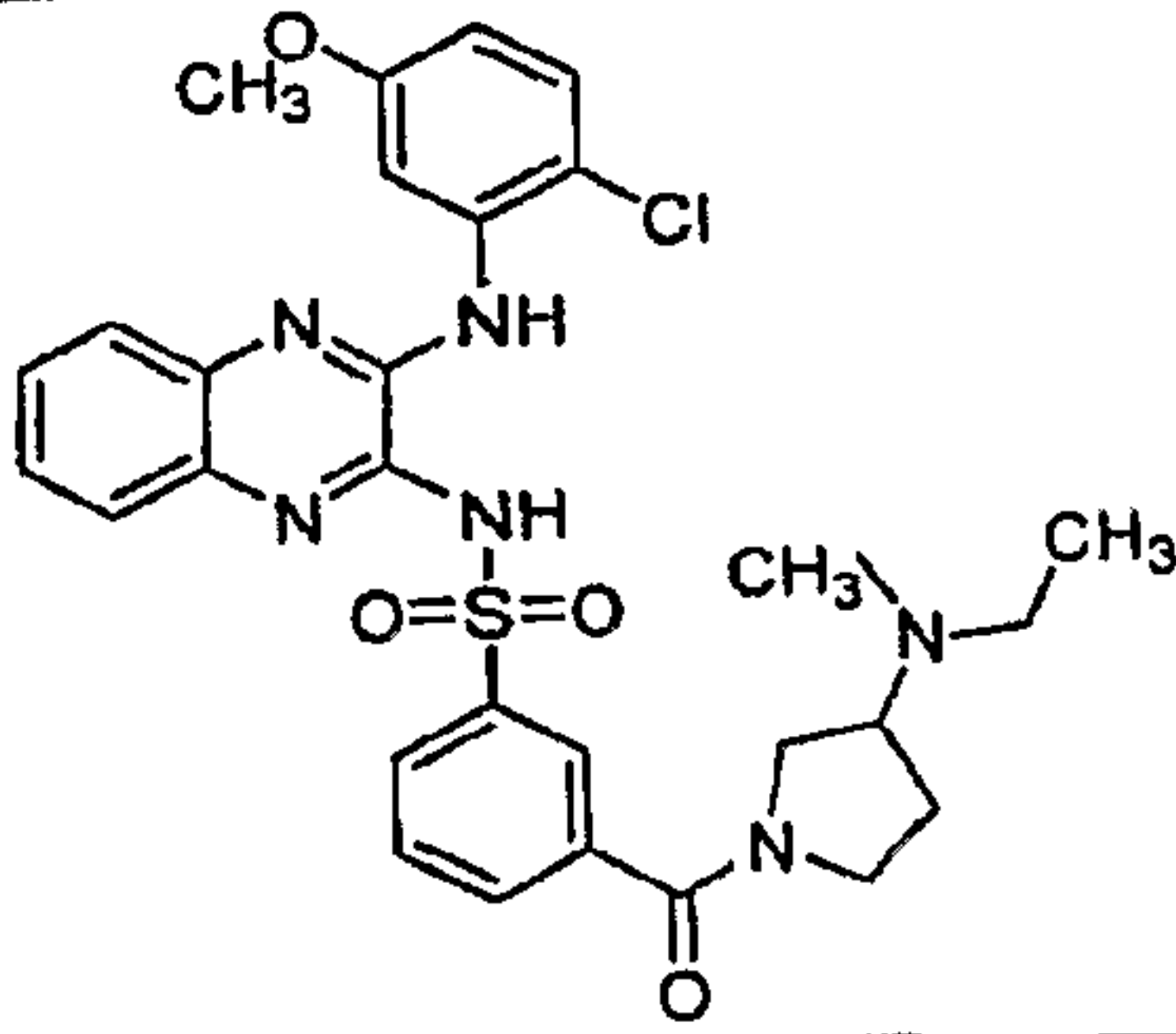
Table 1		
Cpd. No.	Structure	IUPAC Name
727		<i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[3-(dimethylamino)pyrrolidin-1-yl]carbonyl}benzenesulfonamide
728		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}- <i>N</i> -(pyridin-4-ylmethyl)benzamide
729		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}- <i>N</i> -methyl- <i>N</i> -(1-methylpyrrolidin-3-yl)benzamide
730		<i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[3-(diethylamino)pyrrolidin-1-yl]carbonyl}benzenesulfonamide

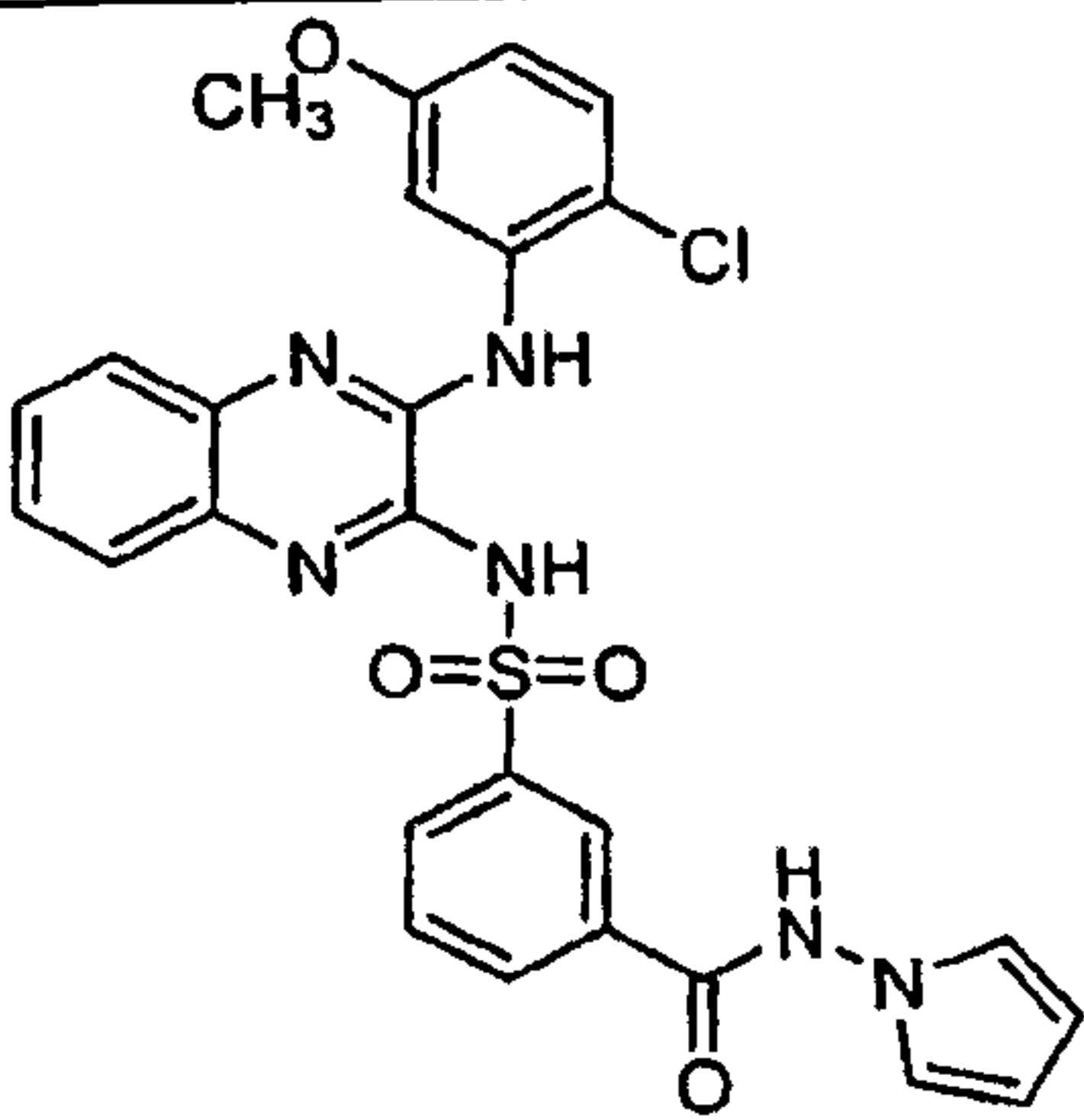
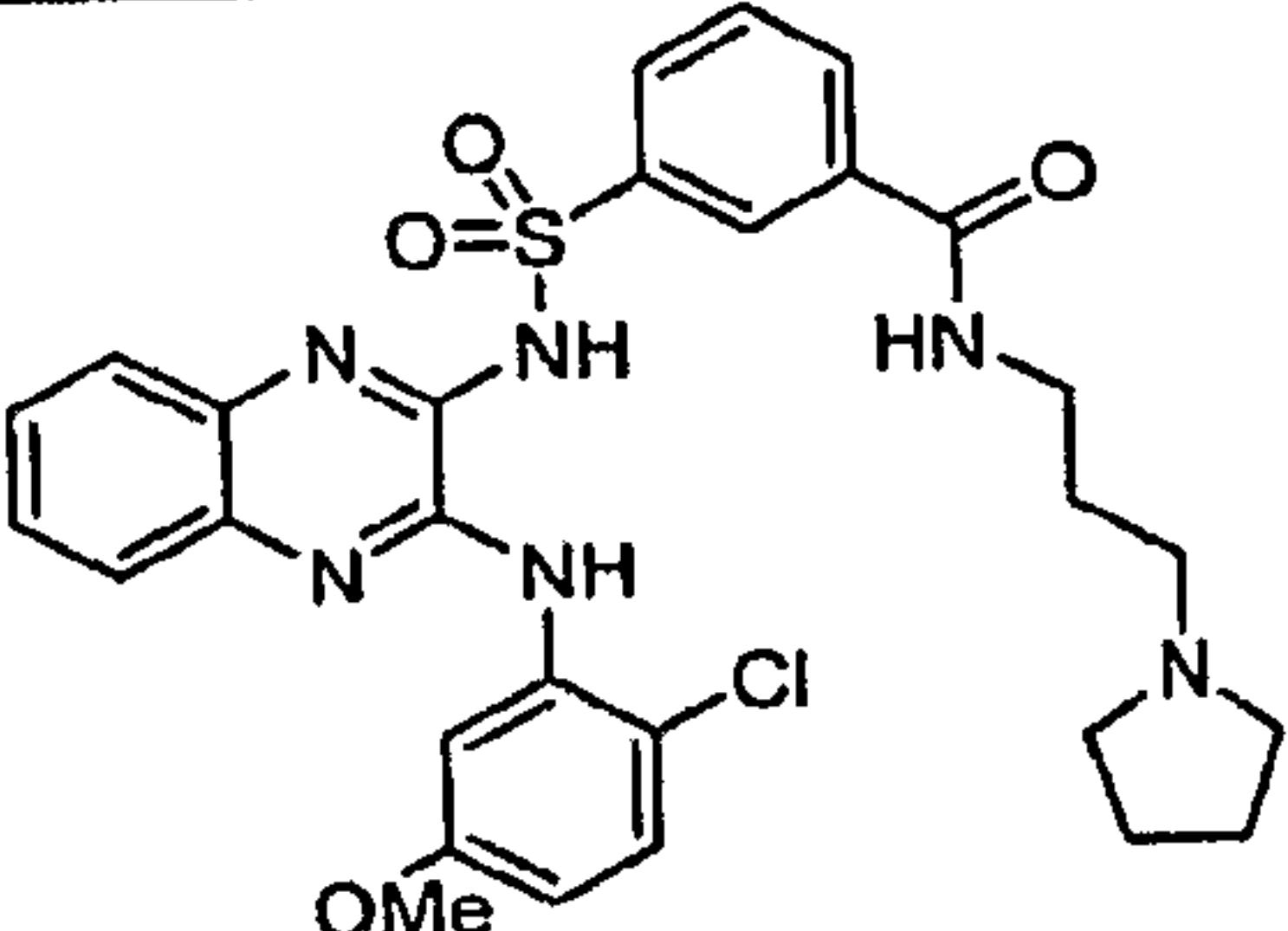
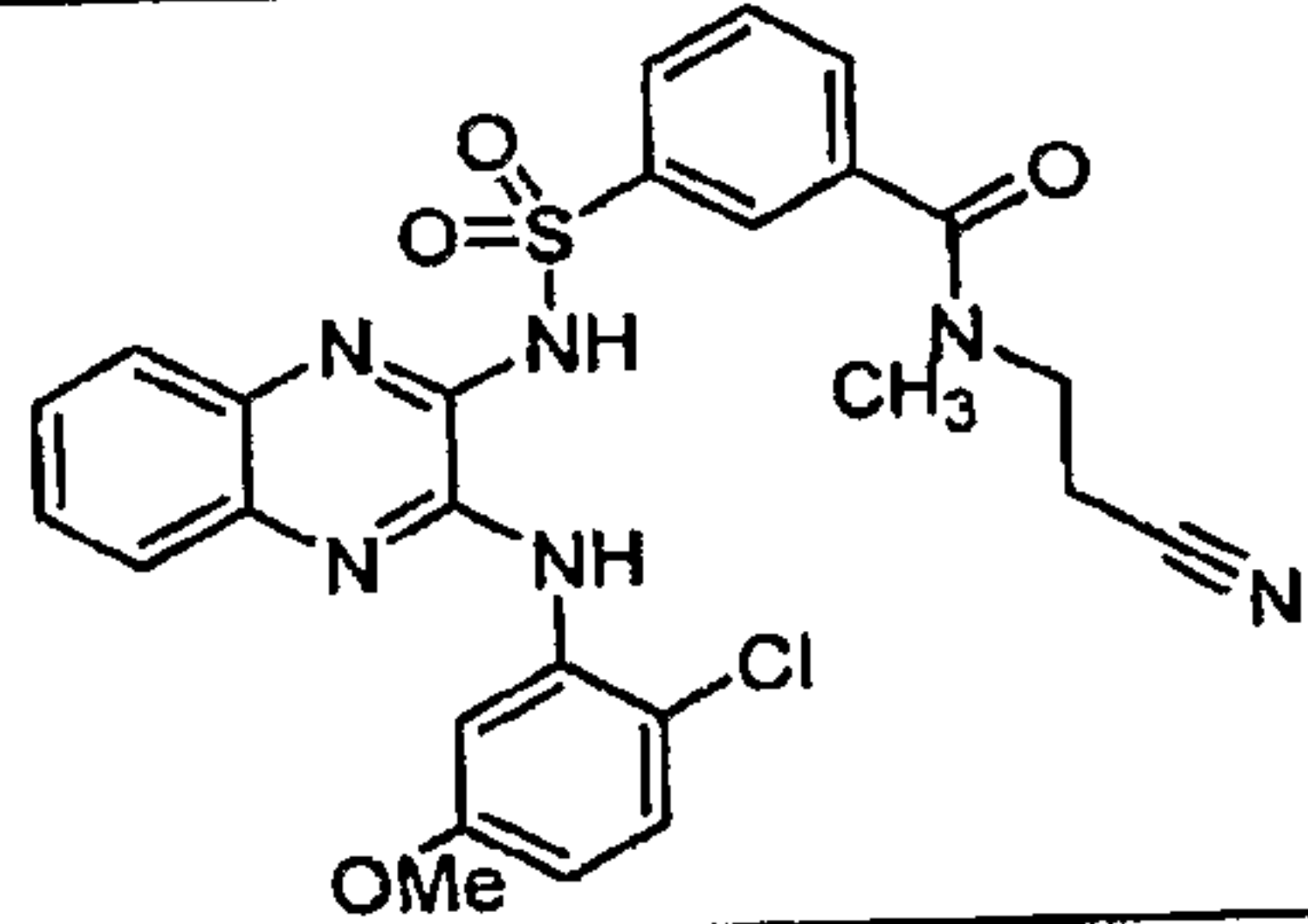
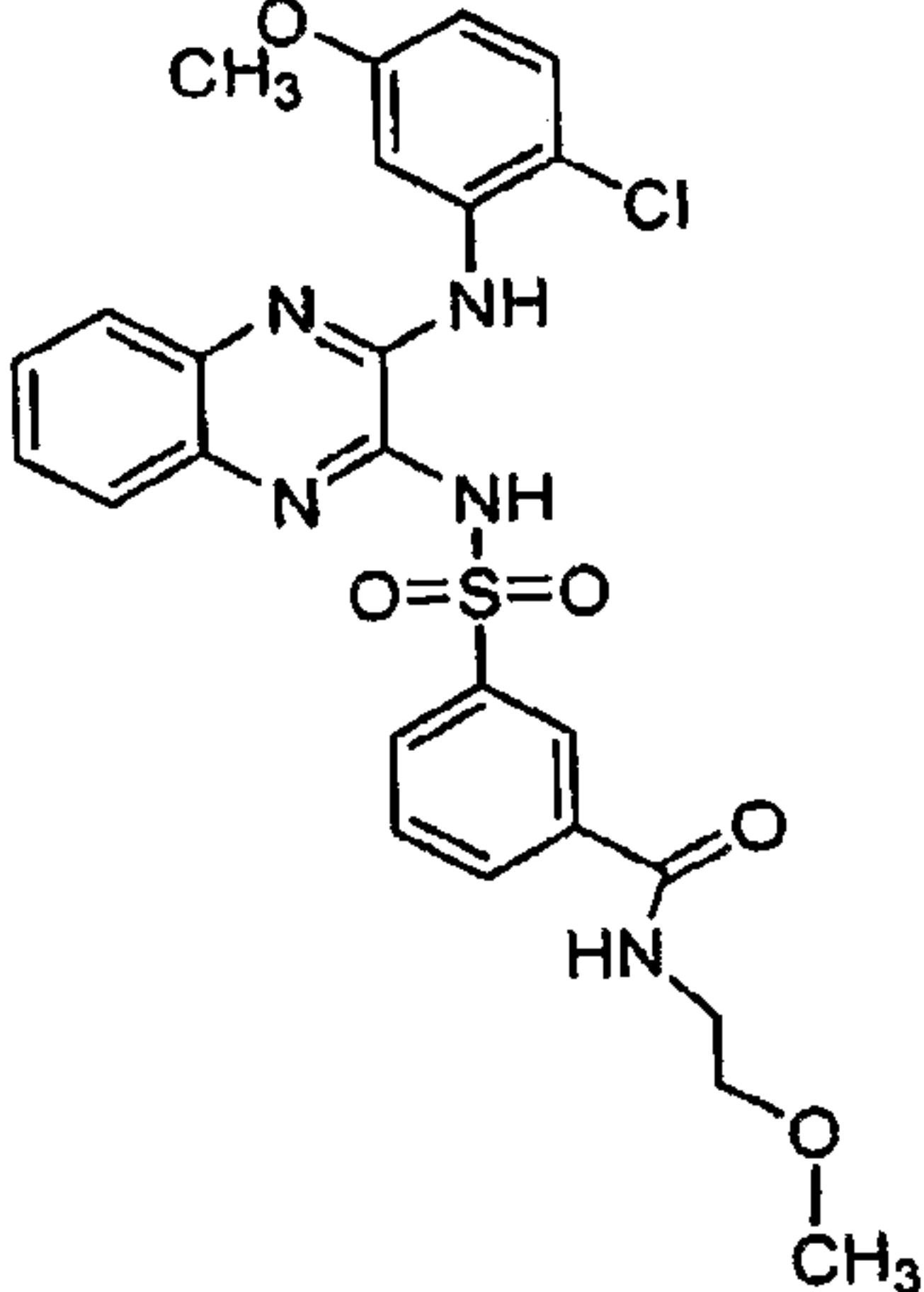
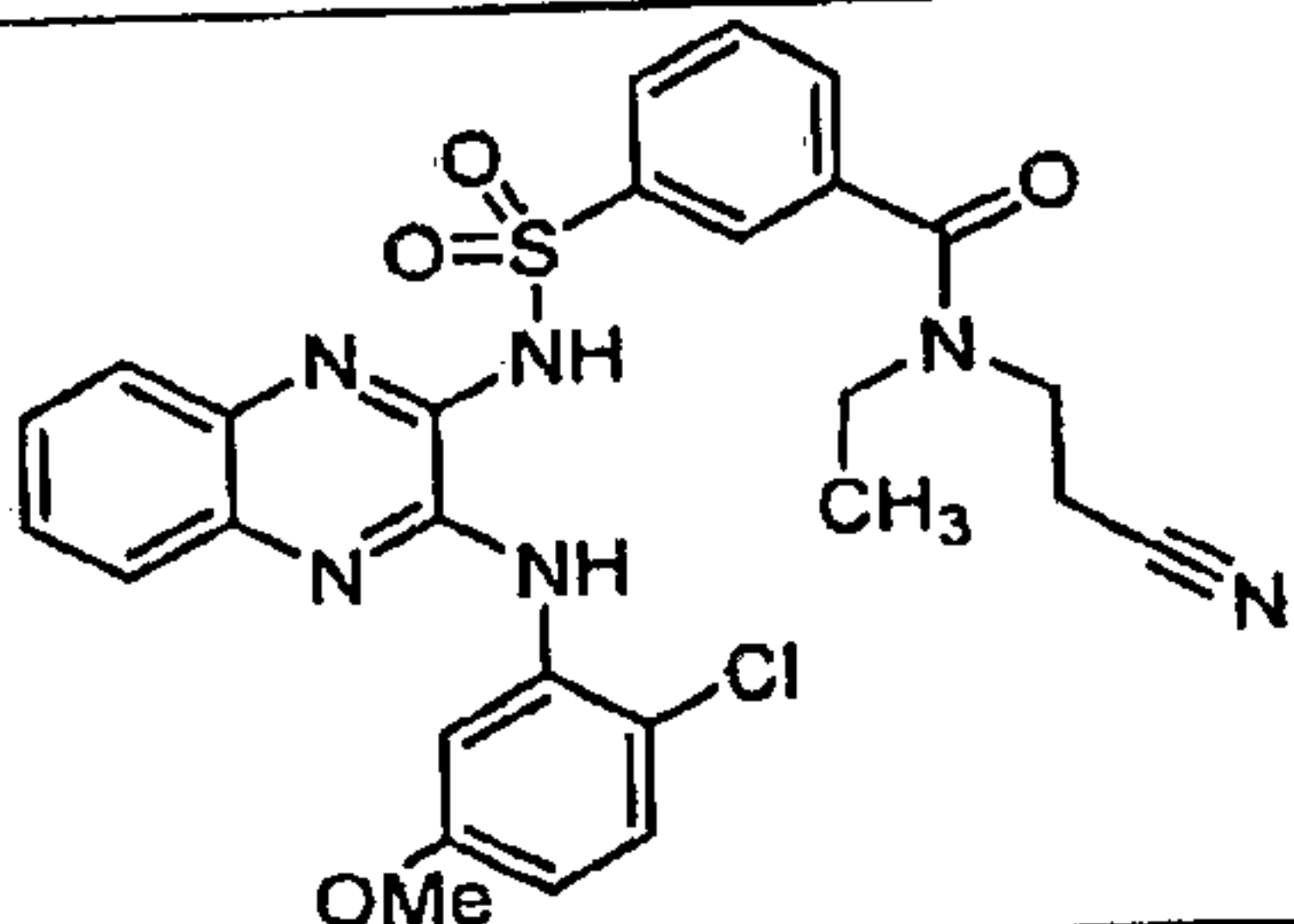
Table 1		
Cpd. No.	Structure	IUPAC Name
731		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl]- <i>N</i> -1 <i>H</i> -pyrrol-1-ylbenzamide
732		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl]- <i>N</i> -(3-pyrrolidin-1-ylpropyl)benzamide
733		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl]- <i>N</i> -(2-cyanoethyl)- <i>N</i> -methylbenzamide
734		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl]- <i>N</i> -[2-(methyloxy)ethyl]benzamide
735		3-[[[3-[[2-chloro-5-(methyloxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl]- <i>N</i> -(2-cyanoethyl)- <i>N</i> -ethylbenzamide

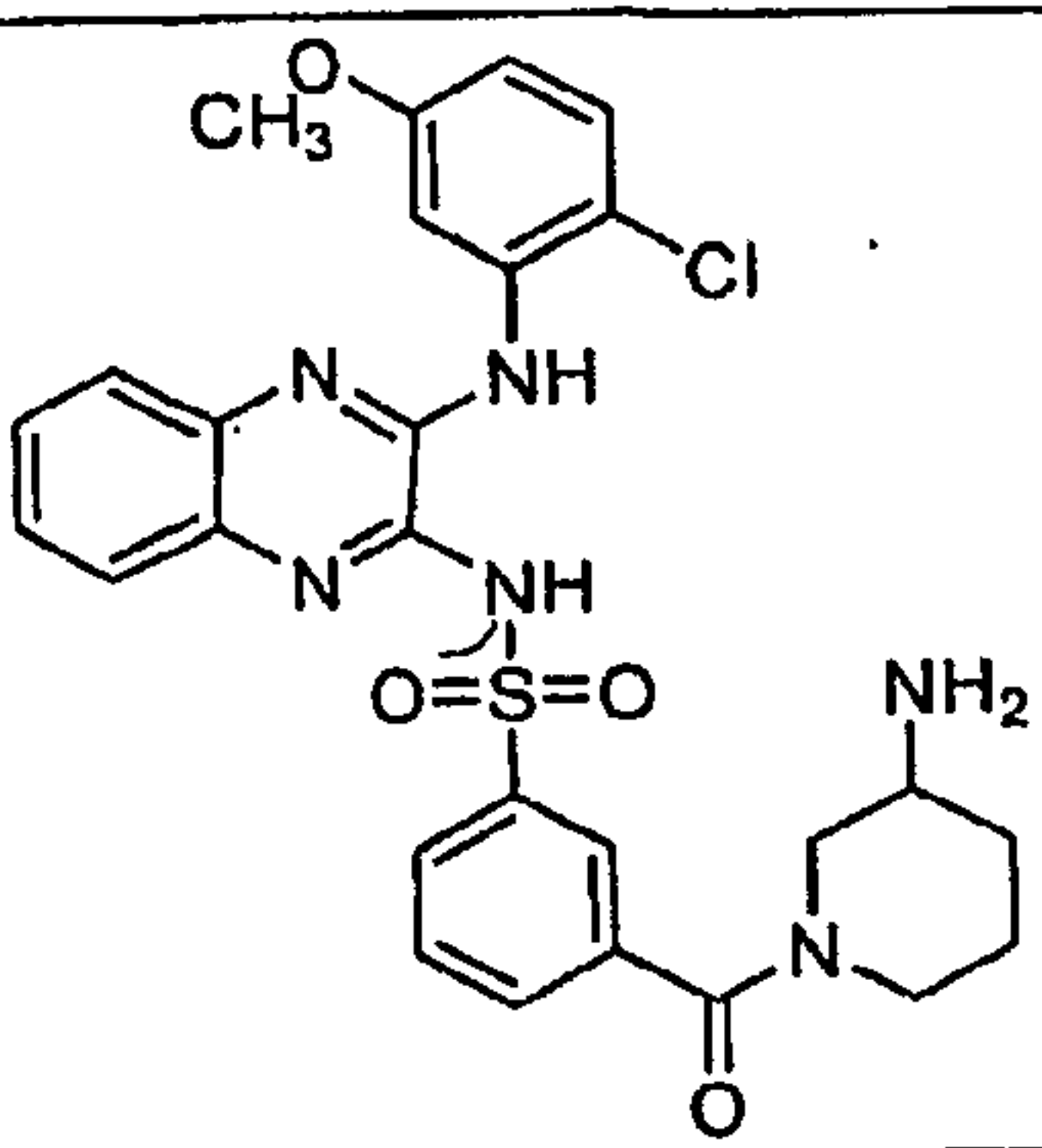
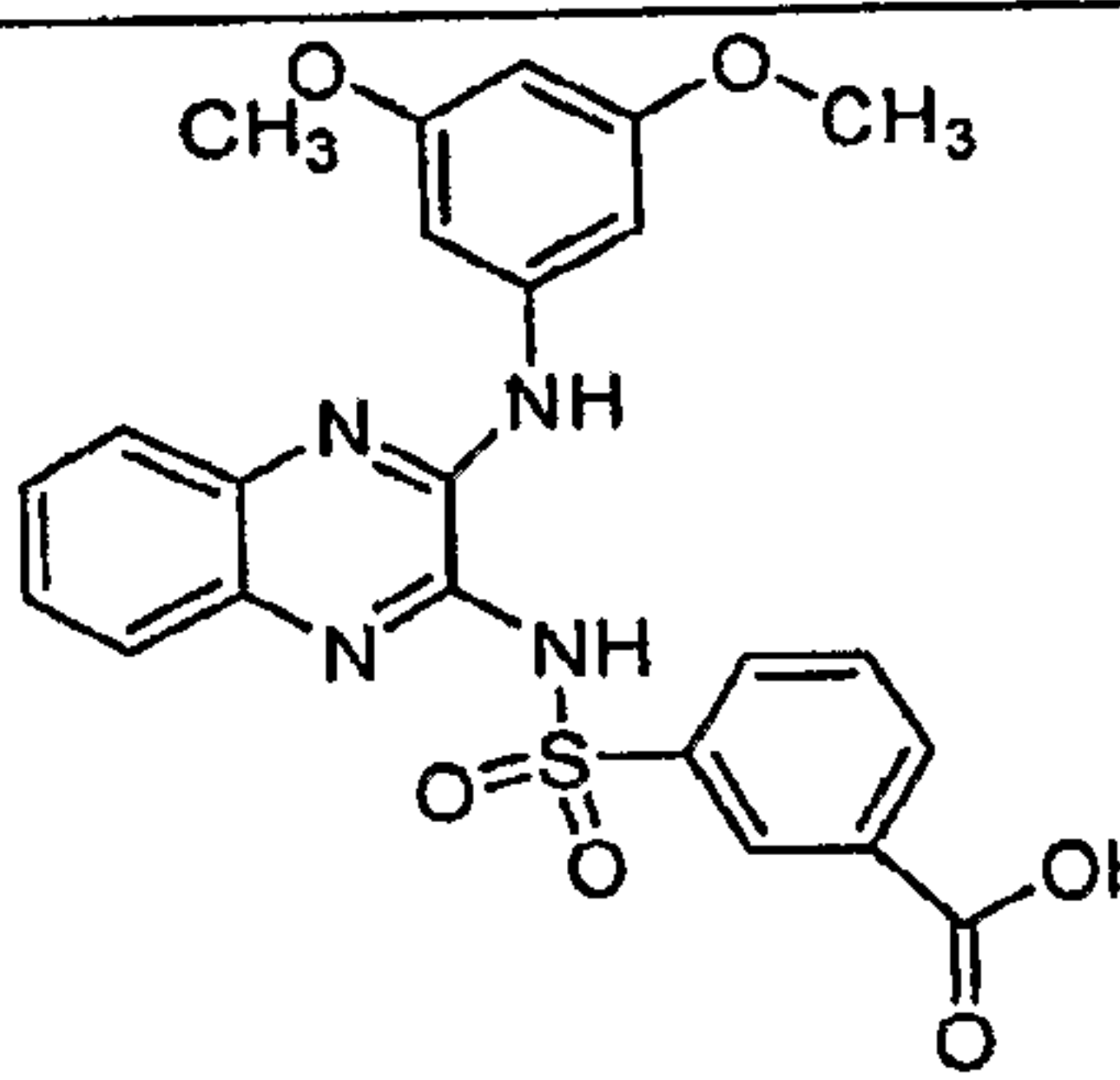
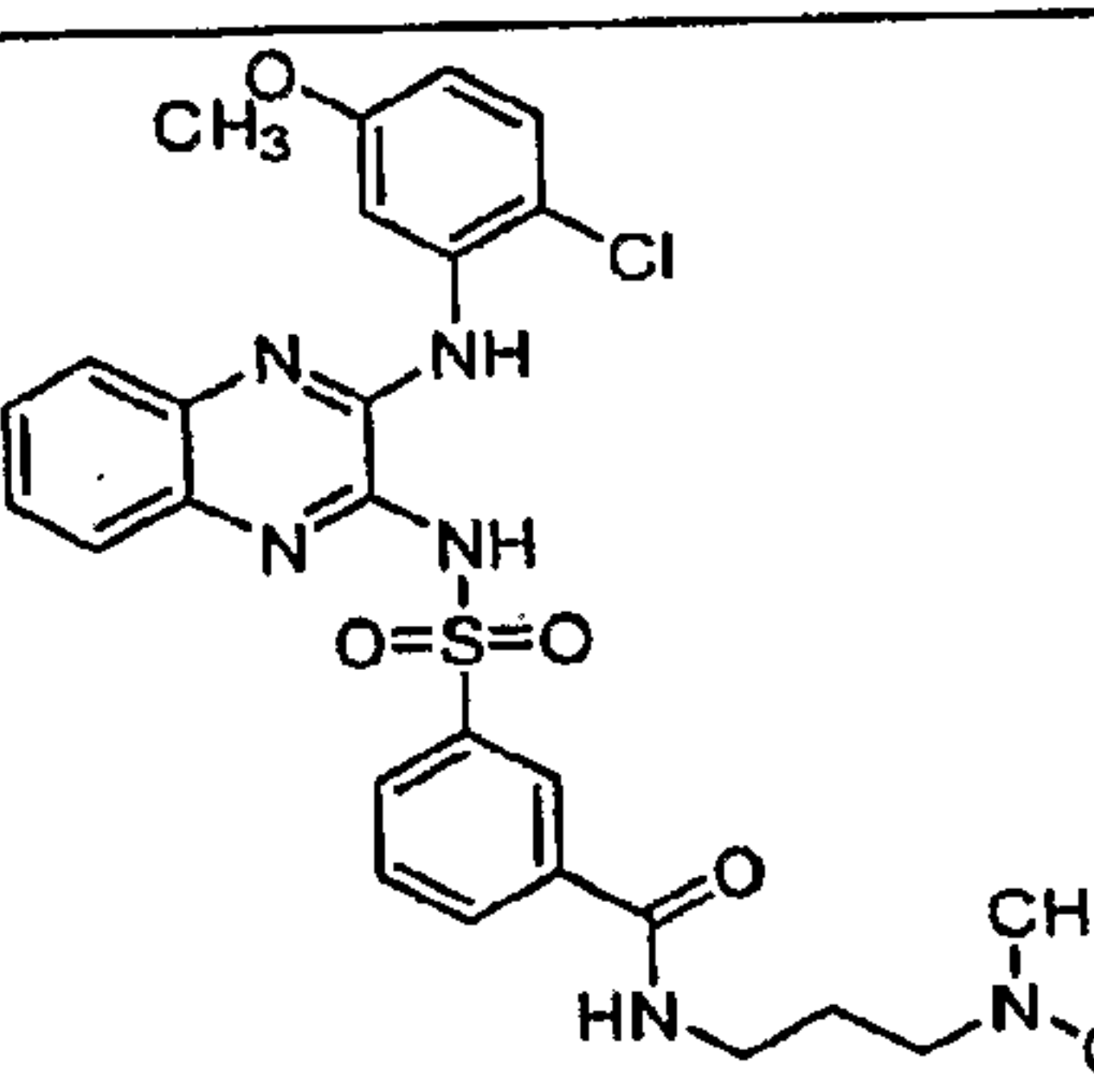
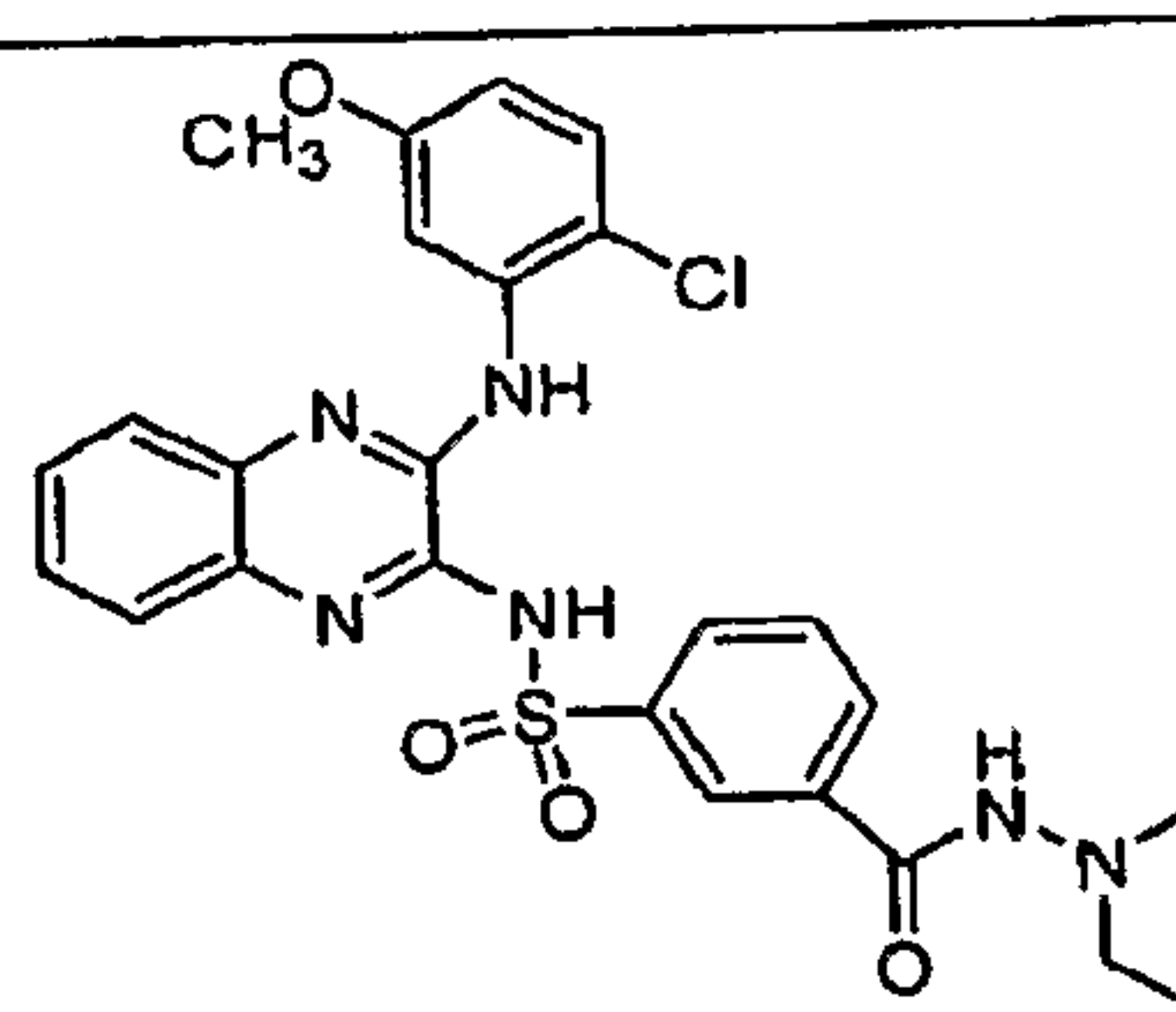
Table 1		
Cpd. No.	Structure	IUPAC Name
736		3-[(3-aminopiperidin-1-yl)carbonyl]-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
737		3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzoic acid
738		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(dimethylamino)propyl]benzamide
739		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-morpholin-4-ylbenzamide

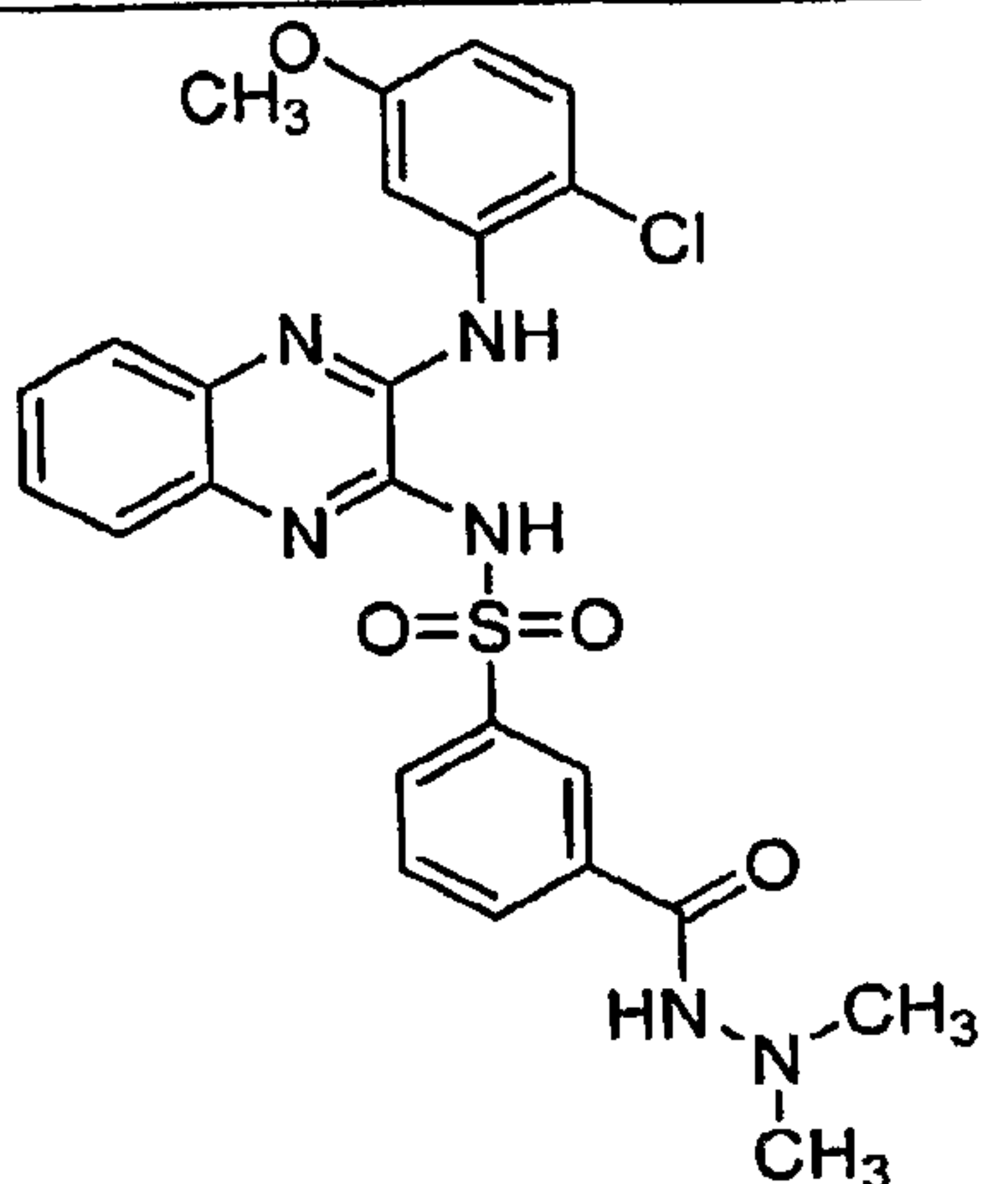
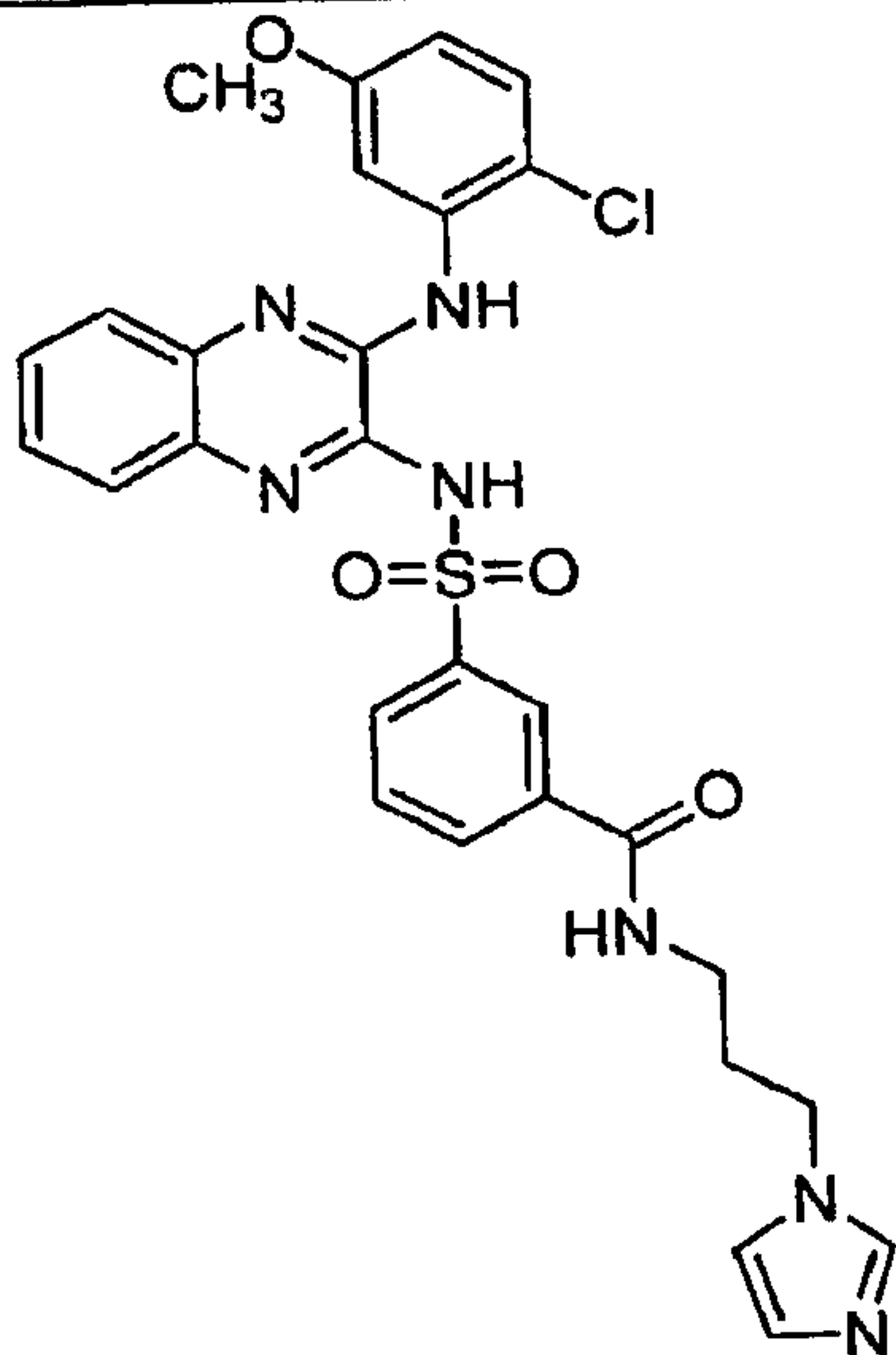
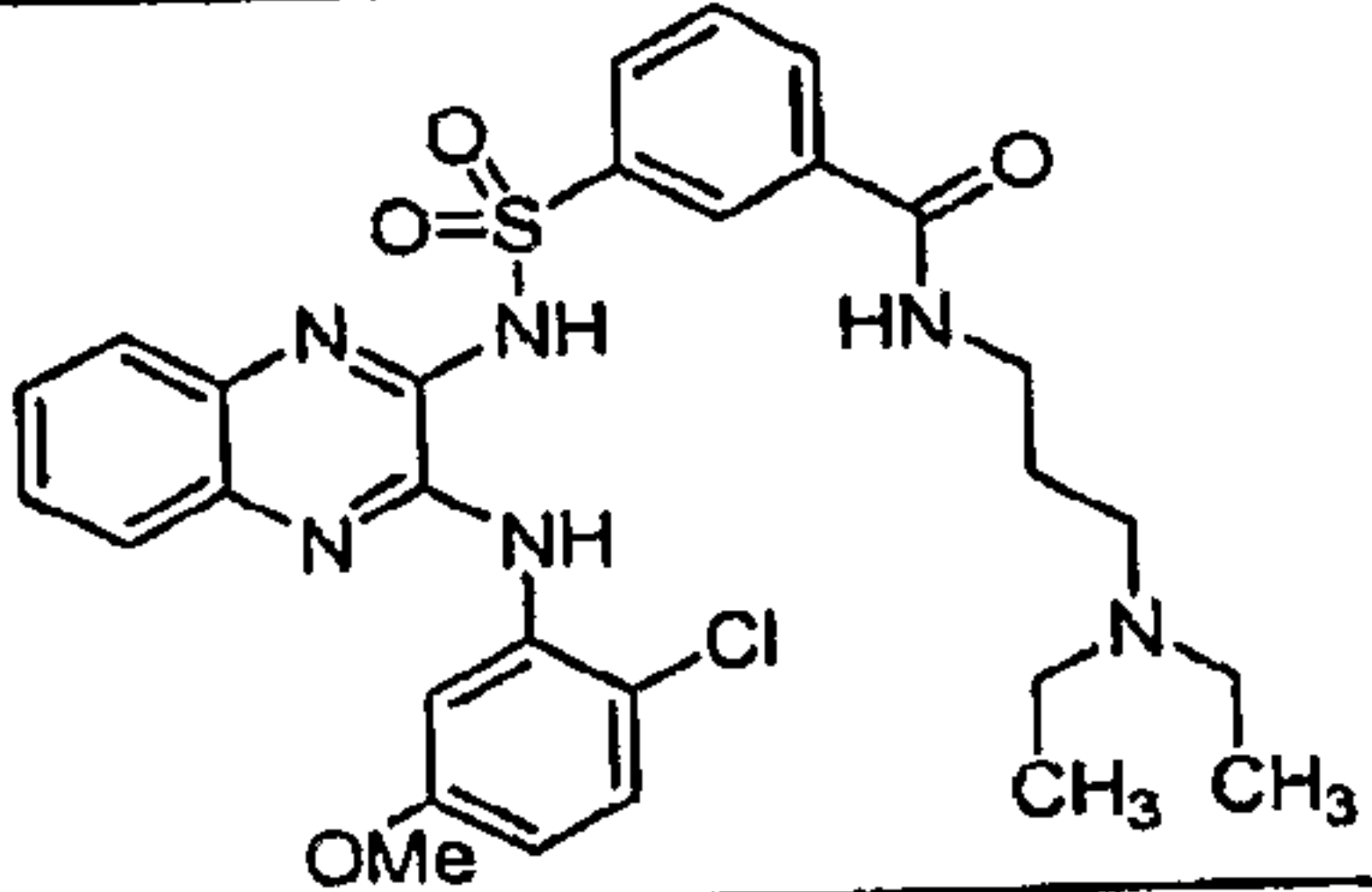
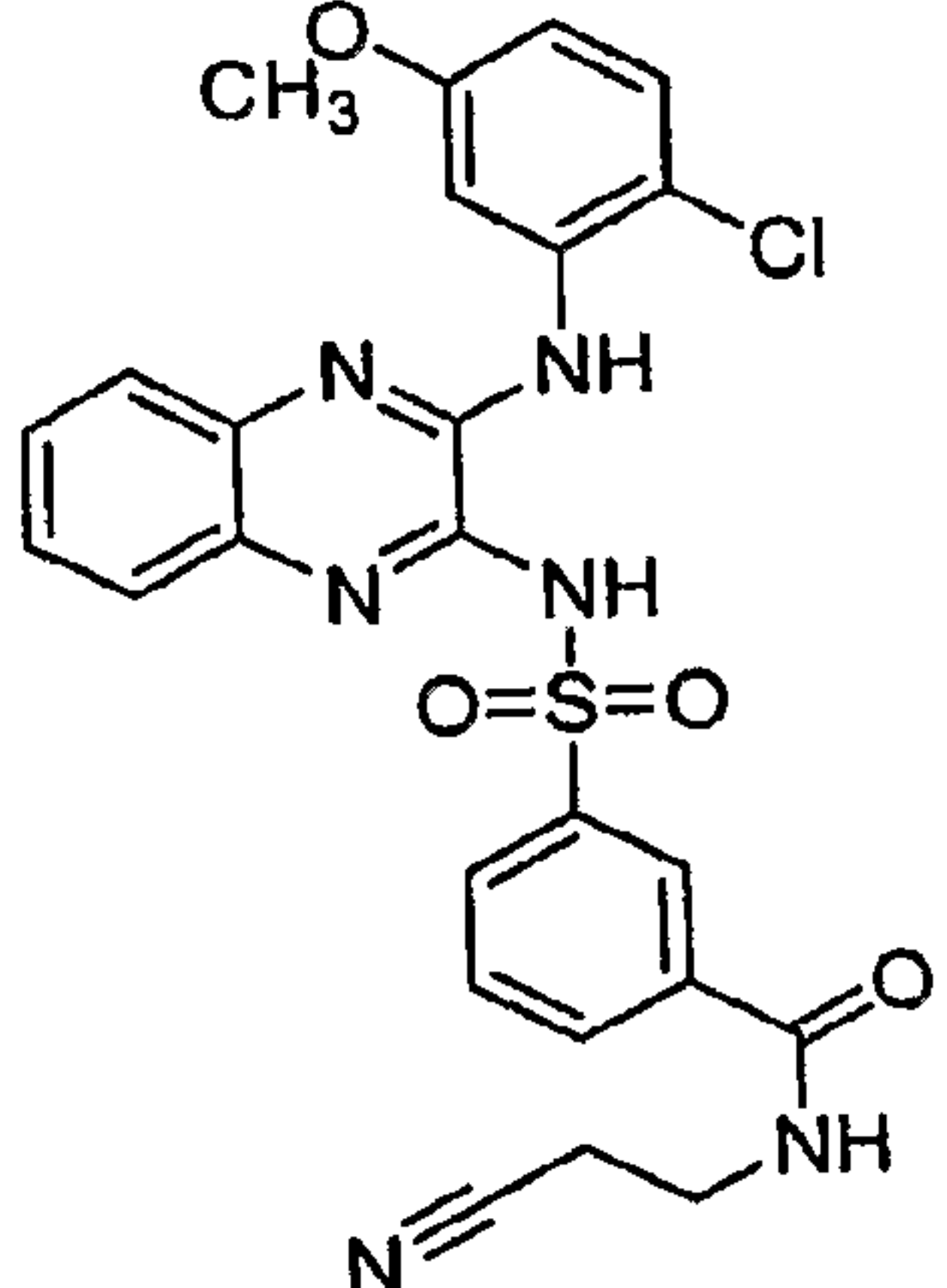
Table 1		
Cpd. No.	Structure	IUPAC Name
740		<i>N</i> -(3-{{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-[(2,2-dimethylhydrazino)carbonyl]benzenesulfonamide
741		3-{{{[3-{{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}}- <i>N</i> -[3-(1 <i>H</i> -imidazol-1-yl)propyl]benzamide
742		3-{{{[3-{{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}}- <i>N</i> -[3-(diethylamino)propyl]benzamide
743		3-{{{[3-{{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}}- <i>N</i> -(2-cyanoethyl)benzamide

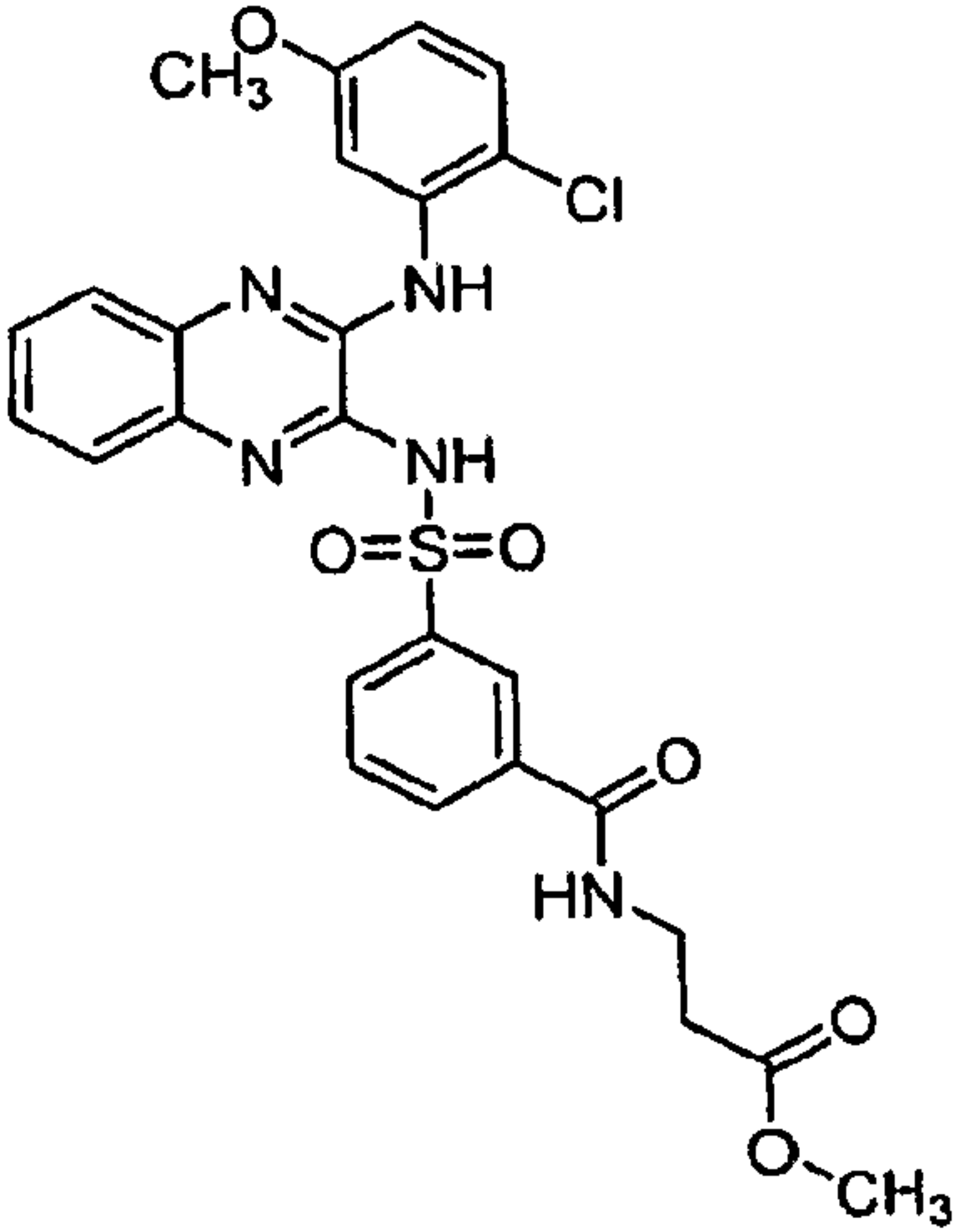
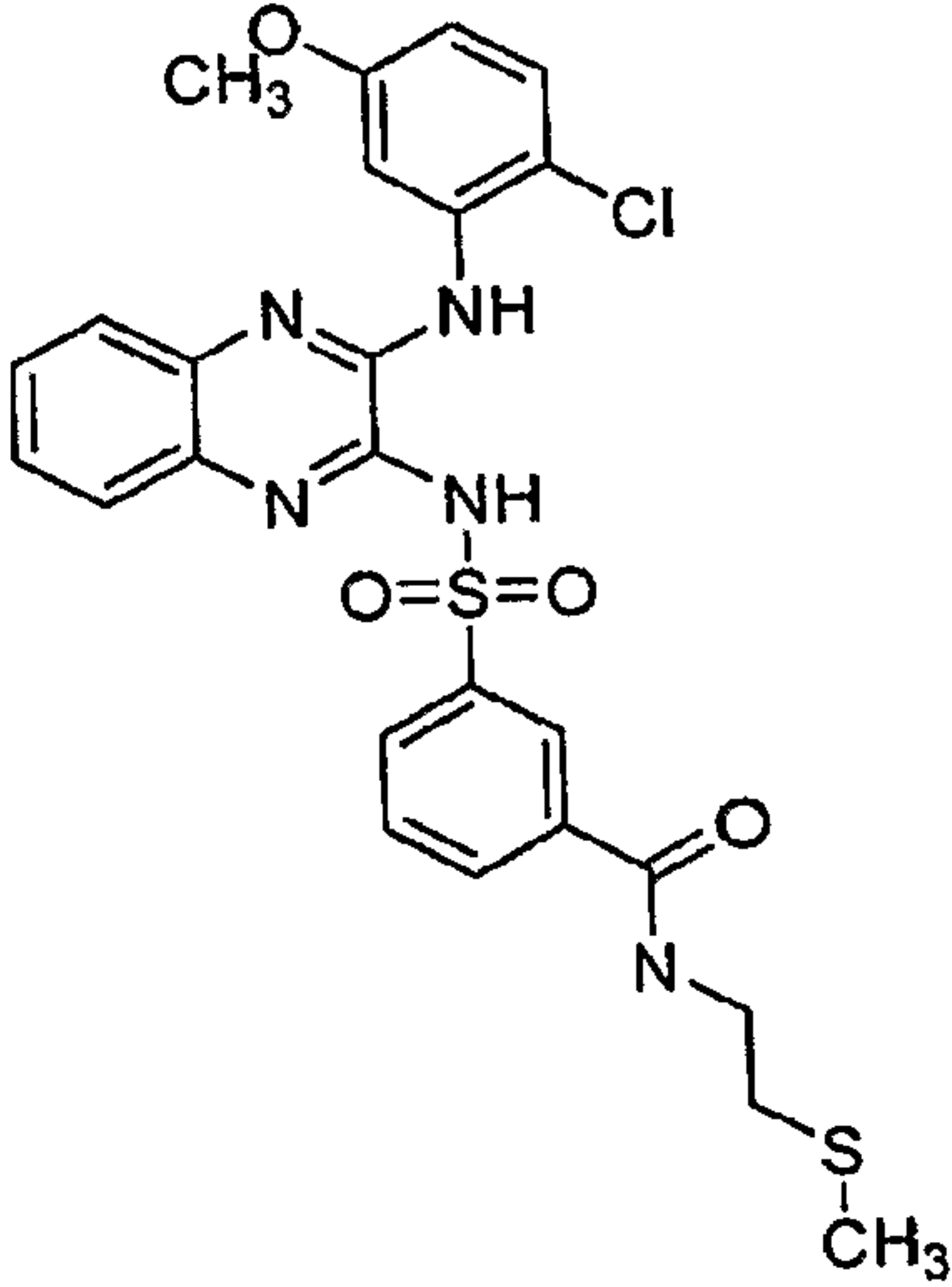
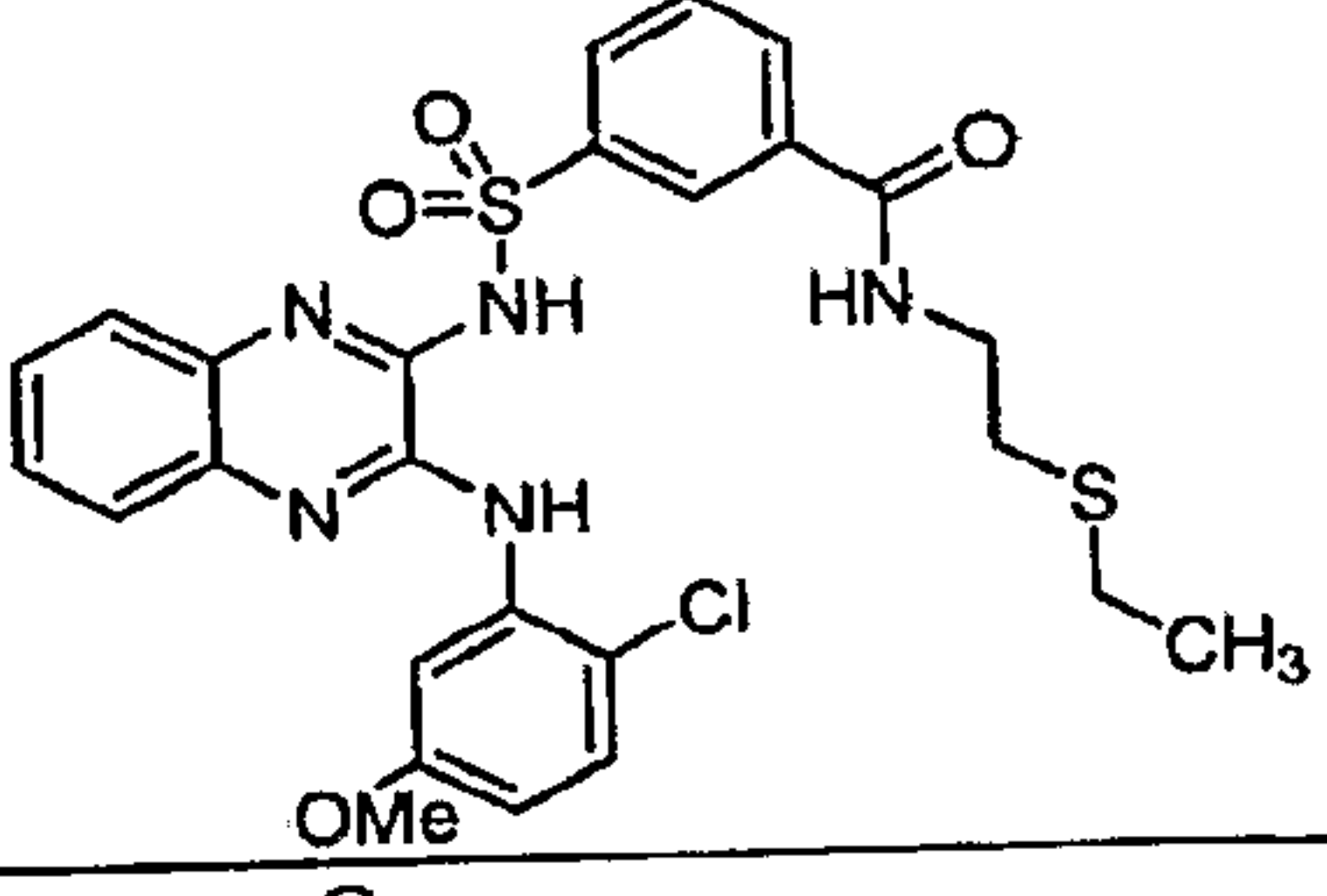
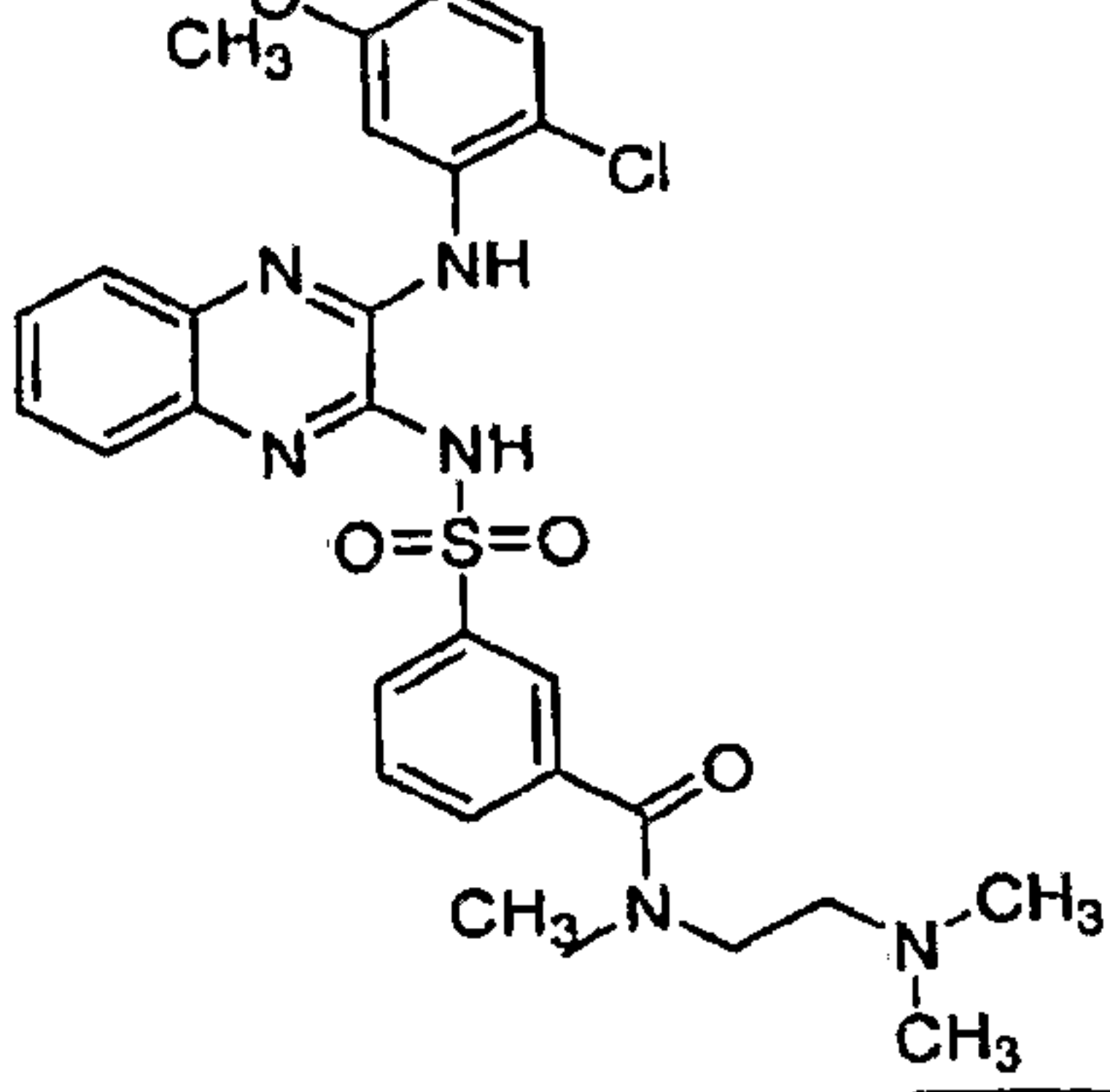
Table 1		
Cpd. No.	Structure	IUPAC Name
744		methylN-[(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)carbonyl]-beta-alaninate
745		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}-N-[2-(methylthio)ethyl]benzamide
746		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}-N-[2-(ethylthio)ethyl]benzamide
747		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}-N-[2-(dimethylamino)ethyl]-N-ethylbenzamide

Table 1		
Cpd. No.	Structure	IUPAC Name
748		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-[3-(2-oxopyrrolidin-1-yl)propyl]benzamide
749		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-(2-pyridin-4-ylethyl)benzamide
750		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-[3-(ethyloxy)propyl]benzamide
751		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-(3-morpholin-4-ylpropyl)benzamide
752		3-[[[(3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-[3-(methyloxy)propyl]benzamide

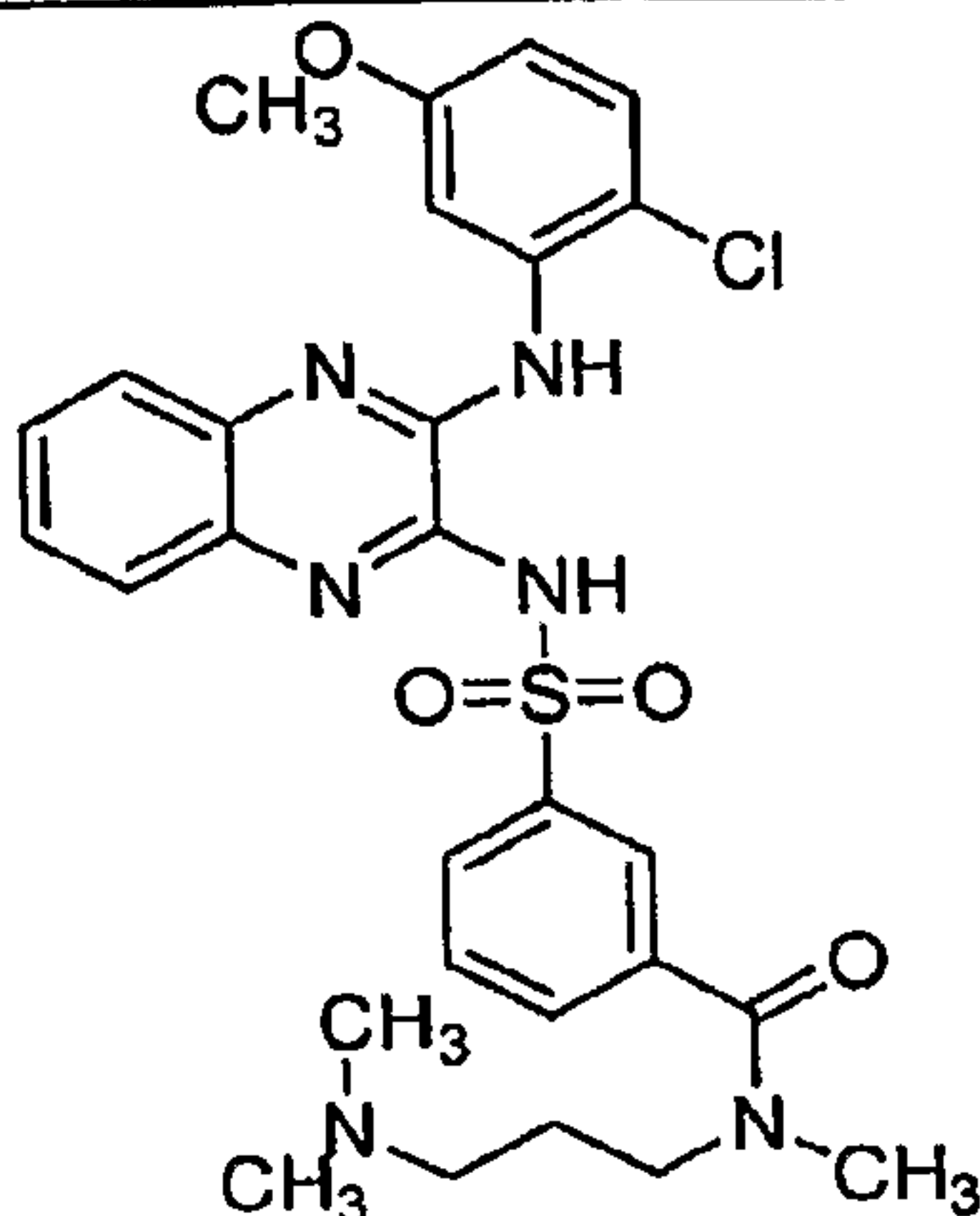
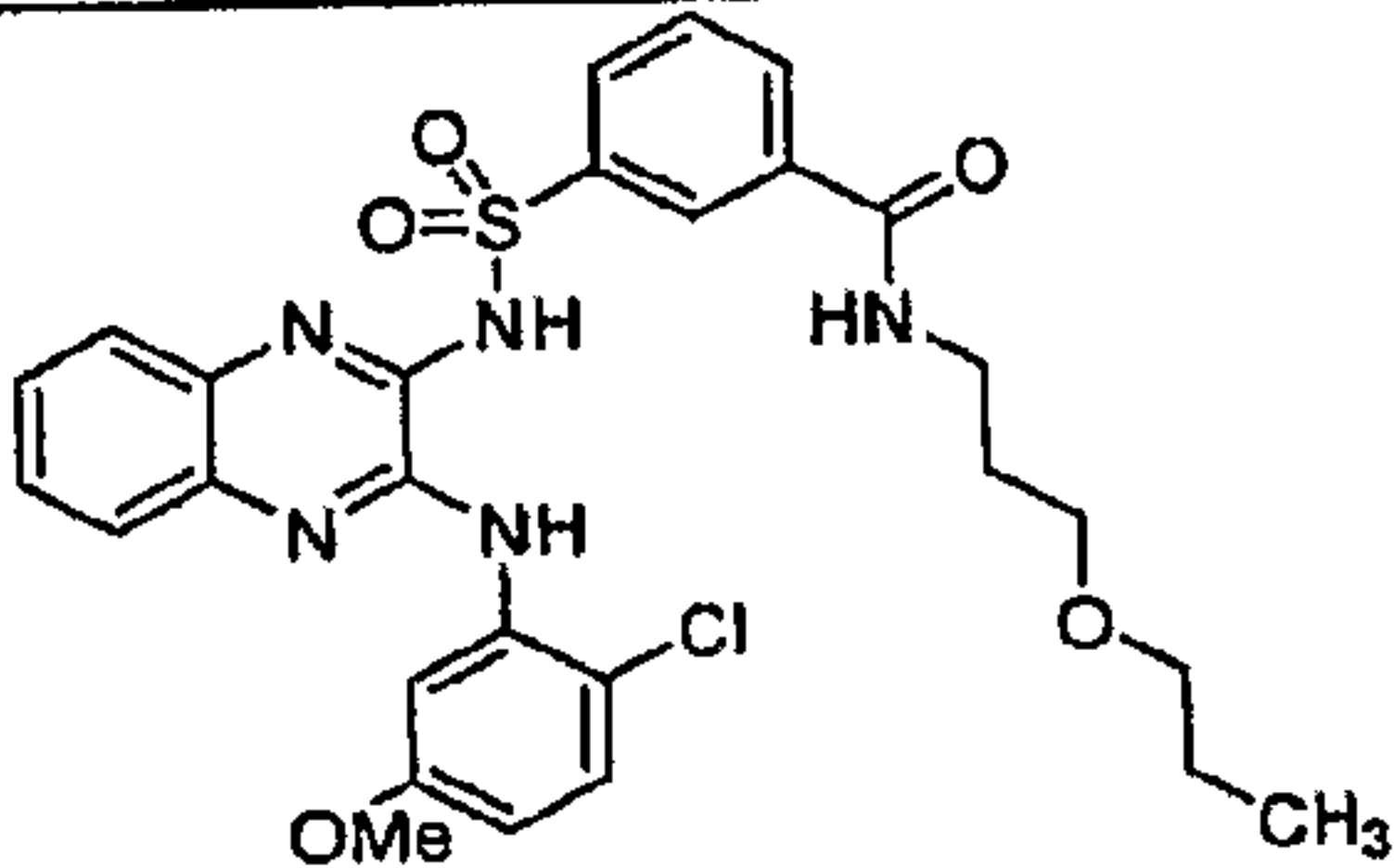
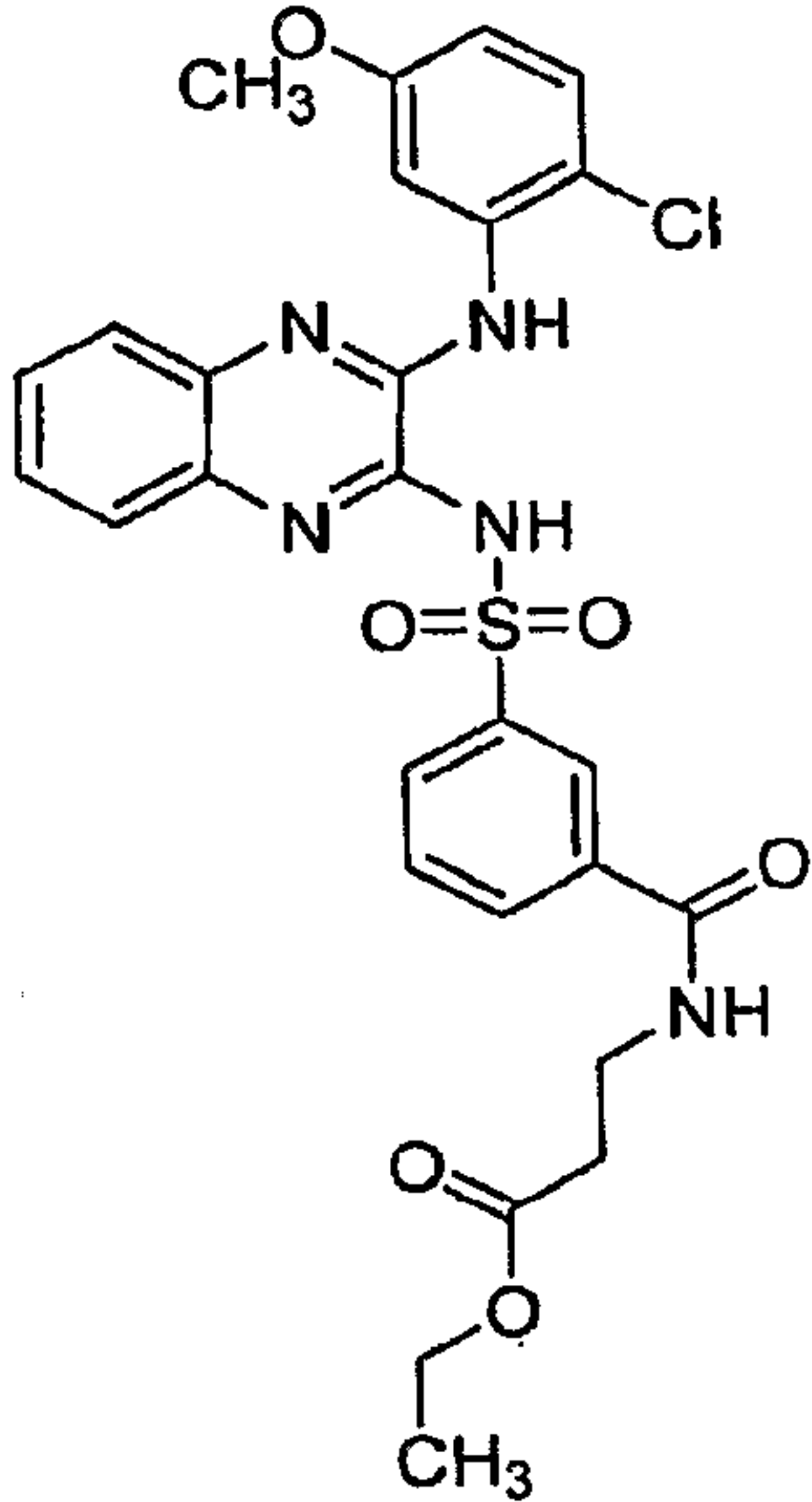
Table 1		
Cpd. No.	Structure	IUPAC Name
753		3-[[[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-[3-(dimethylamino)propyl]-N-methylbenzamide
754		3-[[[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]-N-[3-(propyloxy)propyl]benzamide
755		ethylN-[(3-{[[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl]phenyl)carbonyl]-beta-alaninate

Table 1		
Cpd. No.	Structure	IUPAC Name
756		3-[[3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}-N-{3-[(1-methylethyl)oxy]propyl}benzamide
757		3-[[3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}-N-(1,1-dimethyl-2-piperidin-1-ylethyl)benzamide
758		3-[[3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}-N-methyl-N-propylbenzamide
759		3-[[3-[[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl]amino]sulfonyl}-N-piperidin-1-ylbenzamide

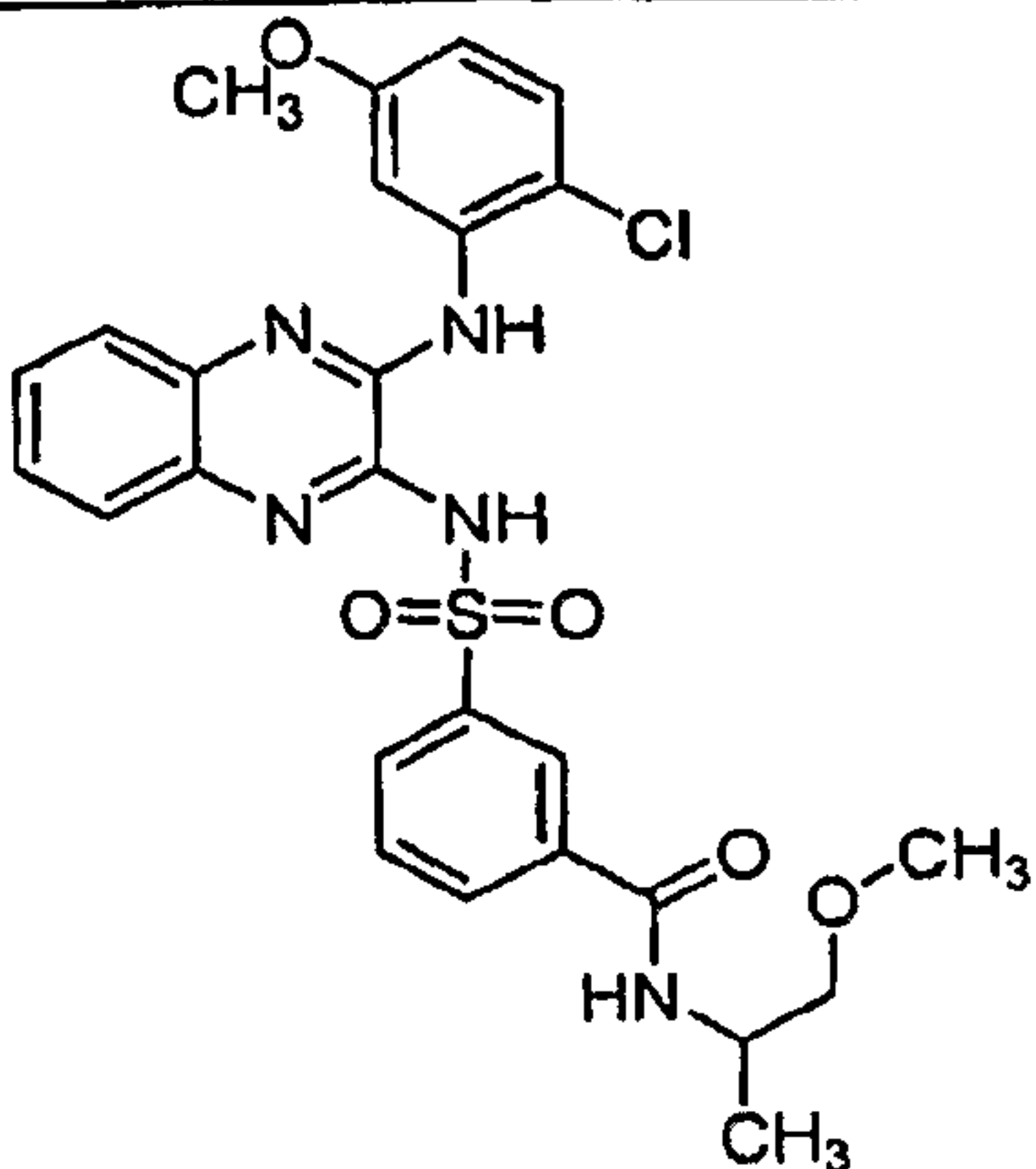
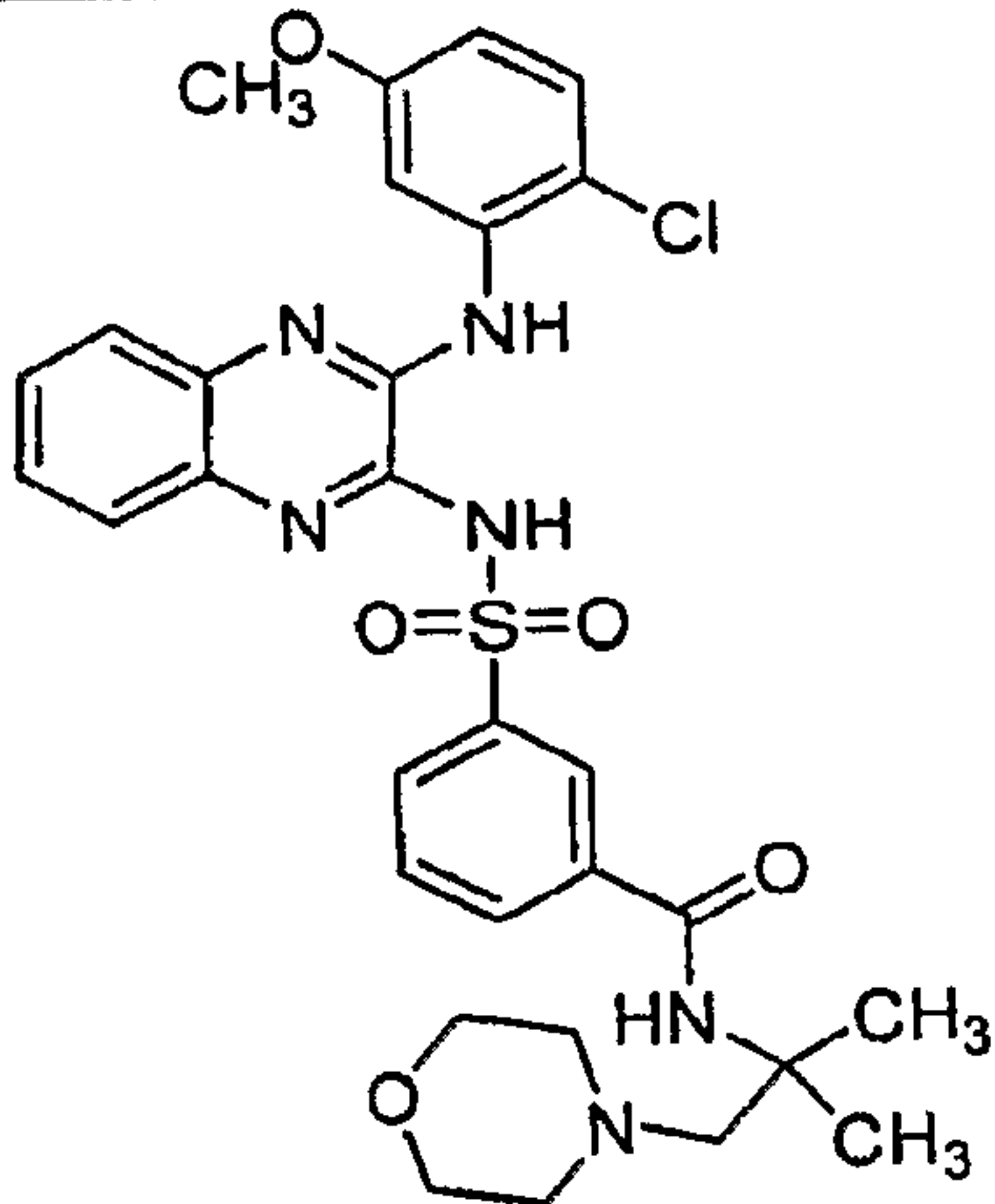
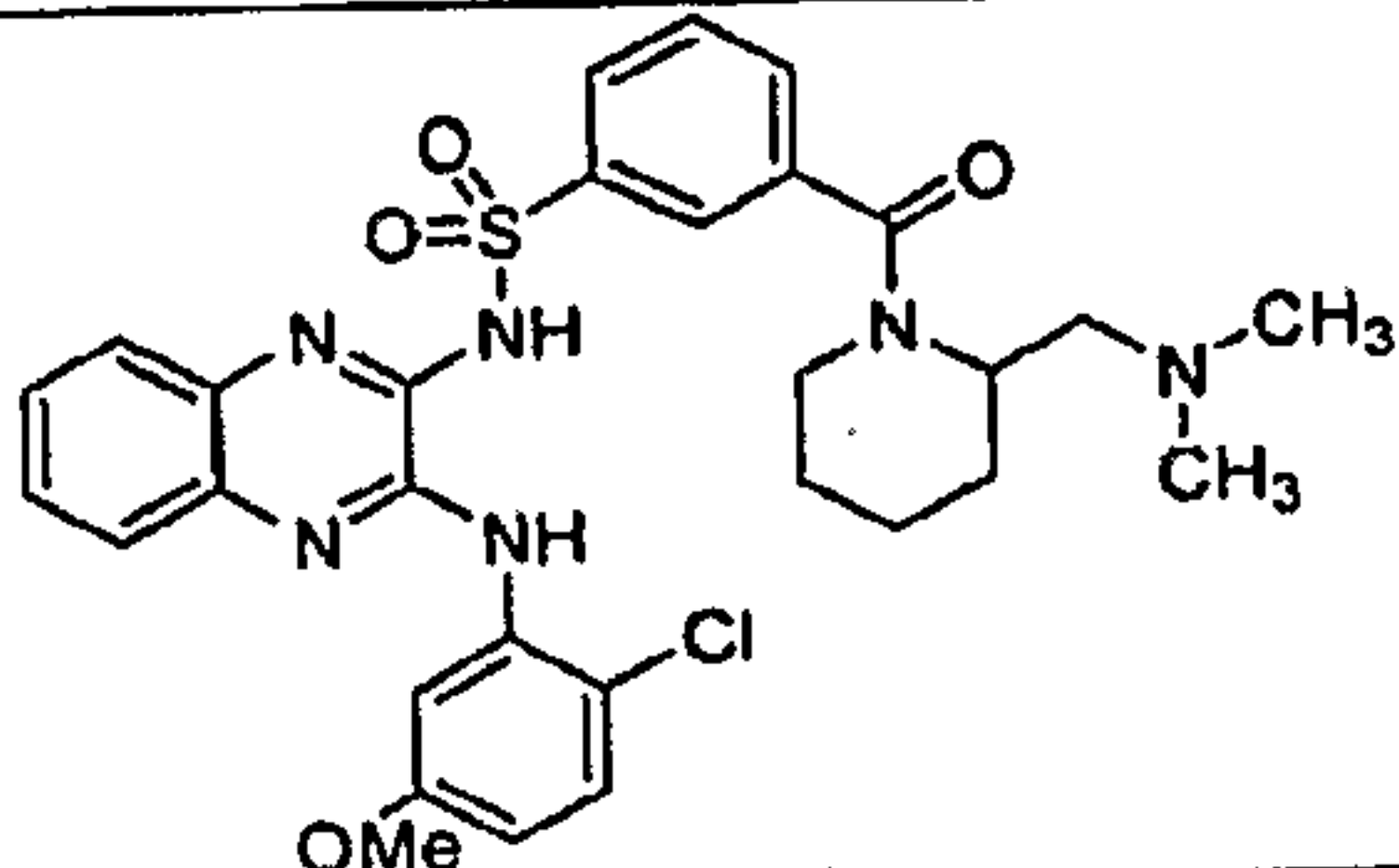
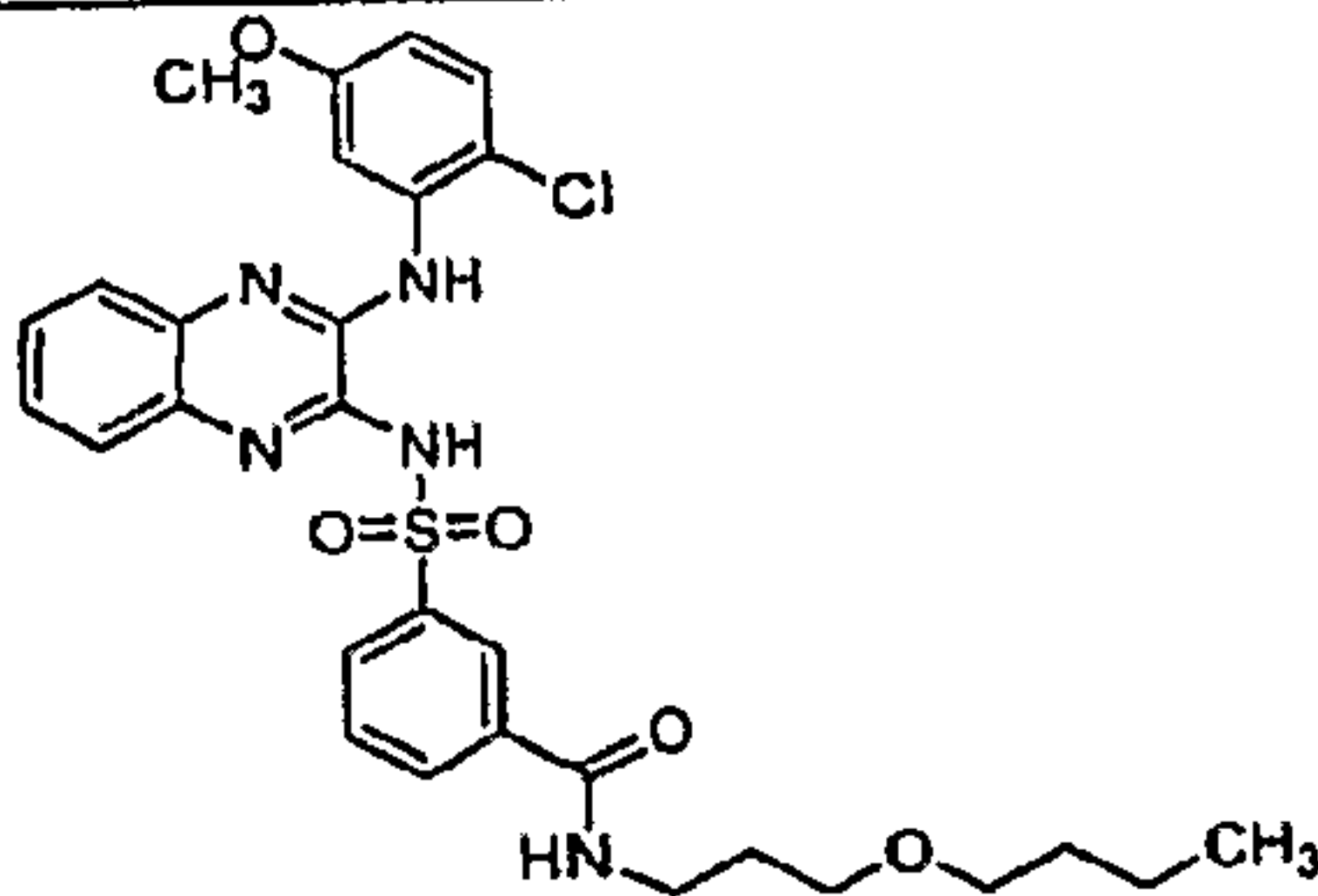
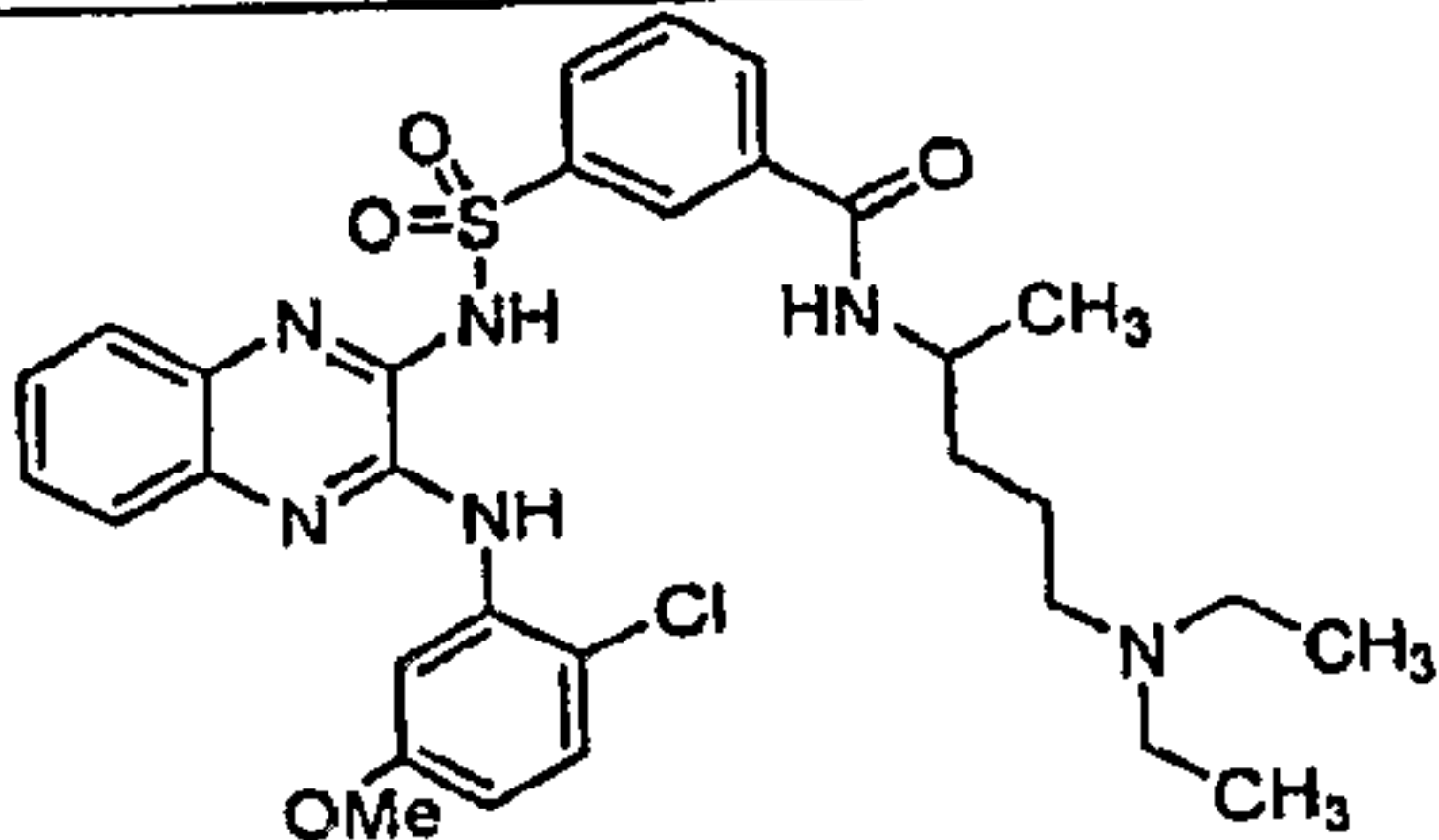
Table 1		
Cpd. No.	Structure	IUPAC Name
760		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[1-methyl-2-(methyloxy)ethyl]benzamide
761		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1,1-dimethyl-2-morpholin-4-ylethyl)benzamide
762		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-({2-[(dimethylamino)methyl]piperidin-1-yl}carbonyl)benzenesulfonamide
763		N-[3-(butyloxy)propyl]-3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide
764		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[4-(diethylamino)-1-methylbutyl]benzamide

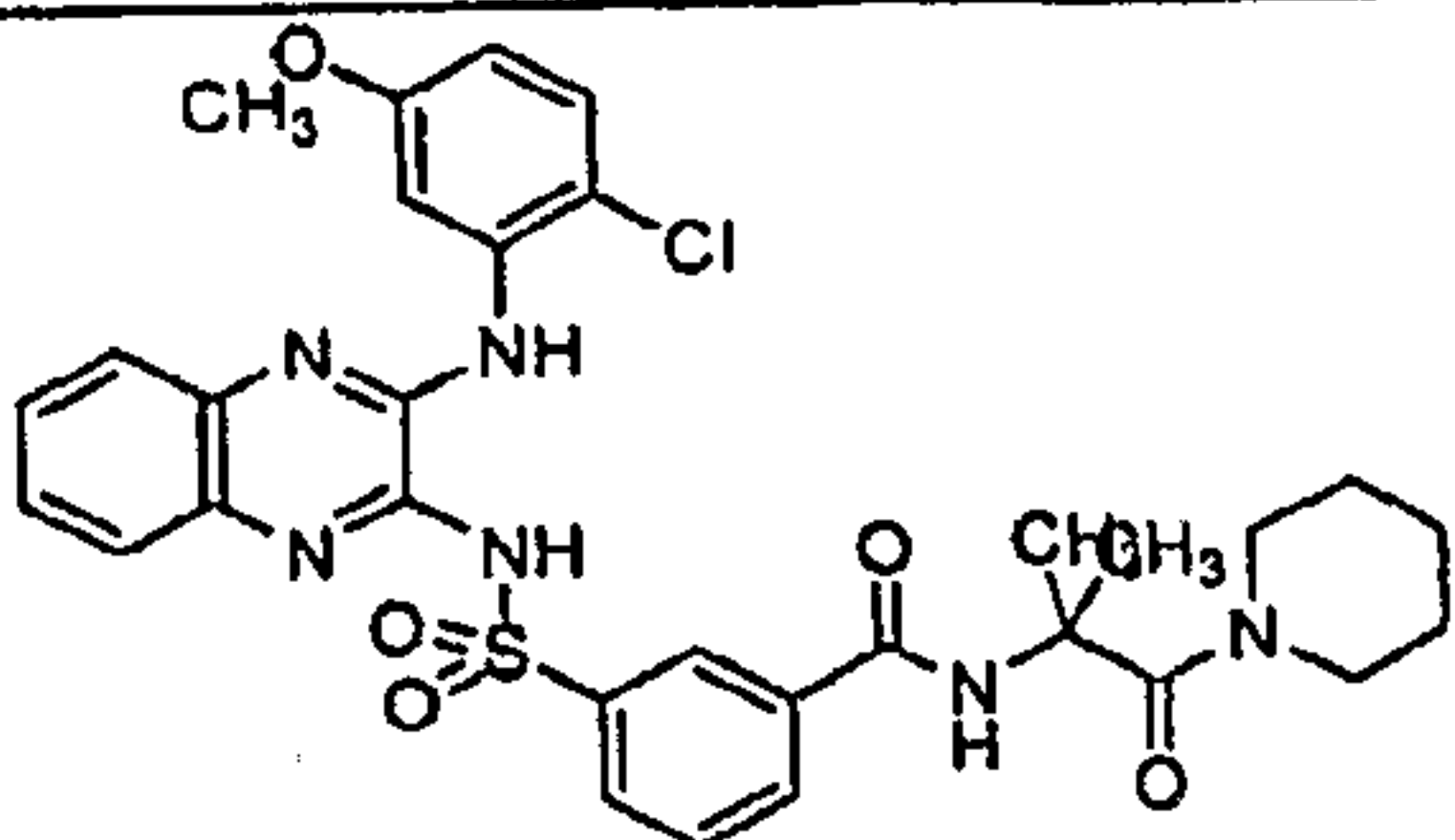
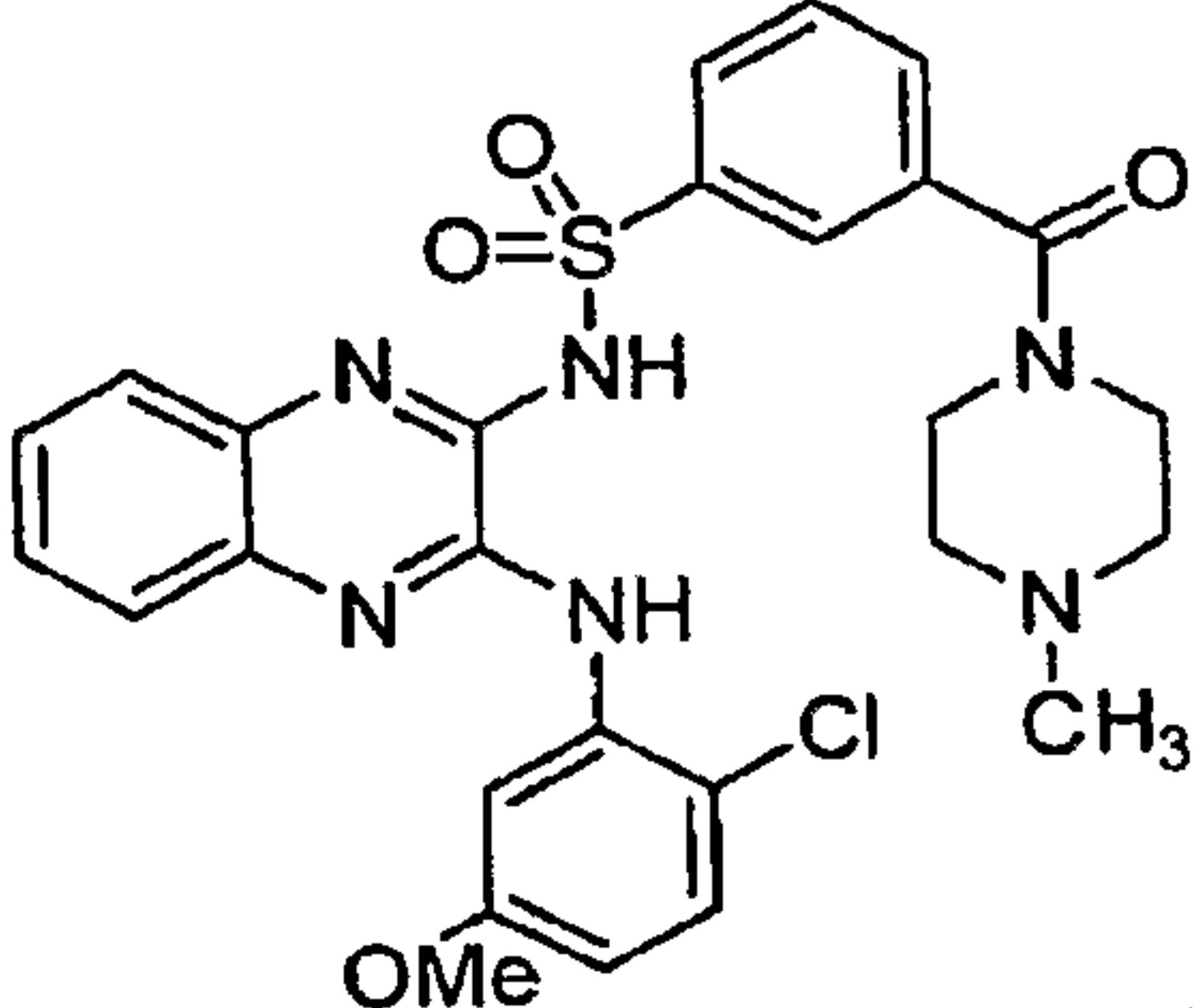
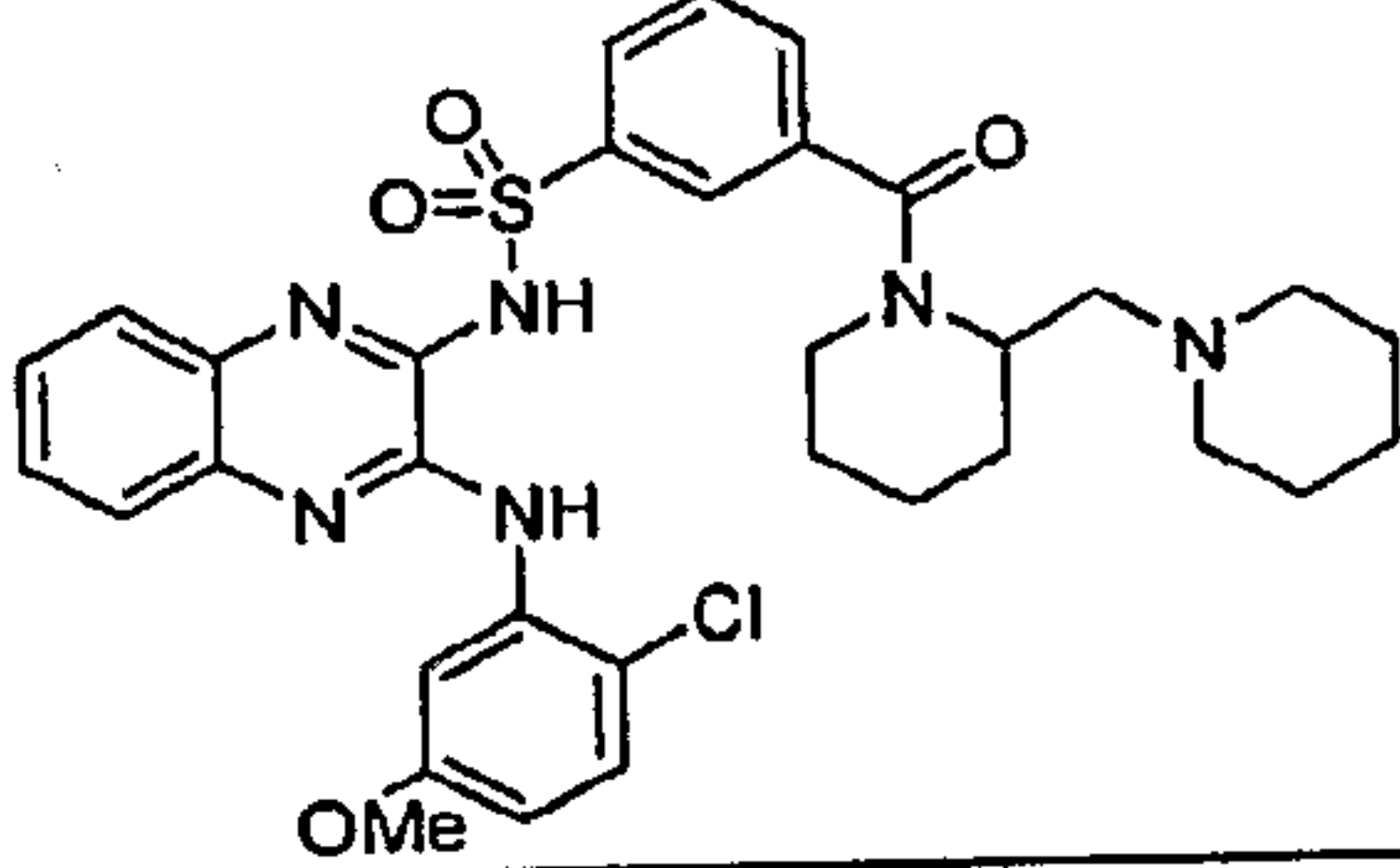
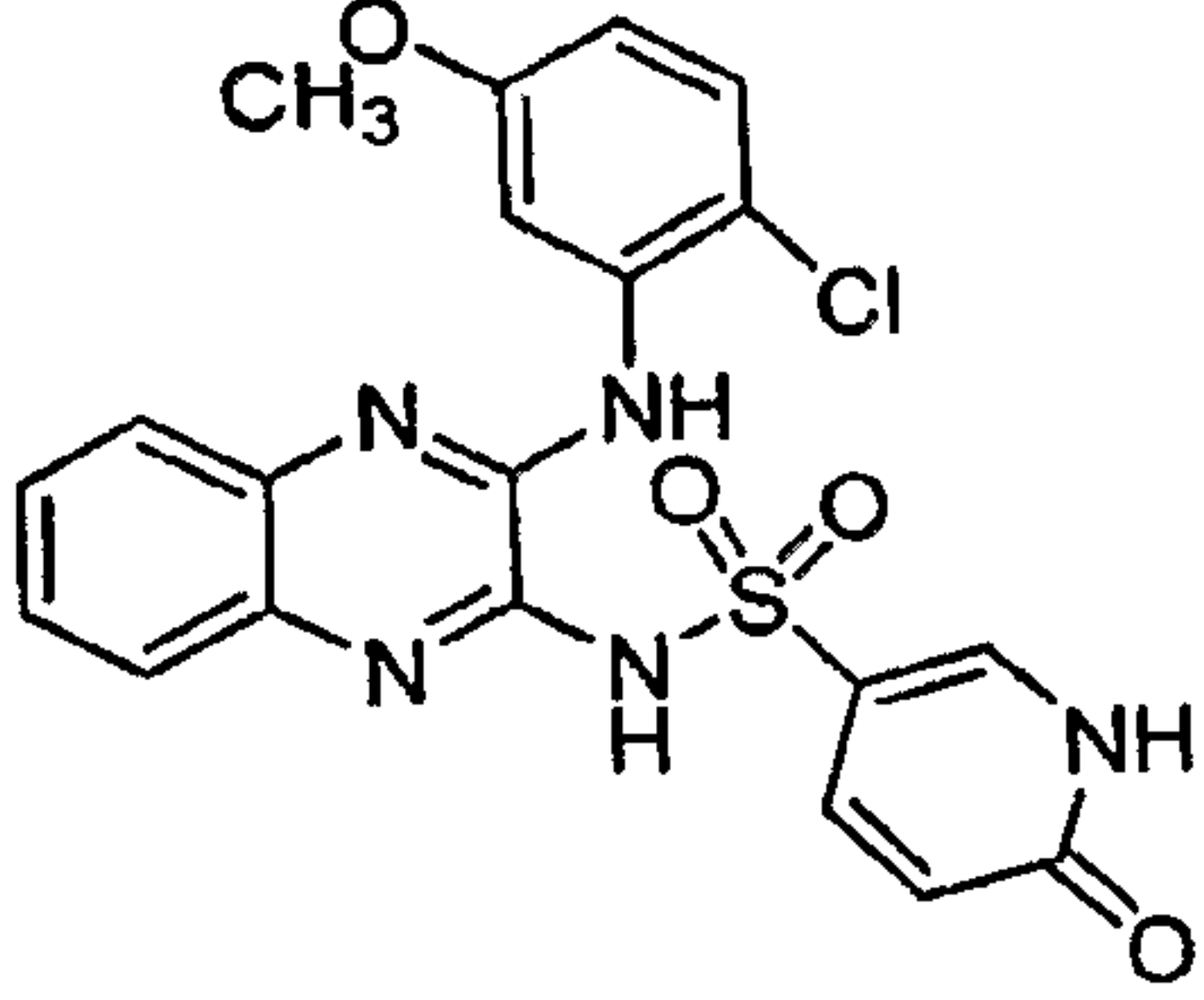
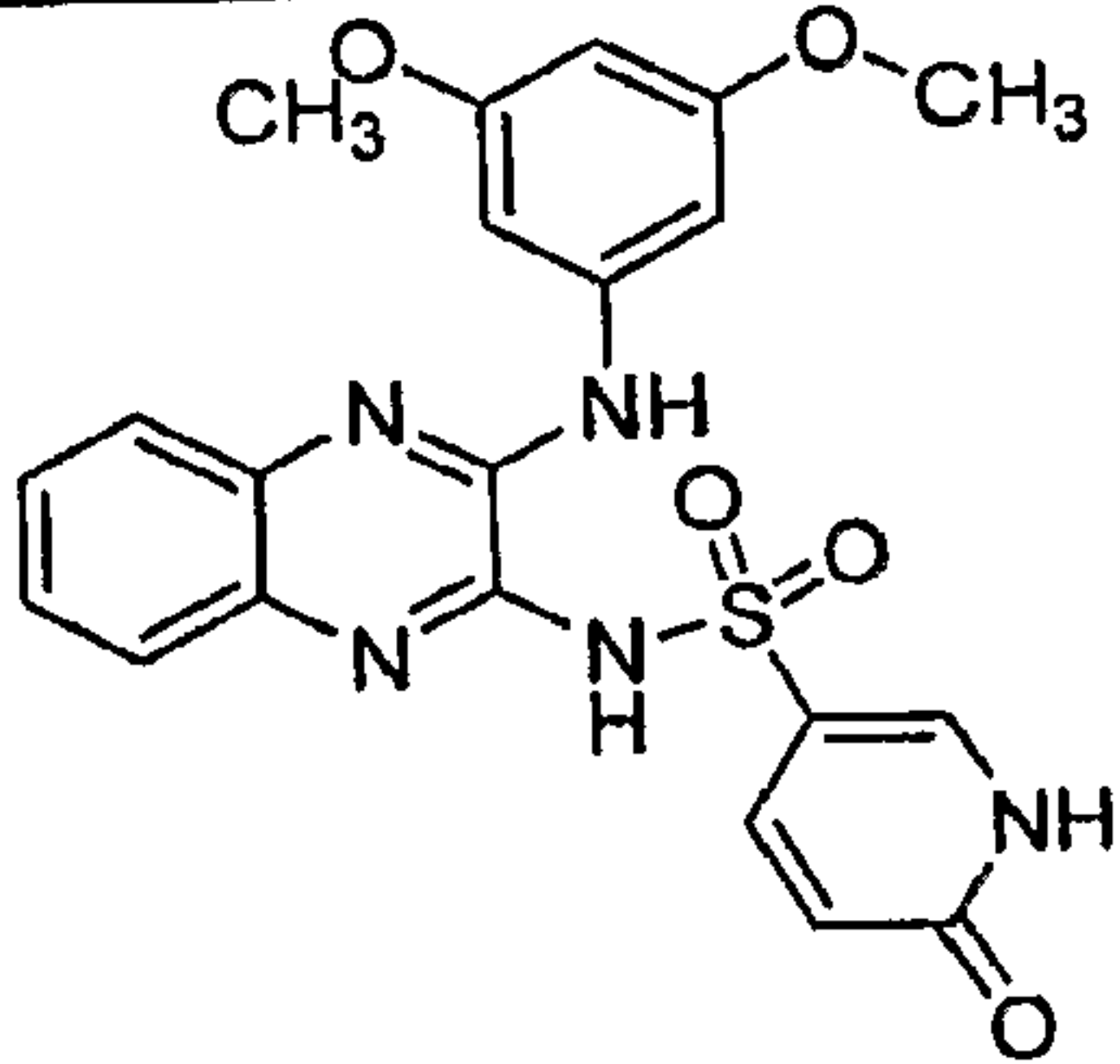
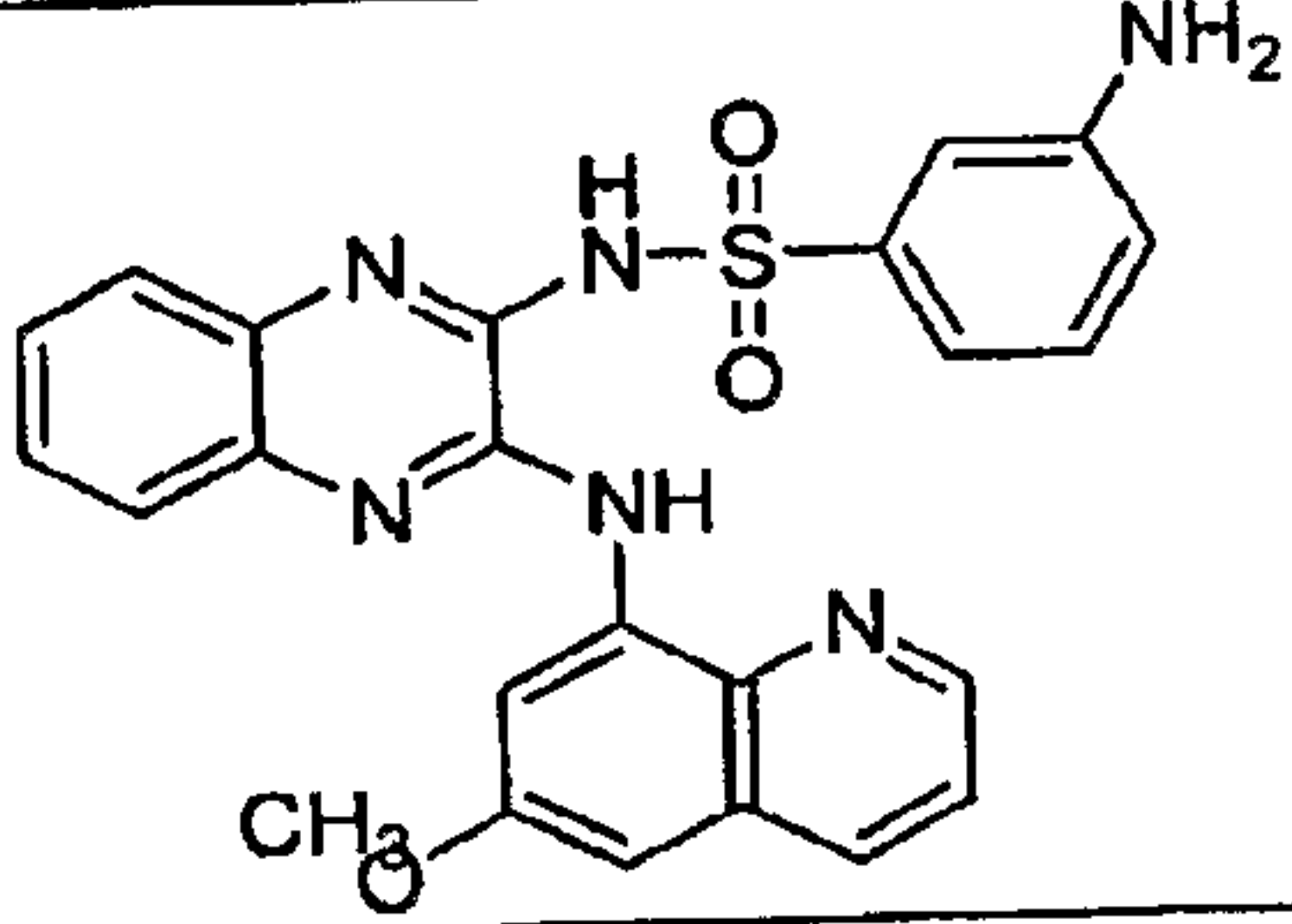
Table 1		
Cpd. No.	Structure	IUPAC Name
765		3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1,1-dimethyl-2-oxo-2-piperidin-1-ylethyl)benzamide
766		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-[(4-methylpiperazin-1-yl)carbonyl]benzenesulfonamide
767		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[2-(piperidin-1-ylmethyl)piperidin-1-yl]carbonyl}benzenesulfonamide
768		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide
769		N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide
770		3-amino-N-(3-{[6-(methyloxy)quinolin-8-yl]amino}quinoxalin-2-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
771		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)thiophene-2-sulfonamide
772		<i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-cyanobenzenesulfonamide
773		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-3-(methylamino)benzenesulfonamide
774		<i>N</i> -(2-{[3,5-bis(methoxy)phenyl]amino}pyrido[2,3-b]pyrazin-3-yl)-3-nitrobenzenesulfonamide
775		<i>N</i> -(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(1-{2-(dimethylamino)ethyl}amino)ethyl)benzenesulfonamide
776		3-amino- <i>N</i> -(3-{[3-(methyloxy)-5-nitrophenyl]amino}quinoxalin-2-yl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
777		3-acetyl-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
778		3-amino-N-(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
779		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-N'-(2-(dimethylamino)ethyl)benzene-1,3-disulfonamide
780		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-N'-(3-(dimethylamino)propyl)benzene-1,3-disulfonamide
781		N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-chloropyridine-3-sulfonamide
782		N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{5-[(dimethylamino)methyl]-1,3,4-oxadiazol-2-yl}benzenesulfonamide
783		N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-{[2-(dimethylamino)ethyl]amino}pyridine-3-sulfonamide

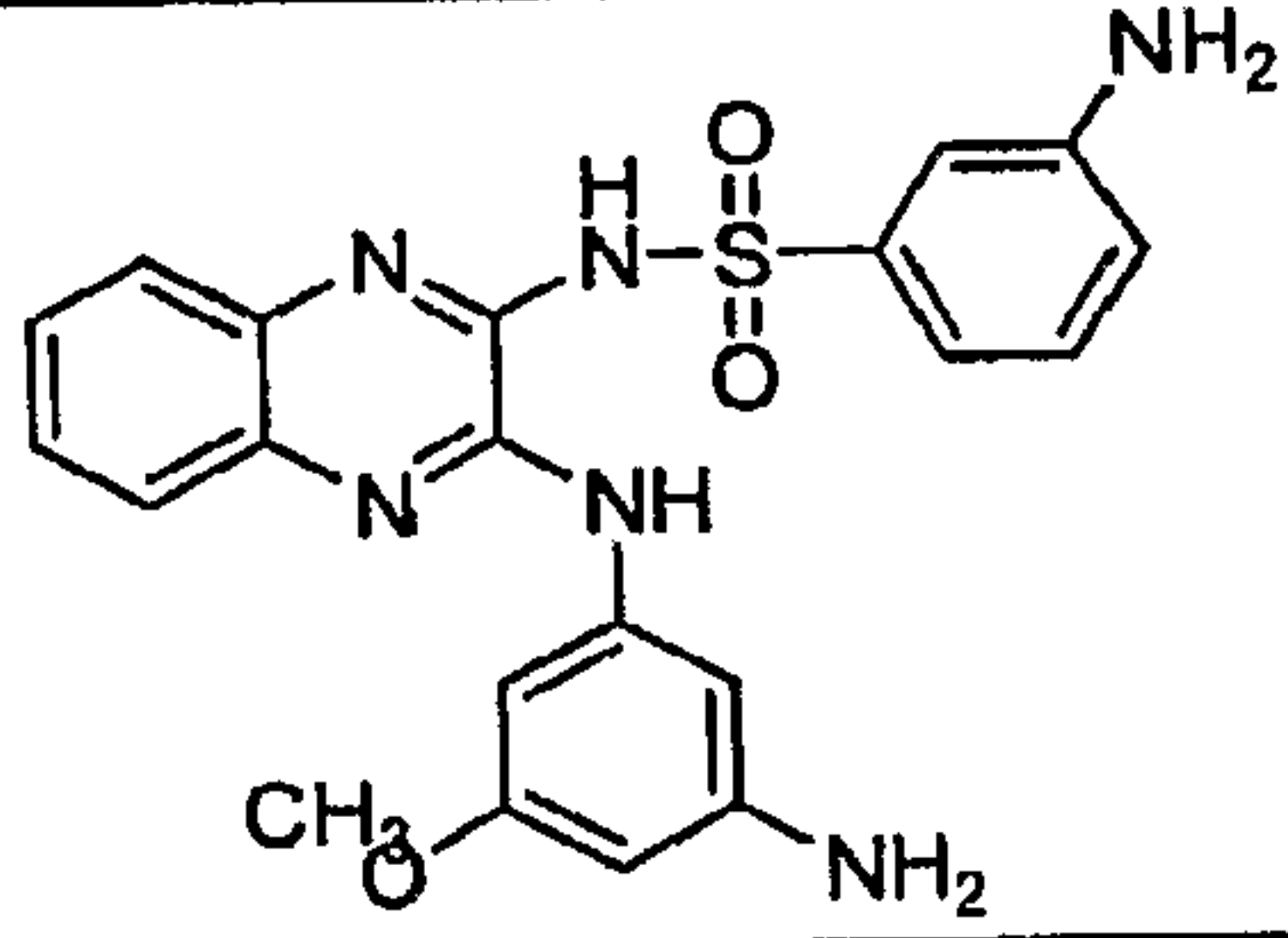
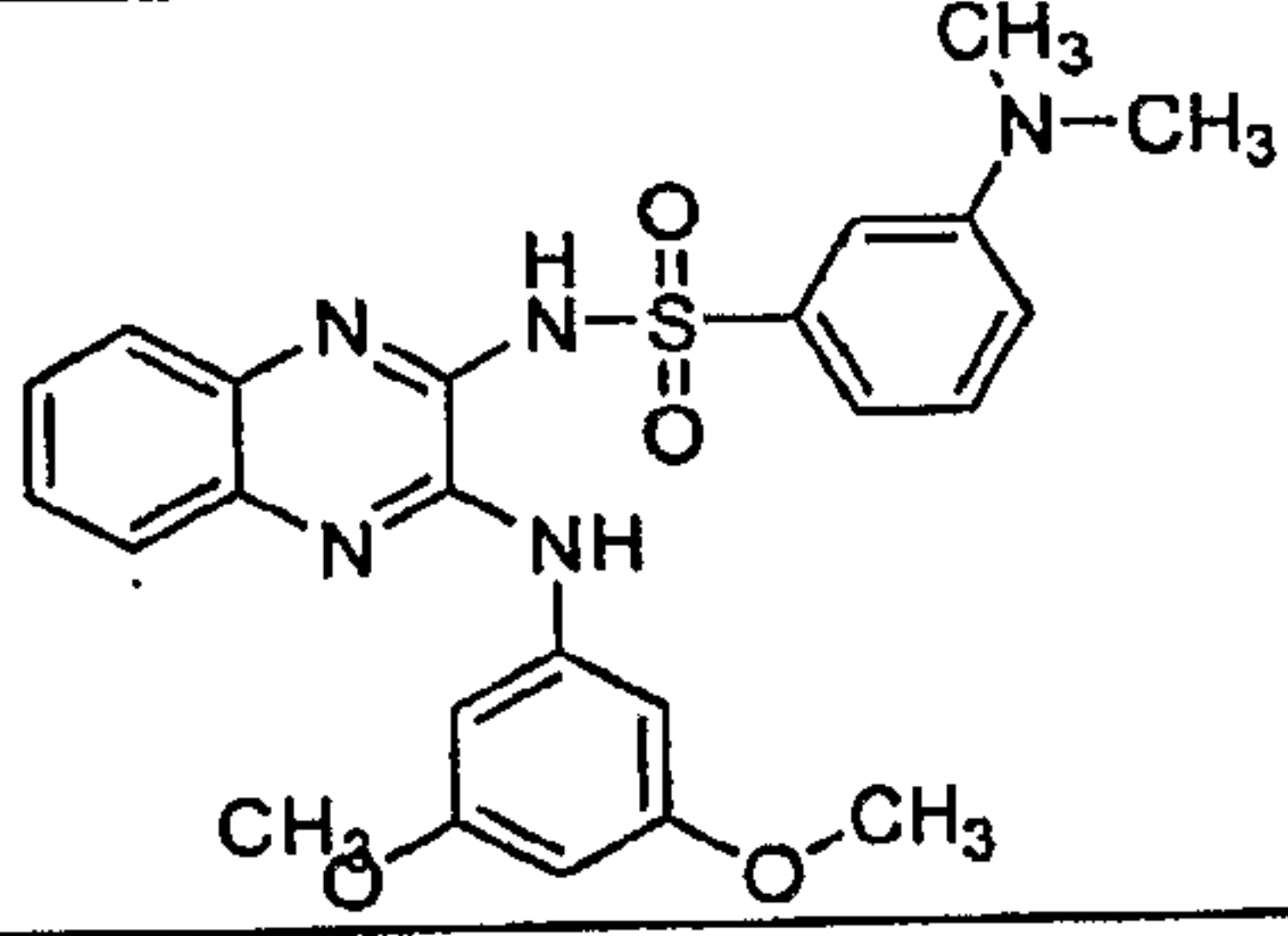
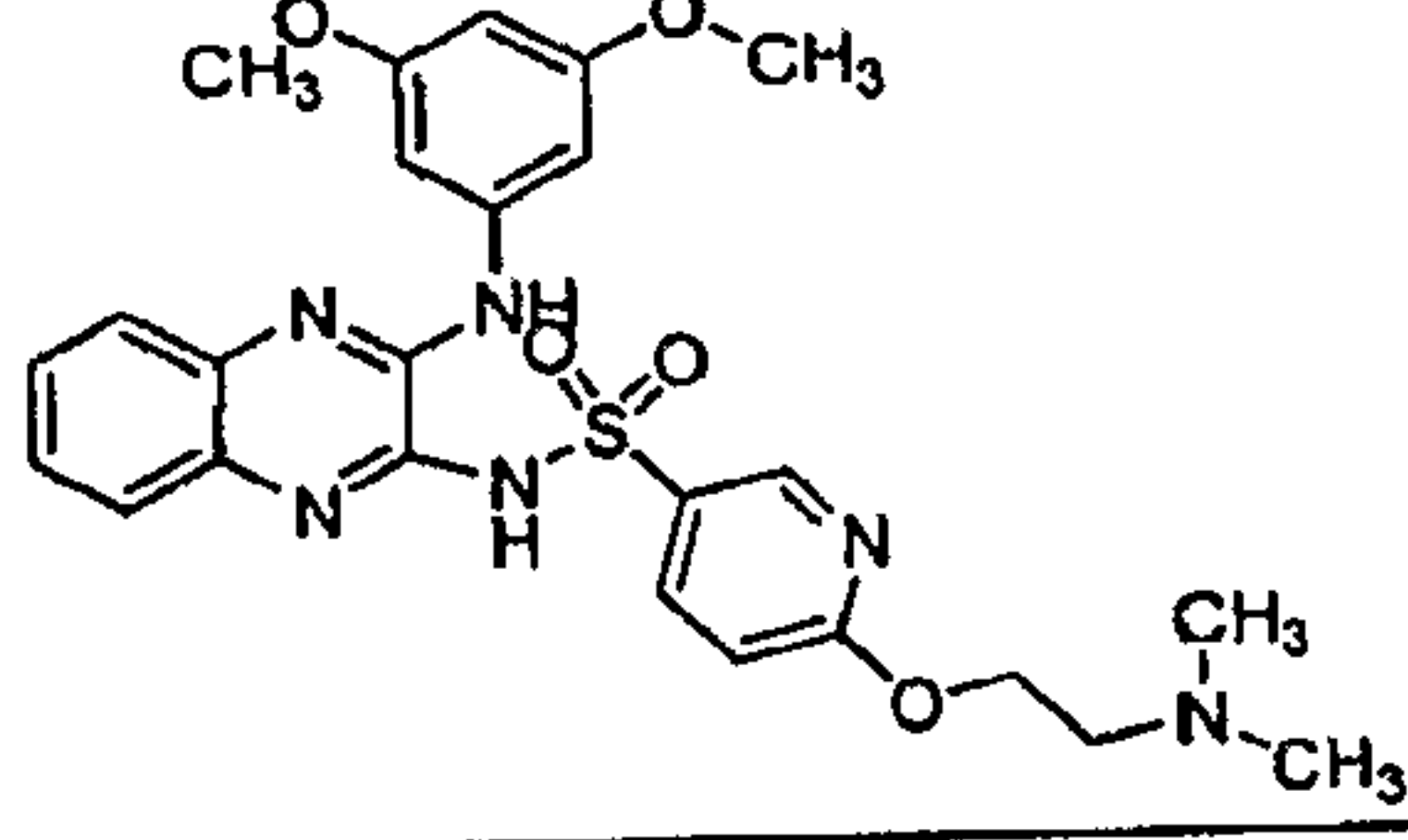
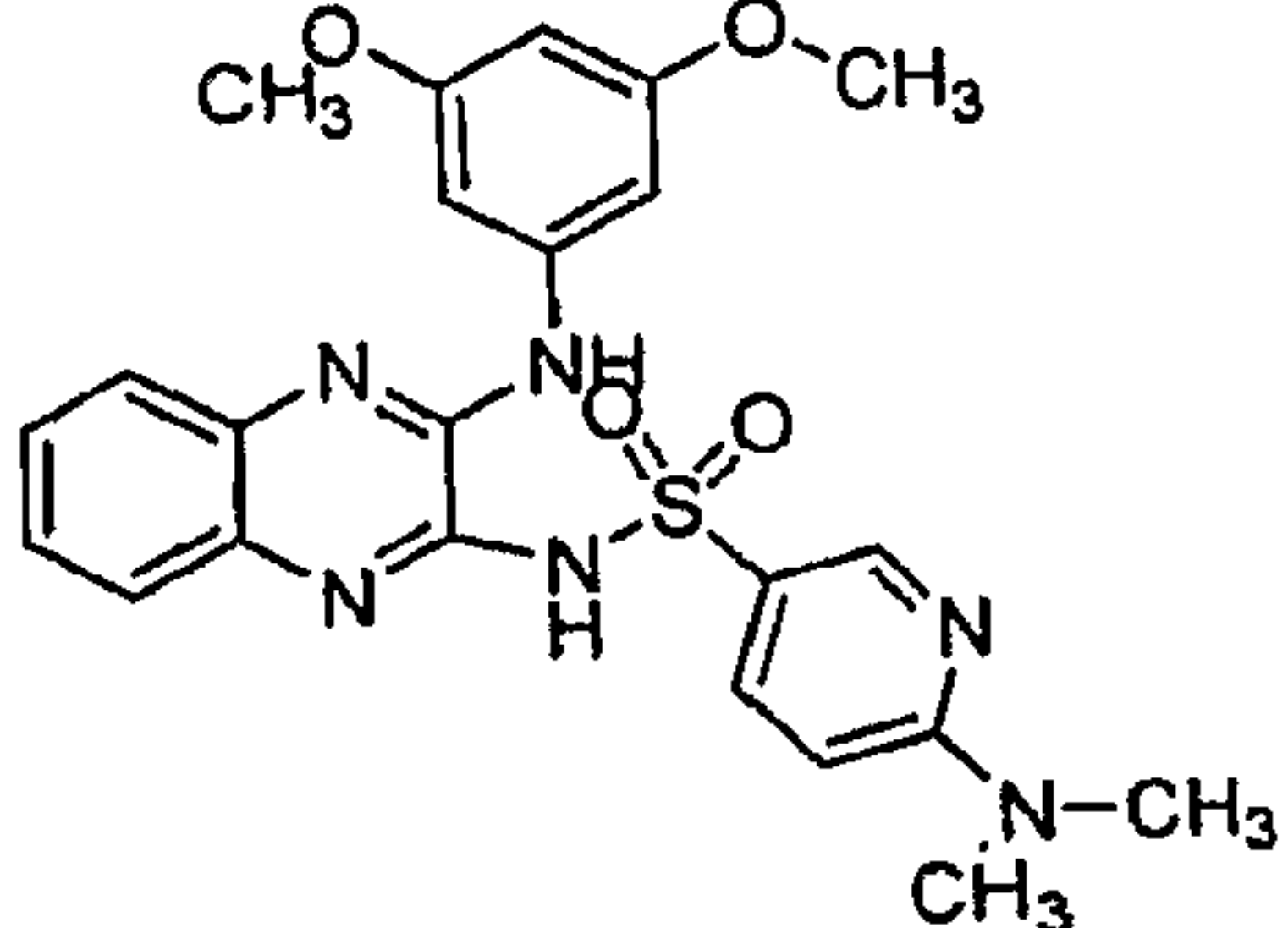
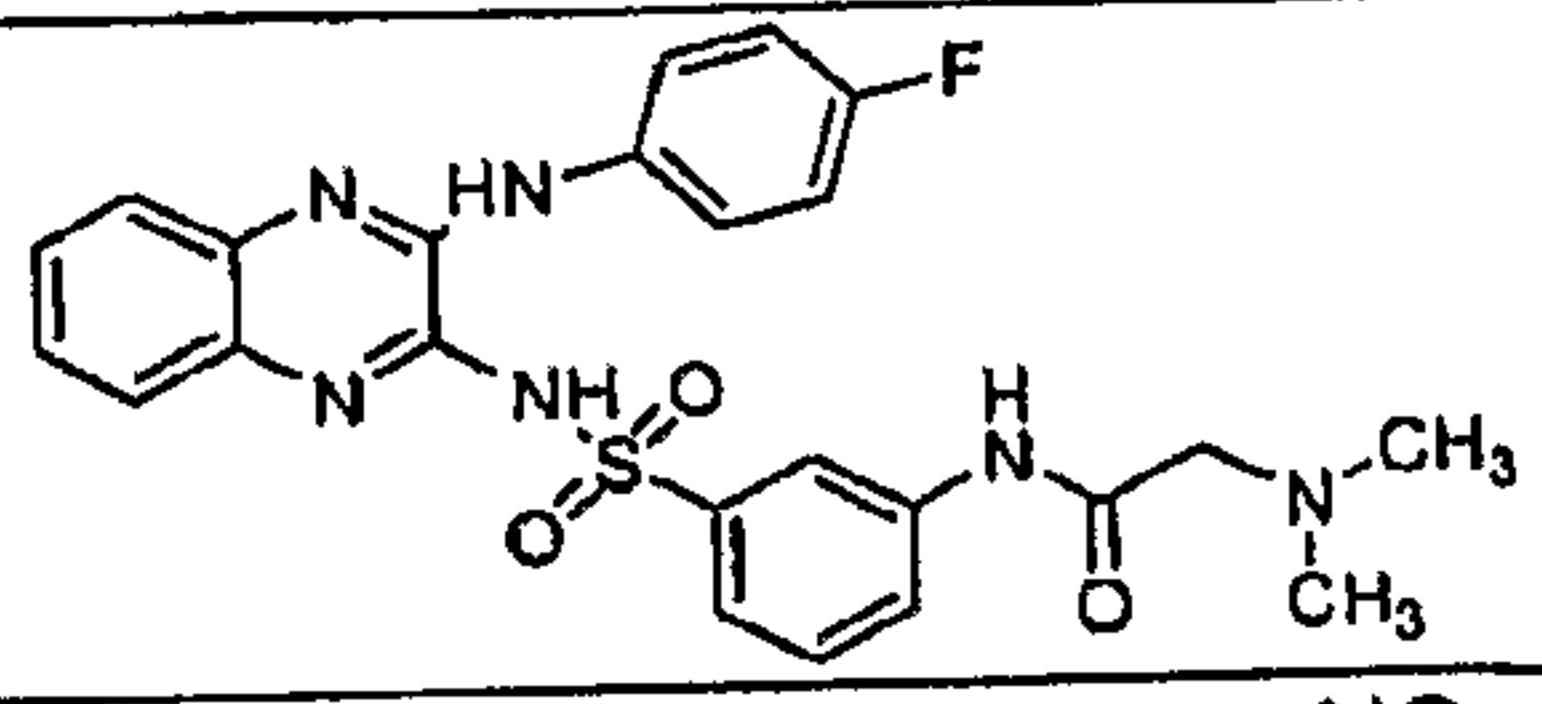
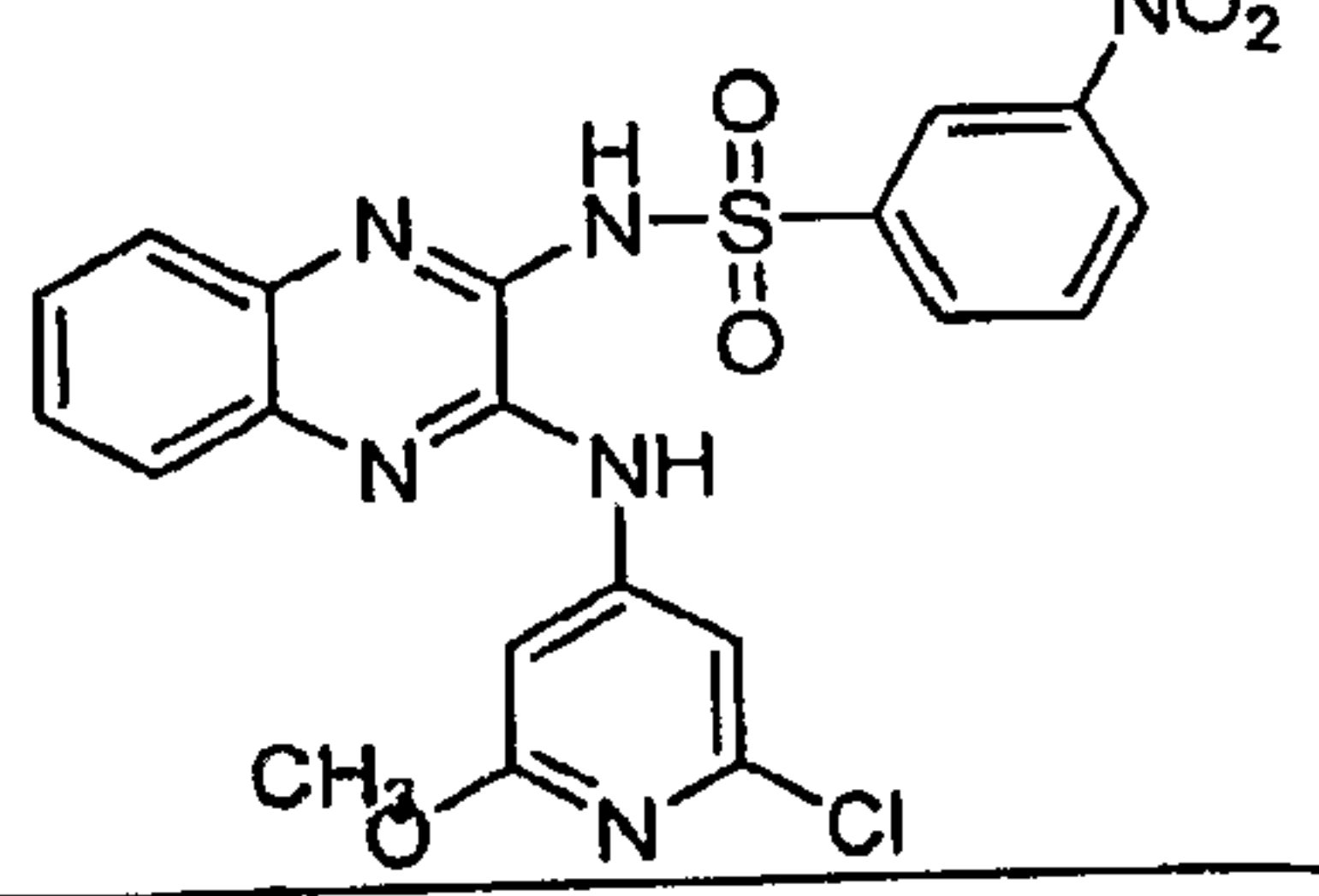
Table 1		
Cpd. No.	Structure	IUPAC Name
784		3-amino-N-(3-{[3-amino-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide
785		N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(dimethylamino)benzenesulfonamide
786		N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-{[2-(dimethylamino)ethyl]oxy}pyridine-3-sulfonamide
787		N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-(dimethylamino)pyridine-3-sulfonamide
788		N-{3-[(3-[(4-fluorophenyl)amino]quinoxalin-2-yl)amino]sulfonylphenyl}-N-2,N-2-dimethylglycinamide
789		N-(3-{[2-chloro-6-(methyloxy)pyridin-4-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide

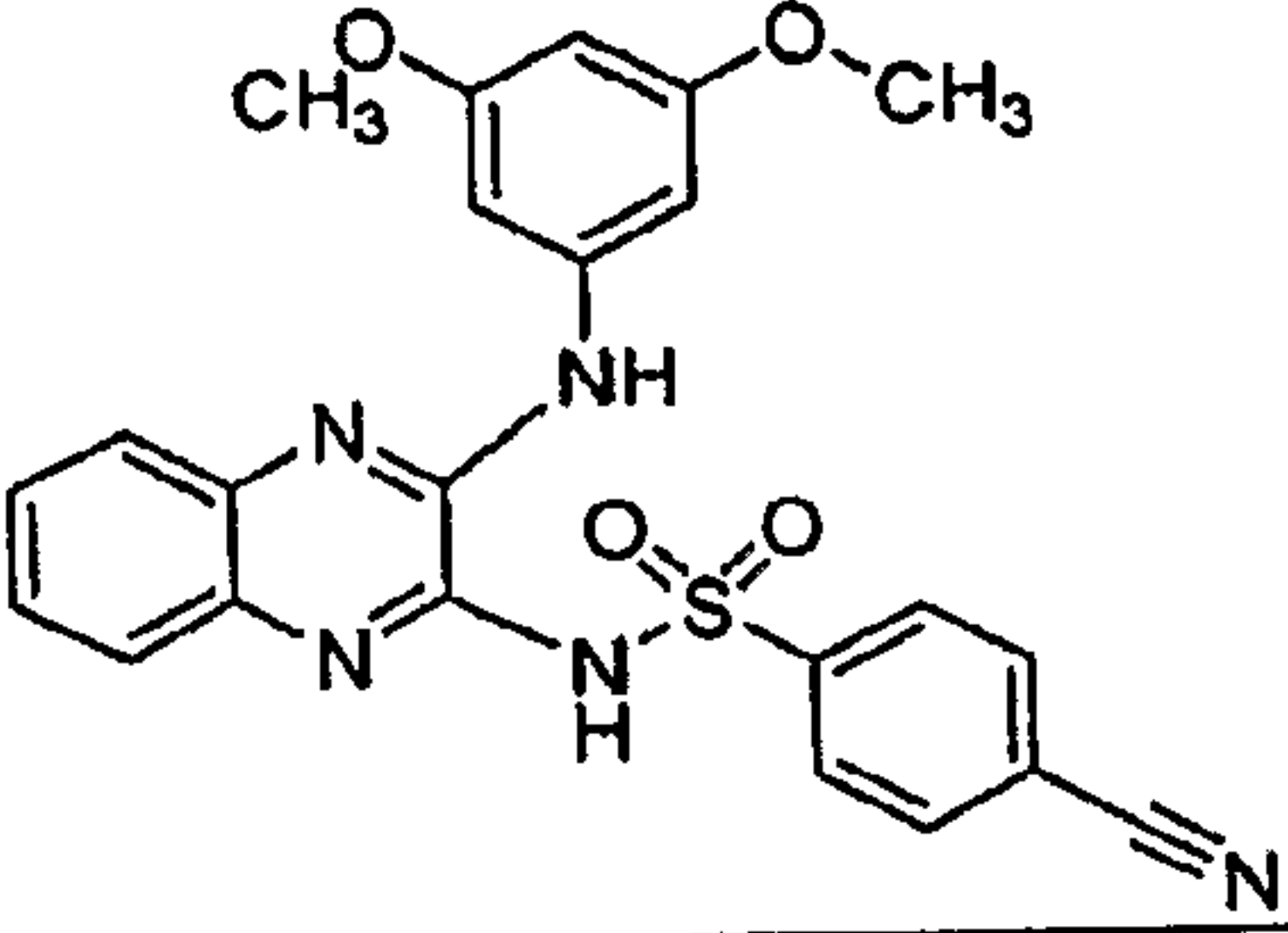
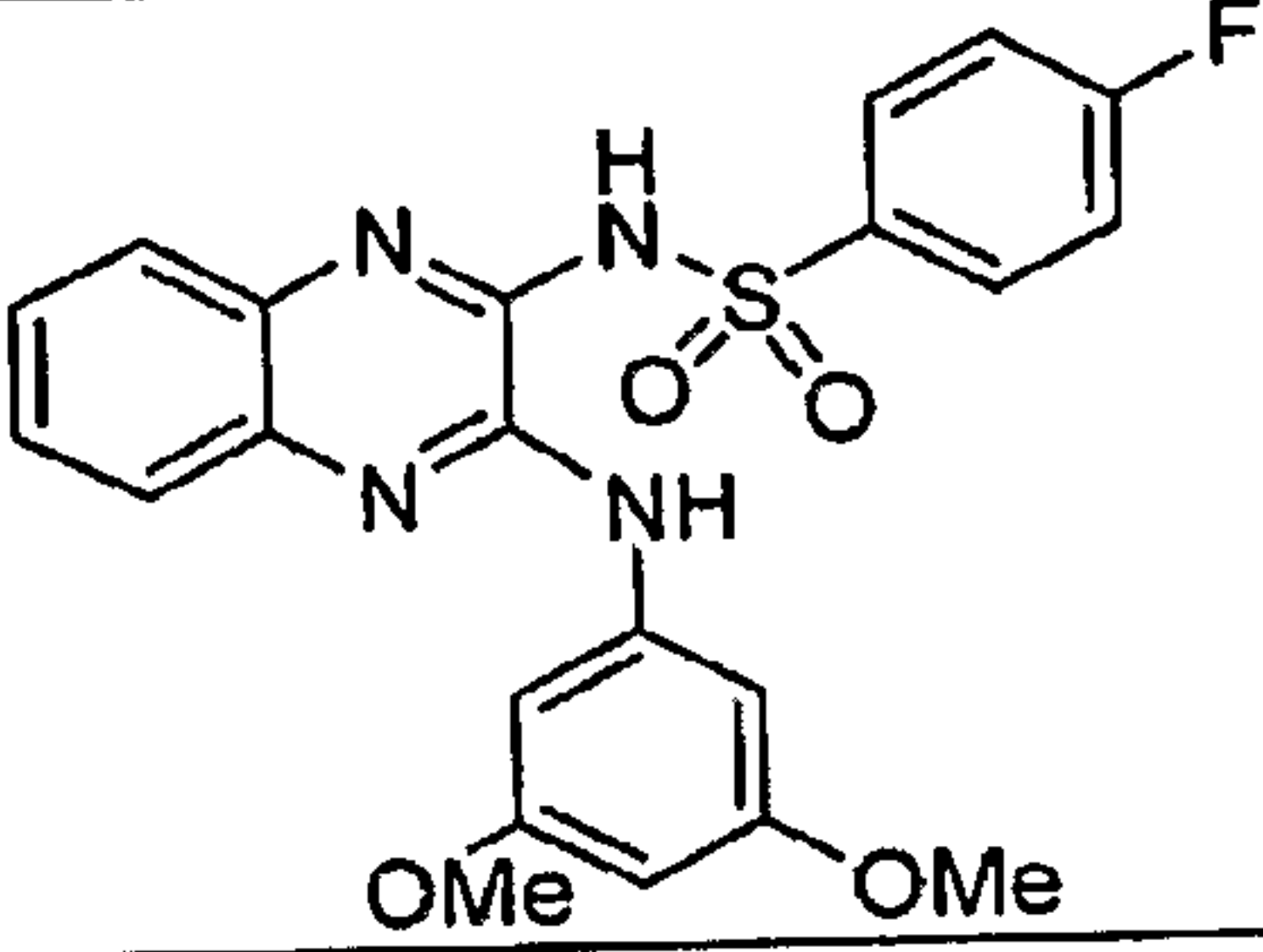
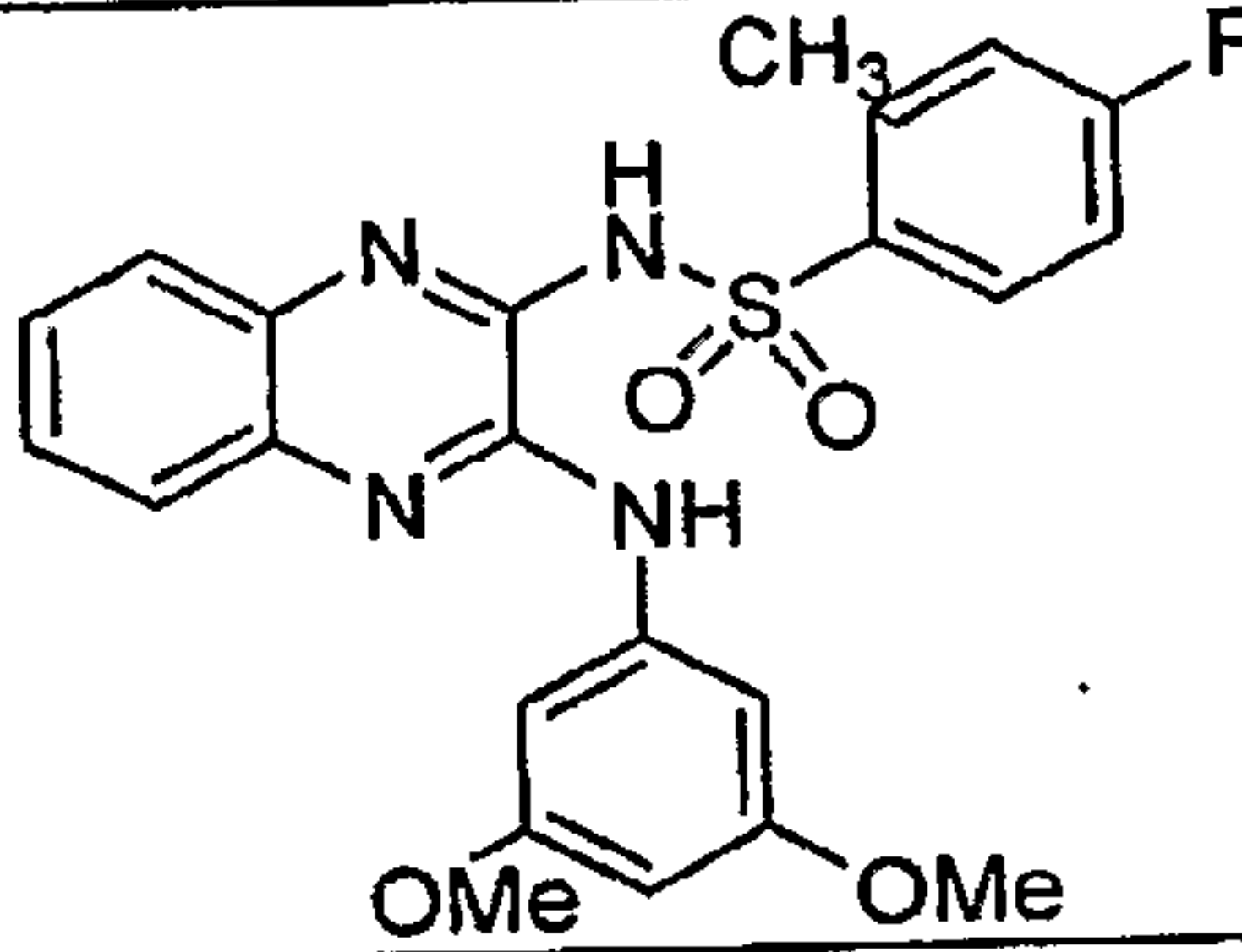
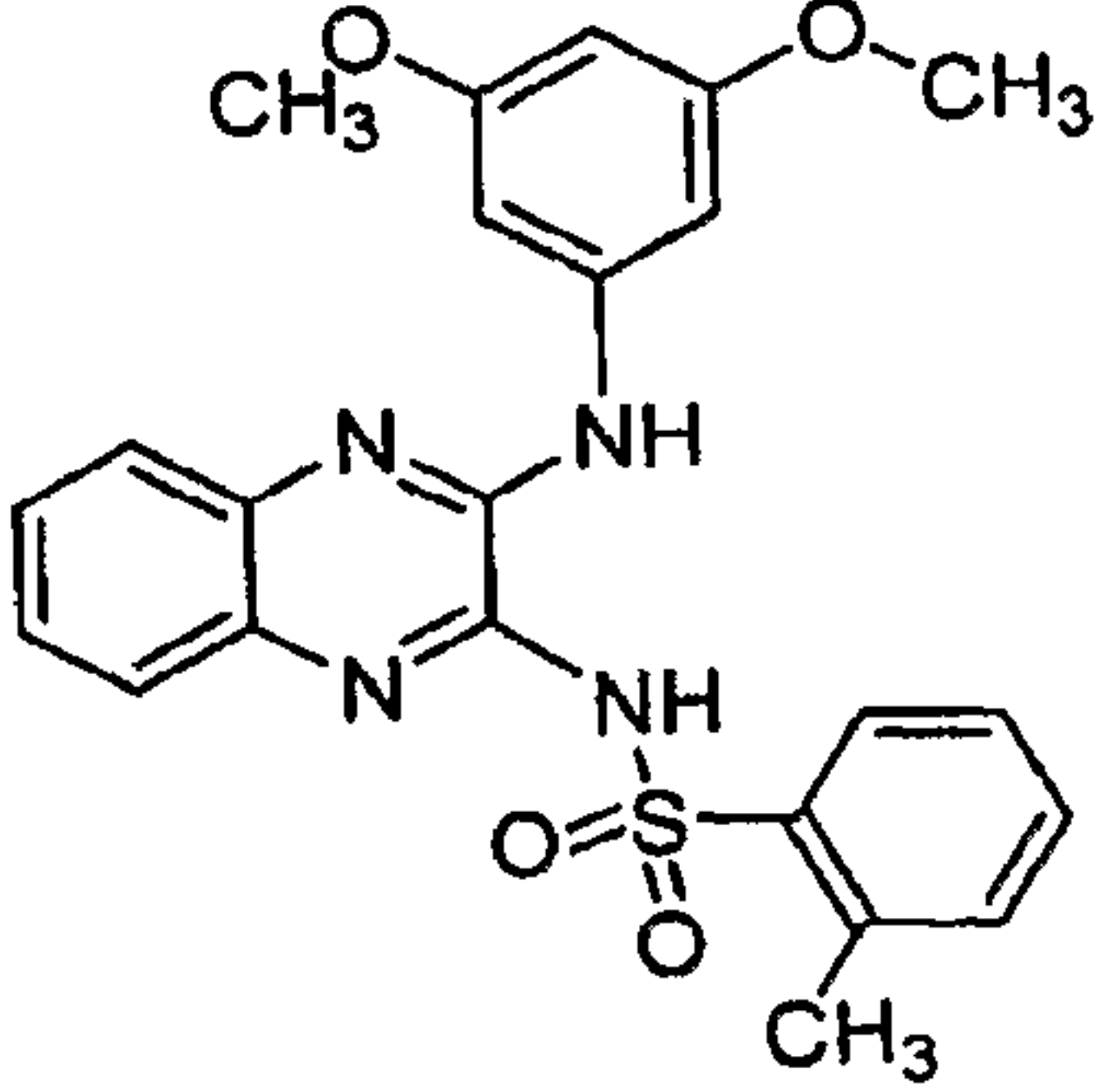
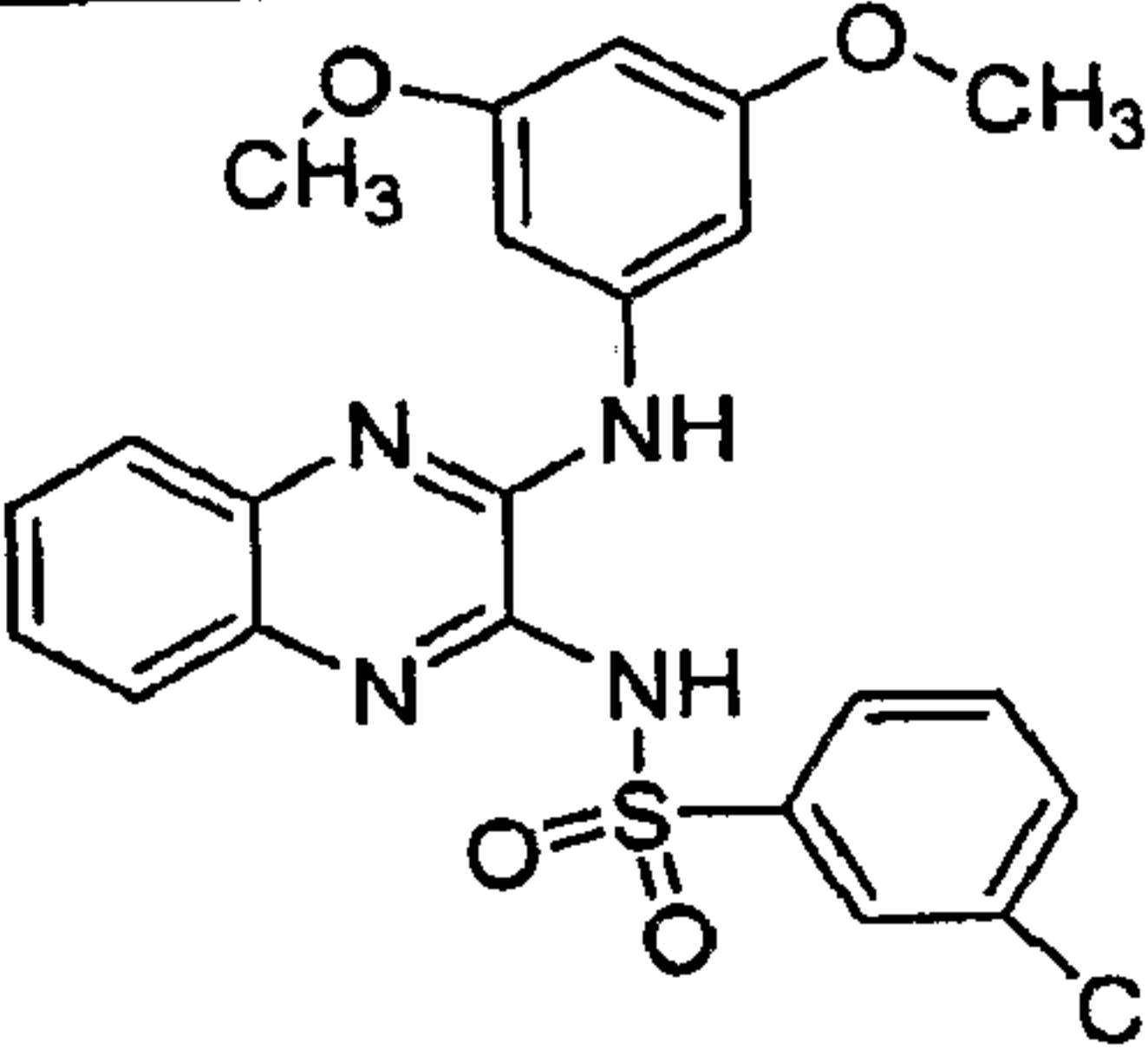
Table 1		
Cpd. No.	Structure	IUPAC Name
790		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-cyanobenzenesulfonamide
791		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-fluorobenzenesulfonamide
792		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-fluoro-2-methylbenzenesulfonamide
793		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-methylbenzenesulfonamide
794		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-cyanobenzenesulfonamide

Table 1

Cpd. No.	Structure	IUPAC Name
795		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3,5-difluorobenzenesulfonamide
796		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-chlorobenzenesulfonamide
797		<i>N</i> -(4-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide
798		<i>N</i> -(3-{[6-(methyloxy)quinolin-8-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
799		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(2 <i>H</i> -tetrazol-5-yl)benzenesulfonamide
800		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)naphthalene-1-sulfonamide

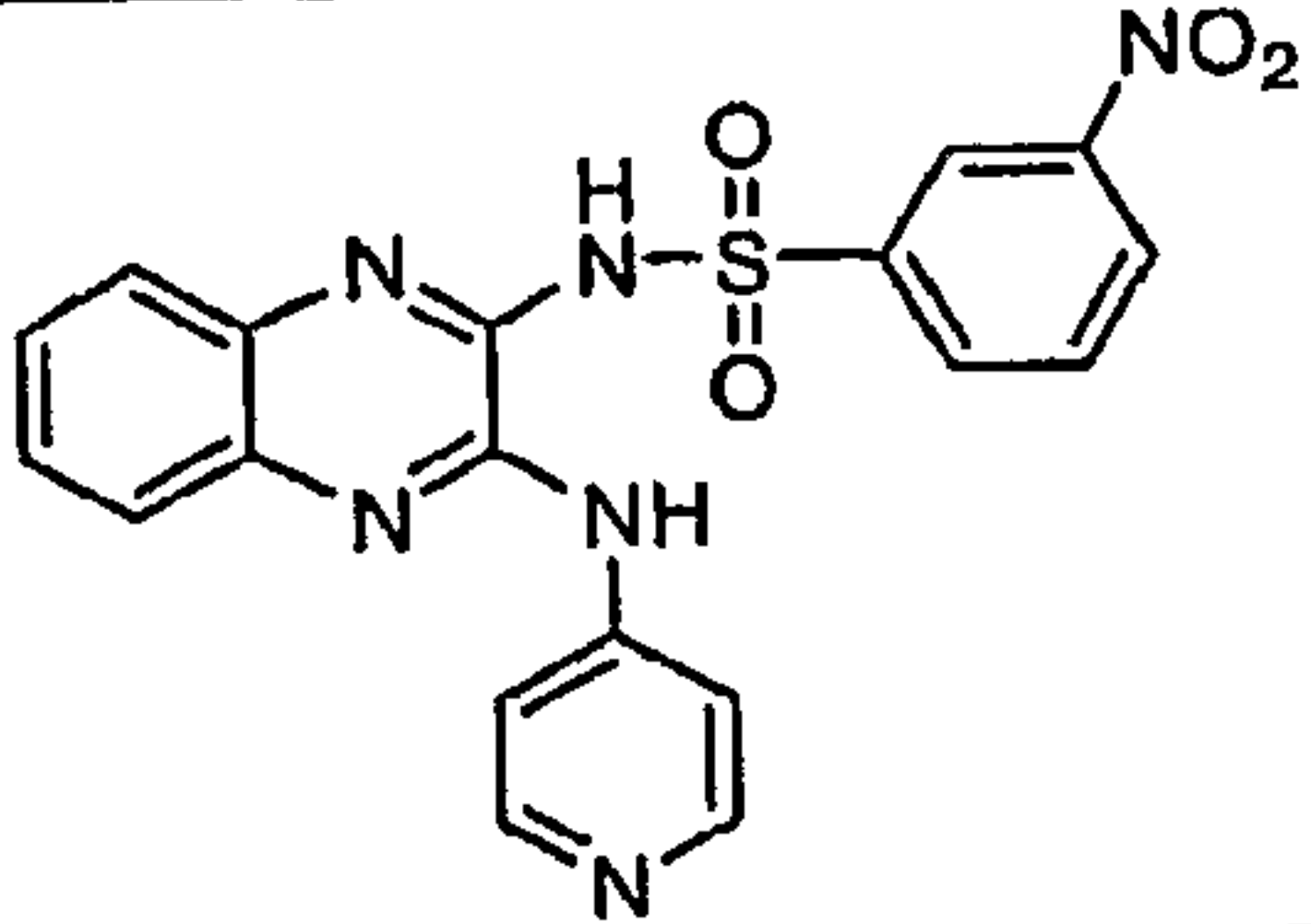
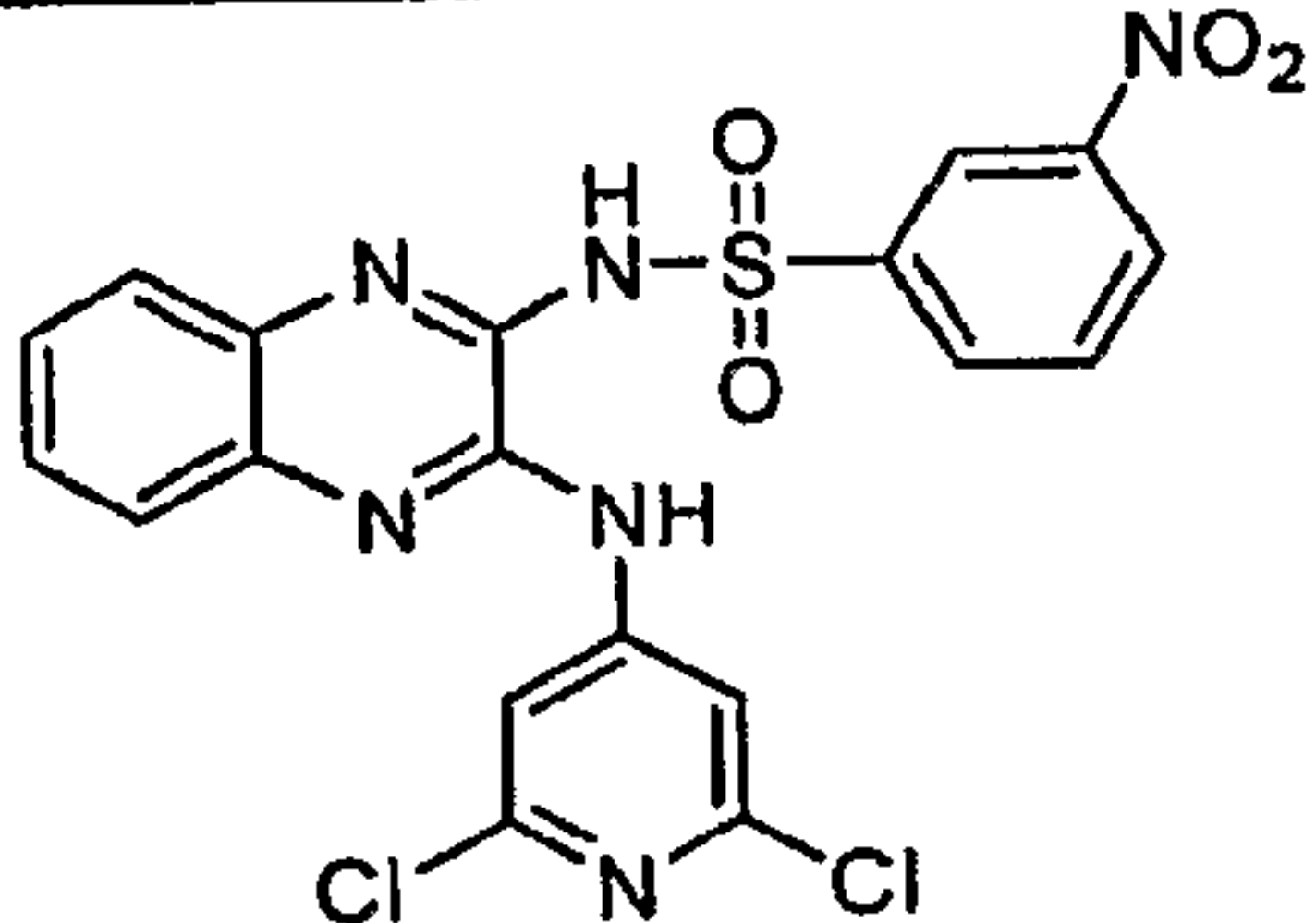
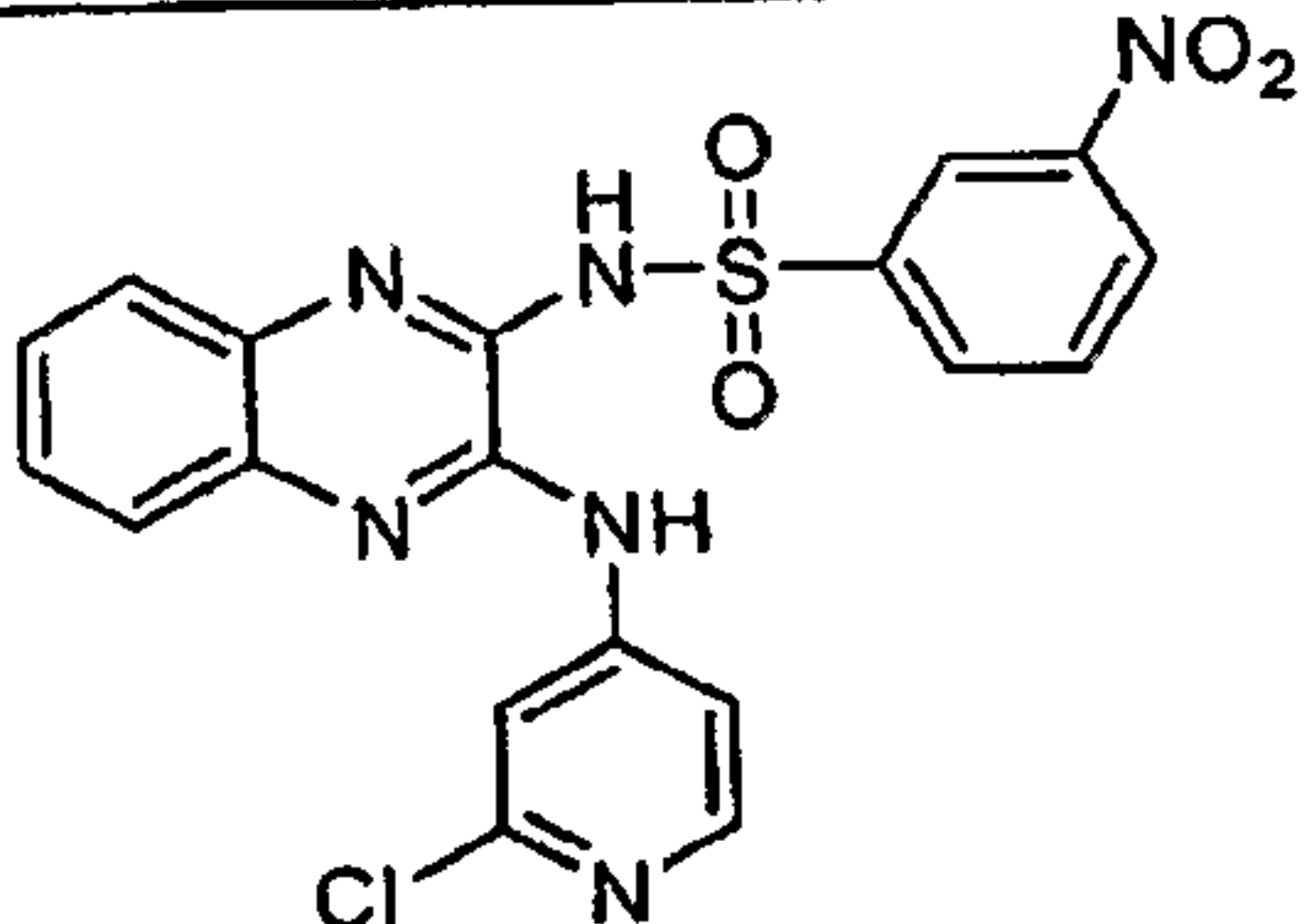
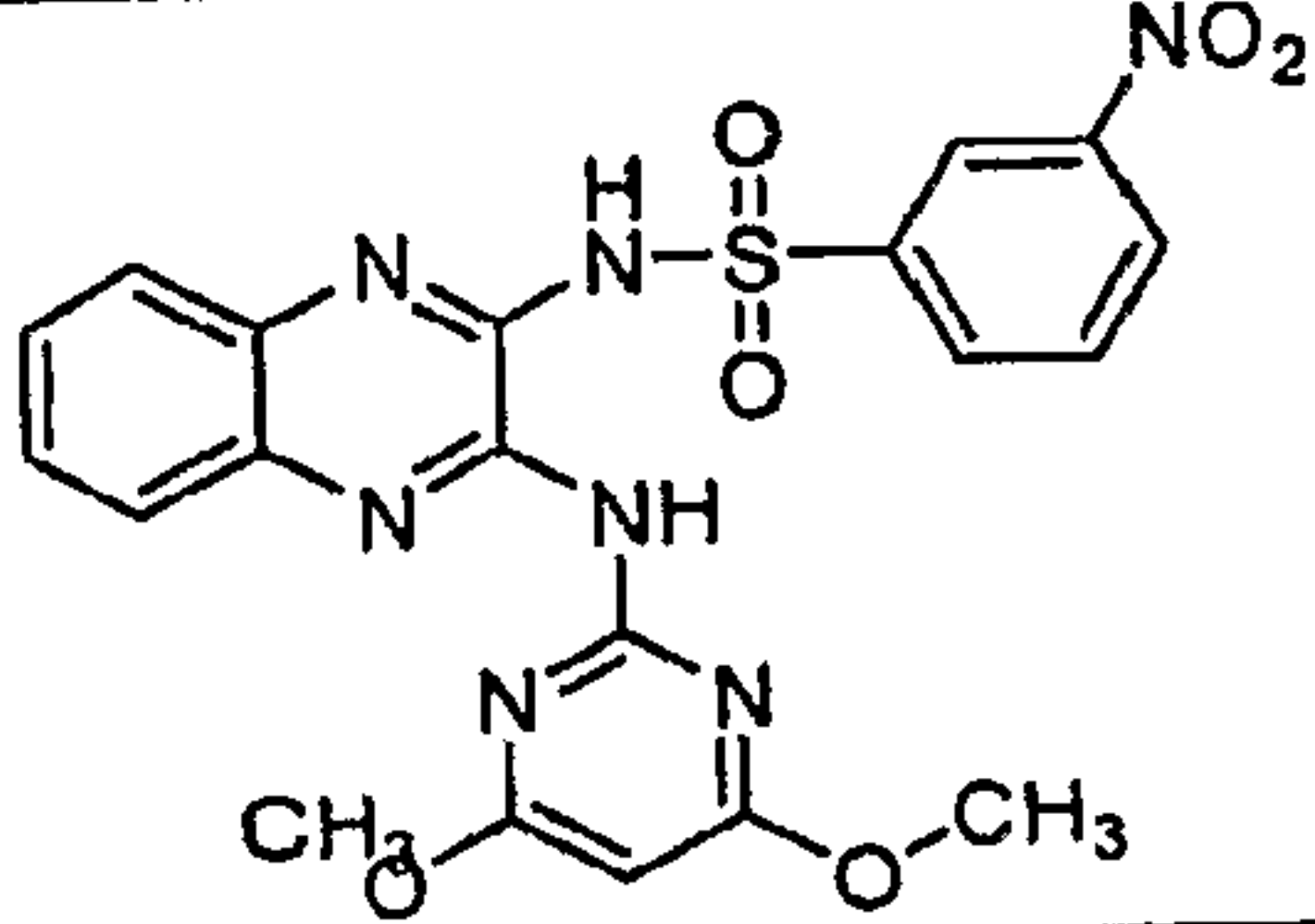
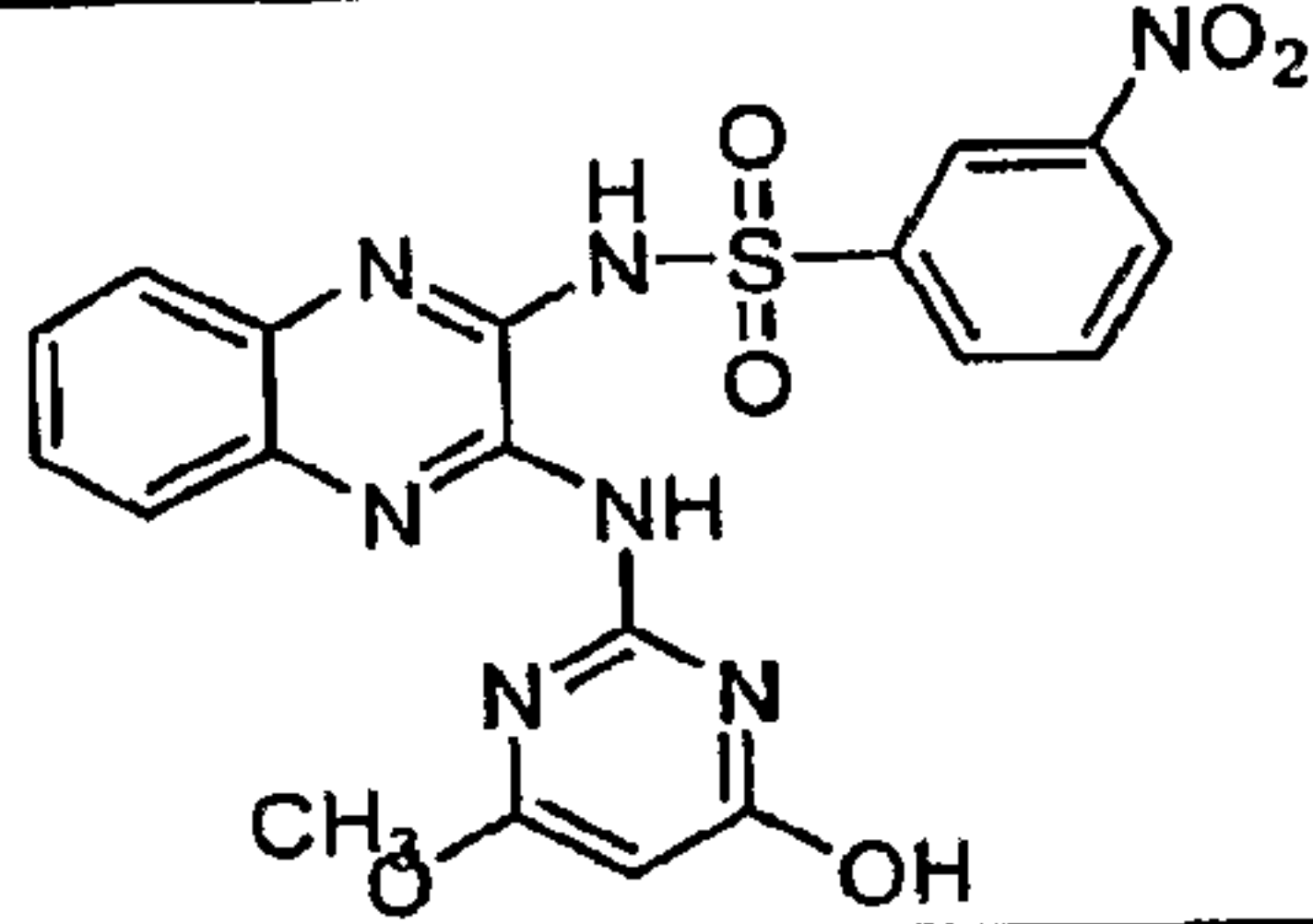
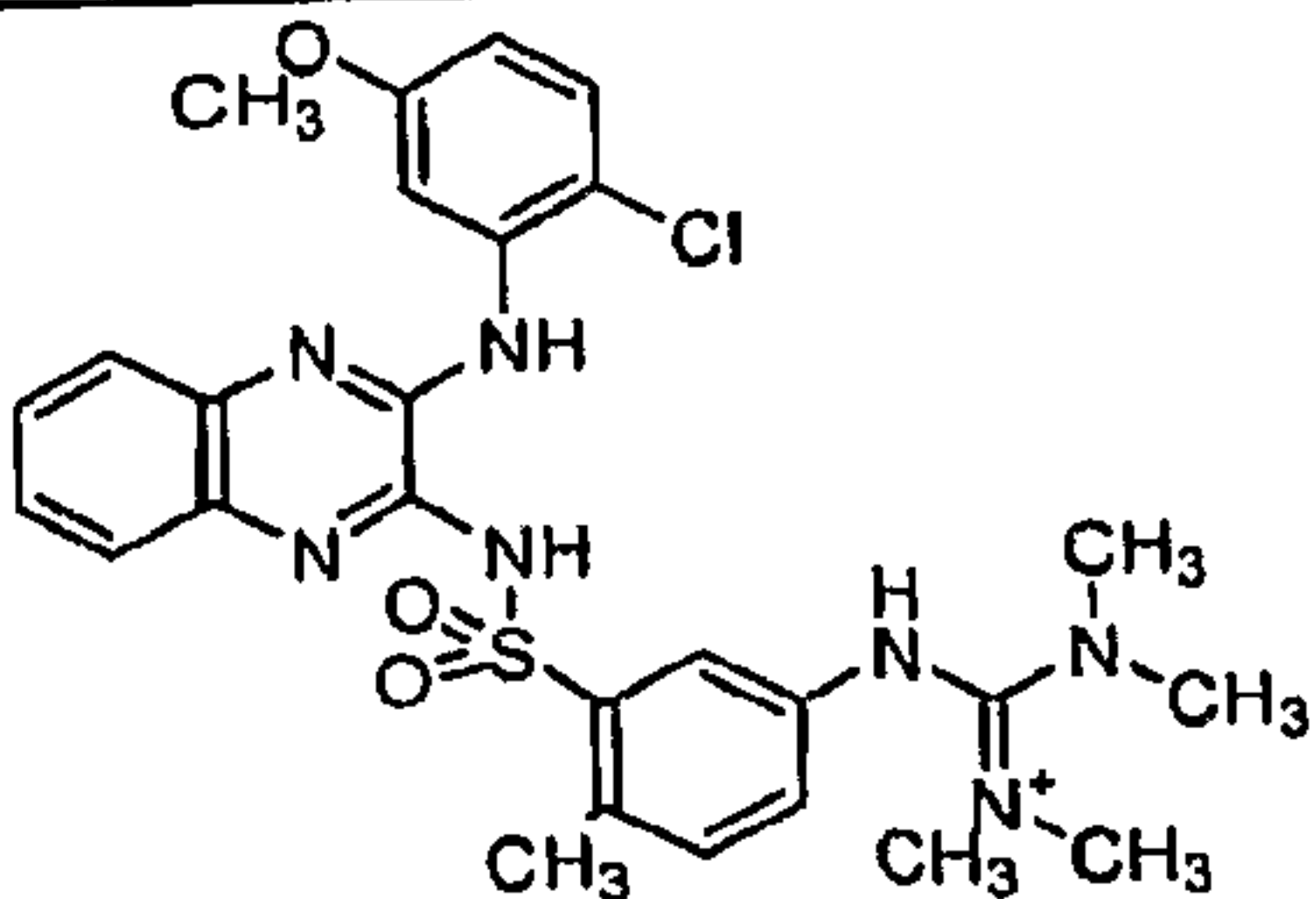
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Cpd. No.	Structure	IUPAC Name
801		3-nitro- <i>N</i> -[3-(pyridin-4-ylamino)quinoxalin-2-yl]benzenesulfonamide
802		<i>N</i> -{3-[(2,6-dichloropyridin-4-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
803		<i>N</i> -{3-[(2-chloropyridin-4-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
804		<i>N</i> -(3-{[4,6-bis(methoxy)pyrimidin-2-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
805		<i>N</i> -(3-{[4-hydroxy-6-(methoxy)pyrimidin-2-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
806		<i>N</i> -[[3-[[3-[[2-chloro-5-(methoxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl]-4-methylphenyl]amino](dimethylamino)methylidene}- <i>N</i> -methylmethanaminium

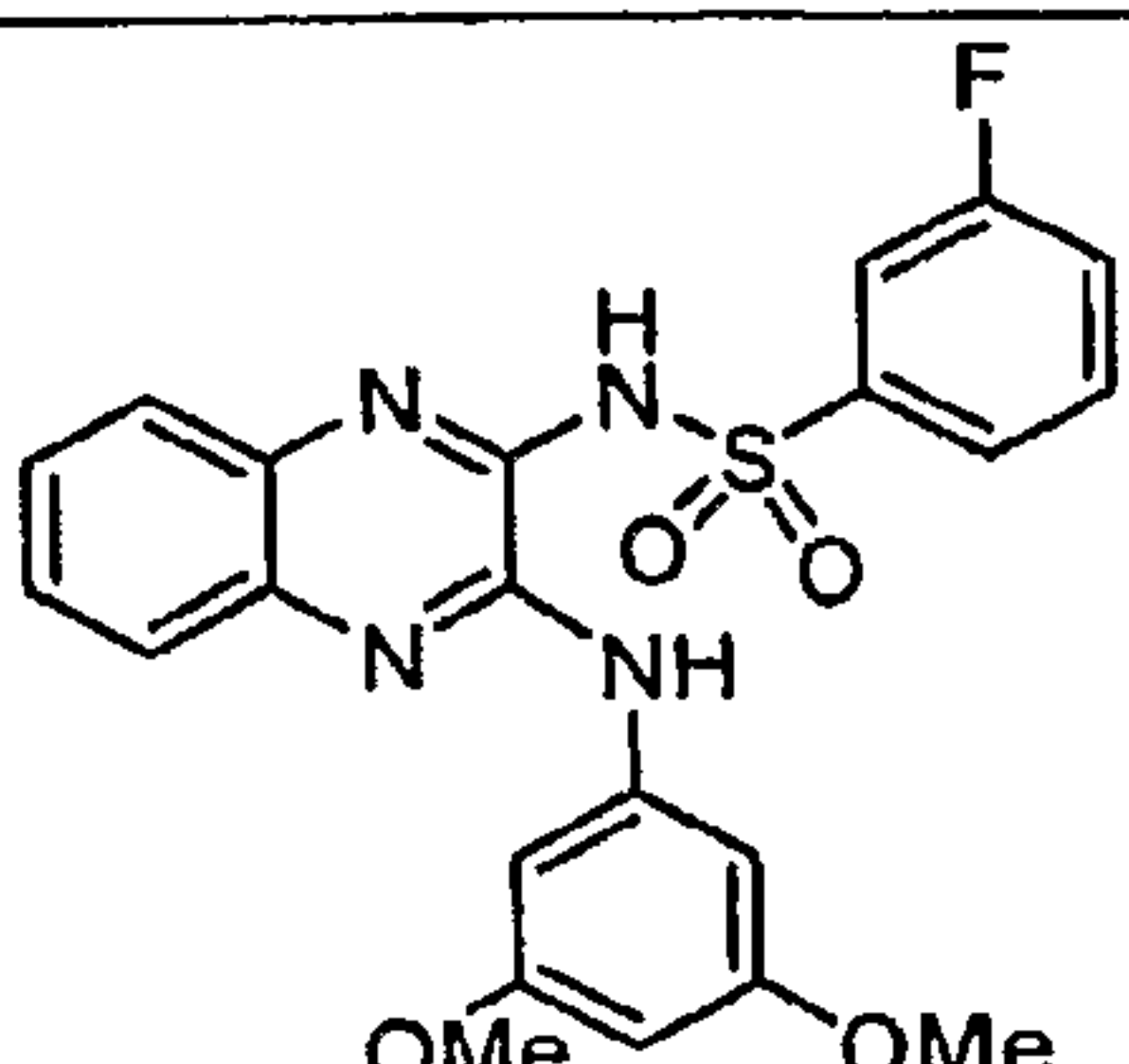
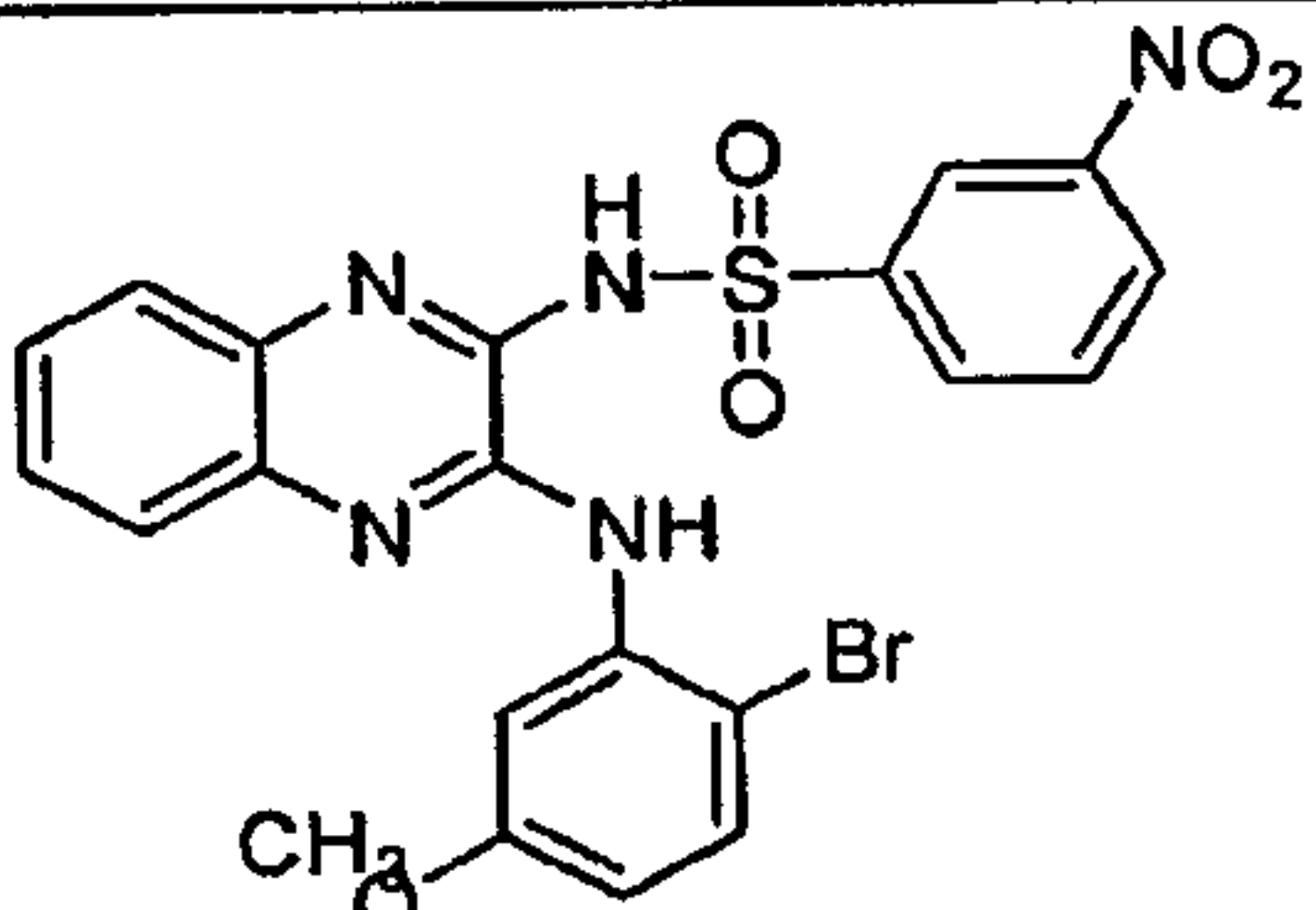
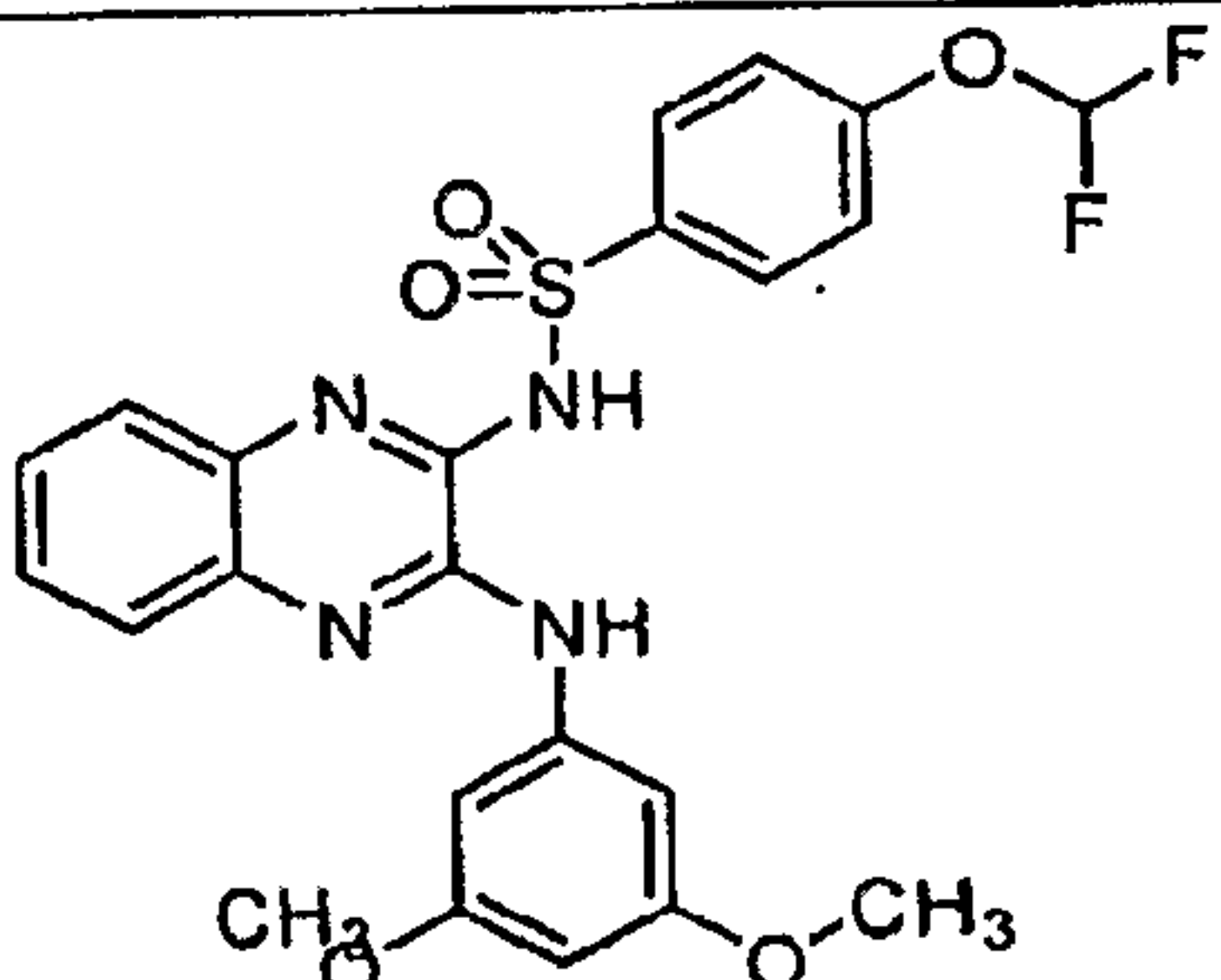
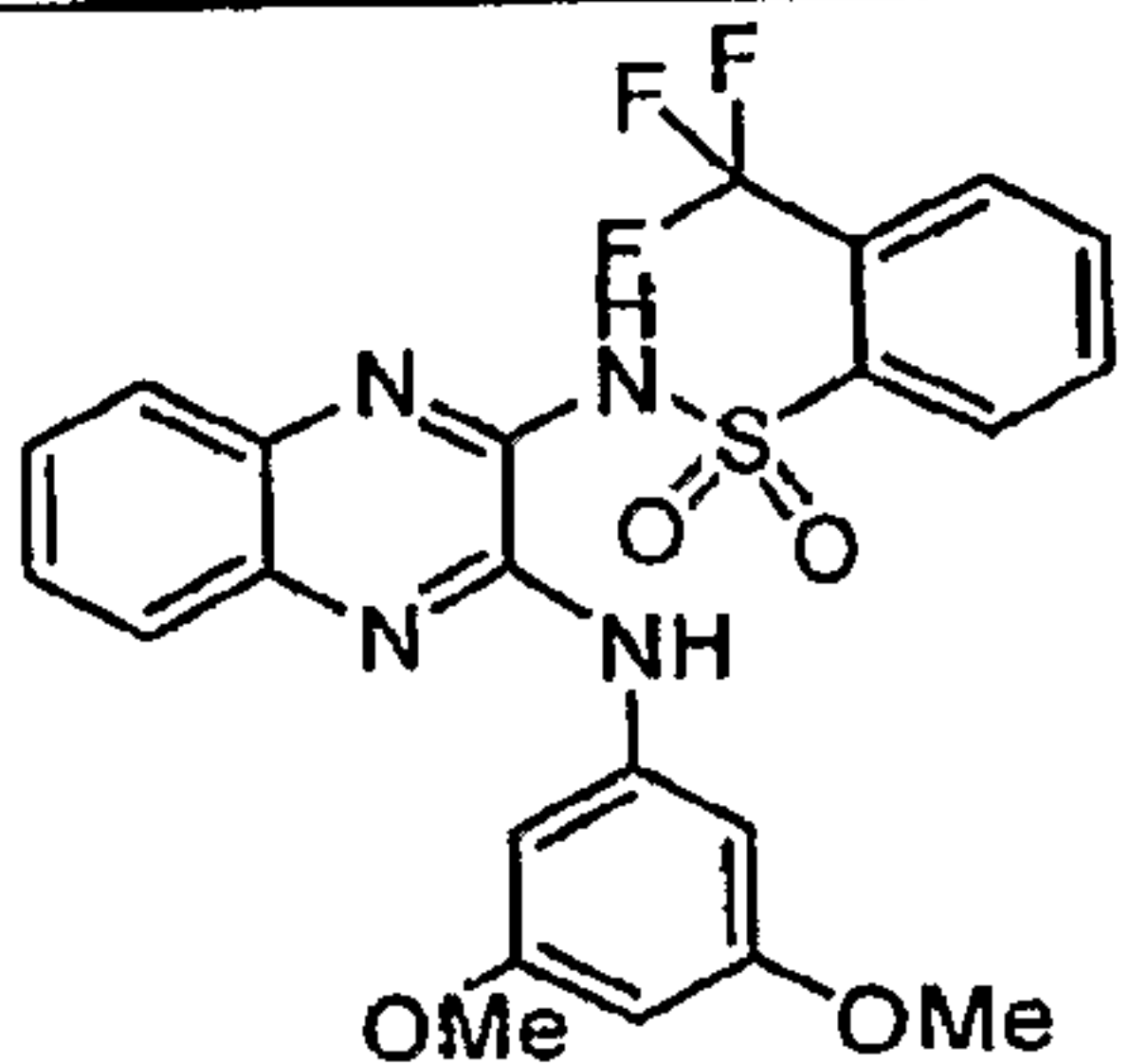
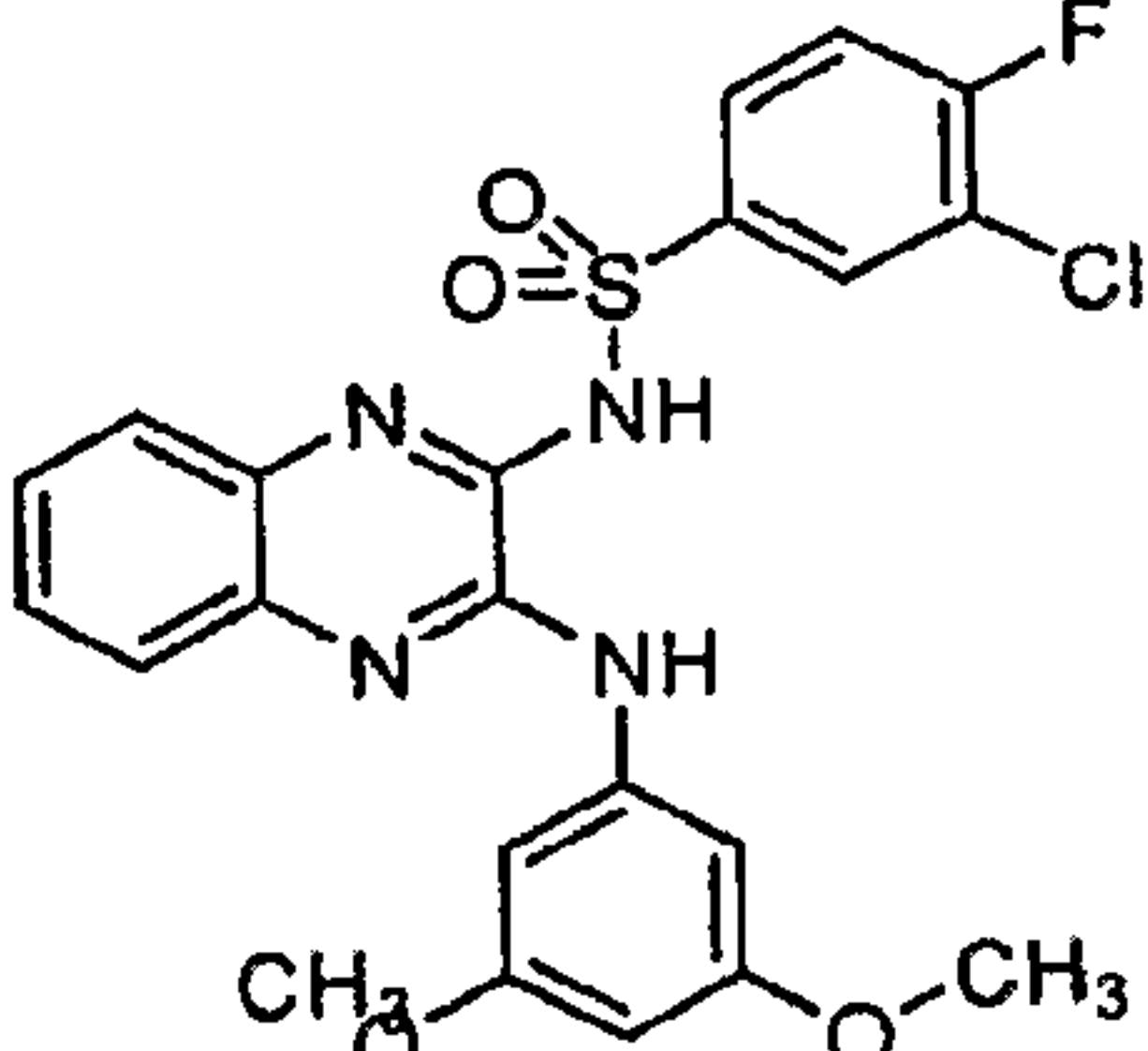
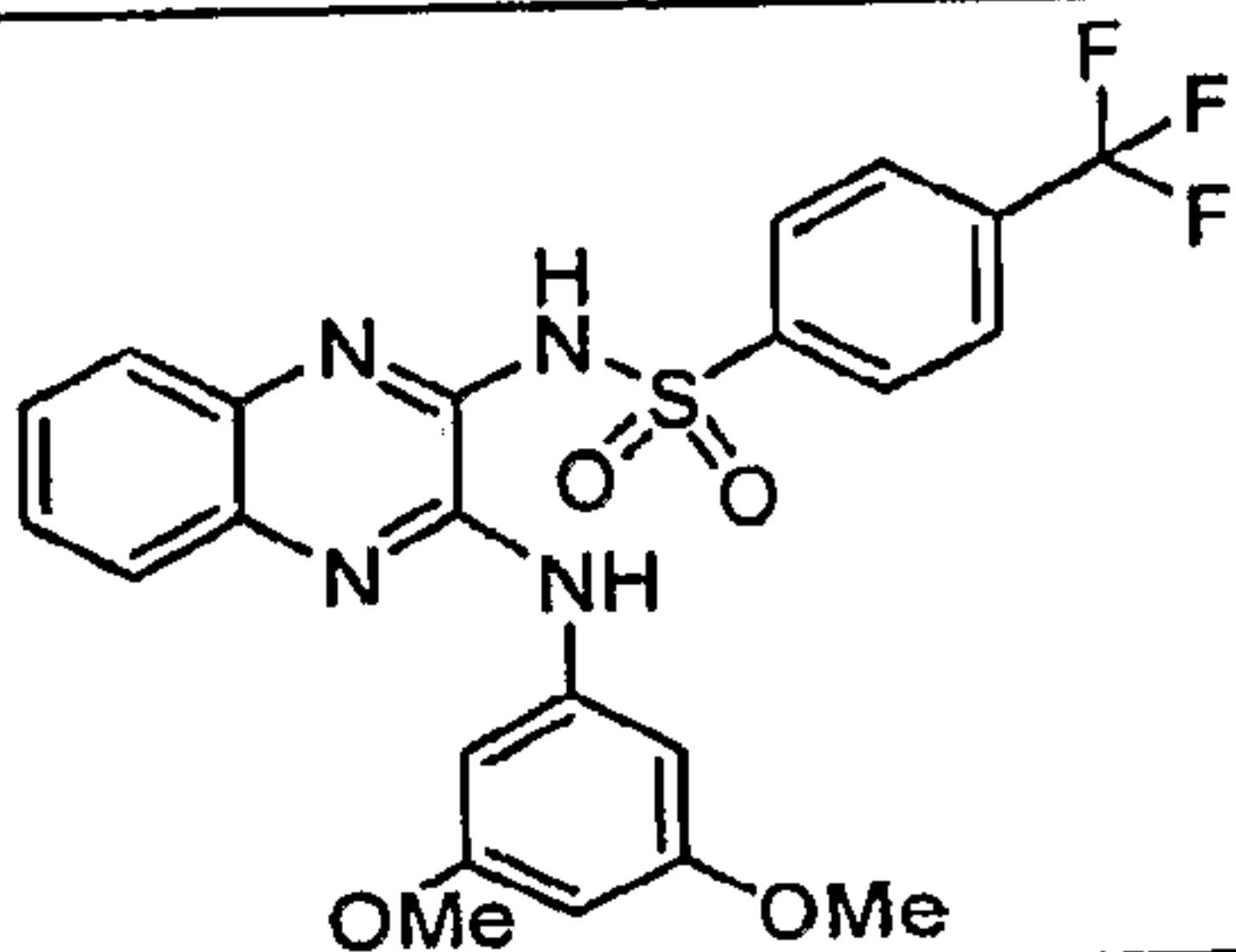
Table 1		
Cpd. No.	Structure	IUPAC Name
807		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-fluorobenzenesulfonamide
808		<i>N</i> -(3-{[2-bromo-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
809		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-[(difluoromethyl)oxy]benzenesulfonamide
810		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-(trifluoromethyl)benzenesulfonamide
811		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-chloro-4-fluorobenzenesulfonamide
812		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-(trifluoromethyl)benzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
813		<i>N</i> -(3-{{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl}-3-(methylsulfonyl)benzenesulfonamide
814		<i>N</i> -(3-{{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl}-2,5-dichlorothiophene-3-sulfonamide
815		<i>N</i> -(3-{{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl}-3,5-dichlorobenzenesulfonamide
816		<i>N</i> -(3-{{[2-methyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl}-3-nitrobenzenesulfonamide
817		<i>N</i> -(3-{{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl}-4-[(trifluoromethyl)oxy]benzenesulfonamide
818		<i>N</i> -(3-{{[(3-{{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(dimethylamino)piperidin-1-yl]acetamide

Table 1		
Cpd. No.	Structure	IUPAC Name
819		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-5-chloro-2-(methoxy)benzenesulfonamide
820		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-3-(trifluoromethyl)benzenesulfonamide
821		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-2,5-bis(methoxy)benzenesulfonamide
822		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-3,5-dimethylisoxazole-4-sulfonamide
823		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-5-bromo-2-(methoxy)benzenesulfonamide
824		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-4-fluoro-3-(trifluoromethyl)benzenesulfonamide

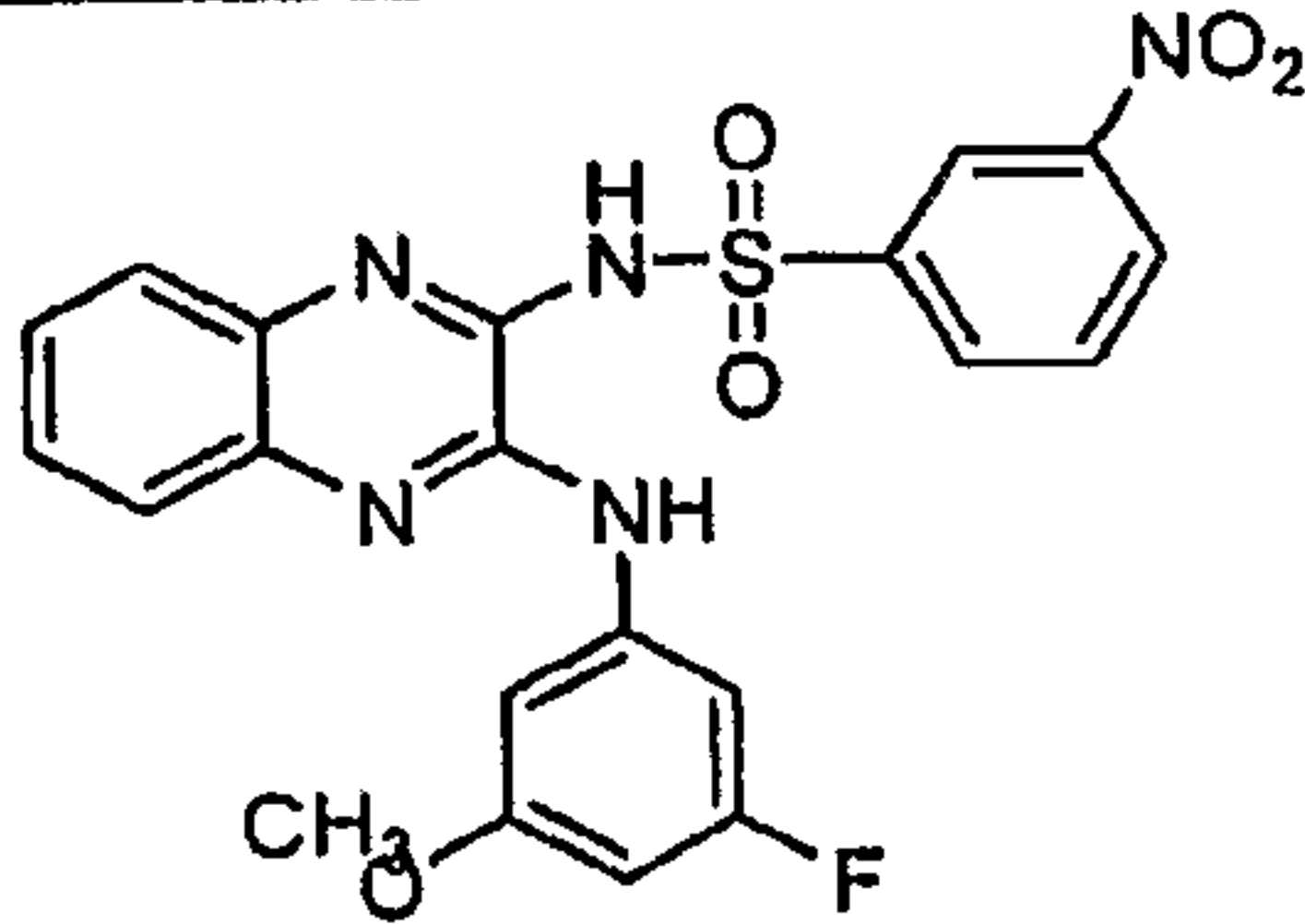
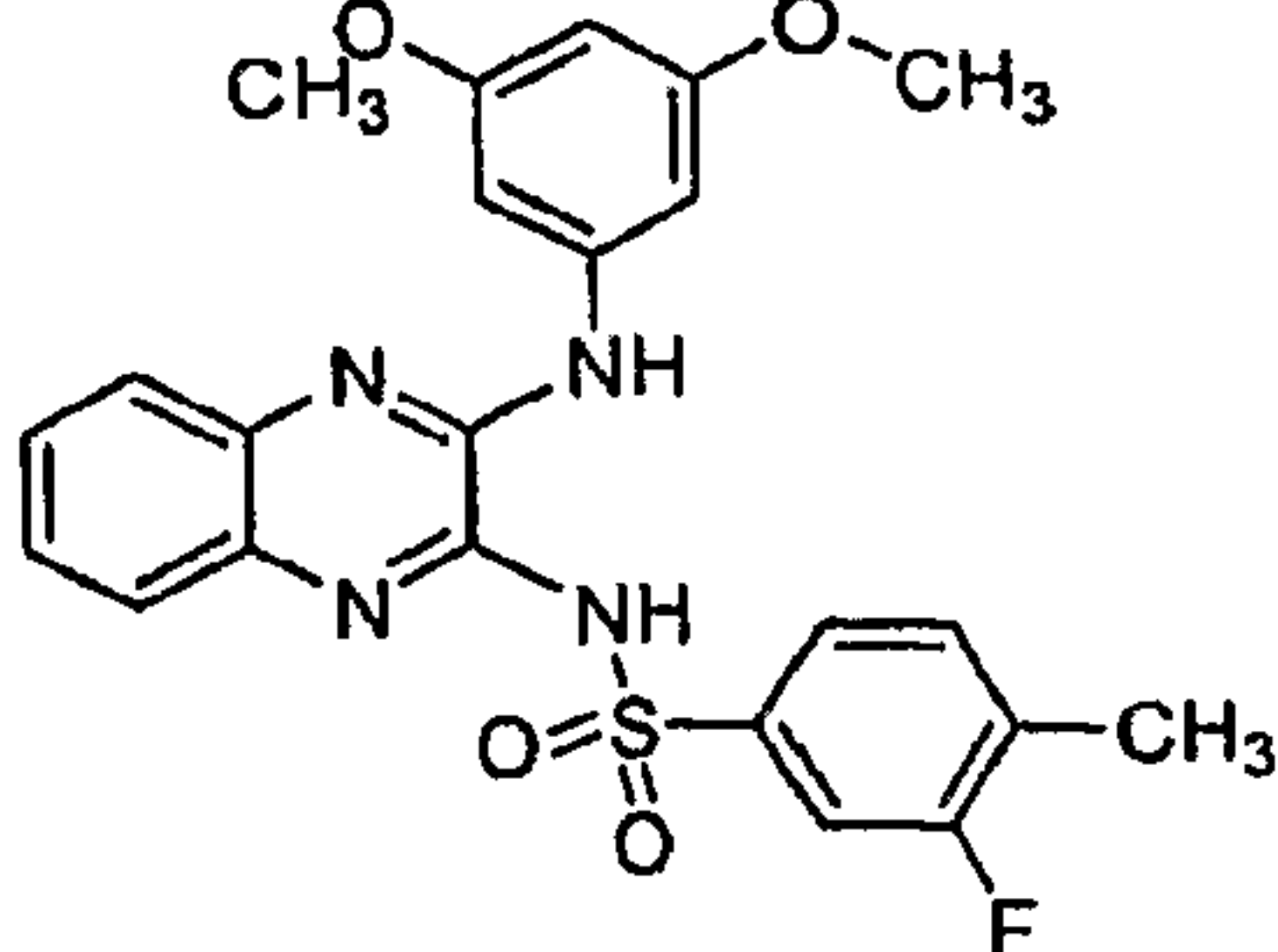
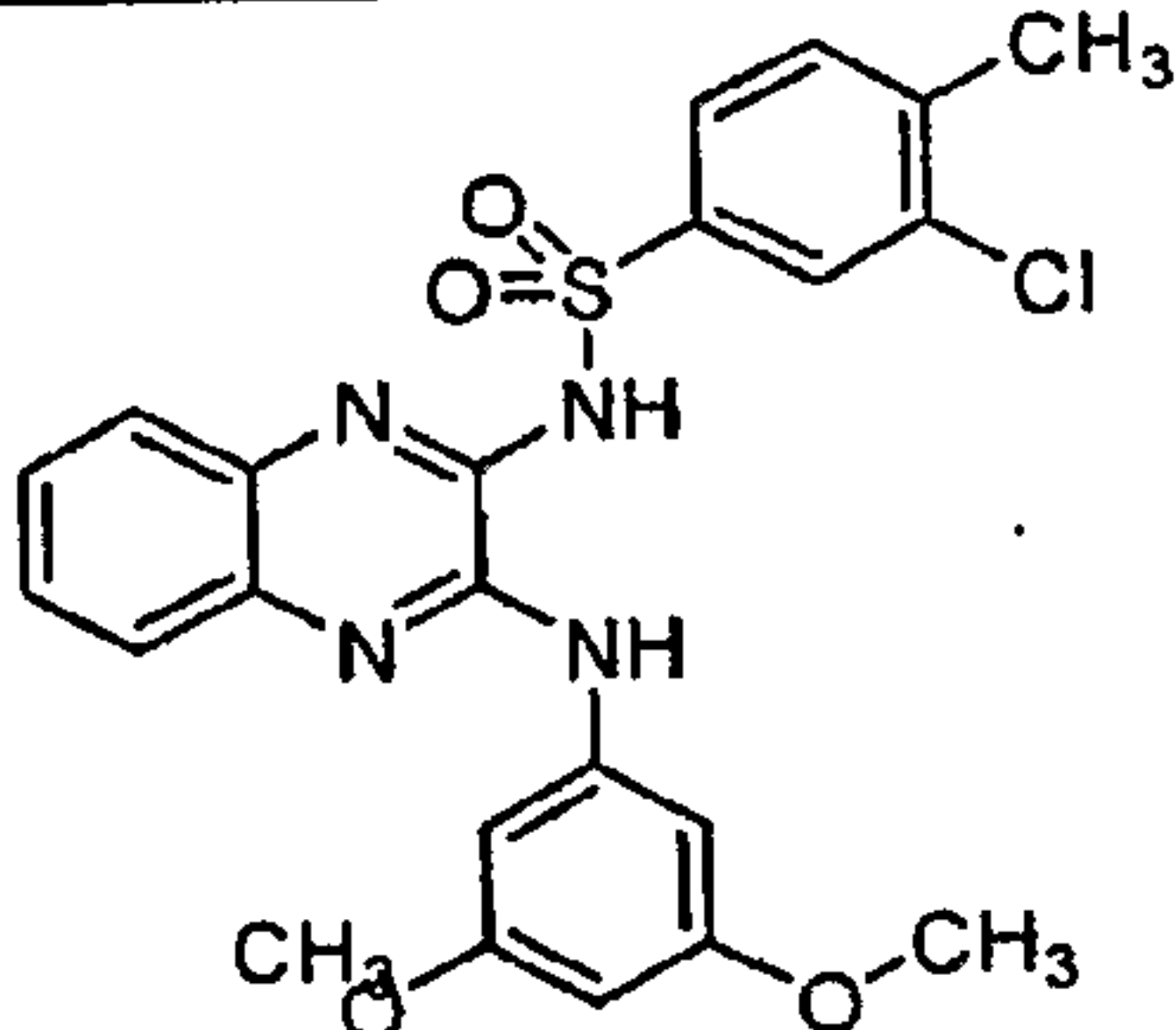
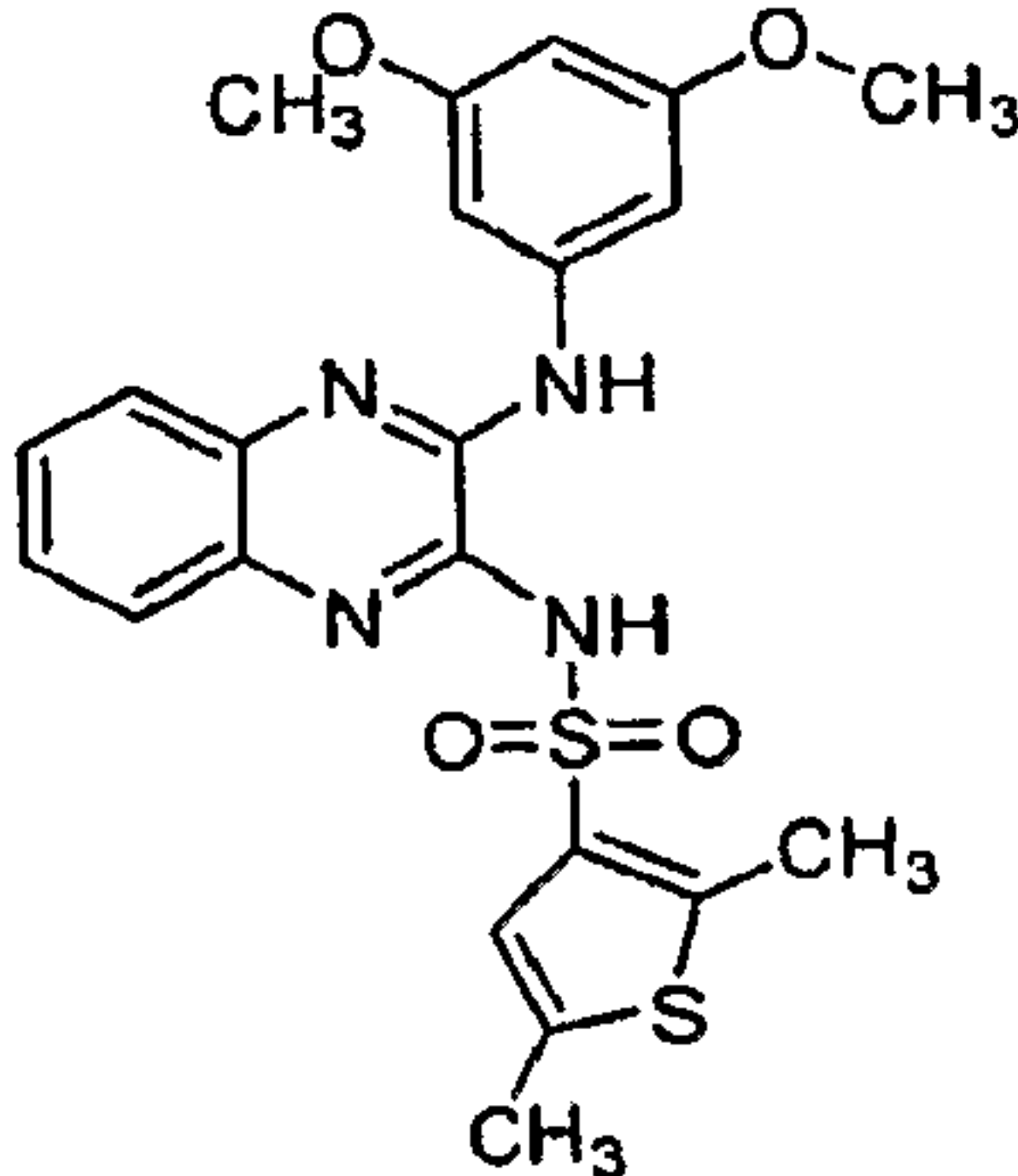
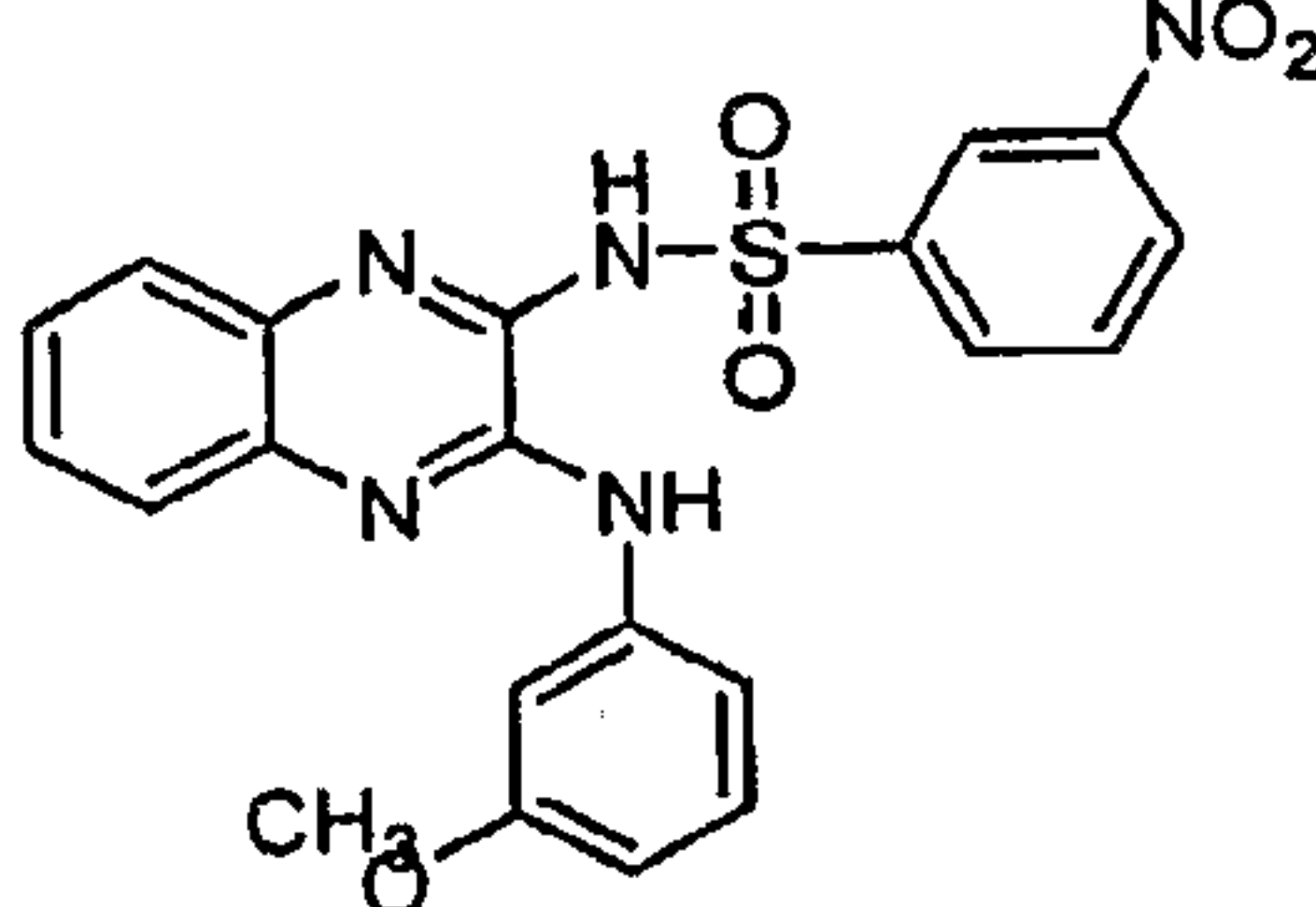
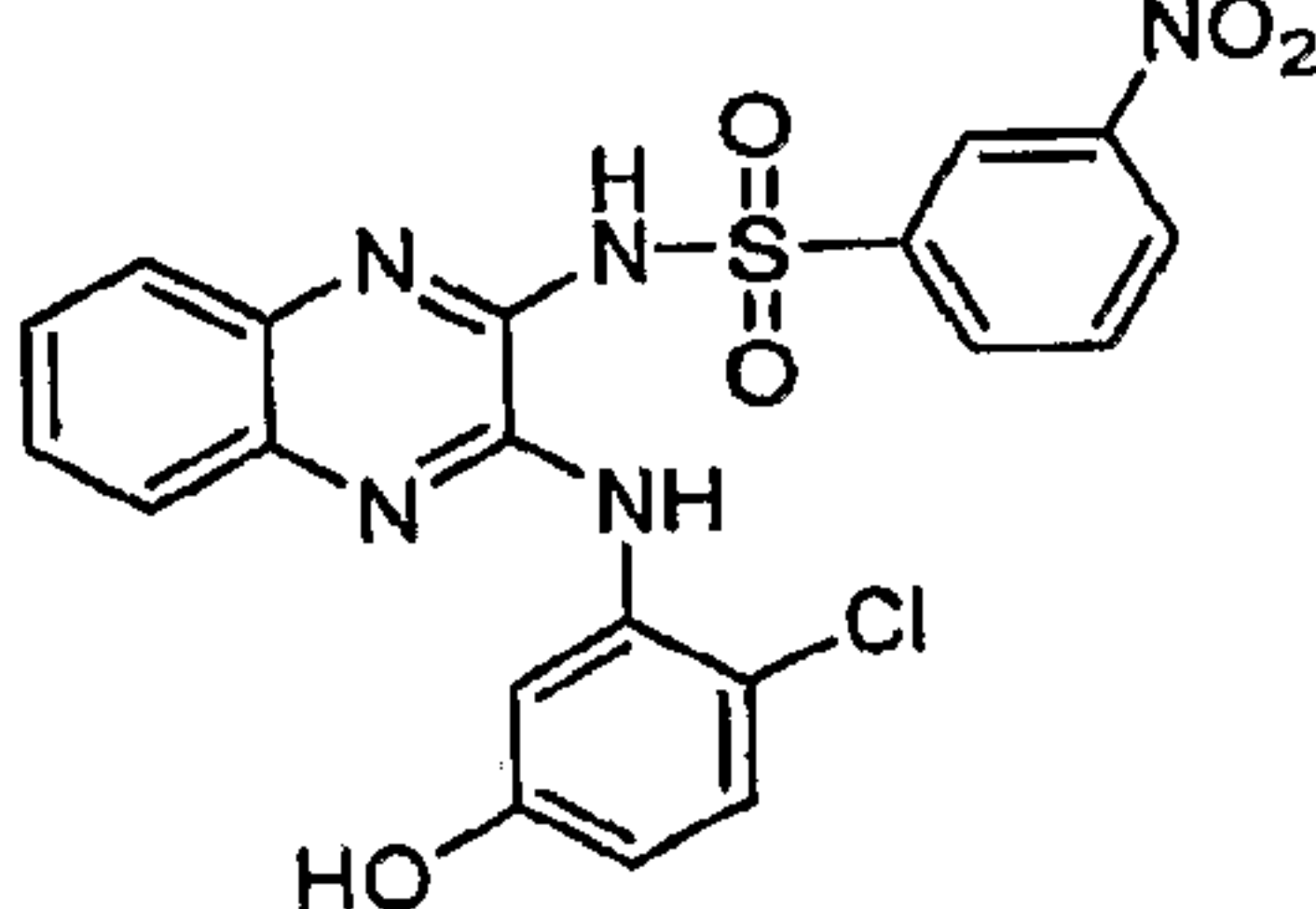
Table 1		
Cpd. No.	Structure	IUPAC Name
825		<i>N</i> -(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
826		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-fluoro-4-methylbenzenesulfonamide
827		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-chloro-4-methylbenzenesulfonamide
828		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2,5-dimethylthiophene-3-sulfonamide
829		<i>N</i> -(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
830		<i>N</i> -{3-[(2-chloro-5-hydroxyphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
831		<i>N</i> -(3-({[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-4-methyl-3-(methoxy)benzamide
832		<i>N</i> -(3-({[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-1-phenylmethanesulfonamide
833		<i>N</i> -(3-({[3-(methoxy)-5-nitrophenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
834		<i>N</i> -(3-({[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-1-(3-chlorophenyl)methanesulfonamide
835		<i>N</i> -(3-({[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-4,5-dichlorothiophene-2-sulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
836		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-5-chloro-1,3-dimethyl-1 <i>H</i> -pyrazole-4-sulfonamide
837		<i>N</i> -(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide
838		<i>N</i> -{3-[(3-hydroxyphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
839		3-nitro- <i>N</i> -[3-({3-[(trifluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide
840		3-nitro- <i>N</i> -[3-(pyridin-3-ylamino)quinoxalin-2-yl]benzenesulfonamide
841		<i>N</i> -[3-(morpholin-4-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide

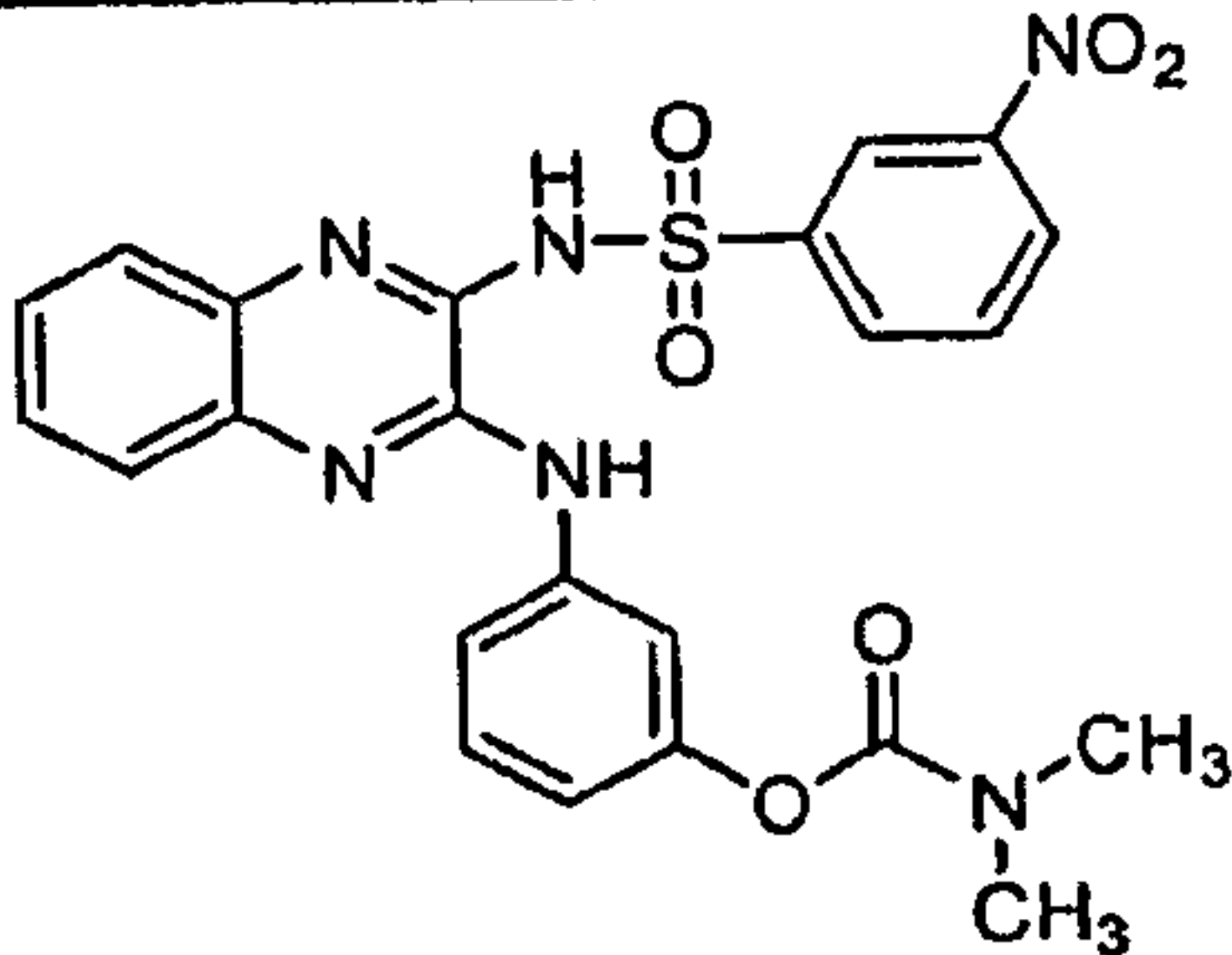
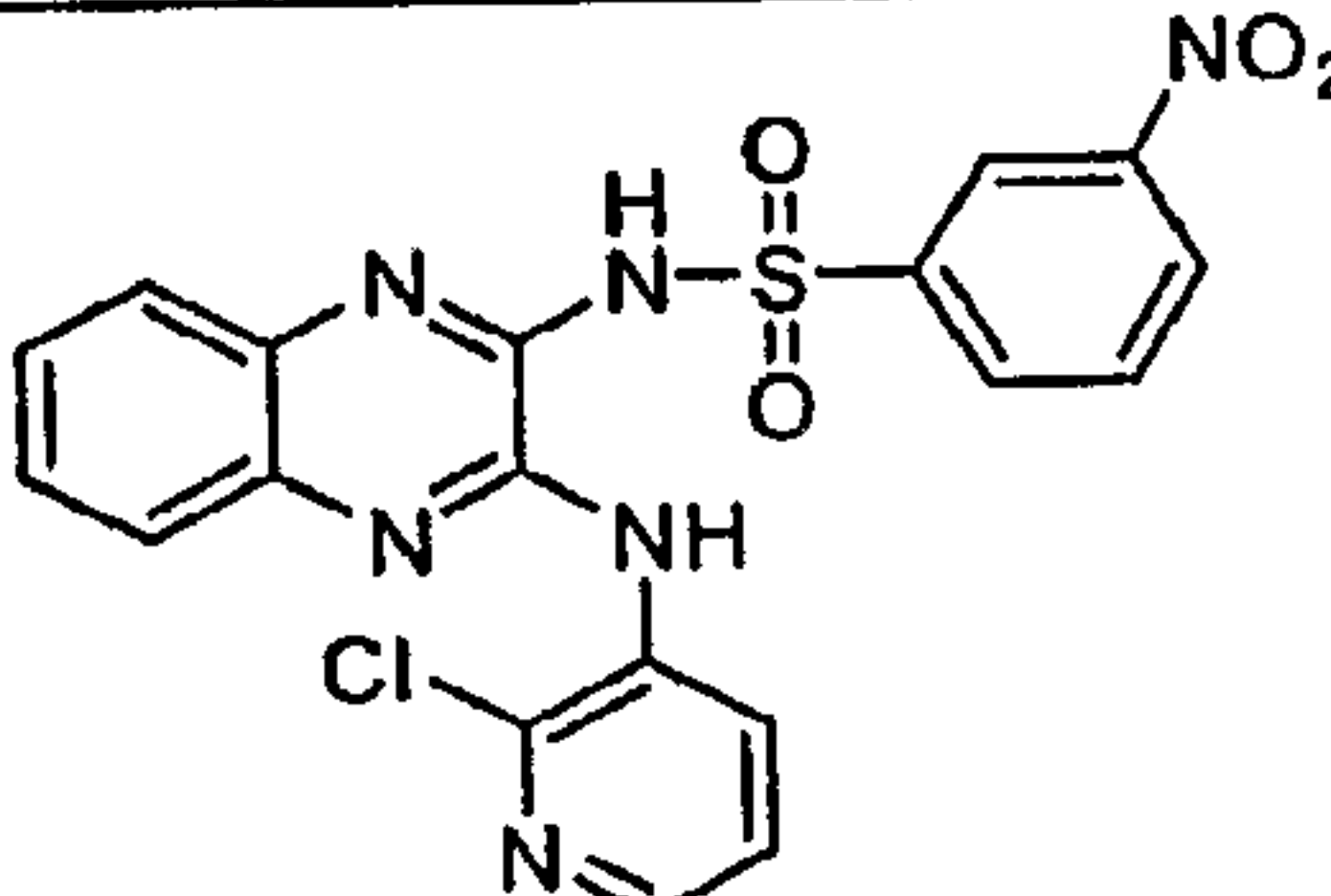
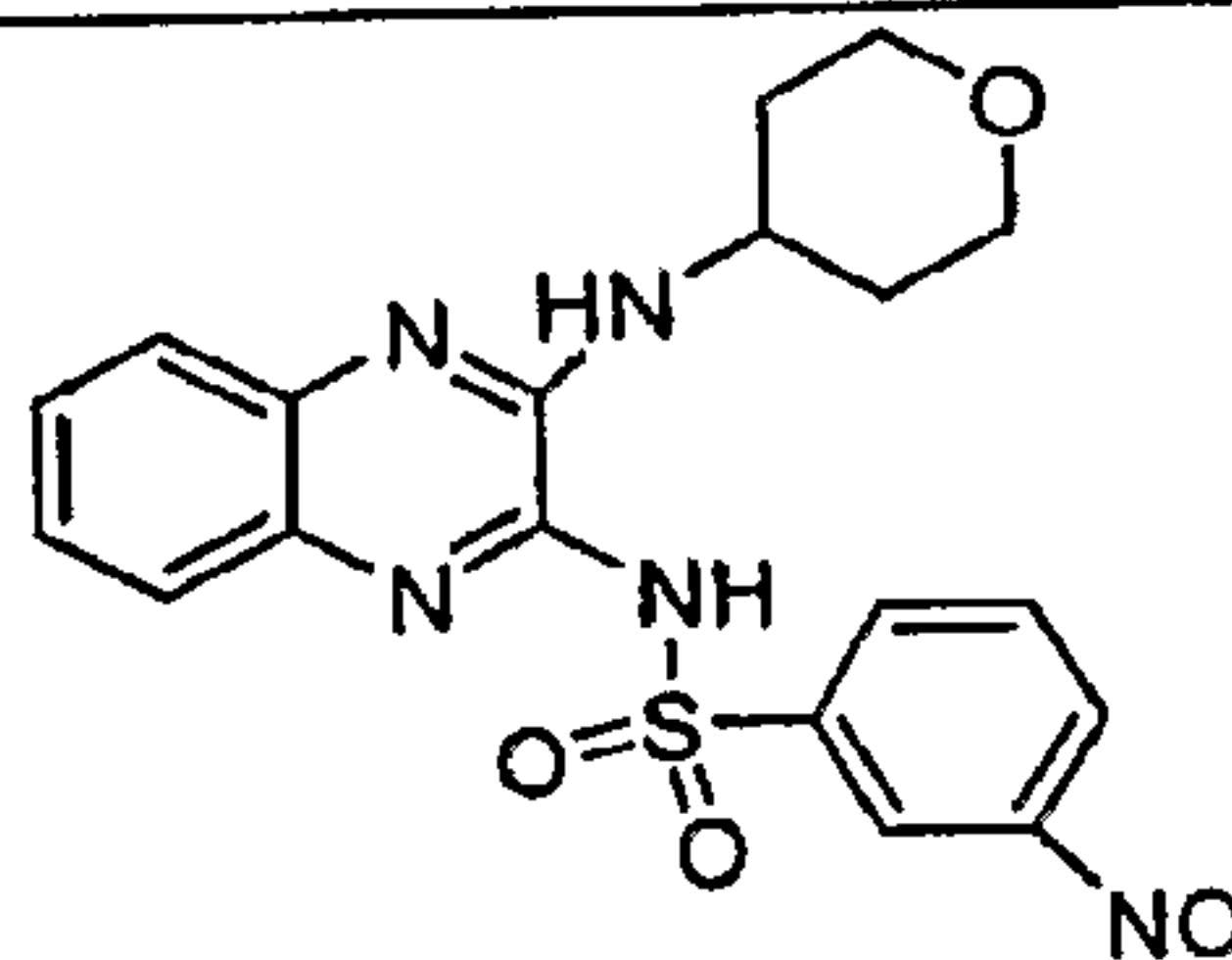
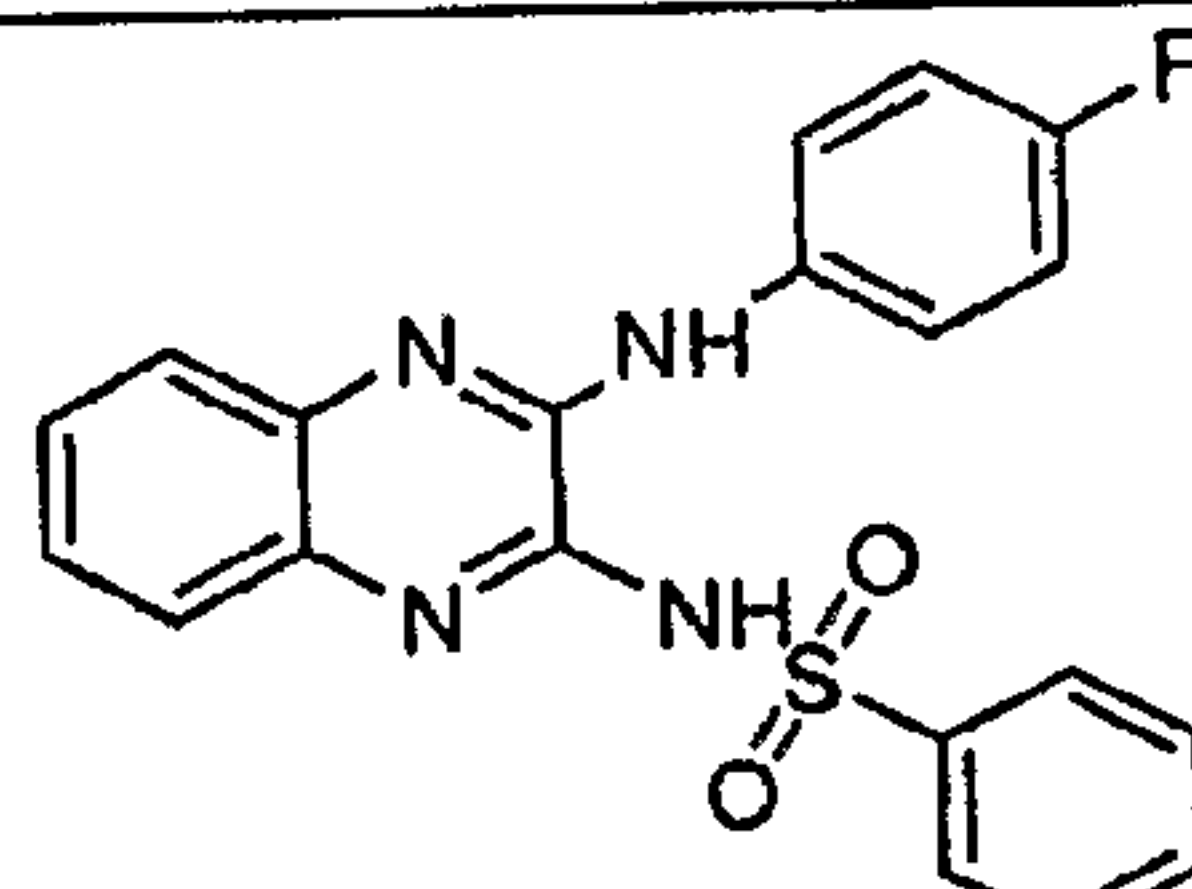
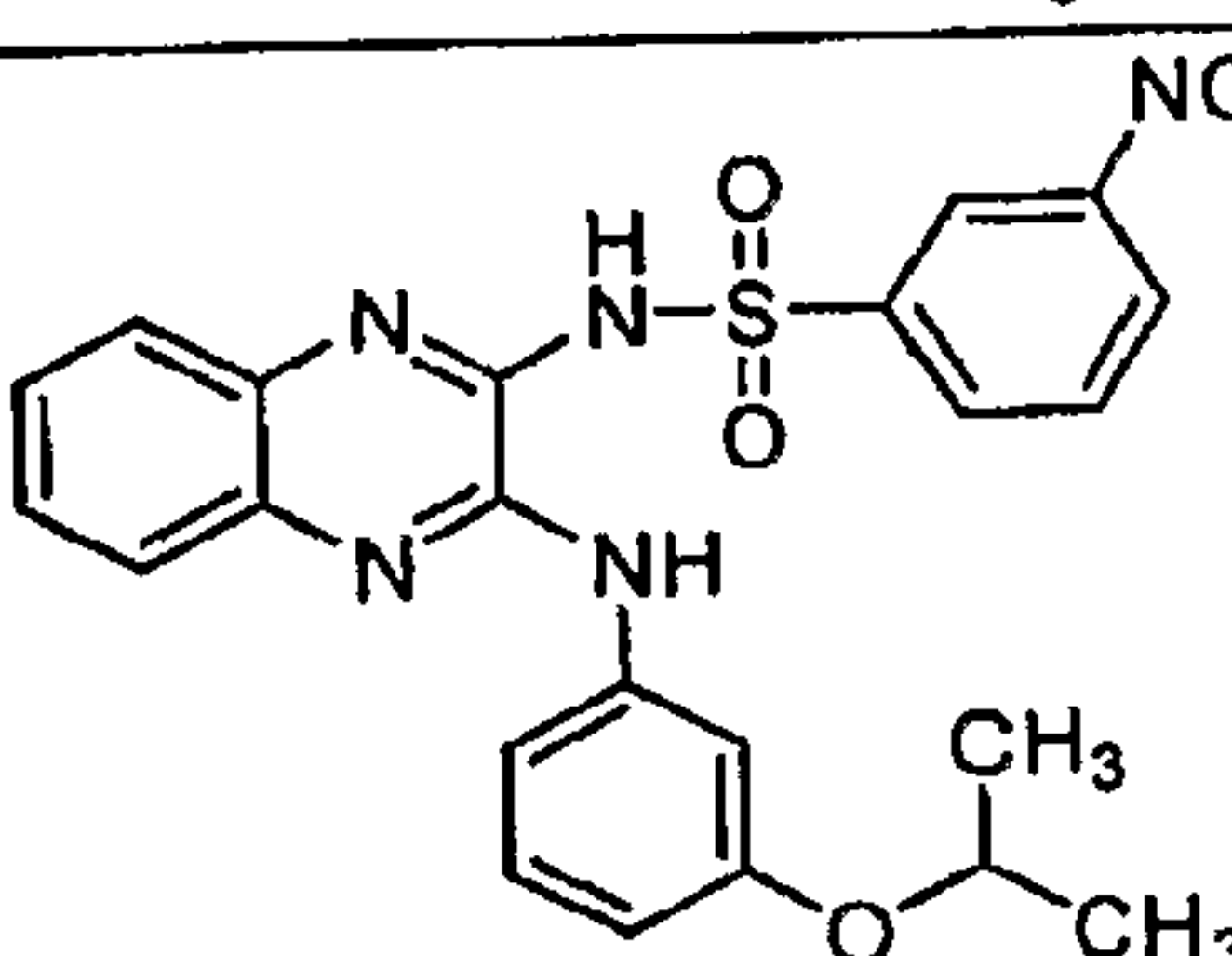
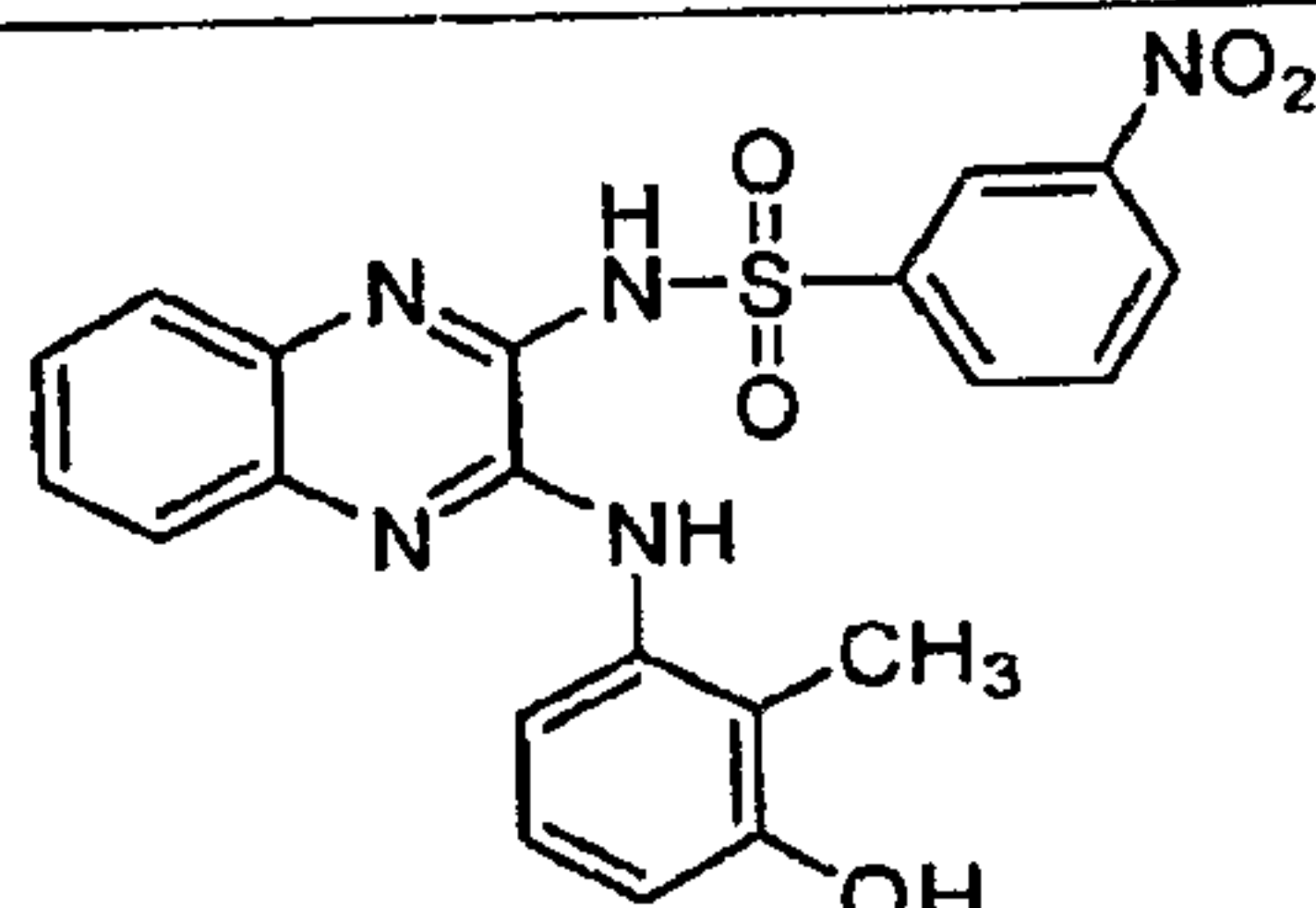
Table 1		
Cpd. No.	Structure	IUPAC Name
842		3-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyldimethylcarbamate
843		<i>N</i> -{3-[(2-chloropyridin-3-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
844		3-nitro- <i>N</i> -[3-(tetrahydro-2 <i>H</i> -pyran-4-ylamino)quinoxalin-2-yl]benzenesulfonamide
845		<i>N</i> -{3-[(4-fluorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide
846		<i>N</i> -[3-({3-[(1-methylethyl)oxy]phenyl}amino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
847		<i>N</i> -{3-[(3-hydroxy-2-methylphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

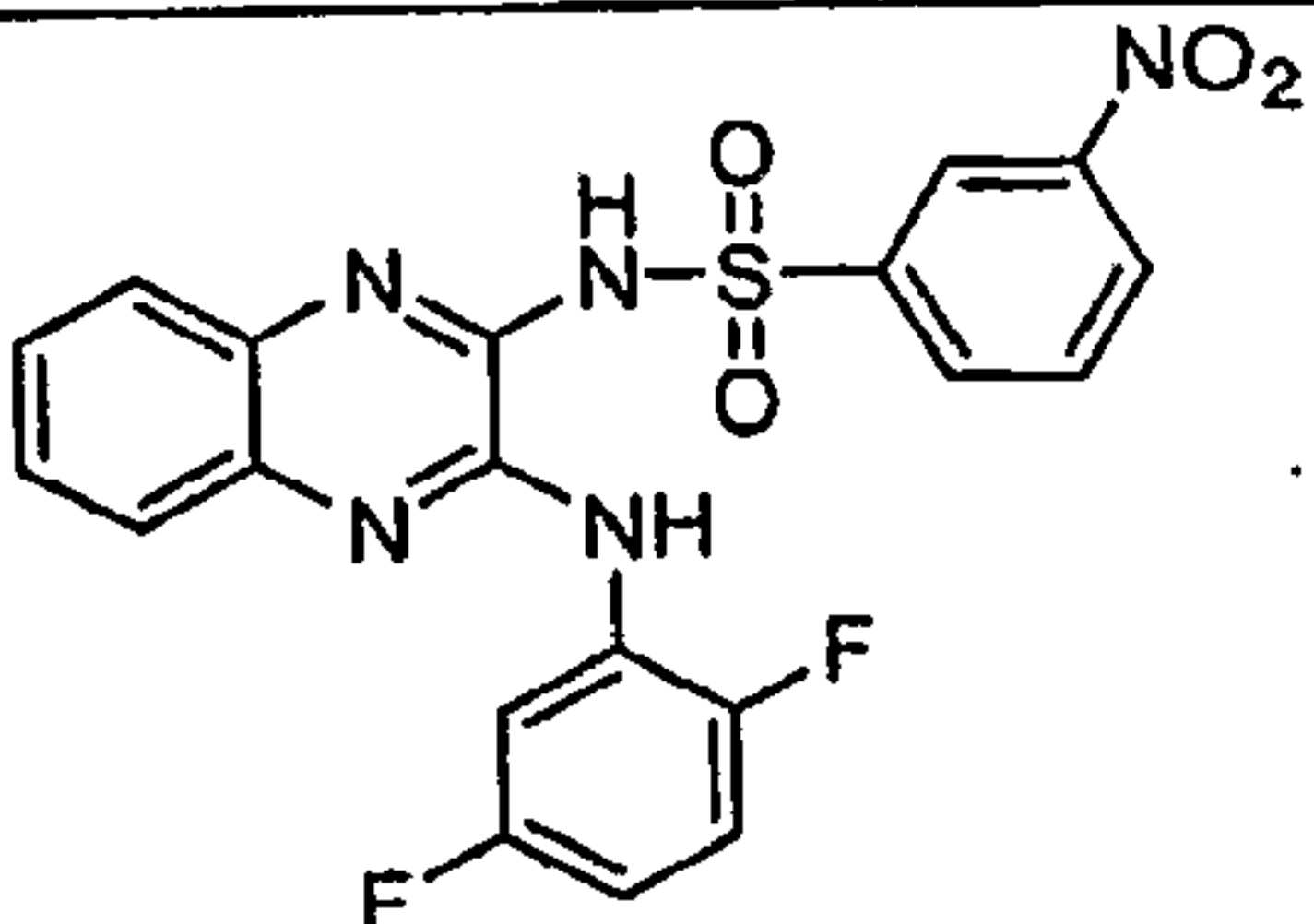
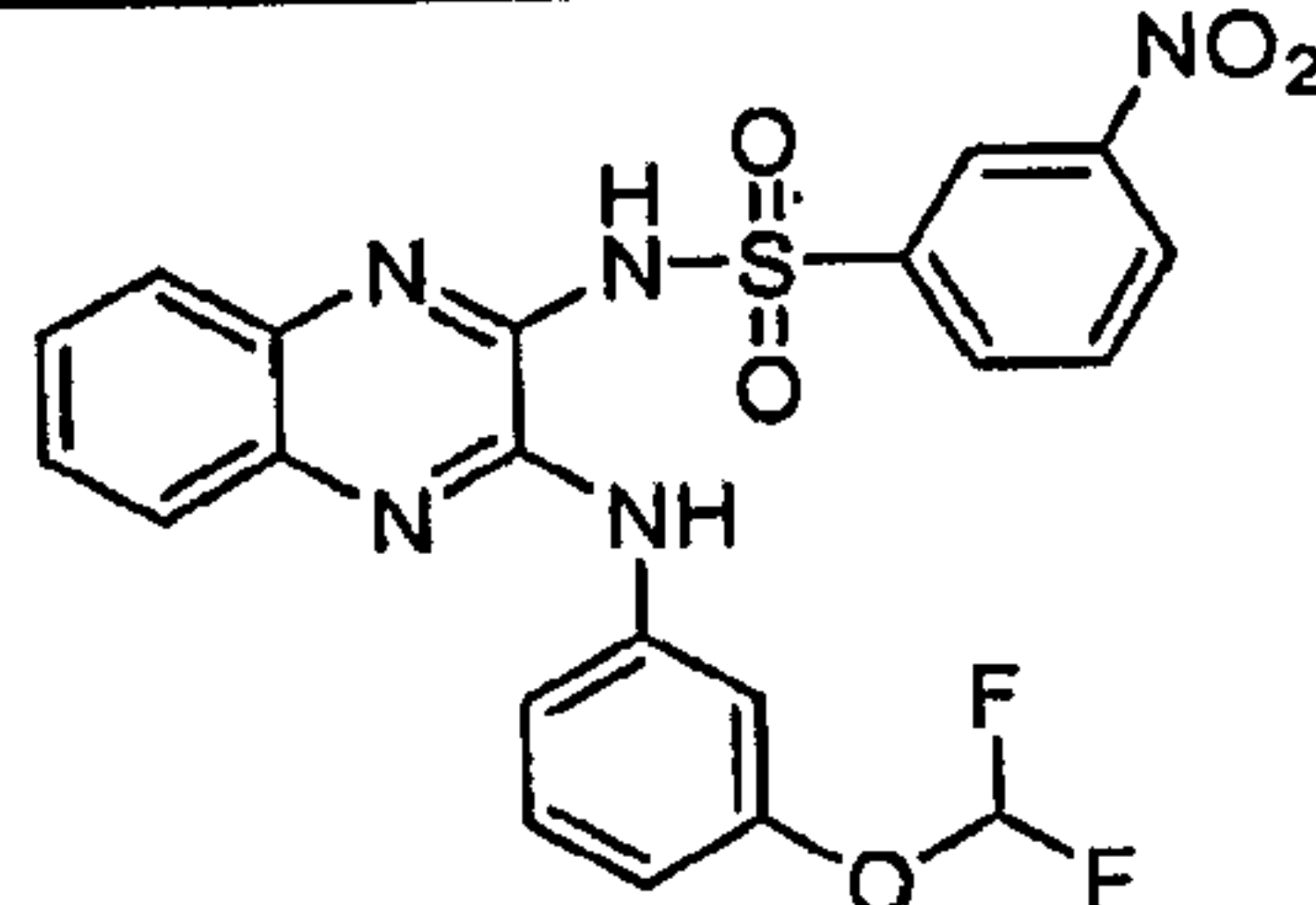
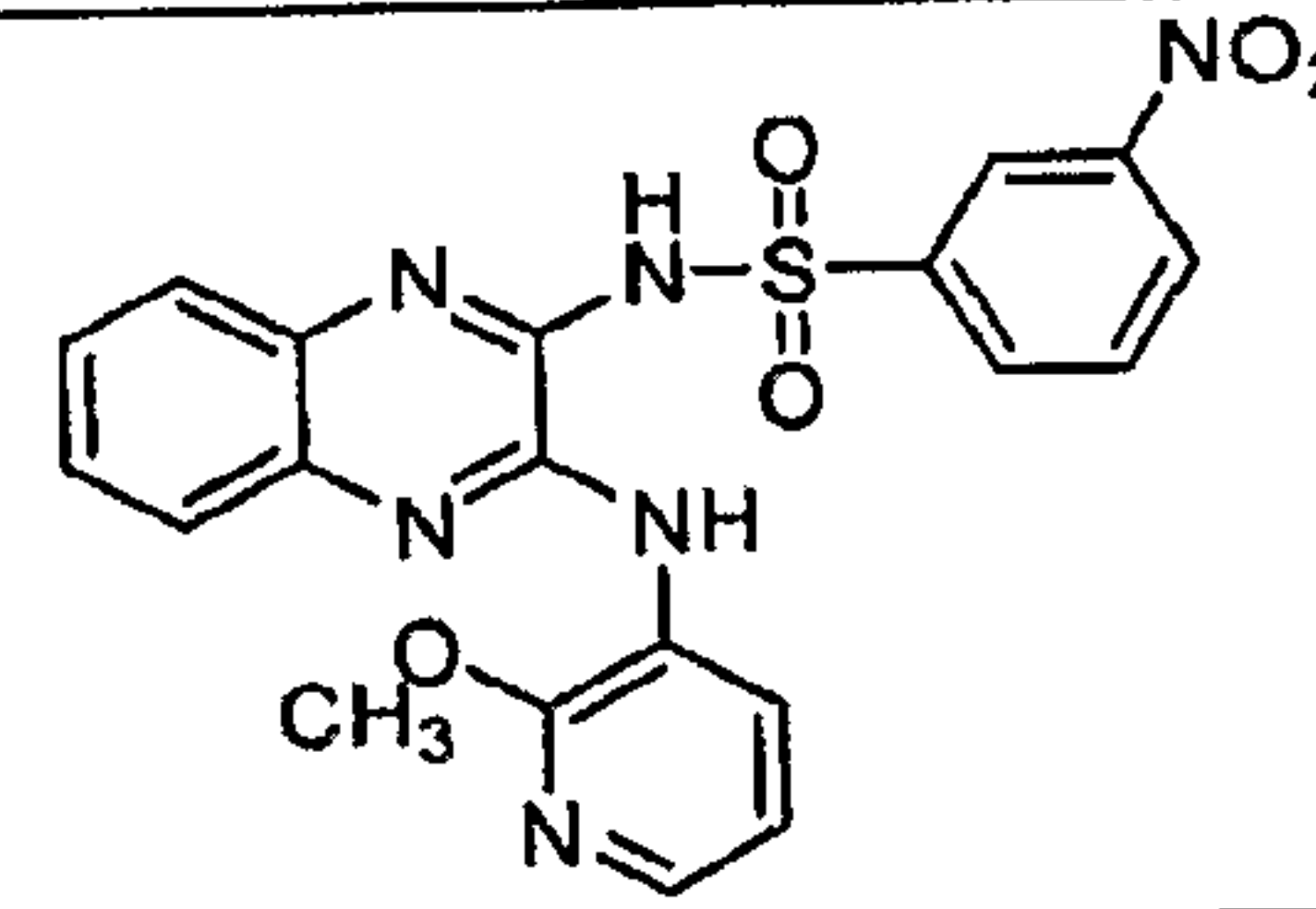
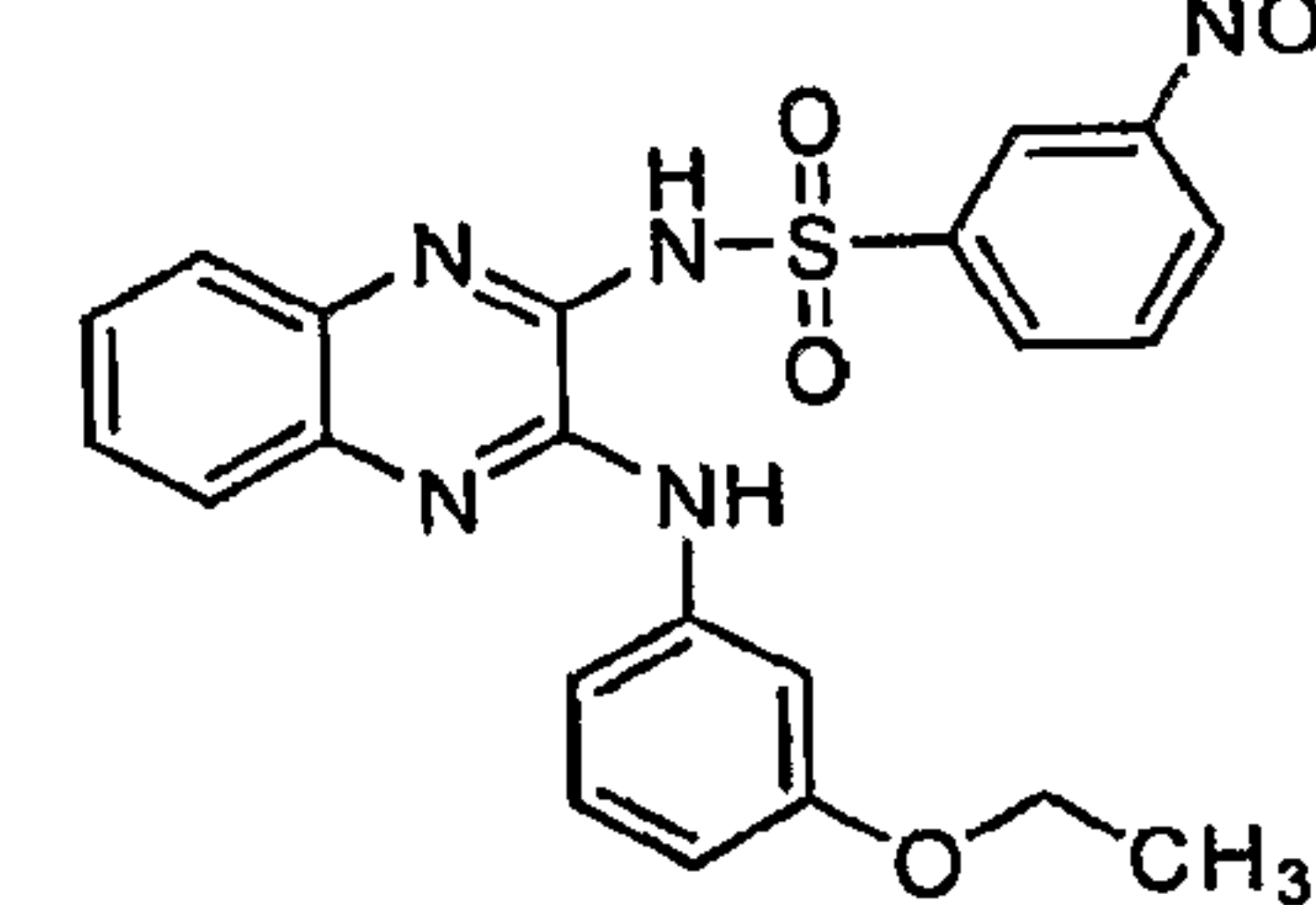
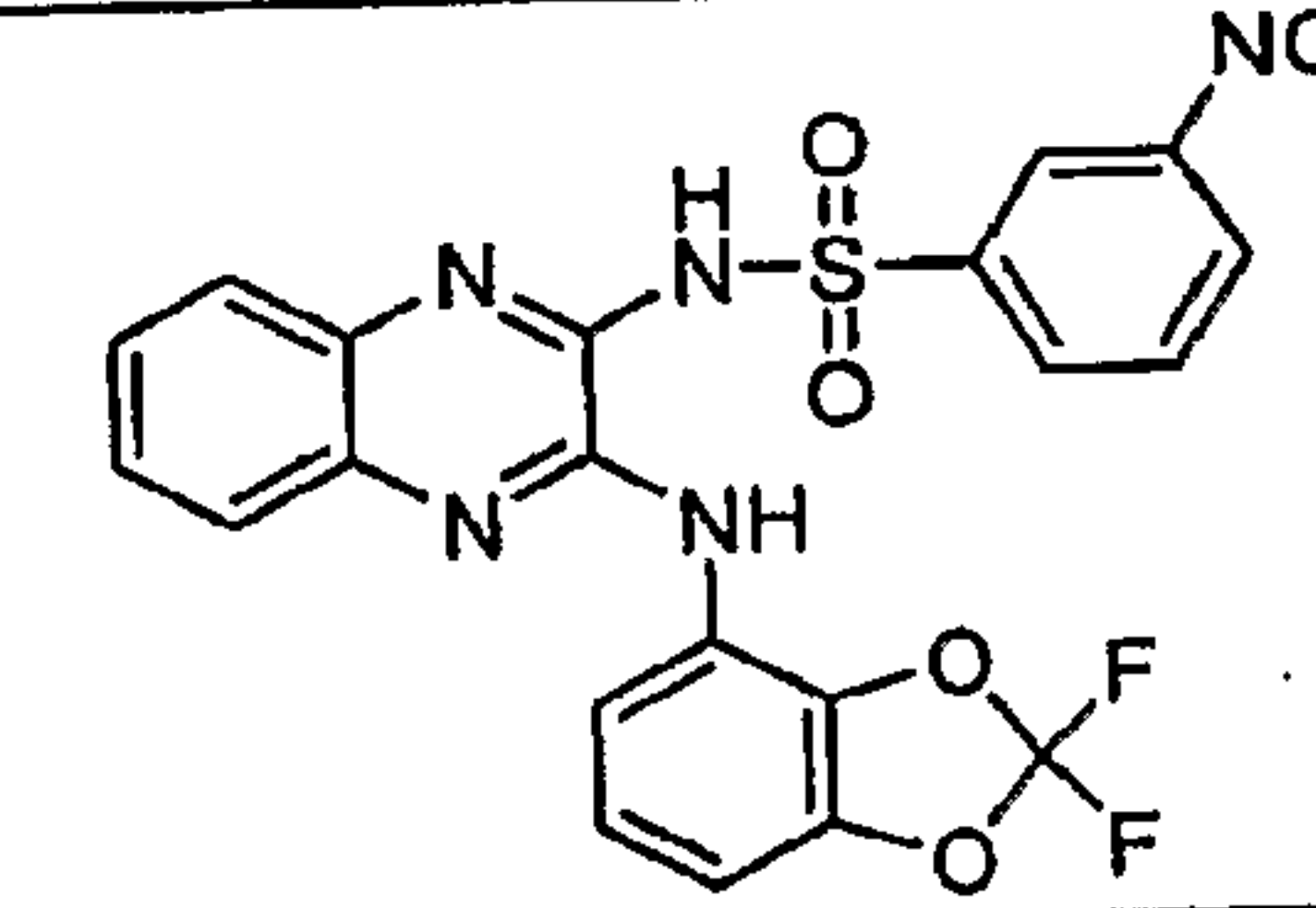
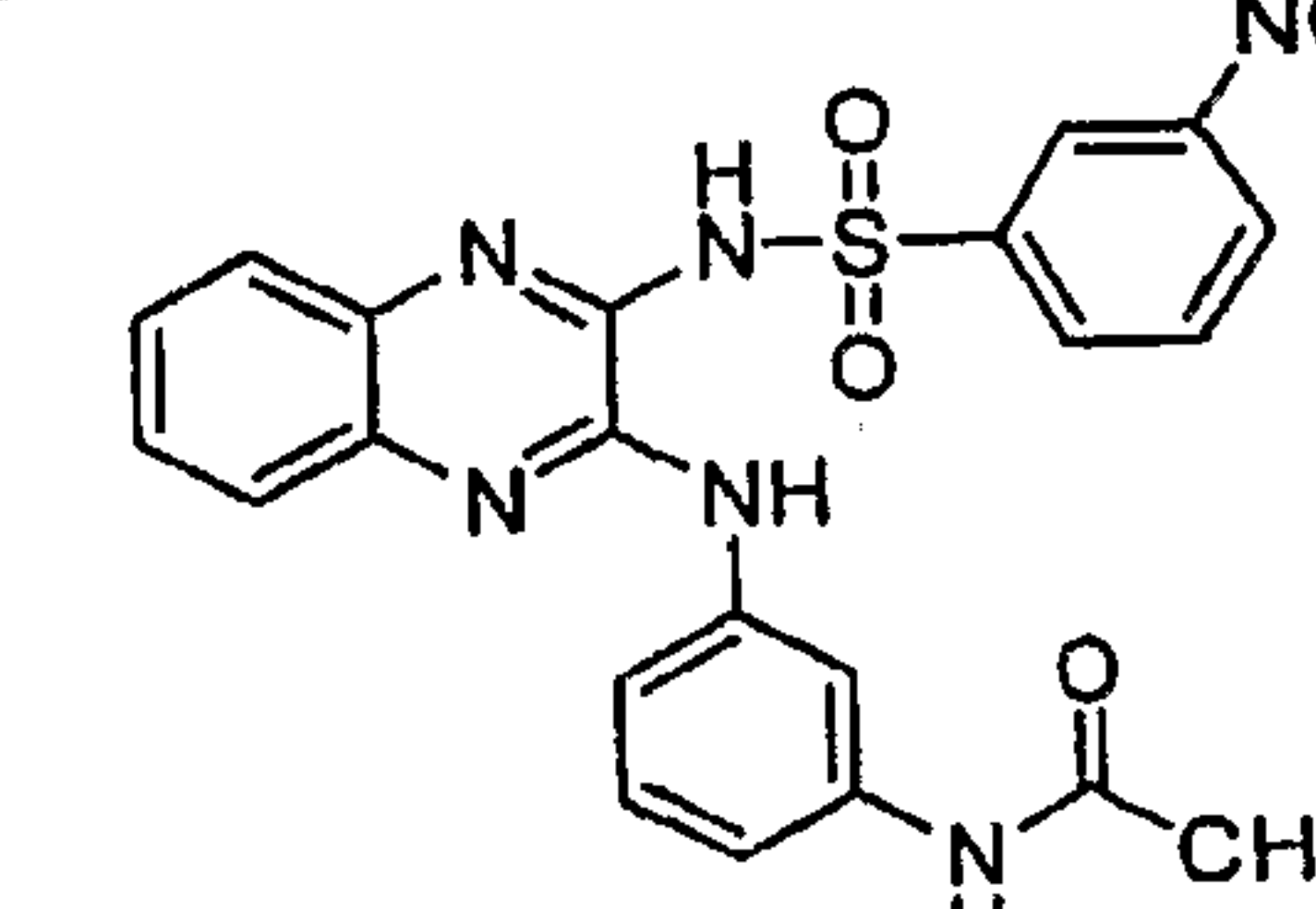
Table 1		
Cpd. No.	Structure	IUPAC Name
848		<i>N</i> -{3-[(2,5-difluorophenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
849		<i>N</i> -[3-({3-[(difluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
850		<i>N</i> -(3-{[2-(methyloxy)pyridin-3-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
851		<i>N</i> -(3-{[3-(ethyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
852		<i>N</i> -{3-[(2,2-difluoro-1,3-benzodioxol-4-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
853		<i>N</i> -{3-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide

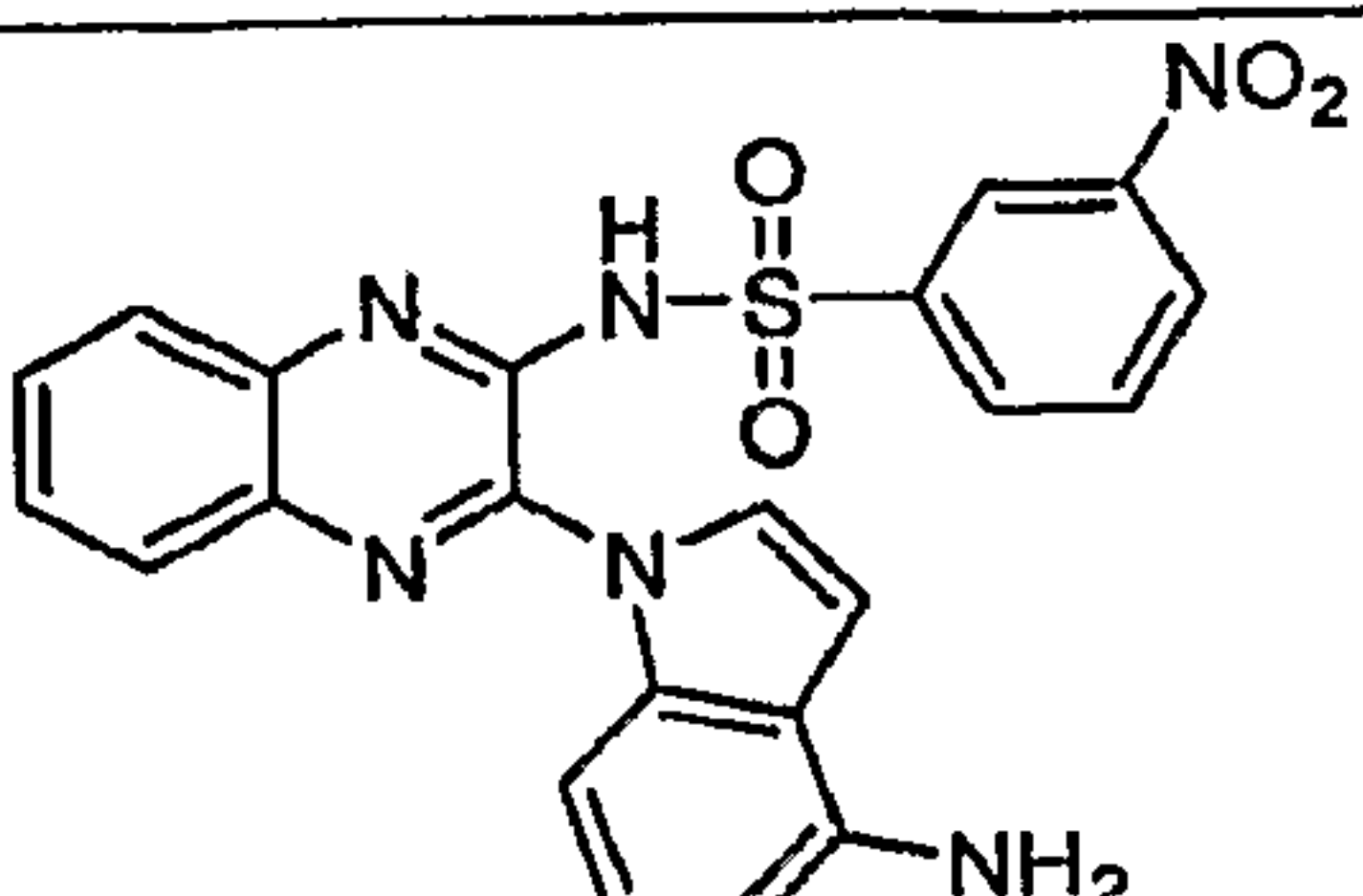
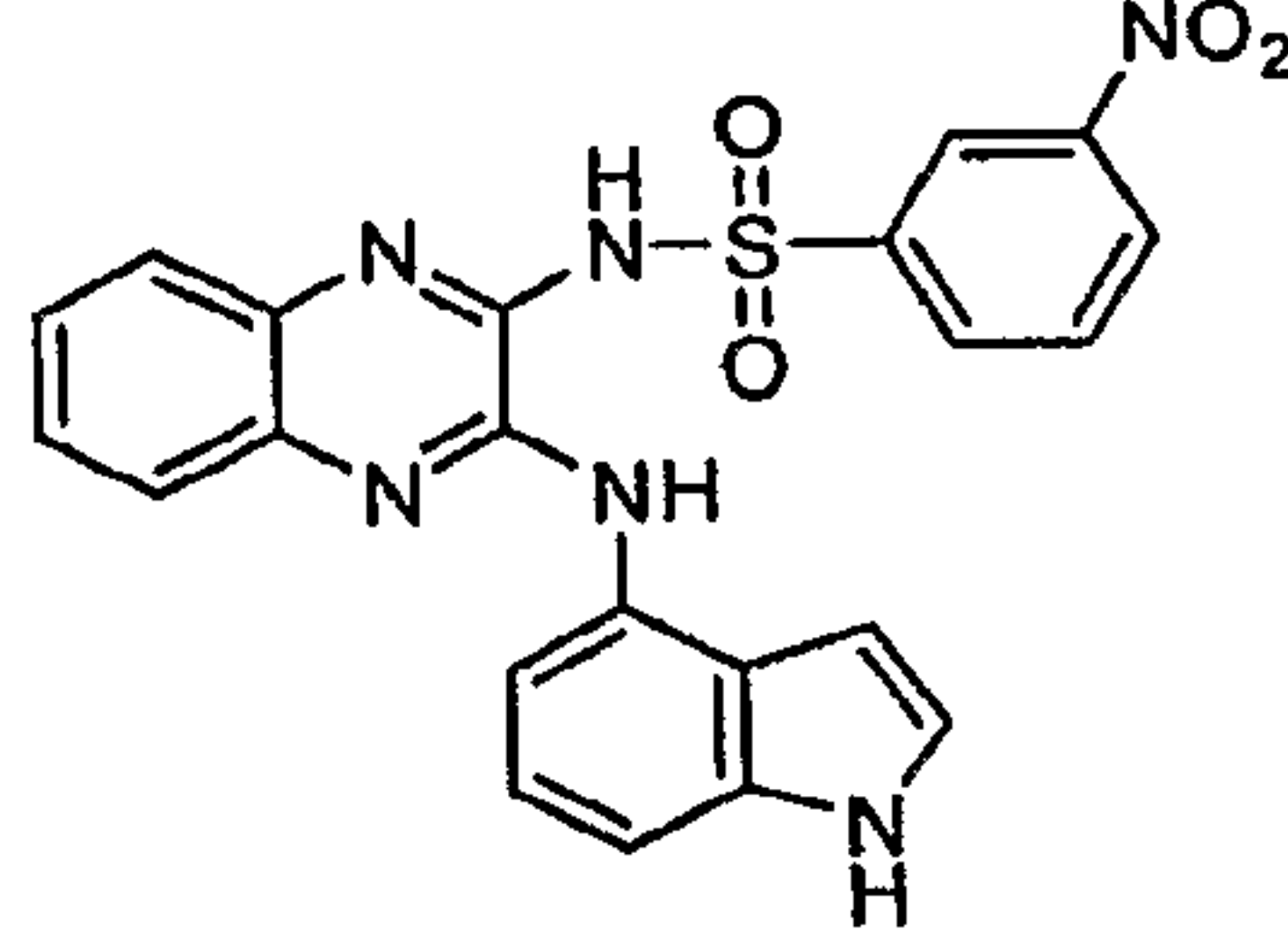
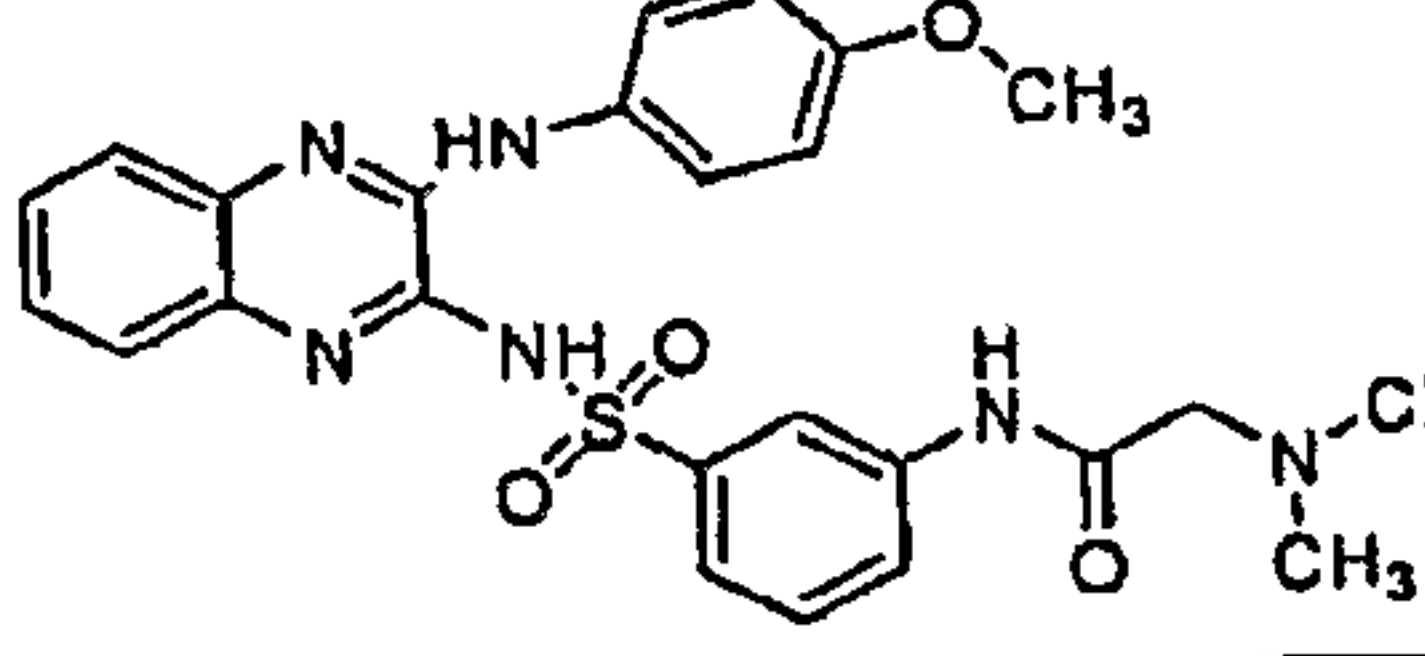
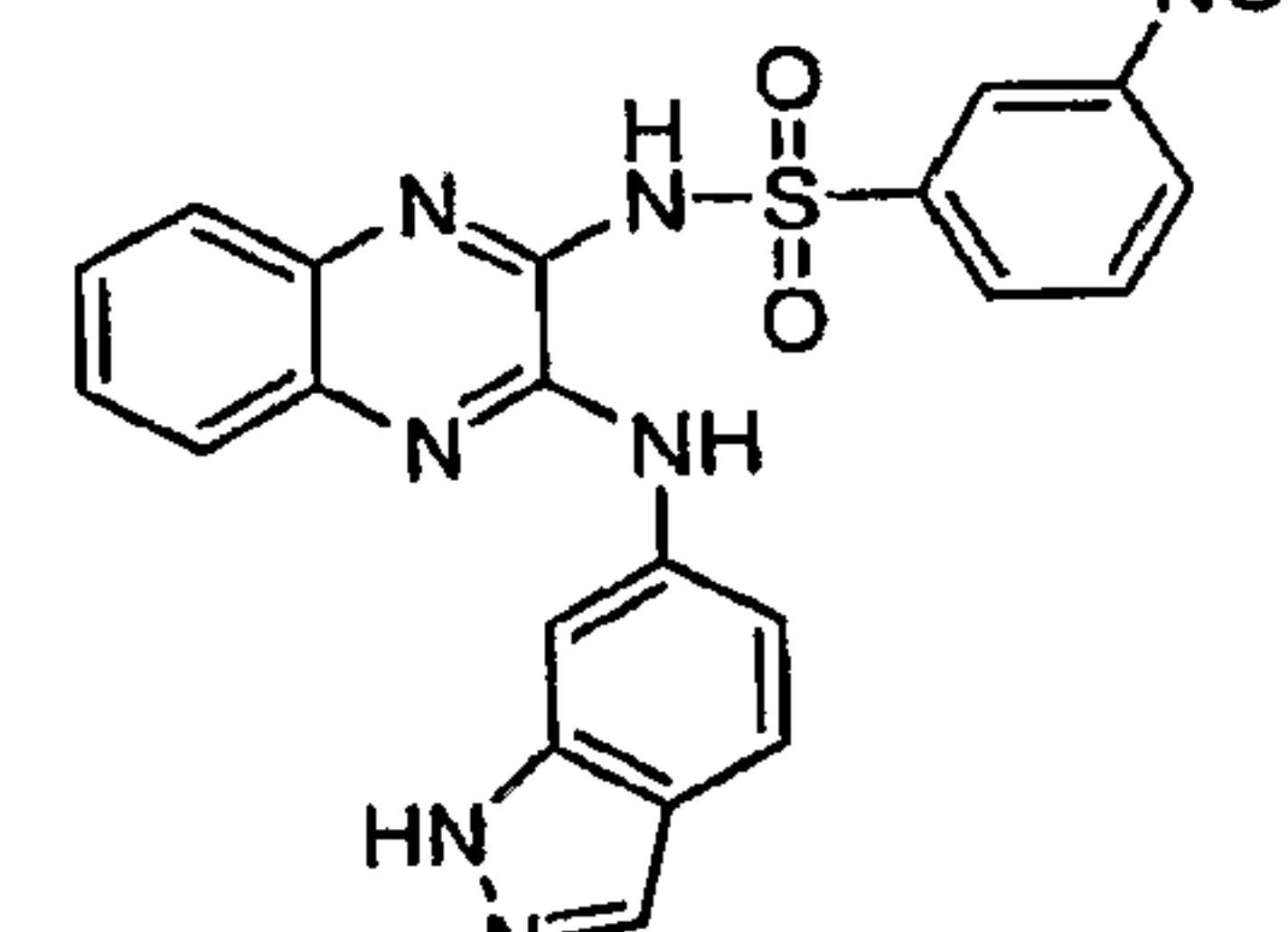
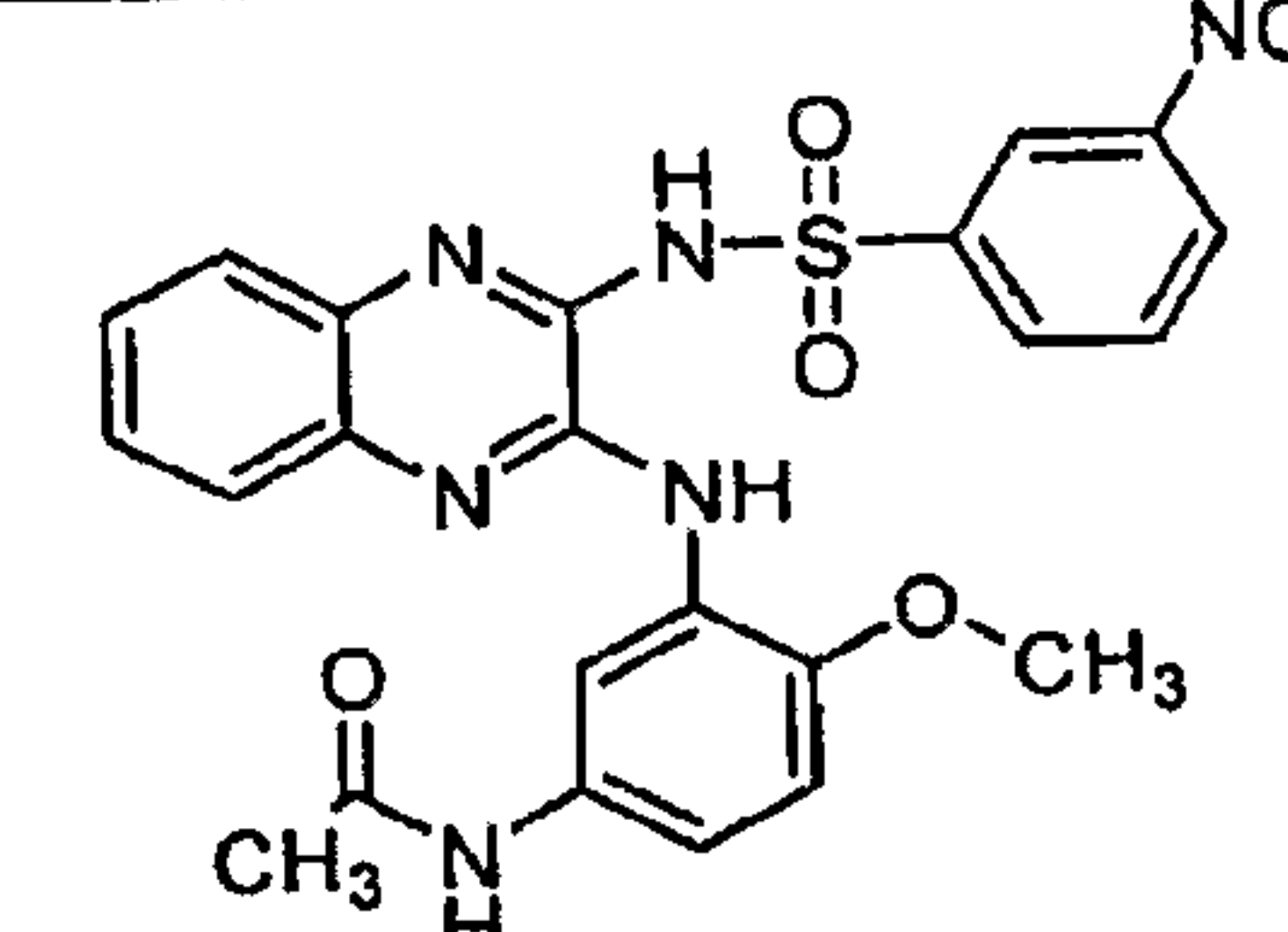
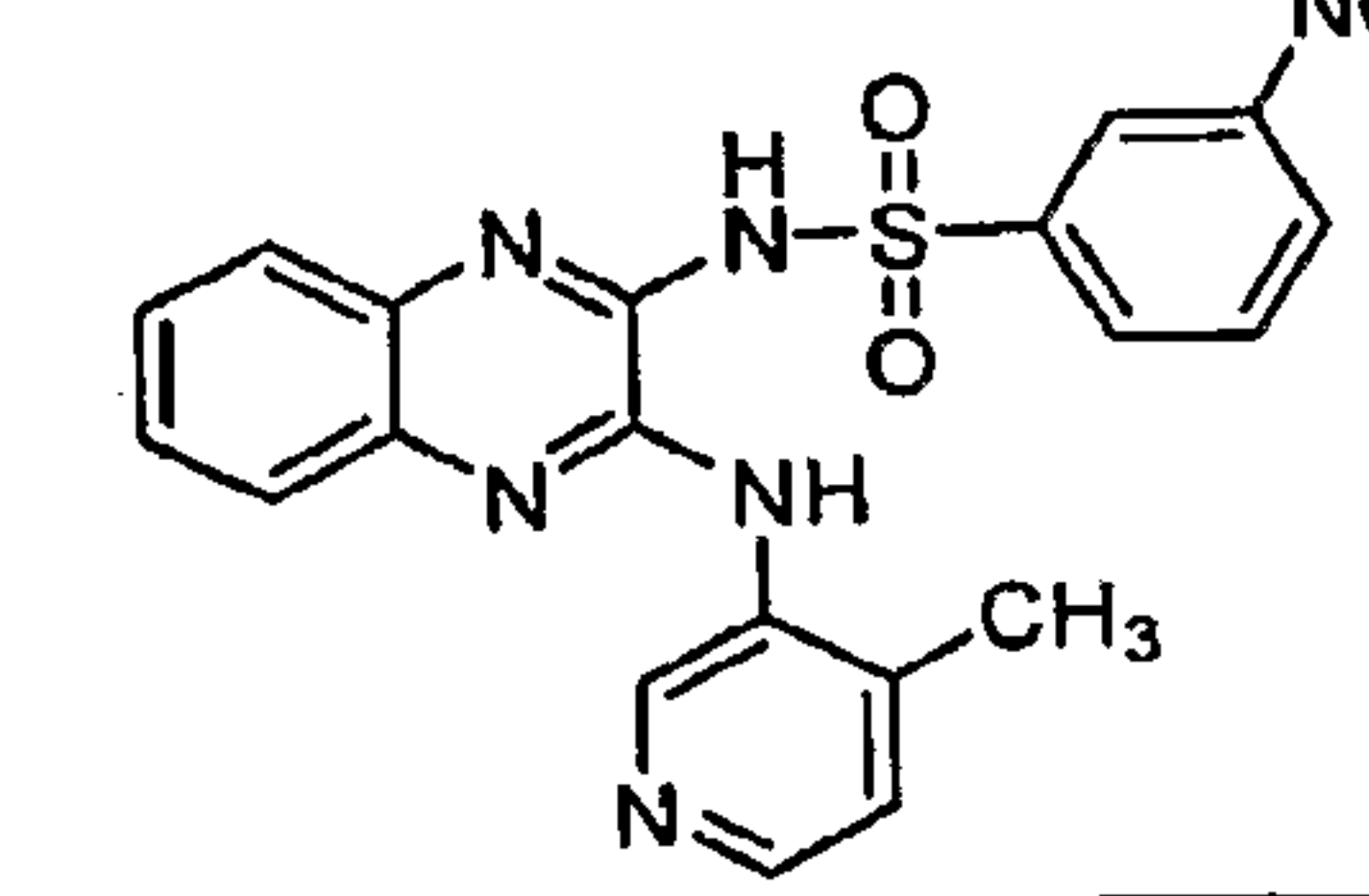
Table 1		
Cpd. No.	Structure	IUPAC Name
854		<i>N</i> -[3-(4-amino-1 <i>H</i> -indol-1-yl)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
855		<i>N</i> -[3-(1 <i>H</i> -indol-4-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
856		<i>N</i> -2,2-dimethyl- <i>N</i> -(3-{[(3-{[4-(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide
857		<i>N</i> -[3-(1 <i>H</i> -indazol-6-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
858		<i>N</i> -{4-(methoxy)-3-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide
859		<i>N</i> -{3-[(4-methylpyridin-3-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide

Table 1		
Cpd. No.	Structure	IUPAC Name
860		<i>N</i> -(3-{[2,3-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
861		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-2-cyanobenzenesulfonamide
862		3-nitro- <i>N</i> -[3-(1 <i>H</i> -pyrazolo[3,4- <i>d</i>]pyrimidin-4-ylamino)quinoxalin-2-yl]benzenesulfonamide
863		<i>N</i> -[3-(1,3-benzoxazol-4-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide
864		<i>N</i> -(3-{[2,6-difluoro-3-(methoxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide
865		<i>N</i> -{3-[(3-[(4-fluoro-3-methylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide
866		<i>N</i> -{3-[(3-[(3,5-dimethylphenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide

Table 1		
Cpd. No.	Structure	IUPAC Name
867		<i>N</i> -(3-{[(3-{[2,4-bis(methoxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide
868		<i>N</i> -{3-[(3,5-dihydroxyphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide
869		<i>N</i> -[3-({[3-(2,3-dihydro-1 <i>H</i> -inden-5-ylamino)quinoxalin-2-yl]amino}sulfonyl)phenyl]- <i>N</i> -2-, <i>N</i> -2-dimethylglycinamide
870		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)-4-[(1-methylethyl)oxy]benzenesulfonamide
871		<i>N</i> -(3-{[3,5-bis(methoxy)phenyl]amino}quinoxalin-2-yl)biphenyl-4-sulfonamide
872		<i>N</i> -[3-({2-chloro-5-[(difluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide

[00331] In addition to the preferred embodiments recited hereinabove, also preferred are embodiments comprising combinations of preferred embodiments.

[00332] One of ordinary skill in the art would understand that certain crystallized, protein-ligand complexes, in particular PI3K-ligand complexes, and their corresponding x-ray

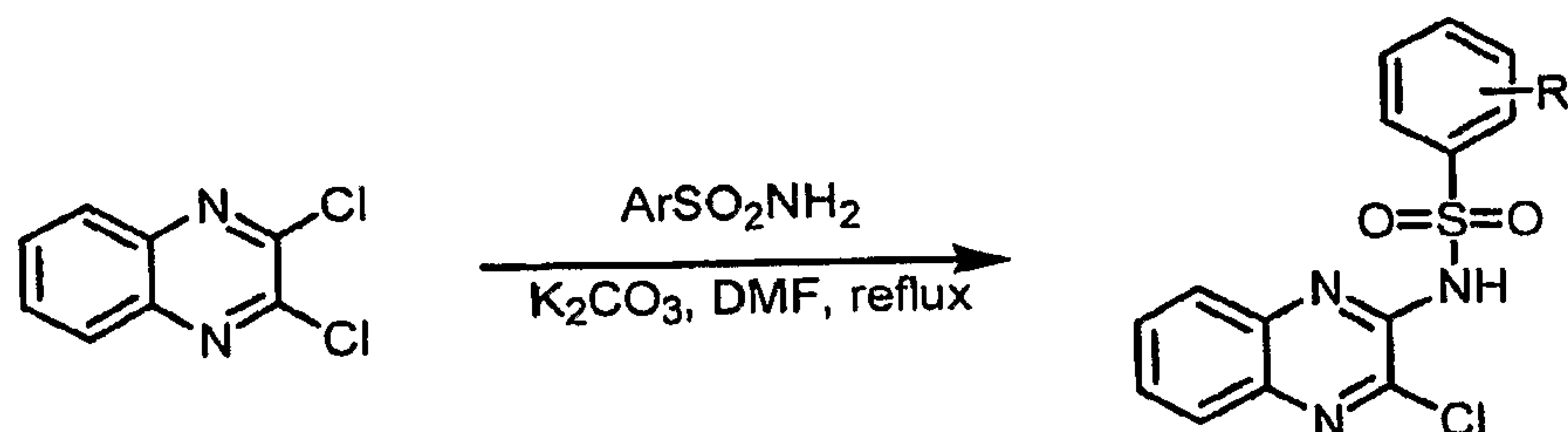
structure coordinates can be used to reveal new structural information useful for understanding the biological activity of kinases as described herein. As well, the key structural features of the aforementioned proteins, particularly, the shape of the ligand binding site, are useful in methods for designing or identifying selective modulators of kinases and in solving the structures of other proteins with similar features. Such protein-ligand complexes, having compounds of the invention as their ligand component, are an embodiment of the invention.

[00333] In one embodiment of the invention, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 8 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 4 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 3 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 2 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 1.5 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 1 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.750 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.5 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.3 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.2 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.1 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.075 μ M or less. In another embodiment, the PI3K inhibitor is selected from the compounds in Table I having a PI3K-binding affinity of about 0.050 μ M or less.

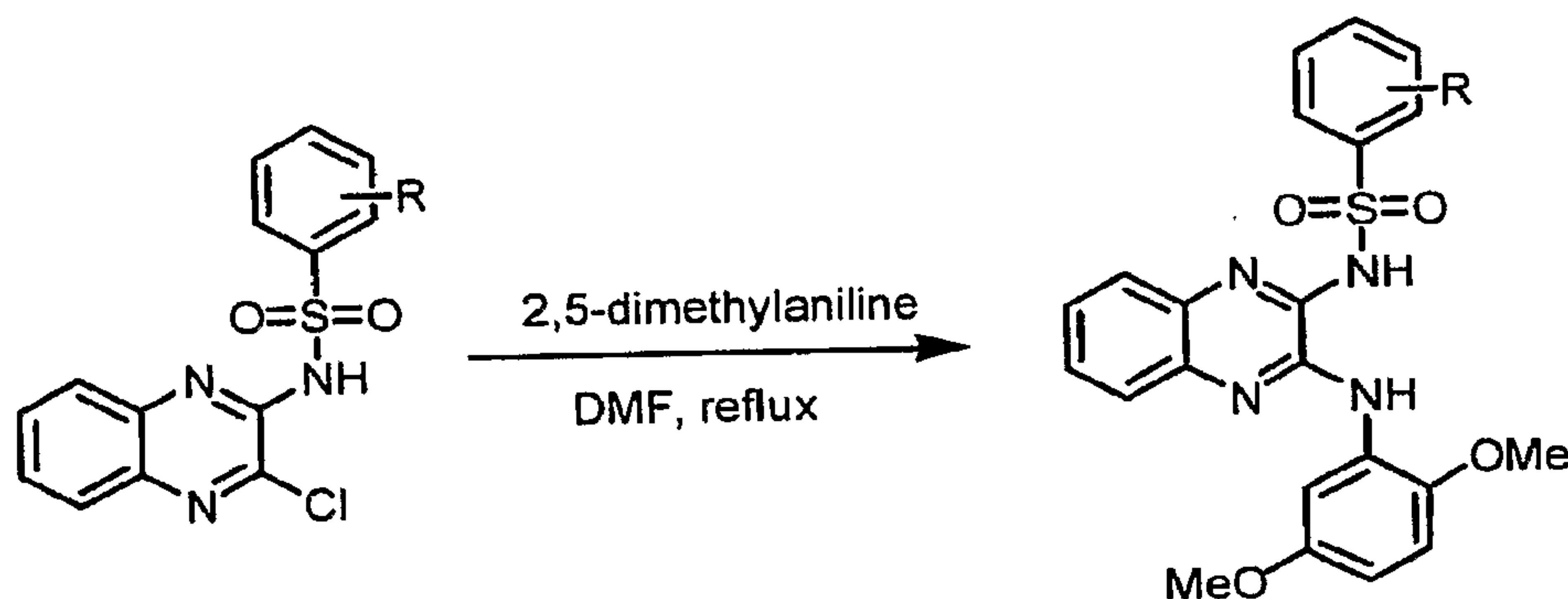
Synthetic Procedures

[00334] Fusion of the reagents at 180 °C in the presence of K_2CO_3 and metallic copper was known to provide these compounds in low yield (S. H. Dandegaonker and C. K. Mesta, *J. Med. Chem.* 1965, 8, 884). New method was utilized that brief heating of the reagents in

DMF in the presence of K_2CO_3 , commercially available 2,3-dichloroquinoxaline and substituted arylsulfonamides were formed in quantitative yields (S. V. Litvinenko, V. I. Savich, D. D. Bobrovnik, *Chem. Heterocycl. Compd.* (Engl. Transl), **1994**, 30, 340).

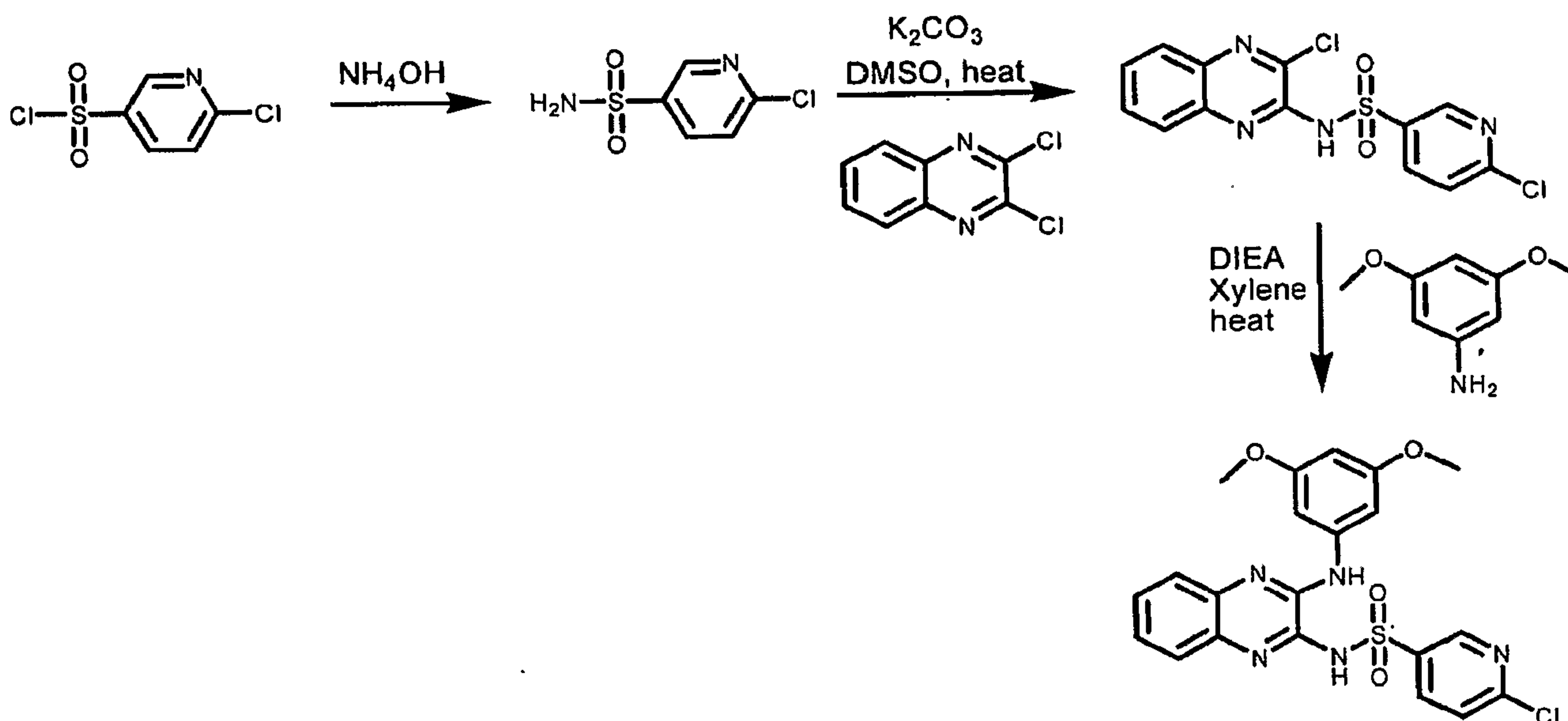


- 5 **[00335]** The displacement of the active chlorine atom in above compounds was treated with 2,5-dimethoxy-phenylamine (nucleophile) in refluxing DMF to give the desired compounds in quantitative yields (S. V. Litvinenko, V. I. Savich, D. D. Bobrovnik, *Chem. Heterocycl. Compd.* (Engl. Transl), **1994**, 30, 340).



- 10 **[00336]** On the other hand, the syntheses of other quinoxaline derivatives were well documented (W. C. Lumma, R. D. Hartman, *J. Med. Chem.* **1981**, 24, 93).

- [00337]** The following compounds were prepared in a manner similar to that described above: *N*-(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide; *N*-(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-chlorobenzenesulfonamide; *N*-(3-chloroquinoxalin-2-yl)-3-nitrobenzenesulfonamide; and 4-chloro-*N*-(3-chloroquinoxalin-2-yl)benzenesulfonamide.
- 15

Synthetic Examples**Example 1****6-chloro-N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)pyridine-3-sulfonamide**

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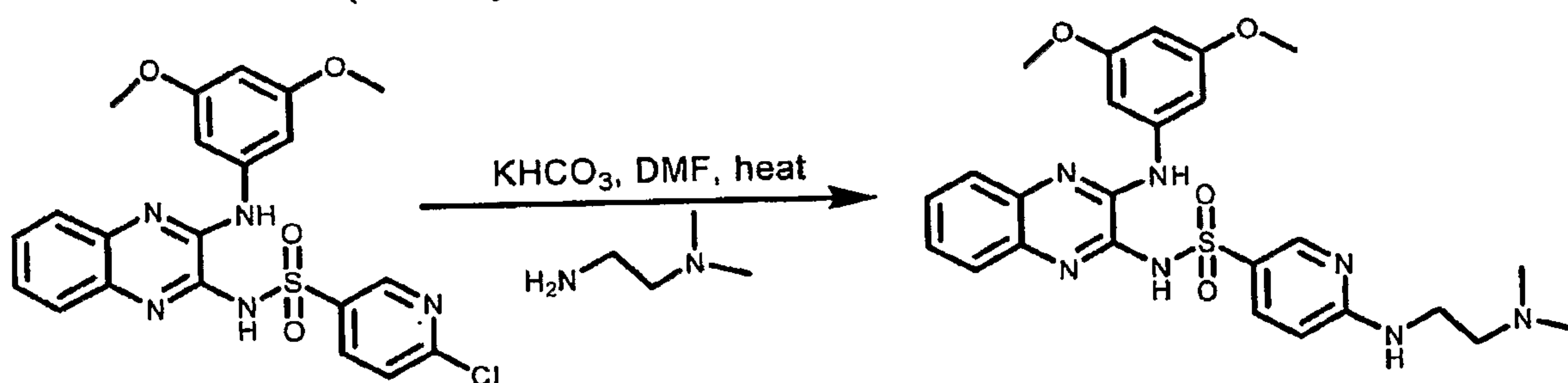
[00338] 6-chloropyridine-3-sulfonamide. 6-chloropyridine-3-sulfonyl chloride (4.1 g, 19.3 mmol) was stirred in ammonium hydroxide (30 mL) at room temperature for 2 hr. The reaction mixture was diluted with EtOAc (150 mL) and any insoluble material filtered. The filtrate was transferred to a separatory funnel and the phases were separated. The aqueous phase was further extracted with EtOAc (1 x 15 mL). The combined EtOAc extractions were washed with H₂O (1 x 50 mL), saturated NaCl (1 x 50 mL), dried (Na₂SO₄), and concentrated *in vacuo* to give 6-chloropyridine-3-sulfonamide (2.58g, 69%). MS (EI) for C₅H₃Cl₂NO₂S: 190.9 (MH⁻).

[00339] 6-chloro-N-(3-chloroquinoxalin-2-yl)pyridine-3-sulfonamide. 2,3-dichloroquinoxaline (1.09 g, 5.48 mmol), 6-chloropyridine-3-sulfonamide (1.05 g, 5.45 mmol), K₂CO₃ (753 mg, 5.45 mmol) and dry DMSO (30 mL) were combined and heated to 150°C with vigorous stirring for 3-4 hr. The reaction mixture was allowed to cool to room temperature, then poured into 1% AcOH in ice water (300 mL) with vigorous stirring. The resulting solids were filtered, washed with H₂O and dried under high vacuum to give 6-chloro-N-(3-chloroquinoxalin-2-yl)pyridine-3-sulfonamide (1.87g, 96%). MS (EI) for C₁₃H₈Cl₂N₄O₂S: 354.99 (MH⁺).

[00340] 6-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)pyridine-3-sulfonamide. 6-Chloro-*N*-(3-chloroquinoxalin-2-yl)pyridine-3-sulfonamide (775 mg, 2.2 mmol), 3,5-dimethoxyaniline (355 mg, 2.3 mmol) and toluene (12 mL) were combined and heated to 125°C with stirring overnight. The reaction was allowed to cool to room temperature and diluted with Et₂O with vigorous stirring. The resulting solids were filtered, washed with Et₂O and dried to give 6-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)pyridine-3-sulfonamide (920 mg, 89%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.20 (br s, 1H), 9.12 (d, 1H), 9.01 (br s, 1H), 8.53 (dd, 1H), 7.91 (br d, 1H), 7.77 (d, 1H), 7.60 (dd, 1H), 7.40 (m, 4H), 6.26 (m, 1H), 3.78 (s, 6H). MS (EI) for C₂₁H₁₈ClN₅O₄S: 472.0 (MH⁺).

Example 2

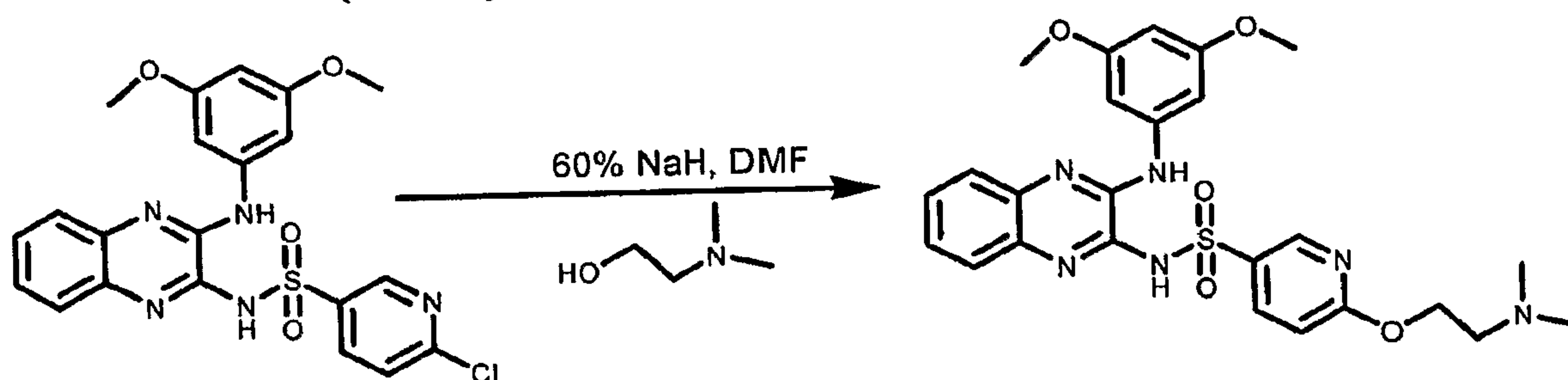
N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-(2-(dimethylamino)ethylamino)pyridine-3-sulfonamide



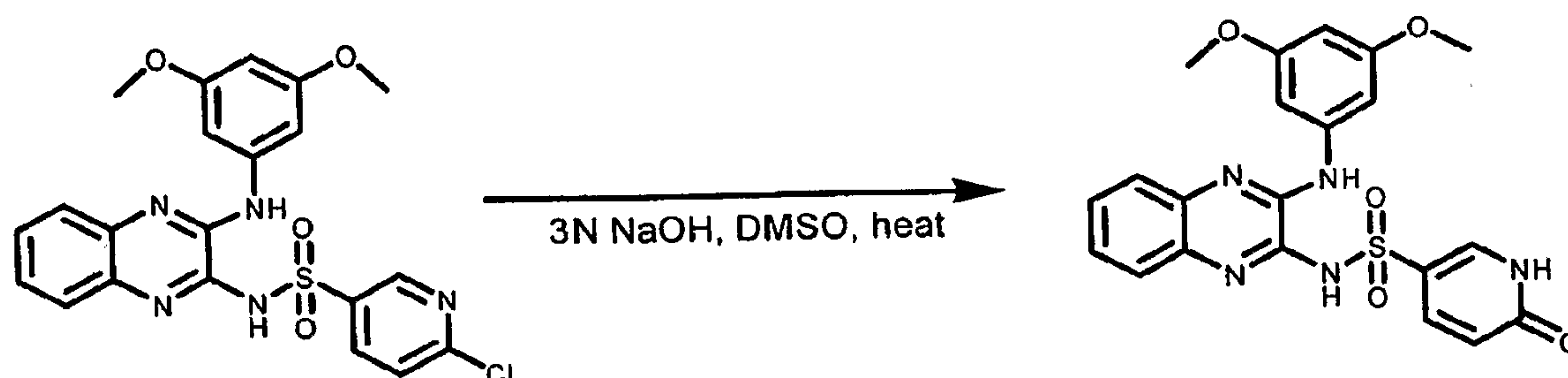
[00341] *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)pyridine-3-sulfonamide (100 mg, 0.21 mmol), KHCO₃ (40 mg, 0.40 mmol), *N*¹,*N*¹-dimethylethane-1,2-diamine (225 μl, 2.0 mmol) and dry DMF (1.0 mL) were combined and heated to 130°C with stirring overnight. The reaction mixture was concentrated *in vacuo* and purified by preparative HPLC to give *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-(2-(dimethylamino)ethylamino)pyridine-3-sulfonamide (21.0 mg, 19%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.76 (br s, 1H), 8.63 (d, 1H), 8.07 (dd, 1H), 7.40 (m, 1H), 7.34 (m, 1H), 7.28 (d, 2H), 7.14 (m, 4H), 6.47 (d, 1H), 6.12 (m, 1H), 3.75 (s, 6H), 3.35 (m, 2H), 3.14 (m, 2H), 2.74 (s, 6H). MS (EI) for C₂₅H₂₉N₇O₄S: 524.1 (MH⁺).

Example 3***N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-(dimethylamino)pyridine-3-sulfonamide**

[00342] The title compound was prepared according to the Examples above. ¹H NMR (400 MHz, DMSO-d₆) δ 12.00 (br s, 1H), 8.92 (br s, 1H), 8.74 (d, 1H), 8.10 (dd, 1H), 7.38 (br s, 1H), 7.54 (m, 1H), 7.33 (m, 4H), 6.70 (d, 1H), 6.22 (s, 1H), 3.77 (s, 6H), 3.08 (s, 6H). MS (EI) for C₂₃H₂₄N₆O₄S: 481.1 (MH⁺).

Example 4***N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-(2-(dimethylamino)ethoxy)pyridine-3-sulfonamide**

[00343] *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)pyridine-3-sulfonamide (100 mg, 0.21 mmol), 2-(dimethylamino)ethanol (50 μl, 0.50 mmol) and dry DMF were combined and 60% NaH in oil (80 mg, 2.0 mmol) added. The mixture was stirred at room temperature overnight. The reaction mixture was concentrated in vacuo and purified by preparative HPLC to give *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-(2-(dimethylamino)ethoxy)pyridine-3-sulfonamide (23 mg, 21%). ¹H NMR (400 MHz, DMSO-d₆) δ 8.78 (d, 1H), 8.73 (s, 1H), 8.38 (dd, 1H), 7.40 (dd, 1H), 7.31 (m, 3H), 7.14 (m, 2H), 6.85 (d, 1H), 6.12 (m, 1H), 4.56 (m, 2H), 3.76 (s, 6H), 3.43 (m, 2H), 2.77 (s, 6H). MS (EI) for C₂₅H₂₈N₆O₅S: 525.1 (MH⁺).

Example 5***N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide**

5 [00344] *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)pyridine-3-sulfonamide (220 mg, 0.47 mmol), DMSO (5 mL), and 3*N* NaOH (5 mL) are combined and heated to 100°C overnight with stirring. Upon cooling to room temperature, the reaction mixture was diluted with H₂O and the pH was adjusted to 7.0 with 1*N* HCl. The resulting solid was filtered, washed with H₂O, and air-dried. The solid was then sonicated in EtOAc, filtered, washed

10 with EtOAc, and dried under high vacuum to give *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide (190 mg, 90%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.23 (br s, 1H), 12.10 (br s, 1H), 8.97 (s, 1H), 8.23 (s, 1H), 7.95 (m, 2H), 7.59 (m, 1H), 7.37 (m, 4H), 6.43 (d, 1H), 6.25 (s, 1H), 3.77 (s, 6H). MS (EI) for C₂₁H₁₉N₅O₅S: 454.0 (MH⁺).

15 [00345] The following title compounds were prepared according to the above Examples.

Example 6: *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.22 (br s, 1H), 12.10 (br s, 1H), 9.16 (s, 1H), 8.60 (s, 1H), 8.14 (d, 1H), 7.94 (m, 1H), 7.85 (dd, 1H), 7.62 (m, 1H), 7.40 (m, 3H) 6.69 (dd, 1H), 6.43 (d, 1H), 3.81 (s, 3H). MS (EI) for C₂₀H₁₆ClN₅O₄S: 456.0 (MH⁺).

Example 7: 5-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(dimethylamino)ethyl)-2-methoxybenzamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.45 (s, 1H), 8.95 (d, 1H), 8.57 (d, 1H), 8.28 (t, 1H), 8.14 (dd, 1H), 7.46 (dd, 1H), 7.39 (m, 2H), 7.17 (m, 4H), 6.60 (dd, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 3.38 (m, 2H), 2.43 (m, 2H), 2.21 (s, 6H). MS (EI) for C₂₇H₂₉ClN₆O₅S: 585.3 (MH⁺).

Example 8: 5-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(dimethylamino)ethyl)-2-fluorobenzamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.40 (br s, 1H), 9.16 (s, 1H), 8.73 (m, 1H), 8.67 (d, 1H), 8.36 (dd, 1H), 8.26 (m, 1H), 7.94 (br s, 1H),

7.66 (m, 1H), 7.59 (t, 1H), 7.43 (m, 3H), 6.71 (dd, 1H), 3.83 (s, 3H), 3.62 (m, 2H), 3.27 (m, 2H), 2.85 (d, 6H). MS (EI) for $C_{26}H_{26}ClFN_6O_4S$: 573.1 (MH⁺).

Example 9: *N*-(2-chloro-5-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)acetamide. The title compound was prepared

5 according to the Examples above. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 9.14 (s, 1H), 9.03 (m, 2H), 8.63 (d, 1H), 8.44 (d, 1H), 7.98 (m, 1H), 7.91 (dd, 1H), 7.80 (d, 1H), 7.67 (m, 1H), 7.44 (m, 3H), 6.71 (dd, 1H), 4.06 (m, 2H), 3.83 (s, 3H), 2.64 (t, 3H). MS (EI) for $C_{24}H_{22}Cl_2N_6O_4S$: 561.0 (MH⁺).

Example 10: (S)-2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)propanamide hydrochloride. ¹H NMR (400 MHz, CD₃OD) δ 8.72-8.71 (d, 1H), 8.48-8.46 (t, 1H), 7.86-7.84 (m, 1H), 7.80-7.78 (m, 1H), 7.63-7.59 (m, 2H), 7.58-7.55 (t, 1H), 7.41-7.38 (m, 2H), 7.24-7.22 (d, 1H), 6.60-6.58 (dd, 1H), 4.10-4.04 (q, 1H), 3.83 (s, 3H), 1.61-1.60 (d, 3H); MS (EI) for $C_{24}H_{23}ClN_6O_4S.HCl$: 527.2 (MH⁺).

Example 11: (S)-2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)butanamide hydrochloride. ¹H NMR (400 MHz, CD₃OD) δ 8.74-8.73 (d, 1H), 8.80-8.47 (t, 1H), 7.87-7.85 (m, 1H), 7.80-7.78 (m, 1H), 7.67-7.61 (m, 2H), 7.59-7.55 (t, 1H), 7.42-7.39 (m, 2H), 7.26-7.24 (d, 1H), 6.62-6.59 (dd, 1H), 3.96-3.93 (t, 1H), 3.84 (s, 3H), 2.02-1.94 (m, 2H), 1.09-1.06 (t, 3H); MS (EI) for $C_{25}H_{25}ClN_6O_4S.HCl$: 541.3 (MH⁺).

Example 12: (S)-*N*-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pyrrolidine-2-carboxamide hydrochloride. ¹H NMR (400 MHz, CD₃OD) δ 8.78-8.77 (d, 1H), 8.47-8.46 (t, 1H), 7.87-7.85 (m, 1H), 7.80-7.75 (m, 1H), 7.69-7.65 (m, 2H), 7.59-7.55 (t, 1H), 7.45-7.41 (m, 2H), 7.31-7.28 (d, 1H), 6.65-6.63 (dd, 1H), 4.42-4.38 (m, 1H), 3.86 (s, 3H), 3.48-3.42 (m, 2H), 2.55-2.49 (m, 1H), 2.18-2.08 (m, 3H); MS (EI) for $C_{26}H_{25}ClN_6O_4S.HCl$: 553.3 (MH⁺).

Example 13: (S)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pyrrolidine-2-carboxamide hydrochloride. ¹H NMR (400 MHz, CD₃OD) δ 10.62 (br s, 1H), 8.50-8.49 (t, 1H), 7.90-7.87 (m, 1H), 7.76-7.73 (m, 1H), 7.63-7.58 (m, 3H), 7.43-7.35 (m, 2H), 7.14 (s, 2H), 6.27-6.26 (t, 1H), 4.43-4.38 (m, 1H), 3.78 (s, 6H), 3.48-3.41 (m, 1H), 3.40-3.36 (m, 1H), 2.54-2.48 (m, 1H), 2.19-2.05 (m, 3H); MS (EI) for $C_{27}H_{28}N_6O_5S.HCl$: 549.3 (MH⁺).

Example 14: (R)-2-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-hydroxypropanamide hydrochloride. ¹H NMR (400 MHz,

CD3OD) δ 8.49-8.48 (t, 1H), 7.89-7.87 (m, 1H), 7.75-7.72 (m, 1H), 7.65-7.62 (m, 2H), 7.62-7.55 (t, 1H), 7.44-7.38 (m, 2H), 7.23-7.22 (d, 2H), 6.27-6.26 (t, 1H), 4.07-4.05 (m, 1H), 3.99-3.93 (m, 2H), 3.80 (s, 6H); MS (EI) for $C_{25}H_{26}N_6O_6S.HCl$: 539.1 (MH⁺).

Example 15: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-

5 **2-yl)sulfamoyl)phenyl)piperidine-3-carboxamide hydrochloride.** ¹H NMR (400 MHz, CD3OD) δ 8.79-8.78 (d, 1H), 8.45 (m, 1H), 7.83-7.81 (d, 1H), 7.76-7.74 (m, 1H), 7.636 (m, 2H), 7.54-7.50 (t, 1H), 7.41 (m, 2H), 7.30-7.28 (d, 1H), 6.65-6.62 (dd, 1H), 3.86 (s, 3H), 3.40-3.32 (m, 2H), 3.20-3.13 (m, 3H), 2.93 (m, 1H), 2.15-2.11 (m, 1H), 1.98-1.93 (m, 2H), 1.83 (m, 1H); MS (EI) for $C_{27}H_{27}ClN_6O_4S . HCl$: 567.3 (MH⁺).

10 **Example 16: (S)-2-amino-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)butanamide hydrochloride.** MS (EI) for $C_{26}H_{28}N_6O_5S.HCl$: 537.1 (MH⁺).

Example 17: (R)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-

15 **2-yl)sulfamoyl)phenyl)pyrrolidine-2-carboxamide hydrochloride.** MS (EI) for $C_{27}H_{28}N_6O_5S.HCl$: 549.1 (MH⁺).

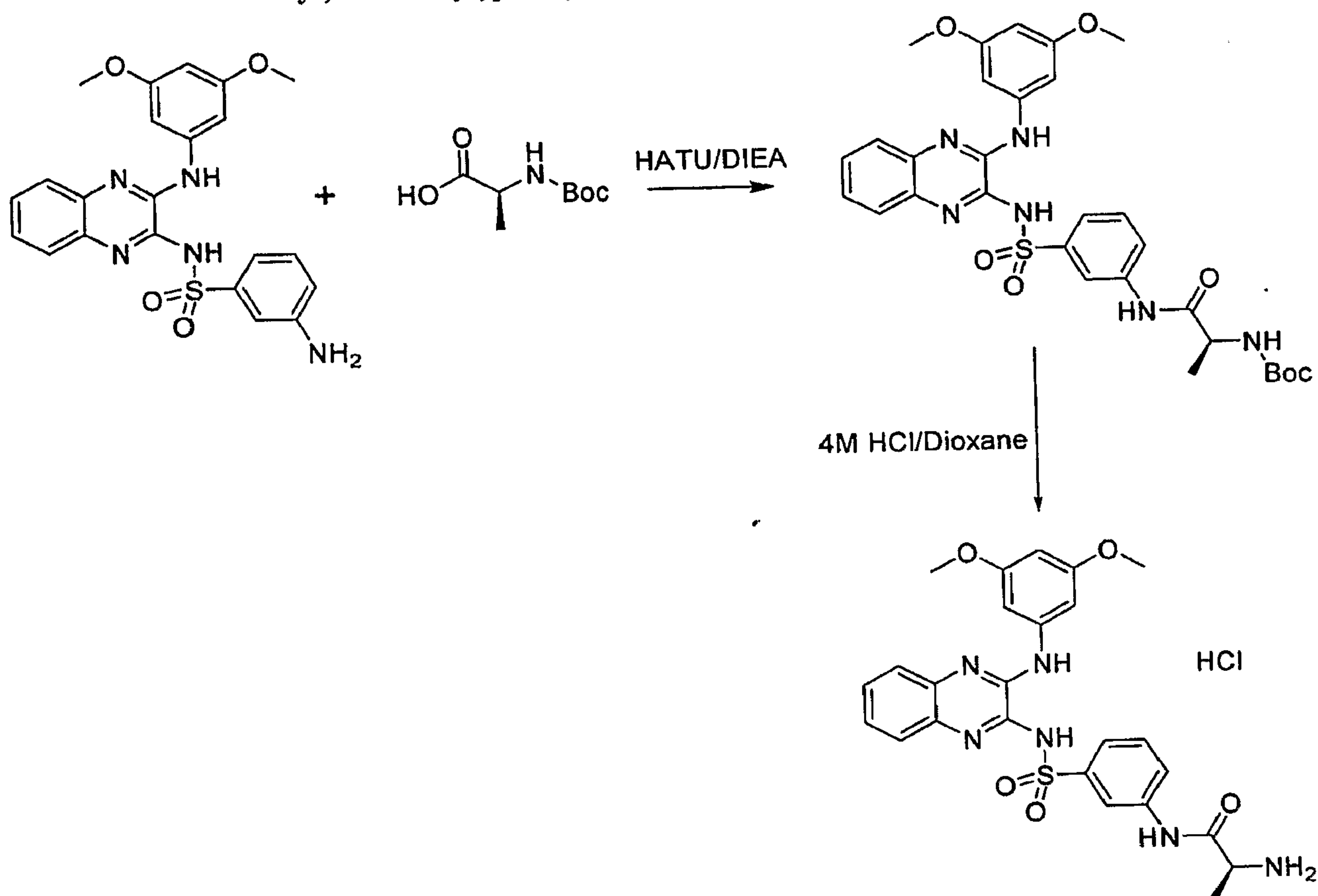
Example 18: (R)-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pyrrolidine-2-carboxamide hydrochloride. MS (EI) for $C_{26}H_{25}ClN_6O_4S.HCl$: 553 (MH⁺).

20 **Example 19: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)morpholine-4-carboxamide:** MS (EI) for $C_{26}H_{25}ClN_6O_5S$: 567 (MH⁻).

Example 20: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. MS (EI) for $C_{26}H_{28}N_6O_5S$: 535.1 (MH⁻).

Example 21

(S)-2-amino-N-(3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)propanamide hydrochloride.



5

[00346] (S)-tert-butyl 1-(3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenylamino)-1-oxopropan-2-ylcarbamate. 3-amino-N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide (1.1 mmol, 500 mg), (L)-Boc-Ala-OH (1.5 mmol, 284 mg), dichloromethane (15 mL), DMF (10 mL), DIEA (2 mmol, 330 ul), and HATU (2 mmol, 760 mg) stirred at r.t. over night. The crude mixture was column purified using 1/1 ethyl acetate/hexanes on silica to gave 160 mg.

10

[00347] (S)-2-amino-N-(3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)propanamide hydrochloride. 4 M HCl in dioxane (10 mL) was added to a solution of (S)-tert-butyl 1-(3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenylamino)-1-oxopropan-2-ylcarbamate (160 mg) and DCM (15 mL). The mixture was stirred at r.t. for 3 hours. The solvent decanted and ether added to the solid, ether decanted to gave 80 mg product as HCl salt. ¹H NMR (400 MHz, CD₃OD) δ 8.50-8.49 (t, 1H), 7.89-7.87 (m, 1H), 7.74-7.72 (m, 1H), 7.61-7.5 (m, 3H), 7.40-7.36 (m, 2H),

15

7.21-7.20 (d, 2H), 6.23-6.21 (t, 1H), 4.09-4.03 (q, 1H), 3.78 (s, 6H), 1.60-1.58 (d, 3H); MS (EI) for $C_{25}H_{26}N_6O_5S.HCl$: 523.1 (MH⁺).

[00348] The following title compounds were prepared according to the above Examples.

[00349] **Example 22: 4-chloro-*N*-(3-(2,5-dimethoxyphenylamino)quinoxalin-2-**

5 **yl)benzenesulfonamide.** ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.18 (s, 1H), 8.78 (s, 1H), 8.40-8.60 (m, 3H), 7.98 (t, 2H), 7.62 (d, 1H), 7.41 (m, 2H), 6.98 (d, 1H), 6.59 (d, 1H), 3.78 (s, 3H), 3.76 (s, 3H); MS (EI) for $C_{22}H_{19}N_5O_6S$: 482.1 (MH⁺).

[00350] **Example 23: *N*-(3-(2,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-**

10 **nitrobenzenesulfonamide.** ¹H NMR (400 MHz, CDCl₃) δ 12.68 (br s, 1H), 9.18 (s, 1H), 8.55 (s, 1H), 8.08 (d, 2H), 7.98 (d, 1H), 7.78 (d, 2H), 7.62 (dd, 1H), 7.40 (m, 2H), 7.00 (d, 1H), 6.60 (dd, 1H), 3.78 (s, 6H); MS (EI) for $C_{22}H_{19}ClN_4O_4S$: 471.1 (MH⁺).

[00351] **Example 24: *N*-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-**

15 **yl)sulfamoyl)-4-methylphenyl)-2-(dimethylamino)acetamide.** ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.0 (br s, 1H), 10.6 (s, 1H), 10.0 (br s, 1H), 9.52 (s, 1H), 8.91 (d, 1H), 8.25 (d, 1H), 7.69 (dd, 1H), 7.47 (m, 1H), 7.39 (d, 1H), 7.16 (m, 3H), 6.01 (dd, 1H); MS (EI) for $C_{26}H_{27}ClN_6O_4S$: 555 (MH⁺).

[00352] **Example 25: (R)-2-amino-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-**

20 **2-yl)sulfamoyl)phenyl)propanamide.** ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.2 (br s, 1H), 8.82 (s, 1H), 8.27 (m, 1H), 7.75 (m, 2H), 7.33 (m, 5H), 7.13 (m, 2H), 6.14 (t, 1H), 3.77 (s, 6H), 1.39 (d, 3H); MS (EI) for $C_{25}H_{26}N_6O_5S$: 523 (MH⁺).

[00353] **Example 26: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-**

25 **yl)sulfamoyl)phenyl)-2-(methylamino)acetamide.** ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.6 (s, 1H), 9.48 (s, 1H), 8.95 (br s, 1H), 8.75 (br s, 1H), 8.19 (br s, 1H), 7.77 (dd, 1H), 7.69 (dd, 1H), 7.41 (m, 4H), 7.17 (m, 2H), 6.60 (dd, 1H), 3.91 (s, 2H), 3.82 (s, 6H), 2.62 (s, 3H); MS (EI) for $C_{24}H_{23}ClN_6O_4S$: 527 (MH⁺).

[00354] **Example 27: (R)-2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-**

30 **phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)propanamide.** ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.5 (s, 1H), 9.47 (s, 1H), 8.95 (d, 1H), 8.22 (d, 2H), 8.14 (br s, 2H), 7.76 (m, 2H), 7.40 (m, 4H), 7.17 (m, 2H), 6.60 (m, 1H), 3.97 (q, 1H), 3.96 (s, 3H), 1.45 (d, 3H); MS (EI) for $C_{24}H_{23}ClN_6O_4S$: 527 (MH⁺).

[00355] **Example 28: 2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-**

phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methylpropanamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.1 (s, 1H), 9.46 (s, 1H), 8.95 (d, 1H), 8.50 (br s, 1H), 8.27 (m, 1H),

7.81 (m, 2 H), 7.47 (m, 1 H), 7.37 (m, 3 H), 7.17 (m, 2 H), 6.61 (dd, 1 H), 3.83 (s, 3 H), 1.60 (s, 6 H); MS (EI) for $C_{25}H_{25}ClN_6O_4S$: 541 (MH⁺).

[00356] Example 29: 2-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methylpropanamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.33 (s, 1 H), 8.89 (s, 1 H), 8.32 (br s, 4 H), 7.92 (m, 3 H), 7.59 (m, 2 H), 7.37 (m, 4 H), 6.24 (s, 1 H), 3.76 (s, 6 H), 1.61 (s, 6 H); MS (EI) for $C_{26}H_{28}N_6O_5S$: 537 (MH⁺).

[00357] Example 30: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-4-methylphenyl)-2-(dimethylamino)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.58 (s, 1 H), 9.80 (br s, 1 H), 8.85 (s, 1 H), 8.25 (s, 1 H), 7.67 (dd, 1 H), 7.30 (m, 7 H), 6.16 (m, 1 H), 4.02 (br s, 2 H), 3.77 (s, 6 H), 2.81 (s, 6 H), 2.54 (s, 3 H); MS (EI) for $C_{27}H_{30}N_6O_5S$: 551 (MH⁺).

[00358] Example 31: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-((2-(dimethylamino)ethyl)(methyl)amino)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.0 (s, 1 H), 9.48 (s, 1 H), 8.96 (d, 1 H), 8.16 (m, 1 H), 7.76 (m, 2 H), 7.39 (m, 4 H), 7.17 (m, 2 H), 6.61 (dd, 1 H), 3.82 (s, 3 H), 3.40 (br s, 2 H), 2.94 (br s, 2 H), 2.71 (br t, 2 H), 2.60 (s, 6 H), 2.33 (s, 3 H); MS (EI) for $C_{28}H_{32}ClN_7O_4S$: 598 (MH⁺).

[00359] Example 32: 2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.5 (s, 1 H), 9.48 (s, 1 H), 8.94 (s, 1 H), 8.15 (s, 1 H), 8.06 (br s, 3 H), 7.74 (m, 2 H), 7.39 (m, 4 H), 7.18 (m, 2 H), 6.61 (dd, 1 H), 3.83 (s, 3 H), 3.77 (s, 2 H); MS (EI) for $C_{23}H_{21}ClN_6O_4S$: 513 (MH⁺).

[00360] Example 33: *N*-(3-(*N*-(3-(2-acetyl-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.4 (s, 1 H), 10.5 (s, 1 H), 9.27 (s, 1 H), 8.25 (s, 1 H), 8.01 (d, 1 H), 7.82 (d, 1 H), 7.71 (d, 1 H), 7.42 (m, 3 H), 7.21 (m, 2 H), 6.63 (dd, 1 H), 3.91 (m, 5 H), 2.75 (s, 6 H), 2.61 (s, 3 H); MS (EI) for $C_{27}H_{28}N_6O_5S$: 549 (MH⁺).

[00361] Example 34: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)formamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.6 (s, 1 H), 10.5 (s, 1 H), 9.16 (s, 1 H), 8.53 (br s, 1 H), 8.35 (m, 2 H), 8.02 (s, 1 H), 7.56 (m, 7 H), 6.70 (dd, 1 H), 3.83 (s, 3 H); MS (EI) for $C_{22}H_{18}ClN_5O_4S$: 484 (MH⁺).

[00362] Example 35: 2-amino-*N*-(5-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-2-methylphenyl)acetamide. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.4 (s, 1 H),

10.1 (br s, 1 H), 8.82 (s, 1 H), 8.20 (m, 3 H), 7.82 (m, 1 H), 7.30 (m, 6 H), 6.20 (s, 1 H), 3.85 (s, 2 H), 3.77 (s, 6 H), 2.26 (s, 3 H); MS (EI) for $C_{25}H_{26}N_6O_5S$: 523 (MH⁺).

[00363] Example 36: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methyl-2-(methylamino)propanamide. ¹H NMR (400 MHz,

5 DMSO-d₆) δ 10.09 (s, 1 H), 9.46 (s, 1 H), 8.95 (m, 3 H), 8.28 (s, 1 H), 7.81 (m, 2 H), 7.41 (m, 4 H), 7.17 (m, 2 H), 6.60 (dd, 1 H), 3.82 (s, 3 H), 2.53 (s, 3 H), 1.60 (s, 6 H); MS (EI) for $C_{26}H_{27}ClN_6O_4S$: 555 (MH⁺).

[00364] Example 37: (S)-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)propanamide. ¹H NMR (400 MHz, DMSO-d₆)

10 δ 10.61 (s, 1 H), 9.47 (s, 1 H), 8.95 (s, 1 H), 8.82 (br s, 2 H), 8.27 (m, 1 H), 7.74 (m, 2 H), 7.42 (m, 4 H), 7.17 (m, 2 H), 6.60 (dd, 1 H), 3.90 (m, 1 H), 3.82 (s, 3 H), 2.59 (s, 3 H), 1.49 (d, 3 H); MS (EI) for $C_{25}H_{25}ClN_6O_4S$: 541 (MH⁺).

[00365] Example 38: 3-amino-*N*-(5-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-2-methylphenyl)propanamide. ¹H NMR (400 MHz, DMSO-d₆) δ 12.25

15 (s, 1 H), 9.77 (s, 1 H), 8.82 (s, 1 H), 7.84 (m, 5 H), 7.50 (d, 1 H), 7.37 (m, 5 H), 6.22 (m, 1 H), 3.74 (s, 6 H), 3.08 (m, 2 H), 2.77 (m, 2 H), 2.27 (s, 3 H); MS (EI) for $C_{26}H_{28}N_6O_5S$: 537 (MH⁺).

[00366] Example 39: 1-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-

20 **phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)cyclopropanecarboxamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 9.54 (br s, 1 H), 9.42 (s, 1 H), 8.91 (s, 1 H), 8.21 (s, 1 H), 8.20 (br s, 2 H), 7.81 (m, 2 H), 7.48 (m, 4 H), 7.22 (m, 2 H), 6.61 (dd, 1 H), 3.82 (s, 3 H), 1.63 (m, 2 H), 1.26 (m, 2 H); MS (EI) for $C_{25}H_{23}ClN_6O_4S$: 539 (MH⁺).

[00367] Example 40: (S)-2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-

25 **phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-6-(dimethylamino)hexanamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 9.47 (br s, 1 H), 8.95 (d, 1 H), 8.26 (m, 1 H), 7.73 (m, 2 H), 7.30 (m, 4 H), 7.26 (m, 4 H), 7.16 (m, 2 H), 6.59 (dd, 1 H), 3.82 (s, 3 H), 3.34 (m, 1 H), 2.20 (m, 2 H), 2.09 (s, 6 H), 1.50 (m, 6 H); MS (EI) for $C_{29}H_{34}ClN_7O_4S$: 610 (MH⁺).

[00368] Example 41: 1-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-

30 **phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)cyclopentanecarboxamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 10.12 (br s, 1 H), 9.46 (s, 1 H), 8.95 (d, 1 H), 8.26 (m, 1 H), 8.16 (m, 3 H), 7.84 (m, 2 H), 7.35 (m, 6 H), 6.60 (dd, 1 H), 3.82 (s, 3 H), 2.34 (m, 2 H), 1.91 (m, 6 H); MS (EI) for $C_{27}H_{27}ClN_6O_4S$: 567 (MH⁺).

[00369] **Example 42: 2-amino-*N*-(5-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-2-methylphenyl)acetamide.**

[00370] **Example *N*-(5-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-2-methylphenyl)-2-(dimethylamino)acetamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 12.0 (br s, 1 H), 9.98 (s, 1 H), 9.43 (s, 1 H), 8.91 (m, 1 H), 8.08 (s, 1 H), 7.84 (dd, 1 H), 7.32 (m, 6 H), 6.61 (dd, 1 H), 4.07 (s, 2 H), 3.82 (s, 3 H), 2.82 (s, 6 H), 2.21 (s, 3 H); MS (EI) for C₂₆H₂₇ClN₆O₄S: 555 (MH⁺).

[00371] **Example 43: 1-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)cyclobutanecarboxamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 10.34 (br s, 1 H), 8.81 (s, 1 H), 8.49 (br s, 3 H), 8.34 (s, 1 H), 7.83 (m, 2 H), 7.43 (m, 3 H), 7.31 (m, 2 H), 7.16 (m, 2 H), 6.16 (s, 1 H), 3.77 (s, 6 H), 2.83 (m, 2 H), 2.25 (m, 3 H), 2.05 (m, 1 H); MS (EI) for C₂₇H₂₈N₆O₅S: 549 (MH⁺).

[00372] **Example 44: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-(3-(2-(dimethylamino)ethyl)ureido)benzenesulfonamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 8.91 (br s, 1 H), 8.81 (s, 1 H), 8.08 (s, 1 H), 7.60 (s, 1 H), 7.38 (m, 9 H), 6.28 (m, 1 H), 6.15 (s, 1 H), 3.78 (s, 6 H), 3.40 (m, 2 H), 3.08 (m, 2 H), 2.74 (s, 6 H); MS (EI) for C₂₇H₃₁N₇O₅S: 566 (MH⁺).

[00373] **Example 45: 1-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)cyclopentanecarboxamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 12.40 (br s, 1 H), 10.58 (s, 1 H), 8.46 (m, 4 H), 7.80 (m, 3 H), 7.59 (m, 2 H), 7.34 (m, 4 H), 6.25 (m, 1 H), 3.76 (s, 6 H), 2.35 (m, 2 H), 1.90 (m, 8 H); MS (EI) for C₂₈H₃₀N₆O₅S: 563 (MH⁺).

[00374] **Example 46: 1-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)cyclopropanecarboxamide.** ¹H NMR (400 MHz, DMSO-d₆) δ 9.54 (br s, 1 H), 8.84 (s, 1 H), 8.29 (s, 1 H), 7.75 (m, 2 H), 7.39 (m, 6 H), 7.17 (m, 2 H), 6.16 (m, 1 H), 3.78 (s, 6 H), 1.52 (m, 2 H), 1.17 (m, 2 H); MS (EI) for C₂₆H₂₆N₆O₅S: 535 (MH⁺).

[00375] **Example 47: 2-(dimethylamino)ethyl 3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenylcarbamate.** ¹H NMR (400 MHz, DMSO-d₆) δ 9.78 (br s, 1 H), 8.79 (s, 1 H), 8.19 (s, 1 H), 7.66 (d, 1 H), 7.31 (m, 9 H), 6.14 (m, 1 H), 4.17 (t, 2 H), 3.78 (s, 6 H), 2.54 (t, 2 H), 2.21 (s, 6 H); MS (EI) for C₂₇H₃₀N₆O₆S: 567 (MH⁺).

[00376] **Example 48: 4-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)tetrahydro-2H-pyran-4-carboxamide.** ¹H NMR (400 MHz, DMSO-

d6) δ 12.2 (br s, 1 H), 10.6 (s, 1 H), 8.74 (m, 5 H), 7.93 (m, 2 H), 7.47 (m, 6 H), 6.24 (m, 1 H), 3.77 (m, 10 H), 2.45 (m, 2 H), 1.81 (m, 2 H); MS (EI) for $C_{28}H_{30}N_6O_6S$: 579 (MH⁺).

[00377] **Example 49: *N*1-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)-*N*3-(2-(dimethylamino)ethyl)benzene-1,3-disulfonamide.** ¹H NMR (400 MHz, DMSO-d₆)

5 δ 9.35 (m, 2 H), 8.92 (m, 1 H), 8.64 (s, 1 H), 8.30 (m, 1 H), 8.11 (s, 1 H), 7.86 (m, 1 H), 7.68 (m, 1 H), 7.49 (s, 1 H), 7.42 (m, 2 H), 7.21 (m, 2 H), 6.61 (m, 1 H), 3.82 (s, 3 H), 3.05 (m, 4 H), 2.74 (s, 6 H); MS (EI) for $C_{25}H_{27}ClN_6O_5S_2$: 591 (MH⁺).

[00378] **Example 50: *N*1-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)-*N*3-(3-(dimethylamino)propyl)benzene-1,3-disulfonamide.** ¹H NMR (400 MHz, DMSO-d₆)

10 δ 9.38 (m, 2 H), 8.90 (m, 1 H), 8.60 (s, 1 H), 8.32 (m, 1 H), 8.12 (s, 1 H), 7.88 (m, 1 H), 7.72 (m, 1 H), 7.59 (s, 1 H), 7.40 (m, 2 H), 7.20 (m, 2 H), 6.67 (m, 1 H), 3.82 (s, 3 H), 2.97 (m, 2 H), 2.78 (m, 2 H), 2.71 (s, 6 H), 1.70 (m, 2 H); MS (EI) for $C_{26}H_{29}ClN_6O_5S_2$: 605 (MH⁺).

[00379] **Example 51: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-4-methylphenyl)-2-(methylamino)acetamide.** MS (EI) for $C_{25}H_{25}ClN_6O_4S$:

15 541.0 (MH⁺).

[00380] **Example 52: (*S*)-2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-4-methylphenyl)propanamide.** MS (EI) for $C_{25}H_{25}ClN_6O_4S$: 541.2 (MH⁺).

[00381] **Example 53: (*R*)-2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-**

20 **phenylamino)quinoxalin-2-yl)sulfamoyl)-4-methylphenyl)propanamide.** MS (EI) for $C_{25}H_{25}ClN_6O_4S$: 541.0 (MH⁺).

[00382] **Example 54: (*S*)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)propanamide.** MS (EI) for $C_{26}H_{28}N_6O_5S$: 537.1 (MH⁺).

25 [00383] **Example 55: (*R*)-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)propanamide.** MS (EI) for $C_{25}H_{25}ClN_6O_4S$: 541.1 (MH⁺).

[00384] **Example 56: (*R*)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)propanamide.** MS (EI) for $C_{26}H_{28}N_6O_5S$: 537.3

30 (MH⁺).

[00400] **Example 57: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)piperidine-2-carboxamide.** MS (EI) for $C_{28}H_{30}N_6O_5S$: 563.1 (MH⁺).

[00401] **Example 58:** *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-(dimethylamino)ethylamino)acetamide. MS (EI) for $C_{28}H_{33}N_7O_5S$: 580.1 (MH⁺).

[00402] **Example 59:** *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-(methylamino)piperidin-1-yl)acetamide. MS (EI) for $C_{30}H_{35}N_7O_6S$: 606.1 (MH⁺).

[00403] **Example 60:** *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-((3-(dimethylamino)propyl)(methyl)amino)acetamide. MS (EI) for $C_{30}H_{37}N_7O_5S$: 608.1 (MH⁺).

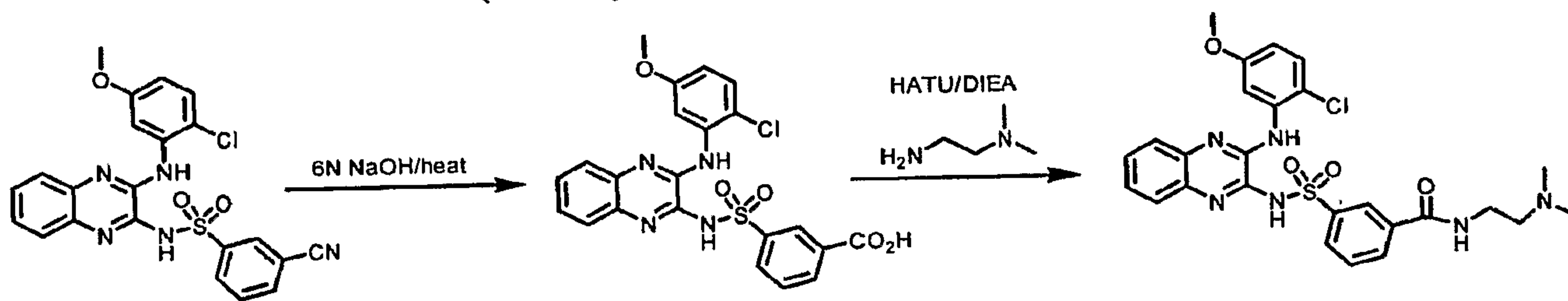
[00404] **Example 61:** 2-(1,4'-bipiperidin-1'-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) for $C_{34}H_{41}N_7O_5S$: 660.1 (MH⁺).

[00405] **Example 62:** *tert*-butyl 2-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenylcarbamoyl)piperidine-1-carboxylate. MS (EI) for $C_{33}H_{38}N_6O_7S$: 663.1 (MH⁺).

[00406] **Example 63:** 3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(1-(dimethylamino)propan-2-yl)benzamide. MS (EI) for $C_{27}H_{29}ClN_6O_4S$: 569.0 (MH⁺).

Example 64

3-{{(3-{{2-chloro-5-(methyloxy)phenyl}amino}quinoxalin-2-yl)amino}sulfonyl}-*N*-[2-(dimethylamino)ethyl]benzamide



[00407] **3-{{(3-{{2-chloro-5-(methyloxy)phenyl}amino}quinoxalin-2-yl)amino}sulfonyl}benzoic acid.** To a solution of *N*-(3-{{2-chloro-5-(methyloxy)phenyl}amino}quinoxalin-2-yl)-3-cyanobenzenesulfonamide (6.02 g, 12.95 mmol) in methanol (20 mL) and 1,4-dioxane (20 mL) was added 6.0 *N* aqueous sodium hydroxide (40 mL) at room temperature. The solution was stirred at 90 °C for 3.5 h. The reaction was cooled to room temperature and neutralized slowly by adding 2.0 *N*

- hydrochloric acid until the pH of the solution became in the 2-3 range at 0° C. The solution was diluted with ethyl acetate (300 mL). The organic layer was washed with saturated aqueous sodium chloride (50 mL) and dried over magnesium sulfate. Filtration and concentration at reduced pressure afforded 3-{{(3-{{(2-chloro-5-(methyloxy)phenyl)amino}quinoxalin-2-yl)amino}sulfonyl}benzoic acid (5.921 g, 94%). MS (EI) for C₂₂H₁₇ClN₄O₅S: 485.0 (MH⁺)
- [00408]** 3-{{(3-{{(2-chloro-5-(methyloxy)phenyl)amino}quinoxalin-2-yl)amino}sulfonyl}-N-[2-(dimethylamino)ethyl]benzamide. To a solution of 3-{{(3-{{(2-chloro-5-(methyloxy)phenyl)amino}quinoxalin-2-yl)amino}sulfonyl}benzoic acid (0.20 g, 0.42 mmol) in dimethylformamide (4 mL) were added 2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU, 0.32 g, 0.83 mmol) and N-ethyl-diisopropylamine (DIEA, 0.13 g, 1.04 mmol) at room temperature. The reaction was stirred for 15 min before N,N-dimethylethane-1,2-diamine (73 mg, 0.83 mmol) was added. The reaction mixture was allowed to stir overnight. The reaction was diluted with ethyl acetate (200 mL) and washed with water (50 mL), saturated aqueous sodium bicarbonate (40 mL), 1.0 N aqueous hydrochloric acid (30 mL), and saturated aqueous sodium chloride (25 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated at reduced pressure to afford 3-{{(3-{{(2-chloro-5-(methyloxy)phenyl)amino}quinoxalin-2-yl)amino}sulfonyl}-N-[2-(dimethylamino)ethyl]benzamide (0.20 g, 87%) as yellow solid. MS (EI) for C₂₆H₂₇ClN₆O₄S: 555.1 (MH⁺).
- [00409]** The following title compounds were prepared according to the above Examples.
- [00410]** **Example 65:** 3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-(2-(dimethylamino)ethyl)benzamide. MS (EI) for C₂₇H₃₀N₆O₅S: 551.1 (MH⁺).
- [00411]** **Example 66:** 3-(N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide. MS (EI) for C₂₇H₂₉ClN₆O₄S: 569.1 (MH⁺).
- [00412]** **Example 67:** 3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-(2-(dimethylamino)ethyl)-N-methylbenzamide. MS (EI) for C₂₈H₃₂N₆O₅S: 565.1 (MH⁺).
- [00413]** **Example 69:** 3-(N-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)benzamide. MS (EI) for C₂₂H₁₈ClN₅O₄S: 484.0 (MH⁺).
- [00414]** **Example 70:** 3-(N-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)benzoic acid. MS (EI) for C₂₂H₁₇ClN₄O₅S: 485.0 (MH⁺).

[00415] **Example 71:** 3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-morpholinoethyl)benzamide. MS (EI) for $C_{28}H_{29}ClN_6O_5S$: 597.0 (MH⁺).

[00416] **Example 72:** 3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-methylbenzamide. MS (EI) for $C_{23}H_{20}ClN_5O_4S$: 498.0 (MH⁺).

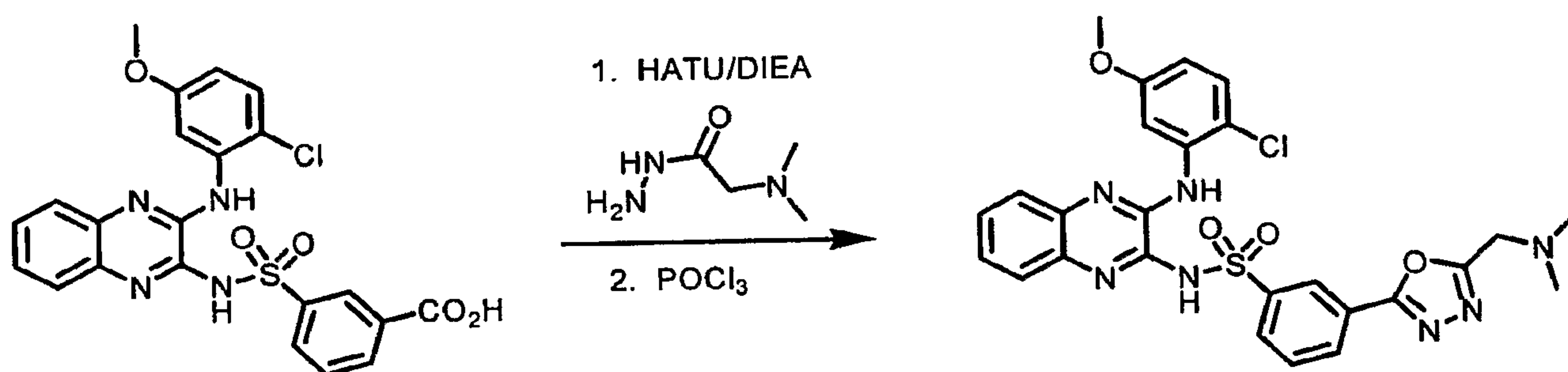
[00417] **Example 73:** 3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzoic acid. MS (EI) for $C_{23}H_{20}N_4O_6S$: 481.0 (MH⁺).

[00418] **Example 74:** 3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-morpholinobenzamide. MS (EI) for $C_{26}H_{25}ClN_6O_5S$: 569.0 (MH⁺).

[00419] **Example 75:** *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-cyanobenzenesulfonamide. MS (EI) for $C_{22}H_{16}ClN_5O_3S$: 465.9 (MH⁺).

Example 76

N-(3-{[2-chloro-5-(methoxy)phenyl]amino}quinoxalin-2-yl)-3-{5-[(dimethylamino)methyl]-1,3,4-oxadiazol-2-yl}benzenesulfonamide

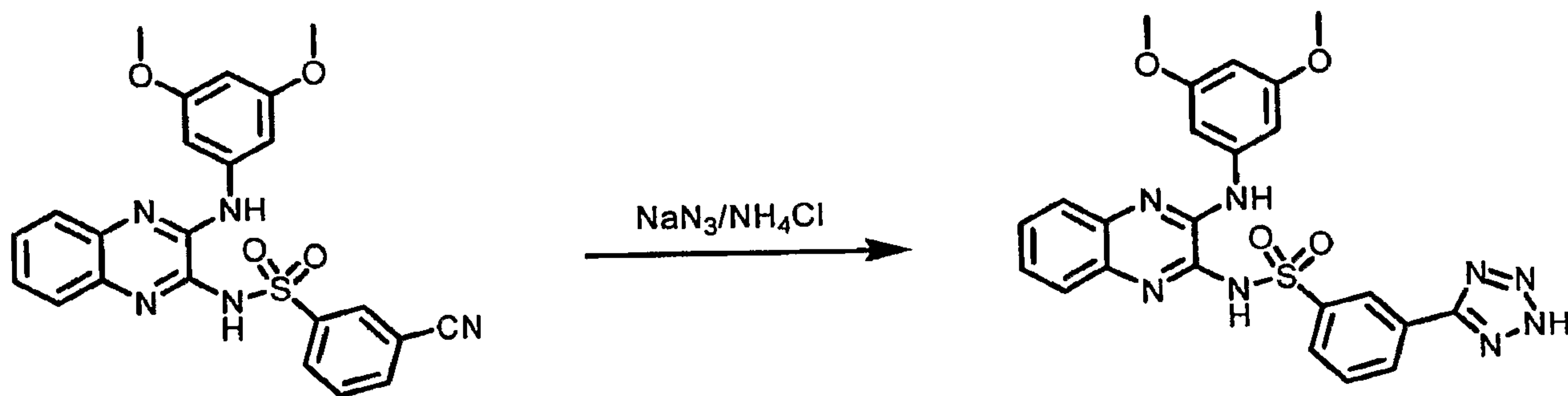


[00420] To a solution of 3-[[3-[[2-chloro-5-(methoxy)phenyl]amino]quinoxalin-2-yl]amino]sulfonyl}benzoic acid (0.25 g, 0.52 mmol) in dimethylformamide (2.6 mL) were added 2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU, 0.25 g, 0.67 mmol) and *N*-ethyldiisopropylamine (DIEA, 0.11 g, 0.88 mmol) at room temperature. The reaction was stirred for 15 min before 2-(dimethylamino)acetohydrazide (78 mg, 0.67 mmol) was added. The reaction mixture was allowed to stir overnight. The reaction was diluted with ethyl acetate (200 mL) and washed with water (30 mL), saturated aqueous sodium bicarbonate (30 mL), 1.0 *N* aqueous hydrochloric acid (20 mL), and saturated aqueous sodium chloride (25 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated at reduced pressure to afford 180 mg of a coupled intermediate which was then heated in phosphorus oxychloride (5 mL) at 100 °C for 4h. The reaction was cooled to room temperature and treated with ice

water (50 mL) and extracted with dichloromethane (3 X 50 mL). The organic layer was dried over magnesium sulfate, filtered and concentrated at reduced pressure to afford a crude product which was subjected to reverse phase HPLC to afford *N*-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{5-[(dimethylamino)methyl]-1,3,4-oxadiazol-2-yl}benzenesulfonamide (16 mg, 5 %) as yellow solid. MS (EI) for C₂₆H₂₄ClN₇O₄S: 566.0 (MH⁺).

Example 78

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(2H-tetrazol-5-yl)benzenesulfonamide



[00421] To a stirred solution of 3-cyano-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide (0.20 g, 0.44 mmol) in dimethylformamide (1.2 mL) at 50 °C were added sodium azide (0.11 g, 1.76 mmol) and ammonium chloride (94 mg, 1.76 mmol). The crude mixture was heated at 100 °C overnight. The reaction was cooled to room temperature treated with ice water (20 mL) followed by concentrated hydrochloric acid (10 mL). The solid obtained was filtered under reduced pressure and washed with hexane (20 mL), diethyl ether (20 mL), and ethyl acetate (5 mL) to afford *N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(2H-tetrazol-5-yl)benzenesulfonamide (55 mg, 25%) as light yellow solid. MS (EI) for C₂₃H₂₀N₈O₄S: 505.0 (MH⁺).

[00422] The following title compounds were prepared according to the above Examples.

Example 77: 3-cyano-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₃H₁₉N₅O₄S: 462.3 (MH⁺).

Example 79: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-(dimethylamino)piperidin-1-yl)acetamide. MS (EI) for C₃₁H₃₇N₇O₅S: 620.1 (MH⁺).

Example 80: *N*-(3-(2,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-fluorobenzenesulfonamide. MS (EI) for C₂₂H₁₉FN₄O₄S: 456.0 (MH⁺).

- Example 81:** 3-bromo-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{22}H_{19}BrN_4O_4S$: 516.9 (MH⁺).
- Example 82:** 3-bromo-*N*-(3-(2,5-dimethoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{22}H_{19}BrN_4O_4S$: 516.9 (MH⁺).
- 5 **Example 83:** *N*-(3-(3-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{21}H_{18}N_4O_3S$: 407.0 (MH⁺).
- Example 84:** *N*-(3-(morpholinoamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{18}H_{18}N_6O_5S$: 431.0 (MH⁺).
- Example 85:** 3-nitro-*N*-(3-(tetrahydro-2H-pyran-4-ylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{19}H_{19}N_5O_5S$: 430.0 (MH⁺)
- 10 **Example 86:** *N*-(3-(4-fluoro-3-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{21}H_{17}FN_4O_3S$: 425.0 (MH⁺).
- Example 87:** *N*-(3-(2,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-methoxybenzenesulfonamide. MS (EI) for $C_{23}H_{22}N_4O_5S$: 467.0 (MH⁺).
- 15 **Example 88:** *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-methoxybenzenesulfonamide. MS (EI) for $C_{23}H_{22}N_4O_5S$: 467.0 (MH⁺).
- Example 89:** *N*-(3-(4-chloro-3-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{21}H_{17}ClN_4O_3S$: 440.9 (MH⁺).
- Example 90:** *N*-(3-(2-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{21}H_{18}N_4O_3S$: 407.0 (MH⁺).
- 20 **Example 91:** *N*-(3-(3-(benzyloxy)phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{27}H_{22}N_4O_3S$: 483.0 (MH⁺).
- Example 92:** *N*-(3-(3-phenoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{26}H_{20}N_4O_3S$: 469.0 (MH⁺).
- 25 **Example 93:** *N*-(3-(3-methoxy-5-(trifluoromethyl)phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{22}H_{17}F_3N_4O_3S$: 475.0 (MH⁺).
- Example 94:** *N*-(3-(2,5-diethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{24}H_{24}N_4O_4S$: 465.0 (MH⁺).
- Example 95:** *N*-(3-(2'-methoxybiphenyl-4-ylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{27}H_{22}N_4O_3S$: 483.0 (MH⁺).
- 30 **Example 96:** *N*-(3-(2-methoxy-5-methyl-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{22}H_{20}N_4O_3S$: 421.0 (MH⁺).
- Example 97:** *N*-(3-(5-chloro-2-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{21}H_{17}ClN_4O_3S$: 441.0 (MH⁺).

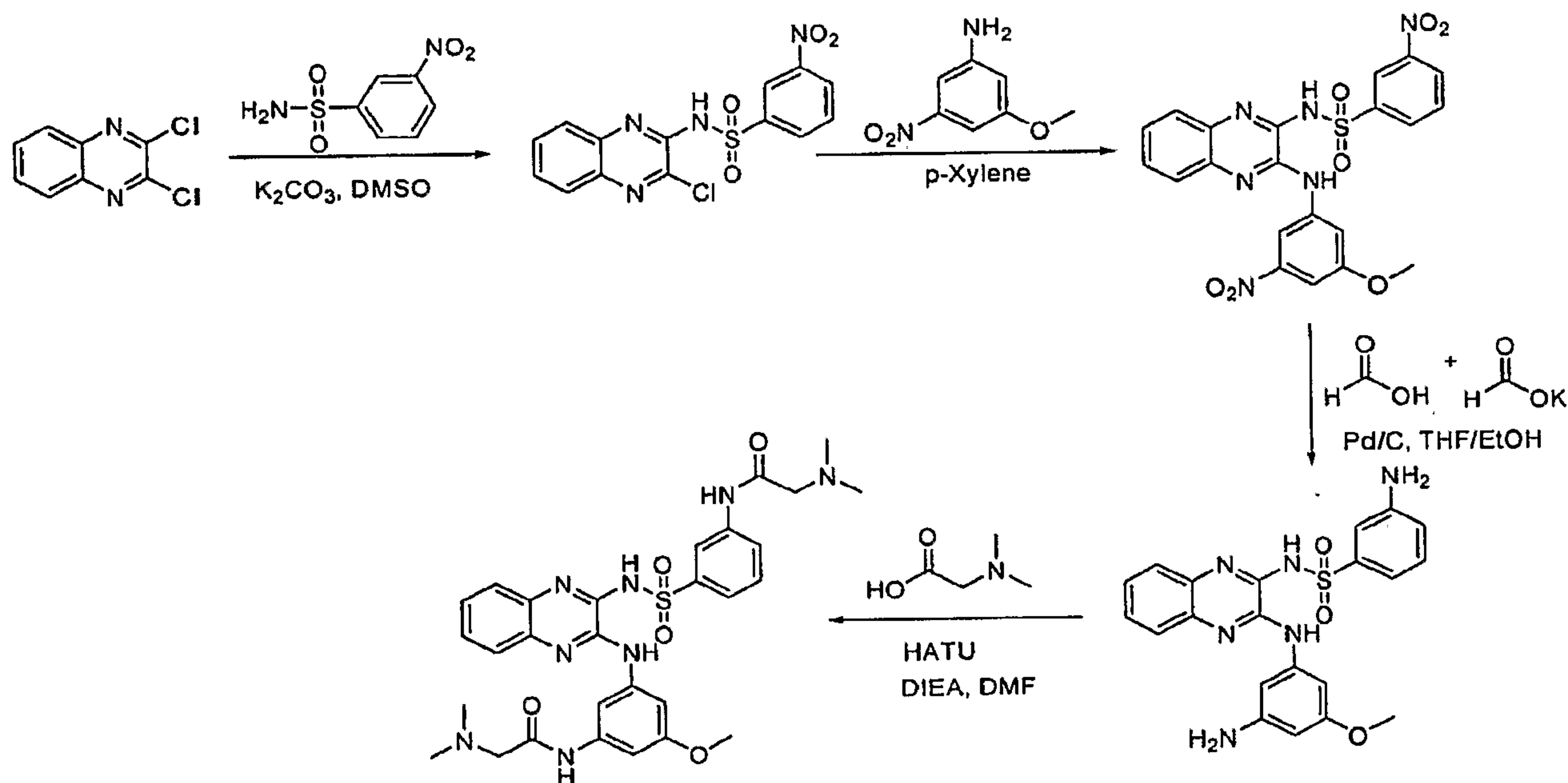
Example 98: *N*-(3-(2-methoxy-5-(trifluoromethyl)-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{22}H_{17}F_3N_4O_3S$: 475.0 (MH⁺).

Example 99: *N*-(3-(2-methoxybiphenyl-4-ylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{27}H_{22}N_4O_3S$: 483.3 (MH⁺).

5 **Example 100:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. ¹H NMR (400 MHz, DMSO) δ 12.4 (br s, 1H), 10.9 (s, 1H), 9.8 (s, 1H), 8.9 (s, 1H), 8.3 (br s, 1H), 7.9 (d, 2H), 7.8 (d, 1H), 7.6 (t, 2H), 7.4 (q, 2H), 7.3 (s, 1H), 6.25 (s, 1H), 4.15 (s, 2H), 3.8 (s, 6H), 2.9 (s, 6H). MS (EI) for $C_{26}H_{28}N_6O_5S$ 2.0 x $C_2H_1O_2F_3$: 537.1 (MH⁺).

Example 101

2-(dimethylamino)-*N*-(3-(*N*-(3-(3-(2-(dimethylamino)acetamido)-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide



15 **[00423] *N*-(3-chloroquinoxalin-2-yl)-3-nitrobenzenesulfonamide.** 2,3-Dichloroquinoxaline (26.1 g, 131.1 mmol), *m*-Nitrobenzene sulfonamide (26.5 g, 131.1 mmol) and potassium carbonate (18.1 g, 131.1) were dissolved in anhydrous DMSO (500 mL). The reaction was heated to 150°C for 2 h. The reaction mixture was poured into water (400 mL), followed by addition of 2M HCl (60 mL). The product was extracted with EtOAc
20 (3 x 500 mL). The organic layers were combined and washed water (2 x 500 mL) and brine (2 x 500 mL). The product was then dried with sodium sulfate to give *N*-(3-chloroquinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{14}H_9ClN_4O_4S$: 364.94, 366.97 (MH⁺)

[00424] *N*-(3-(3-methoxy-5-nitrophenylamino)quinoxalin-2-yl)-3-nitro-

benzenesulfonamide. *N*-(3-chloroquinoxalin-2-yl)-3-nitrobenzenesulfonamide (700 mg, 1.92 mmol), 3-methoxy-5-nitroaniline (645 mg, 3.84 mmol) and *p*-xylene (7 mL) were combined and heated to 140°C, then stirred for 16 hours at 130°C. The reaction was allowed to cool, placed in a sep. funnel, diluted with DCM, and washed with 2M HCl and brine and concentrated in vacuo. The resulting solid was washed with Et₂O to give *N*-(3-(3-methoxy-5-nitrophenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide (400 mg, 42%). MS (EI) for C₂₁H₁₆N₆O₇S: 496.94 (MH⁺)

[00425] 3-amino-*N*-(3-(3-amino-5-methoxyphenylamino)quinoxalin-

2-yl)benzenesulfonamide. *N*-(3-(3-Methoxy-5-nitrophenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide (400 mg, 0.81 mmol) was dissolved in 1:1 THF:EtOH (4 mL), to which was added formic acid (938 µl, 2.42 mmol) and potassium formate (203 mg, 2.42 mmol). The system was flushed with nitrogen, and then 10%wt Pd/C (50 mg) was added. The reaction was then heated to 60°C. Once the reaction was determined complete by LC-MS, it was allowed to cool, and DMF was added for solubility. The solution was then filtered through a nylon frit to remove the catalyst. The filtrate was diluted water and the pH adjusted to 7 and extracted with DCM (2x) and EtOAc (2x). All organic layers were combined and evaporated to dryness to give 3-amino-*N*-(3-(3-amino-5-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide (330 mg, 93%). MS (EI) for C₂₁H₂₀N₆O₃S: 437.06 (MH⁺)

[00426] 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-(2-(dimethylamino)acetamido)-5-methoxyphenylamino)quinoxalin-2-yl)-sulfamoyl)phenyl)acetamide.

3-Amino-*N*-(3-(3-amino-5-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide (330 mg, 0.76 mmol), DMF (4 mL), *N,N*-Dimethylglycine (312 mg, 3.02 mmol), HATU (1.15 g, 3.02 mmol), and 1.29(mL) (7.56 mmol) DIEA (1.29 mL, 7.56 mmol) were combined and heated to 90°C, followed by heating at 50°C for over 16 hours. The reaction was allowed to cool, placed into a sep. funnel diluted with water and aqueous LiCl and extracted with EtOAc. The final compound was then purified by prep. HPLC to give 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-(2-(dimethylamino)acetamido)-5-methoxy-phenylamino)-quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. ¹H NMR (400 MHz, CD₃OD) δ 8.45 (t, 1H), 7.93 (t, 1H), 7.85-7.88 (m, 1H), 7.70-7.74 (m, 1H), 7.65-7.68 (m, 1H), 7.58-7.62 (m, 1H), 7.58 (t, 1H), 7.34-7.42 (m, 3H), 7.0 (t, 1H), 4.05 (d, 2H), 3.8 (s, 3H), 2.9-3.0 (d, 12H). MS (EI) for C₂₉H₃₄N₈O₅S: 607.2 (MH⁺).

[00427] The following title compounds were prepared according to the above Examples.

Example 102: *N*-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-

yl)sulfamoyl)phenyl)-2-(ethylamino)acetamide. ¹H NMR (400 MHz, DMSO) δ 10.8 (s, 1H), 9.20 (s, 1H), 8.84 (br s, 2H), 8.64 (br s, 1H), 8.30 (s, 1H), 7.9-8.0 (br s, 1H), 7.80 (t, 2H), 7.55-7.68 (m, 2H), 7.4 (d, 3H), 6.70 (m, 1H), 3.97 (br s, 2H), 3.83 (s, 3H), 3.04 (br s, 2H), 1.3 (t, 3H). MS (EI) for C₂₅H₂₅ClN₆O₄S 2.0 x C₂H₁O₂F₃: 541.3, 543.2 (MH⁺).

Example 103: 2-(azetidin-1-yl)-*N*-(3-(*N*-(3-(2-chloro-5-

methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. ¹H NMR (400 MHz, DMSO) δ 10.8 (s, 1H), 10.2 (s, 1H), 9.2 (s, 1H), 8.7 (s, 1H), 8.3 (s, 1H), 7.9-8.0 (br s, 1H), 7.80 (d, 1H), 7.72 (d, 1H), 7.65 (br s, 1H), 7.56 (t, 1H), 7.40 (d, 3H), 6.70 (m, 1H), 4.28 (s, 2H), 4.15 (m, 4H), 3.82 (s, 3H), 2.32 (br s, 1H). MS (EI) for C₂₆H₂₅ClN₆O₄S 2.0 x C₂H₁O₂F₃: 553.3, 555.2 (MH⁺).

Example 104: *N*-(3-(*N*-(3-(2-bromo-5-methoxy-phenylamino)quinoxalin-2-*yl*)sulfamoyl)phenyl)-2-(methylamino)acetamide. The title compound was prepared

according to the Examples above. ¹H NMR (400 MHz, DMSO) δ 10.6 (s, 1H), 9.5 (s, 1H), 8.95 (d, 1H), 8.18 (t, 1H), 7.78 (m, 1H), 7.70 (m, 1H), 7.54 (d, 1H), 7.46 (m, 1H), 7.38 (t, 1H), 7.32 (d, 1H), 7.12-7.22 (m, 2H), 6.56 (m, 1H), 3.90 (s, 2H), 3.82 (s, 3H), 2.62 (s, 3H). MS (EI) for C₂₄H₂₃BrN₆O₄S: 572.77, 570.90 (MH⁺).

Example 105: 2-(dimethylamino)-*N*-(3-(*N*-(3-(6-methoxy-quinolin-8-

ylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. The title compound was prepared according to the Examples above. ¹H NMR (400 MHz, DMSO) δ 10.9 (s, 1H), 10.6 (s, 1H), 9.13 (s, 1H), 8.80 (d, 1H), 8.26-8.30 (m, 2H), 7.85 (d, 1H), 7.70 (d, 1H), 7.60 (q, 1H), 7.54 (m, 1H), 7.44 (t, 2H), 7.20 (t, 2H), 6.80 (d, 1H), 4.00 (s, 2H), 3.94 (s, 3H), 2.78 (s, 6H). MS (EI) for C₂₈H₂₇N₇O₄S: 558.3 (MH⁺).

Example 106: *N*-(3-(*N*-(3-(2-bromo-5-methoxy-phenylamino)quinoxalin-2-*yl*)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. The title compound was prepared

according to the Examples above. ¹H NMR (400 MHz, DMSO) δ 10.6 (s, 1H), 9.4 (s, 1H), 8.9 (s, 1H), 8.25 (s, 1H), 7.78 (d, 1H), 7.70 (d, 1H), 7.54 (d, 1H), 7.48 (d, 1H), 7.40 (t, 2H), 6.56 (d, 1H), 4.02 (s, 2H), 3.82 (s, 3H), 2.80 (s, 6H). MS (EI) for C₂₅H₂₅BrN₆O₄S: 586.79, 584.91 (MH⁺).

Example 107: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-*yl*)-3-

(hydroxyamino)benzenesulfonamide. MS (EI) for C₂₂H₂₁N₅O₅S: 468.1 (MH⁺).

Example 108: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-

yl)sulfamoyl)phenyl)-2-(2-fluoroethylamino)acetamide. The title compound was prepared

according to the Examples above. ¹H NMR (400 MHz, DMSO) δ 10.6 (s, 1H), 9.4 (s, 1H), 8.9 (d, 1H), 8.20 (s, 1H), 7.78 (d, 1H), 7.70 (d, 1H), 7.48 (m, 1H), 7.36-7.44 (m, 3H), 7.20 (q, 3H), 6.6 (m, 1H), 4.78 (t, 1H), 4.66 (t, 1H), 3.94 (s, 2H), 3.82 (s, 3H), 3.4 (t, 1H), 3.3 (t, 1H). MS (EI) for C₂₅H₂₄ClFN₆O₄S: 559.2, 561.2 (MH⁺).

5 **Example 109:** *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)formamide. ¹H NMR (400 MHz, DMSO) δ 12.4 (br s, 1H), 10.5 (s, 1H), 8.90 (s, 1H), 8.3 (s, 1H), 7.9 (br s, 1H), 7.85 (d, 1H), 7.75 (d, 1H), 7.5-7.6 (m, 2H), 7.3-7.4 (m, 4H), 6.2 (s, 1H), 3.8 (s, 3H). MS (EI) for C₂₃H₂₁N₅O₅S: 480.1 (MH⁺).

10 **Example 110:** *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-(dimethylamino)azetidin-1-yl)acetamide. ¹H NMR (400 MHz, DMSO) δ 10.2 (br s, 1H), 9.5 (s, 1H), 8.95 (d, 1H), 8.2 (s, 1H), 7.75 (d, 1H), 7.65 (d, 1H), 7.45 (d, 1H), 7.40 (d, 1H), 7.30-7.35 (t, 1H), 7.1-7.2 (q, 2H), 6.60 (m, 1H), 3.82 (s, 3H). MS (EI) for C₂₈H₃₀ClN₇O₄S: 480.1 (MH⁺).

15 **Example 111:** *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(pyrrolidin-1-yl)acetamide. MS (EI) for C₂₈H₃₀N₆O₅S: 563.18 (MH⁺).

20 **Example 112:** 3-amino-*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. ¹H NMR (400 MHz, DMSO) δ 12.2 (br s, 1H), 8.85 (s, 1H), 7.90 (br s, 1H), 7.50-7.60 (m, 1H), 7.3-7.4 (m, 4H), 7.2 (m, 3H), 6.74 (m, 1H), 6.24 (m, 1H), 5.56 (br s, 2H), 3.76 (s, 6H). MS (EI) for C₂₂H₂₁N₅O₄S: 452.0 (MH⁺).

25 **Example 113:** *N*-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(ethyl(methyl)amino)acetamide. ¹H NMR (400 MHz, DMSO) δ 12.0 (s, 1H), 10.6 (s, 1H), 9.65 (s, 1H), 9.5 (s, 1H), 8.95 (s, 1H), 8.25 (s, 1H), 7.8 (d, 1H), 7.70 (d, 1H), 7.45-7.50 (d, 1H), 7.3-7.4 (m, 3H), 7.2 (t, 2H), 6.60 (d, 1H), 4.02 (br s, 2H), 3.82 (s, 3H), 3.14 (br s, 2H), 2.80 (s, 3H) 1.2 (t, 3H). MS (EI) for C₂₆H₂₇ClN₆O₄S: 555.2, 557.3 (MH⁺).

Example 114: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-(piperidin-1-yl)azetidin-1-yl)acetamide. MS (EI) for C₃₁H₃₄ClN₇O₄S 2.0 x C₂H₁O₂F₃: 636.3, 638.3 (MH⁺).

30 **Example 115:** *N*-(3-(*N*-(3-(3-fluoro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)acetamide. MS (EI) for C₂₄H₂₃FN₆O₄S: 511.04 (MH⁺).

Example 116: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-methylpiperidine-4-carboxamide. MS (EI) for $C_{29}H_{32}N_6O_5S$ 1.0 x $C_2H_4O_2$: 577.2 (MH⁺).

Example 117: *N*-(3-(*N*-(3-(3-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)acetamide. 1H NMR (400 MHz, DMSO) δ 10.6 (s, 1H), 8.82 (s, 1H), 8.22 (t, 1H), 7.86 (t, 1H), 7.76 (m, 1H), 7.66 (m, 1H), 7.46 (m, 1H), 7.41 (m, 1H), 7.38 (t, 1H), 7.28 (m, 1H), 7.24 (t, 1H), 7.12 (m, 2H), 6.56 (d, 1H), 3.88 (s, 2H), 3.80 (s, 3H), 2.60 (s, 3H). MS (EI) for $C_{24}H_{24}N_6O_4S$: 492.99 (MH⁺).

Example 118: *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2,2,2-trifluoroethylamino)acetamide. 1H NMR (400 MHz, DMSO) δ 10.4 (s, 1H), 9.2 (s, 1H), 8.65 (s, 1H), 8.4 (s, 1H), 8.00 (m, 1H), 7.80 (d, 1H), 7.75 (d, 1H), 7.65 (q, 1H), 7.55 (t, 1H), 7.40-7.5 (m, 3H), 6.7 (m, 1H), 3.82 (s, 3H), 3.62 (br s, 2H), 3.55 (br d, 2H). MS (EI) for $C_{25}H_{22}ClF_3N_6O_4S$ 1.0 x $C_2H_1O_2F_3$: 595.0, 597.0 (MH⁺).

Example 119: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-(piperidin-1-yl)propanamide. MS (EI) for $C_{30}H_{34}N_6O_5S$: 591.2 (MH⁺).

Example 120: 3-amino-*N*-(3-(2,5-dimethoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. 1H NMR (400 MHz, DMSO) δ 12.4 (br s, 1H), 9.20 (s, 1H), 8.56 (d, 1H), 7.95 (d, 1H), 7.62 (m, 1H), 7.38 (m, 2H), 7.24 (q, 2H), 7.14 (d, 1H), 6.98 (d, 1H), 6.8 (m, 1H), 6.60 (m, 1H), 5.6 (br s, 2H), 3.78 (d, 6H). MS (EI) for $C_{22}H_{21}N_5O_4S$: 452.3 (MH⁺).

Example 121: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-(dimethylamino)butanamide. MS (EI) for $C_{28}H_{32}N_6O_5S$ 1.0 x $C_2H_4O_2$: 565.2 (MH⁺).

Example 122: 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-fluoro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. 1H NMR (400 MHz, DMSO) δ 10.9 (s, 1H), 9.8 (br s, 1H), 9.1 (s, 1H), 8.34 (s, 1H), 7.90 (d, 1H), 7.76 (d, 1H), 7.52-7.68 (m, 4H), 7.40 (m, 2H), 6.54 (m, 1H), 4.16 (s, 2H), 3.82 (s, 3H), 2.86 (s, 6H). MS (EI) for $C_{25}H_{25}FN_6O_4S$: 525.05 (MH⁺).

Example 123: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(piperidin-1-yl)acetamide. MS (EI) for $C_{29}H_{32}N_6O_5S$: 577.37 (MH⁺).

Example 124: 3-amino-*N*-(3-(2-chloro-5-hydroxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{20}H_{16}ClN_5O_3S$ 1.0 x $C_2H_1O_2F_3$: 442.2, 444.2 (MH⁺).

Example 125: 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. ¹H NMR (400 MHz, DMSO) δ 10.5 (s, 1H), 8.8 (s, 1H), 8.25 (s, 1H), 7.83 (t, 1H), 7.76 (d, 1H), 7.64 (d, 1H), 7.3-7.48 (m, 4H), 7.22 (t, 1H), 7.12 (t, 2H), 6.56 (m, 1H), 3.96 (s, 2H), 3.78 (s, 3H), 2.76 (s, 6H). MS (EI) for C₂₅H₂₆N₆O₄S: 507.1 (MH⁺).

Example 126: *N*-(3-(*N*-(3-(2-chloro-5-hydroxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. ¹H NMR (400 MHz, DMSO) δ 10.8 (s, 1H), 9.9 (s, 1H), 9.8 (s, 1H), 9.1 (s, 1H), 8.55 (s, 1H), 8.34 (s, 1H), 7.9-8.0 (br s, 1H), 7.82 (d, 1H), 7.76 (d, 1H), 7.52-7.66 (m, 2H), 7.42 (t, 1H), 7.26 (d, 1H), 6.50 (m, 1H), 4.16 (s, 2H), 2.86 (s, 6H). MS (EI) for C₂₄H₂₃ClN₆O₄S: 527.1, 529.0 (MH⁺).

Example 127: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-morpholinoacetamide. MS (EI) for C₂₈H₃₀N₆O₆S: 579.1 (MH⁺).

Example 128: 3-amino-*N*-(3-(6-methoxyquinolin-8-ylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₄H₂₀N₆O₃S: 473.0 (MH⁺).

Example 129: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)thiophene-2-sulfonamide. MS (EI) for C₂₀H₁₈N₄O₄S₂: 443.0 (MH⁺).

Example 130: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-(methylamino)benzenesulfonamide. MS (EI) for C₂₃H₂₃N₅O₄S: 466.05 (MH⁺).

Example 131: 3-amino-*N*-(3-(3-methoxy-5-nitro-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₁H₁₈N₆O₅S: 467.00 (MH⁺).

Example 132: 3-amino-*N*-(3-(3-fluoro-5-methoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₁H₁₈FN₅O₃S: 439.99 (MH⁺).

Example 134: 3-amino-*N*-(3-(3-amino-5-methoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₁H₂₀N₆O₃S: 437.2 (MH⁺).

Example 135: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-(dimethylamino)benzenesulfonamide. MS (EI) for C₂₄H₂₅N₅O₄S: 480.04 (MH⁺).

Example 136: *N*-(3-(2-chloro-6-methoxypyridin-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₀H₁₅ClN₆O₅S: 496.94 (MH⁺).

Example 137: *N*-(3-(6-methoxyquinolin-8-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₄H₁₈N₆O₅S: 502.95 (MH⁺).

Example 138: 3-nitro-*N*-(3-(pyridin-4-ylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₁₉H₁₄N₆O₄S: 423.2 (MH⁺).

Example 139: *N*-(3-(2,6-dichloropyridin-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₁₉H₁₂Cl₂N₆O₄S: 491.1, 493.1 (MH⁺).

Example 140: *N*-(3-(2-chloropyridin-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₁₉H₁₃ClN₆O₄S: 456.93, 458.90 (MH⁺).

Example 141: *N*-(3-(4,6-dimethoxypyrimidin-2-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₀H₁₇N₇O₆S: 484.03 (MH⁺).

5 **Example 142:** *N*-(3-(4-hydroxy-6-methoxypyrimidin-2-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₁₉H₁₅N₇O₆S: 469.97 (MH⁺).

Example 143: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2-fluorobenzenesulfonamide. MS (EI) for C₂₂H₁₉FN₄O₄S: 455.3 (MH⁺).

10 **Example 144:** *N*-(3-(2-bromo-5-methoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₆BrN₅O₅S: 531.82, 532.84 (MH⁺).

Example 145: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-methylbenzenesulfonamide. MS (EI) for C₂₃H₂₂N₄O₄S: 451.0 (MH⁺).

Example 146: *N*-(3-(2,5-dimethoxyphenylamino)-7-methylquinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₃H₂₂N₄O₄S: 451.0 (MH⁺).

15 **Example 147:** *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₂H₁₉N₅O₆S: 481.9 (MH⁺).

Example 148: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) for C₂₄H₂₃N₅O₅S: 494.0 (MH⁺).

20 **Example 149:** *N*-(3-(2,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-methylbenzenesulfonamide. MS (EI) for C₂₃H₂₂N₄O₄S: 451.0 (MH⁺).

Example 150: *N*-(3-(3-fluoro-5-methoxy-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₆FN₅O₅S: 470.0 (MH⁺).

Example 151: 4-bromo-*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₂H₁₉BrN₄O₄S: 516.9, 514.9 (MH⁺).

25 **Example 152:** *N*-(3-(3-methoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₇N₅O₅S: 451.93 (MH⁺).

Example 153: *N*-(3-(2-chloro-5-hydroxy-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₀H₁₄ClN₅O₅S: 472.15, 474.13 (MH⁺).

30 **Example 154:** *N*-(3-(3-methoxy-5-nitro-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₆N₆O₇S: 496.94 (MH⁺).

Example 155: *N*-(3-(benzo[d][1,3]dioxol-5-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₅N₅O₆S: 466.2 (MH⁺).

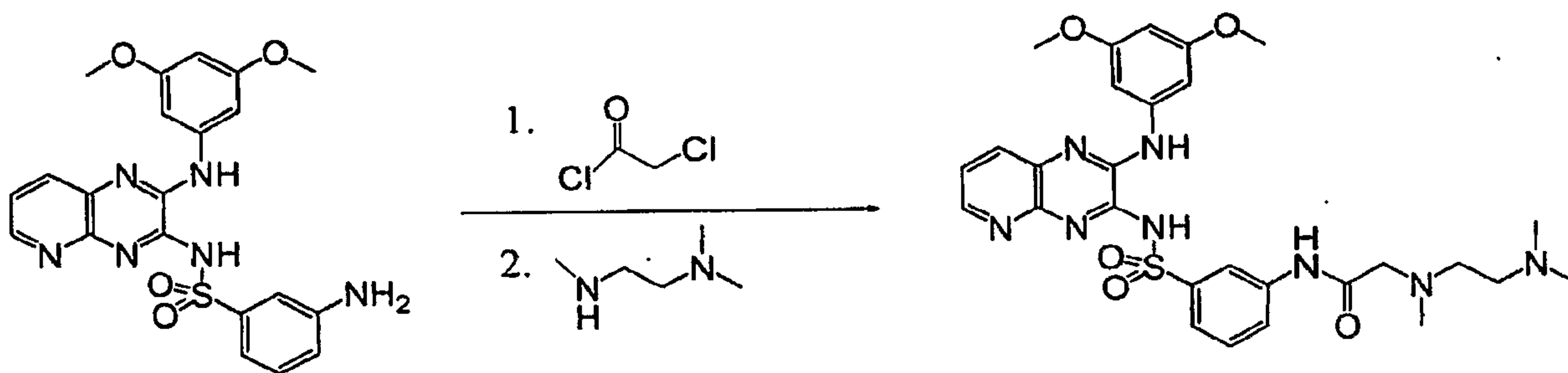
Example 156: *N*-(3-(3-hydroxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₀H₁₅N₅O₅S: 438.16 (MH⁺).

- Example 157:** 3-nitro-*N*-(3-(3-(trifluoromethoxy)-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{21}H_{14}F_3N_5O_5S$: 506.19 (MH⁺).
- Example 158:** 3-nitro-*N*-(3-(pyridin-3-ylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for $C_{19}H_{14}N_6O_4S$: 423.15 (MH⁺).
- 5 **Example 159:** 3-(3-(3-nitrophenylsulfonamido)quinoxalin-2-ylamino)phenyl dimethylcarbamate. MS (EI) for $C_{23}H_{20}N_6O_6S$: 509.01 (MH⁺).
- Example 160:** *N*-(3-(2-chloropyridin-3-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{19}H_{13}ClN_6O_4S$: 456.91 (MH⁺).
- Example 161:** *N*-(3-(3-isopropoxyphenylamino)quinoxalin-2-yl)-3-
10 nitrobenzenesulfonamide. MS (EI) for $C_{23}H_{21}N_5O_5S$: 480.3 (MH⁺).
- Example 162:** *N*-(3-(3-hydroxy-2-methyl-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{21}H_{17}N_5O_5S$: 452.2 (MH⁺).
- Example 163:** *N*-(3-(2,5-difluorophenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{20}H_{13}F_2N_5O_4S$: 458.2 (MH⁺).
- 15 **Example 164:** *N*-(3-(3-(difluoromethoxy)phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{21}H_{15}F_2N_5O_5S$: 488.2 (MH⁺).
- Example 165:** *N*-(3-(2-methoxypyridin-3-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{20}H_{16}N_6O_5S$: 453.01 (MH⁺).
- Example 166:** *N*-(3-(3-ethoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide.
20 MS (EI) for $C_{22}H_{19}N_5O_5S$: 466.2 (MH⁺).
- Example 167:** *N*-(3-(2,2-difluorobenzo[d][1,3]dioxol-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{21}H_{13}F_2N_5O_6S$: 502.2 (MH⁺).
- Example 168:** *N*-(3-(3-(3-nitrophenylsulfonamido)quinoxalin-2-ylamino)phenyl)acetamide. MS (EI) for $C_{22}H_{18}N_6O_5S$: 479.2 (MH⁺).
- 25 **Example 169:** *N*-(3-(4-amino-1*H*-indol-1-yl)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{22}H_{16}N_6O_4S$: 461.2 (MH⁺).
- Example 170:** *N*-(3-(1*H*-indol-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{22}H_{16}N_6O_4S$: 461.2 (MH⁺).
- Example 171:** *N*-(3-(1*H*-indazol-6-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide.
30 MS (EI) for $C_{21}H_{15}N_7O_4S$: 461.96 (MH⁺).
- Example 172:** *N*-(4-methoxy-3-(3-(3-nitro-phenylsulfonamido)quinoxalin-2-ylamino)phenyl)acetamide. MS (EI) for $C_{23}H_{20}N_6O_6S$: 508.97 (MH⁺).
- Example 173:** *N*-(3-(4-methylpyridin-3-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for $C_{20}H_{16}N_6O_4S$: 436.93 (MH⁺).

- Example 174:** *N*-(3-(2,3-dimethoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₂H₁₉N₅O₆S: 481.94 (MH⁺).
- Example 175:** *N*-(3-(1H-pyrazolo[3,4-d]pyrimidin-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₁₉H₁₃N₉O₄S: 463.96 (MH⁺).
- 5 **Example 176:** *N*-(3-(benzo[d]oxazol-4-ylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₄N₆O₅S: 462.99 (MH⁺).
- Example 177:** *N*-(3-(2,6-difluoro-3-methoxy-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₅F₂N₅O₅S: 487.89 (MH⁺).
- Example 178:** *N*-(3-(3,5-dihydroxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₀H₁₅N₅O₆S: 453.96 (MH⁺).
- 10 **Example 179:** *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)naphthalene-2-sulfonamide. MS (EI) for C₂₆H₂₂N₄O₄S: 487.0 (MH⁺).
- Example 180:** *N*-(3-(2,5-dimethoxyphenylamino)-6,7-dimethylquinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₄H₂₄N₄O₄S: 465.3 (MH⁺).
- 15 **Example 181:** 2-amino-*N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-4-methylphenyl)-2-methylpropanamide. MS (EI) for C₂₆H₂₇ClN₆O₄S: 556.12 (MH⁺).
- Example 182:** *N*-(3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. MS (EI) for C₂₅H₂₅ClN₆O₄S: 542.05
- 20 (MH⁺).
- Example 183:** 2-amino-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) for C₂₄H₂₄N₆O₅S: 509.59 (MH⁺).
- Example 184:** 3-amino-*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₁H₁₈ClN₅O₃S: 457.02 (MH⁺).
- 25 **Example 185:** 3-amino-*N*-(2-(3,5-dimethoxy-phenylamino)pyrido[2,3-*b*]pyrazin-3-yl)benzenesulfonamide. MS (EI) for C₂₁H₂₀N₆O₄S: 453.62 (MH⁺).

Example 186

***N*-(3-{{(2-{{[3,5-bis(methoxy)phenyl]amino}pyrido[2,3-*b*]pyrazin-3-yl)amino)sulfonyl}phenyl)-*N*-2-[2-(dimethylamino)ethyl]-*N*-2-methylglycinamide**



5

[00428] To a THF suspension (1.3 mL) of 3-amino-*N*-(3-{{[3,5-bis(methoxy)phenyl]amino} quinoxalin-2-yl)benzenesulfonamide (126 mg, 0.28 mmol) was added 0.143 mL of 2M aqueous Na₂CO₃. To this yellow suspension is added dropwise 33 uL (0.42 mmol) of chloroacetyl chloride. The reaction mixture turns clear after a few minutes and is allowed to stir at 23°C for 1h. To the reaction is added a DMSO (1 mL) solution containing 180 uL (1.4 mmol) of *N,N,N* trimethylethylenediamine. The reaction is then warmed to 60°C and stirred for 18h. The product is isolated by preparative RP-HPLC (NH₄OAc/ACN) gradient, the appropriate fractions were pooled and lyophilize to give a solid yellow as the acetic acid salt: 59 mg (51%). ¹H-NMR (400 MHz, CDCl₃): δ10.1 (br s, 1), 8.37 (br s, 2), 8.18 (d, 1), 7.97 (d, 1), 7.60 (br d, 1), 7.27 (s, 2), 7.20 (br s, 3), 6.15 (s, 1), 3.82 (m, 2), 3.65 (s, 6), 3.20 (br m, 2), 2.82 (br s, 8), 2.42 (s, 3), 2.02 (s, 3). MS (EI) for C₂₈H₃₄N₈O₅S: 595.84 (MH⁺).

15

[00429] The following title compounds were prepared according to the above Examples.

20 **Example 187:** *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-ureidobenzenesulfonamide. MS (EI) for C₂₃H₂₂N₆O₅S: 495.40 (MH⁺).

Example 188: 3-amino-*N*-(3-(5-methoxy-2-methyl-phenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₂H₂₁N₅O₃S: 436.32 (MH⁺).

25 **Example 189:** 2-(dimethylamino)-*N*-(3-(*N*-(3-(5-methoxy-2-methylphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) for C₂₆H₂₈N₆O₄S: 521.69 (MH⁺).

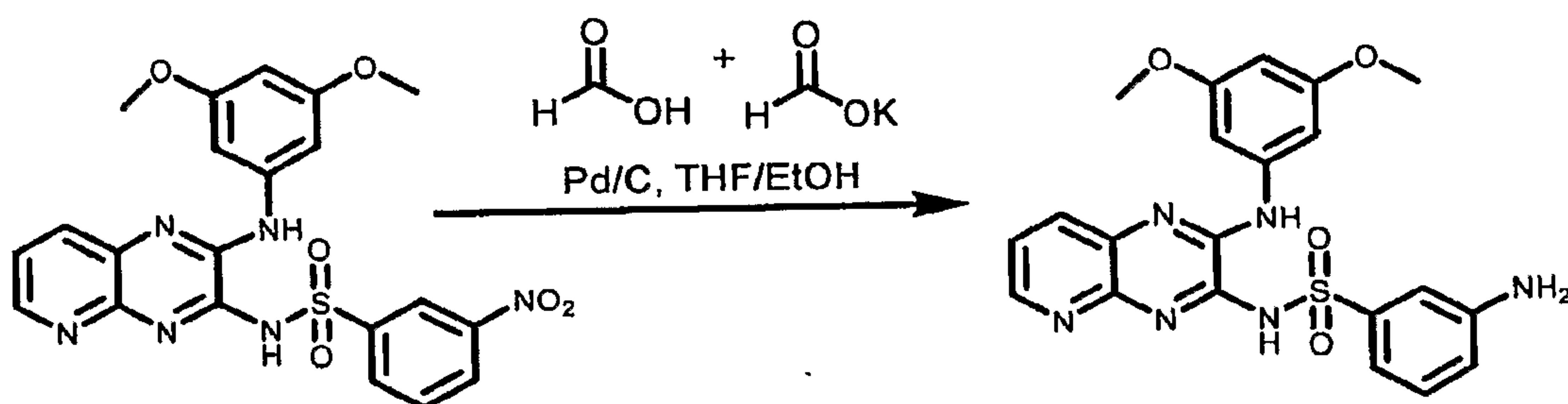
Example 190: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-methylpiperazin-1-yl)acetamide. MS (EI) for C₂₉H₃₃N₇O₅S: 592.61 (MH⁺).

Example 191: 2-acetamido-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) for C₂₆H₂₆N₆O₆S: 550.59 (MH⁺).

Example 192: *tert*-butyl 2-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenylamino)-2-oxoethylcarbamate. MS (EI) for C₂₉H₃₂N₆O₇S: 609.32 (MH⁺).

Example 193

3-amino-*N*-(3-{[3,5-bis(methyloxy)phenyl]amino}pyrido[2,3-*b*]pyrazin-2-yl)benzenesulfonamide



[00430] To a 1:1 THF/EtOH suspension (1 mL) of 3-nitro-*N*-(3-{[3,5-bis(methyloxy)-phenyl]amino}pyrido[2,3-*b*]pyrazin-2-yl)benzenesulfonamide (100 mg, 0.21 mmol) was added 46 μ L (0.63 mmol) of formic acid plus 100mg (0.63 mmol) of potassium formate and 100 mg of 10% palladium on charcoal. After refluxing the reaction for 1h, hot filtration

through celite, and concentration, the product is isolated by preparative RP-HPLC (NH₄OAc/ACN) gradient. The appropriate fractions were pooled and lyophilize to give solid yellow product: 3.2 mg (4%). ¹H-NMR (400 MHz, CDCl₃): δ 8.62 (d, 1), 8.52 (s, 1), 7.62 (d, 1), 7.3 (m, 4), 7.18 (d, 2), 6.88 (d, 1), 6.27 (t, 1), 3.96 (br s, 2), 3.83 (s, 6). MS (EI) for C₂₁H₂₀N₆O₄S: 453.22 (MH⁺).

[00431] The following title compounds were prepared according to the above Examples.

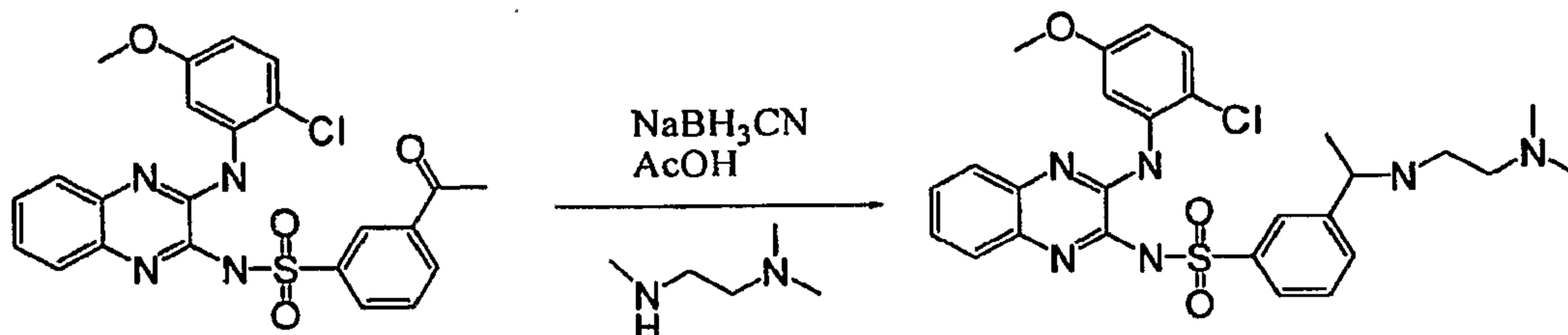
Example 194: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-methyl-1-(piperidin-1-yl)propan-2-yl)benzamide. MS (EI) for C₃₁H₃₅ClN₆O₄S: 623.06 (MH⁺).

Example 195: 3-(*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-methyl-1-oxo-1-(piperidin-1-yl)propan-2-yl)benzamide. MS (EI) for C₃₁H₃₃ClN₆O₅S: 637.65 (MH⁺).

Example 196: *N*-(2-(3,5-dimethoxyphenylamino)pyrido[2,3-*b*]pyrazin-3-yl)-3-nitrobenzenesulfonamide. MS (EI) for C₂₁H₁₈N₆O₆S: 483.78 (MH⁺).

Example 197

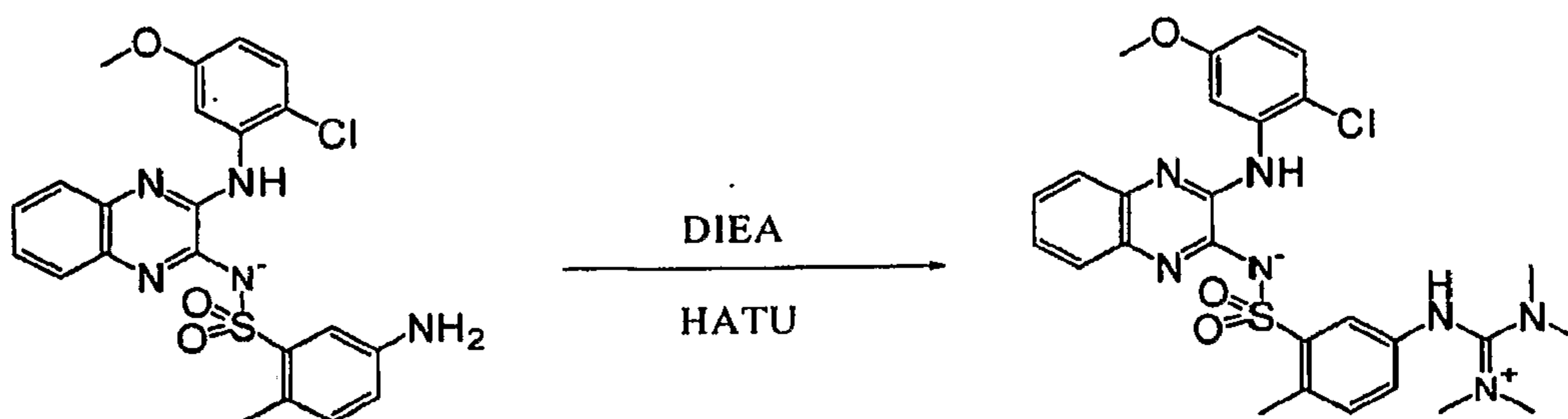
***N*-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(1-{[2-(dimethylamino)ethyl]amino}ethyl)benzenesulfonamide trifluoroacetic acid salt**



[00432] To a dichloroethane solution (0.6 mL) of 3-acetyl-*N*-(3-{[2-chloro-5-(methyloxy)-phenyl]amino} quinoxalin-2-yl)benzenesulfonamide (150 mg, 0.31 mmol) and 51 μ L (0.37 mmol) of *N,N*-dimethylethylenediamine was added 19 μ L of acetic acid followed by 132 mg (0.62 mmol) of sodium cyanoborohydride. The reaction mixture was refluxed for 18h under a nitrogen atmosphere. After concentration (in vacuo), the product is isolated by preparative RP-HPLC (0.1 % TFA/ACN) gradient, followed by lyophilization of appropriate fractions to give solid yellow solid: 189 mg (90%). $^1\text{H-NMR}$ (400 MHz, d_3 -MeOD): δ 8.74 (s, 1), 8.18 (s, 1), 8.12 (d, 1), 7.71 (m, 3), 7.48 (m, 4), 7.28 (d, 1), 6.63 (d, 1), 4.38 (q, 1), 3.80 (s, 3), 3.30 (m, 3), 3.12 (m, 1), 2.84 (s, 3), 1.60 (d, 3). MS (EI) for $\text{C}_{27}\text{H}_{31}\text{ClN}_6\text{O}_3\text{S}$: 555.56 (MH $^+$).

Example 198

***N,N*-{[(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)amino](dimethylamino)methylidene}-*N*-methylethaniminium**

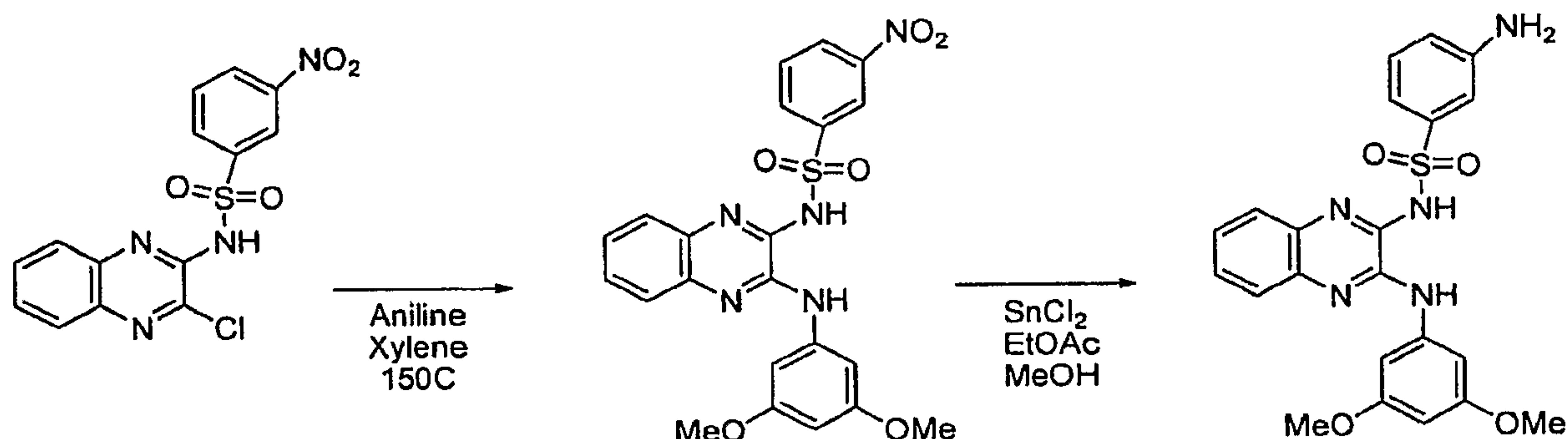


[00433] To a dimethylformamide solution (1 mL) of 3-amino-*N*-(3-{[2-chloro-5-(methyloxy)-phenyl]amino}quinoxalin-2-yl)2-methylbenzenesulfonamide (200 mg, 0.40 mmol) is added 312 μ L (1.8 mmol) of hunigs base and 122 mg (0.6 mmol) of HATU. After stirring for 18h at 60°C, the product was precipitated from a 1:1 mixture of hexane/ethyl acetate, filtered and dried to afford 60 mg (26%). $^1\text{H NMR}$ (400 MHz, d_6 -DMSO): δ 9.26 (b

rs, 1), 8.96 (br s, 1), 7.80 (s, 1), 7.51 (br s, 1), 7.45 (d, 1), 7.18 (brm, 4), 6.91 (br s, 1), 6.60 (br d, 1), 3.82 (s, 3), 3.36 (s, 3), 2.85 (s, 6), 2.58 (s, 3). MS (EI) for $C_{27}H_{31}ClN_7O_3S^+$: 569.32 (MH⁺).

[00434] The following title compounds were prepared according to the above Examples.

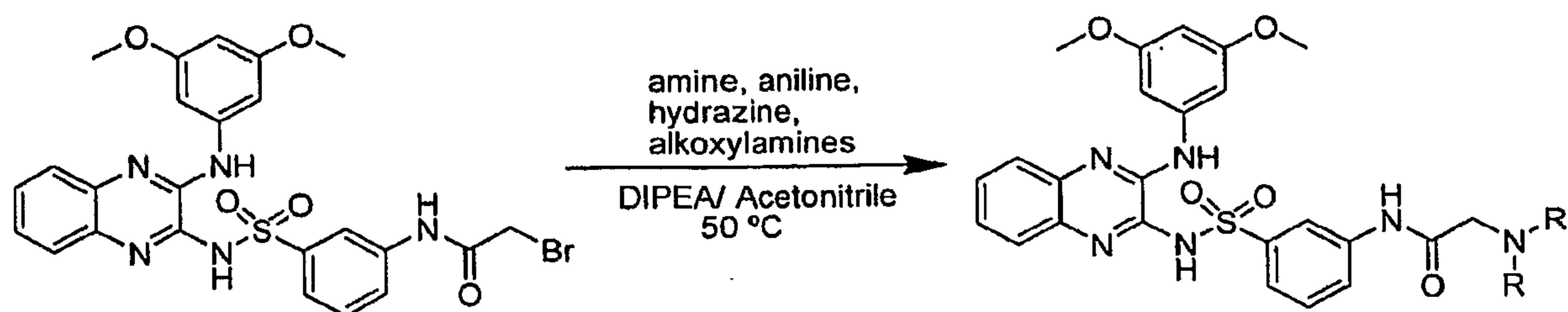
- 5 **Example 199: 3-acetyl-*N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{23}H_{19}ClN_4O_4S$: 483.08 (MH⁺).
- Example 200: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{22}H_{20}N_4O_4S$: 437.49 (MH⁺).
- Example 201: *N*-(3-(5-methoxy-2-methyl-phenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{22}H_{20}N_4O_3S$: 421.46 (MH⁺).
- 10 **Example 202: *N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{21}H_{17}ClN_4O_3S$: 440.59 (MH⁺).
- Example 203: *N*-(3-(2,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{22}H_{20}N_4O_4S$: 437.53 (MH⁺).
- 15 **Example 204: 4-chloro-*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{22}H_{19}ClN_4O_4S$: 470.54 (MH⁺).
- Example 205: *N*-(3-(5-methoxy-2-methyl-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide.** MS (EI) for $C_{22}H_{19}N_5O_5S$: 466.32 (MH⁺).
- Example 206: *N*-(3-(2-chloro-5-methoxy-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide.** MS (EI) for $C_{21}H_{16}ClN_5O_5S$: 485.86 (MH⁺).
- 20 **Example 207: *N*-(3-(2-chloro-5-(difluoromethoxy)-phenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide.** MS (EI) for $C_{21}H_{14}ClF_2N_5O_5S$: 521.92 (MH⁺).
- Example 208: *N*-(3-(4-chloro-2,5-dimethoxy-phenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{22}H_{19}ClN_4O_4S$: 470.99 (MH⁺).
- 25 **Example 209: *N*-(3-(4-morpholinophenylamino)quinoxalin-2-yl)benzenesulfonamide.** MS (EI) for $C_{24}H_{23}N_5O_3S$: 461.54 (MH⁺).

Example 210**3-amino-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide.****[00435] *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide.**

- 5 A flask was charged with *N*-(3-chloroquinoxalin-2-yl)-3-nitrobenzenesulfonamide (5 g, 13.7 mmol), 3,5-dimethoxyaniline (4.2 g, 27.4 mmol), and 80 mL of Xylene. The reaction mixture was stirred under an N₂ atmosphere at 150 °C for 3 hours, after which time, solvent was removed on a rotary evaporator, and 10 mL of Dichloromethane and 50 mL of Methanol were added. The slurry was heated to reflux and filtered while hot, resulting in 4.6 g (69.7
- 10 %) of *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide MS (EI) for C₂₂H₁₉N₅O₆S: 482.2 (MH⁺).

Example 211**[00436] 3-amino-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide**

- 15 A flask was charged with *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-nitrobenzenesulfonamide (3.4g, 7.06 mmol), tin chloride hydrate (6.4 g, 28.2 mmol), and 30 mL of DMA. A few drops of water were added and the reaction mixture was stirred at 80 °C for 3 hours, after which time, solvent was removed on a rotary evaporator, and 50 mL of water and 10 mL of Methanol were added. The slurry was filtered, and the filtrate was washed with
- 20 MeOH, water, and diethyl ether (20 mL of each), resulting in 3.25 g 3-amino-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) for C₂₂H₂₁N₅O₄S: 461.5 (MH⁺).

General Library Alkylation Procedure 1

[00437] Into a 2-dram vial was placed 2-bromo-N-(3-(N-(3-(3,5-dimethoxy-
 5 phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide (86 mg, 0.15 mmol) along with 2 mL of acetonitrile. Eight equivalents (1.2 mmol) of the desired amine, aniline, hydrazine or alkoxyamine were added followed by the addition of Hunig's Base (41 μ L, 0.25 mmol). The reaction then was stirred at 50° C for one hour (overnight for aniline reagents). Preparative reverse-phase HPLC was used to isolate the desired product directly from the crude reaction
 10 mixture. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μ M, 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification.

[00438] The following title compounds were prepared according to **General Library**
 15 **Alkylation Procedure 1**

Example 212: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methylamino)acetamide. $^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$): 8.81 (s, 1H), 8.23 (t, 1H), 7.75 (d, 1H), 7.66 (d, 1H), 7.41-7.38 (m, 1H), 7.35 (m, 1H), 7.32 (d, 2H), 7.29-7.27 (m, 1H), 7.14-7.11 (m, 2H), 6.14 (t, 1H), 3.80 (s, 1H), 3.78 (s, 6H), 2.58 (s, 20 3H), 1.91 (s, 2H); MS (EI) $\text{C}_{25}\text{H}_{26}\text{N}_6\text{O}_5\text{S}$: 523.6 (MH^+).

Example 213: 2-(cyclopropylmethylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. $^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$): 10.58 (s, 1H), 8.81 (s, 1H), 8.20 (t, 1H), 7.76 (d, 1H), 7.67 (d, 1H), 7.42-7.36 (m, 2H), 7.32 (d, 2H), 7.27 (s, 1H), 7.14-7.12 (m, 2H), 6.15 (t, 1H), 3.93 (s, 2H), 25 3.78 (s, 6H), 2.89 (s, 1H), 2.88 (s, 1H), 1.05-1.00 (m, 1H), 0.59 (d, 1H), 0.57 (d, 1H), 0.35 (d, 1H), 0.34 (d, 1H); MS (EI) $\text{C}_{28}\text{H}_{30}\text{N}_6\text{O}_5\text{S}$: 563.6 (MH^+).

Example 214: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-hydroxypropylamino)acetamide. $^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$): 10.49 ppm (s, 1H), 8.81 ppm (s, 1H), 8.23 ppm (t, 1H), 8.13 ppm (s, 1H), 7.76 ppm (d, 1H), 7.765-7.763 (dd, 1H), 7.41-7.37 ppm (m, 2H), 7.33-7.32 ppm (d, 1H), 7.30-7.28 ppm
 30 (d, 1H), 7.27-7.26 (m, 1H), 6.14 ppm (t, 1H), 3.80 ppm (s, 1H), 3.78 ppm (s, 6H), 2.58 ppm (s, 2H), 1.91 ppm (s, 2H), 1.05-1.00 ppm (m, 1H), 0.59 ppm (d, 1H), 0.57 ppm (d, 1H), 0.35 ppm (d, 1H), 0.34 ppm (d, 1H); MS (EI) $\text{C}_{27}\text{H}_{30}\text{N}_6\text{O}_6\text{S}$: 539.6 (MH^+).

(m, 1H), 7.16-7.09 ppm (m, 2H), 6.55 ppm (s, 1H), 6.14 ppm (t, 1H), 5.49 ppm (d, 2H), 5.25 ppm (s, 1H), 3.85 ppm (s, 1H), 3.78 ppm (s, 6H) 3.67-3.59 ppm (m, 1H), 3.00-2.89 ppm (dd, 1H), 2.79-2.76 ppm (m, 1H), 1.10 ppm (d, 1H), 1.01-0.99 ppm (d, 1H); MS (EI) $C_{27}H_{30}N_6O_6S$: 566.6 (MH^+).

- 5 **Example 215:** *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-fluorobenzylamino)acetamide. ^1H -NMR (400MHz, d_6 -DMSO): 10.42 ppm (s, 1H), 8.82 ppm (s, 1H), 8.23 ppm (s, 1H), 8.14 ppm (s, 1H), 7.75 ppm (d, 1H), 7.65 ppm (d, 1H), 7.49-7.32 ppm (m, 6H), 7.25-7.20 ppm (m, 1H), 7.14-7.12 ppm (m, 2H), 6.55 ppm (s, 1H), 6.15 ppm (t, 1H), 4.14 ppm (s, 2H), 3.78 ppm (s, 6H), 3.74 ppm (s, 2H); MS (EI) $C_{31}H_{29}FN_6O_5S$: 616.7 (MH^+).

Example 216: 2-(benzylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{31}H_{30}N_6O_5S$: 599 (MH^+).

Example 217: 2-(diethylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{28}H_{32}N_6O_5S$: 565 (MH^+).

- 15 **Example 218:** 2-(4-(3,4-dichlorophenyl)piperazin-1-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{34}H_{33}Cl_2N_7O_5S$: 722 (MH^+).

Example 219: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2,2-dimethylhydrazinyl)acetamide. MS (EI) $C_{26}H_{29}N_7O_5S$: 552 (MH^+).

Example 220: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(*p*-tolylamino)acetamide. MS (EI) $C_{31}H_{30}N_6O_5S$: 599 (MH^+).

Example 221: 2-(benzyloxyamino)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{31}H_{30}N_6O_6S$: 615 (MH^+).

- 25 **Example 222:** 2-(2-chlorophenylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{30}H_{27}ClN_6O_5S$: 619 (MH^+).

Example 223: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(isopropylamino)acetamide. MS (EI) $C_{27}H_{30}N_6O_5S$: 551 (MH^+).

- 30 **Example 224:** 2-(4-cyclopentylpiperazin-1-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{33}H_{39}N_7O_5S$: 646 (MH^+).

Example 225: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-propylpiperidin-1-yl)acetamide. MS (EI) C₃₂H₃₈N₆O₅S: 619 (MH⁺).

Example 226: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(isobutoxyamino)acetamide. MS (EI) C₂₈H₃₂N₆O₆S: 581 (MH⁺).

Example 227: 2-(3-tert-butylphenylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₄H₃₆N₆O₅S: 641 (MH⁺).

Example 228: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-phenylpropan-2-ylamino)acetamide. MS (EI) C₃₃H₃₄N₆O₅S: 627 (MH⁺).

Example 229: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-fluoro-4-hydroxyphenylamino)acetamide. MS (EI) C₃₀H₂₇FN₆O₆S: 619 (MH⁺).

Example 230: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-(methylthio)benzylamino)acetamide. MS (EI) C₃₂H₃₂N₆O₅S₂: 645 (MH⁺).

Example 231: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(5-fluoro-2-methylbenzylamino)acetamide. MS (EI) C₃₂H₃₁FN₆O₅S: 631 (MH⁺).

Example 232: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-phenylpyrrolidin-1-yl)acetamide. MS (EI) C₃₄H₃₄N₆O₅S: 639 (MH⁺).

Example 233: 2-(2-benzylpyrrolidin-1-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₅H₃₆N₆O₅S: 653 (MH⁺).

Example 234: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-phenylmorpholino)acetamide. MS (EI) C₃₄H₃₄N₆O₆S: 655 (MH⁺).

Example 235: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-(pyridin-4-yl)piperidin-1-yl)acetamide. MS (EI) C₃₄H₃₅N₇O₅S: 654 (MH⁺).

Example 236: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(*o*-tolylamino)acetamide. MS (EI) C₃₁H₃₀N₆O₅S: 599 (MH⁺).

Example 237: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2,4-dimethylbenzylamino)acetamide. MS (EI) C₃₃H₃₄N₆O₅S: 627 (MH⁺).

Example 238: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methyl(pyridin-3-ylmethyl)amino)acetamide. MS (EI) C₃₁H₃₁N₇O₅S: 614 (MH⁺).

Example 239: 2-(3-chloro-4-methylbenzylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₂H₃₁ClN₆O₅S: 647 (MH⁺).

Example 240: *N*-(3-(*N*-(3-(3,5-dimethoxy-phenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-((2-(dimethylamino)-ethyl)(methyl)amino)acetamide. MS (EI) C₂₉H₃₅N₇O₅S: 594 (MH⁺).

Example 241: 2-(4-acetylpiperazin-1-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₃₃N₇O₆S: 620 (MH⁺).

Example 242: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(methyl(1-methylpyrrolidin-3-yl)amino)acetamide. MS (EI) C₃₀H₃₅N₇O₅S: 606 (MH⁺).

Example 243: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-methyl-1,4-diazepan-1-yl)acetamide. MS (EI) C₃₀H₃₅N₇O₅S: 606 (MH⁺).

Example 244: 2-(4-allylpiperazin-1-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₁H₃₅N₇O₅S: 618 (MH⁺).

Example 245: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-isopropylpiperazin-1-yl)acetamide MS (EI) C₃₁H₃₇N₇O₅S: 620 (MH⁺).

Example 246: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-(dimethylamino)pyrrolidin-1-yl)acetamide. MS (EI) C₃₀H₃₅N₇O₅S: 606 (MH⁺).

Example 247: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-(dimethylamino)azetidin-1-yl)acetamide. MS (EI) C₂₉H₃₃N₇O₅S: 592 (MH⁺).

Example 248: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-oxopiperidin-1-yl)acetamide. MS (EI) C₂₉H₃₀N₆O₆S: 591 (MH⁺).

- Example 249: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-((2-methoxyethyl)(methyl)amino)acetamide. MS (EI) C₂₈H₃₂N₆O₆S: 581 (MH⁺).
- Example 250: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-methylbenzyloxyamino)acetamide. MS (EI) C₃₂H₃₂N₆O₆S: 629 (MH⁺).
- 5 Example 251: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methoxybenzyloxyamino)acetamide. MS (EI) C₃₂H₃₂N₆O₇S: 645 (MH⁺).
- Example 252: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(propylamino)acetamide. MS (EI) C₂₇H₃₀N₆O₅S: 551 (MH⁺).
- Example 253: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-10 (ethyl(methyl)amino)acetamide. MS (EI) C₂₇H₃₀N₆O₅S: 551 (MH⁺).
- Example 254: 2-(allyl(methyl)amino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₈H₃₀N₆O₅S: 563 (MH⁺).
- Example 255: 2-(tert-butylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₈H₃₂N₆O₅S: 565 (MH⁺).
- 15 Example 256: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(isobutylamino)acetamide. MS (EI) C₂₈H₃₂N₆O₅S: 565 (MH⁺).
- Example 257: 2-(butylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₈H₃₂N₆O₅S: 565 (MH⁺).
- Example 258: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-20 (isopropyl(methyl)amino)acetamide. MS (EI) C₂₈H₃₂N₆O₅S: 565 (MH⁺).
- Example 259: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-formylpiperazin-1-yl)acetamide. MS (EI) C₂₉H₃₁N₇O₆S: 606 (MH⁺).
- Example 260: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-ethylpiperazin-1-yl)acetamide. MS (EI) C₃₀H₃₅N₇O₅S: 606 (MH⁺).
- 25 Example 261: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-formyl-1,4-diazepan-1-yl)acetamide. MS (EI) C₃₀H₃₃N₇O₆S: 620 (MH⁺).
- Example 262: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(ethyl(2-hydroxyethyl)amino)acetamide. MS (EI) C₂₈H₃₂N₆O₆S: 581 (MH⁺).
- Example 263: (S)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-hydroxypyrrolidin-1-yl)acetamide. MS (EI) C₂₈H₃₀N₆O₆S: 57930 (MH⁺).
- Example 264: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2,6-dimethylmorpholino)acetamide. MS (EI) C₃₀H₃₄N₆O₆S: 607 (MH⁺).

Example 265: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methylbenzylamino)acetamide. MS (EI) C₃₂H₃₂N₆O₅S: 613 (MH⁺).

Example 266: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methoxyethylamino)acetamide. MS (EI) C₂₇H₃₀N₆O₆S: 567 (MH⁺).

5 Example 267: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(thiazolidin-3-yl)acetamide. MS (EI) C₂₇H₂₈N₆O₅S₂: 581 (MH⁺).

Example 268: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-(hydroxymethyl)piperidin-1-yl)acetamide MS (EI) C₃₀H₃₄N₆O₆S: 607 (MH⁺).

10 Example 268: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-phenylpropylamino)acetamide. MS (EI) C₃₃H₃₄N₆O₅S: 627 (MH⁺).

Example 269: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(isobutyl(methyl)amino)acetamide. MS (EI) C₂₉H₃₄N₆O₅S: 579 (MH⁺).

Example 270: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(phenylamino)acetamide. MS (EI) C₃₀H₂₈N₆O₅S: 585 (MH⁺).

15 Example 271: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-propylphenylamino)acetamide. MS (EI) C₃₃H₃₄N₆O₅S: 627 (MH⁺).

Example 272: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-isopropylphenylamino)acetamide. MS (EI) C₃₃H₃₄N₆O₅S: 627 (MH⁺).

20 Example 273: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-fluoro-4-methylphenylamino)acetamide. MS (EI) C₃₁H₂₉FN₆O₅S: 617 (MH⁺).

Example 274: 2-(4-chlorophenylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₂₇ClN₆O₅S: 619 (MH⁺).

Example 275: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methoxyphenylamino)acetamide. MS (EI) C₃₁H₃₀N₆O₆S: 615 (MH⁺).

25 Example 276: 2-(3-chlorophenylamino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₂₇ClN₆O₅S: 619 (MH⁺).

Example 277: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2,3-dimethylphenylamino)acetamide. MS (EI) C₃₂H₃₂N₆O₅S: 613 (MH⁺).

30 Example 278: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-fluorophenylamino)acetamide. MS (EI) C₃₀H₂₇FN₆O₅S: 603 (MH⁺).

Example 279: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-fluorophenylamino)acetamide. MS (EI) C₃₀H₂₇FN₆O₅S: 603 (MH⁺).

Example 280: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(thiophen-2-ylmethylamino)acetamide. MS (EI) C₂₉H₂₈N₆O₅S₂: 605 (MH⁺).

Example 281: 2-(cyclohexyl(ethyl)amino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{32}H_{38}N_6O_5S$: 619 (MH^+).

Example 282: 2-((cyclopropylmethyl)(propyl)amino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{31}H_{36}N_6O_5S$: 605 (MH^+).

Example 283: 2-(allyl(cyclopentyl)amino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{32}H_{36}N_6O_5S$: 617 (MH^+).

Example 284: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(ethyl(isopropyl)amino)acetamide. MS (EI) $C_{29}H_{34}N_6O_5S$: 579 (MH^+).

Example 285: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(ethyl(phenyl)amino)acetamide. MS (EI) $C_{32}H_{32}N_6O_5S$: 613 (MH^+).

Example 286: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methylpyrrolidin-1-yl)acetamide. MS (EI) $C_{29}H_{32}N_6O_5S$: 577 (MH^+).

Example 287: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methylpiperidin-1-yl)acetamide. MS (EI) $C_{30}H_{34}N_6O_5S$: 591 (MH^+).

Example 288: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(pyridin-2-ylmethylamino)acetamide. MS (EI) $C_{30}H_{29}N_7O_5S$: 600 (MH^+).

Example 289: 2-(benzyl(methyl)amino)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) $C_{32}H_{32}N_6O_5S$: 613 (MH^+).

Example 290: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(1-phenylethylamino)acetamide. MS (EI) $C_{32}H_{32}N_6O_5S$: 613 (MH^+).

Example 291: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-methylpiperidin-1-yl)acetamide. MS (EI) $C_{30}H_{34}N_6O_5S$: 591 (MH^+).

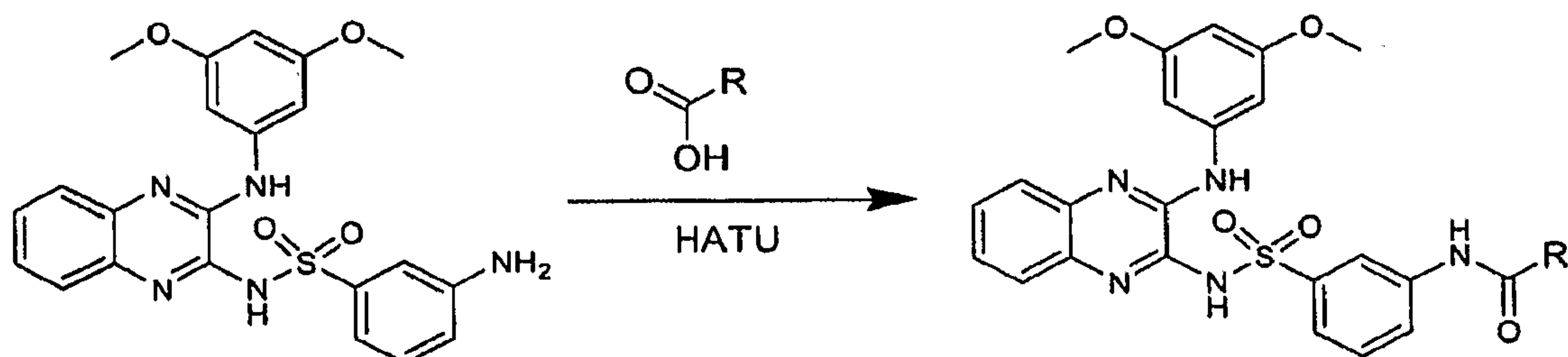
Example 292: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-methylpiperidin-1-yl)acetamide. MS (EI) $C_{30}H_{34}N_6O_5S$: 591 (MH^+).

Example 293: 2-(3,4-dihydroisoquinolin-2(1H)-yl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI)

$C_{33}H_{32}N_6O_5S$: 625 (MH^+).

Example 294: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2,6-dimethylpiperidin-1-yl)acetamide. MS (EI) $C_{31}H_{36}N_6O_5S$: 605 (MH^+).

Example 295: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-hydroxybenzylamino)acetamide. MS (EI) $C_{31}H_{30}N_6O_6S$: 615 (MH^+).

General Library Acylation Procedure 2

[00439] Into a 2-dram vial were added 3-amino-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide (54 mg, 0.12 mmol), DMA (2 mL) and the desired carboxylic acid (0.17 mmol). Hunig's Base (70 μ L, 0.4 mmol) followed by HATU (53 mg, 0.14 mmol) were added to the vial and the reaction mixture stirred at 50° C overnight. Preparative reverse-phase HPLC was used to isolate the desired product directly from the crude reaction mixture. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μ M, 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification.

[00440] The following title compounds were prepared according to **General Library Acylation Procedure 2**.

- 15 **Example 296:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)propionamide. $^1\text{H-NMR}$ (400MHz, d_6 -DMSO): 12.37 (s, 1H), 10.20 (s, 1H), 8.88 (s, 1H), 8.37 (s, 1H), 7.93 (s, 1H), 7.77 (t, 2H), 7.59 (t, 1H), 7.51 (t, 1H), 7.41-7.34 (m, 4H), 6.24 (t, 1H), 3.76 (s, 6H), 2.36-2.31 (dd, 2H), 1.10 (s, 1H), 1.08 (s, 1H), 1.06 (s, 1H); MS (EI) $\text{C}_{25}\text{H}_{25}\text{N}_5\text{O}_5\text{S}$: 508.6 (MH^+).
- 20 **Example 297:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pyridazine-4-carboxamide. $^1\text{H-NMR}$ (400MHz, d_6 -DMSO): 11.01 (s, 1H), 9.66 (dd, 1H), 9.52 (dd, 1H), 8.90 (s, 1H), 8.55 (s, 1H), 8.13 (dd, 1H), 7.99 (d, 1H), 7.93 (d, 1H), 7.65-7.58 (m, 2H), 7.42-7.35 (m, 4H), 6.24 (t, 1H), 3.75 (s, 6H); MS (EI) $\text{C}_{27}\text{H}_{23}\text{N}_7\text{O}_5\text{S}$: 558.6 (MH^+).
- 25 **Example 298:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methylnicotinamide. $^1\text{H-NMR}$ (400MHz, d_6 -DMSO): 10.78 ppm (s, 1H), 8.90 ppm (s, 1H), 8.58-8.57 ppm (dd, 2H), 7.90-7.86 (m, 4H), 7.60-7.56 ppm (m, 2H), 7.42-7.34 (m, 5H), 6.23 ppm (t, 1H), 3.74 ppm (s, 6H), 2.57 ppm (s, 3H); MS (EI) $\text{C}_{29}\text{H}_{26}\text{N}_5\text{O}_5\text{S}$: 570.6 (MH^+).

Example 299: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-2-(*o*-tolylloxy)acetamide. ¹H-NMR (400MHz, d₆-DMSO): 12.37

ppm (s, 1H), 10.41 ppm (s, 1H), 8.90 ppm (s, 1H), 8.41 ppm (s, 1H), 7.93 ppm (s, 1H), 7.90-

7.8 (m, 2H), 7.59-7.53 ppm (m, 2H), 7.42-7.33 ppm (m, 4H), 7.17-7.12 ppm (m, 2H), 6.89-

6.85 ppm (m, 2H), 6.24 ppm (t, 1H), 4.74 ppm (s, 2H), 3.76 ppm (s, 6H), 2.33 ppm (s, 2H);

MS (EI) C₃₁H₂₉N₅O₆S: 599.7 (MH⁺).

Example 300: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-3-methoxy-4-methylbenzamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

Example 301: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-3-methoxy-4-methylbenzamide. MS (EI) C₂₈H₂₄N₆O₅S: 557 (MH⁺).

Example 302: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)thiazole-4-carboxamide. MS (EI) C₂₆H₂₂N₆O₅S₂: 563 (MH⁺).

Example 303: 2-bromo-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)thiophene-3-carboxamide. MS (EI) C₂₇H₂₂BrN₅O₅S₂: 640 (MH⁺).

Example 304: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)pivalamide. MS (EI) C₂₇H₂₉N₅O₅S: 536 (MH⁺).

Example 305: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)pent-4-enamide. MS (EI) C₂₇H₂₇N₅O₅S: 534 (MH⁺).

Example 306: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₅N₅O₅S: 556 (MH⁺).

Example 307: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)butyramide. MS (EI) C₂₆H₂₇N₅O₅S: 522 (MH⁺).

Example 308: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-2-methoxyacetamide. MS (EI) C₂₅H₂₅N₅O₆S: 524 (MH⁺).

Example 309: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)cyclobutanecarboxamide. MS (EI) C₂₇H₂₇N₅O₅S: 534 (MH⁺).

Example 310: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-2-methylcyclopropanecarboxamide. MS (EI) C₂₇H₂₇N₅O₅S: 534 (MH⁺).

Example 311: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-1-methylcyclopropanecarboxamide. MS (EI) C₂₇H₂₇N₅O₅S: 534 (MH⁺).

Example 312: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-

*yl*sulfamoyl)phenyl)-3-methylbutanamide. MS (EI) C₂₇H₂₉N₅O₅S: 536 (MH⁺).

Example 313: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-ethoxyacetamide. MS (EI) C₂₆H₂₇N₅O₆S: 538 (MH⁺).

Example 314: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-methoxypropanamide. MS (EI) C₂₆H₂₇N₅O₆S: 538 (MH⁺).

5 **Example 315:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-hydroxyacetamide. MS (EI) C₂₄H₂₃N₅O₆S: 510 (MH⁺).

Example 316: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)isobutyramide. MS (EI) C₂₆H₂₇N₅O₅S: 522 (MH⁺).

10 **Example 317:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-hydroxycyclopropanecarboxamide. MS (EI) C₂₆H₂₅N₅O₆S: 536 (MH⁺).

Example 318: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)furan-3-carboxamide. MS (EI) C₂₇H₂₃N₅O₆S: 546 (MH⁺).

15 **Example 319:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)tetrahydrofuran-3-carboxamide. MS (EI) C₂₇H₂₇N₅O₆S: 550 (MH⁺).

Example 320: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)tetrahydrofuran-2-carboxamide. MS (EI) C₂₇H₂₇N₅O₆S: 550 (MH⁺).

Example 321: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)furan-2-carboxamide. MS (EI) C₂₇H₂₃N₅O₆S: 546 (MH⁺).

20 **Example 322:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)isonicotinamide. MS (EI) C₂₈H₂₄N₆O₅S: 557 (MH⁺).

Example 323: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1H-pyrrole-2-carboxamide. MS (EI) C₂₇H₂₄N₆O₅S: 545 (MH⁺).

25 **Example 324:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pyrazine-2-carboxamide. MS (EI) C₂₇H₂₃N₇O₅S: 558 (MH⁺).

Example 325: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-methyl-1H-pyrrole-2-carboxamide. MS (EI) C₂₈H₂₆N₆O₅S: 559 (MH⁺).

30 **Example 326:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-5-methylisoxazole-3-carboxamide. MS (EI) C₂₇H₂₄N₆O₆S: 561 (MH⁺).

Example 327: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)thiophene-2-carboxamide. MS (EI) C₂₇H₂₃N₅O₅S₂: 562 (MH⁺).

Example 328: (S)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-methylpyrrolidine-2-carboxamide. MS (EI) C₂₈H₃₀N₆O₅S: 563 (MH⁺).

Example 329: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methylbenzamide. MS (EI) C₃₀H₂₇N₅O₅S: 570 (MH⁺).

Example 330: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-phenylacetamide. MS (EI) C₃₀H₂₇N₅O₅S: 570 (MH⁺).

Example 331: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-methylpicolinamide. MS (EI) C₂₉H₂₆N₆O₅S: 571 (MH⁺).

Example 332: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(pyridin-3-yl)acetamide. MS (EI) C₂₉H₂₆N₆O₅S: 571 (MH⁺).

Example 333: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-6-hydroxypicolinamide. MS (EI) C₂₈H₂₄N₆O₆S: 573 (MH⁺).

Example 334: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-fluorobenzamide. MS (EI) C₂₉H₂₄FN₅O₅S: 574 (MH⁺).

Example 335: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-fluorobenzamide. MS (EI) C₂₉H₂₄FN₅O₅S: 574 (MH⁺).

Example 336: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-fluorobenzamide. MS (EI) C₂₉H₂₄FN₅O₅S: 574 (MH⁺).

Example 337: 2-cyclohexyl-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₃₃N₅O₅S: 576 (MH⁺).

Example 338: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-oxocyclopentyl)acetamide. MS (EI) C₂₉H₂₉N₅O₆S: 576 (MH⁺).

Example 339: 4-cyclopropyl-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-oxobutanamide. MS (EI) C₂₉H₂₉N₅O₆S: 576 (MH⁺).

Example 340: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-oxocyclohexanecarboxamide. MS (EI) C₂₉H₂₉N₅O₆S: 576 (MH⁺).

Example 341: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-(pyridin-3-yl)propanamide. MS (EI) C₃₀H₂₈N₆O₅S: 585 (MH⁺).

Example 342: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methoxybenzamide. MS (EI) C₃₀H₂₇N₅O₆S: 586 (MH⁺).

Example 343: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-methoxybenzamide. MS (EI) C₃₀H₂₇N₅O₆S: 586 (MH⁺).

Example 344: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-phenoxyacetamide. MS (EI) C₃₀H₂₇N₅O₆S: 586 (MH⁺).

Example 345: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-methoxybenzamide. MS (EI) C₃₀H₂₇N₅O₆S: 586 (MH⁺).

5 **Example 346:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-fluorophenyl)acetamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

Example 347: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-fluorophenyl)acetamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

10 **Example 348:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-fluorophenyl)acetamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

Example 349: 2-chloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₄ClN₅O₅S: 590 (MH⁺).

Example 350: 4-chloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₄ClN₅O₅S: 590 (MH⁺).

15 **Example 351:** 3-chloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₄ClN₅O₅S: 590 (MH⁺).

Example 352: (1*R*,2*R*)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-phenylcyclopropanecarboxamide. MS (EI) C₃₂H₂₉N₅O₅S: 596 (MH⁺).

20 **Example 353:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-phenylcyclopropanecarboxamide. MS (EI) C₃₂H₂₉N₅O₅S: 596 (MH⁺).

Example 354: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(1*H*-imidazol-4-yl)acetamide. MS (EI) C₂₇H₂₅N₇O₅S: 560 (MH⁺).

25 **Example 355:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-methoxy-2-methylbenzamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

Example 356: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-fluorophenoxy)acetamide. MS (EI) C₃₀H₂₆FN₅O₆S: 604 (MH⁺).

30 **Example 357:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-5-fluoro-2-methoxybenzamide. MS (EI) C₃₀H₂₆FN₅O₆S: 604 (MH⁺).

Example 358: 2-(4-chlorophenyl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₂₆ClN₅O₅S: 604 (MH⁺).

Example 359: 2-(2-chlorophenyl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₂₆ClN₅O₅S: 604 (MH⁺).

Example 360: 2-(3-chlorophenyl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₃₀H₂₆ClN₅O₅S: 604 (MH⁺).

Example 361: 1-acetyl-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)piperidine-4-carboxamide. MS (EI) C₃₀H₃₂N₆O₆S: 605 (MH⁺).

5 **Example 362:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(pyridin-4-yl)acetamide. MS (EI) C₂₉H₂₆N₆O₅S: 571 (MH⁺).

Example 363: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(pyridin-2-yl)acetamide. MS (EI) C₂₉H₂₆N₆O₅S: 571 (MH⁺).

10 **Example 364:** 2,4-dichloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₃Cl₂N₅O₅S: 624 (MH⁺).

Example 365: 3,4-dichloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₃Cl₂N₅O₅S: 624 (MH⁺).

Example 366: 2,5-dichloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₃Cl₂N₅O₅S: 624 (MH⁺).

15 **Example 367:** 3,5-dichloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₃Cl₂N₅O₅S: 624 (MH⁺).

Example 368: 2,3-dichloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzamide. MS (EI) C₂₉H₂₃Cl₂N₅O₅S: 624 (MH⁺).

20 **Example 369:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pentanamide. MS (EI) C₂₇H₂₉N₅O₅S: 536 (MH⁺).

Example 370: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methylbutanamide. MS (EI) C₂₇H₂₉N₅O₅S: 536 (MH⁺).

Example 371: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1H-imidazole-2-carboxamide. MS (EI) C₂₆H₂₃N₇O₅S: 546 (MH⁺).

25 **Example 372:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1H-imidazole-4-carboxamide. MS (EI) C₂₆H₂₃N₇O₅S: 546 (MH⁺).

Example 373: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)isoxazole-5-carboxamide. MS (EI) C₂₆H₂₂N₆O₆S: 547 (MH⁺).

30 **Example 374:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3,3-dimethylbutanamide. MS (EI) C₂₈H₃₁N₅O₅S: 550 (MH⁺).

Example 375: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methylpentanamide. MS (EI) C₂₈H₃₁N₅O₅S: 550 (MH⁺).

Example 376: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2,2-dimethylbutanamide. MS (EI) C₂₈H₃₁N₅O₅S: 550 (MH⁺).

Example 377: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-methylpentanamide. MS (EI) C₂₈H₃₁N₅O₅S: 550 (MH⁺).

Example 378: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)pyrimidine-5-carboxamide. MS (EI) C₂₇H₂₃N₇O₅S: 558 (MH⁺).

5 **Example 379:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-methylfuran-2-carboxamide. MS (EI) C₂₈H₂₅N₅O₆S: 560 (MH⁺).

Example 380: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)thiophene-3-carboxamide. MS (EI) C₂₇H₂₃N₅O₅S₂: 562 (MH⁺).

10 **Example 381:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-oxocyclopentanecarboxamide. MS (EI) C₂₈H₂₇N₅O₆S: 562 (MH⁺).

Example 382: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methoxyethoxy)acetamide. MS (EI) C₂₇H₂₉N₅O₇S: 568 (MH⁺).

Example 383: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-methylbenzamide. MS (EI) C₃₀H₂₇N₅O₅S: 570 (MH⁺).

15 **Example 384:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-methylisoxazol-4-yl)acetamide. MS (EI) C₂₈H₂₆N₆O₆S: 575 (MH⁺).

Example 385: 3-cyclopentyl-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)propanamide. MS (EI) C₃₀H₃₃N₅O₅S: 576 (MH⁺).

20 **Example 386:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-*o*-tolylacetamide. MS (EI) C₃₁H₂₉N₅O₅S: 584 (MH⁺).

Example 387: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methoxynicotinamide. MS (EI) C₂₉H₂₆N₆O₆S: 587 (MH⁺).

25 **Example 388:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-fluoro-3-methylbenzamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

Example 389: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-fluoro-2-methylbenzamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

Example 390: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-fluoro-4-methylbenzamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

30 **Example 391:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-fluoro-5-methylbenzamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

Example 392: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-5-fluoro-2-methylbenzamide. MS (EI) C₃₀H₂₆FN₅O₅S: 588 (MH⁺).

Example 393: 6-chloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)nicotinamide. MS (EI) C₂₈H₂₃ClN₆O₅S: 591 (MH⁺).

Example 394: 2-chloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)nicotinamide. MS (EI) C₂₈H₂₃ClN₆O₅S: 591 (MH⁺).

5 **Example 395:** 2-chloro-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)isonicotinamide. MS (EI) C₂₈H₂₃ClN₆O₅S: 591 (MH⁺).

Example 396: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-4-(dimethylamino)benzamide. MS (EI) C₃₁H₃₀N₆O₅S: 599 (MH⁺).

10 **Example 397:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-(dimethylamino)benzamide. MS (EI) C₃₁H₃₀N₆O₅S: 599 (MH⁺).

Example 398: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)benzo[d][1,3]dioxole-5-carboxamide. MS (EI) C₃₀H₂₅N₅O₇S: 600 (MH⁺).

15 **Example 399:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(*m*-tolylloxy)acetamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

Example 400: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(4-methoxyphenyl)acetamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

Example 401: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(2-methoxyphenyl)acetamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

20 **Example 402:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(3-methoxyphenyl)acetamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

Example 403: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-methoxy-4-methylbenzamide. MS (EI) C₃₁H₂₉N₅O₆S: 600 (MH⁺).

25 **Example 404:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-fluoro-4-methoxybenzamide. MS (EI) C₃₀H₂₆FN₅O₆S: 604 (MH⁺).

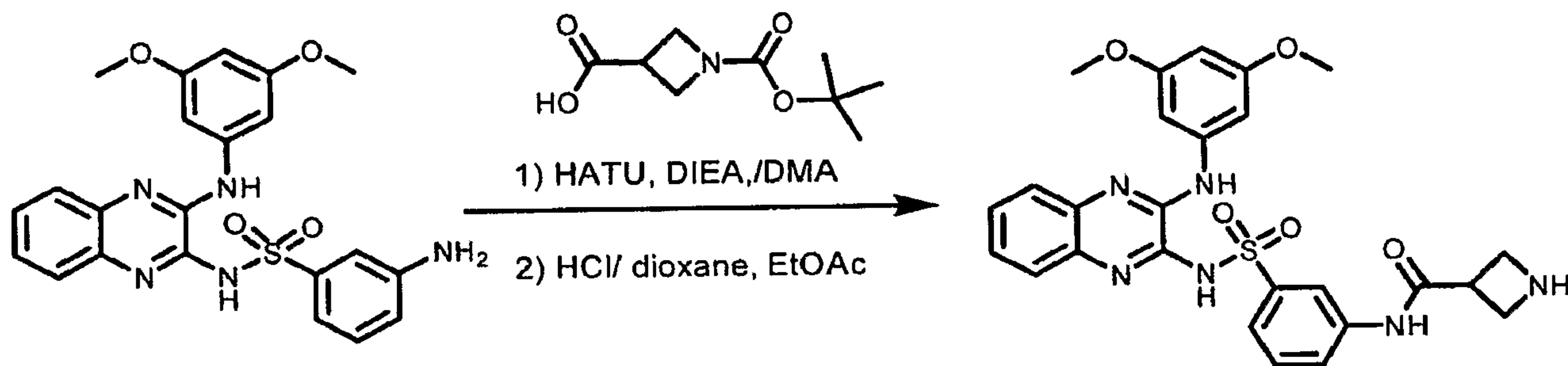
Example 405: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-fluoro-6-methoxybenzamide. MS (EI) C₃₀H₂₆FN₅O₆S: 604 (MH⁺).

Example 406: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-(4-methoxyphenyl)propanamide. MS (EI) C₃₂H₃₁N₅O₆S: 614 (MH⁺).

30 **Example 407:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-(2-methoxyphenyl)propanamide. MS (EI) C₃₂H₃₁N₅O₆S: 614 (MH⁺).

Example 408: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-3-(3-methoxyphenyl)propanamide. MS (EI) C₃₂H₃₁N₅O₆S: 614 (MH⁺).

5 General Library Acylation Procedure 2a



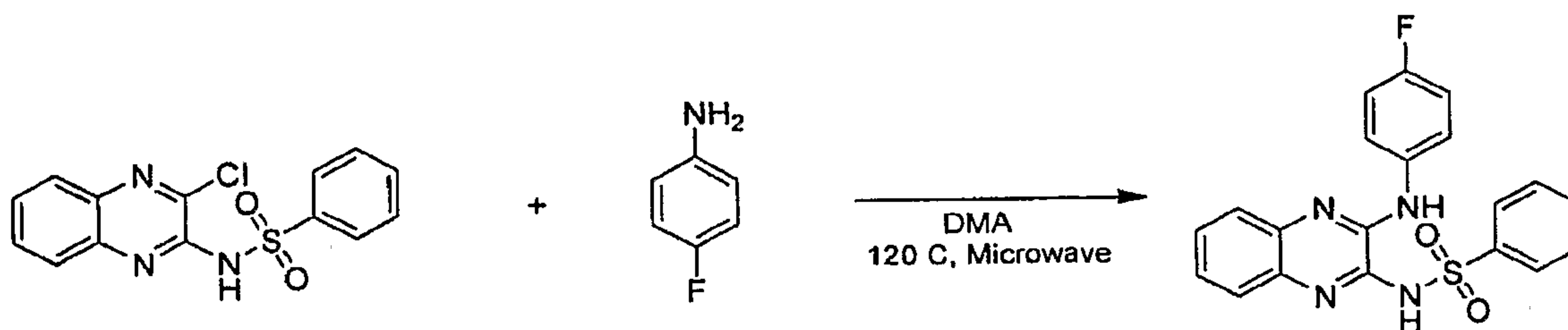
[00441] Into a 20 mL vial was added 3-amino-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide (0.24 mmol, 1 equiv), DMA (5 mL) and 1-(tert-butoxycarbonyl)azetidine-3-carboxylic acid (0.336 mmol, 1.4 equiv). Hunig's Base (0.792 mmol, 3.3 equiv) and HATU (0.288 mmol, 1.2 equiv) were added to the vial and the reaction mixture was then stirred at room temperature overnight. Completion of the reaction was indicated by LCMS. The solvent was removed by rotary evaporation. The crude mixture was carried forward without further purification. The residue was suspended in 5 mL ethyl acetate and chilled in an ice bath. A solution of 4 N HCl in dioxane (3 mL, 5 equiv) was added with stirring. The reaction mixture was then stirred at room temperature overnight. The solid materials were collected by filtration, washed with ethylacetate then purified further by preparative reverse-phase HPLC (ammonium acetate/ACN). A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μ M, 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification.

[00442] The following title compounds were prepared according to **General Library Acylation Procedure 2a**

Example 409: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide. ¹H-NMR (400MHz, d₆-DMSO): 10.26 (s, 1H), 8.81 (s, 1H), 8.25 (t, 1H), 8.14 (s, 1H), 7.74 (d, 1H), 7.69 (d, 1H), 7.41-7.39 (m, 1H), 7.36 (d, 1H), 7.32 (d, 2H), 7.30-7.28 (dd, 1H), 7.14-7.11 (m, 2H), 6.14 (t, 1H), 4.09 (d, 4H), 3.78 (s, 6H); MS (EI) C₂₆H₂₆N₆O₅S: 535.6 (MH⁺).

Procedure 3: *N*-(3-chloroquinoxalin-2-yl)benzenesulfonamide

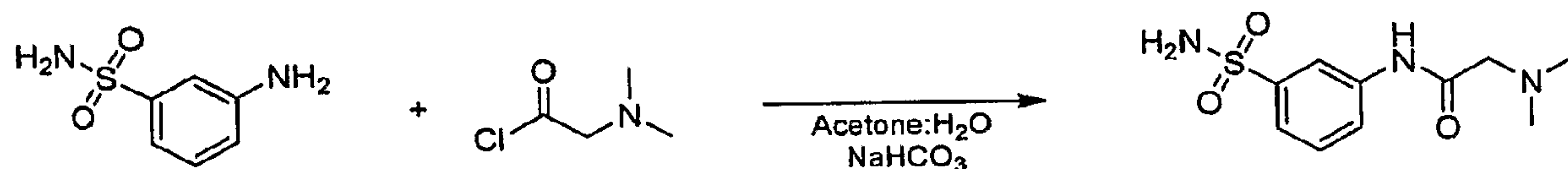
- 5 [00443] A flask was charged with 2,3-dichloroquinoxaline (3.5 g, 18 mmol), 85 mL of dimethylsulfoxide, benzene sulfonamide (2.8 g, 18 mmol), and cesium carbonate (5.8 g, 18 mmol). The reaction mixture was stirred under an N₂ atmosphere for 15 h at 150°C, after which time, it was transferred to a separatory funnel and 100 mL of water were added. Concentrated HCl was then added in order to acidify the reaction mixture to pH<2. The aqueous layer was subsequently washed three times with 90 mL ethyl acetate. The ethyl acetate layers were then washed two times with 150 mL water, three times with 100 mL brine and then dried over sodium sulfate. The ethyl acetate was removed on a rotary-evaporator. A slurry was formed by adding ethyl acetate and dichloromethane to the dried crude product, filtration yielded *N*-(3-chloroquinoxalin-2-yl)benzenesulfonamide which was submitted to
- 10
- 15 the next step without further purification. MS (EI) C₁₄H₁₀ClN₃O₂S: 319.9 (MH⁺)⁺.

Example 410***N*-(3-(4-fluorophenylamino)quinoxalin-2-yl)benzenesulfonamide**

- 20 [00444] A CEM microwave reaction vessel was charged with *N*-(3-chloroquinoxalin-2-yl)benzenesulfonamide (52 mg, 0.16 mmol), 4-fluoroaniline (36 mg, 0.32 mmol), and 0.8 mL of dimethylacetamide. The vessel was sealed and the reaction mixture was heated under microwave radiation for 25 m at 120 °C in a CEM Discover microwave instrument. Methanol (1 mL) was added to the reaction mixture and after 20 minutes the product
- 25 precipitated out of the solution. Filtration yielded 39 mg (62 %) of *N*-(3-(4-

fluorophenylamino)quinoxalin-2-yl)benzenesulfonamide. ¹H-NMR (400MHz, d₆-DMSO): δ 12.30 (s, 1H), 9.11 (s, 1H), 8.16-8.10 (d, 2H), 8.02-7.90 (m, 3H), 7.68-7.58 (m, 3H), 7.55-7.51 (m, 1H), 7.41-7.32 (m, 2H), 7.25-7.16 (m, 2H); MS (EI) C₂₀H₁₅FN₄O₂S: 395.0 (MH⁺).

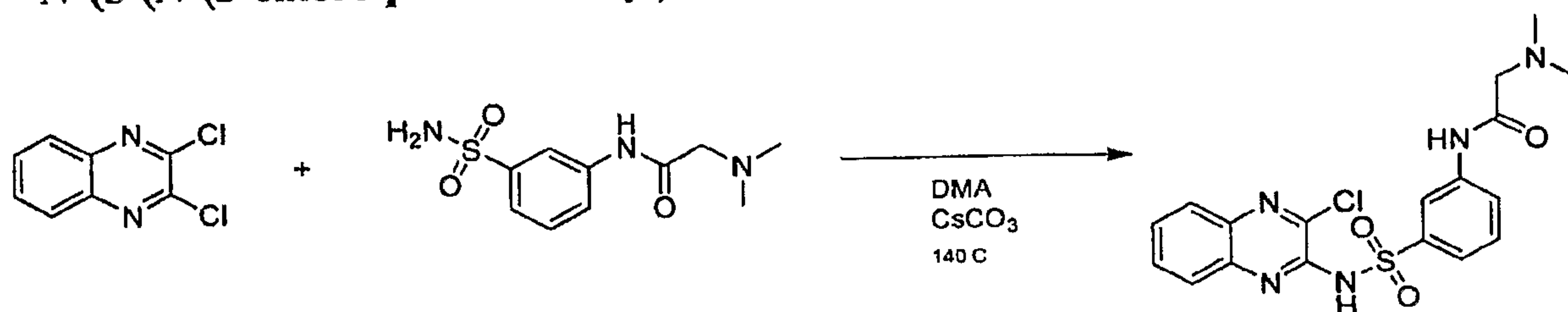
5 Procedure 4: 2-(dimethylamino)-N-(3-sulfamoylphenyl)acetamide



[00445] A flask was charged with 3-aminobenzene sulfonamide (3.3 g, 19 mmol), and 20 mL of 1:1 acetone:H₂O. The solution was stirred at room temperature until the aminobenzene sulfonamide had dissolved. The flask was then cooled in an ice bath and dimethylamino-acetyl chloride HCl (4.6 g, 29 mmol) was added. To the resulting slurry sodium bicarbonate (4.8 g, 57 mmol) was added over a 15 m period. After 30 min the reaction was removed from the ice bath and allowed to stir at room temperature for 15 h. The reaction mixture was then filtered and washed with methanol and acetonitrile. The filtrate was dried on a rotary evaporator to yield 2-(dimethylamino)-N-(3-sulfamoylphenyl)acetamide, which was submitted to the next step without further purification. MS (EI) C₁₀H₁₅N₃O₃S: 258.0 (MH⁺).

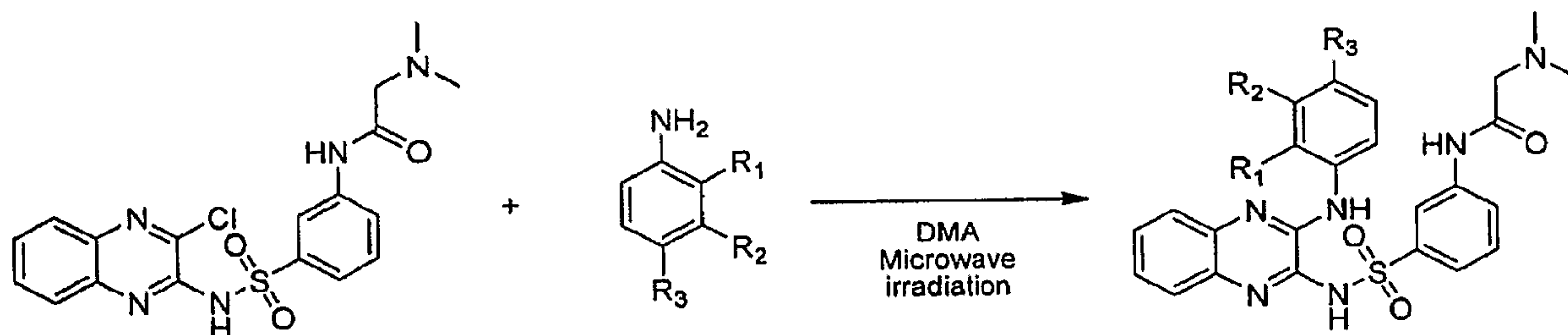
Example 411

N-(3-(*N*-(3-chloroquinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide



[00446] A flask was charged with dichloroquinoxaline (1.0 g, 5.8 mmol), 10 mL of dimethylacetamide, 2-(dimethylamino)-*N*-(3-sulfamoylphenyl)acetamide (0.70 g, 2.7 mmol), and cesium carbonate (1.8 g, 5.5 mmol). The reaction mixture was stirred for 3 h at 140 °C and then filtered. The solvent was evaporated from the filtrate on a rotary- evaporator to yield *N*-(3-(*N*-(3-chloroquinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide which was submitted to the next step without further purification. MS (EI) C₁₈H₁₈ClN₅O₃S: 420.0 (MH⁺).

Two similar procedures were then used to conduct the general reaction shown.



[00447] A CEM microwave reaction vessel was charged with *N*-(3-(*N*-(3-chloroquinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide (30 mg, 0.071 mmol), the desired
 5 aniline (16 mg, 0.14 mmol, 2 eq), and 0.5 mL of Dimethylacetamide. The vessel was sealed and the reaction mixture was heated under microwave radiation for 70 min at 140 °C in a CEM Discover microwave instrument. The solvent was then removed by rotary-evaporation. Purification of the final product was accomplished by preparatory reverse-phase HPLC with the eluents 25 mM aqueous NH₄OAc/ACN to yield 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-
 10 fluorophenylamino)quinoxalin-2-yl) sulfamoyl)phenyl)acetamide.

[00448] The following compounds were prepared according to the above Examples.

Example 412: 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-fluorophenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-

fluorophenylamino)quinoxalin-2-yl) sulfamoyl)phenyl)acetamide. ¹H-NMR (400MHz,

15 CDCl₃): 9.40 ppm (s, 1H), 8.43 ppm (s, 1H), 8.22 ppm (s, 1H), 8.07-8.02 ppm (d, 1H), 7.97-7.93 ppm (d, 1H), 7.76-7.71 (m, 2H), 7.53-7.48 ppm (t, 1H), 7.45-7.36 ppm (m, 4H), 7.35-7.28 ppm (m, 2H), 6.84-6.77 ppm (t, 1H), 3.10 ppm (s, 2H), 2.38 ppm (s, 6H); MS (EI)

C₂₄H₂₃FN₆O₃S: 495 (MH⁺).

Example 413: 2-(dimethylamino)-*N*-(3-(*N*-(3-(4-fluorophenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₄H₂₃FN₆O₃S: 495 (MH⁺).

Example 414: 2-(dimethylamino)-*N*-(3-(*N*-(3-(4-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₅H₂₆N₆O₄S: 507 (MH⁺).

Example 415: *N*-(3-(*N*-(3-(4-chlorophenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. MS (EI) C₂₄H₂₃ClN₆O₃S: 511 (MH⁺).

Example 416

***N*-(3-(*N*-(3-(3-chlorophenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide.** MS (EI) C₂₄H₂₃ClN₆O₃S: 511 (MH⁺)

[00449] A CEM microwave reaction vessel was charged with *N*-(3-(*N*-(3-chloroquinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide (62 mg, 0.147 mmol), the desired aniline (0.567 mmol, 4 eq), and 1.0 mL of toluene. The vessel was sealed and the reaction mixture was heated under microwave radiation for 60 min at 180 °C in a CEM Discover microwave instrument. The solvent was removed on a rotary-evaporator. Purification of the final product was done by preparatory HPLC with NH₄OAc/ACN as eluent to yield 2-(dimethylamino)-*N*-(3-(*N*-(3-(4-fluoro-3-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl).

[00450] The following compounds were prepared according to the above Examples.

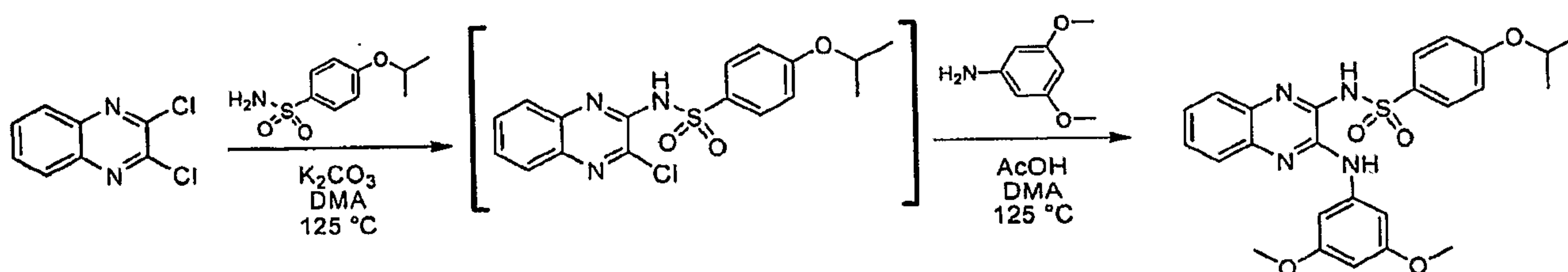
Example 417: 2-(dimethylamino)-*N*-(3-(*N*-(3-(4-fluoro-3-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. 2-(dimethylamino)-*N*-(3-(*N*-(3-(4-fluoro-3-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl). ¹H-NMR (400MHz, CDCl₃): δ 9.47 (s, 1H), 8.36 (s, 1H), 8.29 (s, 1H), 7.91-7.87 (d, 1H), 7.80-7.73 (m, 2H), 7.66-7.63 (d, 1H), 7.53-7.47 (t, 1H), 7.43-7.30 (m, 4H), 7.10-7.04 (t, 1H), 6.55-5.95 (br s, 1H), 3.96 (s, 3H), 3.12 (s, 2H), 2.39 (s, 6H), 2.08 (s, 3H) (AcOH); MS (EI) C₂₅H₂₅FN₆O₄S: 525 (MH⁺).

Example 418: 2-(dimethylamino)-*N*-(3-(*N*-(3-(4-fluoro-3-methylphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₅H₂₅FN₆O₃S: 509 (MH⁺).

Example 419: 2-(dimethylamino)-*N*-(3-(*N*-(3-(3,5-dimethylphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₆H₂₈N₆O₃S: 505 (MH⁺).

Example 420: *N*-(3-(*N*-(3-(2,4-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. MS (EI) C₂₆H₂₈N₆O₅S: 537 (MH⁺).

Example 421: *N*-(3-(*N*-(3-(2,3-dihydro-1H-inden-5-ylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-2-(dimethylamino)acetamide. MS (EI) C₂₇H₂₈N₆O₃S: 517 (MH⁺).

Example 422**Procedure 5*****N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-isopropoxybenzenesulfonamide**

5

[00451] *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-

isopropoxybenzenesulfonamide: A solution of 2,3-dichloroquinoxaline (2.0 mL, 0.38 M) was combined with K₂CO₃ (105 mg, 0.76 mmol) in a glass vial. A solution of 4-isopropoxybenzene sulfonamide (1.75 mL, 0.43 M) was added and the solution was stirred

10 overnight at 125 °C. After cooling, acetic acid (45 mL, 0.79 mmol) and 3,5-dimethoxyaniline (230 mg, 1.5 mmol) were added. The reaction mixture was stirred again at 125 °C overnight. Upon cooling, the reaction mixture was diluted with 8 mL of methanol and then 8 mL of water. The precipitate was collected by filtration and recrystallized from *N,N*-dimethylacetamide/water to give 45 mg of product. ¹H-NMR (400MHz, d₆-DMSO): 12.16 (bs, 1H), 8.93 (s, 1H), 8.03 (d, 2H), 7.92 (bs, 1H), 7.56 (d, 1H), 7.36 (m, 4H), 7.07 (d, 2H), 6.24 (s, 1H), 4.72 (m, 1H), 3.76 (s, 6H), 1.27 (d, 6H); MS (EI) C₂₅H₂₆N₄O₅S: 495 (MH⁺).

15

[00452] The remaining examples were synthesized in similar fashion. In the cases where the product did not precipitate, the mixture was purified by reverse phase HPLC.

20 **Example 423:** 3-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-methylbenzenesulfonamide. ¹H-NMR (400MHz, d₆-DMSO): 12.31 (bs, 1H), 8.96 (s, 1H), 8.18 (s, 1H), 7.98 (d, 1H), 7.92 (bs, 1H), 7.58 (d, 2H), 7.43-7.33 (m, 4H), 6.24 (t, 1H), 3.76 (s, 6H), 2.39 (s, 3H); MS (EI) C₂₃H₂₁ClN₄O₄S: 485 (MH⁺).

Example 424: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)naphthalene-1-sulfonamide. MS (EI) C₂₆H₂₂N₄O₄S: 487 (MH⁺).

25

Example 425: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-fluorobenzenesulfonamide. MS (EI) C₂₂H₁₉FN₄O₄S: 455 (MH⁺).

Example 426: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-fluorobenzenesulfonamide. MS (EI) C₂₂H₁₉FN₄O₄S: 455 (MH⁺).

Example 427: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-(trifluoromethyl)benzenesulfonamide. MS (EI) C₂₃H₁₉F₃N₄O₄S: 505 (MH⁺).

Example 428: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-(trifluoromethyl)benzenesulfonamide. MS (EI) C₂₃H₁₉F₃N₄O₄S: 505 (MH⁺).

5 **Example 429:** 2-cyano-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) C₂₃H₁₉N₅O₄S: 462 (MH⁺).

Example 430: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-(trifluoromethoxy)benzenesulfonamide. MS (EI) C₂₃H₁₉F₃N₄O₅S: 521 (MH⁺).

10 **Example 431:** *N*-(4-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide. MS (EI) C₂₄H₂₃N₅O₅S: 494 (MH⁺).

Example 432: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-fluoro-2-methylbenzenesulfonamide. MS (EI) C₂₃H₂₁FN₄O₄S: 469 (MH⁺).

Example 433: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2-methylbenzenesulfonamide. MS (EI) C₂₃H₂₂N₄O₄S: 451 (MH⁺).

15 **Example 434:** 2-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) C₂₂H₁₉ClN₄O₄S: 471 (MH⁺).

Example 435: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3,5-difluorobenzenesulfonamide. MS (EI) C₂₂H₁₈F₂N₄O₄S: 473 (MH⁺).

20 **Example 436:** 3,5-dichloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) C₂₂H₁₈Cl₂N₄O₄S: 505 (MH⁺).

Example 437: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-fluoro-4-methylbenzenesulfonamide. MS (EI) C₂₃H₂₁FN₄O₄S: 469 (MH⁺).

Example 438: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2-(trifluoromethyl)benzenesulfonamide. MS (EI) C₂₃H₁₉F₃N₄O₄S: 505 (MH⁺).

25 **Example 439:** 4-cyano-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) C₂₃H₁₉N₅O₄S: 462 (MH⁺).

Example 440: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-1-phenylmethanesulfonamide. MS (EI) C₂₃H₂₂N₄O₄S: 451 (MH⁺).

30 **Example 441:** 4,5-dichloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)thiophene-2-sulfonamide. MS (EI) C₂₀H₁₆Cl₂N₄O₄S₂: 511 (MH⁺).

Example 442: 1-(3-chlorophenyl)-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)methanesulfonamide. MS (EI) C₂₃H₂₁ClN₄O₄S: 485 (MH⁺).

Example 443: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2,5-dimethylthiophene-3-sulfonamide. MS (EI) C₂₂H₂₂N₄O₄S₂: 471 (MH⁺).

Example 444: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide. MS (EI) C₂₄H₁₈F₆N₄O₄S: 573 (MH⁺).

Example 445: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-fluoro-3-(trifluoromethyl)benzenesulfonamide. MS (EI) C₂₃H₁₈F₄N₄O₄S: 523 (MH⁺).

5 **Example 446:** 5-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-1,3-dimethyl-1H-pyrazole-4-sulfonamide. MS (EI) C₂₁H₂₁ClN₆O₄S: 489 (MH⁺).

Example 447: 5-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2-methoxybenzenesulfonamide. MS (EI) C₂₃H₂₁ClN₄O₅S: 501 (MH⁺).

10 **Example 448:** 5-bromo-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2-methoxybenzenesulfonamide. MS (EI) C₂₃H₂₁BrN₄O₅S: 545 (MH⁺).

Example 449: 2,5-dichloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)thiophene-3-sulfonamide. MS (EI) C₂₀H₁₆Cl₂N₄O₄S₂: 511 (MH⁺).

Example 450: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3,5-dimethylisoxazole-4-sulfonamide. MS (EI) C₂₁H₂₁N₅O₅S: 456 (MH⁺).

15 **Example 451:** *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-2,5-dimethoxybenzenesulfonamide. MS (EI) C₂₄H₂₄N₄O₆S: 497 (MH⁺).

Example 452: 3-chloro-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-4-fluorobenzenesulfonamide. MS (EI) C₂₂H₁₈ClFN₄O₄S: 489 (MH⁺).

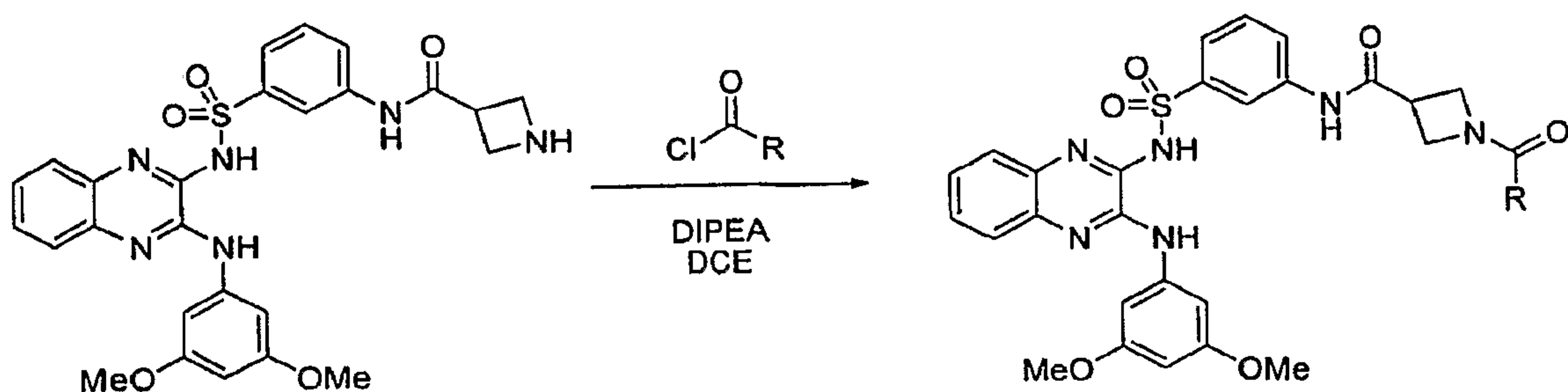
20 **Example 453:** *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)biphenyl-4-sulfonamide. MS (EI) C₂₈H₂₄N₄O₄S: 513 (MH⁺).

Example 454: 4-(difluoromethoxy)-*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide MS (EI) C₂₃H₂₀F₂N₄O₅S: 503 (MH⁺).

Example 455: *N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)-3-(methylsulfonyl)benzenesulfonamide. MS (EI) C₂₃H₂₂N₄O₆S₂: 515 (MH⁺).

25

General Procedure 6



[00453] *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide (125 mg, 0.23 mmol) was dissolved into 5 mL

DCE in a 10 mL round-bottom flask. DIPEA (1.17 mmol, 5.0 eq.) was then added with stirring followed by acid chloride (0.47 mmol, 2.0 eq.). The reaction was then stirred at room temperature for 1 hour or until complete as indicated by LCMS. The solvent was subsequently removed under reduced pressure on a rotary evaporator. The crude material was then redissolved in methanol. Purification of the final product was accomplished by preparatory reverse-phase HPLC with the eluents 25 mM aqueous NH_4OAc /CAN. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μM , 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification.

[00454] The following title compounds were prepared according to **General Procedure 6**.

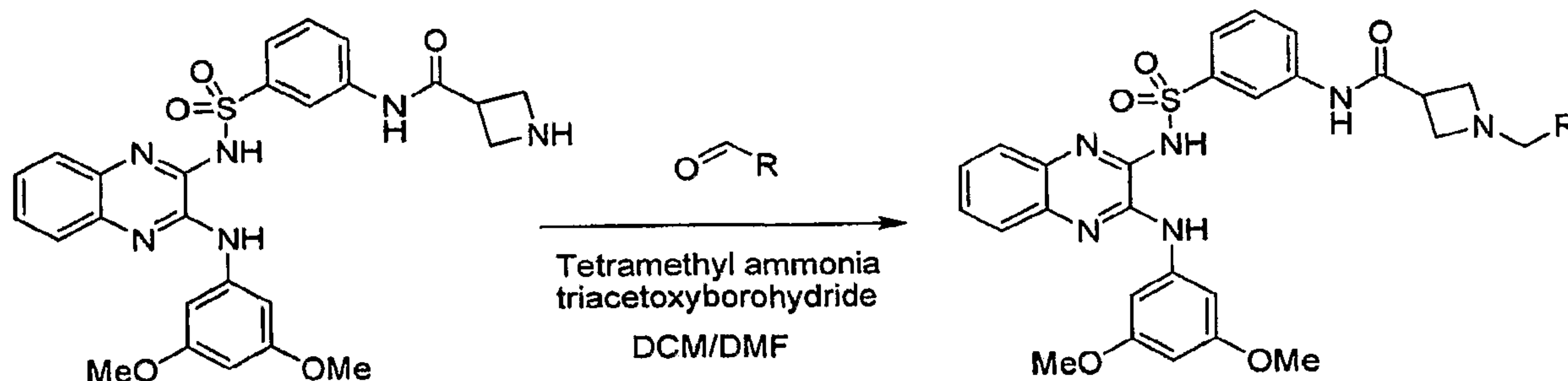
Example 456: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-propionylazetidine-3-carboxamide.

$^1\text{H-NMR}$ (400MHz, d_6 -DMSO): 12.40 (s, 1H), 10.45 (s, 1H), 8.88 (s, 1H), 8.40 (s, 1H), 7.93 (s, 1H), 7.82 (d, 1H), 7.77 (d, 1H), 7.60-7.45 (m, 2H), 7.41-7.30 (m, 4H), 6.24 (s, 1H), 4.26 (t, 1H), 4.22-4.17 (m, 1H), 3.99 (t, 1H), 3.95-3.89 (m, 1H), 3.76 (s, 6H), 3.59-3.45 (m, 1H), 2.05 (dd, 2H), 0.95 (t, 3H); MS (EI) $\text{C}_{29}\text{H}_{30}\text{N}_6\text{O}_6\text{S}$: 591 (MH^+).

Example 457: 1-acetyl-*N*-(3-((3-((3,5-bis(methoxy)phenyl)amino)quinoxalin-2-yl)amino)sulfonyl)phenyl)azetidine-3-carboxamide. MS (EI) $\text{C}_{28}\text{H}_{28}\text{N}_6\text{O}_6\text{S}$: 577 (MH^+).

Example 458: 1-(cyclopropanecarbonyl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide. MS (EI) $\text{C}_{30}\text{H}_{30}\text{N}_6\text{O}_6\text{S}$: 603 (MH^+).

General Procedure 7



[00455] To a solution of *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide (110 mg, 0.19 mmol) in 3 mL of DCE and 200 μL of DMF, aldehyde (0.77 mmol, 4.0 eq.) was added slowly followed by tetramethylammonium triacetoxyborohydride (1.16 mmol, 6.0 eq). The reaction was stirred

at room temperature overnight. LC/MS indicated the reaction was completed. The solvent was subsequently removed under reduced pressure on a rotary evaporator. The crude material was then redissolved in methanol. Purification of the final product was accomplished by preparatory reverse-phase HPLC with the eluents 25 mM aqueous

5 $\text{NH}_4\text{OAc}/\text{CAN}$. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μM , 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification.

[00456] The following title compounds were prepared according to **General Procedure 7**.

10 **Example 459:** *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-ethylazetidine-3-carboxamide. $^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$):

10.29 (s, 1H), 8.82 (s, 1H), 8.25 (t, 1H), 7.75-7.68 (m, 2H), 7.43-7.38 (m, 1H), 7.375-7.340 (m, 1H), 7.338-7.310 (d, 2H), 7.305-7.262 (m, 1H), 7.15-7.08 (m, 2H), 6.56 (s, 1H), 6.15 (t, 1H), 4.15-4.08 (m, 2H), 4.06-3.95 (m, 2H), 3.78 (s, 6H), 3.65-3.56 (m, 1H), 3.12-3.04 (m, 15 2H), 1.03 (t, 3H); MS (EI) $\text{C}_{28}\text{H}_{30}\text{N}_6\text{O}_5\text{S}$: 563 (MH^+).

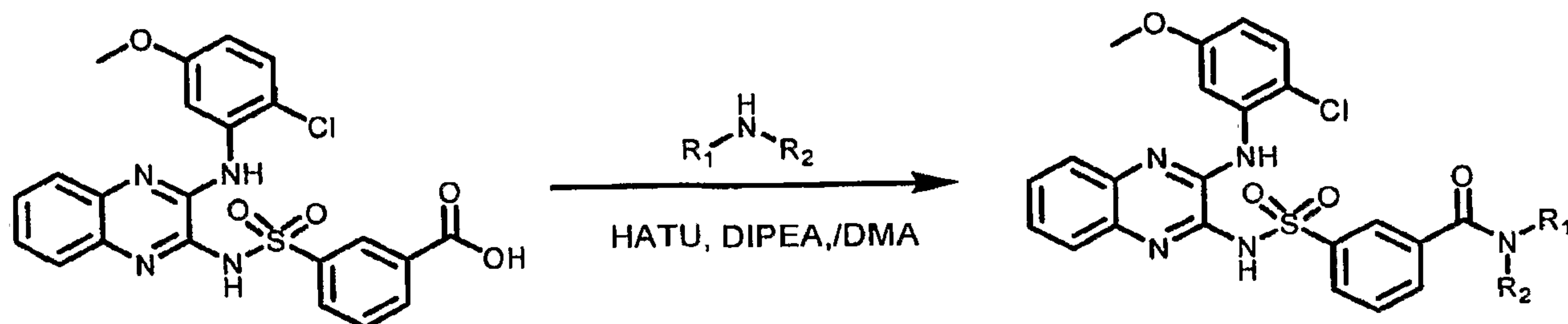
Example 460: 1-(cyclopropylmethyl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide. MS (EI) $\text{C}_{30}\text{H}_{32}\text{N}_6\text{O}_5\text{S}$: 589 (MH^+).

Example 461: 1-benzyl-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide. MS (EI) $\text{C}_{33}\text{H}_{32}\text{N}_6\text{O}_5\text{S}$: 625 (MH^+).

Example 462: *N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)-1-(furan-2-ylmethyl)azetidine-3-carboxamide. MS (EI) $\text{C}_{31}\text{H}_{30}\text{N}_6\text{O}_6\text{S}$: 615 (MH^+).

Example 463: 1-((1H-imidazol-5-yl)methyl)-*N*-(3-(*N*-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)azetidine-3-carboxamide. MS (EI) $\text{C}_{30}\text{H}_{30}\text{N}_8\text{O}_5\text{S}$: 615 (MH^+).

General Library Procedure 8



[00457] Into a small 1 dram vial was added 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzoic acid (61 mg, .13 mmol, 1.1 equiv). The acid was dissolved in 1 mL of DMA and DIPEA (42 μ L, .24 mMol, 2 equiv) was added then added to the solution. The amine reagent (1 mL of .12 M solution in DMA) was added
 5 to solution with stirring followed by HATU (64 mg, .17 mMol, 1.4 equiv). Reaction was stirred overnight at room temperature. Upon completion as indicated by LCMS analysis, 2 mL of methanol was added to the solution. Preparative reverse-phase HPLC was used to isolate the desired product directly from this crude reaction solution. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μ M, 30
 10 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification.

[00458] The following compounds were prepared according to **General Library Procedure 8**.

- Example 464 :** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(dimethylamino)propyl)benzamide. 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(dimethylamino)propyl)benzamide:
 15 ¹H NMR (400 MHz, d₆-DMSO): 9.44 (s, 1H), 8.94 (s, 1H), 8.79 (t, 1H), 8.54 (s, 1H), 8.24 (d, 1H), 7.87 (d, 1H), 7.48 (m, 3H), 7.33 (d, 1H), 7.18 (m, 2H), 6.60 (dd, 1H), 3.82 (1H), 3.04 (m, 3H), 2.51 (m, 5H), 1.91 (s, 1H), 1.86 (m, 3H); MS (EI) for C₂₇H₂₉ClN₆O₄S: 569 (MH⁺).
- Example 465:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(1-methylazetidin-3-yl)benzamide. 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(1-methylazetidin-3-yl)benzamide: ¹H NMR (400 MHz, d₆-DMSO): 9.43 (s, 1H), 9.23 (d, 1H), 8.94 (d, 1H), 8.58 (s, 1H), 8.29 (d, 1H), 7.89 (d, 1H), 7.56 (t, 1H), 7.47 (d, 1H), 7.44 (d, 1H), 7.33 (d, 1H), 7.18 (m, 2H), 6.60 (dd, 1H), 4.81 (m, 1H), 4.33 (m, 2H),
 20 4.19 (m, 2H), 3.82 (s, 1H), 2.51 (s, 3H); MS (EI) for C₂₆H₂₅ClN₆O₄S: 553 (MH⁺).
- Example 466:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(pyridin-4-ylmethyl)benzamide. MS (EI) C₂₈H₂₃ClN₆O₄S: 575 (MH⁺).
- Example 467:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(dimethylamino)propyl)benzamide. MS (EI) C₂₈H₂₆ClN₇O₄S: 592 (MH⁺).
- Example 468:** *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(2,2-dimethylhydrazinecarbonyl)benzenesulfonamide. MS (EI) C₂₄H₂₃ClN₆O₄S: 527 (MH⁺).
- Example 469:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-methoxyethyl)benzamide. MS (EI) C₂₅H₂₄ClN₅O₅S: 542 (MH⁺).

- Example 470:** *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(4-methylpiperazine-1-carbonyl)benzenesulfonamide. MS (EI) $C_{27}H_{27}ClN_6O_4S$: 567 (MH^+).
- Example 471:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(pyrrolidin-1-yl)ethyl)benzamide. MS (EI) $C_{28}H_{29}ClN_6O_4S$: 581 (MH^+).
- 5 **Example 472:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(pyridin-4-yl)ethyl)benzamide. MS (EI) $C_{29}H_{25}ClN_6O_4S$: 589 (MH^+).
- Example 473:** *N*-(2-(1H-imidazol-4-yl)ethyl)-3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzamide. MS (EI) $C_{27}H_{24}ClN_7O_4S$: 578 (MH^+).
- 10 **Example 474:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(piperidin-1-yl)benzamide. MS (EI) $C_{27}H_{27}ClN_6O_4S$: 567 (MH^+).
- Example 475:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-hydroxyethyl)benzamide. MS (EI) $C_{24}H_{22}ClN_5O_5S$: 528 (MH^+).
- Example 476:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-ethoxypropyl)benzamide. MS (EI) $C_{27}H_{28}ClN_5O_5S$: 570 (MH^+).
- 15 **Example 477:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(pyrrolidin-1-yl)propyl)benzamide. MS (EI) $C_{29}H_{31}ClN_6O_4S$: 595 (MH^+).
- Example 478111:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(diethylamino)propyl)benzamide. MS (EI) $C_{29}H_{33}ClN_6O_4S$: 597 (MH^+).
- 20 **Example 479:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(2-oxopyrrolidin-1-yl)propyl)benzamide. MS (EI) $C_{29}H_{29}ClN_6O_5S$: 609 (MH^+).
- Example 480:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(pyridin-2-ylmethyl)benzamide. MS (EI) $C_{28}H_{23}ClN_6O_4S$: 575 (MH^+).
- Example 481:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-cyanoethyl)-*N*-methylbenzamide. MS (EI) $C_{26}H_{23}ClN_6O_4S$: 551 (MH^+).
- 25 **Example 482:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-cyanoethyl)-*N*-ethylbenzamide. MS (EI) $C_{27}H_{25}ClN_6O_4S$: 565 (MH^+).
- Example 483:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(ethylthio)ethyl)benzamide. MS (EI) $C_{26}H_{26}ClN_5O_4S_2$: 572 (MH^+).
- 30 **Example 484:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-propoxypropyl)benzamide. MS (EI) $C_{28}H_{30}ClN_5O_5S$: 584 (MH^+).
- Example 485:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(5-(diethylamino)pentan-2-yl)benzamide. MS (EI) $C_{31}H_{37}ClN_6O_4S$: 625 (MH^+).

Example 486: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-methoxypropyl)benzamide. MS (EI) C₂₆H₂₆ClN₅O₅S: 556 (MH⁺).

Example 487: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-morpholinopropyl)benzamide MS (EI) C₂₉H₃₁ClN₆O₅S: 611 (MH⁺).

5 **Example 488:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(pyridin-3-ylmethyl)benzamide MS (EI) C₂₈H₂₃ClN₆O₄S: 575 (MH⁺).

Example 489: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-cyanoethyl)benzamide. MS (EI) C₂₅H₂₁ClN₆O₄S: 537 (MH⁺).

10 **Example 490:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(1-methoxypropan-2-yl)benzamide. MS (EI) C₂₆H₂₆ClN₅O₅S: 556 (MH⁺).

Example 491: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(methylthio)ethyl)benzamide. MS (EI) C₂₅H₂₄ClN₅O₄S₂: 558 (MH⁺).

Example 492: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-(dimethylamino)propyl)-*N*-methylbenzamide. MS (EI) C₂₈H₃₁ClN₆O₄S: 583 (MH⁺).

15 **Example 493:** 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-isopropoxypropyl)benzamide. MS (EI) C₂₈H₃₀ClN₅O₅S: 584 (MH⁺).

Example 494: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(dimethylamino)ethyl)-*N*-ethylbenzamide. MS (EI) C₂₈H₃₁ClN₆O₄S: 583 (MH⁺).

20 **Example 495:** *N*-(3-butoxypropyl)-3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzamide. MS (EI) C₂₉H₃₂ClN₅O₅S: 598 (MH⁺).

Example 496: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(diethylamino)ethyl)benzamide. MS (EI) C₂₈H₃₁ClN₆O₄S: 583 (MH⁺).

25 **Example 497XEL-04286749:** methyl 3-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzamido)propanoate. MS (EI) C₂₆H₂₄ClN₅O₆S: 570 (MH⁺).

Example 498: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-methyl-*N*-propylbenzamide. MS (EI) C₂₆H₂₆ClN₅O₄S: 540 (MH⁺).

30 **Example 499:** ethyl 3-(3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzamido)propanoate. MS (EI) C₂₇H₂₆ClN₅O₆S: 584 (MH⁺).

Example 500: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-(piperidin-1-yl)ethyl)benzamide. MS (EI) C₂₉H₃₁ClN₆O₄S: 595 (MH⁺).

Example 501: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-((1-ethylpyrrolidin-2-yl)methyl)benzamide. MS (EI) C₂₉H₃₁ClN₆O₄S: 595 (MH⁺).

Example 502: *N*-(2-(bis(2-hydroxyethyl)amino)ethyl)-3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzamide. MS (EI) C₂₈H₃₁ClN₆O₆S: 615 (MH⁺).

Example 503: *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(3-(diethylamino)pyrrolidine-1-carbonyl)benzenesulfonamide. MS (EI) C₃₀H₃₃ClN₆O₄S: 609 (MH⁺).

Example 504: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-methyl-*N*-(1-methylpyrrolidin-3-yl)benzamide. MS (EI) C₂₈H₂₉ClN₆O₄S: 581 (MH⁺).

Example 505: *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(3-(dimethylamino)pyrrolidine-1-carbonyl)benzenesulfonamide. MS (EI) C₂₈H₂₉ClN₆O₄S: 581 (MH⁺).

Example 506: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(2-methyl-1-morpholinopropan-2-yl)benzamide. MS (EI) C₃₀H₃₃ClN₆O₅S: 625 (MH⁺).

Example 507: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(1H-pyrrol-1-yl)benzamide. MS (EI) C₂₆H₂₁ClN₆O₄S: 549 (MH⁺).

Example 508: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(3-oxopyrazolidin-4-yl)benzamide. MS (EI) C₂₅H₂₂ClN₇O₅S: 568 (MH⁺).

Example 509: *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(2-((dimethylamino)methyl)piperidine-1-carbonyl)benzenesulfonamide. MS (EI) C₃₀H₃₃ClN₆O₄S: 609 (MH⁺).

Example 510: *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(2-(piperidin-1-ylmethyl)piperidine-1-carbonyl)benzenesulfonamide. MS (EI) C₃₃H₃₇ClN₆O₄S: 649 (MH⁺).

Example 511: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(1-ethylpiperidin-3-yl)benzamide MS (EI) C₂₉H₃₁ClN₆O₄S: 595 (MH⁺).

General Procedure 8A

[00459] The General Library Procedure outlined in Procedure 8 was used to incorporate a number of amines that contained a second amine group protected as the *tert*-butylcarbamate. A subsequent deprotection after HPLC purification was performed to unmask this second amine group. Into a small 1 dram vial was added 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzoic acid (61 mg, .13 mmol, 1.1 equiv). The acid was dissolved in 1 mL of DMA and DIPEA (42 uL, .24 mmol, 2 equiv) was added then added to the solution. The mono-Boc-protected diamine reagent (1 mL of .12 M

solution in DMA, 1 equiv) was added to solution with stirring followed by HATU (64 mg, .17 mmol, 1.4 equiv). Reaction was stirred overnight at room temperature. Upon completion as indicated by LCMS analysis, 2 mL of methanol was added to the solution. Preparative reverse-phase HPLC was used to isolate the desired product directly from this crude reaction solution. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μ M, 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification. The product fractions were combined and concentrated to dryness under reduced pressure by rotary evaporation. A solution of 4 N HCl in dioxane (2 mL) was added. The solution was then stirred at room temperature until no starting material was detected. The deprotected product precipitated out of solution as an HCL salt and was collected by filtration, washed with ether and dried under vacuum.

[00460] The following compounds were prepared according to **General Procedure 8A**

Example 512: 3-(N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-

(piperidin-3-yl)benzamide. 3-(N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-(piperidin-3-yl)benzamide: ^1H NMR (400 MHz, d_6 -DMSO): 12.82 (s, 1H), 9.12 (s, 1H), 9.04 (s, 1H), 8.85 (d, 1H), 8.65 (s, 1H), 8.55 (s, 1H), 8.18 (m, 1H), 7.98 (s, 1H), 7.69 (m, 2H), 7.43 (m, 2H), 6.69 (dd, 1H), 4.21 (s, 1H), 3.83 (s, 3H), 3.69 (m, 1H), 3.48 (m, 1H), 3.18 (s, 1H), 2.84 (q, 2H), 1.91 (s, 2H); MS (EI) for $\text{C}_{27}\text{H}_{27}\text{ClN}_6\text{O}_4\text{S}$: 567 (MH^+).

Example 513: 3-(N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-
(piperidin-2-ylmethyl)benzamide. 3-(N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-(piperidin-2-ylmethyl)benzamide: NMR (400 MHz, d_6 -DMSO): 12.78 (s, 1H), 9.16 (s, 1H), 9.09 (s, 1H), 8.79 (s, 1H), 8.59 (d, 2H), 8.22 (t, 2H), 7.99 (s, 1H), 7.74 (t, 1H), 7.66 (s, 1H), 7.42 (m, 2H), 6.69 (dd, 1H), 3.82 (s, 3H), 3.69 (dd, 1H), 3.57 (m, 1H), 3.50 (m, 3H), 3.22 (s, 2H), 2.82 (d, 1H), 1.68 (m, 5H); MS (EI) for $\text{C}_{28}\text{H}_{29}\text{ClN}_6\text{O}_4\text{S}$: 581 (MH^+).

Example 514: 3-(3-aminopyrrolidine-1-carbonyl)-N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) $\text{C}_{26}\text{H}_{25}\text{ClN}_6\text{O}_4\text{S}$: 553 (MH^+).

Example 515: 3-(3-aminoazetidine-1-carbonyl)-N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) $\text{C}_{25}\text{H}_{23}\text{ClN}_6\text{O}_4\text{S}$: 539 (MH^+).

Example 516: 3-(3-aminopiperidine-1-carbonyl)-*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) C₂₇H₂₇ClN₆O₄S: 567 (MH⁺).

Example 517: 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(pyrrolidin-3-yl)benzamide. MS (EI) C₂₆H₂₅ClN₆O₄S: 553 (MH⁺).

Example 518: *N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)-3-(3-(methylamino)pyrrolidine-1-carbonyl)benzenesulfonamide. MS (EI) C₂₇H₂₇ClN₆O₄S: 567 (MH⁺).

Example 519: *N*-(2-aminoethyl)-3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)benzamide. MS (EI) C₂₄H₂₃ClN₆O₄S: 527 (MH⁺).

Example 520: 3-(4-amino-3-oxopyrazolidine-1-carbonyl)-*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)benzenesulfonamide. MS (EI) C₂₅H₂₂ClN₇O₅S: 568 (MH⁺).

15

Example 521

3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-((1-methylpiperidin-2-yl)methyl)benzamide

[00461] A measured amount of 3-(*N*-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-*N*-(piperidin-2-ylmethyl)benzamide (299 mg, .51 mmol, 1 eq) was dissolved in 2.3 mL of DMA. Formic acid (388 ul, 10.28 mmol, 20 eq) was added to solution with stirring followed by the addition of formaldehyde (508 ul of 37% aq. solution). The reaction was then stirred at room temperature overnight. Analysis of an aliquot of the reaction mixture by LCMS indicated the complete consumption of starting material. The reaction was diluted with methanol (2 mL). Preparative reverse-phase HPLC was used to isolate the desired product directly from the crude reaction mixture. A Waters Fractionlynx preparative reverse-phase HPLC; equipped with a Waters SunFire Prep C18, OCD 5 μM, 30 X 70 mm column and running a 5-100 % gradient with a binary solvent system of 25 mM ammonium acetate in water/acetonitrile; was used to carry out the purification. ¹H NMR (400 MHz, d₆-DMSO): 9.44 (s, 1H), 8.94 (s, 1H), 8.79 (t, 1H), 8.57 (s, 1H), 8.27 (d, 1H), 7.90 (d, 1H) 7.54 (t, 1H), 7.46 (d, 1H), 7.39 (d, 1H), 7.33 (d, 1H), 7.18 (m, 2H), 6.60 (dd, 1H), 3.82 (s, 3H), 3.59 (m, 2H), 3.00 (s, 1H), 2.90 (s, 3H), 1.62 (m, 7H); MS (EI) for C₂₉H₃₁ClN₆O₄S: 595 (MH⁺).

30

Example 522**3-(N-(3-(2-chloro-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)-N-(1-methylpiperidin-3-yl)benzamide**

[00462] The title compound was prepared according to the above Examples. ¹H NMR (400 MHz, d₆-DMSO): 9.43 (s, 1H), 8.93 (s, 1H), 8.59 (s, 1H), 8.24 (d, 1H), 7.87 (d, 1H), 7.47 (m, 2H), 7.40 (d, 1H), 7.33 (d, 1H), 7.19 (m, 2H), 6.60 (dd, 1H), 4.21 (s, 1H), 3.82 (s, 1H), 2.76 (s, 1H), 2.50 (m, 7H), 1.91 (m, 2H), 1.63 (m, 2H); MS (EI) for C₂₈H₂₉ClN₆O₄S: 581 (MH⁺).

Biological Assays

10 [00463] The compounds of the invention demonstrated the ability to bind to PI3K when tested in the assays described in Section II above. In another embodiment, the compounds in Section II and Section III bind to the PI3K with a binding affinity, for example, of about 50 μM or less, 20 μM or less, 10 μM or less, 5 μM or less, 2.5 μM or less or 1 μM or less. In an advantageous embodiment, the IC₅₀ of the binding compounds is about 0.5 μM or less, about 15 0.3 μM or less, about 0.1 μM or less, about 0.08 μM or less, about 0.06 μM or less, about 0.05 μM or less, about 0.04 μM or less, 0.03 μM or less, in another embodiment, about 0.03 μM or less.

Biological Models

20 [00464] Several biological models were used to test the efficacy of a MEK compound of Formula I, Ia, Ic, Id, II, III, IV, or V in combination with a PI3K compound of Formula VI, VIa, VIb or VII or a PI3K compound of Formula VIII, VIIIa, VIIIb, or IX in inhibiting tumor cell proliferation. In brief, either A2058 or WM-266 melanoma cell lines (ATCC) were transplanted intradermally in the hindflank of athymic nude mice (Jackson Laboratories).
25 Both cell lines contain the B-RAF V600E mutation (Solit et al., *Nature* 439: pages 358-362, February 2006) and the PTEN gene is deleted. The xenograft was allowed to grow and divide for 10 days. Starting on day 10, mice were treated daily with a vehicle control or with a selected compound from section I (MEK inhibitor of Formula I, Ia, Ic, Id, II, III, IV, or V) either alone or in combination with a compound from section II (PI3K inhibitor of Formulae
30 Formula VI, VIa, VIb or VII) or a compound from section III (PI3K inhibitor of Formulae Formula VIII, VIIIa, VIIIb, or IX). The xenografts were allowed to grow for another 15 days and then the tumors were weighed.

[00465] Mice treated with the MEK inhibitor alone exhibited a 50-75% reduction in tumor growth over the 15 day treatment period. Mice carrying the A2058 xenograft and treated

with a select MEK inhibitor at 10 mgs/kg showed a 60% reduction in tumor growth relative to mice treated with vehicle alone. Mice carrying the A2058 xenograft and treated with vehicle had a mean tumor weight of approximately 1100 mgs versus mice who were treated with the select MEK inhibitor who had a mean tumor weight of 450 mgs. Mice carrying the WM-266 xenograft and treated with vehicle had a mean tumor weight of 700 mgs while mice carrying the same xenograft and treated with the select MEK inhibitor had a mean tumor weight of 200 mgs. The MEK inhibitor inhibited the tumor growth of both tumors by 60-75% over the 15 day period of treatment.

[00466] Mice treated with a combination of MEK inhibitor and a selected Section II or Section III PI3K inhibitor also exhibited a reduction in tumor growth over the 15 day treatment period. Mice carrying the A2058 xenograft and treated with a select Section III PI3K inhibitor at 100 mgs/kg exhibited a 65% reduction in growth relative to animals treated with the vehicle alone (mean tumor size of 375 mgs for Section III PI3K inhibitor treated animals vs 1100 mgs for vehicle treated animals). Animals treated with a combination of a select MEK inhibitor (10mgs/kg) and a selected Section III PI3K inhibitor (100 mgs/kg) exhibited an 80% reduction in tumor growth over the 15 day treatment period (mean tumor size of 200 mgs for the tumors treated with the combination of compounds vs 1100 mgs for the vehicle treated tumors).

[00467] Mice carrying the A2058 xenograft and treated with a select Section II PI3K inhibitor at 100 mgs/kg exhibited a 65% reduction in growth relative to animals treated with the vehicle alone (mean tumor size of 350 mgs for PI3K inhibitor treated animals vs 1100 mgs for vehicle treated animals). Animals treated with a combination of a select MEK inhibitor (10mgs/kg) and a selected Section II PI3K inhibitor (100 mgs/kg) exhibited an 75% reduction in tumor growth over the 15 day treatment period (mean tumor size of 250 mgs for the tumors treated with the combination of compounds vs 1100 mgs for the vehicle treated tumors).

[00468] Similar results were observed in animals carrying the WM-266 xenograft and treated with the same combination of drugs. Mean tumor weights for the animals treated with the vehicle alone were 700 mgs after 15 days of treatment. Animals that had received the Section III PI3K or Section II PI3K inhibitors exhibited a 50% reduction in tumor growth (mean tumor size of 500 mgs for the tumors treated with each compound) and an 85% reduction in tumor growth for tumors treated with the combination of a select MEK and either the Section II PI3K or Section III PI3K inhibitors (mean tumor size of 100 mgs after 15 days of combination treatment).

[00469] Xenographs treated with the combination of a select MEK inhibitor and either a select Section III PI3K inhibitor or a select Section II PI3K inhibitor exhibited a greater reduction in tumor growth than tumors treated with either compound alone.

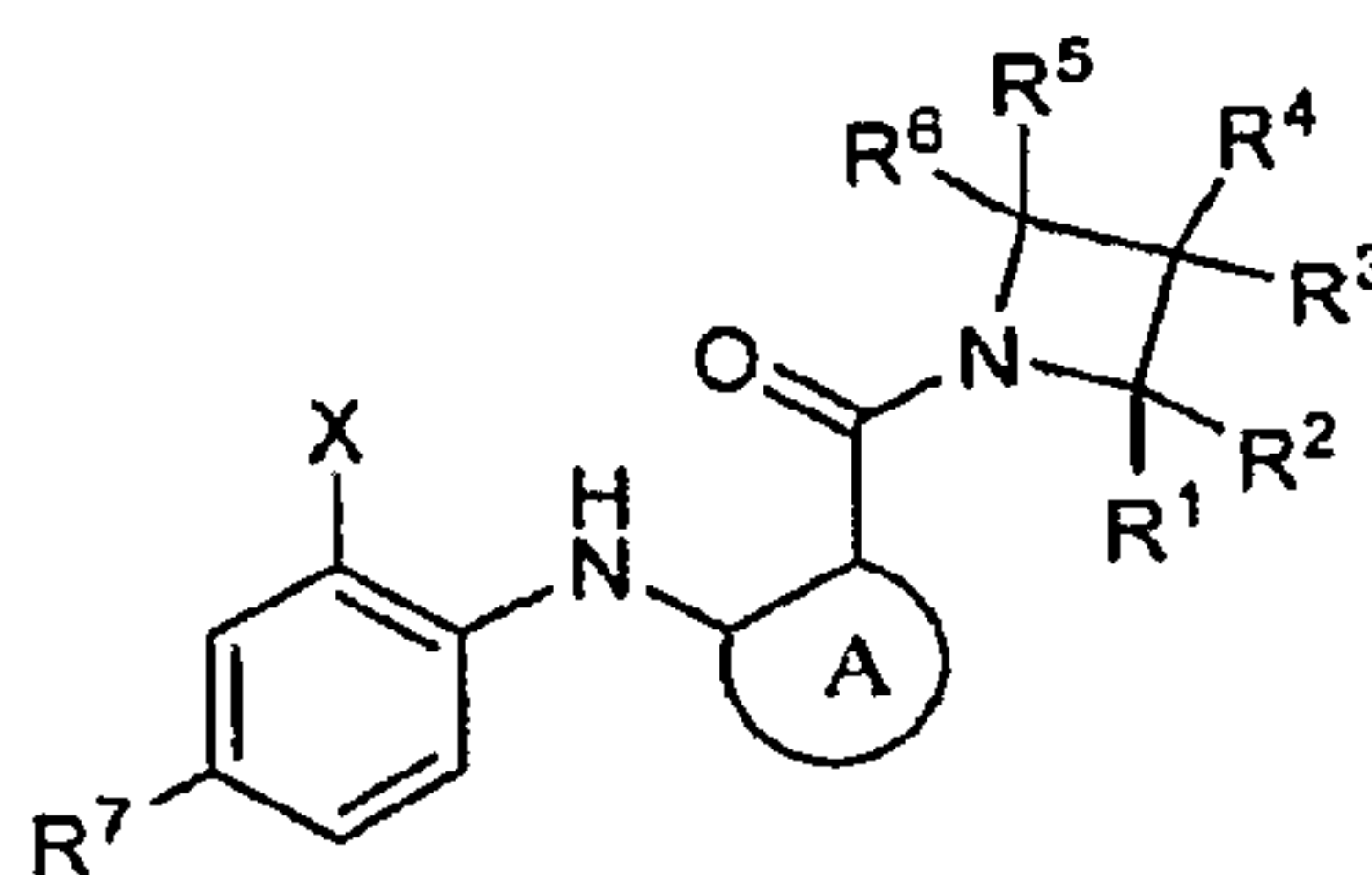
5 [00470] The foregoing invention has been described in some detail by way of illustration and example, for purposes of clarity and understanding. The invention has been described with reference to various specific and preferred embodiments and techniques. However, it should be understood that many variations and modifications may be made while remaining within the spirit and scope of the invention. It will be obvious to one of skill in the art that changes and modifications may be practiced within the scope of the appended claims.

10 Therefore, it is to be understood that the above description is intended to be illustrative and not restrictive. The scope of the invention should, therefore, be determined not with reference to the above description, but should instead be determined with reference to the following appended claims, along with the full scope of equivalents to which such claims are entitled. All patents, patent applications and publications cited in this application are hereby

15 incorporated by reference in their entirety for all purposes to the same extent as if each individual patent, patent application or publication were so individually denoted.

We claim:

1. A method of treating cancer which method comprises administering to a patient a therapeutically effective amount of a compound of Formula Ia, Ic, Id, II, or V or a pharmaceutically acceptable composition, thereof, in combination with a compound(s)
 5 selected from the group consisting of a compound of Formula VIa, VIb, VII, VIIla, and VIIlb, or a pharmaceutically acceptable composition thereof,
 where Formula Ia is as follows:



Formula Ia

- 10 and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein the A ring represents an arylene or heteroarylene group and the A ring is optionally substituted with one, two, three or four groups selected from R^{10} , R^{12} , R^{14} , and R^{16} where R^{10} , R^{12} , R^{14} , and R^{16} are independently hydrogen, lower alkanyl, lower alkenyl, lower alkynyl, halo, haloalkoxy, hydroxy, lower alkoxy, amino, alkylamino,
 15 dialkylamino, haloalkyl, $-NHS(O)_2R^8$, $-CN$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$ or $-NR^8C(O)R^{8'}$;
 X is lower alkyl, halo, haloalkyl, or haloalkoxy;
 R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are independently hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$,
 20 $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$, $-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$,
 $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^{8'}$,
 lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl,
 25 optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$,
 $-NHS(O)_2R^9$, $-CN$, $-S(O)_mR^9$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^8R^{8''}$,
 $-NR^8C(O)OR^8$, and $-NR^8C(O)R^{8'}$; or

one of R^1 and R^2 together with the carbon to which they are attached, R^3 and R^4 together with the carbon to which they are attached, and R^5 and R^6 together with the carbon to which they are attached form $C(O)$ or $C(=NOH)$;

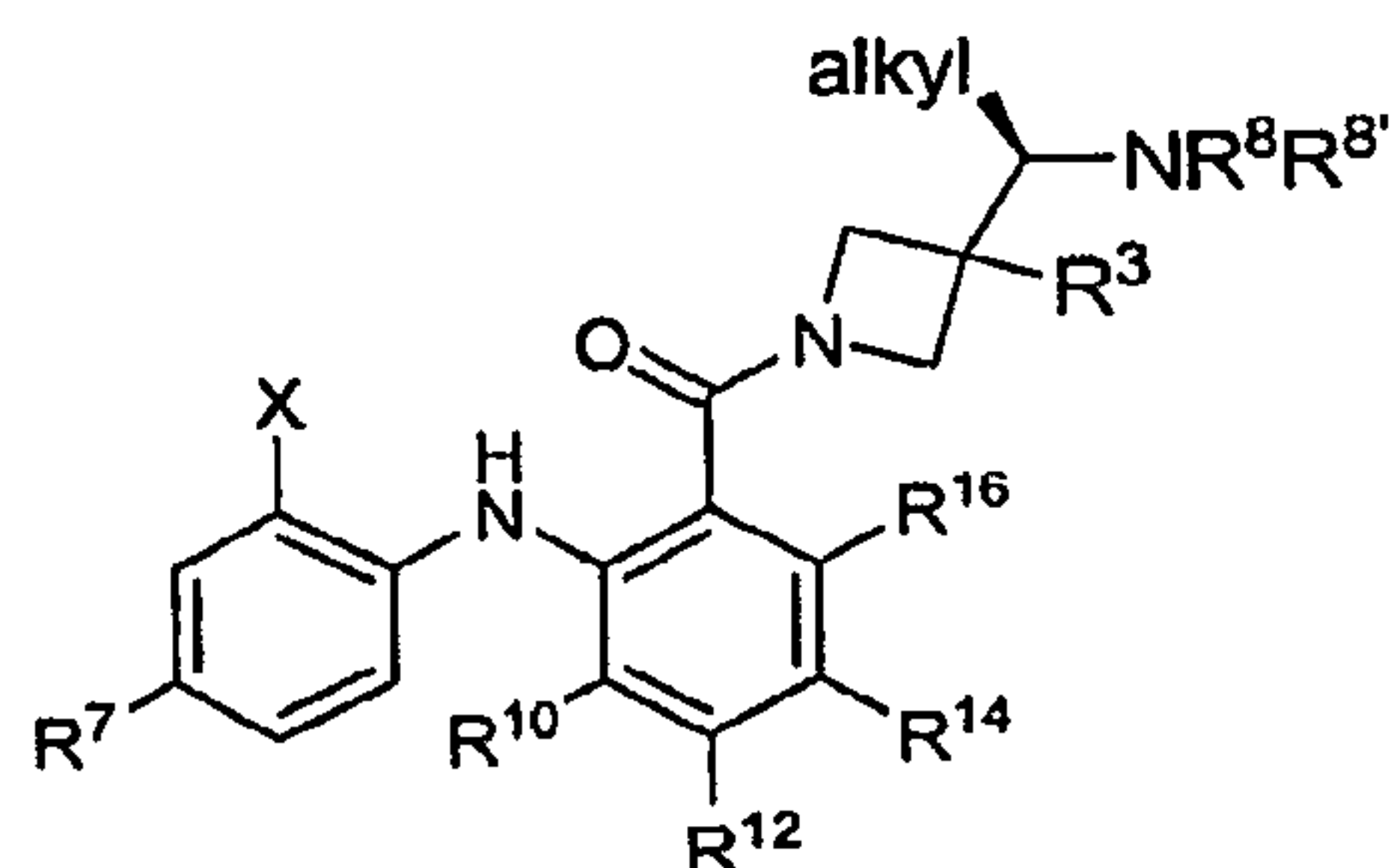
m is 1 or 2;

5 R^7 is hydrogen, halo or lower alkyl;

R^8 , $R^{8'}$ and $R^{8''}$ are independently hydrogen, hydroxy, alkoxy, substituted alkoxy, lower alkanyl, haloalkyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from lower alkanyl, halo, hydroxy, hydroxyalkyl, lower alkoxy, substituted alkoxy, alkoxyalkyl, haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and R^{31} is alkyl, substituted alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{34}SO_2R^{34a}$ (where R^{34} is hydrogen or lower alkyl and R^{34a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl), $-SO_2NR^{35}R^{35a}$ (where R^{35} is hydrogen or alkyl and R^{35a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, aryloxy, arylalkyloxy, optionally substituted heteroaryl, $-NHC(O)R^{32}$ (where R^{32} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl) and $-NR^{30}R^{30'}$ (where R^{30} and $R^{30'}$ are independently hydrogen, lower alkyl, or hydroxyalkyl), and $-C(O)NHR^{33}$ (where R^{33} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl); and

R^9 is lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, or five groups selected from lower alkanyl, halo, hydroxy, haloalkoxy, haloalkyl, amino, alkylamino, and dialkylamino;

where Formula Ic is as follows:



Formula Ic

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein

R^{10} , R^{12} , R^{14} , and R^{16} are independently hydrogen, lower alkanyl, halo, haloalkoxy, hydroxy, lower alkoxy, or haloalkyl;

X is halo;

R^3 is hydrogen, halo, nitro, $-NR^8R^{8'}$, $-OR^8$, $-NHS(O)_2R^8$, $-CN$, $-S(O)_mR^8$,

$-S(O)_2NR^8R^{8'}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)OR^8$,

$-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, $-NR^8C(O)R^8$, lower alkanyl, lower alkenyl, lower

alkynyl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower

alkenyl, lower alkynyl, cycloalkyl, heteroaryl, and heterocycloalkyl are optionally substituted with one, two, three, four, five, six or seven groups independently selected from halo, lower alkanyl, haloalkyl, nitro, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted

arylalkyl, optionally substituted heteroaryl, $-OR^8$, $-NR^8R^{8'}$, $-NHS(O)_2R^9$, $-CN$,

$-S(O)_mR^9$,

$-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^8R^{8'}$, $-NR^8C(O)NR^{8'}R^{8''}$, $-NR^8C(O)OR^8$, and

$-NR^8C(O)R^8$;

R^7 is hydrogen, halo or lower alkyl;

R^8 , $R^{8'}$ and $R^{8''}$ are independently hydrogen, hydroxy, alkoxy, substituted alkoxy, lower

alkanyl, haloalkyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or

heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two three, four, or five groups independently selected from lower alkanyl,

halo, hydroxy, hydroxyalkyl, lower alkoxy, substituted alkoxy, alkoxyalkyl,

haloalkyl, carboxy, carboxy ester, nitro, cyano, $-S(O)_nR^{31}$ (where n is 0, 1, or 2 and

R^{31} is alkyl, substituted alkyl, optionally substituted aryl, optionally substituted

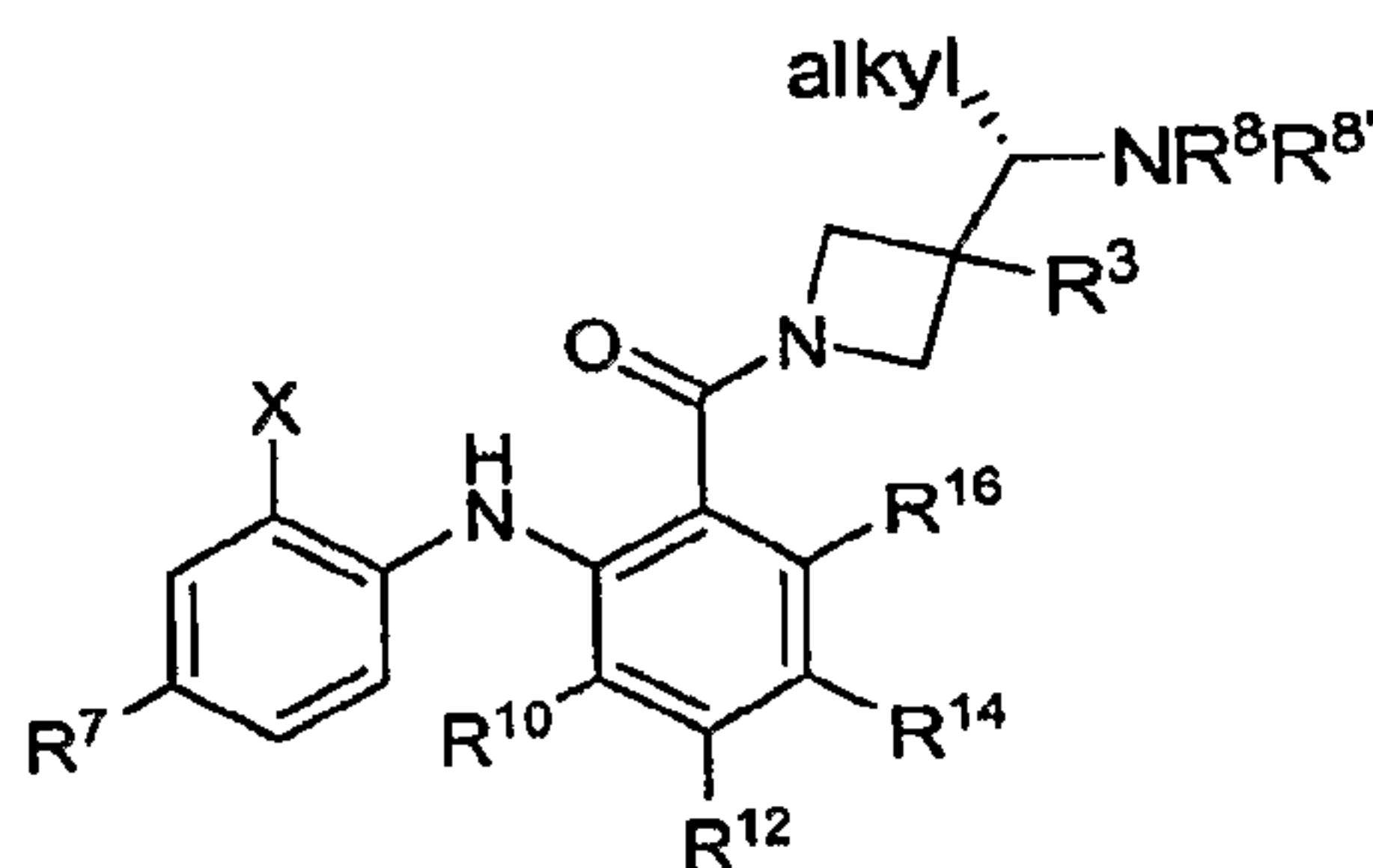
heterocycloalkyl, or optionally substituted heteroaryl), $-NR^{34}SO_2R^{34a}$ (where R^{34} is

hydrogen or lower alkyl and R^{34a} is lower alkyl, lower alkenyl, optionally substituted

aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl),
 $-\text{SO}_2\text{NR}^{35}\text{R}^{35a}$ (where R^{35} is hydrogen or alkyl and R^{35a} is lower alkyl, lower alkenyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted cycloalkyl, or optionally substituted heteroaryl), optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, aryloxy, arylalkyloxy, optionally substituted heteroaryl, $-\text{NHC}(\text{O})\text{R}^{32}$ (where R^{32} is lower alkanyl, lower alkenyl, alkoxy, or cycloalkyl) and $-\text{NR}^{30}\text{R}^{30'}$ (where R^{30} and $\text{R}^{30'}$ are independently hydrogen, lower alkyl, or hydroxyalkyl), and $-\text{C}(\text{O})\text{NHR}^{33}$ (where R^{33} is lower alkanyl, lower alkenyl, lower alkynyl, or cycloalkyl); and

R^9 is lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, or heterocycloalkyl; where the lower alkanyl, lower alkenyl, lower alkynyl, aryl, cycloalkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with one, two, three, four, or five groups selected from lower alkanyl, halo, hydroxy, haloalkoxy, haloalkyl, amino, alkylamino, and dialkylamino;

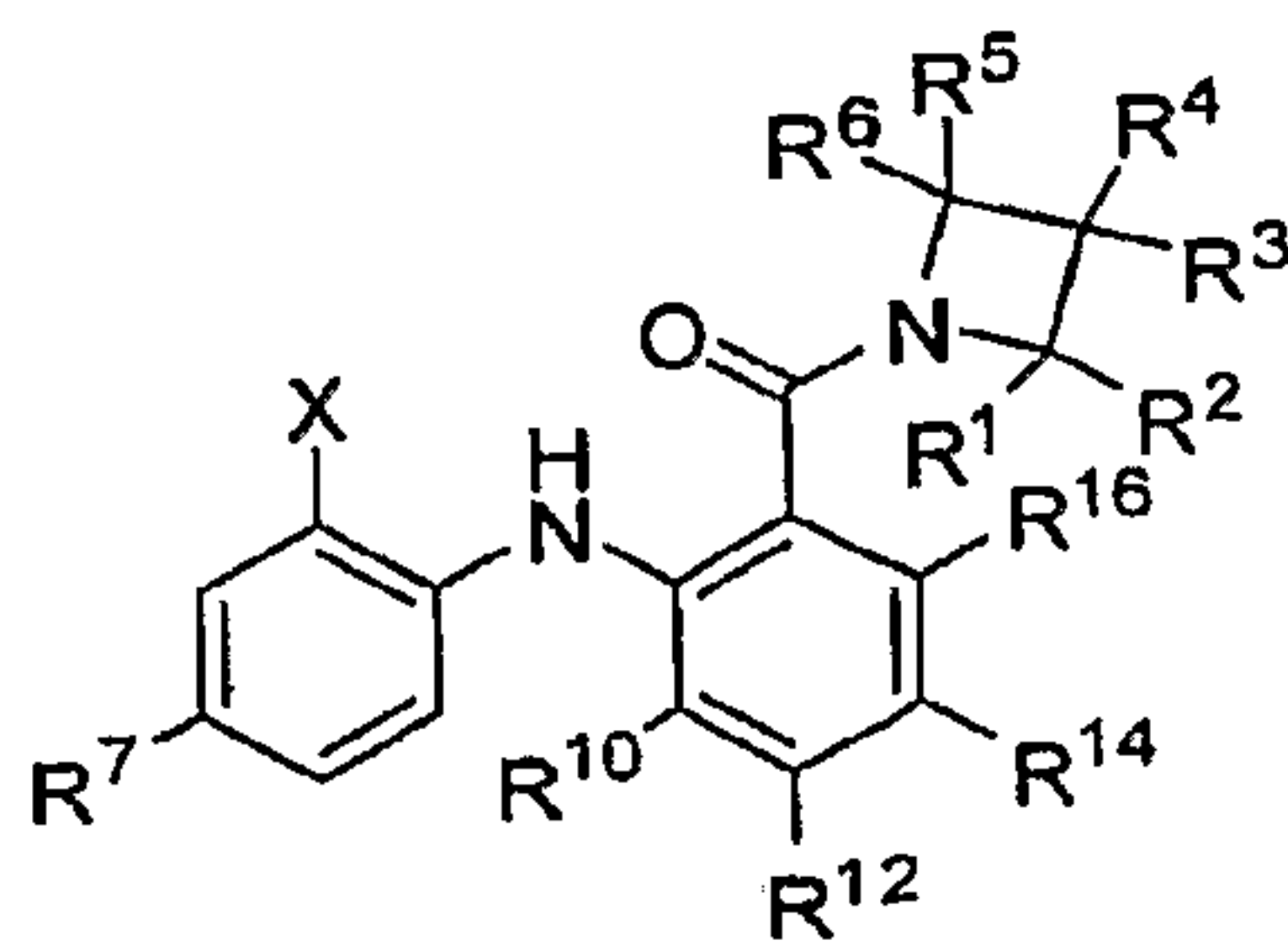
where Formula Id is as follows:



Formula Id

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein X, R^7 , R^{10} , R^{12} , R^{14} , R^{16} , R^3 , R^8 , and $\text{R}^{8'}$ are as defined above for Formula Ic;

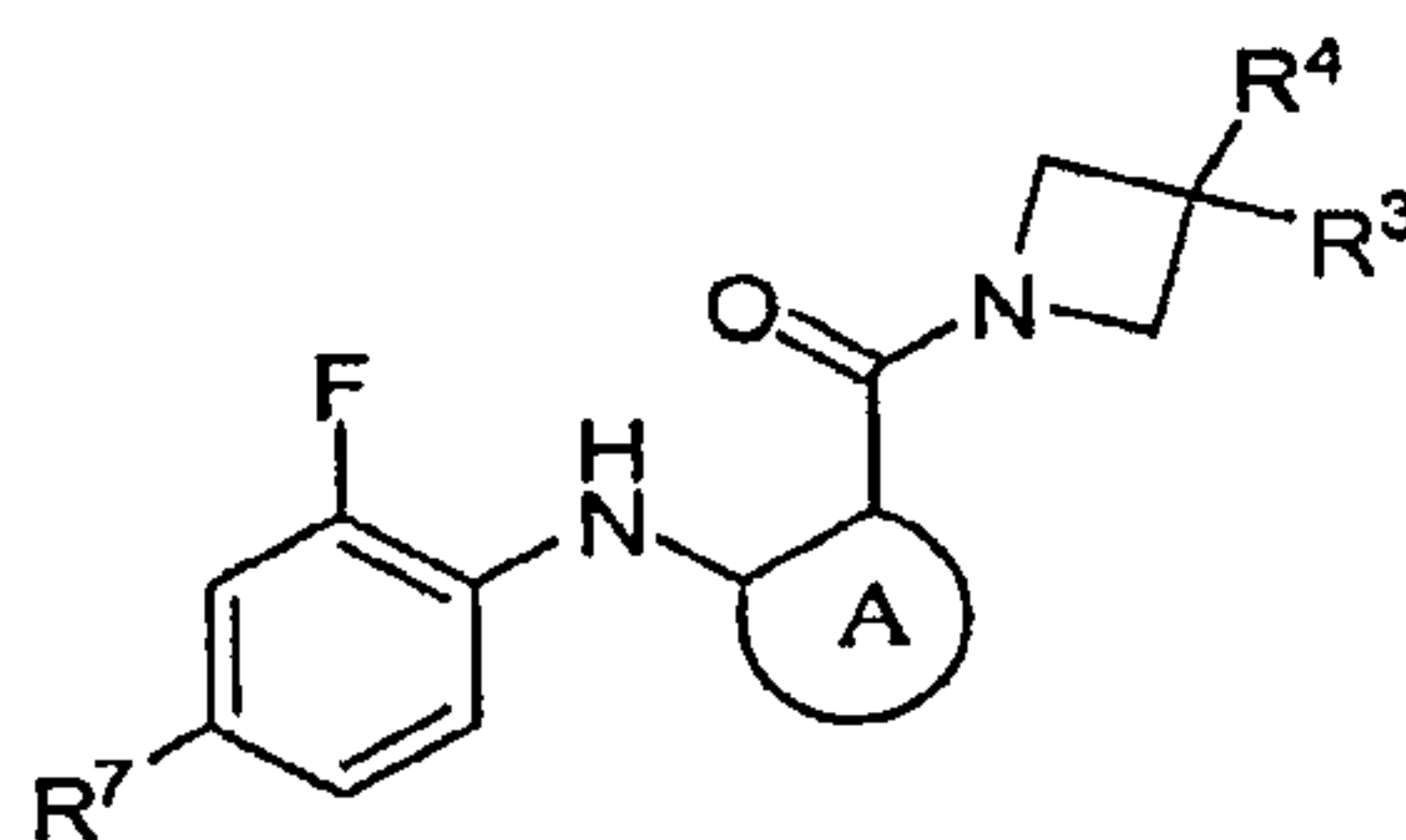
where Formula II is as follows:



II

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein X, R¹, R², R³, R⁴, R⁵, R⁶, and R⁷ are as defined above for Formula Ia;

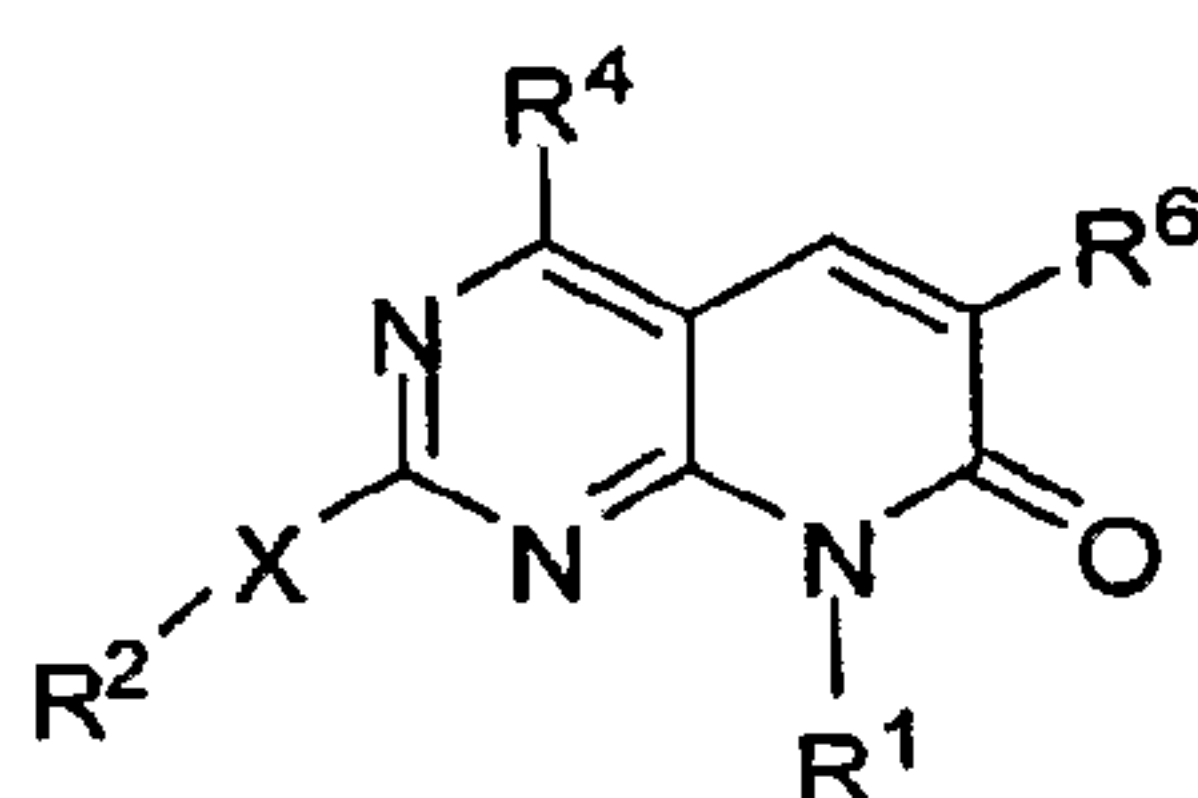
where Formula V is as follows:



V

and optionally as a pharmaceutically acceptable salt or solvate thereof, wherein the A ring, R³, R⁴, and R⁴ are as defined above for Formula Ia;

where Formula VIa is as follows:



(VIa)

and optionally as a pharmaceutically acceptable salt or hydrate thereof, wherein

R¹ is hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

X is -NR³-;

R² is hydrogen, optionally substituted C₁-C₆ alkyl, C₃-C₇ cycloalkyl, aryl, aryl-C₁₋₆ alkyl, heteroalicyclic, heterocyclalkyl, heterocyclalkyl-aryl- or heteroaryl; where the cycloalkyl, aryl, aryl-C₁₋₆ alkyl, heteroalicyclic, heterocyclalkyl, heterocyclalkyl-aryl-, and heteroaryl groups in R² are optionally substituted with 1, 2, 3, or 4 R⁸ groups;

R³ is hydrogen;

R⁴ is optionally substituted C₁-C₆ alkyl;

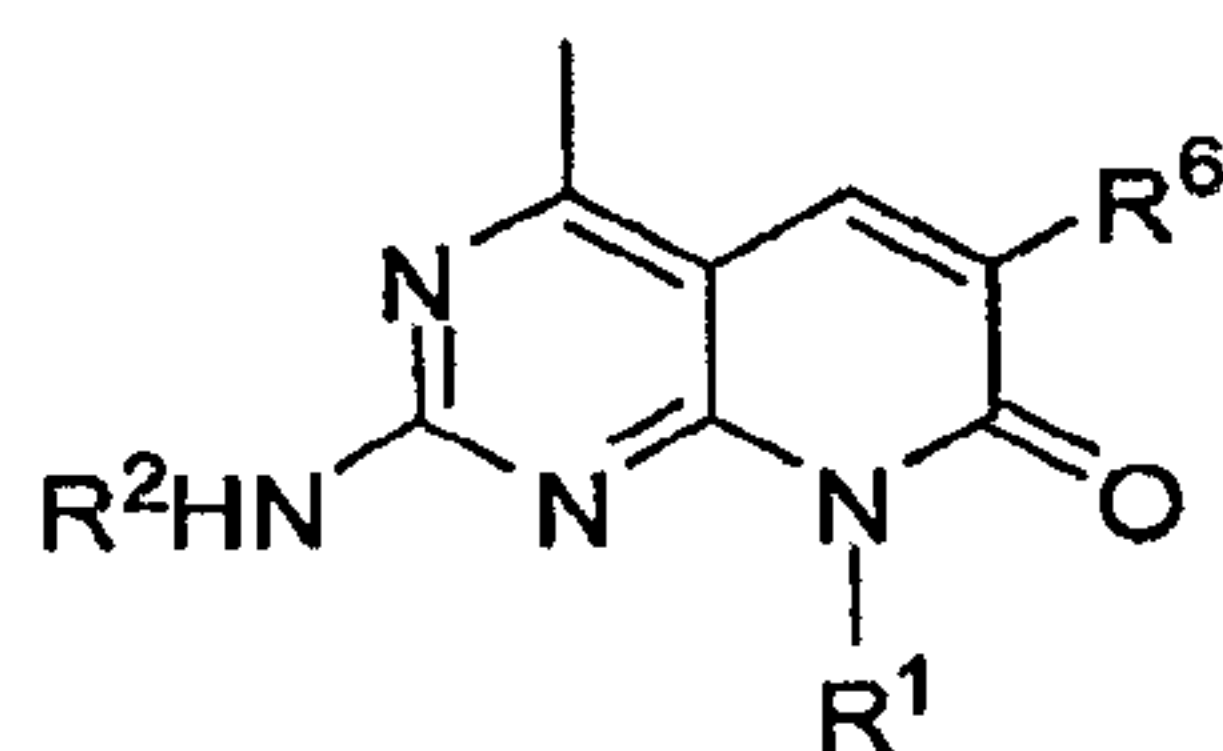
R⁶ is hydrogen, acyl, phenyl, heteroalicyclic, or heteroaryl; where the phenyl, heteroalicyclic, and heteroaryl in R⁶ are optionally substituted with 1, 2, 3, or 4 R⁹ groups;

R⁸ at each occurrence is independently hydroxy, halo, haloalkyl, C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, C₁-C₆ alkoxyalkylaminoalkyl, C₁-C₆

alkylcarboxyheterocyclyl, -O-C₁-C₆alkylheterocyclyl, aminoalkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted aryl C₁-C₆ alkyl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl; and

R⁹ at each occurrence is independently halo, haloalkyl, haloalkoxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, C₁-C₆ carboxyalkyl, alkoxycarbonyl, aminoalkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted aryl C₁-C₆ alkyl, optionally substituted aryloxy, optionally substituted heteroalicyclic, or optionally substituted heteroaryl;

where Formula VIb is as follows:



(VIb)

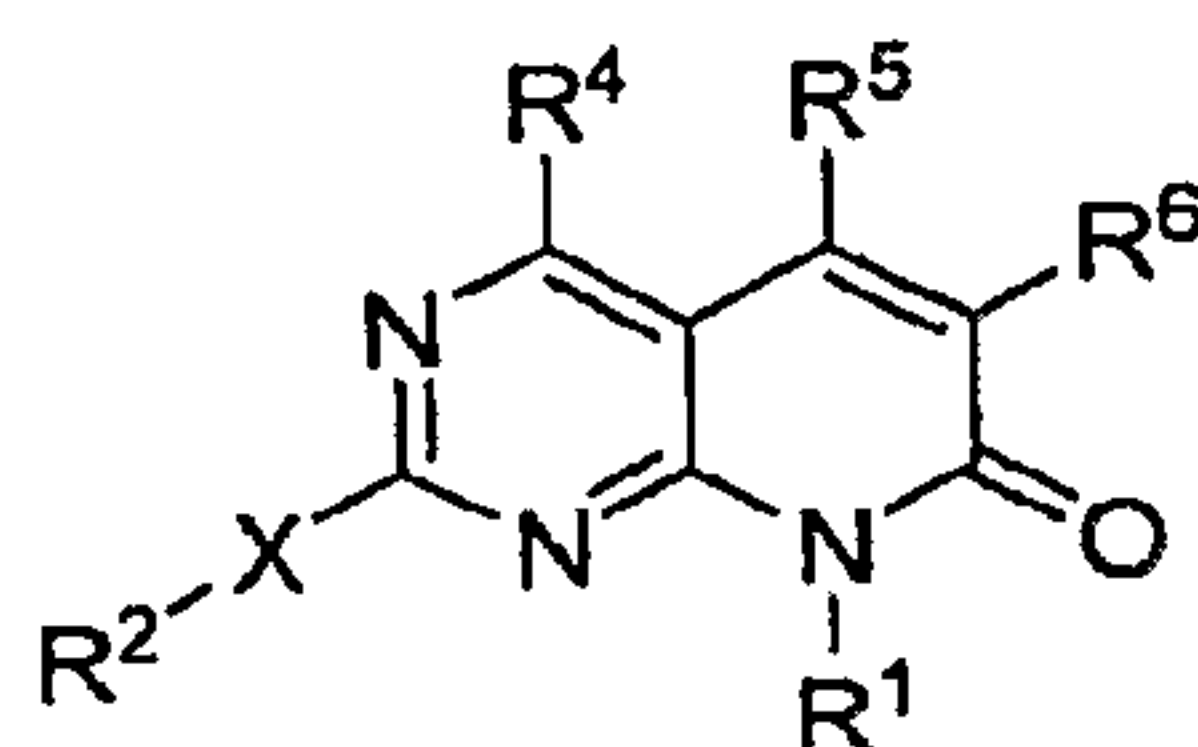
and optionally a pharmaceutically acceptable salt or solvate thereof, wherein

R¹ is hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

R⁶ is phenyl, acyl, or heteroaryl wherein the phenyl and heteroaryl are optionally substituted with 1, 2, 3, or 4 R⁹ groups; and

R⁹ at each occurrence is independently halo, haloalkyl, haloalkoxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxyalkyl, C₁-C₆ carboxyalkyl, alkoxycarbonyl, aminoalkyl, optionally substituted C₃-C₇ cycloalkyl, optionally substituted aryl, optionally substituted aryl C₁-C₆ alkyl, aryloxy, optionally substituted heteroalicyclic, or optionally substituted heteroaryl;

where Formula VII is as follows:



VII

R^1 is hydrogen, optionally substituted C_1 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

5 X is $-NR^3$ -;

R^3 is hydrogen;

R^4 is optionally substituted C_1 - C_6 alkyl;

R^5 is hydrogen;

R^6 is acyl and R^2 is heterocycl-aryl- optionally substituted with 1, 2, 3, or 4 R^8 groups; or

10 R^6 is halo and R^2 is optionally substituted C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, phenyl, aryl- C_{1-6} alkyl, heteroalicyclicalkyl, or heterocycl-aryl-; where the C_3 - C_7 cycloalkyl, phenyl, phenyl, aryl- C_{1-6} alkyl, heteroalicyclicalkyl, and heterocycl-aryl- groups in R^2 are optionally substituted with 1, 2, 3, or 4 R^8 groups; or

R^6 is phenyl optionally substituted with 1, 2, or 3 halo; and R^2 is phenyl or heterocycl-aryl-;

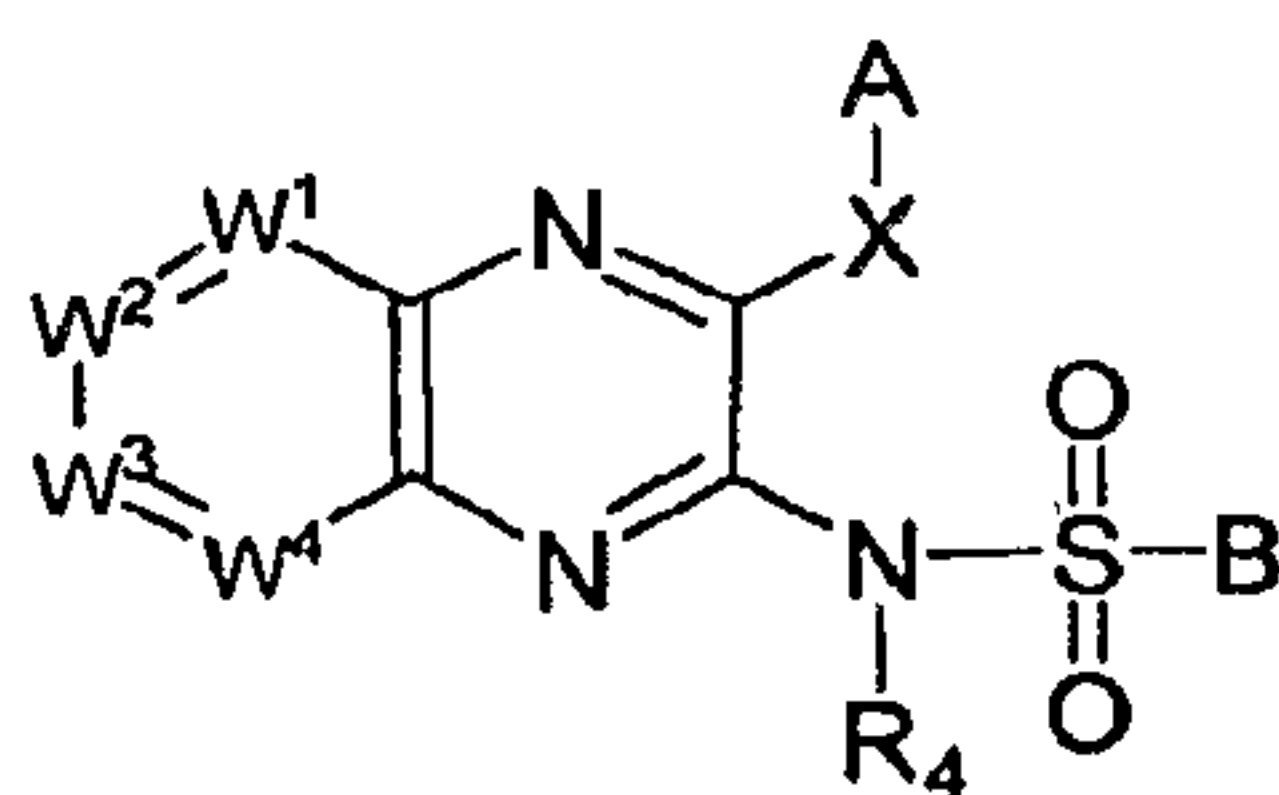
15 where the phenyl and heterocycl-aryl- groups in R^2 are optionally substituted with 1, 2, 3, or 4 R^8 groups; or

R^6 is heteroaryl optionally substituted with 1, 2, or 3 halo; and R^2 is heterocycl-aryl- optionally substituted with 1, 2, 3, 4, or 5 R^8 groups;

each R^8 at each instance is independently hydroxy, halo, C_1 - C_6 alkyl, haloalkyl, optionally

20 substituted C_1 - C_6 alkoxy, C_1 - C_6 alkoxyalkyl, C_1 - C_6 alkoxycarbonyl, C_1 - C_6 alkoxyalkylaminoalkyl, $-O-C_1$ - C_6 alkylheterocycl, aminoalkyl, optionally substituted C_3 - C_7 cycloalkyl, optionally substituted aryl, optionally substituted aryl C_1 - C_6 alkyl, optionally substituted heteroalicyclic, optionally substituted heteroalicyclicalkyl, optionally substituted heteroaryl or optionally substituted heteroarylalkyl;

25 where Formula VIIIa is as follows:



VIIIa

or a pharmaceutically acceptable salt or solvate thereof, wherein

W^1 , W^2 , W^3 , and W^4 are $-C(R_1)-$ or W^2 and W^3 are $-C(R_1)-$ and one of W^1 and W^4 is $-N-$ and

30 the other is $-C(R_1)-$;

X is -N(R₅)-;

A is aryl, heteroaryl, or heterocycloalkyl where the aryl, heteroaryl, and heterocycloalkyl are optionally substituted with (R₂)_{n1}; or

B is aryl, -C₁-C₆ alkylaryl, heteroaryl, or heterocycloalkyl, where the aryl, C₁-C₆-alkyl, heteroaryl, and heterocycloalkyl are independently optionally substituted with (R₃)_{n2};

n₁ is 0, 1, 2, or 3;

n₂ is or an integer from 1 to 5;

each R₁ is independently hydrogen, C₁-C₆-alkyl, haloalkyl, C₁-C₆-alkoxy, haloalkoxy, or -NO₂;

each R₂ (when R₂ is present) is independently -C₁-C₆-alkanyl, -C₁-C₆-alkenyl, -OR₆, -N(R₇)-C(O)-R₆, -N(R₇)-C(O)-C₀-C₆ alkyl-N(R_{7b})R_{7a}, -OC(O)-C₀-C₆ alkyl-N(R₇)R_{7a}, -C₀-C₆alkyl-C(O)R₆, heterocycloalkyl, aryl, halo, -NO₂, or -C₀-C₆-alkyl-N(R₇)R_{7a}, wherein each alkyl, aryl, and heterocycloalkyl groups, each either alone or as part of another group within R₂, is independently optionally substituted with one, two, three, four, or five groups selected from C₁-C₆-alkyl, C₁-C₆-alkoxy, halo, haloalkyl, and haloalkoxy;

each R₃ (when R₃ is present) is independently hydroxy, -NO₂, halo, -CN, C₁-C₆-alkanyl, C₂-C₆-alkenyl, C₁-C₆ alkoxy, -C₀-C₆ alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})C(O)R_{7a}, -C₀-C₆ alkyl-C(O)N(R₇)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-C(O)N(R₇)-C₁-C₆-alkyl-C(O)OR_{7a}, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-(R₇), -C₀-C₆-alkyl-N(R₇)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})-C₀-C₆-alkyl-N(R_{7c})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-alkyl-N(R₇)-C₀-C₆ alkyl-C(=N(R_{7b})(R_{7a}))(NR_{7c}R_{7d}), -C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-OR₆, -C₀-C₆-alkyl-C(O)OR₆, -C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)-NR₇R_{7a}, -C₀-C₆-alkyl-C(O)-R₇, -S(O)₂R₇, -SO₂N(R₇)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)-heterocycloalkyl (dupe of C(O)R₇), -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl-aryl, or -N(R₇)C(O)R_{7a}, wherein each of the alkyl, alkanyl, alkenyl, cycloalkyl, aryl, alkoxy, heterocycloalkyl, and heteroaryl groups, either alone or as part of another group within R₃, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C₁-C₆-alkanyl, C₁-C₆ alkenyl, cycloalkyl, halo, -C(O)-R₆, oxo,

hydroxy, $-C_0-C_6$ -alkyl- $N(R_8)R_{8a}$, $-C_0-C_6$ -alkyl-heterocycloalkyl, $-C_0-C_6$ -alkyl-aryl, $-C_0-C_6$ -alkyl-heteroaryl, $-C(O)OR_6$, and hydroxyalkyl;

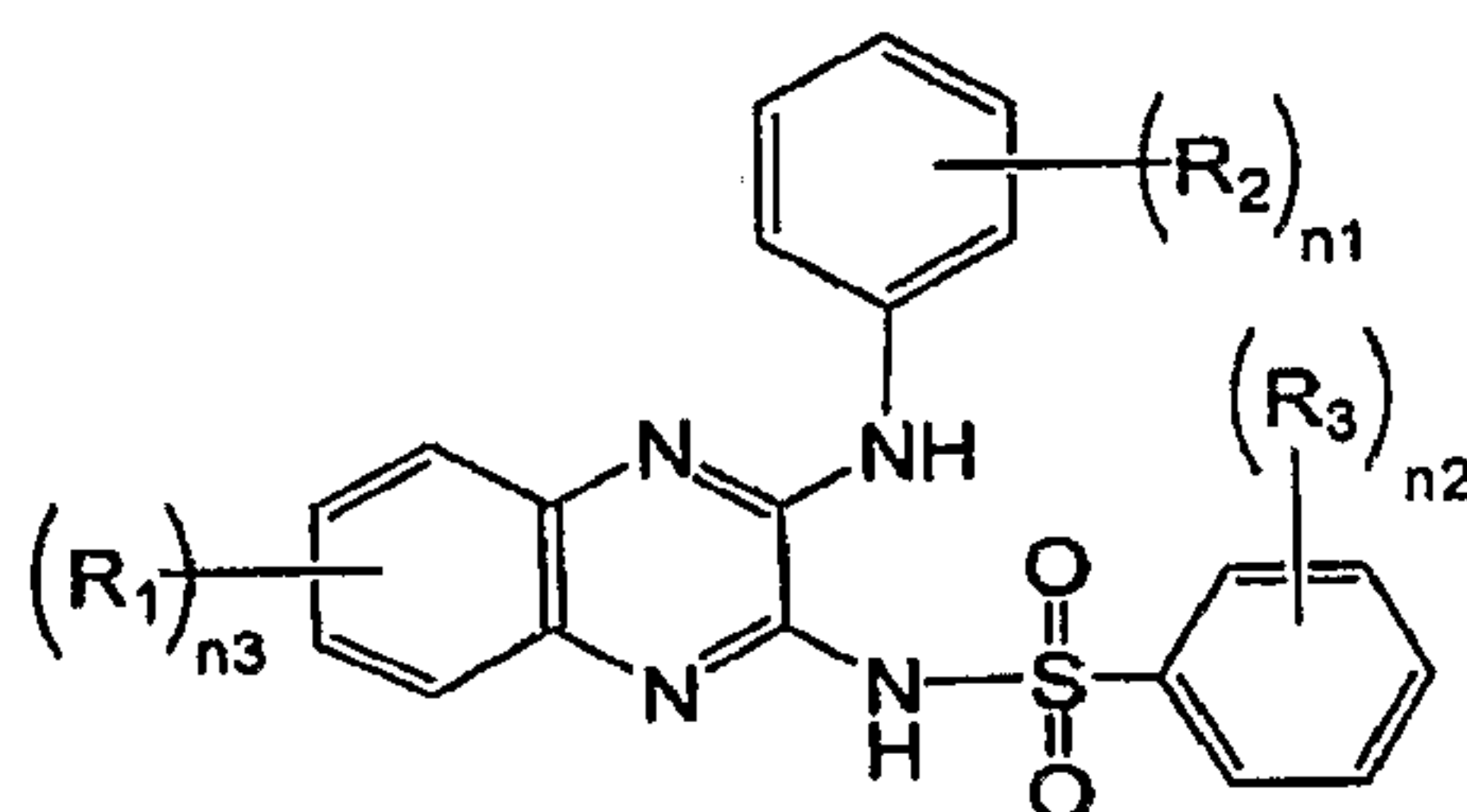
R_4 is hydrogen;

R_5 is hydrogen;

5 R_6 and R_9 are independently hydrogen, C_1-C_6 -alkyl, aryl, arylalkyl, or cycloalkyl, where each of the $-C_1-C_6$ -alkyl, aryl, arylalkyl, and cycloalkyl, is independently optionally substituted with 1, 2, 3, 4, or 5 groups selected from C_1-C_6 -alkoxy, C_1-C_6 -alkyl, and halo; and

10 R_7 , R_{7a} , R_{7b} , R_{7c} , and R_{7d} are independently hydrogen, $-C_1-C_6$ -alkanyl, $-C_1-C_6$ -alkenyl, $-OH$, $-O-C_1-C_6$ alkanyl, $-O-C_1-C_6$ alkenyl, $-O-C_0-C_6$ -alkyl-aryl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or heterocycloalkylalkyl, wherein each of the alkyl, aryl, heteroaryl, and heterocycloalkyl, either alone or part of another group within R_7 , R_{7a} , R_{7b} , R_{7c} , and R_{7d} , is independently optionally substituted with 1, 2, 3, 4, or 5 $-NH_2$, alkylamino, dialkylamino, $-S-C_1-C_6$ -alkyl, $-CN$, hydroxy, oxo, C_1-C_6 alkoxy, C_1-C_6 alkyl, or halo;

15 and where Formula VIIIb is as follows:



VIIIb

or a pharmaceutically acceptable salt or solvate thereof, wherein

20 n_1 is one or two; and n_2 is one or two; n_3 is 0, 1, or two;

each R_1 is independently hydrogen, C_1-C_6 -alkyl, haloalkyl, C_1-C_6 -alkoxy, haloalkoxy, $-NO_2$, halo, hydroxy, hydroxyalkyl, $-CN$, cyanoalkyl, or $-C_0-C_6$ alkyl- $N(R_{10})R_{10a}$ where R_{10} and R_{10a} are independently hydrogen, $-C_1-C_6$ -alkyl, $-OH$, $-O-C_1-C_6$ alkyl, haloalkyl, or haloalkoxy;

25 each R_2 (when R_2 is present) is independently C_1-C_6 -alkanyl, C_1-C_6 -alkenyl, $-OR_6$, $-N(R_7)-C(O)-R_6$, $-N(R_7)-C(O)-C_0-C_6$ alkyl- $N(R_{7b})R_{7a}$, $-OC(O)-C_0-C_6$ alkyl- $N(R_7)R_{7a}$, $-C_0-C_6$ alkyl- $C(O)R_6$, heterocycloalkyl, aryl, halo, $-NO_2$, or $-C_0-C_6$ -alkyl- $N(R_7)R_{7a}$, wherein each alkyl, aryl, and heterocycloalkyl groups, each either alone or as part of another group within R_2 , is independently optionally substituted with one, two, three,

four, or five groups selected from C₁-C₆-alkyl, C₁-C₆-alkoxy, halo, haloalkyl, and haloalkoxy;

each R₃ (when R₃ is present) is independently hydroxy, -NO₂, halo, -CN, C₁-C₆-alkanyl,

C₂-C₆-alkenyl, C₁-C₆ alkoxy, -C₀-C₆ alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})R_{7a}, -C₀-C₆-

5 alkyl-N(R₇)C(O)-C₀-C₆-alkyl-N(R_{7b})C(O)R_{7a}, -C₀-C₆ alkyl-C(O)N(R₇)-C₀-C₆-alkyl-

N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)N(R₇)-C₁-C₆-alkyl-C(O)OR_{7a}, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-

C₆-alkyl-(R₇), -C₀-C₆-alkyl-N(R₇)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-

alkyl-N(R_{7b})-C₀-C₆-alkyl-N(R_{7c})R_{7a}, -C₀-C₆-alkyl-N(R₇)C(O)O-C₀-C₆-alkyl-N(R_{7b})R_{7a},

-C₀-C₆-alkyl-N(R₇)-C₀-C₆ alkyl-C(=N(R_{7b})(R_{7a}))(NR_{7c}R_{7d}), -C₀-C₆-alkyl-heteroaryl, -C₀-

10 C₆-alkyl-OR₆, -C₀-C₆-alkyl-C(O)OR₆, -C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-alkyl-C(O)-

NR₇R_{7a}, -C₀-C₆-alkyl-C(O)-R₇, -S(O)₂R₇, -SO₂N(R₇)-C₀-C₆-alkyl-N(R₇)R_{7a}, -C₀-C₆-

alkyl-C(O)-heterocycloalkyl (dupe of C(O)R₇), -C₀-C₆-alkyl-C(O)N(R₇)-C₀-C₆-alkyl-

heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-cycloalkyl, -C₀-C₆-alkyl-N(R₇)-

C(O)-C₀-C₆-alkyl-aryl, -C₀-C₆-alkyl-N(R₇)-C(O)-C₀-C₆-alkyl-heteroaryl, -C₀-C₆-alkyl-

15 N(R₇)C(O)-C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-N(R₇)C(O)-C₀-C₆-alkyl-

heterocycloalkyl-aryl, or -N(R₇)C(O)R_{7a}, wherein each of the alkyl, alkanyl, alkenyl,

cycloalkyl, aryl, alkoxy, heterocycloalkyl, and heteroaryl groups, either alone or as part

of another group within R₃, is independently optionally substituted with 1, 2, 3, 4, or 5

groups selected from C₁-C₆-alkanyl, C₁-C₆ alkenyl, cycloalkyl, halo, -C(O)-R₆, oxo,

20 hydroxy, -C₀-C₆-alkyl-N(R₈)R_{8a}, -C₀-C₆-alkyl-heterocycloalkyl, -C₀-C₆-alkyl-aryl,

-C₀-C₆-alkyl-heteroaryl, -C(O)OR₆, and hydroxyalkyl;

R₄ is hydrogen;

R₅ is hydrogen;

R₆ is hydrogen, C₁-C₆-alkyl, aryl, arylalkyl, or cycloalkyl, where each of the -C₁-C₆-alkyl,

25 aryl, arylalkyl, and cycloalkyl, is independently optionally substituted with 1, 2, 3, 4, or 5

groups selected from C₁-C₆-alkoxy, C₁-C₆-alkyl, and halo; and

R₇, R_{7a} R_{7b}, R_{7c}, and R_{7d} are independently hydrogen, -C₁-C₆-alkanyl, -C₁-C₆-alkenyl, -OH,

-O-C₁-C₆ alkanyl, -O-C₁-C₆ alkenyl, -O-C₀-C₆-alkyl-aryl, aryl, arylalkyl, heteroaryl,

heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, or

30 heterocycloalkylalkyl, wherein each of the alkyl, aryl, heteroaryl, and

heterocycloalkyl, either alone or part of another group within R₇, R_{7a} R_{7b}, R_{7c}, and

R_{7d}, is independently optionally substituted with 1, 2, 3, 4, or 5 -NH₂, alkylamino,

dialkylamino, -S-C₁-C₆-alkyl, -CN, hydroxy, oxo, C₁-C₆ alkoxy, C₁-C₆ alkyl, or halo.

2. The method of claim 1 wherein the cancer is melanoma, bladder cancer, Wilm's cancer, ovarian cancer, pancreatic cancer, gastrointestinal stroma cancer, breast cancer, prostate cancer, bone cancer, small cell lung cancer, non-small cell lung cancer, colorectal cancer, cervical cancer, endometrium cancer, synovial sarcoma, vasoactive intestinal peptide secreting tumors, acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), Philadelphia Chromosome-Associated Acute Lymphoblastic Leukemia (Ph+ ALL), chronic lymphocytic leukemia (CLL), or chronic myelogenous leukemia (CML).
3. The method of claim 2, wherein the cancer is melanoma.
4. The method of claim 2, wherein the cancer is further characterized by having a mutation in the B-RAF gene.
5. The method of claim 4, wherein the mutation in B-RAF is an activating mutation.
6. The method of claim 2, wherein the cancer is further characterized by having a mutation in the PTEN gene.
7. The method of claim 6, wherein the mutation eliminates PTEN function.
8. The method of claim 7, wherein the cancer also contains a mutation in the B-RAF gene and wherein the mutation is an activating mutation.
9. The method of Claim 1 where the cancer is mediated, at least in part, by inhibiting MEK and PI3K.
10. The method of Claims 1, 2, 3, 4, 5, 6, 7, 8, or 9, wherein the MEK Compound is selected from:
 - 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;
 - 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one;
 - 6-(azetidin-1-ylcarbonyl)-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline;
 - 6-[(3,3-difluoroazetidin-1-yl)carbonyl]-2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)aniline;
 - 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(hydroxymethyl)azetidin-3-ol;
 - 2,3-difluoro-*N*-(2-fluoro-4-iodophenyl)-6-{[3-(methyloxy)azetidin-1-yl]carbonyl}aniline;
 - 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(trifluoromethyl)azetidin-3-ol;
 - 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-prop-2-en-1-ylazetidin-3-ol;

- 3-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]propane-1,2-diol;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethylazetidin-3-ol;
- 5 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-methylazetidin-3-ol;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-2-carboxylic acid;
- 10 [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-2-yl]methanol;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-ethenylazetidin-3-ol;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxylic acid;
- 15 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-one oxime;
- [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanol;
- 1-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-hydroxyazetidin-3-yl]ethane-1,2-diol;
- 20 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-3-carboxamide;
- 25 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-2-carboxamide;
- 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-hydroxyazetidine-2-carboxamide;
- 30 *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]methanesulfonamide;
- N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]acetamide;

1,1-dimethylethyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate;
 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-(pyrrolidin-1-ylmethyl)azetidin-3-ol;
 5 3-[(diethylamino)methyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-ol;
 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(dimethylamino)methyl]azetidin-3-ol;
 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methyl-*N*-prop-2-en-1-ylazetidine-3-carboxamide;
 10 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-methylazetidine-3-carboxamide;
N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidine-3-carboxamide;
 15 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-prop-2-en-1-ylazetidine-3-carboxamide;
 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N*-ethyl-*N*-(2-hydroxyethyl)azetidine-3-carboxamide;
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-2-methylpropanamide;
 20 *N*-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]formamide;
N-[1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]-3,4-dihydroxybutanamide;
 25 methyl [1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-yl]carbamate;
N-butyl-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)azetidin-3-amine;
 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-*N,N*-diprop-2-en-1-ylazetidin-3-amine;
 30 1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-amine;
 1-({4-[(2-fluoro-4-iodophenyl)amino]-3-thienyl}carbonyl)azetidin-3-ol;
 1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*S*)-piperidin-2-yl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[(2*R*)-
piperidin-2-yl]azetidin-3-ol;

1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}carbonyl)-3-[2-pyrrolidin-
2-yl]azetidin-3-ol;

5 3-(aminomethyl)-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-
carbonyl)azetidin-3-ol;

3-[1-aminoethyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-
carbonyl)azetidin-3-ol; and

10 3-[1-aminopropyl]-1-({3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]phenyl}-
carbonyl)azetidin-3-ol.

11. The method of Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 wherein the PI3K Compound is
selected from:

- 15 6-bromo-8-ethyl-4-methyl-2-(methylamino)pyrido[2,3-d]pyrimidin-7(8H)-one;
6-bromo-8-ethyl-4-methyl-2-[(phenylmethyl)amino]pyrido[2,3-d]pyrimidin-7(8H)-
one;
6-bromo-8-ethyl-4-methyl-2-(phenylamino)pyrido[2,3-d]pyrimidin-7(8H)-one;
8-ethyl-2-(ethylamino)-4-methyl-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
6-bromo-8-ethyl-4-methyl-2-[(1-methylethyl)amino]pyrido[2,3-d]pyrimidin-7(8H)-
20 one;
6-bromo-2-[(1,1-dimethylethyl)amino]-8-ethyl-4-methylpyrido[2,3-d]pyrimidin-
7(8H)-one;
6-bromo-2-(cyclopentylamino)-8-ethyl-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
8-ethyl-4-methyl-6-phenyl-2-(phenylamino)pyrido[2,3-d]pyrimidin-7(8H)-one;
25 6-biphenyl-4-yl-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
6-(2,4-difluorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-
7(8H)-one;
6-(3-chloro-4-fluorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-
7(8H)-one;
30 8-ethyl-2-(ethylamino)-4-methyl-6-[4-(methyloxy)phenyl]pyrido[2,3-d]pyrimidin-
7(8H)-one;
6-(2,4-dichlorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-
7(8H)-one;

- 6-(3,4-difluorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methyl-6-[2-(methyloxy)phenyl]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 5 6-bromo-2-(cyclohexylamino)-8-ethyl-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-ethyl-4-methyl-2-[(2-morpholin-4-ylethyl)amino]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-ethyl-4-methyl-2-[(3-morpholin-4-ylpropyl)amino]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 10 6-bromo-2-{[3-(dimethylamino)propyl]amino}-8-ethyl-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methyl-6-[4-(phenyloxy)phenyl]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-[2,4-bis(methyloxy)phenyl]-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 15 6-bromo-8-ethyl-2-[(2-fluorophenyl)amino]-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-6-(3-fluorophenyl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-6-(2-fluorophenyl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 20 8-ethyl-2-(ethylamino)-4-methyl-6-[3-(trifluoromethyl)phenyl]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-6-(4-fluorophenyl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 25 8-ethyl-2-(ethylamino)-4-methyl-6-(2-thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methyl-6-[3-(methyloxy)phenyl]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-(3-chlorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 30 6-bromo-8-ethyl-4-methyl-2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-(4-chlorophenyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;

- 8-ethyl-2-(ethylamino)-4-methyl-6-(3-thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
 8-ethyl-2-(ethylamino)-4-methyl-6-(4-methyl-2-thienyl)pyrido[2,3-d]pyrimidin-
 7(8H)-one;
 8-ethyl-2-(ethylamino)-4-methyl-6-(4-methyl-3-thienyl)pyrido[2,3-d]pyrimidin-
 7(8H)-one;
 1,1-dimethylethyl 2-[8-ethyl-2-(ethylamino)-4-methyl-7-oxo-7,8-dihydropyrido[2,3-
 d]pyrimidin-6-yl]-1H-pyrrole-1-carboxylate;
 6-bromo-8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methylpyrido[2,3-
 d]pyrimidin-7(8H)-one;
 6-bromo-8-ethyl-4-methyl-2-[(4-morpholin-4-ylphenyl)amino]pyrido[2,3-
 d]pyrimidin-7(8H)-one;
 6-bromo-8-ethyl-4-methyl-2-({4-[4-(phenylmethyl)piperazin-1-
 yl]phenyl}amino)pyrido[2,3-d]pyrimidin-7(8H)-one;
 8-ethyl-2-(ethylamino)-4-methyl-6-(1H-pyrrol-2-yl)pyrido[2,3-d]pyrimidin-7(8H)-
 one;
 6-(5-chloro-2-thienyl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-
 7(8H)-one;
 8-ethyl-4-methyl-2-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-6-(2-
 thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
 8-ethyl-2-(ethylamino)-4-methyl-6-pyrimidin-5-ylpyrido[2,3-d]pyrimidin-7(8H)-one;
 8-ethyl-2-(ethylamino)-6-(3-fluoropyridin-4-yl)-4-methylpyrido[2,3-d]pyrimidin-
 7(8H)-one;
 8-ethyl-2-(ethylamino)-6-furan-3-yl-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
 8-ethyl-2-(ethylamino)-4-methyl-6-[1-(phenylmethyl)-1H-pyrazol-4-yl]pyrido[2,3-
 d]pyrimidin-7(8H)-one;
 6-(3,5-dimethylisoxazol-4-yl)-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-
 d]pyrimidin-7(8H)-one;
 8-ethyl-4-methyl-2-({4-[4-(phenylmethyl)piperazin-1-yl]phenyl}amino)-6-(2-
 thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
 6-bromo-2-(ethylamino)-4-methyl-8-(1-methylethyl)pyrido[2,3-d]pyrimidin-7(8H)-
 one;
 2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(2-thienyl)pyrido[2,3-d]pyrimidin-
 7(8H)-one;

- 8-ethyl-2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(2-thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-6-(1H-indol-6-yl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methyl-6-(5-phenyl-2-thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-(ethylamino)-6-furan-3-yl-4-methyl-8-(1-methylethyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methyl-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-ethyl-2-(ethylamino)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-(ethylamino)-4-methyl-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-6-furan-3-yl-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-(2-thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-6-(3-fluorophenyl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-[(4-{{[2-(diethylamino)ethyl]oxy}phenyl)amino]-8-ethyl-4-methyl-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-[(4-hydroxyphenyl)amino]-4-methyl-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-cyclohexyl-2-(ethylamino)-4-methyl-6-(2-thienyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-(3,5-difluorophenyl)-8-ethyl-2-{{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;

- 8-ethyl-4-methyl-6-phenyl-2-({4-[(2-piperidin-1-ylethyl)oxy]phenyl}amino)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-4-methyl-2-({4-[(2-morpholin-4-ylethyl)oxy]phenyl}amino)-6-phenylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 5 6-bromo-2-(ethylamino)-4-methyl-8-[3-(methyloxy)propyl]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-2-(ethylamino)-8-[2-(ethyloxy)ethyl]-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-2-(ethylamino)-4-methyl-8-(2-piperidin-1-ylethyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 10 6-bromo-2-(ethylamino)-8-[3-(ethyloxy)propyl]-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-2-(ethylamino)-4-methyl-8-{3-[(1-methylethyl)oxy]propyl}pyrido[2,3-d]pyrimidin-7(8H)-one;
- 15 6-bromo-2-(ethylamino)-8-(3-hydroxypropyl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-2-(ethylamino)-8-(2-hydroxyethyl)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-cyclopropyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 20 6-bromo-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-acetyl-8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 25 8-ethyl-2-(ethylamino)-4-methyl-6-(1,3-thiazol-2-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-cyclopentyl-2-(ethylamino)-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-cyclopentyl-2-(ethylamino)-4-methyl-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 30 cyclopentyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;

- 8-ethyl-2-(ethylamino)-4-methyl-6-(1H-pyrazol-1-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(1H-pyrazol-1-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 5 8-cyclopentyl-2-(ethylamino)-4-methyl-6-(1H-pyrazol-1-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1H-pyrazol-1-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-8-(1-methylethyl)-6-(1H-pyrazol-1-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 10 8-cyclopentyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1H-pyrazol-1-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-cyclopentyl-2-(ethylamino)-4-methyl-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 15 2-(ethylamino)-4-methyl-8-(1-methylethyl)-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 1,1-dimethylethyl 4-{4-[(6-bromo-8-ethyl-4-methyl-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl)amino]phenyl}piperazine-1-carboxylate;
- 6-bromo-8-ethyl-4-methyl-2-[(4-piperazin-1-ylphenyl)amino]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 20 8-cyclopentyl-2-{[4-(4-ethylpiperazin-1-yl)phenyl]amino}-4-methyl-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-cyclopentyl-2-[(4-fluorophenyl)amino]-4-methyl-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 25 6-bromo-8-ethyl-2-[(4-fluorophenyl)amino]-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 8-ethyl-4-methyl-6-(1H-pyrazol-5-yl)-2-[(2,2,2-trifluoroethyl)amino]pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-cyclopentyl-2-[(4-hydroxyphenyl)amino]-4-methylpyrido[2,3-d]pyrimidin-7(8H)-one;
- 30 2-amino-8-ethyl-4-methyl-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 2-(ethylamino)-4-methyl-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;
- 6-bromo-8-cyclopentyl-4-methyl-2-({4-[(2-piperidin-1-ylethyl)oxy]phenyl}amino)pyrido[2,3-d]pyrimidin-7(8H)-one;

8-ethyl-4-methyl-2-(methylamino)-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;

8-cyclopentyl-4-methyl-2-(phenylamino)-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;

5 1,1-dimethylethyl 4-(4-{[8-cyclopentyl-4-methyl-7-oxo-6-(1H-pyrazol-5-yl)-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino}phenyl)piperazine-1-carboxylate;

8-cyclopentyl-4-methyl-2-[(4-piperazin-1-ylphenyl)amino]-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;

10 2-amino-8-cyclopentyl-4-methyl-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;

8-ethyl-2-[(2-fluoroethyl)amino]-4-methyl-6-(1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-7(8H)-one;

2-amino-4-methyl-8-(1-methylethyl)-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one; and

15 8-cyclopentyl-4-methyl-2-({4-[(2-piperidin-1-ylethyl)oxy]phenyl}amino)-6-(1H-pyrazol-3-yl)pyrido[2,3-d]pyrimidin-7(8H)-one.

12. The method of Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 wherein the PI3K Compound is selected from:

20 4-chloro-*N*-{3-[(3-chloro-4-piperidin-1-ylphenyl)amino]-6-methylquinoxalin-2-yl}benzenesulfonamide;

N-(3-{[2-(ethyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide;

N-(3-{[4-chloro-2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;

25 *N*-[3-({2-[2,5-bis(methyloxy)phenyl]ethyl}amino)quinoxalin-2-yl]benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;

N-(3-{[3,4,5-tris(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;

N-[3-({3-[(phenylmethyl)oxy]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide;

30 *N*-(3-{[3-(phenyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;

N-[3-(piperidin-1-ylamino)quinoxalin-2-yl]benzenesulfonamide;

N-[3-(4-phenylpiperazin-1-yl)quinoxalin-2-yl]benzenesulfonamide;

N-{3-[4-(phenylmethyl)piperidin-1-yl]quinoxalin-2-yl}benzenesulfonamide;

N-{3-[(4-morpholin-4-ylphenyl)amino]quinoxalin-2-yl}benzenesulfonamide;

- N*-(3-{[3-(methyloxy)-5-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[2,5-bis(ethyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-(3-morpholin-4-ylquinoxalin-2-yl)benzenesulfonamide;
- 5 *N*-(3-{[2,5-bis(methyloxy)phenyl]amino}pyrazin-2-yl)-4-chlorobenzenesulfonamide;
- N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-methylbenzenesulfonamide;
- N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- 10 *N*-(3-azidoquinoxalin-2-yl)benzenesulfonamide;
- N*-[3-({[2,5-bis(methyloxy)phenyl]methyl}amino)quinoxalin-2-yl]benzenesulfonamide;
- N*-(3-{[2-methyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-[3-(dimethylamino)quinoxalin-2-yl]benzenesulfonamide;
- 15 *N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)naphthalene-2-sulfonamide;
- 4-(3-Benzensulfonylamino-quinoxalin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester;
- N*-[3-(2-Chloro-5-methoxy-phenylamino)-quinoxalin-2-yl]-benzensulfonamide;
- 3-amino-*N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 20 *N*-(3-piperazin-1-ylquinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-chlorobenzenesulfonamide;
- N*-(3-{4-[(9-oxo-9*H*-fluoren-1-yl)carbonyl]piperazin-1-yl}quinoxalin-2-yl)benzenesulfonamide;
- 25 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide;
- N*-(3-{[4-chloro-3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[4-fluoro-3-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 30 *N*-(3-{[2'-(methyloxy)biphenyl-4-yl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[5-methyl-2-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 3-amino-*N*-(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;

- N*-(3-{[2,5-bis(methyloxy)phenyl]amino}-6,7-dimethylquinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-bromobenzenesulfonamide;
- 5 *N*-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- N*-(3-{[5-chloro-2-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[2-(methyloxy)-5-(trifluoromethyl)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 10 *N*-(3-{[2-(methyloxy)biphenyl-4-yl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 3-amino-*N*-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-,*N*-2-dimethylglycinamide;
- 15 *N*-(3-{[2,5-bis(methyloxy)phenyl]amino}-7-methylquinoxalin-2-yl)benzenesulfonamide;
- N*-(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-(methyloxy)benzenesulfonamide;
- N*-(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-bromobenzenesulfonamide;
- 20 *N*-(3-{[2,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-fluorobenzenesulfonamide;
- N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-fluorobenzenesulfonamide;
- 25 *N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-(methyloxy)benzenesulfonamide;
- N*-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-bromobenzenesulfonamide;
- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-methylpiperidine-4-carboxamide;
- 30 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-piperidin-1-ylpropanamide;
- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-(dimethylamino)butanamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(hydroxyamino)benzenesulfonamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-morpholin-4-ylacetamide;

5 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-*N*-2-methylglycinamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-*L*-alaninamide;

10 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-2-methylalaninamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-*N*-2-*N*-2-dimethylglycinamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*D*-alaninamide;

15 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methylglycinamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-*D*-alaninamide;

20 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methylglycinamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*L*-alaninamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*D*-alaninamide;

25 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylalaninamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylalaninamide;

30 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)-*N*-2-,*N*-2-dimethylglycinamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-[2-(dimethylamino)ethyl]-*N*-2-methylglycinamide;

(2*S*)-2-amino-*N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)butanamide;

- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-[2-(dimethylamino)ethyl]-*N*-2-methylglycinamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-,*N*-2-dimethylglycinamide;
- 5 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methyl-L-alaninamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
- 10 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
- N*-(2-chloro-5-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methylglycinamide;
- 2-(dimethylamino)-*N*-(3-(*N*-(3-(3-(2-(dimethylamino)acetamido)-5-methoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide;
- 15 *N*-(3-{[(3-{[2-acetyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-,*N*-2-dimethylglycinamide;
- N*-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(formylamino)benzenesulfonamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-ethylglycinamide;
- 20 *N*-(5-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-2-methylphenyl)glycinamide;
- 2-azetidin-1-yl-*N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide;
- 25 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-L-prolinamide;
- N*-(3-{[(3-{[2-bromo-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methylglycinamide;
- N*-2-,*N*-2-dimethyl-*N*-(3-{[(3-{[6-(methyloxy)quinolin-8-yl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
- 30 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-L-alaninamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methyl-D-alaninamide;

- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-L-prolinamide;
- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-D-serinamide;
- 5 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)azetidine-3-carboxamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-,2-dimethylalaninamide;
- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methyl-D-alaninamide;
- 10 *N*-(3-{[(3-{[2-bromo-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-,*N*-2-dimethylglycinamide;
- N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-propylglycinamide;
- 15 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-methyl-L-alaninamide;
- N*-(5-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-2-methylphenyl)-beta-alaninamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)piperidine-3-carboxamide;
- 20 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-methyl-1,4-diazepan-1-yl)acetamide;
- (2*S*)-2-amino-*N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)butanamide;
- 25 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-(2-hydroxypropyl)glycinamide;
- N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-(2-fluoroethyl)glycinamide;
- 3-amino-*N*-(2-{[3,5-bis(methyloxy)phenyl]amino}pyrido[2,3-*b*]pyrazin-3-yl)benzenesulfonamide;
- 30 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-[(2-methylpropyl)oxy]glycinamide;
- 1-amino-*N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopropanecarboxamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(formylamino)benzenesulfonamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-(cyclopropylmethyl)glycinamide;

5 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*D*-prolinamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(dimethylamino)azetidin-1-yl]acetamide;

10 *N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*D*-prolinamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)piperidine-2-carboxamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)morpholine-4-carboxamide;

15 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyrrolidin-1-ylacetamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-6-,*N*-6-dimethyl-*L*-lysineamide;

20 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-ethyl-*N*-2-methylglycinamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(1*H*-imidazol-4-yl)acetamide;

1-amino-*N*-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopentanecarboxamide;

25 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-(2-methylpropyl)glycinamide;

N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-*N*-2-ethyl-*N*-2-methylglycinamide;

30 *N*-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(1*H*-imidazol-4-ylmethyl)azetidine-3-carboxamide;

N-(5-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-2-methylphenyl)-*N*-2-,*N*-2-dimethylglycinamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-ethylazetidine-3-carboxamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-(1-methylpyrrolidin-3-yl)glycinamide;
 N-(3-{[(2-{[3,5-bis(methyloxy)phenyl]amino}pyrido[2,3-b]pyrazin-3-yl)amino]sulfonyl}phenyl)-N-2-[2-(dimethylamino)ethyl]-N-2-methylglycinamide;
 5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(3S)-3-hydroxypyrrolidin-1-yl]acetamide;
 1-amino-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclobutanecarboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-butylglycinamide;
 10 N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3-piperidin-1-ylazetidin-1-yl)acetamide;
 3-[(aminocarbonyl)amino]-N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
 15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-hydroxycyclopropanecarboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2,2-dimethylhydrazino)acetamide;
 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-[(2-(dimethylamino)ethyl)amino]benzenesulfonamide;
 20 N-(3-{[(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methylglycinamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-hydroxyacetamide;
 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyridazine-4-carboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(1-methylethyl)glycinamide;
 1-amino-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopentanecarboxamide;
 30 1-amino-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclopropanecarboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(dimethylamino)pyrrolidin-1-yl]acetamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[2-(dimethylamino)ethyl]glycinamide;
2-(dimethylamino)ethyl(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)carbamate;
5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(cyclopropylmethyl)azetidine-3-carboxamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(1,1-dimethylethyl)glycinamide;
N-2-methyl-N-(3-{[(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1H-imidazole-2-carboxamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)isoxazole-5-carboxamide;
15 N-(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2,2,2-trifluoroethyl)glycinamide;
3-amino-N-(3-{[2-methyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-oxocyclopentanecarboxamide;
20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-6-hydroxypyridine-2-carboxamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(3-fluoro-4-hydroxyphenyl)glycinamide;
25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-(furan-2-ylmethyl)azetidine-3-carboxamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyrimidine-5-carboxamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1H-pyrrole-2-carboxamide;
30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-(1-methylethyl)glycinamide;
N-(3-{[(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-,N-2-dimethylglycinamide;

- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-1H-imidazole-4-carboxamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-N-2-,N-2-diethylglycinamide;
- 5 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(3-methylisoxazol-5-yl)acetamide;
- N-2-,N-2-dimethyl-N-(3-{{(3-{{(2-methyl-5-(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)glycinamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-N-2-[(3-hydroxyphenyl)methyl]glycinamide;
- 10 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-1-methyl-1H-pyrrole-2-carboxamide;
- 4-amino-N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)tetrahydro-2H-pyran-4-carboxamide;
- 15 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-[4-(methylamino)piperidin-1-yl]acetamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-piperidin-1-ylacetamide;
- N-(4-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-N-2-,N-2-dimethylglycinamide;
- 20 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-1-methyl-L-prolinamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)thiophene-3-carboxamide;
- 25 3-amino-N-{3-[(2-chloro-5-hydroxyphenyl)amino]quinoxalin-2-yl}benzenesulfonamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-1-(cyclopropylcarbonyl)azetidine-3-carboxamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-(4-methylpiperazin-1-yl)acetamide;
- 30 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-1-(phenylmethyl)azetidine-3-carboxamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino)sulfonyl}phenyl)-2-chloropyridine-3-carboxamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyridin-4-ylacetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-prop-2-en-1-ylglycinamide;
- 5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(phenylmethyl)glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(methyloxy)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-propanoylazetidine-3-carboxamide;
- 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyridine-3-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[2-(methyloxy)ethyl]glycinamide;
- 15 1-acetyl-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)piperidine-4-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-methylpyrrolidin-1-yl)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)furan-3-carboxamide;
- 20 N-2-,N-2-dimethyl-N-(3-{[(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-6-chloropyridine-3-carboxamide;
- 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-chlorobenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyridin-2-ylacetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(dimethylamino)azetidin-1-yl]acetamide;
- 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-pyridin-3-ylacetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-chlorophenyl)acetamide;

- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[3-(dimethylamino)propyl]-N-2-methylglycinamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-ethyl-N-2-(2-hydroxyethyl)glycinamide;
- 5 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[2-(phenylmethyl)pyrrolidin-1-yl]acetamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)propanamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)furan-2-carboxamide;
- 10 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-chloropyridine-4-carboxamide;
- N-2-acetyl-N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
- 15 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)butanamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-chlorobenzamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-methylbenzamide;
- 20 1,1-dimethylethyl{2-[(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)amino]-2-oxoethyl}carbamate;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1,3-benzodioxole-5-carboxamide;
- 25 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-([2-(methyloxy)phenyl]methyl)oxy)glycinamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyridine-4-carboxamide;
- N-(3-{{(3-{{(4-fluoro-3-(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-,N-2-dimethylglycinamide;
- 30 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(3,4-dichlorophenyl)piperazin-1-yl]acetamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl}amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-pyridin-3-ylpropanamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)tetrahydrofuran-3-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[(2-methylphenyl)methyl]glycinamide;
- 5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylbutanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3-fluorophenyl)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(1-methyl-1-phenylethyl)glycinamide;
- 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylcyclopropanecarboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methyl-4-(methyloxy)benzamide;
- 15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylpyridine-3-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-(methyloxy)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-ethylpiperazin-1-yl)acetamide;
- 20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)thiophene-2-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluoro-2-methylbenzamide;
- 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-bromothiophene-3-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-fluorobenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3-methylpiperidin-1-yl)acetamide;
- 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylpropanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino} quinoxalin-2-yl)amino]sulfonyl}phenyl)pentanamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(ethyloxy)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2-fluorophenyl)glycinamide;
- 5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-(dimethylamino)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-methylpiperidin-1-yl)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2-propylphenyl)glycinamide;
- 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pyrazine-2-carboxamide;
- 15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluoro-4-(methyloxy)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,2-dimethylbutanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(4-fluorophenyl)oxy]acetamide;
- 20 1-acetyl-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)azetidine-3-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(4-methylphenyl)glycinamide;
- 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-phenylglycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-prop-2-en-1-ylpiperazin-1-yl)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylbenzamide;
- 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-(methyloxy)propanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-methylfuran-2-carboxamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,2-dimethylpropanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[(phenylmethyl)oxy]glycinamide;
- 5 N-{3-[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl}-N-2,N-2-dimethylglycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(3-chlorophenyl)glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)cyclobutanecarboxamide;
- 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[3-(methyloxy)phenyl]acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-methylcyclopropanecarboxamide;
- 15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluorobenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-(dimethylamino)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3,4-dichlorobenzamide;
- 20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-{[2-(methylthio)phenyl]methyl}glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-fluorophenyl)acetamide;
- 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-ethyl-N-2-(1-methylethyl)glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1,3-thiazole-4-carboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-(phenylmethyl)glycinamide;
- 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2-thienylmethyl)glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(pyridin-2-ylmethyl)glycinamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-(methyloxy)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[(3-chloro-4-methylphenyl)methyl]glycinamide;
- 5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-methylpentanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-chlorophenyl)acetamide;
- 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-fluoro-4-methylbenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(2-methylphenyl)oxy]acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-cyclohexylacetamide;
- 15 (1R,2R)-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-phenylcyclopropanecarboxamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-chlorobenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[2-(methyloxy)phenyl]acetamide;
- 20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-[3-(methyloxy)phenyl]propanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2-fluoro-4-methylphenyl)glycinamide;
- 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[(3-fluorophenyl)methyl]glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(methyloxy)phenyl]acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-phenylacetamide;
- 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,4-dichlorobenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-oxocyclohexanecarboxamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(3-fluorophenyl)glycinamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3-chlorophenyl)acetamide;
5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2-phenylpropyl)glycinamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[(2,4-dimethylphenyl)methyl]glycinamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-methylpiperidin-1-yl)acetamide;
10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[2-(methyloxy)phenyl]glycinamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(3,4-dihydroisoquinolin-2(1H)-yl)acetamide;
15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)pent-4-enamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2-methylphenyl)glycinamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-oxopiperidin-1-yl)acetamide;
20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-fluorobenzamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(1-phenylethyl)glycinamide;
25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-fluoro-6-(methyloxy)benzamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[2-(1-methylethyl)phenyl]glycinamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-[2-(methyloxy)phenyl]propanamide;
30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-methylpentanamide;
N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-phenylmorpholin-4-yl)acetamide;

- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-[4-(methyloxy)phenyl]propanamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-cyclopentyl-N-2-prop-2-en-1-ylglycinamide;
- 5 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-[2-(methyloxy)ethyl]glycinamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-cyclopropyl-4-oxobutanamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[3-(1,1-dimethylethyl)phenyl]glycinamide;
- 10 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(cyclopropylmethyl)-N-2-propylglycinamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-oxocyclopentyl)acetamide;
- 15 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(4-chlorophenyl)glycinamide;
- 2-(1,4'-bipiperidin-1'-yl)-N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-cyclopentylpiperazin-1-yl)acetamide;
- 20 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-methylphenyl)acetamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-[(5-fluoro-2-methylphenyl)methyl]glycinamide;
- 25 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3,3-dimethylbutanamide;
- 2-(2-chlorophenylamino)-N-(3-(N-(3-(3,5-dimethoxyphenylamino)quinoxalin-2-yl)sulfamoyl)phenyl)acetamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-5-fluoro-2-methylbenzamide;
- 30 N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-fluoro-3-methylbenzamide;
- N-(3-{{(3-{{(3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,3-dichlorobenzamide;

- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(phenyloxy)acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-(2,3-dimethylphenyl)glycinamide;
- 5 3-amino-N-(3-{[3,5-bis(methyloxy)phenyl]amino}pyrido[2,3-b]pyrazin-2-yl)benzenesulfonamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-fluoro-5-methylbenzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-{[(4-methylphenyl)methyl]oxy}glycinamide;
- 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(1-methylethyl)piperazin-1-yl]acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-fluorophenyl)acetamide;
- 15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-methylbutanamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-methyl-2-(methyloxy)benzamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-propylpiperidin-1-yl)acetamide;
- 20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[(3-methylphenyl)oxy]acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)tetrahydrofuran-2-carboxamide;
- 25 1,1-dimethylethyl 2-{[(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)amino]carbonyl}piperidine-1-carboxylate;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-(pyridin-3-ylmethyl)glycinamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-ethyl-N-2-phenylglycinamide;
- 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-{[2-(methyloxy)ethyl]oxy}acetamide;
- N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-cyclopentylpropanamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2,5-dichlorobenzamide;
 2-(4-acetylpiperazin-1-yl)-N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide;
 5 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-5-fluoro-2-(methyloxy)benzamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-cyclohexyl-N-2-ethylglycinamide;
 10 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-5-methylisoxazole-3-carboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3-methylpyridine-2-carboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(methyloxy)pyridine-3-carboxamide;
 15 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-3,5-dichlorobenzamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(1,3-thiazolidin-3-yl)acetamide;
 20 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-formylpiperazin-1-yl)acetamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(methyloxy)benzamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-methyl-N-2-(2-methylpropyl)glycinamide;
 25 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(4-formyl-1,4-diazepan-1-yl)acetamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-1-phenylcyclopropanecarboxamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2,6-dimethylmorpholin-4-yl)acetamide;
 30 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2-phenylpyrrolidin-1-yl)acetamide;
 N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-(2,6-dimethylpiperidin-1-yl)acetamide;

- N-{3-[(3-[(4-chlorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}-N-2-,N-2-dimethylglycinamide;
- N-{3-[(3-[(3-fluorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}-N-2-,N-2-dimethylglycinamide;
- 5 N-{3-[(3-[(3-chlorophenyl)amino]quinoxalin-2-yl)amino)sulfonyl]phenyl}-N-2-,N-2-dimethylglycinamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(dimethylamino)-1-methylethyl]benzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(dimethylamino)ethyl]benzamide;
- 10 5-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(dimethylamino)ethyl]-2-fluorobenzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-pyrrolidin-3-ylbenzamide;
- 15 3-{[(3-[(3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(dimethylamino)ethyl]benzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-(2-pyrrolidin-1-ylethyl)benzamide;
- N-(2-aminoethyl)-3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}benzamide;
- 20 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-(piperidin-2-ylmethyl)benzamide;
- 25 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-(1-methylazetidin-3-yl)benzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-(2-piperidin-1-ylethyl)benzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(diethylamino)ethyl]benzamide;
- 30 3-{[(3-[(3,5-bis(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-[2-(dimethylamino)ethyl]-N-methylbenzamide;
- 3-{[(3-[(2-chloro-5-(methyloxy)phenyl]amino)quinoxalin-2-yl)amino)sulfonyl}-N-(1-methylpiperidin-3-yl)benzamide;

- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-piperidin-3-ylbenzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[(1-methylpiperidin-2-yl)methyl]benzamide;
- 5 N-{2-[bis(2-hydroxyethyl)amino]ethyl}-3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1-ethylpiperidin-3-yl)benzamide;
- 10 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide;
- 3-[(3-aminopyrrolidin-1-yl)carbonyl]-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 5-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(dimethylamino)ethyl]-2-(methyloxy)benzamide;
- 15 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[3-(methylamino)pyrrolidin-1-yl]carbonyl}benzenesulfonamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzoic acid;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-morpholin-4-ylethyl)benzamide;
- 20 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[(1-ethylpyrrolidin-2-yl)methyl]benzamide;
- 3-[(4-amino-3-oxopyrazolidin-1-yl)carbonyl]-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 25 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-methylbenzamide;
- 3-[(3-aminoazetidin-1-yl)carbonyl]-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(pyridin-3-ylmethyl)benzamide;
- 30 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(pyridin-2-ylmethyl)benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-hydroxyethyl)benzamide;

- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(3-oxopyrazolidin-4-yl)benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(1H-imidazol-4-yl)ethyl]benzamide;
- 5 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[3-(dimethylamino)pyrrolidin-1-yl]carbonyl}benzenesulfonamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(pyridin-4-ylmethyl)benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-methyl-N-(1-methylpyrrolidin-3-yl)benzamide;
- 10 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[3-(diethylamino)pyrrolidin-1-yl]carbonyl}benzenesulfonamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-1H-pyrrol-1-ylbenzamide;
- 15 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(3-pyrrolidin-1-ylpropyl)benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-cyanoethyl)-N-methylbenzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(methyloxy)ethyl]benzamide;
- 20 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-cyanoethyl)-N-ethylbenzamide;
- 3-[(3-aminopiperidin-1-yl)carbonyl]-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 25 3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzoic acid;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(dimethylamino)propyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-morpholin-4-ylbenzamide;
- 30 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-[(2,2-dimethylhydrazino)carbonyl]benzenesulfonamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(1H-imidazol-1-yl)propyl]benzamide;

- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(diethylamino)propyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-cyanoethyl)benzamide;
- 5 methylN-[(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)carbonyl]-beta-alaninate;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(methylthio)ethyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(ethylthio)ethyl]benzamide;
- 10 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(ethylthio)ethyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[2-(dimethylamino)ethyl]-N-ethylbenzamide;
- 15 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(2-oxopyrrolidin-1-yl)propyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(2-pyridin-4-ylethyl)benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(ethyloxy)propyl]benzamide;
- 20 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(3-morpholin-4-ylpropyl)benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(methyloxy)propyl]benzamide;
- 25 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(propyloxy)propyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-(propyloxy)propyl]benzamide;
- ethylN-[(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)carbonyl]-beta-alaninate;
- 30 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[3-[(1-methylethyl)oxy]propyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1,1-dimethyl-2-piperidin-1-ylethyl)benzamide;

- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-methyl-N-propylbenzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-piperidin-1-ylbenzamide;
- 5 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[1-methyl-2-(methyloxy)ethyl]benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1,1-dimethyl-2-morpholin-4-ylethyl)benzamide;
- 10 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-({2-[(dimethylamino)methyl]piperidin-1-yl}carbonyl)benzenesulfonamide;
- N-[3-(butyloxy)propyl]-3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}benzamide;
- 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-[4-(diethylamino)-1-methylbutyl]benzamide;
- 15 3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-N-(1,1-dimethyl-2-oxo-2-piperidin-1-ylethyl)benzamide;
- N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-[(4-methylpiperazin-1-yl)carbonyl]benzenesulfonamide;
- N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{[2-(piperidin-1-ylmethyl)piperidin-1-yl]carbonyl}benzenesulfonamide;
- 20 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-oxo-1,6-dihydropyridine-3-sulfonamide;
- 25 3-amino-N-(3-{[6-(methyloxy)quinolin-8-yl]amino}quinoxalin-2-yl)benzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)thiophene-2-sulfonamide;
- N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-cyanobenzenesulfonamide;
- 30 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(methylamino)benzenesulfonamide;
- N-(2-{[3,5-bis(methyloxy)phenyl]amino}pyrido[2,3-b]pyrazin-3-yl)-3-nitrobenzenesulfonamide;

- N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(1-{[2-(dimethylamino)ethyl]amino}ethyl)benzenesulfonamide;
- 3-amino-N-(3-{[3-(methyloxy)-5-nitrophenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 5 3-acetyl-N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 3-amino-N-(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 10 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-N'-[2-(dimethylamino)ethyl]benzene-1,3-disulfonamide;
- N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-N'-[3-(dimethylamino)propyl]benzene-1,3-disulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-chloropyridine-3-sulfonamide;
- 15 N-(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-{5-[(dimethylamino)methyl]-1,3,4-oxadiazol-2-yl}benzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-{[2-(dimethylamino)ethyl]amino}pyridine-3-sulfonamide;
- 3-amino-N-(3-{[3-amino-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)benzenesulfonamide;
- 20 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(dimethylamino)benzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-{[2-(dimethylamino)ethyl]oxy}pyridine-3-sulfonamide;
- 25 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-6-(dimethylamino)pyridine-3-sulfonamide;
- N-{3-[(3-{[4-fluorophenyl]amino}quinoxalin-2-yl)amino)sulfonyl]phenyl}-N-2,N-2-dimethylglycinamide;
- N-(3-{[2-chloro-6-(methyloxy)pyridin-4-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- 30 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-cyanobenzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-fluorobenzenesulfonamide;

- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-fluoro-2-methylbenzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-methylbenzenesulfonamide;
- 5 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-cyanobenzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3,5-difluorobenzenesulfonamide;
- 10 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-chlorobenzenesulfonamide;
- N-(4-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)acetamide;
- N-(3-{[6-(methyloxy)quinolin-8-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- 15 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(2H-tetrazol-5-yl)benzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)naphthalene-1-sulfonamide;
- 3-nitro-N-[3-(pyridin-4-ylamino)quinoxalin-2-yl]benzenesulfonamide;
- N-{3-[(2,6-dichloropyridin-4-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;
- 20 N-{3-[(2-chloropyridin-4-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;
- N-(3-{[4,6-bis(methyloxy)pyrimidin-2-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- N-(3-{[4-hydroxy-6-(methyloxy)pyrimidin-2-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- 25 N-{[(3-{[(3-{[2-chloro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}-4-methylphenyl)amino](dimethylamino)methylidene}-N-methylmethanaminium;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-fluorobenzenesulfonamide;
- 30 N-(3-{[2-bromo-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-[(difluoromethyl)oxy]benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-(trifluoromethyl)benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-chloro-4-fluorobenzenesulfonamide;

5 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-(trifluoromethyl)benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(methylsulfonyl)benzenesulfonamide;

10 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2,5-dichlorothiophene-3-sulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3,5-dichlorobenzenesulfonamide;

N-(3-{[2-methyl-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;

15 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-[(trifluoromethyl)oxy]benzenesulfonamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-2-[4-(dimethylamino)piperidin-1-yl]acetamide;

20 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-5-chloro-2-(methyloxy)benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-(trifluoromethyl)benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2,5-bis(methyloxy)benzenesulfonamide;

25 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3,5-dimethylisoxazole-4-sulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-5-bromo-2-(methyloxy)benzenesulfonamide;

30 N-(3-{[3-fluoro-5-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-fluoro-4-methylbenzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-chloro-4-methylbenzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2,5-dimethylthiophene-3-sulfonamide;

N-(3-{[3-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;

N-{3-[(2-chloro-5-hydroxyphenyl)amino]quinoxalin-2-yl}-3-

5 nitrobenzenesulfonamide;

N-(3-{[(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-4-methyl-3-(methyloxy)benzamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-1-phenylmethanesulfonamide;

10 N-(3-{[3-(methyloxy)-5-nitrophenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-1-(3-chlorophenyl)methanesulfonamide;

15 N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4,5-dichlorothiophene-2-sulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-5-chloro-1,3-dimethyl-1H-pyrazole-4-sulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide;

20 N-{3-[(3-hydroxyphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;
3-nitro-N-[3-({3-[(trifluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]benzenesulfonamide;

3-nitro-N-[3-(pyridin-3-ylamino)quinoxalin-2-yl]benzenesulfonamide;

N-[3-(morpholin-4-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;

25 3-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyldimethylcarbamate;

N-{3-[(2-chloropyridin-3-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;

3-nitro-N-[3-(tetrahydro-2H-pyran-4-ylamino)quinoxalin-2-yl]benzenesulfonamide;

N-{3-[(4-fluorophenyl)amino]quinoxalin-2-yl}benzenesulfonamide;

30 N-[3-({3-[(1-methylethyl)oxy]phenyl}amino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;

N-{3-[(3-hydroxy-2-methylphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;

N-{3-[(2,5-difluorophenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;

- N-[3-({3-[(difluoromethyl)oxy]phenyl}amino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;
- N-(3-{[2-(methyloxy)pyridin-3-yl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- 5 N-(3-{[3-(ethyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- N-{3-[(2,2-difluoro-1,3-benzodioxol-4-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;
- N-{3-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide;
- N-[3-(4-amino-1H-indol-1-yl)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;
- 10 N-[3-(1H-indol-4-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;
- N-2-,N-2-dimethyl-N-(3-{[(3-{[4-(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)glycinamide;
- N-[3-(1H-indazol-6-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;
- N-{4-(methyloxy)-3-[(3-{[(3-nitrophenyl)sulfonyl]amino}quinoxalin-2-yl)amino]phenyl}acetamide;
- 15 N-{3-[(4-methylpyridin-3-yl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;
- N-(3-{[2,3-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-2-cyanobenzenesulfonamide;
- 20 3-nitro-N-[3-(1H-pyrazolo[3,4-d]pyrimidin-4-ylamino)quinoxalin-2-yl]benzenesulfonamide;
- N-[3-(1,3-benzoxazol-4-ylamino)quinoxalin-2-yl]-3-nitrobenzenesulfonamide;
- N-(3-{[2,6-difluoro-3-(methyloxy)phenyl]amino}quinoxalin-2-yl)-3-nitrobenzenesulfonamide;
- 25 N-{3-[(3-{[4-fluoro-3-methylphenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl}-N-2-,N-2-dimethylglycinamide;
- N-{3-[(3-{[3,5-dimethylphenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl}-N-2-,N-2-dimethylglycinamide;
- 30 N-(3-{[(3-{[2,4-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)amino]sulfonyl}phenyl)-N-2-,N-2-dimethylglycinamide;
- N-{3-[(3,5-dihydroxyphenyl)amino]quinoxalin-2-yl}-3-nitrobenzenesulfonamide;
- N-[3-({[3-(2,3-dihydro-1H-inden-5-ylamino)quinoxalin-2-yl]amino}sulfonyl)phenyl]-N-2-,N-2-dimethylglycinamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)-4-[(1-methylethyl)oxy]benzenesulfonamide;

N-(3-{[3,5-bis(methyloxy)phenyl]amino}quinoxalin-2-yl)biphenyl-4-sulfonamide;

N-[3-(2-chloro-5-[(difluoromethyl)oxy]phenyl)amino]quinoxalin-2-yl]-3-nitrobenzenesulfonamide; and

a pharmaceutically acceptable salt or solvate thereof.

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