

QUINOLINE DERIVATIVES AS AXL KINASE INHIBITORS

The present invention relates to novel compounds which are inhibitors of
5 receptor tyrosine kinases of the AXL receptor family. These compounds are
suitable for the treatment or prevention of disorders associated with,
accompanied by or caused by hyperfunction of a receptor of the AXL family.
The compounds are suitable for the treatment of hyperproliferative disorders,
such as cancer, particularly cancer metastases.

10 Breast cancer is the most common malignant disease in western women. In
these patients, it is not the primary tumour, but its metastases at distant sites
that are the main cause of death (1). Despite surgical removal of the primary
tumour, relapse at local or distant sites may occur because of incomplete
15 removal of primary tumour tissue or the presence of micrometastases
undetectable at the time of diagnosis. The development of chemotherapy as
well as endocrine-and radiation therapy, administered as adjuvant treatment
after surgery, has led to a reduction in the risk of relapse to 20-40%.
However, adjuvant treatment has a wide range of acute and long-term side
20 effects. Over the past twenty years, with the advances in understanding the
molecular basis of signalling pathway dysregulation in various cancers, a
new era of cancer therapy has begun, which is characterized by the
identification of critical regulators of malignant properties of cancer cells as
molecular targets (2, 3).

25 Deregulated expression of protein kinases by gene deletion, -mutation or
-amplification has been found to be important for tumour initiation and
-progression, involving cancer cell proliferation, -survival, -motility and
-invasivity as well as tumour angiogenesis and chemotherapy resistance (4,
30 5). Because of the advanced understanding of their critical functions in
oncogenesis, protein kinases have been at the forefront of targeted cancer
therapy development since the 1980s. Most of the novel targeted cancer
therapeutics currently approved by the FDA in clinical use is interfering with

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the signalling action of protein kinases. More than 100 additional protein kinase inhibitors and antibodies are in clinical trials, making kinases after G protein-coupled receptors the second most popular drug target class in the pharmaceutical and biotech industries (3).

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In breast cancer, the receptor tyrosine kinase HER2/neu is overexpressed due to gene amplification in tumours of about 25% of breast cancer patients, and enhanced expression correlates with lack of response to adjuvant therapy and poor prognosis (6). Based on this discovery, Herceptin, a monoclonal antibody against HER2/neu oncoprotein, has been developed and is in clinical use since 1998 both as a single agent and in combination with chemotherapies for HER2/neu overexpressing metastatic breast cancer, which has helped to significantly prolong survival of patients (7, 8). However, metastatic breast cancer patients showing no overexpression of HER2/neu do not benefit from this therapy. Therefore, novel therapeutic targets are still urgently needed for intervention in breast cancer metastatic progression.

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To identify the genes that mediate progression of breast cancer, we have focused on key elements of the phosphoprotein-mediated signalling system because of its established role in human cancer. After systematically analyzing expression profiles of kinases of thirteen weakly invasive and eight highly invasive breast cancer cell lines and normal mammary epithelia cell lines by cDNA array hybridization analysis, we identified a cluster of genes characteristic for highly invasive cell types. The RTK AXL was part of the gene cluster predictive of the aggressiveness of breast cancer cells.

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The mammalian AXL RTK subfamily includes three closely related members: AXL, SKY, and MER. The subfamily is characterised by an extracellular domain, consisting of two immunoglobulin-like domains followed by two fibronectin type 3-like domains. GAS6, originally isolated as a growth arrest-specific gene, is the common ligand for AXL subfamily receptors (9-11). GAS6 has the highest affinity for AXL, followed by SKY, and finally MER (11). GAS6-AXL signalling has been implicated in a host of discrete cellular

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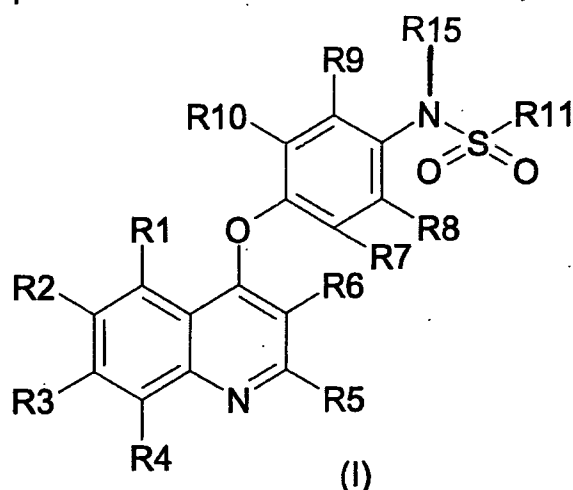
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responses including cell survival, proliferation, migration and adhesion (12).

AXL was originally isolated from patients with chronic myelogenous leukaemia and was shown to have transforming potential when overexpressed (13, 14). Subsequently, AXL expression has been reported in a wide variety of human cancers(15-20). Especially, in breast cancer patients a significant correlation was found between AXL and tumour stage (15). Moreover, some reports indicated that AXL might be involved in cancer progression (21, 22).

SUMMARY OF THE INVENTION

According to the present invention, compounds represented by formula (I) or pharmaceutically acceptable salts or solvates thereof are provided:



wherein

- R¹, R², R³ and R⁴, which may be the same or different, represent hydrogen, hydroxyl, nitro, halogen, cyano, NR¹²R¹³, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, or C₁₋₆ alkoxy,

wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl; halogen, C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxy carbonyl; -(C=O)-NR¹²R¹³, and/or -NR¹²R¹³ wherein R¹² and R¹³, which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or alternatively

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R¹² and R¹³ may combine with the nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group; which is optionally mono- or polysubstituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein R² and/or R³ also may be -O-(CH₂)_n-R¹⁴ wherein n is an integer of 0 to 6, -(CH₂)_n- is optionally substituted by C₁₋₆ alkyl, hydroxyl, or a halogen atom, and R¹⁴ represents a hydrogen atom; hydroxyl; a halogen atom; C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxycarbonyl; -(C=O)-NR¹²R¹³, -NR¹²R¹³ wherein R¹² or R¹³ which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or alternatively R¹² and R¹³ may combine with the nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group; in which the heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; amino in which one or two hydrogen atoms on the amino group are optionally substituted by C₁₋₆ alkyl or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system, and the C₁₋₆ alkyl group is optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or

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unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; when the carbocyclic or heterocyclic group is substituted by two C₁₋₆ alkyl groups, the two alkyl groups may combine together to form an alkylene chain; and the carbocyclic or heterocyclic group may be condensed with
5 another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic group to form a bicyclic group. When n = 0, -(CH₂)_n- represents a bond,

- R⁵ and R⁶, which may be the same or different, represent a hydrogen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, halogen, cyano or nitro,

10 wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl; halogen, C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxycarbonyl; -(C=O)-NR¹²R¹³, and/or -NR¹²R¹³; wherein R¹² and R¹³, which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or
15 alternatively R¹² and R¹³ may combine with the nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group; in which the heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-
20 membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system,

- R⁷, R⁸, R⁹ and R¹⁰, which may be the same or different, represent a
25 hydrogen atom, halogen, nitro, C₁₋₆ alkyl, C₁₋₆ alkoxy,

wherein the C₁₋₆ alkyl or C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl and/or halogen, C₁₋₄ alkyl and/or C₁₋₄ alkoxy, wherein the C₁₋₆ alkyl, C₁₋₆ alkoxy, wherein the C₁₋₆ alkyl or C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl and/or halogen,

30 - R¹¹ represents

(i) a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally mono- or polysubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom,

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or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group,

5 (ii) C₁₋₆ alkyl or C₁₋₆ alkoxy which is unsubstituted or substituted by a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally mono- or polysubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, or

10 (iii) a nitrogen atom substituted with a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally mono- or polysubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and

20 - R¹⁵ represents a hydrogen atom or C₁₋₆ alkyl.

In one embodiment, the present invention relates to compounds as described above, preferably with the proviso that the compound is not N-[4-
25 [(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-benzenemethanesulfonamide, N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-benzeneethanesulfonamide, or N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-benzenepropanesulfonamide. In a further embodiment, the present invention refers to compounds as described above, preferably with the proviso that compounds wherein R⁷ is F and R¹⁰ is H are
30 excluded.

The compounds of the present invention are efficient inhibitors of AXL

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receptor tyrosine kinase autophosphorylation and, thus, are suitable for the treatment of hyperproliferative disorders associated with, accompanied by and/or caused by AXL hyperfunction, particularly AXL receptor tyrosine kinase induced hyperproliferative disorders.

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DETAILED DESCRIPTION OF THE INVENTION

The compounds of the present invention are quinoline-substituted sulfonamide derivatives which are inhibitors of autophosphorylation of
10 receptors of the AXL family, particularly of the human AXL receptor. The compounds of the invention are capable of inhibiting cell proliferation and, thus, are suitable for the treatment and/or prevention of AXL receptor tyrosine kinase induced hyperproliferative disorders, particularly selected from the group consisting of cancer and primary tumor metastases. In a
15 preferred embodiment of the invention, the AXL receptor tyrosine kinase induced disorders are associated with AXL receptor tyrosine kinase receptor overexpression and/or hyperactivity, e.g. an increased degree of autophosphorylation compared to normal tissues. The disorders may be selected from breast, colon, prostate, lung, gastric, ovarian, endometrial,
20 renal, hepatocellular, thyroid, uterine, esophagus, squamous cell cancer, leukemia, osteosarcoma, melanoma, glioblastoma and neuroblastoma. In an especially preferred embodiment, the disorders are selected from breast cancer, glioblastoma, renal cancer, non-small cell lung cancer (NSCLC), and melanoma. Most preferably, the disorder is breast cancer. It should be
25 noted, however, that the compounds of the present invention are also suitable for the prevention and/or treatment for other hyperproliferative disorders, particularly benign hyperproliferative disorders such as benign prostate hyperplasia.

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In a further especially preferred embodiment of the present invention, the compounds as described above are used for the treatment of cancer metastases, particularly primary metastases, optionally in combination with surgery, irradiation and/or administration of further antitumor agents, such as

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chemotherapeutic agents and/or antitumor antibodies.

The compounds of the present invention are characterized by their ability to inhibit AXL receptor tyrosine kinase autophosphorylation in a cellular system, e.g. in NIH3T3 cells. In a preferred embodiment of the present invention, the compounds have an IC₅₀ value of 10 μM or less, more preferably of 5 μM or less, even more preferably of 2.5 μM or less, and most preferably of 1 μM or less.

In the compounds of formula (I), the terms "alkyl," "alkoxy," "alkenyl," and "alkynyl" as used herein as a group or a part of a group respectively mean straight chain or branched chain alkyl, alkoxy, alkenyl, and alkynyl.

C₁₋₆ alkyl is preferably C₁₋₄ alkyl.

C₁₋₆ alkoxy is preferably C₁₋₄ alkoxy.

C₂₋₆ alkenyl is preferably C₂₋₄ alkenyl.

C₂₋₆ alkynyl is preferably C₂₋₄ alkynyl.

Examples of C₁₋₆ alkyl include methyl, ethyl, n-propyl, isopropyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, and n-hexyl.

Examples of C₁₋₆ alkoxy include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, s-butoxy, and t-butoxy.

Examples of C₂₋₆ alkenyl include allyl, butenyl, pentenyl, and hexenyl.

Examples of C₂₋₆ alkynyl include 2-propynyl, butynyl, pentynyl, and hexynyl.

The expression "alkyl optionally substituted by" as used herein refers to alkyl, in which one or more hydrogen atoms on the alkyl group have been

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substituted by one or more substituents which may be the same or different, and unsubstituted alkyl. It will be apparent to a person having ordinary skill in the art that the maximum number of substituents may be determined depending upon the number of substitutable hydrogen atoms on the alkyl group. This is true of a group having a substituent other than the alkyl group.

The term "halogen" means a fluorine, chlorine, bromine, or iodine atom. Preferably, the term halogen means a fluorine or chlorine atom.

The three- to twelve-membered ring system may comprise a saturated or unsaturated three- to eight-membered carbocyclic ring, preferably a four- to seven-membered, more preferably five- or six-membered, saturated or unsaturated carbocyclic ring. Examples of saturated or unsaturated three- to ten-membered carbocyclic rings include phenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

Further, the three- to twelve-membered ring system may comprise a saturated or unsaturated three- to eight-membered heterocyclic group containing at least one hetero-atom selected from oxygen, nitrogen, and sulfur atoms. The heterocyclic group preferably contains one, two or three hetero-atoms with the remaining ring-constituting atoms being carbon atoms. The heterocyclic group preferably comprises a saturated or unsaturated four- to seven-membered heterocyclic ring, more preferably a saturated or unsaturated five- or six-membered heterocyclic ring. Examples of saturated or unsaturated three- to eight-membered heterocyclic groups include thienyl, pyridyl, 1,2,3-triazolyl, thiazolyl, imidazolyl, isoxazolyl, pyrazolyl, piperazinyl, quinoliny, piperidyl, morpholiny, homopiperazinyl, thiomorpholiny, tetrahydropyrrolyl, and azepanyl.

Further, the saturated or unsaturated carboxylic and heterocyclic ring systems include condensed ring systems wherein a cyclic group is condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic ring to form a bicyclic group, preferably a

saturated or unsaturated nine- to twelve-membered bicyclic carbocyclic or heterocyclic group. Such bicyclic groups include naphthyl, quinolyl, 1,2,3,4-tetrahydroquinolyl, 1,4-benzoxanyl, indanyl, indolyl, 1,2,3,4-tetrahydronaphthyl, and phthalimidyl.

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R¹ preferably represents a hydrogen atom or C₁₋₄ alkyl, e.g. methyl. More preferably, R¹ represents a hydrogen atom.

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R² and R³ may be the same or different. Preferably, one of R² and R³ represents a group other than a hydrogen atom. More preferably, R² and/or R³ represent hydroxyl, optionally substituted C₁₋₆ alkoxy, halogen, or cyano. In a preferred embodiment, C₁₋₆ alkoxy is not substituted by amino. In an especially preferred embodiment, R² represents unsubstituted C₁₋₆ alkoxy, still more preferably methoxy or fluorine. In a further preferred embodiment, R² represents unsubstituted C₁₋₆ alkoxy, still more preferably, methoxy, and R³ represents hydroxyl or optionally substituted C₁₋₆ alkoxy, or alternatively R² represents hydroxyl or optionally substituted C₁₋₆ alkoxy and R³ represents unsubstituted C₁₋₆ alkoxy, still more preferably unsubstituted methoxy. For example, R² and R³ both represent methoxy. In a further preferred embodiment, R² is halogen, e.g. fluorine and R³ is hydrogen. According to another preferred embodiment, R³ is preferably selected from the group consisting of benzyloxy, 3-amino-propoxy, 2-morpholin-4-yl-ethoxy, 3-(4-methyl-piperidin-1-yl), 3-(3-methyl-piperidin-1-yl), 3-morpholin-4-yl-propoxy). In a particular preferred embodiment, R² is methoxy and R³ is selected from said group.

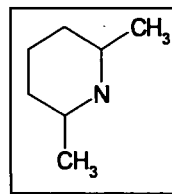
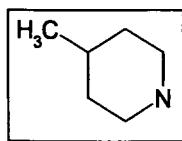
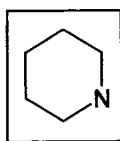
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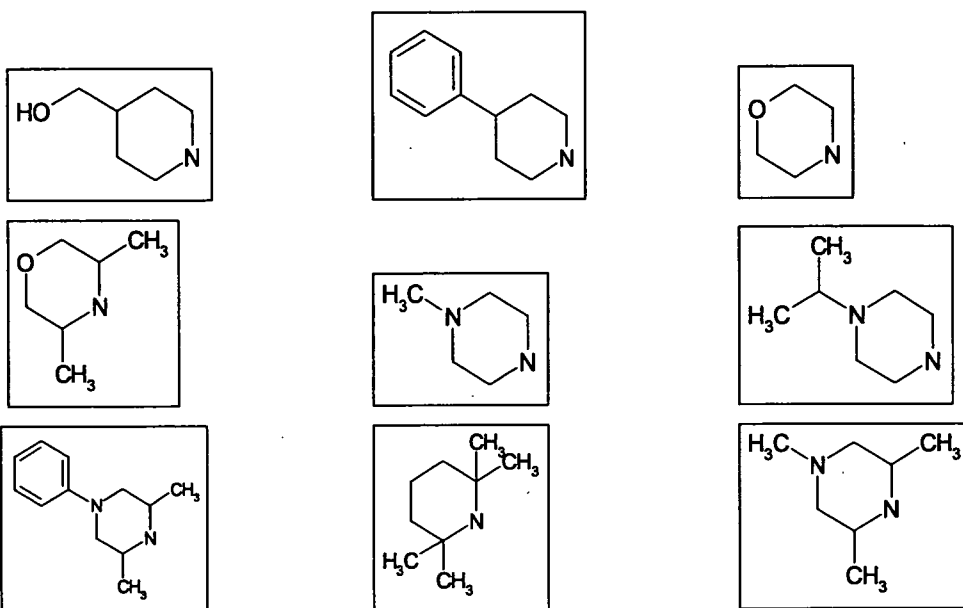
In a still further preferred embodiment, R² and/or R³ may represent -O-(CH₂)_n-R¹⁴ wherein n is an integer of 0 to 6, -(CH₂)_n- is optionally substituted by C₁₋₆ alkyl, hydroxyl, or a halogen atom, and R¹⁴ represents a hydrogen atom; hydroxyl; a halogen atom; C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxy carbonyl; -(C=O)-NR¹²R¹³, -NR¹²R¹³ wherein R¹² or R¹³ which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or alternatively R¹² and R¹³ may combine with the

nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group, in which the heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system, amino in which one or two hydrogen atoms on the amino group are optionally substituted by C₁₋₆ alkyl or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system, and the C₁₋₆ alkyl group is optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; when the carbocyclic or heterocyclic group is substituted by two C₁₋₆ alkyl groups, the two alkyl groups may combine together to form an alkylene chain; and the carbocyclic or heterocyclic group may be condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic group to form a bicyclic group. When n = 0, -(CH₂)_n- represents a bond.

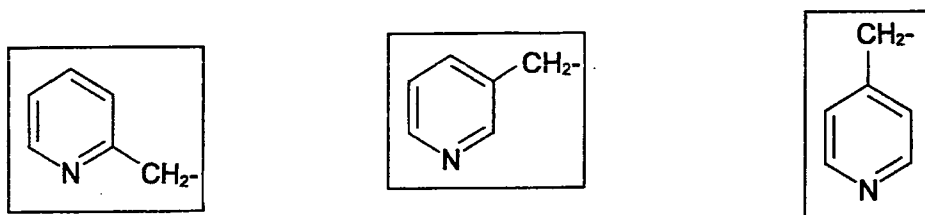
More preferably, R¹⁴ may represent a saturated heterocyclic ring attached through its nitrogen atom, wherein R¹⁴ is selected from the following:



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More preferably, R^{14} may represent an unsaturated heterocyclic ring attached through its CH_2 group, wherein R^{14} is selected from the following:



R^4 is preferably hydrogen, C_{1-6} alkyl or C_{1-6} alkoxy, wherein the C_{1-6} alkyl or C_{1-6} alkoxy group is optionally substituted with one or more halogen atoms. More preferably, R^4 is hydrogen or trifluoromethyl.

- 10 In an especially preferred embodiment, R^1 and R^4 are hydrogen and R^2 and R^3 are C_{1-6} alkoxy, particularly methoxy. In a further especially preferred embodiment, R^1 , R^2 and R^3 are hydrogen and R^4 is C_{1-6} alkyl optionally substituted, particularly trifluoromethyl. In a still further especially preferred embodiment, R^1 , R^3 and R^4 are hydrogen and R^2 is halogen, e.g. fluorine.

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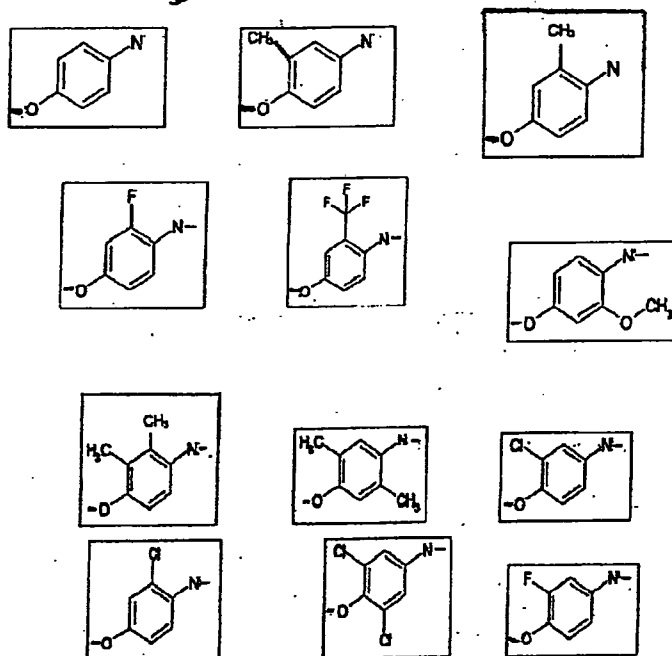
R^5 and R^6 are preferably selected from hydrogen, C_{1-6} alkyl or C_{1-6} alkoxy, optionally substituted, e.g. by halogen and/or $NR^{12}R^{13}$ as described above.

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More preferably, R⁵ and R⁶ are hydrogen.

R⁷, R⁸, R⁹ and R¹⁰, which may be the same or different, preferably represent a hydrogen atom, a halogen atom, nitro or C₁₋₄ alkyl, or C₁₋₄ alkoxy, each optionally halogenated such as methoxy or trifluoromethyl. More preferably, R⁷ and R¹⁰ are hydrogen and at least one of R⁸ and R⁹ is different from hydrogen, e.g. halogen, such as fluorine.

More preferably, the carboxylic ring substituted by R⁷, R⁸, R⁹ and R¹⁰ is selected from the following:

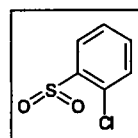
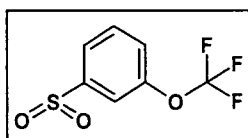
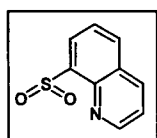
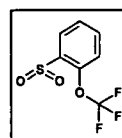
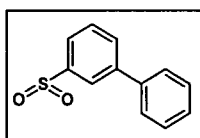
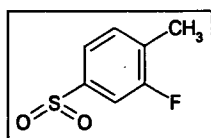
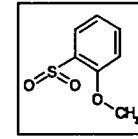
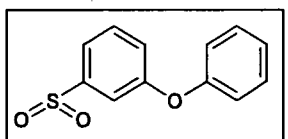
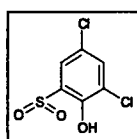
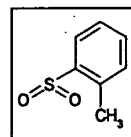
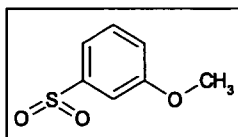
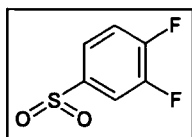
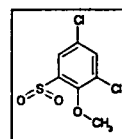
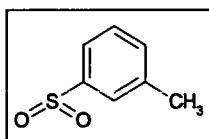
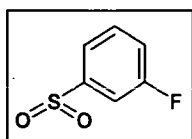
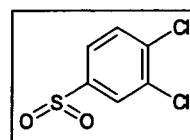
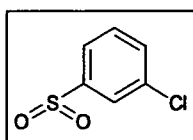
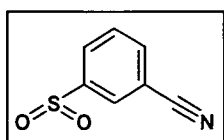


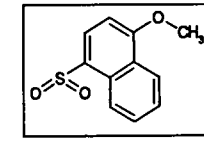
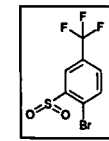
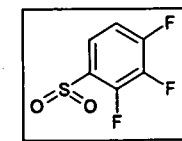
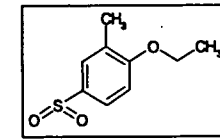
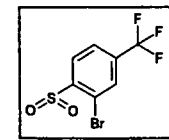
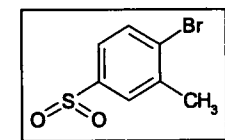
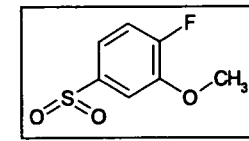
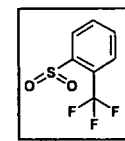
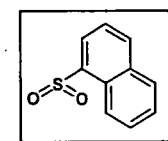
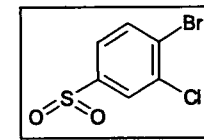
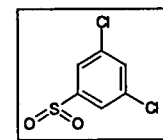
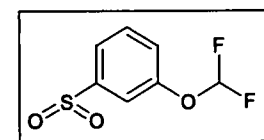
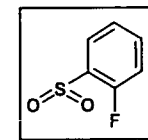
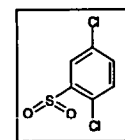
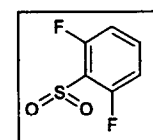
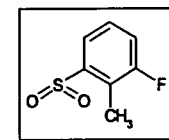
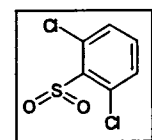
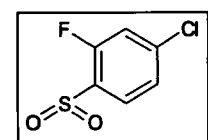
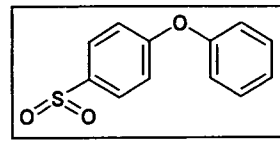
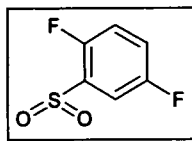
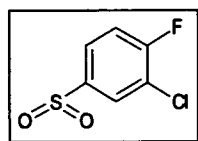
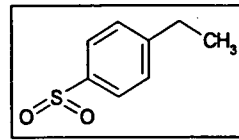
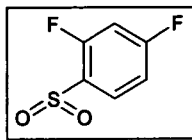
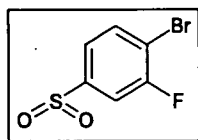
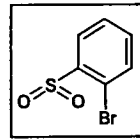
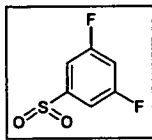
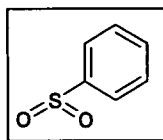
In one embodiment, it is preferred that in case R¹¹ is C₁₋₆ alkyl substituted by a phenyl ring, the phenyl ring is mono- or polysubstituted. R¹¹ preferably represents a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally substituted, e.g. mono-, di- or trisubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group. Examples of preferred substituents on the

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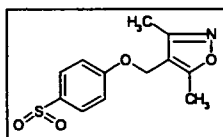
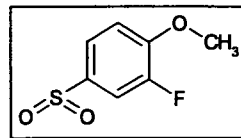
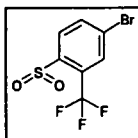
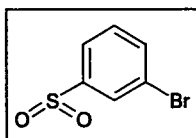
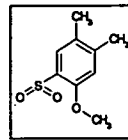
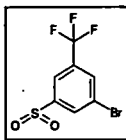
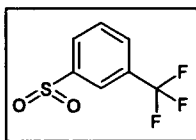
carbocyclic or heterocyclic group are halogen, e.g. F, Cl or Br, C₁₋₄ alkyl optionally halogenated, such as methyl, ethyl, or trifluoromethyl, C₁₋₄ alkoxy, optionally halogenated such as methoxy, difluoromethoxy or trifluoromethoxy, hydroxyl, cyano, and optionally substituted amino. Still
5 more preferably the carbocyclic or heterocyclic group in R¹¹ comprises at least one halogen, e.g. fluorine or chlorine, trifluoromethyl or trifluoromethoxy substituent.

More preferably, R¹¹ represents an optionally substituted carbocyclic ring
10 selected from the following (connecting atom attached to the sulfonyl group):

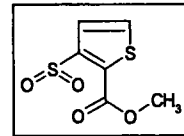
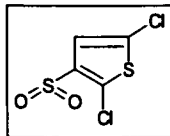
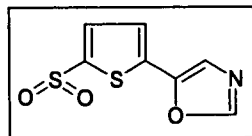
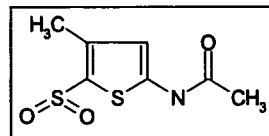
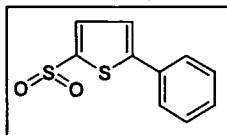
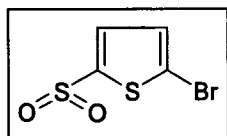
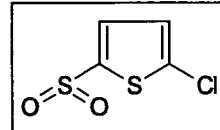
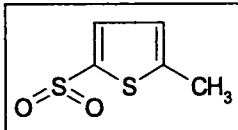
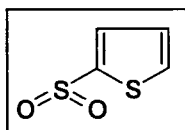




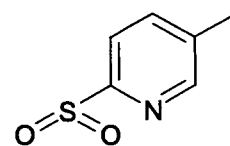
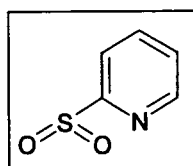
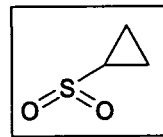
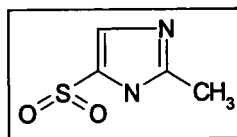
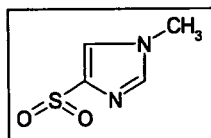
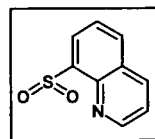
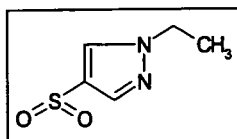
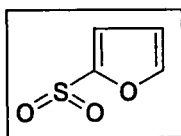
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More preferably, R¹¹ may also represent an optionally substituted carbocyclic or heterocyclic ring selected from the following (connecting atom attached to the sulfonyl group):



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More preferably, R¹¹ represents an optionally substituted nitrogen atom selected from the following (connecting atom labeled by sulfonyl group):

<chem>CS(=O)(=O)N</chem>	<chem>CCN(S(=O)(=O))</chem>	<chem>c1ccccc1CN(S(=O)(=O))</chem>
<chem>C1CCN(S(=O)(=O))CC1</chem>	<chem>CN1CCN(S(=O)(=O))CC1</chem>	<chem>C1CCN(S(=O)(=O))CC1O</chem>

Examples of more preferred compounds according to the present invention include compounds represented by formula:

	Reference
A1	3-Cyano-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A2	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-benzenesulfonamide
A3	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3,4-difluoro-benzenesulfonamide
A4	Thiophene-2-sulfonic acid 4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A5	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-hydroxy-benzenesulfonamide
A6	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-4-methyl-benzenesulfonamide
A7	N-{5-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenylsulfamoyl]-4-methyl-thiophen-2-yl}-acetamide
A8	Quinoline-8-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A9	3-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenylsulfamoyl]-thiophene-2-carboxylic acid methyl ester
A10	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A11	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-benzenesulfonamide
A12	3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-fluoro-benzenesulfonamide
A13	4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-fluoro-benzenesulfonamide
A14	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,6-difluoro-benzenesulfonamide
A15	3-Difluoromethoxy-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A16	2-Phenyl-ethenesulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A17	Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A18	2,5-Dichloro-thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A19	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methyl-benzenesulfonamide
A20	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,3,4-trifluoro-benzenesulfonamide
A21	5-Methyl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A22	Furan-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-

	amide
A23	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-trifluoromethyl-benzenesulfonamide
A24	3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A25	3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A26	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methyl-benzenesulfonamide
A27	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methoxy-benzenesulfonamide
A28	5-Chloro-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A29	5-Bromo-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A30	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-phenoxy-benzenesulfonamide
A31	1-Ethyl-1H-pyrazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A32	1-Methyl-1H-imidazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A33	Cyclopropanesulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A34	Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A35	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-trifluoromethoxy-benzenesulfonamide
A36	5-Phenyl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A37	5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A38	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3,5-difluoro-benzenesulfonamide
A39	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,4-difluoro-benzenesulfonamide
A40	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,5-difluoro-benzenesulfonamide
A41	2,6-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A42	2,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A43	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A44	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethyl-benzenesulfonamide
A45	2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-trifluoromethyl-benzenesulfonamide

A46	2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-5-trifluoromethyl-benzenesulfonamide
A47	3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-5-trifluoromethyl-benzenesulfonamide
A48	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethyl-benzenesulfonamide
A49	3,4-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A50	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-benzenesulfonamide
A51	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methyl-benzenesulfonamide
A52	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-benzenesulfonamide
A53	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A54	2-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A55	2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A56	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-ethyl-benzenesulfonamide
A57	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-phenoxy-benzenesulfonamide
A58	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-2-methyl-benzenesulfonamide
A59	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-fluoro-benzenesulfonamide
A60	4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide
A61	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide
A62	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-ethoxy-3-methyl-benzenesulfonamide
A63	4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A64	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-4,5-dimethyl-benzenesulfonamide
A65	N-{2-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenylsulfamoyl]-4-methyl-phenyl}-acetamide
A66	N-{4-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenylsulfamoyl]-2,6-dimethyl-phenyl}-acetamide
A67	3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide
A68	5-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-methoxy-benzenesulfonamide
A69	5-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-methoxy-4-methyl-

	benzenesulfonamide
A70	3-tert-Butyl-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide
A71	Butane-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A72	2-Methyl-propane-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A73	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-phenyl-methanesulfonamide
A74	3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide
A75	Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide
A76	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-3-phenoxy-benzenesulfonamide
A77	Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide
A78	Isoquinoline-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A79	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-hydroxy-benzenesulfonamide
A80	2-Methyl-3H-imidazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A81	Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A82	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide
A83	Benzo[b]thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A84	Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A85	1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A86	Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A87	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-4-(3,5-dimethyl-isoxazol-4-ylmethoxy)-benzenesulfonamide
A88	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-4-methoxy-benzenesulfonamide
A89	Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide
A90	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-3-phenoxy-benzenesulfonamide
A91	Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide
A92	Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide
A93	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

A94	Benzo[b]thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide
A95	1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide
A96	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethyl-benzenesulfonamide
A97	Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide
A98	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-3-phenoxy-benzenesulfonamide
A99	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2,5-difluoro-benzenesulfonamide
A100	Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide
A101	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide
A102	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide
A103	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide
A104	Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A105	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-4-hydroxy-benzenesulfonamide
A106	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-methoxy-benzenesulfonamide
A107	Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide
A108	Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide
A109	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide
A110	4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-fluoro-benzenesulfonamide
A111	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-methoxy-benzenesulfonamide
A112	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A113	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-trifluoromethyl-benzenesulfonamide
A114	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A115	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-3-phenoxy-benzenesulfonamide
A116	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide
A117	4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-

	benzenesulfonamide
A118	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2,5-difluoro-benzenesulfonamide
A119	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A120	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-3-phenoxy-benzenesulfonamide
A121	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide
A122	4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-benzenesulfonamide
A123	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethyl-benzenesulfonamide
A124	04-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-benzenesulfonamide
A125	1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide
A126	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A127	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-methoxy-benzenesulfonamide
A128	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-trifluoromethyl-benzenesulfonamide
A129	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A130	4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide
A131	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2,5-difluoro-benzenesulfonamide
A132	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide
A133	4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide
A134	4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-fluoro-benzenesulfonamide
A135	4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide
A136	Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A137	1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
A138	Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide
A139	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2,5-difluoro-benzenesulfonamide
A140	Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

A141	4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-fluoro-benzenesulfonamide
A142	Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide
A143	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide
A144	Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide
A145	1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide
A146	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A147	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A148	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A149	4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethoxy-benzenesulfonamide
A150	4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide
A151	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2,5-difluoro-benzenesulfonamide
A152	4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-benzenesulfonamide
A153	4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-fluoro-benzenesulfonamide
A154	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide
A155	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-hydroxy-benzenesulfonamide
A156	3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-hydroxy-benzenesulfonamide
B1	Thiophene-2-sulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B2	3-Cyano-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B3	N-[2-Fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-3-methoxy-benzenesulfonamide
B4	Cyclopropanesulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B5	3-Chloro-4-fluoro-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B6	2,6-Difluoro-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B7	5-Methyl-thiophene-2-sulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B8	N-[2-Fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-3-trifluoromethyl-

	benzenesulfonamide
B9	N-[4-(6-Fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B10	3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B11	3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-methoxy-benzenesulfonamide
B12	2,4-Difluoro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B13	3,5-Difluoro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B14	3-Bromo-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
B15	4-Bromo-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide
B16	Thiophene-3-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B17	3-[4-(6-Fluoro-2-methyl-quinolin-4-yloxy)-phenylsulfamoyl]-thiophene-2-carboxylic acid methyl ester
B18	5-Chloro-thiophene-2-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B19	5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B20	Naphthalene-1-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B21	1-Ethyl-1H-pyrazole-4-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide
B22	3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-hydroxy-benzenesulfonamide
C1	3,5-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
C2	Biphenyl-3-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
C3	N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-3-phenoxy-benzenesulfonamide
C4	Naphthalene-1-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
C5	2,5-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
C6	2,6-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
C7	N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide
C8	4-Methoxy-naphthalene-1-sulfonic acid [3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

C9	3-Fluoro-N-[3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide
C10	N-[3-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-2-methoxy-4,5-dimethyl-benzenesulfonamide
C11	2,5-Difluoro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
C12	3-Chloro-4-fluoro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
C13	2-Methyl-3H-imidazole-4-sulfonic acid [3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
C14	4-(3,5-Dimethyl-isoxazol-4-ylmethoxy)-N-[3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide
C15	Biphenyl-4-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
C16	N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide
C17	Benzo[b]thiophene-2-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
C18	Benzo[b]thiophene-3-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
C19	1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide
D1	Biphenyl-3-sulfonic acid [4-(7-benzyloxy-6-methoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide
D2	Naphthalene-1-sulfonic acid {4-[7-(3-amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-amide
D3	Biphenyl-3-sulfonic acid {4-[7-(3-amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-amide
D4	Biphenyl-3-sulfonic acid {3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-amide
D5	N-{3-Fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethyl-benzenesulfonamide
D6	N-{3-Fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethoxy-benzenesulfonamide
D7	Biphenyl-3-sulfonic acid {4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-amide
D8	N-{4-[6-Methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-2-trifluoromethoxy-benzenesulfonamide
D9	2,5-Difluoro-N-{4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-benzenesulfonamide

D10	2,5-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D11	N-{4-[6-Methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-2-trifluoromethyl-benzenesulfonamide
D12	4-Chloro-2-fluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D13	4-Methoxy-naphthalene-1-sulfonic acid {3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-amide
D14	N-{4-[7-(3-Amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-trifluoromethyl-benzenesulfonamide
D15	N-{4-[7-(3-Amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-trifluoromethoxy-benzenesulfonamide
D16	(3-{4-[2-Fluoro-4-(2-trifluoromethoxy-benzenesulfonylamino)-phenoxy]-6-methoxy-quinolin-7-yloxy}-propyl)-carbamic acid tert-butyl ester
D17	N-(3-Fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-2-trifluoromethyl-benzenesulfonamide
D18	2-Bromo-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D19	2,4-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D20	2,6-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D21	Naphthalene-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide
D22	Propane-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide
D23	2-Cyano-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D24	4-Chloro-2-fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D25	Butane-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide
D26	2-Bromo-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D27	2-Cyano-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D28	2,4-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D29	Biphenyl-3-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide

D30	2-Fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D31	2-Cyano-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D32	2,6-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D33	N-(3-Fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-2-trifluoromethoxy-benzenesulfonamide
D34	2,5-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D35	N-(3-Fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}phenyl)-2-trifluoromethyl-benzenesulfonamide
D36	2,5-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide
D37	Biphenyl-3-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide
D38	4-Fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-3-methoxy-benzenesulfonamide
D39	N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethyl-benzenesulfonamide
D40	N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethoxy-benzenesulfonamide
D41	2,5-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D42	Biphenyl-3-sulfonic acid {3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-amide
D43	4-Chloro-2-fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D44	4-Fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-3-methoxy-benzenesulfonamide
D45	2-Fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D46	N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-nitro-benzenesulfonamide
D47	2,6-Dichloro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide
D48	Naphthalene-1-sulfonic acid {3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-amide
D49	2-Bromo-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

Preparation of starting materials

The compounds of the present invention are suitable for use in medicine, particularly in human medicine, but also in veterinary medicine. The compounds of the present invention may be administered in a pharmaceutically effective amount by any suitable route to subjects in need thereof, e.g. parenterally, topically, rectally, nasally, buccally, vaginally, transdermally, by inhalation, by injection or infusion, by spray or via implanted reservoirs. Preferably, the compounds are administered orally or by injection or infusion, e.g. intravenously. For medical purposes, the compounds are preferably formulated as a pharmaceutical composition, which comprises at least one compound as described above, and pharmaceutically acceptable carriers, diluents and/or adjuvants. The pharmaceutical composition may e.g. be a solid dosage form, e.g. a tablet, a capsule etc., or a liquid dosage form, e.g. an injectable or infundible solution.

The dosage of the compounds may be determined by a skilled practitioner according to the type and severity of the disorder to be treated. In general, the dosage of the compound may vary from 0.0001 to 1000 or even more mg/day.

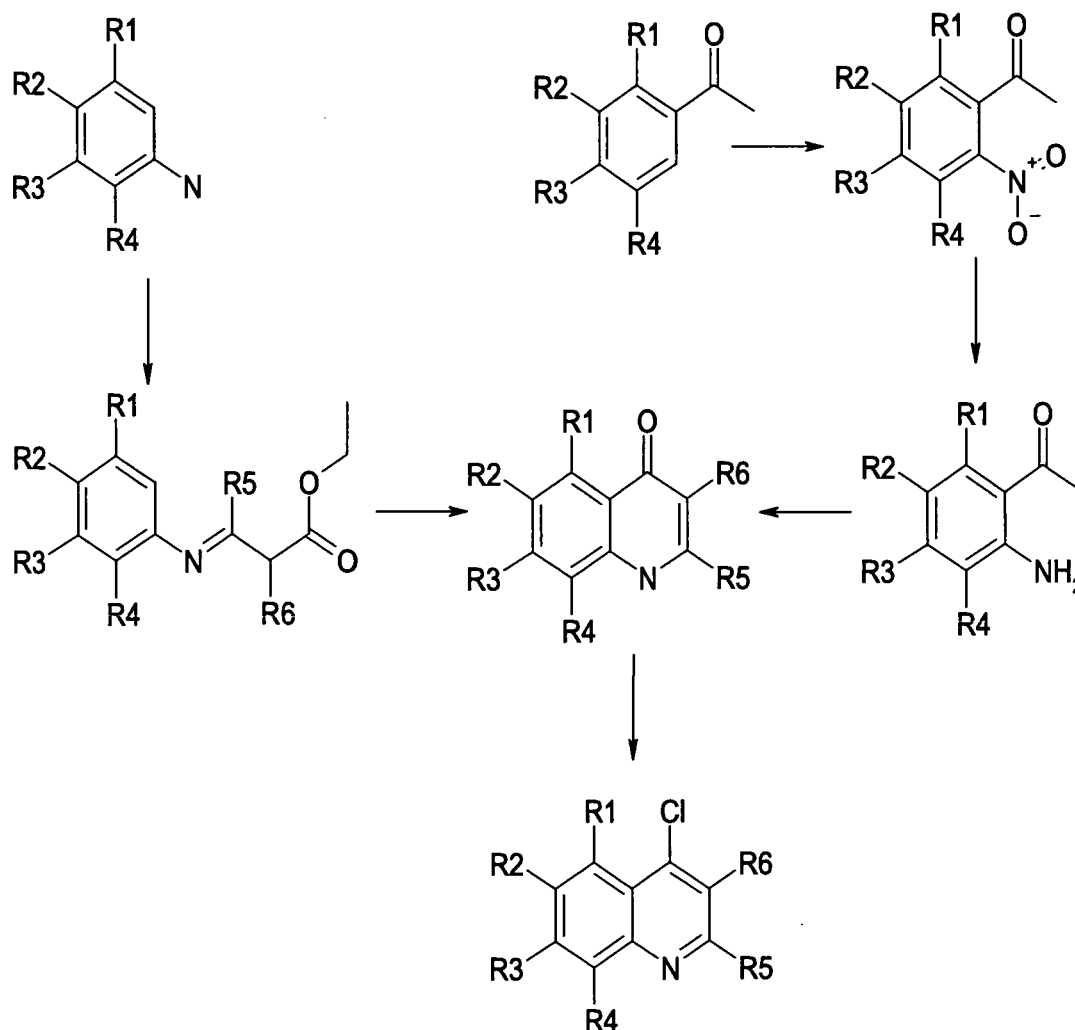
The compounds of the present invention may be administered as a monotherapy or together with further active agents, particularly chemotherapeutic agents or antitumor antibodies.

The compounds according to the present invention may be produced, for example, according to synthesis routes as depicted in schemes 1 to 3. Starting compounds necessary for the synthesis of the compounds according to the present invention are commercially available or alternatively can be easily produced by conventional methods. In the schemes, R^1 to R^{10} are as defined in formula (I).

The 4-chloroquinoline derivatives can be synthesized from substituted

anilines by methods described in Org. Synth. Col. Vol. 3, 272 (1955) or from substituted acetophenones by methods described in EP 1153920 (Scheme 1).

Scheme 1.

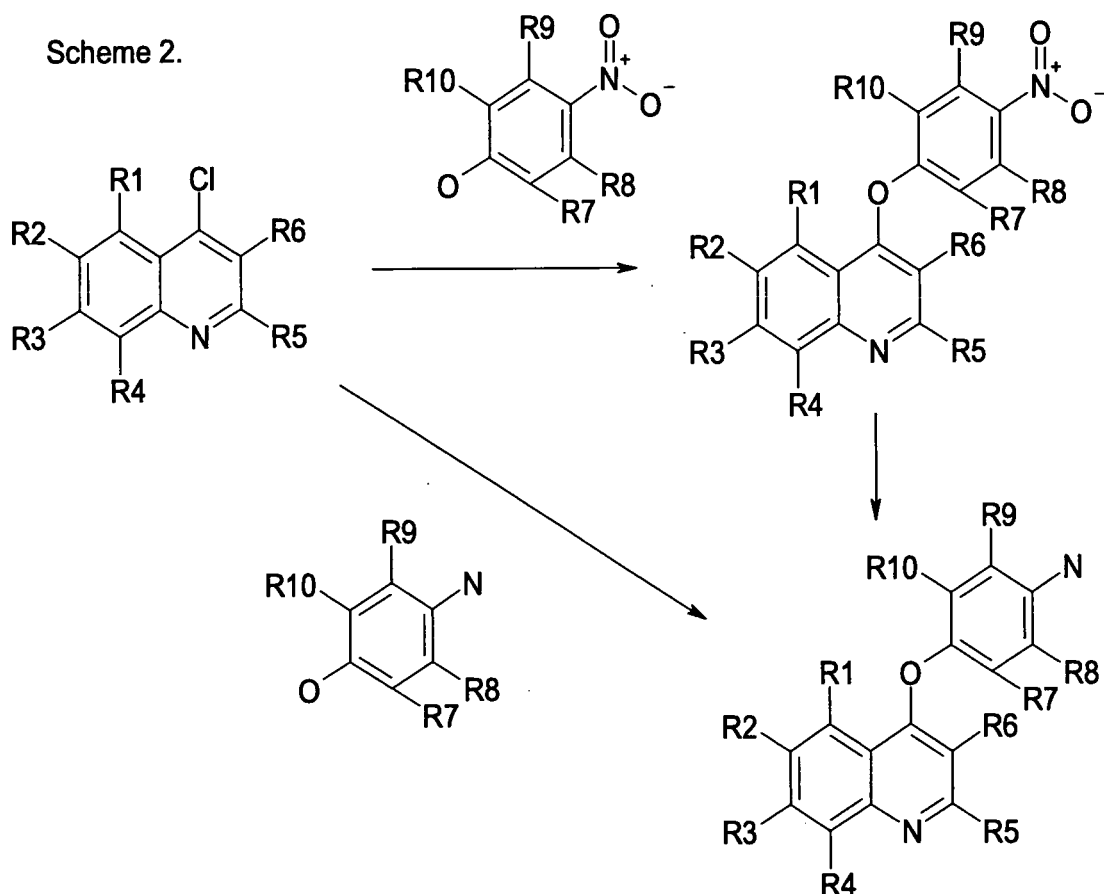


5

10

A 4-(aminophenoxy)quinoline derivative may be produced by reacting a nitrophenol derivative with the 4-chloroquinoline derivative in a suitable solvent, for example, chlorobenzene, to synthesize a 4-(nitrophenoxy)quinoline derivative or a corresponding quinazoline derivative and then reacting the 4-(nitrophenoxy)quinoline derivative in a suitable solvent, for example, N,N-dimethyl formamide, in the presence of a catalyst, for example, palladium hydroxide-carbon or palladium-carbon, under a hydrogen atmosphere. The nitro group can also be reduced with zinc, iron or the like (Scheme 2).

Alternatively, the 4-(aminophenoxy)quinoline derivative can be produced by reacting an aminophenol derivative with the 4-chloroquinoline derivative in a suitable solvent, for example, dimethyl sulfoxide, in the presence of a base, for example, sodium hydride. Alternatively, the 4-(aminophenoxy)quinazoline derivative can also be produced by dissolving an aminophenol derivative in an aqueous sodium hydroxide solution and subjecting the solution to a two-phase reaction with a solution of the 4-chloroquinazoline derivative in a suitable organic solvent, for example, ethyl methyl ketone, in the presence of a phase transfer catalyst, for example, tetra-n-butylammonium chloride, or in the absence of a catalyst (Scheme 2).

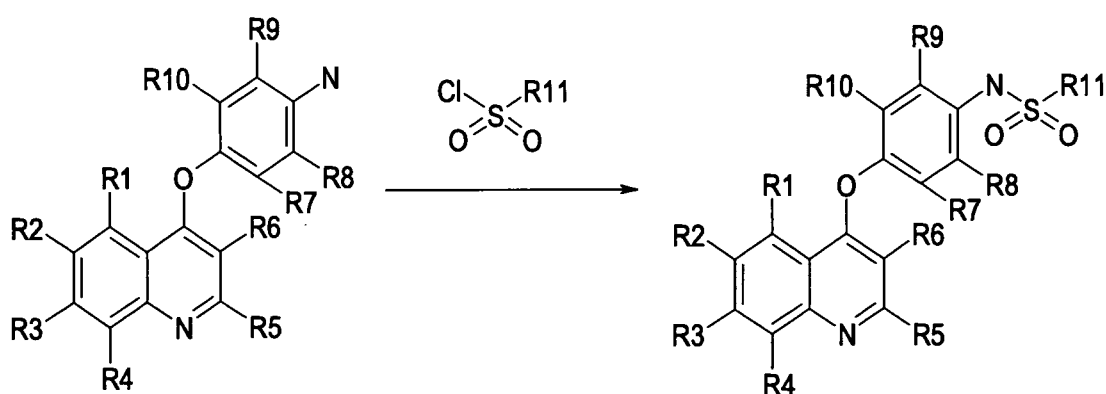


A 4-(sulfamoylphenoxy)quinoline derivative may be produced by reacting a 4-(aminophenoxy)quinoline derivative with sulfonyl chloride derivative in a suitable solvent, for example, pyridine (Scheme 3). The reaction may be carried out in room temperature. The solvent can be diluted with hydrochloric

- 32 -

acid, when the product precipitated. The crystals can be collected by filtration and the obtained solid material can be dissolved in e.g. 10% sodium acetate solution and extracted e.g. with ethyl acetate. The organic layer can be washed e.g. with sodium chloride solution, dried and the solvent can be evaporated. The resulted solid can be treated with diisopropyl ether. The product can be purified with column chromatography (if necessary).

Scheme 3.



Examples

1) Analytical Methods (HPLC, NMR, TLC and melting point)

Analytical HPLC/MS was performed on an Waters HPLC/MS system using reverse phase Waters XTerra MS C18 (5cm x 4.6mm, 5um), gradient 0-95% B (0.00 min 5 % B, 0.50 min 5 % B, 5.50 min 95 % B, 6.00 min 95 %B, 6.50 min 5 % B, 7.00 min 5 % B), Solvent A: Water/ 0.05% HCOOH, Solvent B: AcCN/ 0.05% HCOOH over 7.00 min, flow = 2.0 ml/min. Separation module was Waters Alliance 2795.

UV spectra were recorded using a Waters 996 DAD UV detector. Mass spectra were obtained using Waters SQD MS detector (Ionization: ES⁺/ES⁻, Source block temp: 120 C, Desolvation temp: 350 °C, Desolvation Gas: 400 L/h, Cone Gas: 100 L/h, Capillary: 3000 V, Cone: 25 V, Extractor: 3 V, Rf Lens: 0.2 V, Scan: 120 to 1000 m/z in 1 sec., Inter-scan delay: 0.1 s).

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¹H NMR spectra were recorded on a Bruker Avance 300 MHz AV spectrometer in deuterated solvents (DMSO-d₆). Chemical shifts δ are in parts per million (ppm).

5 Thin-layer chromatography (TLC) analysis was performed with Kieselgel 60 F254 (Merck) plates and visualized using UV light.

Melting point measurement was Büchi melting Point B-54 instrument.

10

2) Manufacture of compounds

The following Examples illustrate the preparation of specific compounds of the invention, and the AXL Kinase inhibitory properties thereof:

15

General procedure for sulfonamide compounds (type A-C):

20

0.31 mmol appropriately substituted sulfonylchloride and 0.3 mmol 4-(4-amino-phenoxy)quinoline derivative was dissolved 3 ml abs. pyridine and stirred at room temperature while the starting amine disappears (2-3 days). The reaction mixture was poured on ice cold 1M hydrochloric acid, stirred for 1 hour and the precipitated crystals were filtered out. The obtained solid material was dissolved in 10% sodium acetate solution and extracted with ethyl acetate. The organic layer was washed with sodium chloride solution, dried and the solvent was evaporated. The resulted solid was treated with diisopropyl ether. The product was purified with column chromatography (if it was necessary).

25

General procedure for sulfonamide compounds (type D):

30

0.31 mmol appropriately substituted sulfonylchloride and 0.3 mmol 4-(4-amino-phenoxy)quinoline derivative was dissolved 3 ml abs. pyridine and stirred at room temperature while the starting amine disappears (2-3 days). The reaction mixture was poured into 50 ml of water, extracted with 30 ml of

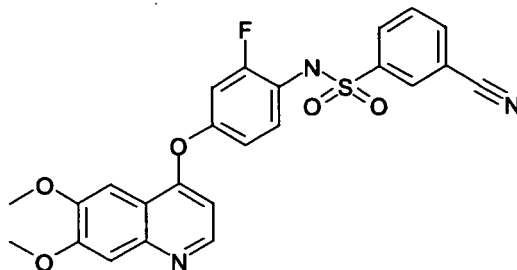
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chloroform, and separated the two layers. The organic phase was dried over anhydrous sodium sulfate, evaporated and the residue was purified on TLC plate (eluent chloroform-methanol 95:5, 9:1). The pure product was solidified over diisopropyl ether.

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Example A1

3-Cyano-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



$C_{24}H_{18}FN_3O_5S$ Mw. 479.49

5 LC/MS purity: 92 %, m/z 480 $[M+H]^+$ Rt. 2.71 min.

1H NMR (300 MHz, DMSO- d_6): 10.46 (s, 1H), 8.51 (d, 1H), 8.15 (m, 2H), 8.04 (d, 2H), 7.82 (t, 1H), 7.41 (s, 1H), 7.40 (s, 1H), 7.28 (m, 2H), 7.07 (d, 1H), 6.56 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

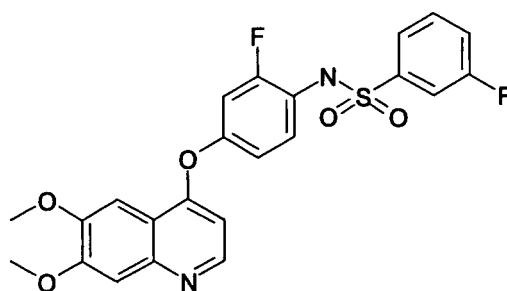
Melting point: 223-224 °C.

Yield: 45 %

10

Example A2

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluorobenzenesulfonamide



$C_{23}H_{18}F_2N_2O_5S$ Mw. 472.47

15 LC/MS purity: 97 %, m/z 471 $[M-H]^-$ Rt. 2.80 min.

1H NMR (300 MHz, DMSO- d_6): 10.37 (s, 1H), 8.51 (d, 1H), 7.76-7.23 (m, 8H), 7.07 (d, 1H), 6.56 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

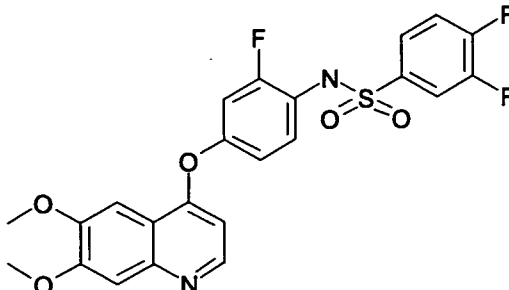
Melting point: 233-235 °C.

Yield: 49 %

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Example A3

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3,4-difluoro-benzenesulfonamide



$C_{23}H_{17}F_3N_2O_5S$ Mw. 490.46

5 LC/MS purity: 94 %, m/z 489 [M-H]⁻ Rt. 2.89 min.

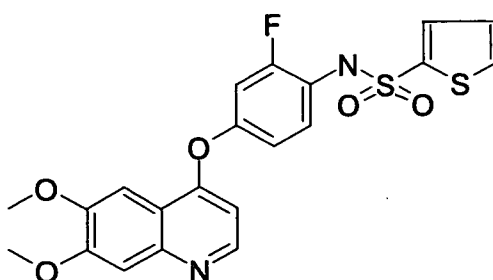
¹H NMR (300 MHz, DMSO-d₆): 10.38 (s, 1H), 8.50 (d, 1H), 7.81-7.61(m, 3H), 7.41 (s, 1H), 7.40 (s, 1H), 7.29 (m, 2H), 7.07 (d, 1H), 6.57 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 217-219 °C.

Yield: 38 %

10 Example A4

Thiophene-2-sulfonic acid 4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



$C_{21}H_{17}FN_2O_5S_2$ Mw. 460.51

15 LC/MS purity: 96 %, m/z 459 [M-H]⁻ Rt. 2.66 min.

¹H NMR (300 MHz, DMSO-d₆): 10.35 (s, 1H), 8.52 (d, 1H), 7.96 (d, 1H), 7.52 (d, 1H), 7.43 (s, 1H), 7.41 (s, 1H), 7.32 (m, 1H), 7.17 (t, 1H), 7.09 (d, 1H), 6.67 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

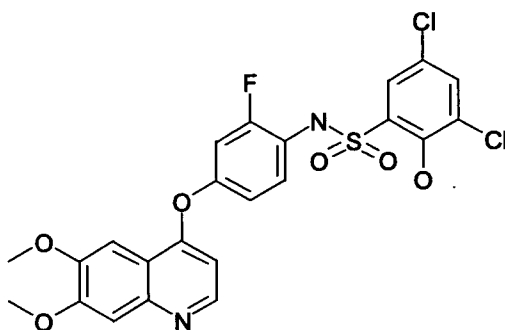
Melting point: 214-216 °C.

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Yield: 37 %

Example A5

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-
 5 hydroxy-benzenesulfonamide



5 $C_{23}H_{17}Cl_2FN_2O_6S$ Mw. 539.37

LC/MS purity: 96 %, m/z 537 [M-H]⁻ Rt. 3.01 min.

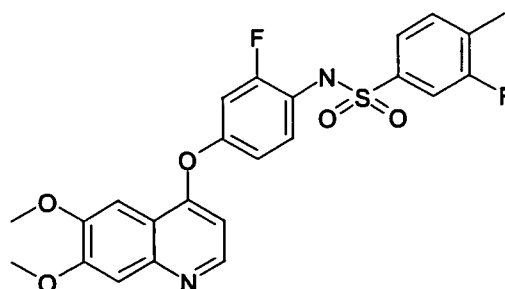
¹H NMR (300 MHz, DMSO-d₆): 8.52 (d, 1H), 7.76 (d, 1H), 7.48 (d, 1H), 7.44
 (s, 1H), 7.41 (s, 1H), 7.35 (m, 1H), 7.25 (dd, 1H), 7.04 (d, 1H), 6.57 (d, 1H),
 10 3.95 (s, 3H), 3.91 (s, 3H), 3.6 (bs, 2H)

Melting point: 232-234 °C.

10 Yield: 35 %

Example A6

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-4-methyl-
 benzenesulfonamide



15 $C_{24}H_{20}F_2N_2O_5S$ Mw. 486.50

LC/MS purity: 95 %, m/z 485 [M-H]⁻ Rt. 2.93 min.

¹H NMR (300 MHz, DMSO-d₆): 10.28 (s, 1H), 8.51 (d, 1H), 7.55-7.23 (m,
 7H), 7.07 (dd, 1H),
 6.56 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.31 (s, 3H)

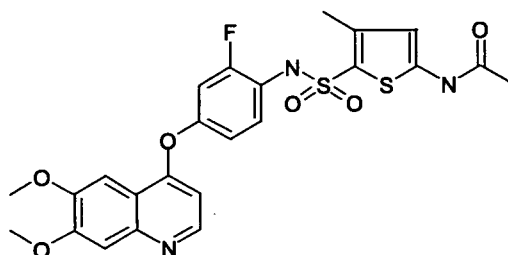
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Melting point: 211-212 °C.

Yield: 54 %

Example A7

5 N-{5-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenylsulfamoyl]-4-methyl-thiophen-2-yl}-acetamide

 $C_{24}H_{22}FN_3O_6S_2$ Mw. 531.59LC/MS purity: 98 %, m/z 533 [M+H]⁺ Rt. 2.53 min.

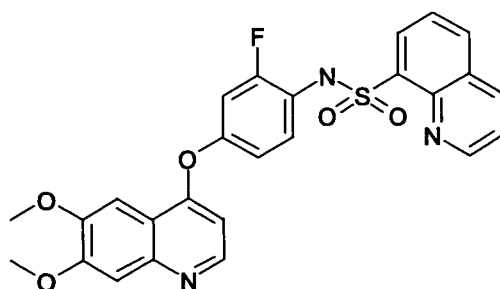
10 ¹H NMR (300 MHz, DMSO-d₆): 12.52 (s, 1H), 10.33 (s, 1H), 8.50 (d, 1H),
7.36 (m, 4H), 7.11 (d, 1H), 6.51 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.30 (s,
3H), 2.16 (s, 3H)

10 Melting point: 133-135 °C.

Yield: 48 %

Example A8

15 Quinoline-8-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



15

 $C_{26}H_{20}FN_3O_5S$ Mw. 505.53LC/MS purity: 97 %, m/z 506 [M+H]⁺ Rt. 2.81 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 9.75 (s, 1H), 9.11 (d, 1H), 8.58 (d, 1H), 8.48
(d, 1H), 8.30 (m, 2H), 7.74 (m, 2H), 7.19 (m, 3H), 7.03 (d, 1H), 6.96 (d, 1H),
6.48 (s, 1H), 3.92 (s, 3H), 3.86 (s, 3H)

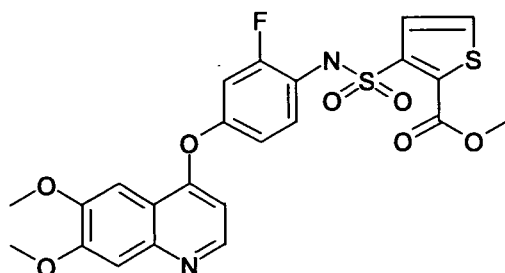
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Melting point: 255-257 °C.

Yield: 36 %

Example A9

5 3-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenylsulfamoyl]-thiophene-2-carboxylic acid methyl ester

 $C_{23}H_{19}FN_2O_7S_2$ Mw. 518.54LC/MS purity: 96 %, m/z 519 [M+H]⁺ Rt. 2.84 min.

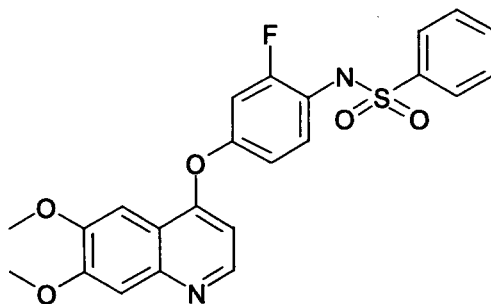
10 ¹H NMR (300 MHz, DMSO-d₆): 9.80 (s, 1H), 8.51 (d, 1H), 7.97 (d, 1H), 7.39 (m, 4H), 7.26 (d, 1H), 7.05 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H).

10 Melting point: 189-190 °C.

Yield: 45 %

Example A10

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



15

 $C_{23}H_{19}FN_2O_5S$ Mw. 454.48LC/MS purity: 98 %, m/z 453 [M-H]⁻ Rt. 2.70 min.

¹H NMR (300 MHz, DMSO-d₆): 10.22 (s, 1H), 8.50 (d, 1H), 7.75-7.56 (m, 5H), 7.41 (s, 1H), 7.40 (s, 1H), 7.32 (t, 1H), 7.23 (dd, 1H), 7.06 (d, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

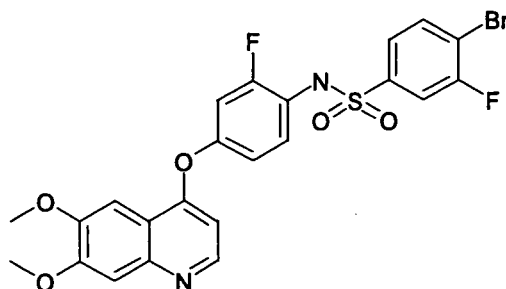
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Melting point: 234-235 °C.

Yield: 59 %

Example A11

5 4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-
benzenesulfonamide

 $C_{23}H_{17}BrF_2N_2O_5S$ Mw. 551.37LC/MS purity: 97 %, m/z 551 [M+H]⁺ Rt. 3.06 min.

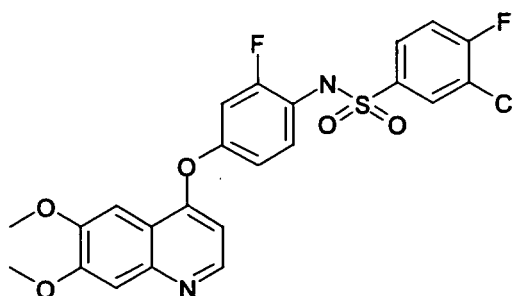
10 ¹H NMR (300 MHz, DMSO-d₆): 10.46 (s, 1H), 8.51 (d, 1H), 7.99 (t, 1H), 7.67
(dd, 1H), 7.50 (dd, 1H), 7.41 (s, 1H), 7.40 (s, 1H), 7.30 (m, 2H), 7.07 (d, 1H),
6.58 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H).

10 Melting point: 209-211 °C.

Yield: 62 %

Example A12

15 3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-fluoro-
benzenesulfonamide



15

 $C_{23}H_{17}ClF_2N_2O_5S$ Mw. 506.92LC/MS purity: 95 %, m/z 505 [M-H]⁻ Rt. 3.00 min.

¹H NMR (300 MHz, DMSO-d₆): 10.39 (s, 1H), 8.51 (d, 1H), 7.89 (dd, 1H),
7.72 (m, 2H), 7.41 (s, 1H), 7.40 (s, 1H), 7.30 (m, 2H), 7.08 (dd, 1H), 6.56 (d,

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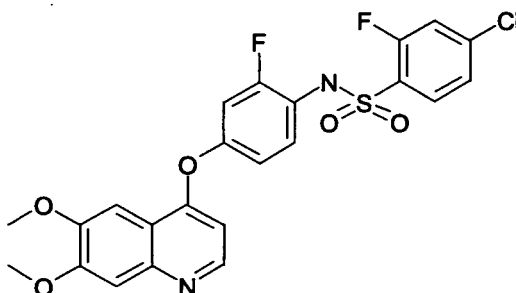
1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 208-210 °C.

Yield: 65 %

5 Example A13

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-fluoro-benzenesulfonamide



C₂₃H₁₇ClF₂N₂O₅S Mw. 506.92

LC/MS purity: 95 %, m/z 505 [M-H]⁻ Rt. 2.97 min.

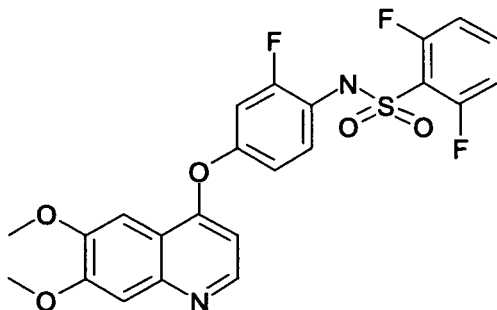
10 ¹H NMR (300 MHz, DMSO-d₆): 10.63 (s, 1H), 8.52 (d, 1H), 7.76 (dd, 1H), 7.70 (t, 1H), 7.48-7.25 (m, 5H), 7.07 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 218-219 °C.

Yield: 53 %

Example A14

15 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,6-difluoro-benzenesulfonamide



C₂₃H₁₇F₃N₂O₅S Mw. 490.46

LC/MS purity: 96 %, m/z 489 [M-H]⁻ Rt. 2.73 min.

¹H NMR (300 MHz, DMSO-d₆): 10.82 (s, 1H), 8.52 (d, 1H), 7.73 (m, 1H),

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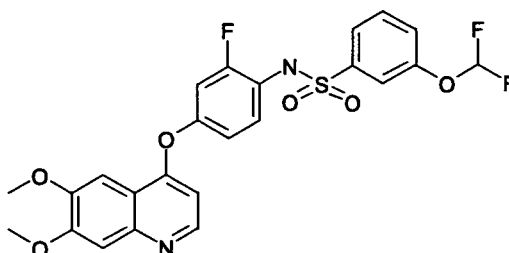
7.41 (s, 1H), 7.40 (s, 1H), 7.32 (m, 4H), 7.09 (d, 1H), 6.54 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 223-225 °C.

Yield: 45 %

5 Example A15

3-Difluoromethoxy-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



$C_{24}H_{19}F_3N_2O_6S$ Mw. 520.49

LC/MS purity: 98 %, m/z 519 [M-H]⁻ Rt. 2.93 min.

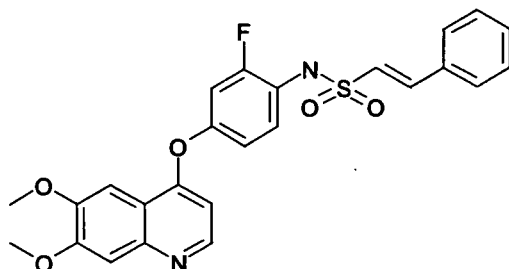
10 ¹H NMR (300 MHz, DMSO-d₆): 10.36 (s, 1H), 8.50 (d, 1H), 7.62 (m, 2H), 7.49 (m, 2H), 7.41 (s, 1H), 7.40 (s, 1H), 7.35-7.23 (m, 2H), 7.07 (d, 1H), 6.64 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 238-239 °C.

Yield: 61 %

Example A16

15 2-Phenyl-ethenesulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



$C_{25}H_{21}FN_2O_5S$ Mw. 480.52

LC/MS purity: 98 %, m/z 479 [M-H]⁻ Rt. 2.91 min.

¹H NMR (300 MHz, DMSO-d₆): 9.94 (s, 1H), 8.48 (d, 1H), 7.71 (m, 2H),

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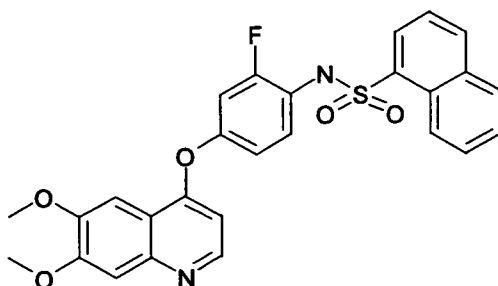
7.52-7.29 (m, 9H), 7.09 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 224-225 °C.

Yield: 26 %

5 Example A17

Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

 $C_{27}H_{21}FN_2O_5S$ Mw. 504.54LC/MS purity: 98 %, m/z 503 [M-H]⁻ Rt. 3.01 min.

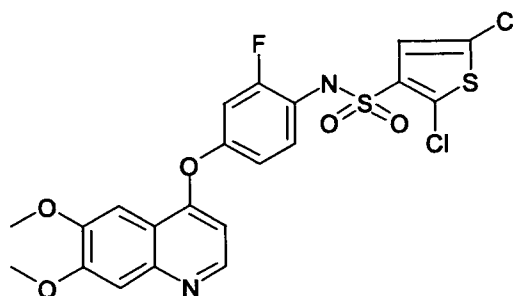
10 ¹H NMR (300 MHz, DMSO-d₆): 10.51 (s, 1H), 8.71 (d, 1H), 8.49 (d, 1H), 8.25 (d, 1H), 8.10 (d, 2H), 7.71 (m, 2H), 7.62 (t, 1H), 7.38 (s, 2H), 7.28 (t, 1H), 7.12 (dd, 1H), 6.99 (d, 1H), 6.44 (d, 1H), 3.93 (s, 3H), 3.87 (s, 3H)

Melting point: 243-245 °C.

Yield: 41 %

15 Example A18

2,5-Dichloro-thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

 $C_{21}H_{15}Cl_2FN_2O_5S_2$ Mw. 529.40LC/MS purity: 93 %, m/z 527 [M-H]⁻ Rt. 3.05 min.

- 44 -

¹H NMR (300 MHz, DMSO-d₆): 10.60 (s, 1H), 8.52 (d, 1H), 7.43-7.26 (m, 5H), 7.09 (d, 1H),

6.57 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

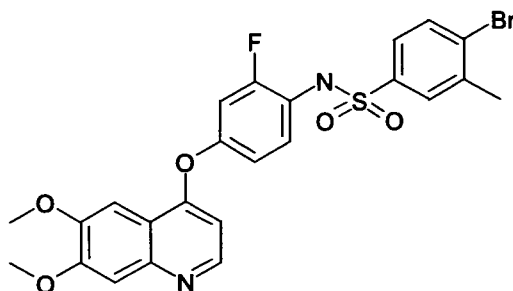
Melting point: 223-225 °C.

Yield: 35 %

5

Example A19

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methylbenzenesulfonamide



C₂₄H₂₀BrFN₂O₅S Mw. 547.40

10 LC/MS purity: 95 %, m/z 545 [M-H]⁻ Rt. 3.10 min.

¹H NMR (300 MHz, DMSO-d₆): 10.28 (s, 1H), 8.51 (d, 1H), 7.82 (d, 1H), 7.71 (s, 1H), 7.46 (d, 1H), 7.41 (s, 1H), 7.40 (s, 1H), 7.30 (m, 1H), 7.06 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H),

2.41 (s, 3H)

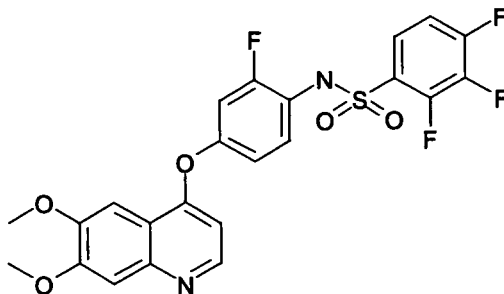
Melting point: 199-201 °C.

Yield: 56 %

15

Example A20

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,3,4-trifluorobenzenesulfonamide



- 45 -

$C_{23}H_{16}F_4N_2O_5S$ Mw. 508.45

LC/MS purity: 95 %, m/z 507 [M-H]⁻ Rt. 2.92 min.

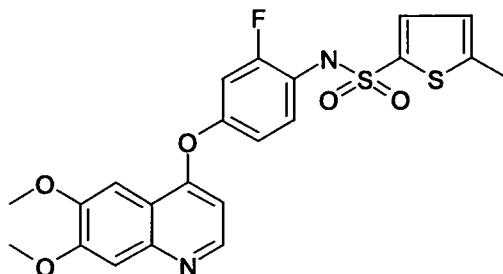
¹H NMR (300 MHz, DMSO-d₆): 10.78 (s, 1H), 8.52 (d, 1H), 7.63-7.27 (m, 6H), 7.07 (d, 1H), 6.57 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 188-190 °C.

5 Yield: 38 %

Example A21

5-Methyl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



10

$C_{22}H_{19}FN_2O_5S_2$ Mw. 474.53

LC/MS purity: 97 %, m/z 475 [M+H]⁺ Rt. 2.60 min.

¹H NMR (300 MHz, DMSO-d₆): 10.30 (s, 1H), 8.52 (d, 1H), 7.43-7.26 (m, 5H), 7.09 (d, 1H), 6.88 (d, 1H), 6.57 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.50 (s, 3H)

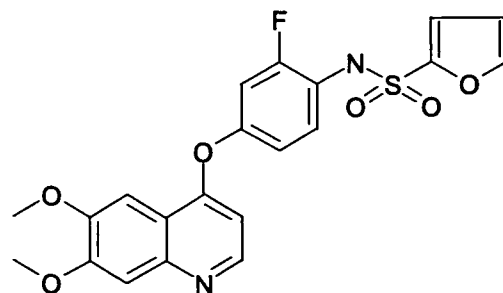
15

Melting point: 218-220 °C.

15 Yield: 68 %

Example A22

Furan-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



20

$C_{21}H_{17}FN_2O_6S$ Mw. 444.44

- 46 -

LC/MS purity: 96 %, m/z 443 [M-H]⁻ Rt. 2.59 min.

¹H NMR (300 MHz, DMSO-d₆): 10.53 (s, 1H), 8.52 (d, 1H), 8.02 (d, 1H), 7.42 (s, 1H), 7.41 (s, 1H), 7.30 (m, 2H), 7.08 (d, 1H), 7.06 (s, 1H), 6.67 (dd, 1H), 6.59 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

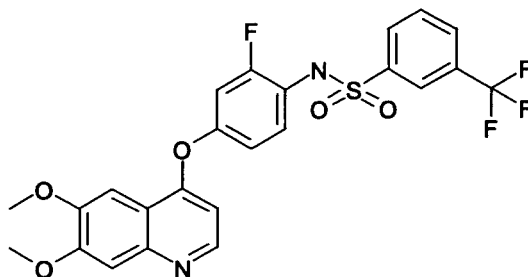
Melting point: 210-212 °C.

Yield: 59 %

5

Example A23

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-trifluoromethyl-benzenesulfonamide



C₂₄H₁₈F₄N₂O₅S Mw. 522.48

10 LC/MS purity: 94 %, m/z 521 [M-H]⁻ Rt. 3.03 min.

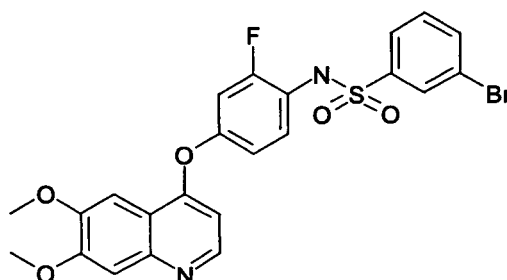
¹H NMR (300 MHz, DMSO-d₆): 10.46 (s, 1H), 8.50 (d, 1H), 8.05 (m, 3H), 7.85 (t, 1H), 7.40 (s, 2H), 7.33 (t, 1H), 7.22 (dd, 1H), 7.08 (d, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 230-231 °C.

15 Yield: 53 %

Example A24

3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



- 47 -

$C_{23}H_{18}BrFN_2O_5S$ Mw. 533.38

LC/MS purity: 96 %, m/z 533 $[M+H]^+$ Rt. 2.96 min.

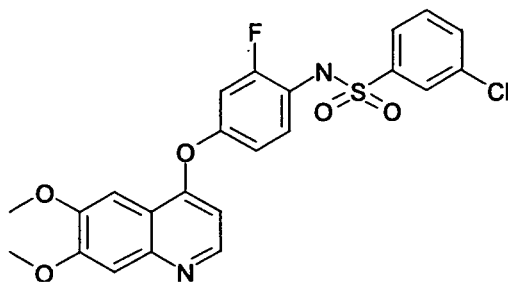
1H NMR (300 MHz, DMSO- d_6): 11.9 (bs, 1H), 8.45 (d, 1H), 7.81 (s, 1H), 7.70 (d, 1H), 7.64 (d, 1H), 7.42 (m, 3H), 7.23 (t, 1H), 6.98 (dd, 1H), 6.79 (d, 1H), 6.44 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H)

Melting point: 255-257 °C.

Yield: 37 %

Example A25

3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



$C_{23}H_{18}ClFN_2O_5S$ Mw. 488.93

LC/MS purity: 96 %, m/z 487 $[M-H]^-$ Rt. 2.93 min.

1H NMR (300 MHz, DMSO- d_6): 10.38 (s, 1H), 8.49 (d, 1H), 7.65 (m, 4H), 7.42 (s, 1H), 7.39 (s, 1H), 7.30 (t, 1H), 7.18 (d, 1H), 7.00 (d, 1H), 6.52 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H)

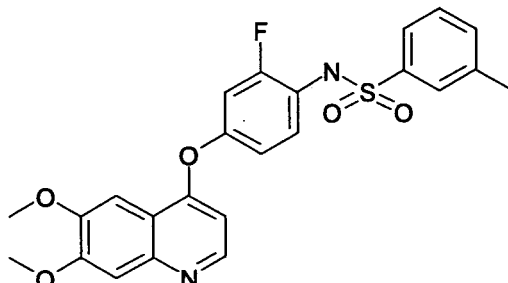
Melting point: 250-251 °C.

Yield: 62 %

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Example A26

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methyl-benzenesulfonamide



5 $C_{24}H_{21}FN_2O_5S$ Mw. 468.51

LC/MS purity: 98 %, m/z 467 [M-H]⁻ Rt. 2.85 min.

¹H NMR (300 MHz, DMSO-d₆): 10.16 (s, 1H), 8.50 (d, 1H), 7.56-7.40 (m, 6H), 7.31 (t, 1H), 7.22 (dd, 1H), 7.04 (dd, 1H), 6.52 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.37 (s, 3H)

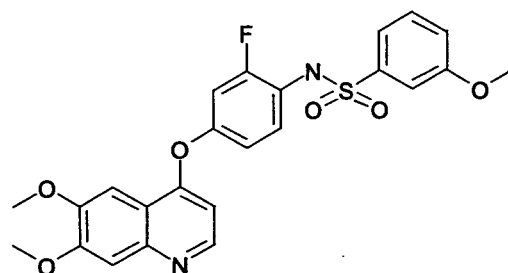
10 Melting point: 244-245 °C.

Yield: 49 %

Example A27

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methoxy-benzenesulfonamide

15



$C_{24}H_{21}FN_2O_6S$ Mw. 484.51

LC/MS purity: 95 %, m/z 483 [M-H]⁻ Rt. 2.78 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.22 (s, 1H), 8.50 (d, 1H), 7.50 (t, 1H), 7.41 (s, 1H), 7.40 (s, 1H), 7.35-7.2 (m, 5H), 7.05 (dd, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.80 (s, 3H)

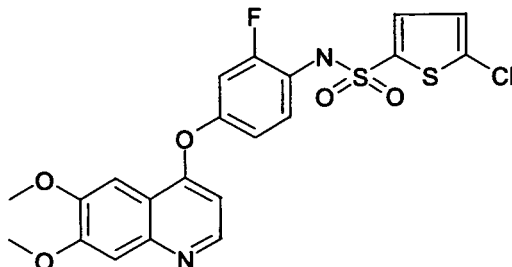
Melting point: 224-225 °C.

Yield: 68 %

- 49 -

Example A28

5-Chloro-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



5 $C_{21}H_{16}ClFN_2O_5S_2$ Mw. 494.95

LC/MS purity: 94 %, m/z 493 [M-H]⁻ Rt. 2.94 min.

¹H NMR (300 MHz, DMSO-d₆): 10.57 (s, 1H), 8.52 (d, 1H), 7.43-7.25 (m, 7H), 7.1 (d, 1H),

6.60 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

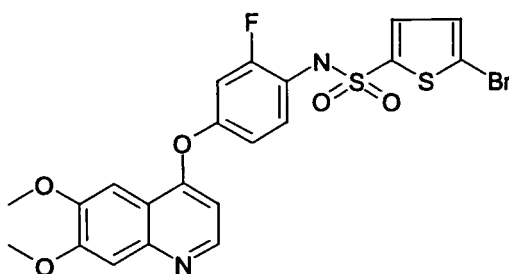
10 Melting point: 187-189 °C.

Yield: 54 %

Example A29

5-Bromo-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

15



$C_{21}H_{16}BrFN_2O_5S_2$ Mw. 539.40

LC/MS purity: 95 %, m/z 537 [M-H]⁻ Rt. 2.83 min.

¹H NMR (300 MHz, DMSO-d₆): 10.55 (s, 1H), 8.52 (d, 1H), 7.40 (m, 6H), 7.1 (d, 1H), 6.59 (d, 1H), 3.95 (s, 3H), 3.91 (s, 3H)

20

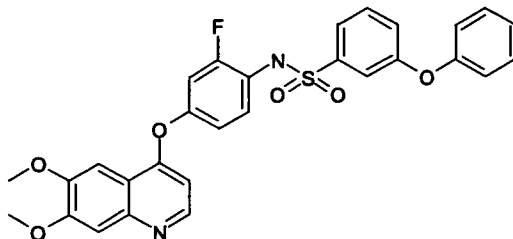
Melting point: 207-209 °C.

Yield: 55 %

- 50 -

Example A30

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-phenoxy-benzenesulfonamide



5 $C_{29}H_{23}FN_2O_6S$ Mw. 546.58

LC/MS purity: 97 %, m/z 545 [M-H]⁻ Rt. 3.23 min.

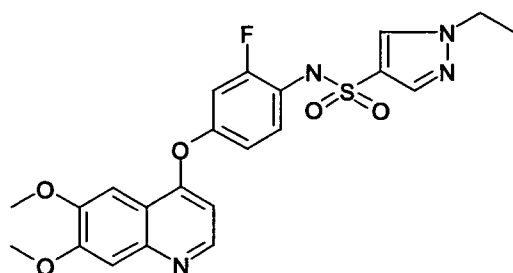
¹H NMR (300 MHz, DMSO-d₆): 10.22 (bs, 1H), 8.49 (d, 1H), 7.61 (t, 1H), 7.44 (m, 5H), 7.27 (m, 5H), 7.04 (m, 3H), 6.54 (d, 1H), 3.95 (s, 3H), 3.90 (s, 3H)

10 Melting point: 179-180 °C.

Yield: 75 %

Example A31

1-Ethyl-1H-pyrazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



15 $C_{22}H_{21}FN_4O_5S$ Mw. 472.50

LC/MS purity: 98 %, m/z 471 [M-H]⁻ Rt. 2.45 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 9.94 (s, 1H), 8.51 (d, 1H), 8.23 (s, 1H), 7.68 (s, 1H), 7.43 (s, 1H), 7.41 (s, 1H), 7.28 (m, 2H), 7.07 (dd, 1H), 6.58 (d, 1H), 4.17 (q, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 1.34 (t, 3H)

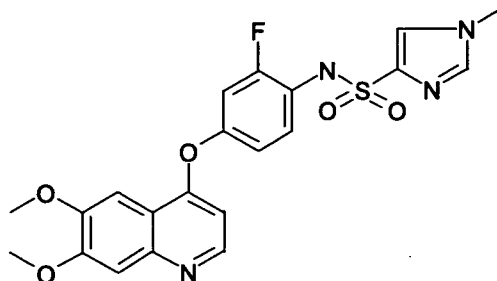
Melting point: 211-213 °C.

Yield: 49 %

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Example A32

1-Methyl-1H-imidazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



5 $C_{21}H_{19}FN_4O_5S$ Mw. 458.47

LC/MS purity: 98 %, m/z 459 $[M+H]^+$ Rt. 2.21 min.

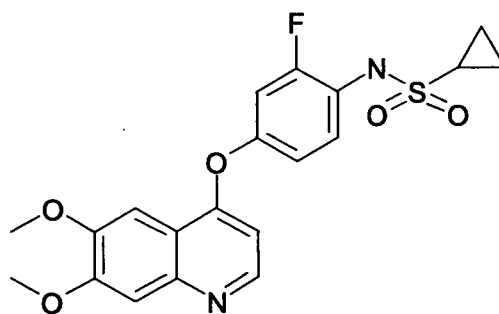
1H NMR (300 MHz, DMSO- d_6): 9.97 (s, 1H), 8.51 (d, 2H), 7.78 (s, 1H), 7.73 (s, 1H), 7.41 (m, 3H), 7.23 (d, 1H), 7.03 (d, 1H); 6.55 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.68 (s, 3H)

10 Melting point: 215-217 °C.

Yield: 35 %

Example A33

Cyclopropanesulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



$C_{20}H_{19}FN_2O_5S$ Mw. 418.45

LC/MS purity: 98 %, m/z 417 $[M-H]^-$ Rt. 2.40 min.

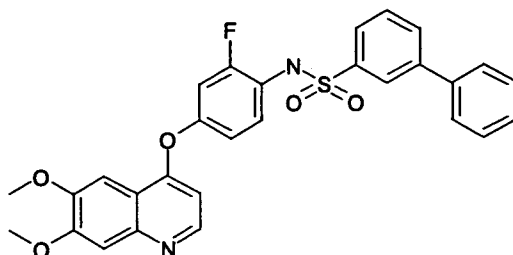
20 1H NMR (300 MHz, DMSO- d_6): 9.64 (bs, 1H), 8.51 (bs, 1H), 7.44 (m, 4H), 7.11 (bs, 1H), 6.62 (bs, 1H), 3.94 (bs, 6H), 2.67 (bs, 1H), 0.97 (bs, 2H), 0.90 (bs, 2H)

Melting point: 179-180 °C.

Yield: 38 %

Example A34

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



$C_{29}H_{23}FN_2O_5S$ Mw. 530.58

LC/MS purity: 98 %, m/z 529 [M-H]⁻ Rt. 3.20 min.

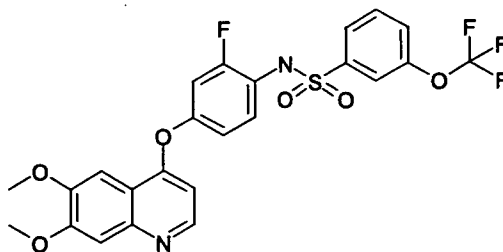
¹H NMR (300 MHz, DMSO-d₆): 10.25 (bs, 1H), 8.44 (d, 1H), 7.96 (m, 2H), 7.70 (m, 4H), 7.54-7.33 (m, 6H), 7.22 (bd, 1H), 7.06 (d, 1H), 6.48 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 193-195 °C.

Yield: 64 %

Example A35

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-trifluoromethoxy-benzenesulfonamide



$C_{24}H_{18}F_4N_2O_6S$ Mw. 538.48

LC/MS purity: 94 %, m/z 537 [M-H]⁻ Rt. 3.09 min.

¹H NMR (300 MHz, DMSO-d₆): 10.41 (s, 1H), 8.50 (d, 1H), 7.75 (m, 3H), 7.63 (s, 1H), 7.41 (s, 2H), 7.33 (t, 1H), 7.23 (dd, 1H), 7.07 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

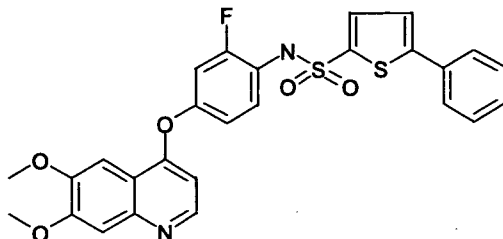
Melting point: 221-223 °C.

Yield: 52 %

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Example A36

5-Phenyl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



5 $C_{27}H_{21}FN_2O_5S_2$ Mw. 536.61

LC/MS purity: 93 %, m/z 535 [M-H] Rt. 3.22 min.

1H NMR (300 MHz, DMSO- d_6): 10.45 (s, 1H), 8.47 (d, 1H), 7.72 (m, 2H), 7.58-7.37 (m, 9H),

7.28 (dd, 1H), 7.10 (d, 1H), 6.56 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

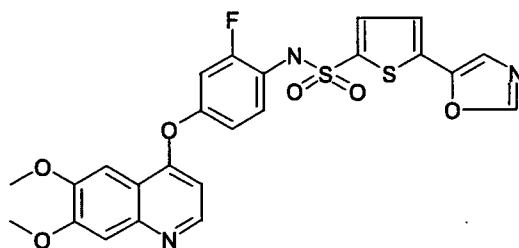
10 Melting point: 186-188 °C.

Yield: 52 %

Example A37

5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

15



$C_{24}H_{18}FN_3O_6S_2$ Mw. 527.55

LC/MS purity: 98 %, m/z 528 [M+H]⁺ Rt. 2.51 min.

1H NMR (300 MHz, DMSO- d_6): 10.56 (s, 1H), 8.52 (s, 1H), 8.51 (d, 1H), 7.77 (s, 1H), 7.53 (m, 2H), 7.39 (m, 3H), 7.29 (dd, 1H), 7.10 (d, 1H), 6.58 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

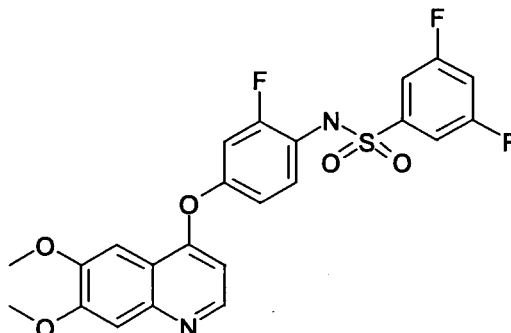
20

Melting point: 206-208 °C.

Yield: 36 %

Example A38

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3,5-difluoro-benzenesulfonamide



5 $C_{23}H_{17}F_3N_2O_5S$ Mw. 490.46

LC/MS purity: 96 %, m/z 489 [M-H]⁻ Rt. 2.91 min.

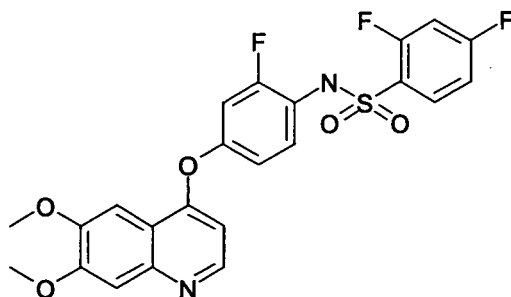
¹H NMR (300 MHz, DMSO-d₆): 10.49 (s, 1H), 8.51 (d, 1H), 7.67 (m, 1H), 7.44-7.25 (m, 6H), 7.07 (dd, 1H), 6.59 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 243-245 °C.

10 Yield: 47 %

Example A39

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,4-difluoro-benzenesulfonamide



15

$C_{23}H_{17}F_3N_2O_5S$ Mw. 490.46

LC/MS purity: 95 %, m/z 489 [M-H]⁻ Rt. 2.81 min.

¹H NMR (300 MHz, DMSO-d₆): 10.56 (s, 1H), 8.51 (d, 1H), 7.78 (dd, 1H), 7.56 (dd, 1H), 7.44-7.23 (m, 5H), 7.06 (dd, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

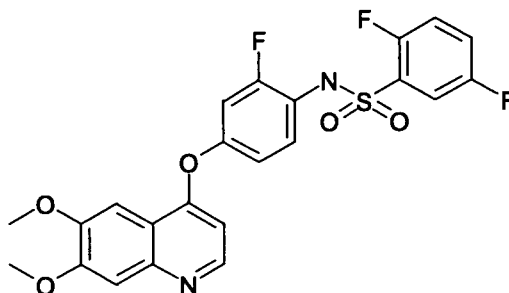
20

Melting point: 212-214 °C.

Yield: 52 %

Example A40

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,5-difluoro-benzenesulfonamide



$C_{23}H_{17}F_3N_2O_5S$ Mw. 490.46

LC/MS purity: 99 %, m/z 489 [M-H]⁻ Rt. 2.82 min.

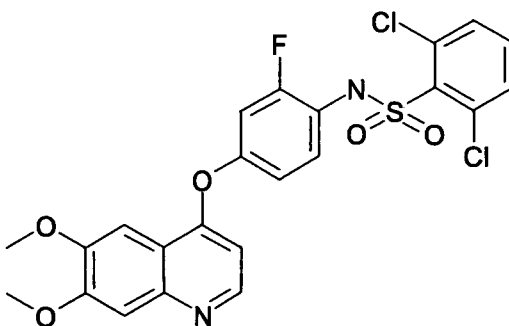
¹H NMR (300 MHz, DMSO-d₆): 10.68 (s, 1H), 8.51 (d, 1H), 7.55 (m, 3H), 7.41 (s, 1H), 7.40 (s, 1H), 7.36 (t, 1H), 7.26 (dd, 1H), 7.06 (dd, 1H), 6.56 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 232-234 °C.

Yield: 45 %

Example A41

2,6-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



$C_{23}H_{17}Cl_2FN_2O_5S$ Mw. 523.37

LC/MS purity: 96 %, m/z 523 [M+H]⁺ Rt. 2.92 min.

¹H NMR (300 MHz, DMSO-d₆): 10.61 (s, 1H), 8.51 (d, 1H), 7.57 (m, 3H), 7.41 (s, 2H), 7.34 (t, 1H), 7.25 (dd, 1H), 7.06 (d, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

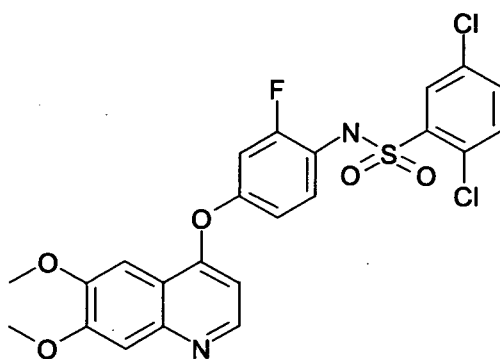
Melting point: 217-218 °C.

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Yield: 58 %

Example A42

2,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

 $C_{23}H_{17}Cl_2FN_2O_5S$ Mw. 523.37LC/MS purity: 95 %, m/z 523 [M-H]⁻ Rt. 3.05 min.

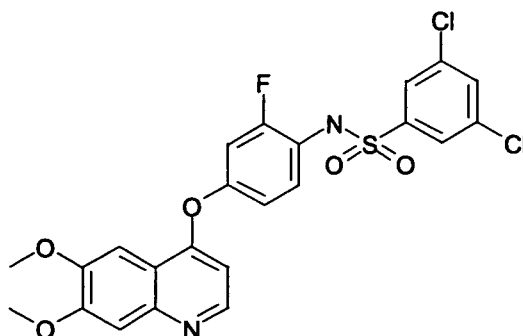
¹H NMR (300 MHz, DMSO-d₆): 10.64 (s, 1H), 8.51 (d, 1H), 7.85 (s, 1H), 7.76 (s, 2H), 7.40 (s, 2H), 7.35 (t, 1H), 7.26 (dd, 1H), 7.06 (d, 1H), 6.56 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 228-230 °C.

Yield: 63 %

Example A43

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

 $C_{23}H_{17}Cl_2FN_2O_5S$ Mw. 523.37LC/MS purity: 95 %, m/z 521 [M-H]⁻ Rt. 3.16 min.

¹H NMR (300 MHz, DMSO-d₆): 10.51 (s, 1H), 8.52 (d, 1H), 8.00 (s, 1H), 7.69

- 57 -

(s, 2H), 7.42 (s, 1H), 7.41 (s, 1H), 7.33 (t, 1H), 7.28 (dd, 1H), 7.09 (d, 1H), 6.57 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

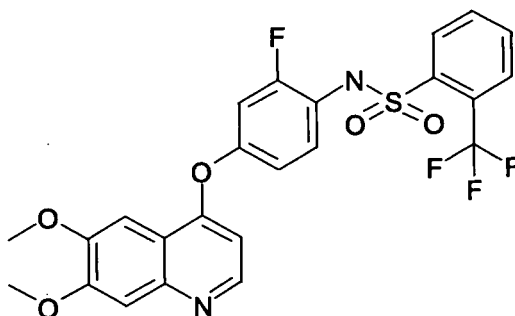
Melting point: 240-242 °C.

Yield: 46 %

5

Example A44

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethyl-benzenesulfonamide



10 $C_{24}H_{18}F_4N_2O_5S$ Mw. 522.48

LC/MS purity: 96 %, m/z 521 [M-H]⁻ Rt. 2.95 min.

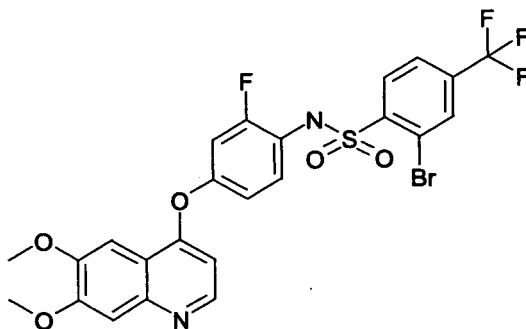
¹H NMR (300 MHz, DMSO-d₆): 10.37 (s, 1H), 8.51 (d, 1H), 8.03 (m, 2H), 7.87 (m, 2H), 7.40 (s, 2H), 7.34 (t, 1H), 7.24 (dd, 1H), 7.06 (d, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

15 Melting point: 237-239 °C.

Yield: 72 %

Example A45

20 2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-trifluoromethyl-benzenesulfonamide



$C_{24}H_{17}BrF_4N_2O_5S$ Mw. 601.38

- 58 -

LC/MS purity: 96 %, m/z 599 [M-H]⁻ Rt. 3.13 min.

¹H NMR (300 MHz, DMSO-d₆): 10.70 (s, 1H), 8.51 (d, 1H), 8.30 (s, 1H), 8.15 (d, 1H), 7.97 (d, 1H), 7.40 (s, 2H), 7.34 (t, 1H), 7.27 (dd, 1H), 7.05 (dd, 1H), 6.57 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

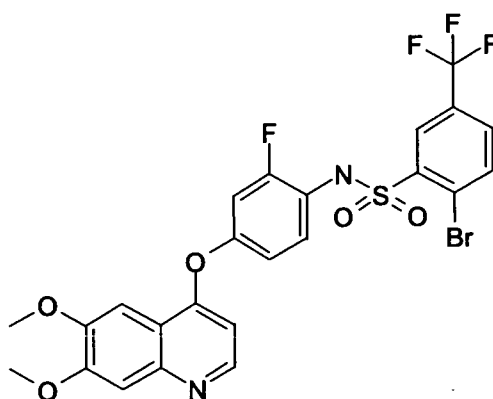
5 Melting point: 236-238 °C.

Yield: 65 %

Example A46

2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-5-trifluoromethyl-benzenesulfonamide

10



C₂₄H₁₇BrF₄N₂O₅S Mw. 601.38

LC/MS purity: 96 %, m/z 599 [M-H]⁻ Rt. 3.17 min.

¹H NMR (300 MHz, DMSO-d₆): 10.72 (s, 1H), 8.50 (d, 1H), 8.16 (d, 1H), 8.14 (s, 1H), 7.95 (dd, 1H), 7.40 (s, 2H), 7.36 (t, 1H), 7.26 (dd, 1H), 7.06 (dd, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

15

Melting point: 227-230 °C.

Yield: 42 %

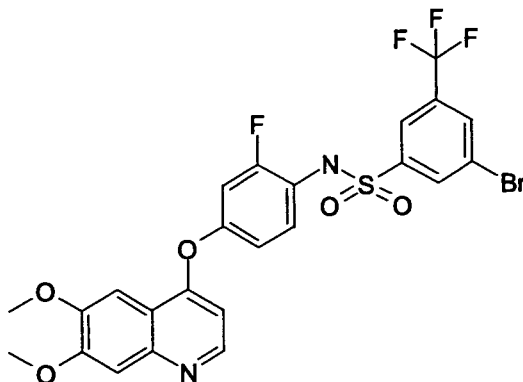
20

25

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Example A47

3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-5-trifluoromethyl-benzenesulfonamide



5 $C_{24}H_{17}BrF_4N_2O_5S$ Mw. 601.38

LC/MS purity: 95 %, m/z 599 [M-H]⁻ Rt. 3.27 min.

¹H NMR (300 MHz, DMSO-d₆): 10.60 (s, 1H), 8.52 (d, 1H), 8.39 (s, 1H), 8.12 (s, 1H), 7.97 (s, 1H), 7.41 (s, 2H), 7.34 (t, 1H), 7.28 (dd, 1H), 7.09 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

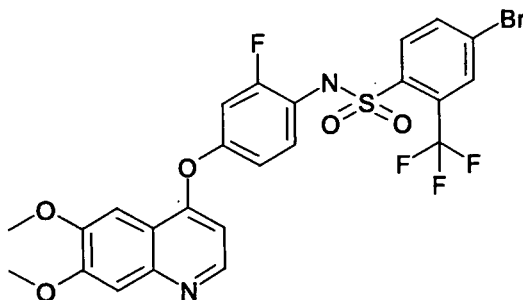
10 Melting point: 214-216 °C.

Yield: 58 %

Example A48

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethyl-benzenesulfonamide

15



$C_{24}H_{17}BrF_4N_2O_5S$ Mw. 601.38

LC/MS purity: 96 %, m/z 599 [M-H]⁻ Rt. 3.14 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.51 (s, 1H), 8.52 (d, 1H), 8.18 (s, 1H), 8.13 (dd, 1H), 7.94 (d, 1H), 7.41 (s, 2H), 7.34 (t, 1H), 7.27 (dd, 1H), 7.07 (dd, 1H), 6.56 (d, 1H), 3.95 (s, 3H), 3.90 (s, 3H)

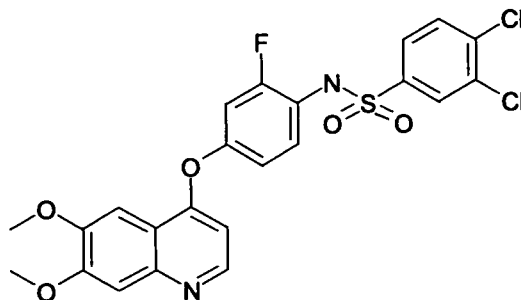
- 60 -

Melting point: 242-244 °C.

Yield: 69 %

Example A49

5 3,4-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide

 $C_{23}H_{17}Cl_2FN_2O_5S$ Mw. 523.37LC/MS purity: 97 %, m/z 521 [M-H]⁻ Rt.3.12 min.

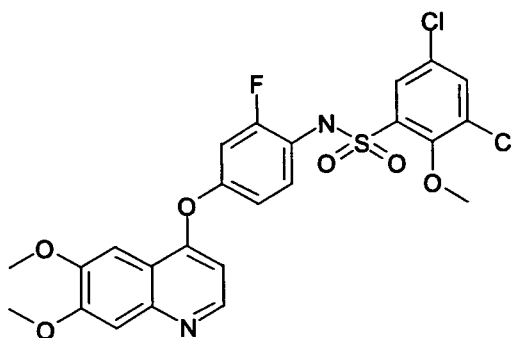
10 ¹H NMR (300 MHz, DMSO-d₆): 10.45 (s, 1H), 8.50 (d, 1H), 8.31 (s, 1H), 7.86 (m, 2H), 7.68 (d, 2H), 7.42 (s, 1H), 7.40 (s, 1H), 7.31(t, 1H), 7.23 (dd, 1H), 7.03 (d, 1H), 6.56 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 225-227 °C.

15 Yield: 38 %

Example A50

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-benzenesulfonamide



20

 $C_{24}H_{19}Cl_2FN_2O_6S$ Mw. 553.40LC/MS purity: 99 %, m/z 551[M-H]⁻ Rt. 3.23 min.

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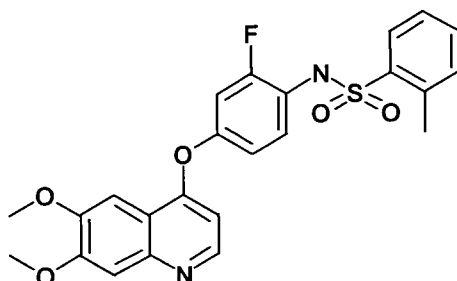
¹H NMR (300 MHz, DMSO-d₆): 10.37 (s, 1H), 8.51 (d, 1H), 8.03 (d, 1H), 7.63 (d, 1H), 7.42 (s, 1H), 7.40 (s, 1H), 7.33 (t, 1H), 7.25 (dd, 1H), 7.04 (dd, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.91(s, 3H), 3.90 (s, 3H)

5 Melting point: 193-195 °C.

Yield: 51 %

Example A51

10 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methyl-benzenesulfonamide



C₂₄H₂₁FN₂O₅S Mw. 468.51

LC/MS purity: 94%, m/z 467 [M-H]⁻ m/z 469 [M-H]⁺ Rt. 2.82 min.

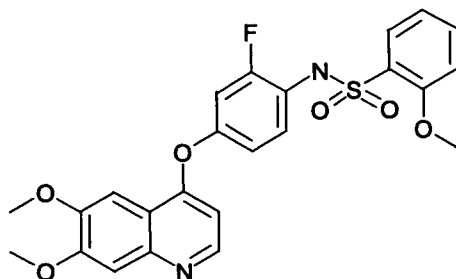
15 ¹H NMR (300 MHz, DMSO-d₆): 10.47 (bs, 1H), 8.49 (d, 1H), 7.92 (d, 1H), 7.68-7.18 (m, 7H), 7.00 (dd, 1H), 6.51 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 2.58 (s, 3H)

Melting point: 218-220 °C.

Yield: 62 %

20 Example A52

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-benzenesulfonamide



C₂₄H₂₁FN₂O₆S Mw. 484.51

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LC/MS purity: 98% m/z 483 [M-H]⁻ m/z 485 [M-H]⁺ Rt. 2.71 min.

¹H NMR (300 MHz, DMSO-d₆): 9.82 (bs, 1H), 8.50 (d, 1H), 7.65 (m, 2H), 7.39-7.01 (m, 7H),

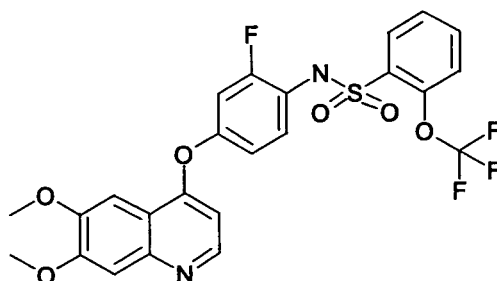
6.50 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H), 2.59 (s, 3H)

5 Melting point: 213-215 °C.

Yield: 55 %

Example A53

10 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonami



C₂₄H₁₈F₄N₂O₆S Mw. 538.48

LC/MS purity: 96% m/z 537 [M-H]⁻ m/z 539 [M-H]⁺ Rt. 3.00 min.

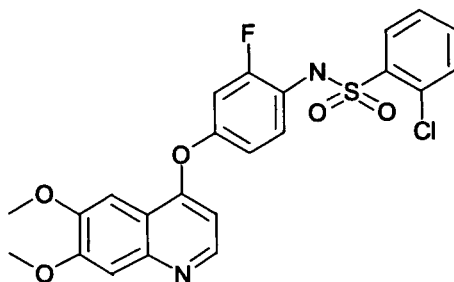
15 ¹H NMR (300 MHz, DMSO-d₆): 10.40 (bs, 1H), 8.52 (d, 1H), 7.90 (d, 1H), 7.80 (m, 1H), 7.70-7.05 (m, 7H), 6.54 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 204-206 °C.

Yield: 69 %

20 Example A54

2-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamid



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$C_{23}H_{18}ClFN_2O_5S$ Mw. 488.93

LC/MS purity: 98% m/z 487 [M-H]⁻, m/z 489 [M-H]⁺ Rt. 2.81 min.

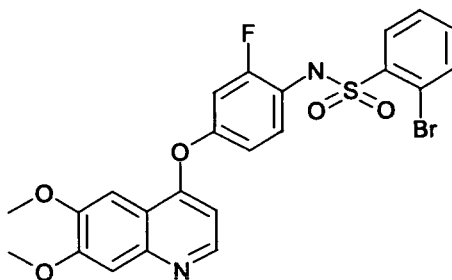
¹H NMR (300 MHz, DMSO-d₆): 10.43 (bs, 1H), 8.50 (d, 1H), 7.69 (d, 1H), 7.64 (m, 2H), 7.51-7.17 (m, 5H), 7.00 (d, 1H), 6.52 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 232-234 °C.

Yield: 76 %

Example A55

2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



$C_{23}H_{18}BrFN_2O_5S$ Mw. 533.38

LC/MS purity: 98%, m/z 531 [M-H]⁻, m/z 533 [M-H]⁺ Rt. 2.85 min.

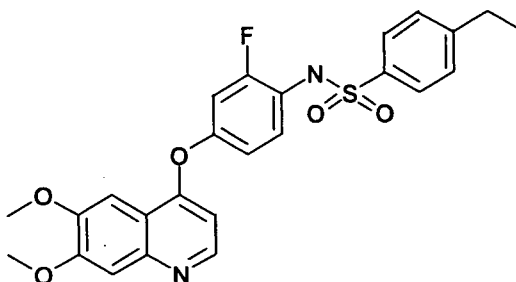
¹H NMR (300 MHz, DMSO-d₆): 10.40 (bs, 1H), 8.50 (d, 1H), 7.95 (dd, 1H), 7.88 (dd, 1H), 7.55 (m, 2H), 7.40 (s, 2H), 7.26 (m, 2H), 7.04 (dd, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 225-227 °C.

Yield: 47 %

Example A56

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-ethylbenzenesulfonamide



- 64 -

$C_{25}H_{23}FN_2O_5S$ Mw. 482.53

LC/MS purity: 94%, m/z 481 [M-H]⁻, m/z 483 [M-H]⁺ Rt. 3.01 min.

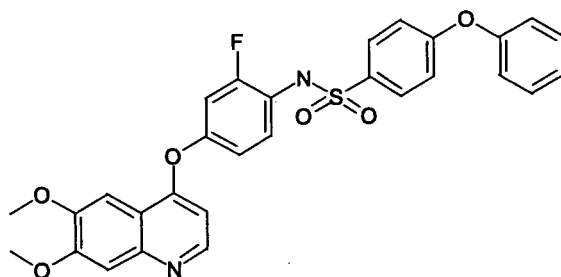
¹H NMR (300 MHz, DMSO-d₆): 10.14 (bs, 1H), 8.50 (d, 1H), 7.66 (d, 2H), 7.41 (m, 3H), 7.32 (t, 1H), 7.22 (dd, 1H), 7.04 (dd, 1H), 6.54 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.68 (q, 2H), 1.20 (t, 3H)

Melting point: 193-195 °C.

Yield: 66 %

Example A57

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-phenoxy-benzenesulfonamide



$C_{29}H_{23}FN_2O_6S$ Mw. 546.58

LC/MS purity: 95%, m/z 545 [M-H]⁻, m/z 547 [M-H]⁺ Rt. 3.23 min.

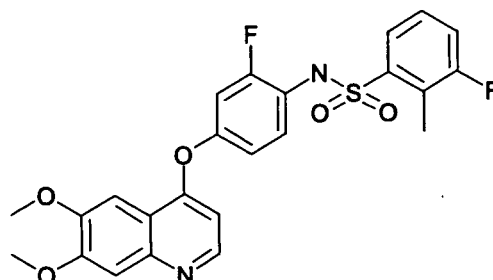
¹H NMR (300 MHz, DMSO-d₆): 10.13 (bs, 1H), 8.49 (d, 1H), 7.73 (d, 2H), 7.43 (m, 4H), 7.32-7.22 (m, 4H), 7.10 (m, 4H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 202-204 °C.

Yield: 76 %

Example A58

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-2-methyl-benzenesulfonamide



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$C_{24}H_{20}F_2N_2O_5S$ Mw. 486.50

LC/MS purity: 94%, m/z 485 [M-H]⁻, m/z 487 [M-H]⁺ Rt. 2.92 min.

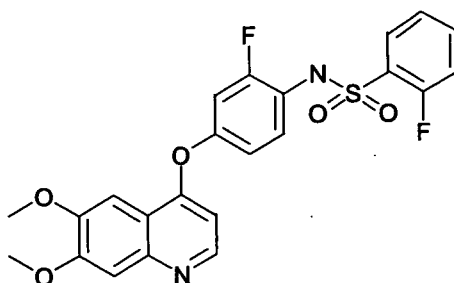
¹H NMR (300 MHz, DMSO-d₆): 10.39 (bs, 1H), 8.57 (d, 1H), 7.60-7.31 (m, 6H), 7.23 (dd, 1H), 7.04 (d, 1H), 6.52 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

5 Melting point: 204-206 °C.

Yield: 78 %

Example A59

10 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-fluoro-benzenesulfonamide



$C_{23}H_{18}F_2N_2O_5S$ Mw. 472.47

LC/MS purity: 98%, m/z 471 [M-H]⁻, m/z 473 [M-H]⁺ Rt. 2.72 min.

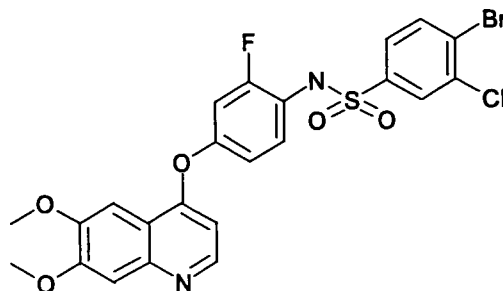
15 ¹H NMR (300 MHz, DMSO-d₆): 10.47 (bs, 1H), 8.51 (d, 1H), 7.70 (m, 1H), 7.70 (m, 2H), 7.37 (m, 5H), 7.22 (dd, 1H), 7.03 (dd, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H)

Melting point: 235-236 °C.

Yield: 51 %

20 Example A60

4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide



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$C_{23}H_{17}BrClFN_2O_5S$ Mw. 567.82

LC/MS purity: 98%, m/z 565 [M-H]⁻, m/z 567 [M-H]⁺ Rt. 3.14 min.

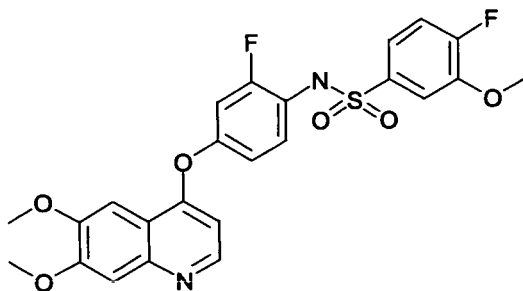
¹H NMR (300 MHz, DMSO-d₆): 10.45 (bs, 1H), 8.51 (d, 1H), 8.02 (d, 1H), 7.87 (s, 1H), 7.58 (dd, 1H), 7.42-7.24 (m, 4H), 7.07 (d, 1H), 6.57 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 231-232 °C.

Yield: 55 %

Example A61

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide



$C_{24}H_{20}F_2N_2O_6S$ Mw. 502.50

LC/MS purity: 100%, m/z 501 [M-H]⁻, m/z 503 [M-H]⁺ Rt. 2.69 min.

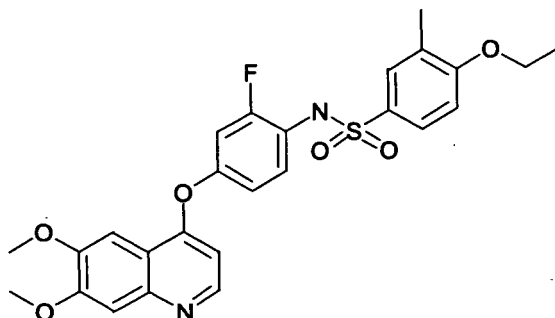
¹H NMR (300 MHz, DMSO-d₆): 10.20 (bs, 1H), 8.50 (d, 1H), 7.49-7.22 (m, 7H), 7.05 (d, 1H), 6.55 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H)

Melting point: 214-216 °C.

Yield: 45 %

Example A62

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-ethoxy-3-methyl-benzenesulfonamid



- 67 -

$C_{26}H_{25}FN_2O_6S$ Mw. 512.56

LC/MS purity: 100%, m/z 521 [M-H]⁻ Rt. 3.09 min.

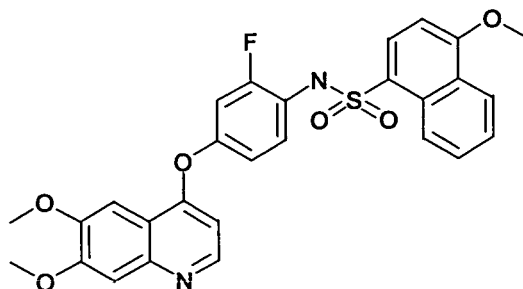
¹H NMR (300 MHz, DMSO-d₆): 9.96 (s, 1H), 8.50 (d, 1H), 7.52 (m, 2H), 7.42 (s, 1H), 7.40 (s, 1H), 7.30 (t, 1H), 7.20 (d, 1H), 7.04 (m, 2H), 6.52 (d, 1H),
5 4.10 (q, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 1.36 (t, 3H)

Melting point: 158-160 °C.

Yield: 61 %

Example A63

10 4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amid



$C_{28}H_{23}FN_2O_6S$ Mw. 534.57

LC/MS purity: 97%, m/z 533 [M-H]⁻ Rt. 3.07 min.

15 ¹H NMR (300 MHz, DMSO-d₆): 10.31 (s, 1H), 8.68 (d, 1H), 8.48 (d, 2H), 8.29 (d, 1H), 8.07 (d, 1H), 7.70 (m, 2H), 7.38 (s, 1H), 7.37 (s, 1H), 7.28 (t, 1H), 7.07 (m, 3H), 6.45 (d, 1H), 4.05 (s, 3H),
3.93 (s, 3H), 3.88 (s, 3H)

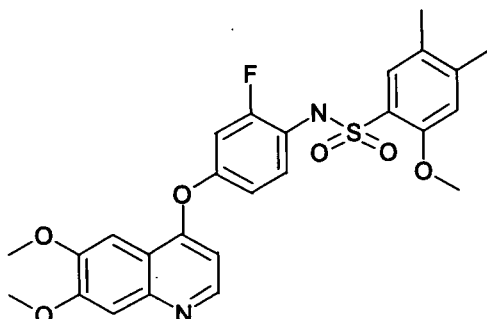
Melting point: 226-227 °C.

20 Yield: 62 %

- 68 -

Example A64

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-4,5-dimethyl-benzenesulfonamide



5 $C_{26}H_{25}FN_2O_6S$ Mw. 512.56

LC/MS purity: 97%, m/z 511 [M-H]⁻ Rt. 2.97 min.

¹H NMR (300 MHz, DMSO-d₆): 9.63 (s, 1H), 8.50 (d, 1H), 7.40 (s, 3H), 7.33 (t, 1H), 7.20 (dd, 1H), 7.02 (m, 2H), 6.51 (d, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.84 (s, 3H), 2.27 (s, 3H), 2.15 (s, 3H)

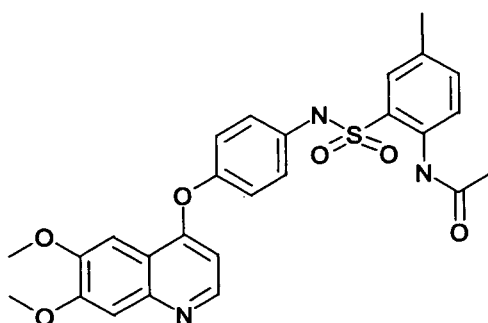
10 Melting point: 238-240 °C.

Yield: 53 %

Example A65

N-{2-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenylsulfamoyl]-4-methyl-phenyl}-acetamide

15



$C_{26}H_{25}N_3O_6S$ Mw. 507.57

LC/MS purity: 99%, m/z 506 [M-H]⁻, m/z 508 [M-H]⁺ Rt. 2.51 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 10.13 (s, 1H), 8.43 (d, 1H), 8.15 (d, 1H), 7.72 (d, 1H), 7.44 (s, 1H), 7.37 (s, 1H), 7.29 (d, 1H), 7.13 (dd, 4H), 6.35 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 2.54 (s, 3H), 2.03 (s, 3H)

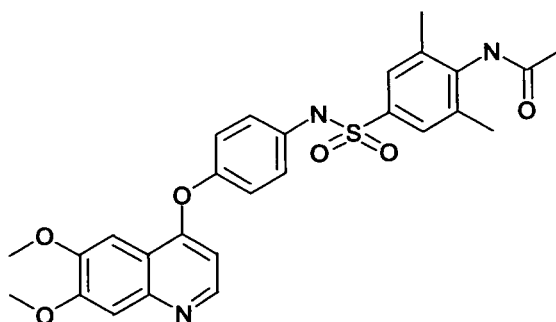
Melting point: 134-136 °C.

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Yield: 49 %

Example A66

N-{4-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenylsulfamoyl]-2,6-dimethyl-phenyl}-acetamide

 $C_{27}H_{27}N_3O_6S$ Mw. 521.60LC/MS purity: 94%, m/z 520 [M-H]⁻, m/z 522 [M-H]⁺ Rt. 2.49 min.

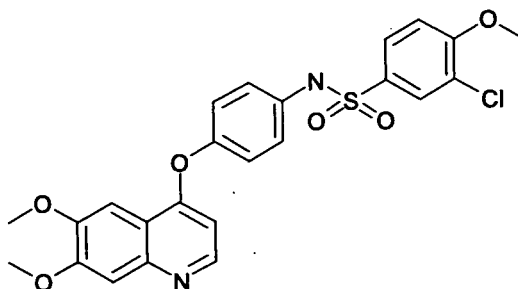
¹H NMR (300 MHz, DMSO-d₆): 13.5 (bs, 1H), 8.44 (d, 1H), 7.73 (d, 1H), 7.45 (s, 1H), 7.37 (s, 1H), 7.25 (d, 1H), 7.14 (m, 4H), 6.37 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 2.44 (s, 3H), 2.17 (s, 3H), 2.07 (s, 3H)

Melting point: 145-147 °C.

Yield: 67 %

Example A67

3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxybenzenesulfonamide

 $C_{24}H_{21}ClN_2O_6S$ Mw. 500.96LC/MS purity: 99%, m/z 499 [M-H]⁻, m/z 501 [M-H]⁺ Rt. 2.89 min.

¹H NMR (300 MHz, DMSO-d₆): 10.27 (bs, 1H), 8.45 (d, 1H), 7.70 (m, 2H), 7.36 (m, 3H), 7.18 (m, 4H), 6.37 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H)

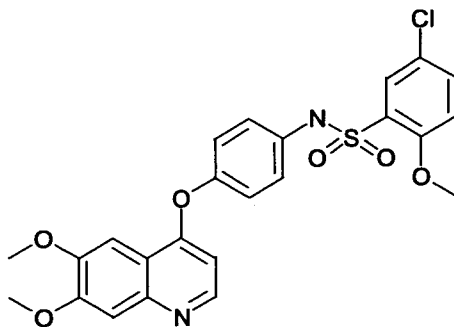
Melting point: 226-227 °C.

- 70 -

Yield: 51%

Example A68

5-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-methoxy-
benzenesulfonamide



$C_{24}H_{21}ClN_2O_6S$ Mw. 500.96

LC/MS purity: 98%, m/z 499 [M-H]⁻ m/z 501 [M-H]⁺ Rt. 2.90 min.

¹H NMR (300 MHz, DMSO-d₆): 10.24 (s, 1H), 8.44 (d, 1H), 7.66 (m, 2H),
7.44 (s, 1H), 7.37 (s, 1H), 7.27-7.13 (m, 5H), 6.32 (d, 1H), 3.93 (s, 3H), 3.92
(s, 3H), 3.89 (s, 3H),

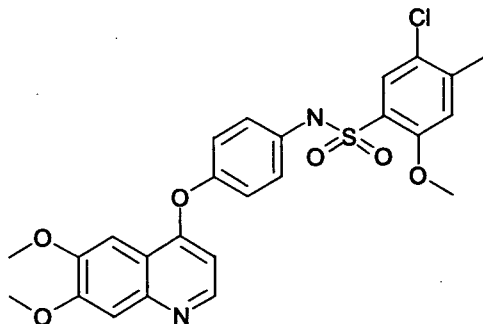
Melting point: 255-257 °C.

Yield: 63 %

15

Example A69

5-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-methoxy-4-methyl-
benzenesulfonamide



$C_{25}H_{23}ClN_2O_6S$ Mw. 514.99

LC/MS purity: 98%, m/z 513 [M-H]⁻ Rt. 3.04 min.

¹H NMR (300 MHz, DMSO-d₆): 12.0 (bs, 1H), 10.17 (bs, 1H), 8.44 (d, 1H),

20

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7.65 (s, 1H), 7.44 (s, 3H), 7.37 (s, 1H), 7.17 (m, 5H), 6.33 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 2.36 (s, 3H)

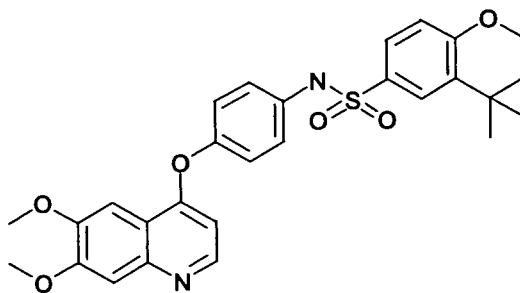
Melting point: 236-238 °C.

Yield: 70 %

5

Example A70

3-tert-Butyl-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide



10 $C_{28}H_{30}N_2O_6S$ Mw. 522.63

LC/MS purity: 98%, m/z 521 [M-H]⁻ Rt. 3.24 min.

¹H NMR (300 MHz, DMSO-d₆): 10.13 (bs, 1H), 8.43 (d, 1H), 7.62 (d, 1H), 7.56 (s, 1H), 7.44 (s, 1H), 7.38 (s, 5H), 7.16 (m, 5H), 6.33 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H), 1.29 (s, 9H).

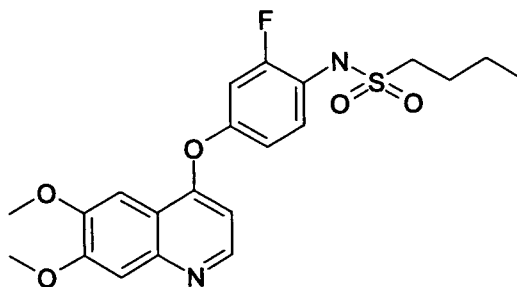
15 Melting point: 229-231 °C.

Yield: 56 %

Example A71

Butane-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

20



$C_{21}H_{23}FN_2O_5S$ Mw. 434.49

LC/MS purity: 99%, m/z 433 [M-H]⁻, m/z 435 [M-H]⁺ Rt. 2.67 min.

¹H NMR (300 MHz, DMSO-d₆): 9.66 (s, 1H), 8.52 (d, 1H), 7.45 (m, 4H), 7.09

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(d, 1H), 6.63 (d, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 3.11 (t, 2H), 1.70 (m, 2H), 1.40 (q, 2H), 0.89 (t, 3H)

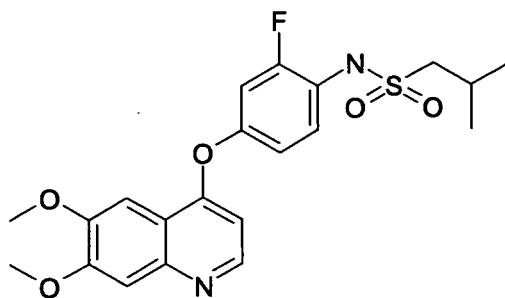
Melting point: 164-166 °C.

Yield: 42 %

5

Example A72

2-Methyl-propane-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



10 $C_{21}H_{23}FN_2O_5S$ Mw. 434.49

LC/MS purity: 100%, m/z 433 [M-H]⁻, m/z 435 [M-H]⁺ Rt. 2.48 min.

¹H NMR (300 MHz, DMSO-d₆): 9.68 (s, 1H), 8.52 (d, 1H), 7.52-7.41 (m, 3H), 7.43 (dd, 1H), 7.09 (dd, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 3.02 (d, 2H), 2.20 (m, 1H), 1.04 (s, 6H)

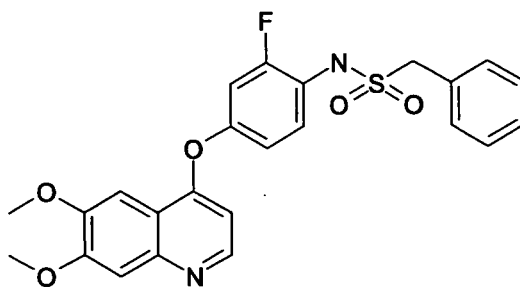
15 Melting point: 175-176 °C.

Yield: 46 %

Example A73

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-C-phenyl-methanesulfonamide

20



$C_{24}H_{21}FN_2O_5S$ Mw. 468.51

LC/MS purity: 99%, m/z 467 [M-H]⁻, m/z 469 [M-H]⁺ Rt. 2.57 min.

¹H NMR (300 MHz, DMSO-d₆): 9.73 (s, 1H), 8.54 (d, 1H), 7.38 (m, 9H), 7.03

- 73 -

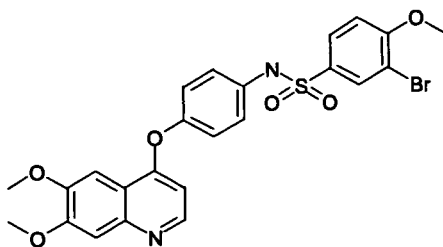
(d, 1H), 6.58 (d, 1H), 3.95 (s, 3H), 3.92 (s, 3H),

Melting point: 204-205 °C.

Yield: 47 %

5 Example A74

3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide



10 $C_{24}H_{21}BrN_2O_6S$ Mw. 545.41

LC/MS purity: 100 %, m/z 543 [M-H]⁻, m/z 545 [M-H]⁺ Rt. 2.78 min.

¹H NMR (300 MHz, DMSO-d₆): 10.25 (bs, 1H), 8.46 (d, 1H), 7.81 (s, 1H), 7.73 (dd, 1H), 7.45 (s, 1H), 7.38 (s, 1H), 7.27 (dd, 1H), 7.17 (m, 4H), 6.35 (s, 1H), 3.93 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H).

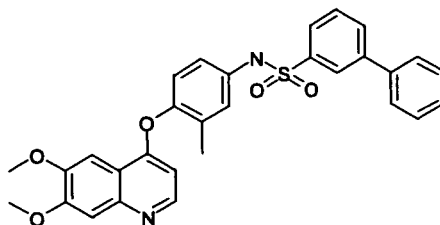
15 Melting point: 211-212°C.

Yield: 74 %

Example A75

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide

20



$C_{30}H_{26}N_2O_5S$ Mw. 526.62

LC/MS purity: 99 %, m/z 525 [M-H]⁻, m/z 527 [M-H]⁺ Rt. 3.19 min.

¹H NMR (300 MHz, DMSO-d₆): 10.29 (s, 1H), 8.32 (d, 1H), 7.97 (m, 1H), 7.77 (d, 1H), 7.67 (m, 3H), 7.50 (s, 5H), 7.37 (s, 1H), 7.15 (s, 1H), 7.05 (s, 2H), 6.0 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 2.01 (s, 3H)

25

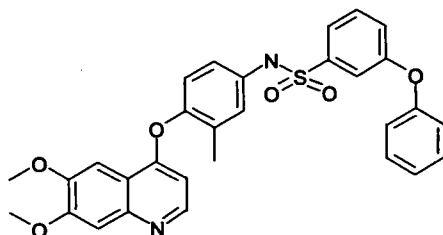
- 74 -

Melting point: 178-180 °C.

Yield: 55 %

Example A76

5 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-3-phenoxy-benzenesulfonamide

 $C_{30}H_{26}N_2O_6S$ Mw. 542.62LC/MS purity: 100 %, m/z 541 [M-H]⁻, m/z 543 [M-H]⁺ Rt. 3.21 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.28 (bs, 1H), 8.40 (d, 1H), 7.63-7.44 (m, 4H), 7.42-7.30 (m, 3H), 7.25-6.97 (m, 7H), 6.28 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H), 2.08 (s, 3H)

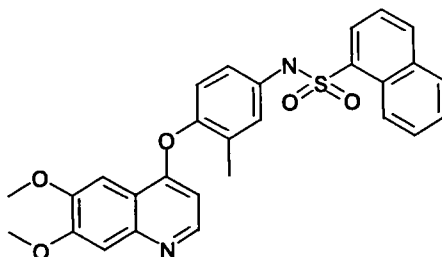
Melting point: 115-117 °C.

Yield: 65 %

15

Example A77

Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide



20 $C_{28}H_{24}N_2O_5S$ Mw. 500.58

LC/MS purity: 95 %, m/z 499 [M-H]⁻, m/z 501 [M-H]⁺ Rt. 2.87 min.

¹H NMR (300 MHz, DMSO-d₆): 10.68 (s, 1H), 8.75 (d, 1H), 8.38 (d, 1H), 8.24 (m, 2H), 8.10 (d, 1H), 7.69 (m, 3H), 7.46 (s, 1H), 7.36 (s, 1H), 7.04 (s, 1H), 6.95 (m, 2H), 6.07 (d, 1H), 3.92 (s, 3H), 3.88 (s, 3H), 1.94 (s, 3H)

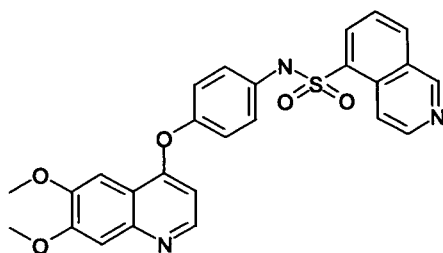
25 Melting point: 118-120 °C.

- 75 -

Yield: 43 %

Example A78

Isoquinoline-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-
amide



$C_{26}H_{21}N_3O_5S$ Mw. 487.54

LC/MS purity: 100 %, m/z 486 [M-H]⁻, m/z 488 [M-H]⁺ Rt. 2.51 min.

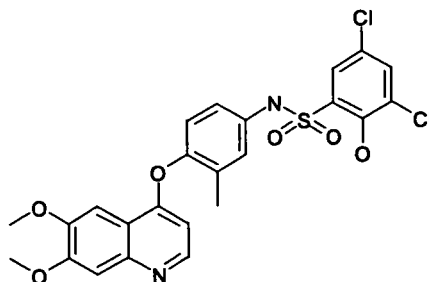
¹H NMR (300 MHz, DMSO-d₆): 10.80 (s, 1H), 9.48 (s, 1H), 8.73 (d, 1H), 8.51 (d, 1H), 8.43 (m, 3H), 7.82 (t, 1H), 7.39 (s, 1H), 7.36 (s, 1H), 7.10 (dd, 4H), 6.26 (d, 1H), 3.92 (s, 3H), 3.87 (s, 3H)

Melting point: 229-231 °C.

Yield: 74 %

Example A79

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-hydroxy-benzenesulfonamide



$C_{24}H_{20}Cl_2N_2O_6S$ Mw. 535.41

LC/MS purity: 91 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 2.90 min.

¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 7.87 (d, 1H), 7.73 (s, 1H), 7.68 (d, 1H), 7.62 (s, 1H), 7.14 (m, 5H), 6.59 (d, 1H), 4.01 (s, 6H), 2.05 (s, 3H)

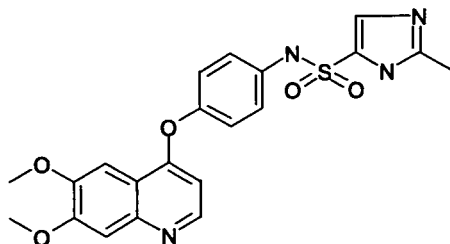
- 76 -

Melting point: 113-117 °C.

Yield: 25 %

Example A80

- 5 2-Methyl-3H-imidazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

 $C_{21}H_{20}N_4O_5S$ Mw. 440.48

- 10 LC/MS purity: 99 %, m/z 439 [M-H]⁻, m/z 441 [M-H]⁺ Rt. 2.02 min.

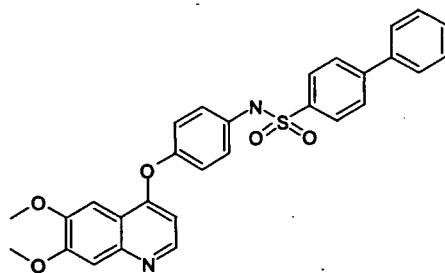
¹H NMR (300 MHz, DMSO-d₆): 12.4 (s, 1H), 8.58 (dd, 1H), 8.45 (d, 1H), 7.78 (t, 1H), 7.65 (d, 1H), 7.47 (s, 1H), 7.26 (d, 2H), 7.13 (d, 1H), 6.39 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.28 (s, 3H)

Melting point: 268-269 °C.

- 15 Yield: 54 %

Example A81

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide



- 20 $C_{29}H_{24}N_2O_5S$ Mw. 512.59

LC/MS purity: 96 %, m/z 511 [M-H]⁻, m/z 513 [M-H]⁺ Rt. 3.12 min.

¹H NMR (300 MHz, DMSO-d₆): 10.42 (bs, 1H), 8.42 (d, 1H), 7.87 (m, 4H), 7.73 (d, 2H), 7.49 (m, 3H), 7.43 (s, 1H), 7.37 (s, 1H), 7.25 (d, 2H), 7.17 (d, 2H), 6.36 (d, 1H), 3.93 (s, 3H), 3.88 (s, 3H)

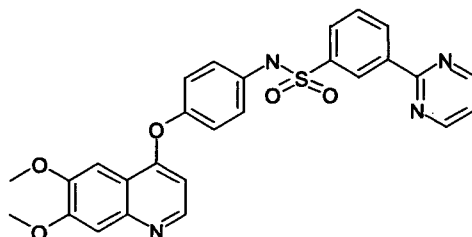
- 25 Melting point: 191-194 °C.

- 77 -

Yield: 52 %

Example A82

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-3-pyrimidin-2-yl-
benzenesulfonamide



$C_{27}H_{22}N_4O_5S$ Mw. 514.56

LC/MS purity: 99 %, m/z 513 [M-H]⁻, m/z 515 [M-H]⁺ Rt. 2.67 min.

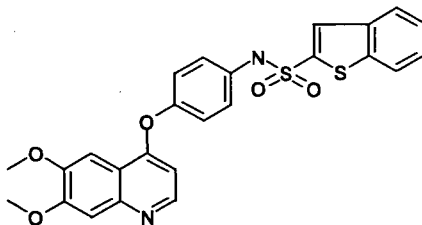
¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 8.96 (d, 2H), 8.82 (s, 1H), 8.62 (d, 1H), 8.36 (d, 1H), 7.90 (d, 1H), 7.75 (t, 1H), 7.54 (t, 1H), 7.42 (s, 1H), 7.36 (s, 1H), 7.22 (d, 2H), 7.15 (d, 2H), 6.28 (d, 1H), 3.92 (s, 3H), 3.87 (s, 3H)

Melting point: 194-195 °C.

Yield: 61 %

Example A83

Benzo[b]thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide



20

$C_{25}H_{20}N_2O_5S_2$ Mw. 492.58

LC/MS purity: 99 %, m/z 491 [M-H]⁻, m/z 493 [M-H]⁺ Rt. 2.90 min.

¹H NMR (300 MHz, DMSO-d₆): 10.72 (s, 1H), 8.44 (d, 1H), 8.08 (d, 1H), 8.02 (d, 1H), 7.51 (m, 3H), 7.44 (s, 1H), 7.37 (s, 1H), 7.29 (d, 2H), 7.19 (d, 2H), 6.36 (d, 1H), 3.93 (s, 3H), 3.88 (s, 3H)

25

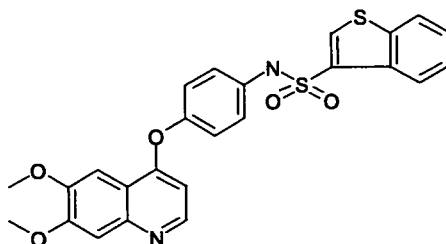
- 78 -

Melting point: 222-225 °C.

Yield: 64 %

Example A84

5 Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

 $C_{25}H_{20}N_2O_5S_2$ Mw. 492.58LC/MS purity: 100 %, m/z 491 [M-H]⁻, m/z 493 [M-H]⁺ Rt. 2.84 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.25 (s, 1H), 8.39 (d, 1H), 8.28 (d, 1H), 8.25 (s, 1H), 8.01 (d, 1H), 7.42 (m, 3H), 7.35 (s, 1H), 7.04 (d, 2H), 6.93 (d, 2H), 6.31 (d, 1H), 3.92 (s, 3H), 3.88 (s, 3H)

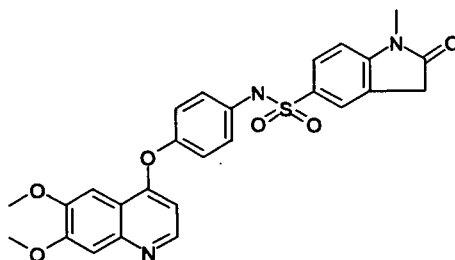
Melting point: 267-270 °C.

Yield: 53 %

15

Example A85

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide



20 $C_{26}H_{23}N_3O_6S$ Mw. 505.55

LC/MS purity: 100 %, m/z 504 [M-H]⁻, m/z 506 [M-H]⁺ Rt. 2.37 min.

¹H NMR (300 MHz, DMSO-d₆): 10.1 (bs, 1H), 8.44 (m, 1H), 7.71 (d, 1H), 7.64 (s, 1H), 7.41 (d, 2H), 7.37 (d, 1H), 7.15 (m, 4H), 6.36 (m, 1H), 3.92 (s, 3H), 3.88 (s, 3H), 3.64 (s, 2H), 3.13 (s, 3H)

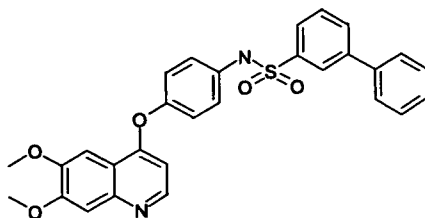
25 Melting point: 119-122 °C.

- 79 -

Yield: 54 %

Example A86

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide



5

 $C_{29}H_{24}N_2O_5S$ Mw. 512.59LC/MS purity: 97 %, m/z 511 [M-H]⁻, m/z 513 [M-H]⁺ Rt. 3.09 min.

¹H NMR (300 MHz, DMSO-d₆): 10.3 (bs, 1H), 8.36 (d, 1H), 7.98 (s, 1H), 7.95 (d, 1H), 7.76 (d, 1H), 7.66 (m, 3H), 7.51 (m, 3H), 7.43 (s, 1H), 7.37 (s, 1H), 7.24 (d, 2H), 7.17 (d, 2H), 6.29 (d, 1H), 3.93 (s, 3H), 3.88 (s, 3H)

10

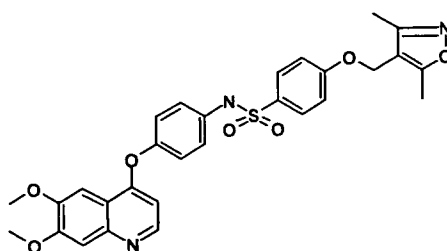
Melting point: 197-200 °C.

Yield: 53 %

15

Example A87

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-4-(3,5-dimethyl-isoxazol-4-ylmethoxy)-benzenesulfonamide



20

 $C_{29}H_{27}N_3O_7S$ Mw. 561.62LC/MS purity: 97 %, m/z 560 [M-H]⁻, m/z 562 [M-H]⁺ Rt. 2.78 min.

¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 8.45 (d, 1H), 7.72 (d, 2H), 7.44 (s, 1H), 7.38 (s, 1H), 7.16 (m, 6H), 6.37 (d, 1H), 4.99 (s, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 2.39 (s, 3H), 2.19 (s, 3H)

25

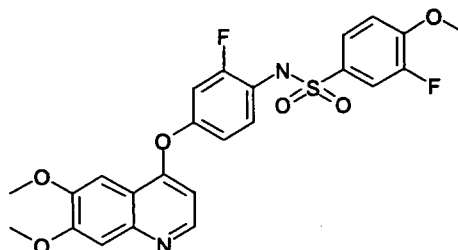
Melting point: 188-190 °C.

Yield: 11 %

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Example A88

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-4-methoxy-benzenesulfonamide



$C_{24}H_{20}F_2N_2O_6S$ Mw. 502.50

LC/MS purity: 100 %, m/z 501 [M-H]⁻, m/z 503 [M-H]⁺ Rt. 2.62 min.

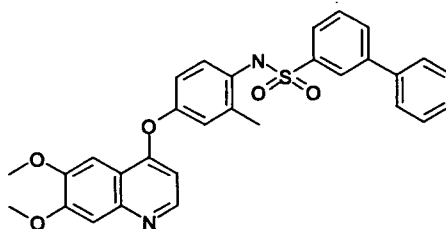
¹H NMR (300 MHz, DMSO-d₆): 10.15 (bs, 1H), 8.50 (d, 1H), 7.51 (m, 3H), 7.41-7.21 (m, 4H), 7.04 (dd, 1H), 6.95 (d, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.89 (s, 3H)

Melting point: 230-232 °C.

Yield: 23 %

Example A89

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide



$C_{30}H_{26}N_2O_5S$ Mw. 526.62

LC/MS purity: 100 %, m/z 525 [M-H]⁻, m/z 527 [M-H]⁺ Rt. 3.18 min.

¹H NMR (300 MHz, DMSO-d₆): 9.69 (s, 1H), 8.40 (d, 1H), 7.97 (t, 1H), 7.87 (s, 1H), 7.66 (m, 4H), 7.48 (m, 4H), 7.38 (s, 1H), 7.06 (m, 3H), 6.39 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.00 (s, 3H)

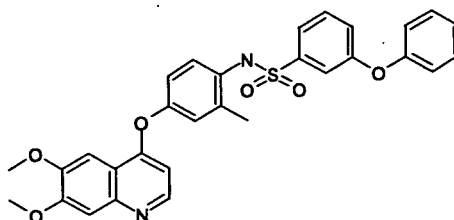
Melting point: 220-222 °C.

Yield: 77 %

- 81 -

Example A90

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-3-phenoxy-benzenesulfonamide



5 $C_{30}H_{26}N_2O_6S$ Mw. 542.62

LC/MS purity: 100 %, m/z 541 [M-H]⁻, m/z 543 [M-H]⁺ Rt. 3.22 min.

¹H NMR (300 MHz, DMSO-d₆): 9.71 (s, 1H), 8.46 (d, 1H), 7.61 (t, 1H), 7.43 (m, 5H), 7.18 (t, 1H), 7.08 (m, 7H), 6.44 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 1.98 (s, 3H)

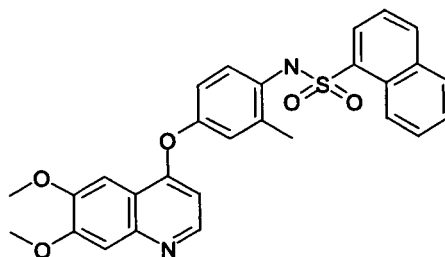
10 Melting point: 169-170 °C.

Yield: 70 %

Example A91

Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide

15



$C_{28}H_{24}N_2O_5S$ Mw. 500.58

LC/MS purity: 98 %, m/z 499 [M-H]⁻, m/z 451 [M-H]⁺ Rt. 3.01 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 9.93 (s, 1H), 8.71 (d, 1H), 8.47 (d, 1H), 8.25 (d, 1H), 8.08 (m, 2H), 7.70 (m, 2H), 7.61 (t, 1H), 7.41 (s, 1H), 7.37 (s, 1H), 7.03 (d, 1H), 6.94 (m, 2H), 6.37 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 1.85 (s, 3H)

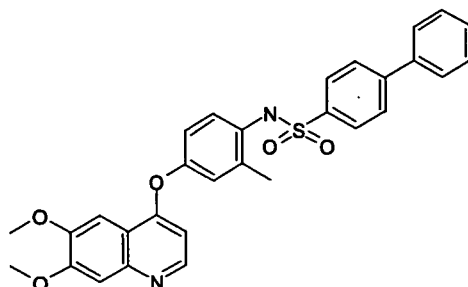
Melting point: 233-235 °C.

Yield: 72 %

- 82 -

Example A92

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide



5 $C_{30}H_{26}N_2O_5S$ Mw. 526.62

LC/MS purity: 96 %, m/z 525 [M-H]⁻, m/z 527 [M-H]⁺ Rt. 3.21 min.

¹H NMR (300 MHz, DMSO-d₆): 9.71 (s, 1H), 8.48 (s, 1H), 7.90 (d, 2H), 7.51 (m, 4H), 7.46 (m, 3H), 7.44 (s, 1H), 7.38 (s, 1H), 7.08 (m, 3H), 6.47 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 2.04 (s, 3H)

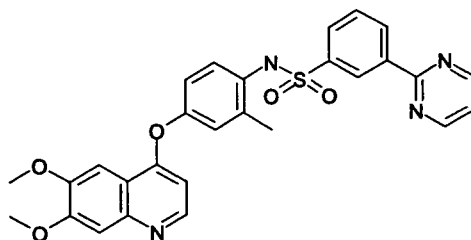
10 Melting point: 228-230 °C.

Yield: 58 %

Example A93

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

15



$C_{28}H_{24}N_4O_5S$ Mw. 528.59

LC/MS purity: 100 %, m/z 527 [M-H]⁻, m/z 529 [M-H]⁺ Rt. 2.81 min.

¹H NMR (300 MHz, DMSO-d₆): 9.79 (bs, 1H), 8.97 (d, 2H), 8.75 (d, 1H), 8.66 (d, 1H), 8.40 (d, 1H), 7.83 (dd, 1H), 7.75 (t, 1H), 7.54 (t, 1H), 7.43 (s, 1H), 7.37 (s, 1H), 7.06 (s, 1H), 7.02 (m, 2H), 6.39 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 2.01 (s, 3H)

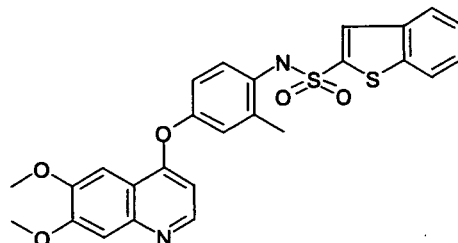
20

Melting point: 103-105 °C.

Yield: 65 %

Example A94

Benzo[b]thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide



$C_{26}H_{22}N_2O_5S_2$ Mw. 506.60

LC/MS purity: 98 %, m/z 505 [M-H]⁻, m/z 507 [M-H]⁺ Rt. 3.05 min.

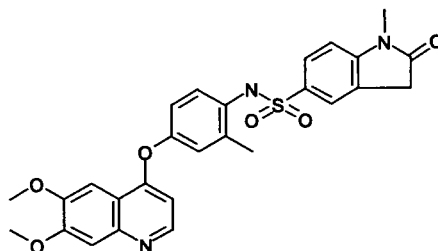
¹H NMR (300 MHz, DMSO-d₆): 10.11 (s, 1H), 8.49 (d, 1H), 8.10 (d, 1H), 8.02 (d, 1H), 7.81 (s, 1H), 7.52 (m, 2H), 7.45 (s, 1H), 7.39 (s, 1H), 7.19 (d, 1H), 7.11 (d, 1H), 7.06 (dd, 1H), 6.48 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.07 (s, 3H)

Melting point: 255-257 °C.

Yield: 34 %

Example A95

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide



$C_{27}H_{25}N_3O_6S$ Mw. 519.58

LC/MS purity: 100 %, m/z 518 [M-H]⁻, m/z 520 [M-H]⁺ Rt. 2.36 min.

¹H NMR (300 MHz, DMSO-d₆): 9.5 (bs, 1H), 8.61 (m, 3H), 7.44 (s, 1H), 7.38 (s, 1H), 7.02 (m, 4H), 6.45 (d, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.64 (s, 2H), 3.14 (s, 3H), 2.50 (s, 3H)

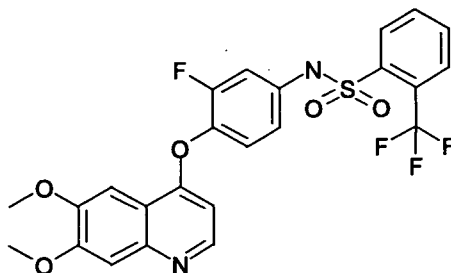
Melting point: 115-116 °C.

Yield: 71 %

- 84 -

Example A96

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethyl-benzenesulfonamide



5

$C_{24}H_{18}F_4N_2O_5S$ Mw. 522.48

LC/MS purity: 99 %, m/z 521 [M-H]⁻, m/z 523 [M-H]⁺ Rt. 2.99 min.

¹H NMR (300 MHz, DMSO-d₆): 11.03 (bs, 1H), 8.45 (d, 1H), 8.16 (d, 1H), 8.04 (d, 1H), 7.90 (m, 3H), 7.47 (s, 1H), 7.40 (s, 1H), 7.38 (t, 1H), 7.16 (d, 1H), 7.03 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H)

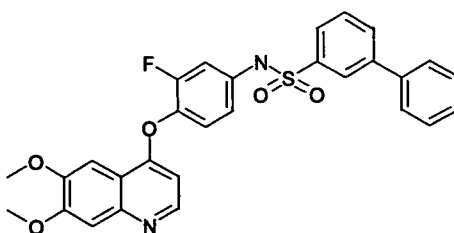
10

Melting point: 80-83 °C.

Yield: 51 %

Example A97

15 Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide



$C_{29}H_{23}FN_2O_5S$ Mw. 530.58

LC/MS purity: 98 %, m/z 529 [M-H]⁻, m/z 531 [M-H]⁺ Rt. 3.27 min.

20

¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 8.37 (d, 1H), 8.04 (s, 1H), 7.98 (d, 1H), 7.80 (d, 1H), 7.69 (m, 3H), 7.55-7.33 (m, 6H), 7.20 (dd, 1H), 7.06 (d, 1H), 6.28 (d, 1H), 3.97 (s, 3H), 3.90 (s, 3H)

Melting point: 109-111 °C.

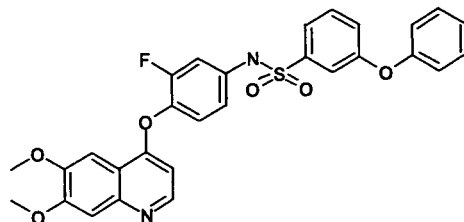
Yield: 67 %

25

- 85 -

Example A98

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-3-phenoxy-benzenesulfonamide



5

$C_{29}H_{23}FN_2O_6S$ Mw. 546.58

LC/MS purity: 99 %, m/z 545 [M-H]⁻, m/z 547 [M-H]⁺ Rt. 3.28 min.

¹H NMR (300 MHz, DMSO-d₆): 10.62 (bs, 1H), 8.45 (d, 1H), 7.62-7.52 (m, 8H), 7.24 (m, 2H), 7.14-7.00 (m, 4H), 6.36 (d, 1H), 3.95 (s, 3H), 3.93 (s, 3H)

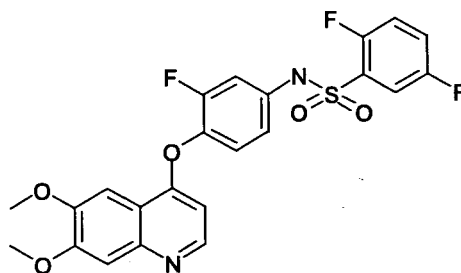
10 Melting point: 197-199 °C.

Yield: 65 %

Example A99

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2,5-difluoro-benzenesulfonamide

15



$C_{23}H_{17}F_3N_2O_5S$ Mw. 490.46

LC/MS purity: 99 %, m/z 489 [M-H]⁻, m/z 491 [M-H]⁺ Rt. 2.87 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 11.12 (bs, 1H), 8.45 (d, 1H), 7.73-7.55 (m, 3H), 7.48 (s, 1H), 7.41 (s, 1H), 7.39 (t, 1H), 7.19 (dd, 1H), 7.05 (d, 1H), 6.36 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H)

Melting point: 232-234 °C.

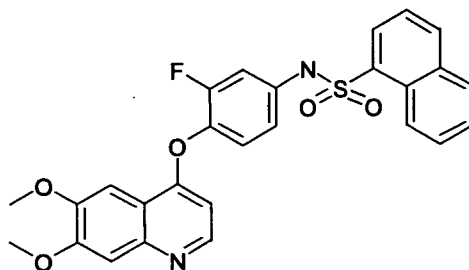
Yield: 51 %

25

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Example A100

Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide



5 $C_{27}H_{21}FN_2O_5S$ Mw. 504.54

LC/MS purity: 100 %, m/z 503 [M-H]⁻, m/z 505 [M-H]⁺ Rt. 3.04 min.

¹H NMR (300 MHz, DMSO-d₆): 11.04 (bs, 1H), 8.73 (d, 1H), 8.41 (d, 1H), 8.28 (m, 2H), 8.12 (d, 1H), 7.71 (m, 3H), 7.42 (s, 1H), 7.37 (s, 1H), 7.26 (t, 1H), 7.08 (dd, 1H), 6.93 (d, 1H), 6.26 (d, 1H), 3.92 (s, 3H), 3.88 (s, 3H)

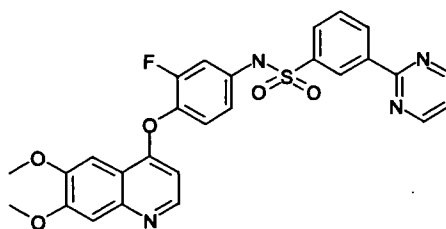
10 Melting point: 118-120 °C.

Yield: 61 %

Example A101

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

15



$C_{27}H_{21}FN_4O_5S$ Mw. 532.55

LC/MS purity: 100 %, m/z 531 [M-H]⁻, m/z 533 [M-H]⁺ Rt. 2.86 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.75 (bs, 1H), 8.97 (d, 2H), 8.85 (s, 1H), 8.65 (d, 1H), 8.37 (d, 1H), 7.96 (d, 1H), 7.78 (t, 1H), 7.55 (t, 1H), 7.45 (s, 1H), 7.37 (s, 1H), 7.34 (d, 1H), 7.19 (dd, 1H), 7.02 (dd, 1H), 6.28 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H)

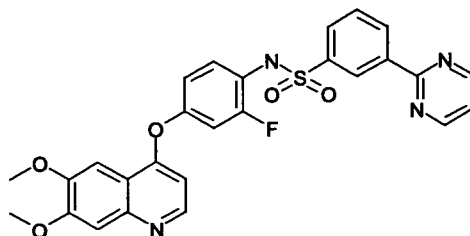
Melting point: 105-107 °C.

Yield: 39 %

- 87 -

Example A102

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide



5 $C_{27}H_{21}FN_4O_5S$ Mw. 532.55

LC/MS purity: 100 %, m/z 531 [M-H]⁻, m/z 533 [M-H]⁺ Rt. 2.79 min.

¹H NMR (300 MHz, DMSO-d₆): 10.33 (bs, 1H), 8.97 (d, 2H), 8.79 (s, 1H), 8.65 (d, 1H), 8.43 (d, 1H), 7.88 (d, 1H), 7.75 (t, 1H), 7.54 (t, 1H), 7.37 (m, 3H), 7.21 (dd, 1H), 7.06 (d, 1H), 6.47 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H)

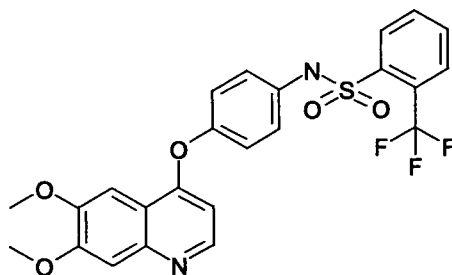
10 Melting point: 137-140 °C.

Yield: 42 %

Example A103

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide

15



$C_{24}H_{19}F_3N_2O_5S$ Mw. 504.49

LC/MS purity: 99 %, m/z 503 [M-H]⁻, m/z 505 [M-H]⁺ Rt. 2.88 min.

¹H NMR (300 MHz, DMSO-d₆): 10.71 (bs, 1H), 8.45 (d, 1H), 8.11 (dd, 1H), 8.02 (dd, 1H), 7.88 (m, 2H), 7.44 (s, 1H), 7.38 (s, 1H), 7.18 (dd, 4H), 6.37 (d, 1H), 3.93 (s, 3H), 3.81 (s, 3H)

20

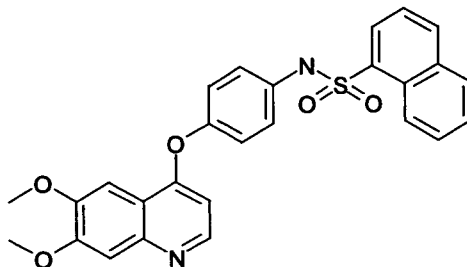
Melting point: 224-227 °C.

Yield: 59 %

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Example A104

Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide



5 $C_{27}H_{22}N_2O_5S$ Mw. 486.55

LC/MS purity: 100 %, m/z 485 [M-H]⁻, m/z 487 [M-H]⁺ Rt. 2.96 min.

¹H NMR (300 MHz, DMSO-d₆): 10.72 (bs, 1H), 8.75 (d, 1H), 8.41 (d, 1H), 8.22 (t, 2H), 8.09 (d, 1H), 7.71 (m, 3H), 7.39 (s, 1H), 7.35 (s, 1H), 7.09 (dd, 4H), 6.27 (d, 1H), 3.92 (s, 3H), 3.86 (s, 3H)

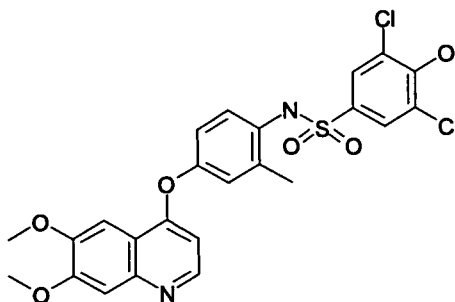
10 Melting point: 250-253 °C.

Yield: 61 %

Example A105

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-4-hydroxy-benzenesulfonamide

15



$C_{24}H_{20}Cl_2N_2O_6S$ Mw. 535.41

LC/MS purity: 93 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 2.69 min.

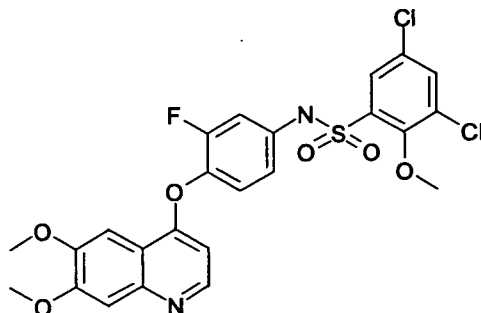
20 ¹H NMR (300 MHz, DMSO-d₆): 9.71 (s, 1H), 8.55 (d, 1H), 7.56 (s, 3H), 7.52 (s, 1H), 7.43 (s, 1H), 7.16 (s, 2H), 7.06 (m, 2H), 6.53 (d, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 2.09 (s, 3H)

Melting point: 255-259 °C.

Yield: 25 %

Example A106

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-methoxy-benzenesulfonamide



5 $C_{24}H_{19}Cl_2FN_2O_6S$ Mw. 553.40

LC/MS purity: 98 %, m/z 551 [M-H]⁻, m/z 553 [M-H]⁺ Rt. 3.31 min.

¹H NMR (300 MHz, DMSO-d₆): 10.86 (bs, 1H), 8.46 (d, 1H), 8.06 (d, 1H), 7.81 (d, 1H), 7.48 (s, 1H), 7.38 (m, 2H), 7.17 (dd, 1H), 7.04 (d, 1H), 6.36 (d, 1H), 3.96 (s, 3H), 3.94 (s, 3H), 3.91 (s, 3H)

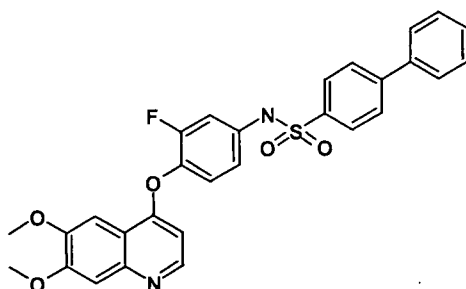
10 Melting point: 155-158 °C.

Yield: 59 %

Example A107

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide

15



$C_{29}H_{23}FN_2O_5S$ Mw. 530.58

LC/MS purity: 98 %, m/z 529 [M-H]⁻, m/z 531 [M-H]⁺ Rt. 3.28 min.

¹H NMR (300 MHz, DMSO-d₆): 10.72 (bs, 1H), 8.43 (d, 1H), 7.90 (s, 3H), 7.74 (d, 2H), 7.53-7.44 (m, 7H), 7.20 (d, 1H), 7.06 (d, 1H), 6.36 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H)

20

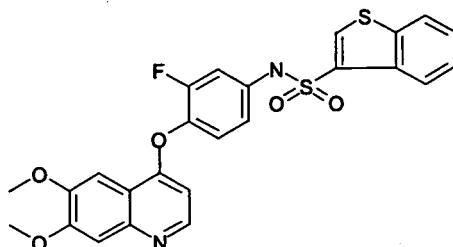
Melting point: 167-171 °C.

Yield: 40 %

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Example A108

Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide



5

$C_{25}H_{19}FN_2O_5S_2$ Mw. 510.57

LC/MS purity: 99 %, m/z 509 [M-H]⁻, m/z 511 [M-H]⁺ Rt. 3.03 min.

¹H NMR (300 MHz, DMSO-d₆): 10.96 (bs, 1H), 8.72 (s, 1H), 8.43 (d, 1H), 8.23 (d, 1H), 8.14 (d, 1H), 7.55 (m, 2H), 7.45 (s, 1H), 7.38 (s, 1H), 7.31 (t, 1H), 7.16 (dd, 1H), 7.09 (d, 1H), 6.30 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H)

10

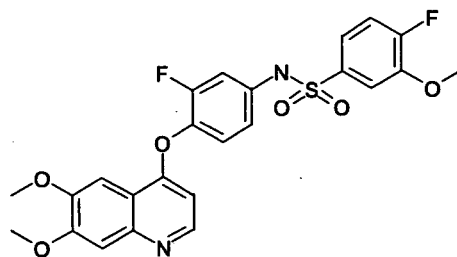
Melting point: 191-193 °C.

Yield: 63 %

Example A109

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide

15



$C_{24}H_{20}F_2N_2O_6S$ Mw. 502.50

LC/MS purity: 97 %, m/z 501 [M-H]⁻, m/z 503 [M-H]⁺ Rt. 2.92 min.

¹H NMR (300 MHz, DMSO-d₆): 10.60 (bs, 1H), 8.46 (d, 1H), 7.54-7.34 (m, 6H), 7.19 (dd, 1H), 7.03 (d, 1H), 6.35 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H)

20

Melting point: 202-204 °C.

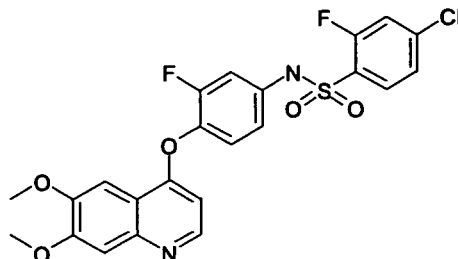
Yield: 61 %

25

- 91 -

Example A110

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-fluoro-benzenesulfonamide



5 $C_{23}H_{17}ClF_2N_2O_5S$ Mw. 506.92

LC/MS purity: 96 %, m/z 505 [M-H]⁻, m/z 507 [M-H]⁺ Rt. 3.01 min.

¹H NMR (300 MHz, DMSO-d₆): 11.08 (bs, 1H), 8.45 (d, 1H), 7.92 (m, 2H), 7.77 (dd, 1H), 7.52 (dd, 1H), 7.48 (s, 1H), 7.19 (s, 1H), 7.18 (t, 1H), 7.16 (dd, 1H), 7.03 (dd, 1H), 6.36 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H)

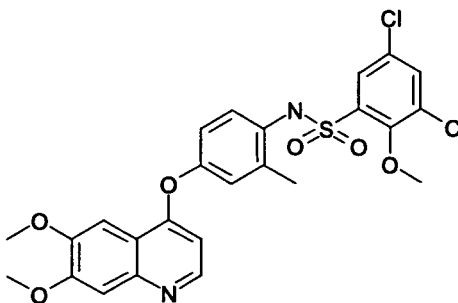
10 Melting point: 99-101 °C.

Yield: 54 %

Example A111

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-methoxy-benzenesulfonamide

15



$C_{25}H_{22}Cl_2N_2O_6S$ Mw. 549.43

LC/MS purity: 97 %, m/z 547 [M-H]⁻, m/z 549 [M-H]⁺ Rt. 3.27 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 9.90 (bs, 1H), 8.48 (d, 1H), 8.05 (d, 1H), 7.56 (d, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 7.07 (m, 3H), 6.45 (d, 1H), 3.94 (s, 6H), 3.90 (s, 3H), 2.07 (s, 3H), 2.08 (s, 3H)

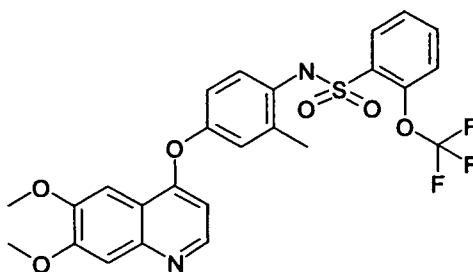
Melting point: 159-162 °C.

Yield: 69 %

- 92 -

Example A112

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-trifluoromethoxy-benzenesulfonamide



5 $C_{25}H_{21}F_3N_2O_6S$ Mw. 534.52

LC/MS purity: 98 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 2.91 min.

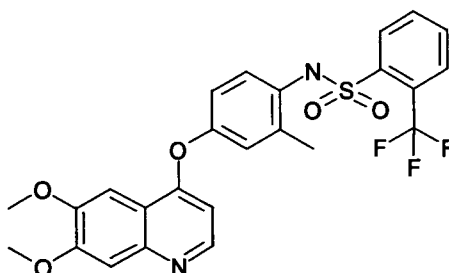
¹H NMR (300 MHz, DMSO-d₆): 9.92 (bs, 1H), 8.48 (d, 1H), 7.86 (d, 1H), 7.79 (t, 1H), 7.69 (d, 1H), 7.53 (d, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 7.09 (d, 1H), 7.07 (s, 1H), 7.01 (dd, 1H), 6.43 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.01 (s, 3H), 2.10 (s, 3H)

Melting point: 230-232 °C.

Yield: 64 %

Example A113

15 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-trifluoromethyl-benzenesulfonamide



$C_{25}H_{21}F_3N_2O_5S$ Mw. 518.52

LC/MS purity: 96 %, m/z 517 [M-H]⁻, m/z 519 [M-H]⁺ Rt. 2.96 min.

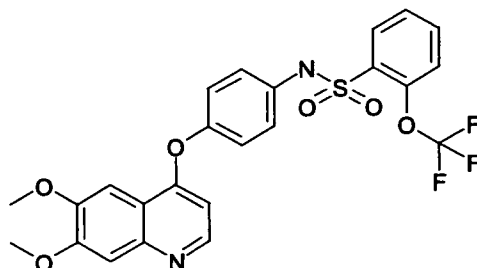
20 ¹H NMR (300 MHz, DMSO-d₆): 9.88 (bs, 1H), 8.48 (d, 1H), 8.02 (dd, 1H), 7.95 (dd, 1H), 7.86 (m, 2H), 7.44 (s, 1H), 7.39 (s, 1H), 7.05 (s, 1H), 6.44 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.01 (s, 3H), 2.11 (s, 3H)

Melting point: 254-257 °C.

Yield: 32 %

Example A114

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethoxy-benzenesulfonamide



5

$C_{24}H_{19}F_3N_2O_6S$ Mw. 520.49

LC/MS purity: 100 %, m/z 519 [M-H]⁻, m/z 521 [M-H]⁺ Rt. 2.96 min.

¹H NMR (300 MHz, DMSO-d₆): 10.61 (bs, 1H), 8.45 (d, 1H), 7.98 (d, 1H), 7.79 (t, 1H), 7.56 (m, 2H), 7.44 (s, 1H), 7.38 (s, 1H), 7.18 (dd, 4H), 6.34 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H),

10

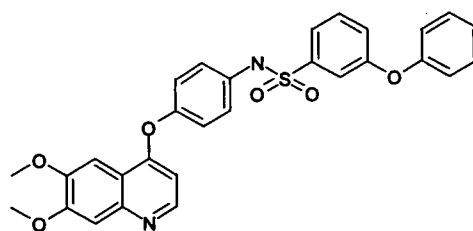
Melting point: 222-223 °C.

Yield: 63 %

Example A115

15

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-3-phenoxy-benzenesulfonamide



$C_{29}H_{24}N_2O_6S$ Mw. 528.59

LC/MS purity: 100 %, m/z 527 [M-H]⁻, m/z 529 [M-H]⁺ Rt. 3.15 min.

20

¹H NMR (300 MHz, DMSO-d₆): 10.32 (bs, 1H), 8.44 (d, 1H), 7.60 (t, 1H), 7.45 (m, 6H), 7.30 (d, 1H), 7.18 (m, 5H), 7.01 (d, 2H), 6.36 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 172-174 °C.

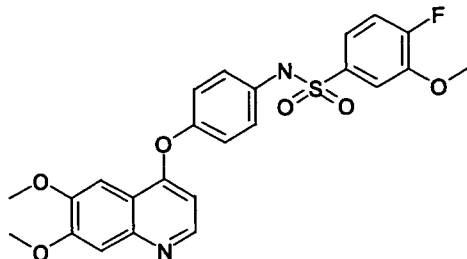
Yield: 57 %

25

- 94 -

Example A116

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide



5 $C_{24}H_{21}FN_2O_6S$ Mw. 484.51

LC/MS purity: 100 %, m/z 483 [M-H]⁻, m/z 485 [M-H]⁺ Rt. 2.81 min.

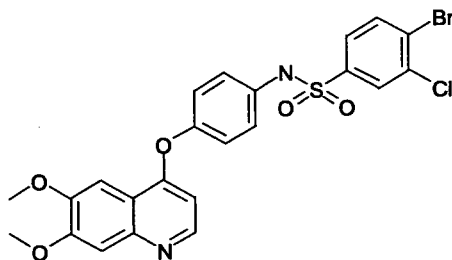
¹H NMR (300 MHz, DMSO-d₆): 10.29 (bs, 1H), 8.45 (d, 1H), 7.38 (m, 5H), 7.19 (m, 4H), 6.36 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H)

Melting point: 222-224 °C.

10 Yield: 69 %

Example A117

4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-benzenesulfonamide



15

$C_{23}H_{18}BrClN_2O_5S$ Mw. 549.83

LC/MS purity: 99 %, m/z 547 [M-H]⁻, m/z 549 [M-H]⁺ Rt. 3.11 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.48 (bs, 1H), 8.46 (d, 1H), 8.02 (d, 1H), 7.88 (s, 1H), 7.59 (d, 1H), 7.45 (s, 1H), 7.38 (s, 1H), 7.20 (dd, 4H), 6.38 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

Melting point: 232-234 °C.

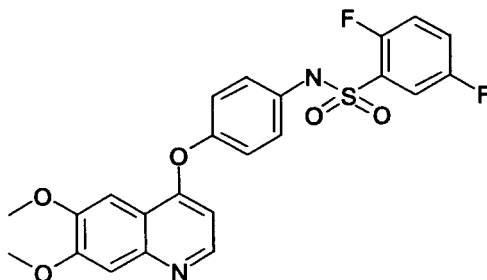
Yield: 73 %

25

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Example A118

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2,5-difluoro-benzenesulfonamide



$C_{23}H_{18}F_2N_2O_5S$ Mw. 472.47

LC/MS purity: 99 %, m/z 471 [M-H]⁻, m/z 473 [M-H]⁺ Rt. 2.77 min.

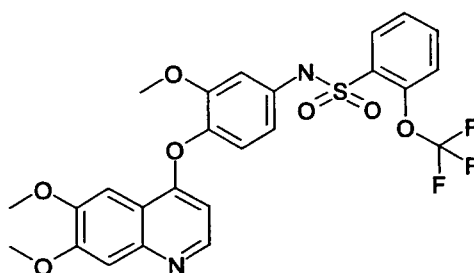
¹H NMR (300 MHz, DMSO-d₆): 10.80 (bs, 1H), 8.45 (d, 1H), 7.65-7.50 (m, 3H), 7.44 (s, 1H), 7.38 (s, 1H), 7.21 (dd, 4H), 6.36 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H)

Melting point: 260-263 °C.

Yield: 39 %

Example A119

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethoxy-benzenesulfonamide



$C_{25}H_{21}F_3N_2O_7S$ Mw. 550.51

LC/MS purity: 100 %, m/z 549 [M-H]⁻, m/z 551 [M-H]⁺ Rt. 2.96 min.

¹H NMR (300 MHz, DMSO-d₆): 10.62 (bs, 1H), 8.39 (d, 1H), 8.03 (dd, 1H), 7.80 (td, 1H), 7.59 (m, 2H), 7.46 (s, 1H), 7.36 (s, 1H), 7.13 (d, 1H), 6.97 (d, 1H), 6.72 (dd, 1H), 6.14 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.61 (s, 3H)

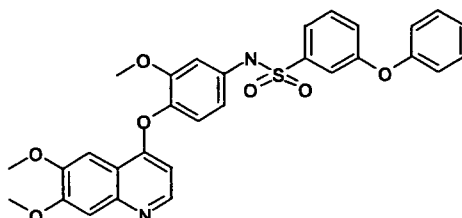
Melting point: 211-212 °C.

- 96 -

Yield: 59 %

Example A120

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-3-phenoxy-
benzenesulfonamide



$C_{30}H_{26}N_2O_7S$ Mw. 558.61

LC/MS purity: 99 %, m/z 557 [M-H]⁻, m/z 559 [M-H]⁺ Rt. 3.19 min.

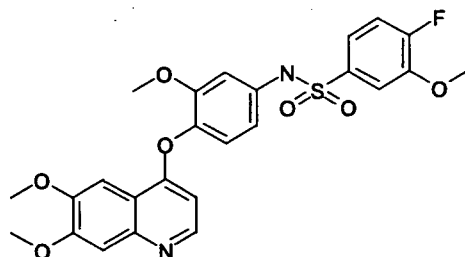
¹H NMR (300 MHz, DMSO-d₆): 10.35 (bs, 1H), 8.38 (d, 1H), 7.59 (t, 1H),
7.47 (dd, 1H), 7.45 (m, 3H), 7.37 (s, 1H), 7.32 (d, 1H), 7.24 (m, 2H), 7.16 (d,
1H), 7.01 (d, 2H), 6.93 (d, 1H), 6.70 (dd, 1H), 6.16 (d, 1H), 3.94 (s, 3H), 3.92
(s, 3H), 3.61 (s, 3H)

Melting point: 106-107 °C.

Yield: 55 %

Example A121

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-4-fluoro-3-
methoxybenzenesulfonamide



$C_{25}H_{23}FN_2O_7S$ Mw. 514.53

LC/MS purity: 99 %, m/z 513 [M-H]⁻, m/z 515 [M-H]⁺ Rt. 2.71 min.

¹H NMR (300 MHz, DMSO-d₆): 10.3 (bs, 1H), 8.39 (d, 1H), 7.52 (dd, 1H),
7.45 (s, 1H), 7.39 (m, 2H), 7.36 (s, 1H), 7.14 (d, 1H), 6.97 (d, 1H), 6.15 (d,
1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 3.64 (s, 3H)

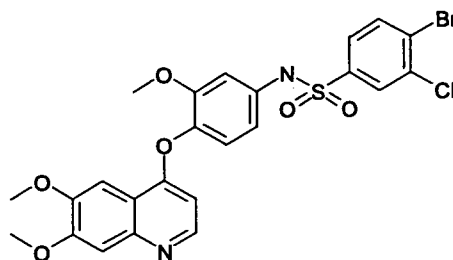
Melting point: 109-110 °C.

- 97 -

Yield: 66 %

Example A122

4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-
benzenesulfonamide

 $C_{24}H_{20}BrClN_2O_6S$ Mw. 579.86LC/MS purity: 99 %, m/z 577 [M-H]⁻, m/z 579 [M-H]⁺ Rt. 3.12 min.

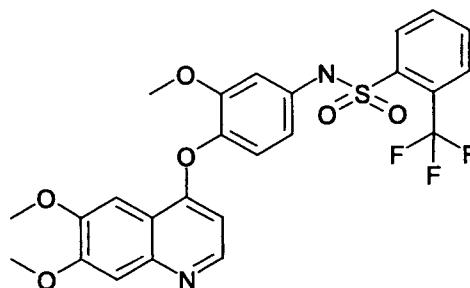
¹H NMR (300 MHz, DMSO-d₆): 10.4 (bs, 1H), 8.40 (d, 1H), 8.30 (d, 1H),
7.92 (d, 1H), 7.63 (dd, 1H), 7.47 (s, 1H), 7.36 (s, 1H), 7.17 (d, 1H), 6.96 (d,
1H), 6.74 (d, 1H), 6.17 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.64 (s, 3H)

Melting point: 110-113 °C.

Yield: 75 %

Example A123

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethyl-
benzenesulfonamide

 $C_{25}H_{21}F_3N_2O_6S$ Mw. 534.52LC/MS purity: 100 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 2.91 min.

¹H NMR (300 MHz, DMSO-d₆): 10.74 (bs, 1H), 8.39 (d, 1H), 8.15 (d, 1H),
7.89 (m, 2H), 7.45 (s, 1H), 7.36 (s, 1H), 7.14 (d, 1H), 6.98 (d, 2H), 6.73 (dd,
1H), 6.16 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.62 (s, 3H)

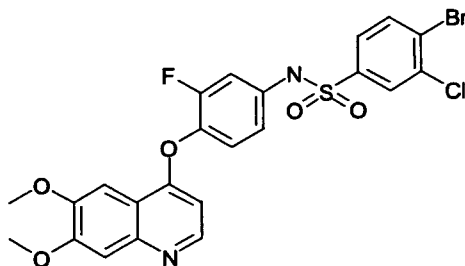
Melting point: 198-199 °C.

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Yield: 49 %

Example A124

4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-
benzenesulfonamide

 $C_{23}H_{17}BrClFN_2O_5S$ Mw. 567.82LC/MS purity: 99 %, m/z 565 [M-H]⁻, m/z 567 [M-H]⁺ Rt. 3.22 min.

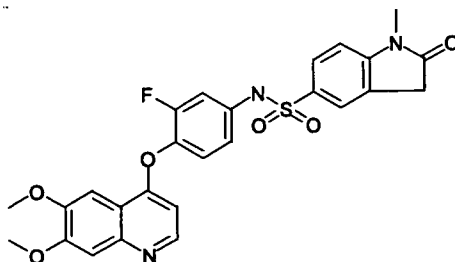
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.46 (d, 1H), 8.01 (d, 1H), 7.93 (s, 1H), 7.63 (dd, 1H), 7.48 (s, 1H), 7.36 (s, 1H), 7.34 (t, 1H), 7.15 (dd, 1H), 6.98 (d, 1H), 6.37 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H)

Melting point: 144-147 °C.

Yield: 43 %

Example A125

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide

 $C_{26}H_{22}FN_3O_6S$ Mw. 523.54LC/MS purity: 99 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 2.60 min.

¹H NMR (300 MHz, DMSO-d₆): 10.7 (bs, 1H), 8.45 (m, 1H), 7.76 (d, 1H), 7.67 (s, 1H), 7.46 (s, 1H), 7.39 (s, 1H), 7.33 (t, 1H), 7.15 (m, 2H), 7.00 (d, 1H), 6.36 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.65 (s, 2H), 3.14 (s, 3H)

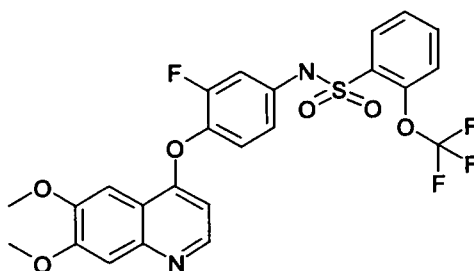
Melting point: 163-165 °C.

- 99 -

Yield: 59 %

Example A126

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethoxy-
benzenesulfonamide

 $C_{24}H_{18}F_4N_2O_6S$ Mw. 538.48LC/MS purity: 100 %, m/z 537 [M-H]⁻, m/z 539 [M-H]⁺ Rt. 3.05 min.

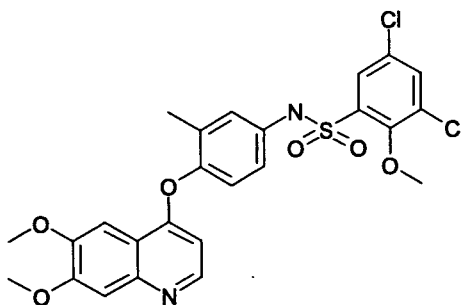
¹H NMR (300 MHz, DMSO-d₆): 10.93 (bs, 1H), 8.45 (d, 1H), 8.04 (dd, 1H),
7.79 (dt, 1H), 7.58 (m, 3H), 7.47 (s, 1H), 7.39 (s, 1H), 7.35 (t, 1H), 7.15 (dd,
1H), 6.98 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H)

Melting point: 203-204 °C.

Yield: 42 %

15 Example A127

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-
methoxy-benzenesulfonamide

 $C_{25}H_{22}Cl_2N_2O_6S$ Mw. 549.4320 LC/MS purity: 98 %, m/z 547 [M-H]⁻, m/z 549 [M-H]⁺ Rt. 3.27 min.

¹H NMR (300 MHz, DMSO-d₆): 10.50 (bs, 1H), 8.41 (d, 1H), 7.74 (d, 1H),
7.51 (s, 1H), 7.44 (s, 1H), 7.38 (s, 1H), 7.07 (m, 3H), 6.17 (d, 1H), 3.96 (s,
3H), 3.94 (s, 3H), 3.91 (s, 3H), 2.03 (s, 3H)

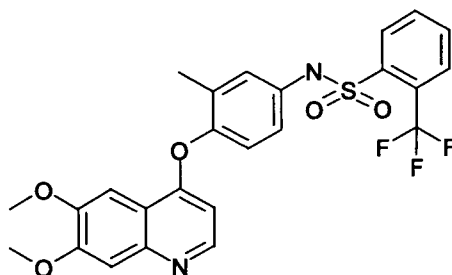
- 100 -

Melting point: 206-208 °C.

Yield: 78 %

Example A128

5 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-trifluoromethyl-benzenesulfonamide

 $C_{25}H_{21}F_3N_2O_5S$ Mw. 518.52LC/MS purity: 100 %, m/z 517 [M-H]⁻, m/z 519 [M-H]⁺ Rt. 2.98 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.66 (bs, 1H), 8.42 (d, 1H), 8.12 (d, 1H), 8.02 (d, 1H), 7.88 (m, 2H), 7.50 (s, 1H), 7.38 (s, 1H), 7.08 (m, 3H), 6.18 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 2.03 (s, 3H)

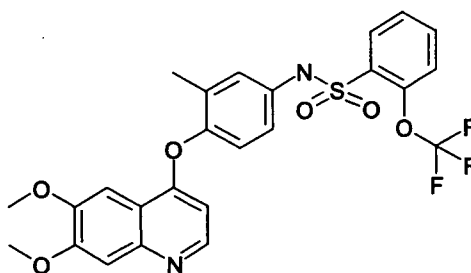
Melting point: 209-211 °C.

Yield: 59 %

15

Example A129

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-trifluoromethoxy-benzenesulfonamide



20 $C_{25}H_{21}F_3N_2O_6S$ Mw. 534.52

LC/MS purity: 100 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 3.04 min.

¹H NMR (300 MHz, DMSO-d₆): 10.55 (s, 1H), 8.41 (d, 1H), 7.99 (d, 1H), 7.79 (t, 1H), 7.55 (m, 2H), 7.51 (s, 1H), 7.38 (s, 1H), 7.12 (d, 1H), 7.08 (d, 1H), 7.01 (d, 1H), 6.15 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 2.02 (s, 3H)

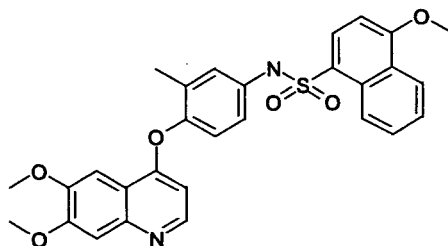
- 101 -

Melting point: 207-209 °C.

Yield: 71 %

Example A130

5 4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide

 $C_{29}H_{26}N_2O_6S$ Mw. 530.60LC/MS purity: 96 %, m/z 529 [M-H]⁻, m/z 531 [M-H]⁺ Rt. 2.97 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.54 (s, 1H), 8.70 (d, 1H), 8.37 (d, 1H), 8.25 (d, 1H), 8.22 (d, 1H), 7.58 (m, 2H), 7.45 (s, 1H), 7.36 (s, 1H), 6.99 (m, 4H), 6.09 (d, 1H), 4.05 (s, 3H), 3.92 (s, 3H), 3.88 (s, 3H), 1.95 (s, 3H)

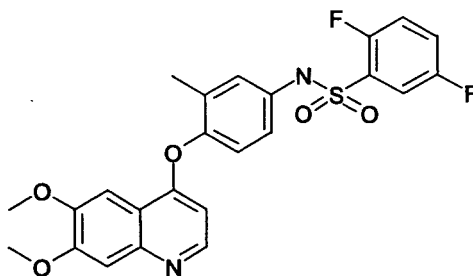
Melting point: 233-235°C.

Yield: 34 %

15

Example A131

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2,5-difluorobenzenesulfonamide



20 $C_{24}H_{20}F_2N_2O_5S$ Mw. 486.50

LC/MS purity: 100 %, m/z 485 [M-H]⁻, m/z 487 [M-H]⁺ Rt. 2.72 min.

¹H NMR (300 MHz, DMSO-d₆): 10.76 (s, 1H), 8.41 (d, 1H), 7.58 (m, 3H), 7.51 (s, 1H), 7.38 (s, 1H), 7.09 (m, 3H), 6.17 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.04 (s, 3H)

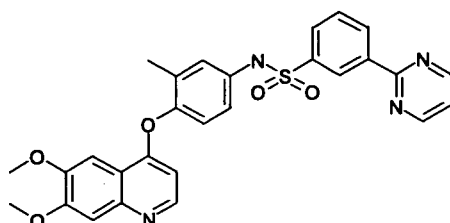
25 Melting point: 239-240 °C.

- 102 -

Yield: 74 %

Example A132

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-3-pyrimidin-2-yl-
benzenesulfonamide

 $C_{28}H_{24}N_4O_5S$ Mw. 528.59LC/MS purity: 99 %, m/z 527 [M-H]⁻, m/z 529 [M-H]⁺ Rt. 2.85 min.

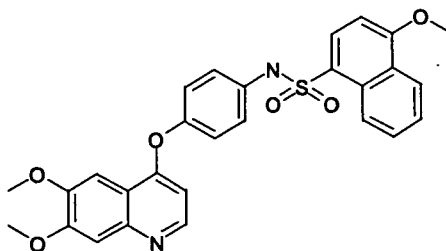
¹H NMR (300 MHz, DMSO-d₆): 11.38 (bs, 1H), 8.97 (d, 2H), 8.83 (s, 1H),
8.62 (d, 1H), 8.31 (d, 1H), 7.92 (d, 1H), 7.75 (t, 1H), 7.54 (t, 1H), 7.48 (s,
1H), 7.36 (s, 1H), 7.14 (s, 1H), 7.05 (dd, 2H), 6.10 (d, 1H), 3.93 (s, 3H), 3.90
(s, 3H), 2.00 (s, 3H)

Melting point: 188-190 °C.

Yield: 16 %

Example A133

4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-
phenyl]-amide

 $C_{28}H_{24}N_2O_6S$ Mw. 516.58LC/MS purity: 96 %, m/z 515 [M-H]⁻, m/z 517 [M-H]⁺ Rt. 2.91 min.

¹H NMR (300 MHz, DMSO-d₆): 10.60 (bs, 1H), 8.70 (d, 1H), 8.40 (d, 1H),
8.19 (d, 1H), 7.75 (t, 1H), 7.65 (t, 1H), 7.39 (s, 1H), 7.35 (s, 1H), 7.07 (m,
6H), 6.27 (d, 1H), 4.04 (s, 3H), 3.92 (s, 3H), 3.86 (s, 3H)

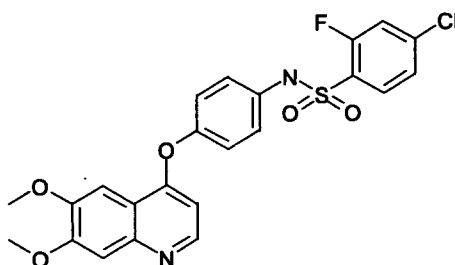
- 103 -

Melting point: 240-242 °C.

Yield: 14 %

Example A134

5 4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-fluoro-benzenesulfonamide

C₂₃H₁₈ClFN₂O₅S Mw. 488.93LC/MS purity: 100 %, m/z 487 [M-H]⁻, m/z 489 [M-H]⁺ Rt. 2.92 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.76 (bs, 1H), 8.45 (d, 1H), 7.83 (t, 1H), 7.75 (d, 1H), 7.49 (d, 1H), 7.44 (s, 1H), 7.38 (s, 1H), 7.18 (dd, 4H), 6.36 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H)

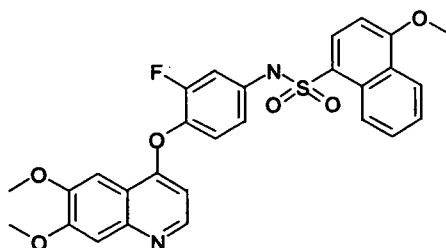
Melting point: 218-220 °C.

Yield: 69 %

15

Example A135

4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide



20 C₂₈H₂₃FN₂O₆S Mw. 534.57

LC/MS purity: 96 %, m/z 533 [M-H]⁻, m/z 535 [M-H]⁺ Rt. 3.14 min.

¹H NMR (300 MHz, DMSO-d₆): 10.91 (bs, 1H), 8.69 (d, 1H), 8.40 (d, 1H), 8.27 (m, 2H), 7.77 (t, 1H), 7.65 (t, 1H), 7.42 (s, 1H), 7.37 (s, 1H), 7.25 (m, 1H), 7.08 (m, 2H), 6.91 (dd, 1H), 6.27 (d, 1H), 4.07 (s, 3H), 3.98 (s, 3H),
25 3.89 (s, 3H)

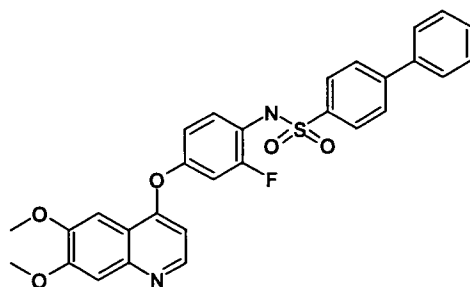
- 104 -

Melting point: 145-147 °C.

Yield: 31 %

Example A136

5 Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

 $C_{29}H_{23}FN_2O_5S$ Mw. 530.58LC/MS purity: 99 %, m/z 529 [M-H]⁻, m/z 531 [M-H]⁺ Rt. 3.20 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.29 (bs, 1H), 8.49 (d, 1H), 7.89 (d, 2H), 7.82 (d, 2H), 7.74 (d, 2H), 7.44 (m, 6H), 7.23 (dd, 1H), 7.04 (d, 1H), 6.55 (d, 1H), 3.93 (s, 3H), 3.89 (s, 3H)

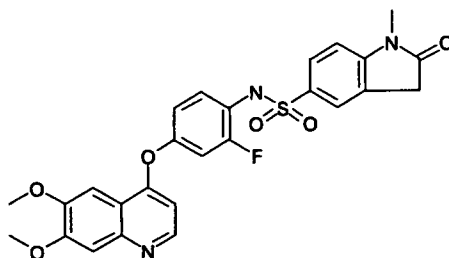
Melting point: 199-201 °C.

Yield: 38 %

15

Example A137

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



20 $C_{26}H_{22}FN_3O_5S$ Mw. 523.54

LC/MS purity: 100 %, m/z 522 [M-H]⁻, m/z 524 [M-H]⁺ Rt. 2.53 min.

¹H NMR (300 MHz, DMSO-d₆): 10 (bs, 1H), 8.49 dm, 1H), 7.65 (m, 2H), 7.42-7.28 (m, 4H), 7.20 (dd, 1H), 7.01 (dd, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.89 (s, 3H), 3.63 (s, 2H), 3.14 (s, 3H)

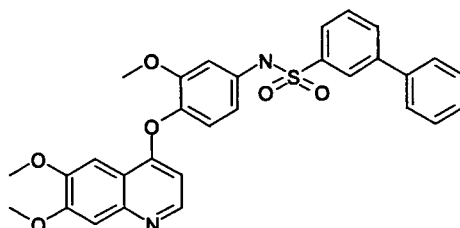
- 105 -

Melting point: 195-197 °C.

Yield: 54 %

Example A138

5 Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

 $C_{30}H_{26}N_2O_6S$ Mw. 542.62LC/MS purity: 99 %, m/z 541 [M-H]⁻, m/z 543 [M-H]⁺ Rt. 3.15 min.

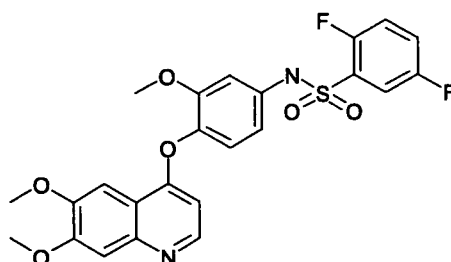
10 ¹H NMR (300 MHz, DMSO-d₆): 0.37 (bs, 1H), 8.29 (d, 1H), 8.03 (s, 1H), 7.97 (d, 1H), 7.79 (d, 1H), 7.68 (m, 3H), 7.49 (m, 4H), 7.35 (s, 1H), 7.14 (d, 1H), 6.98 (d, 1H), 6.78 (dd, 1H), 6.08 (d, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.60 (s, 3H)

Melting point: 108-110 °C.

15 Yield: 47 %

Example A139

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2,5-difluorobenzenesulfonamide



20

 $C_{24}H_{20}F_2N_2O_6S$ Mw. 502.50LC/MS purity: 99 %, m/z 501 [M-H]⁻, m/z 503 [M-H]⁺ Rt. 2.82 min.

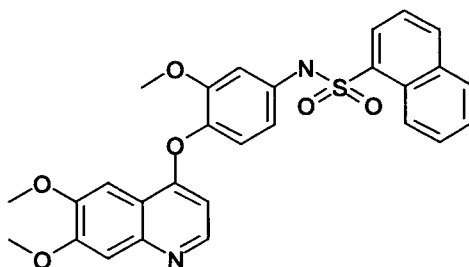
25 ¹H NMR (300 MHz, DMSO-d₆): 10.85 (bs, 1H), 8.39 (d, 1H), 7.70-7.54 (m, 3H), 7.46 (s, 1H), 7.36 (s, 1H), 7.16 (d, 1H), 6.98 (d, 1H), 6.77 (dd, 1H), 6.14 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.64 (s, 3H)

Melting point: 222-224 °C.

Yield: 43 %

Example A140

5 Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide



C₂₈H₂₄N₂O₆S Mw. 516.58

LC/MS purity: 98 %, m/z 515 [M-H]⁻, m/z 517 [M-H]⁺ Rt. 2.98 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 10.75 (bs, 1H), 8.79 (d, 1H), 8.35 (d, 1H),
8.25 (m, 2H), 8.09 (d, 1H), 7.70 (m, 3H), 7.41 (s, 1H), 7.33 (s, 1H), 6.99 (d,
1H), 6.84 (s, 1H), 6.62 (d, 1H), 6.04 (d, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 3.52
(s, 3H)

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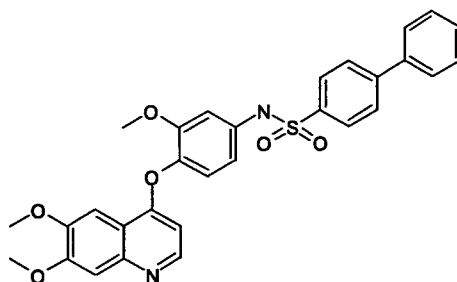
¹H), 6.75 (dd, 1H), 6.15 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.66 (s, 3H)

Melting point: 124-126 °C.

Yield: 43 %

5 Example A142

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide



C₃₀H₂₆N₂O₆S Mw. 542.62

10 LC/MS purity: 98 %, m/z 541 [M-H]⁻, m/z 543 [M-H]⁺ Rt. 3.18 min.

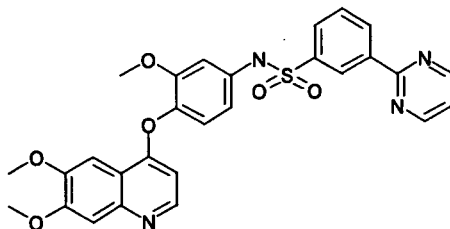
¹H NMR (300 MHz, DMSO-d₆): 10.4 (bs, 1H), 8.35 (d, 1H), 7.89 (dd, 4H), 7.73 (d, 1H), 7.50 (m, 4H), 7.44 (s, 1H), 7.35 (s, 1H), 7.15 (d, 1H), 7.00 (d, 1H), 6.78 (dd, 1H), 6.16 (d, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 3.66 (s, 3H)

Melting point: 128-131 °C.

15 Yield: 39 %

Example A143

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide



20

C₂₈H₂₄N₄O₆S Mw. 544.59

LC/MS purity: 100 %, m/z 543 [M-H]⁻, m/z 545 [M-H]⁺ Rt. 2.80 min.

¹H NMR (300 MHz, DMSO-d₆): 10.48 (bs, 1H), 8.97 (d, 2H), 8.86 (s, 1H), 8.64 (d, 1H), 8.27 (d, 1H), 7.95 (d, 1H), 7.77 (t, 1H), 7.54 (t, 1H), 7.43 (d, 1H), 7.34 (s, 1H), 7.12 (d, 1H), 7.08 (d, 1H), 6.74 (dd, 1H), 6.07 (d, 1H), 3.92

25

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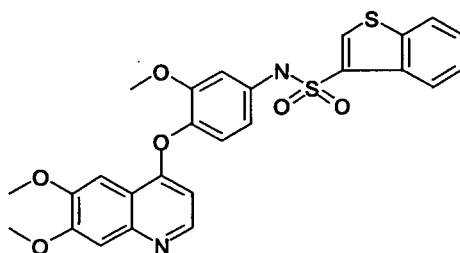
(s, 3H), 3.89 (s, 3H), 3.63 (s, 3H)

Melting point: 135-137 °C.

Yield: 38 %

5 Example A144

Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

 $C_{26}H_{22}N_2O_6S_2$ Mw. 522.6010 LC/MS purity: 100 %, m/z 521 [M-H]⁻, m/z 523 [M-H]⁺ Rt. 2.95 min.

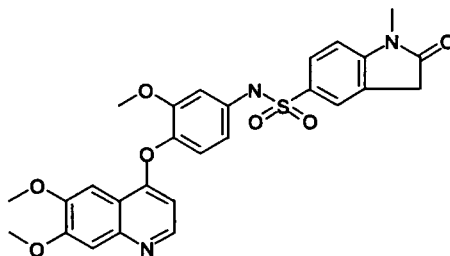
¹H NMR (300 MHz, DMSO-d₆): 10.68 (s, 1H), 8.67 (s, 1H), 8.37 (d, 1H), 8.24 (d, 1H), 8.13 (d, 1H), 7.54 (m, 2H), 7.43 (s, 1H), 7.35 (s, 1H), 7.18 (d, 1H), 6.93 (d, 1H), 6.70 (dd, 1H), 6.08 (d, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.58 (s, 3H),

15 Melting point: 144-146 °C.

Yield: 61 %

Example A145

20 1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

 $C_{27}H_{25}N_3O_7S$ Mw. 535.58LC/MS purity: 100 %, m/z 534 [M-H]⁻, m/z 536 [M-H]⁺ Rt. 2.43 min.

¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 8.38 (d, 1H), 7.76 (d, 1H), 7.67 (s, 1H), 7.45 (s, 1H), 7.35 (s, 1H), 7.10 (t, 2H), 6.96 (d, 1H), 6.72 (d,

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¹H), 6.18 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.64 (s, 2H), 3.63 (s, 3H), 3.13 (s, 3H)

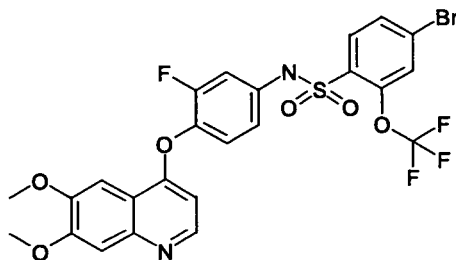
Melting point: 150-152 °C.

Yield: 18 %

5

Example A146

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide



10 $C_{24}H_{17}BrF_4N_2O_6S$ Mw. 617.37

LC/MS purity: 99 %, m/z 615 [M-H]⁻, m/z 617 [M-H]⁺ Rt. 3.30 min.

¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.46 (d, 1H), 7.96 (d, 1H), 7.84 (d, 1H), 7.82 (s, 1H), 7.48 (s, 1H), 7.39 (s, 1H), 7.35 (d, 1H), 7.16 (dd, 1H), 6.99 (d, 1H), 6.35 (d, 1H), 3.94 (s, 3H), 3.92 (s, 3H)

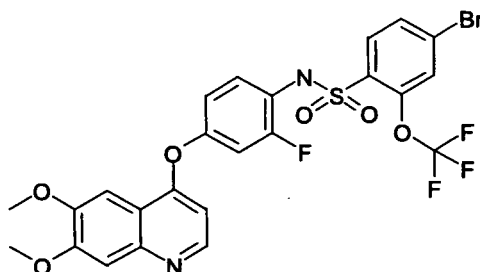
15 Melting point: 226-228 °C.

Yield: 34 %

Example A147

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide

20



$C_{24}H_{17}BrF_4N_2O_6S$ Mw. 617.37

LC/MS purity: 100 %, m/z 615 [M-H]⁻, m/z 617 [M-H]⁺ Rt. 3.27 min.

¹H NMR (300 MHz, DMSO-d₆): 10.4 (bs, 1H), 8.51 (d, 1H), 7.80 (m, 3H),

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7.41 (s, 1H), 7.40 (s, 1H), 7.34 (t, 1H), 7.24 (dd, 1H), 7.04 (d, 1H), 6.53 (d, 1H), 3.94 (s, 3H), 3.90 (s, 3H)

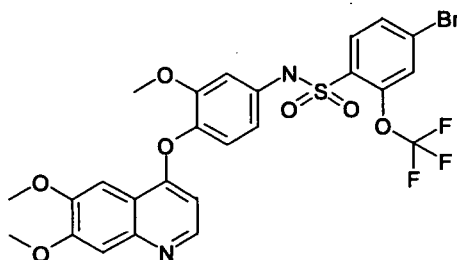
Melting point: 227-229 °C.

Yield: 36 %

5

Example A148

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethoxy-benzenesulfonamide



10 $C_{25}H_{20}BrF_3N_2O_7S$ Mw. 629.41

LC/MS purity: 99 %, m/z 627 [M-H]⁻, m/z 629 [M-H]⁺ Rt. 3.21 min.

¹H NMR (300 MHz, DMSO-d₆): 10.8 (bs, 1H), 8.39 (d, 1H), 7.94 (d, 1H), 7.83 (d, 1H), 7.81 (s, 1H), 7.47 (s, 1H), 7.36 (s, 1H), 7.13 (d, 1H), 6.95 (d, 1H), 6.70 (d, 1H), 6.15 (d, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.63 (s, 3H)

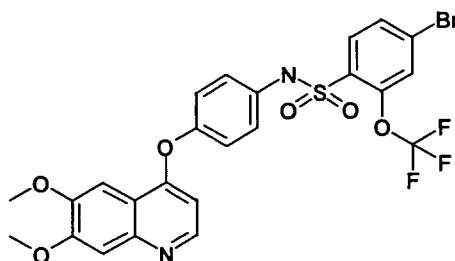
15 Melting point: 176-177 °C.

Yield: 31 %

Example A149

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethoxy-benzenesulfonamide

20



$C_{24}H_{18}BrF_3N_2O_6S$ Mw. 599.38

LC/MS purity: 99 %, m/z 597 [M-H]⁻, m/z 599 [M-H]⁺ Rt. 3.20 min.

¹H NMR (300 MHz, DMSO-d₆): 10.8 (bs, 1H), 8.45 (d, 1H), 7.89 (d, 1H), 7.82 (d, 1H), 7.80 (s, 1H), 7.45 (s, 1H), 7.38 (s, 1H), 7.17 (dd, 4H), 6.35 (d,

25

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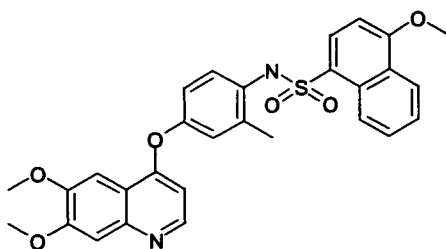
1H), 3.93 (s, 3H), 3.90 (s, 3H)

Melting point: 237-239 °C.

Yield: 30 %

5 Example A150

4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide

 $C_{29}H_{26}N_2O_6S$ Mw. 530.6010 LC/MS purity: 99 %, m/z 529 [M-H]⁻, m/z 531 [M-H]⁺ Rt. 3.10 min.

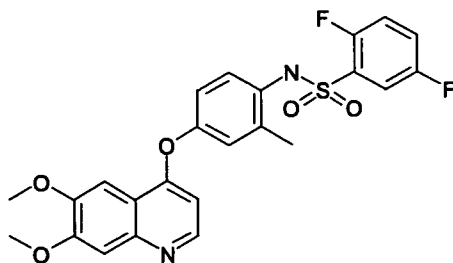
¹H NMR (300 MHz, DMSO-d₆): 10 (bs, 1H), 8.71 (d, 1H), 8.46 (d, 1H), 8.28 (d, 1H), 8.01 (d, 1H), 7.67 (m, 2H), 7.41 (s, 1H), 7.37 (s, 1H), 7.05 (d, 2H), 6.92 (s, 1H), 6.91 (d, 1H), 6.36 (d, 1H), 4.07 (s, 3H), 3.93 (s, 3H), 3.88 (s, 3H), 2.09 (s, 3H)

15 Melting point: 216-217 °C.

Yield: 34 %

Example A151

20 N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2,5-difluorobenzenesulfonamide

 $C_{24}H_{20}F_2N_2O_5S$ Mw. 486.50LC/MS purity: 98 %, m/z 485 [M-H]⁻, m/z 487 [M-H]⁺ Rt. 2.82 min.

25 ¹H NMR (300 MHz, DMSO-d₆): 10.19 (bs, 1H), 8.48 (d, 1H), 7.59 (m, 2H), 7.48 (m, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 7.04 (m, 3H), 6.46 (d, 1H), 3.94 (s,

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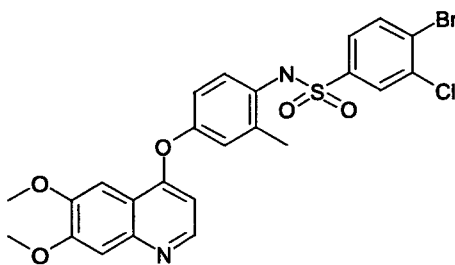
3H), 3.90 (s, 3H), 2.13 (s, 3H)

Melting point: 259-260 °C.

Yield: 37 %

5 Example A152

4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-benzenesulfonamide

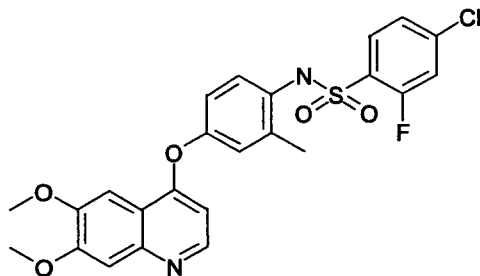
 $C_{24}H_{20}BrClN_2O_5S$ Mw. 563.8610 LC/MS purity: 100 %, m/z 561 [M-H]⁻, m/z 563 [M-H]⁺ Rt. 3.17 min.¹H NMR (300 MHz, DMSO-d₆): 9.91 (bs, 1H), 8.48 (d, 1H), 8.03 (d, 1H), 7.79 (d, 1H), 7.54 (dd, 1H), 7.45 (s, 1H), 7.39 (s, 1H), 7.12 (s, 1H), 7.03 (dd, 2H), 6.47 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 2.06 (s, 3H)

Melting point: 212-213 °C.

15 Yield: 58 %

Example A153

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-fluorobenzenesulfonamide



20

 $C_{24}H_{20}ClFN_2O_5S$ Mw. 502.95LC/MS purity: 99 %, m/z 501 [M-H]⁻, m/z 503 [M-H]⁺ Rt. 2.98 min.¹H NMR (300 MHz, DMSO-d₆): 10.13 (bs, 1H), 8.48 (d, 1H), 7.73 (m, 2H), 7.46 (d, 1H), 7.44 (s, 1H), 7.39 (s, 1H), 7.03 (m, 2H), 7.01 (dd, 1H), 6.45 (d,

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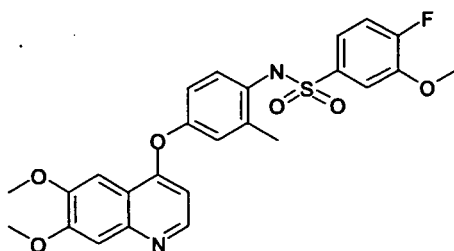
1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.13 (s, 3H)

Melting point: 248-250 °C.

Yield: 43 %

5 Example A154

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide

 $C_{25}H_{23}FN_2O_6S$ Mw. 498.5310 LC/MS purity: 98 %, m/z 497 [M-H]⁻, m/z 499 [M-H]⁺ Rt. 2.87 min.

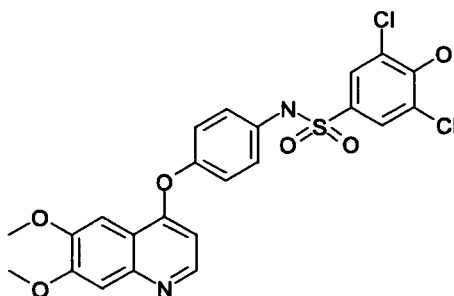
¹H NMR (300 MHz, DMSO-d₆): 9.67 (bs, 1H), 8.47 (d, 1H), 7.40 (m, 4H), 7.28 (m, 1H), 7.10 (s, 1H), 7.03 (dd, 2H), 6.46 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.85 (s, 3H), 2.05 (s, 3H)

Melting point: 228-229 °C.

15 Yield: 38 %

Example A155

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-hydroxy-benzenesulfonamide



20

 $C_{23}H_{18}Cl_2N_2O_6S$ Mw. 521.38LC/MS purity: 92 %, m/z 519 [M-H]⁻, m/z 521 [M-H]⁺ Rt. 2.79 min.

¹H NMR (300 MHz, DMSO-d₆): 9.7 (bs, 1H), 8.42 (d, 1H), 7.49 (s, 1H), 7.37 (s, 1H), 7.27 (s, 2H), 7.10 (m, 4H), 6.35 (d, 1H), 3.94 (s, 3H), 3.91 (s, 3H)

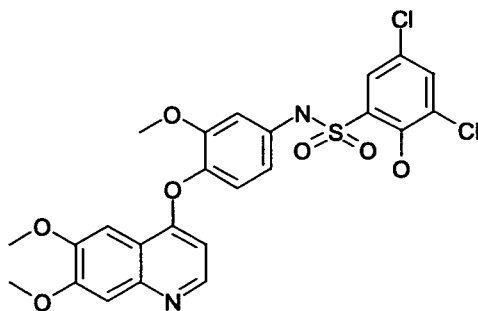
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Melting point: >260 °C.

Yield: 45 %

Example A156

5 3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-hydroxy-benzenesulfonamide

 $C_{24}H_{20}Cl_2N_2O_7S$ Mw. 551.41LC/MS purity: 99 %, m/z 549 [M-H]⁻, m/z 551 [M-H]⁺ Rt. 3.00 min.

10 ¹H NMR (300 MHz, DMSO-d₆): 9.6 (bs, 1H), 8.38 (d, 1H), 7.49 (s, 1H), 7.47 (s, 1H), 7.09 (d, 1H), 6.94 (d, 1H), 6.75 (d, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.59 (s, 3H)

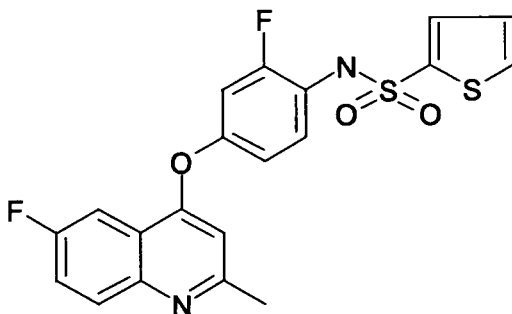
Melting point: >240 °C.

Yield: 26 %

15

Example B1

Thiophene-2-sulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide



20 $C_{20}H_{14}F_2N_2O_3S_2$ Mw. 432.47

LC/MS purity: 96 %, m/z 431 [M-H]⁻ Rt. 3.00 min.¹H NMR (300 MHz, DMSO-d₆): 10.37 (s, 1H), 7.97 (m, 2H), 7.83 (d, 1H),

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7.68 (m, 1H), 7.53 (dd, 1H), 7.31 (m, 2H), 7.19 (m, 1H), 7.11 (d, 1H), 6.65 (s, 1H), 2.54 (s, 3H)

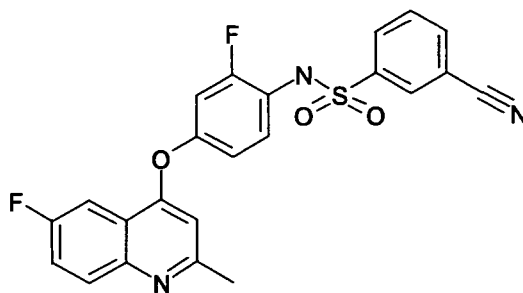
Melting point: 166-167 °C.

Yield: 60 %

5

Example B2

3-Cyano-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide



10 $C_{23}H_{15}F_2N_3O_3S$ Mw. 451.46

LC/MS purity: 97 %, m/z 450 [M-H]⁻ Rt. 3.03 min.

¹H NMR (300 MHz, DMSO-d₆): 10.46 (s, 1H), 8.14 (m, 2H), 8.00 (m, 2H), 7.81 (m, 2H), 7.68 (m, 1H), 7.33 (t, 1H), 7.26 (dd, 1H), 7.08 (d, 1H), 6.65 (s, 1H), 2.54 (s, 3H)

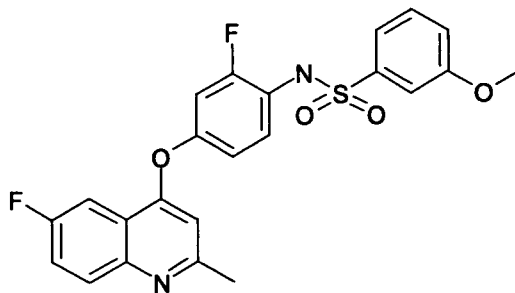
15 Melting point: 190-191 °C.

Yield: 37 %

Example B3

N-[2-Fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-3-methoxy-benzenesulfonamide

20



$C_{23}H_{18}F_2N_2O_4S$ Mw. 456.47

LC/MS purity: 98 %, m/z 455 [M-H]⁻ Rt. 3.16 min.

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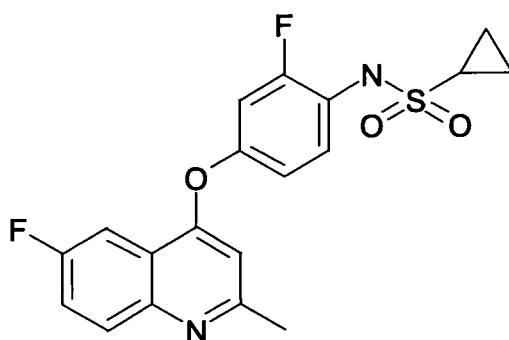
¹H NMR (300 MHz, DMSO-d₆): 10.22 (s, 1H), 8.00 (m, 1H), 7.82 (m, 1H), 7.67 (m, 1H), 7.49 (t, 1H), 7.37-7.21 (m, 6H), 7.07 (d, 1H), 6.62 (s, 1H), 3.80 (s, 3H), 2.53 (s, 3H)

Melting point: 150-151 °C.

5 Yield: 58 %

Example B4

Cyclopropanesulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide



10

C₁₉H₁₆F₂N₂O₃S Mw. 390.41

LC/MS purity: 96 %, m/z 391 [M+H]⁺ Rt. 2.54 min.

¹H NMR (300 MHz, DMSO-d₆): 9.67 (s, 1H), 8.01 (m, 1H), 7.85 (m, 1H), 7.70 (m, 1H), 7.52 (t, 1H), 7.37 (dd, 1H), 7.13 (d, 1H), 6.71 (s, 1H), 2.69 (s, 1H), 2.55 (s, 3H), 0.95 (m, 4H)

15

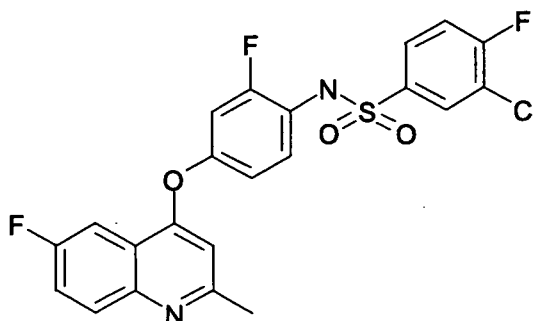
Melting point: 189-190 °C.

Yield: 42 %

Example B5

20

3-Chloro-4-fluoro-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide



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$C_{22}H_{14}ClF_3N_2O_3S$ Mw. 478.88

LC/MS purity: 94 %, m/z 477 [M-H]⁻ Rt. 3.45 min.

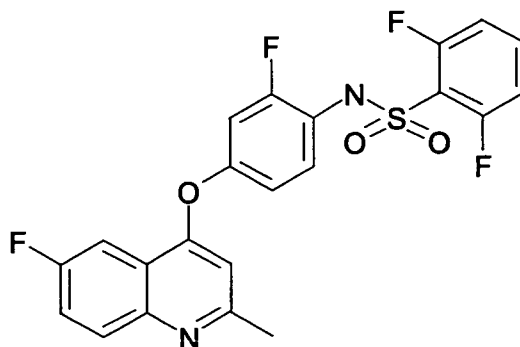
¹H NMR (300 MHz, DMSO-d₆): 10.38 (s, 1H), 8.00 (m, 1H), 7.91 (m, 1H), 7.84-7.66 (m, 4H), 7.31 (m, 2H), 7.11 (dd, 1H), 6.67 (s, 1H), 2.54 (s, 3H)

5 Melting point: 205-207 °C.

Yield: 62 %

Example B6

10 2,6-Difluoro-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide



$C_{22}H_{14}F_4N_2O_3S$ Mw. 462.43

LC/MS purity: 98 %, m/z 461 [M-H]⁻ Rt. 3.06 min.

15 ¹H NMR (300 MHz, DMSO-d₆): 10.81 (s, 1H), 8.00 (m, 1H), 7.82 (dd, 1H), 7.68 (m, 2H), 7.38 (t, 1H), 7.27 (m, 3H), 7.08 (d, 1H), 6.62 (s, 1H), 2.54 (s, 3H)

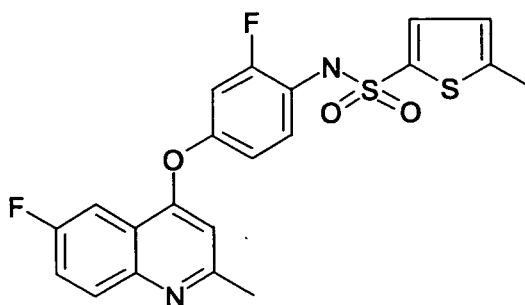
Melting point: 188-190 °C.

Yield: 53 %

20 Example B7

5-Methyl-thiophene-2-sulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

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$C_{21}H_{16}F_2N_2O_3S_2$ Mw. 446.50

LC/MS purity: 97 %, m/z 445 [M-H]⁻ Rt. 3.18 min.

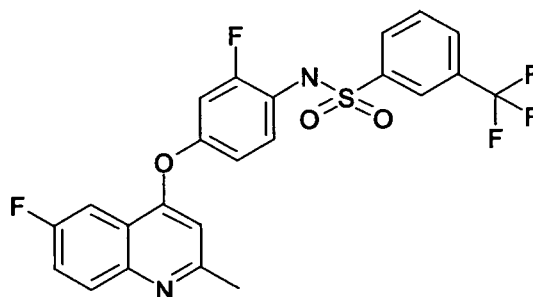
¹H NMR (300 MHz, DMSO-d₆): 10.30 (s, 1H), 8.00 (dd, 1H), 7.83 (dd, 1H),
 5 7.69 (m, 1H), 7.32 (m, 3H), 7.10 (d, 1H), 6.87 (dd, 1H), 6.64 (s, 1H), 2.54 (s,
 3H)

Melting point: 151-153 °C.

Yield: 62 %

10 Example B8

N-[2-Fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-3-trifluoromethyl-
 benzenesulfonamide



$C_{23}H_{15}F_5N_2O_3S$ Mw. 494.44

15 LC/MS purity: 95 %, m/z 493 [M-H]⁻ Rt. 3.51 min.

¹H NMR (300 MHz, DMSO-d₆): 10.45 (s, 1H), 8.00 (m, 4H), 7.83 (m, 2H),
 7.68 (m, 1H), 7.34 (t, 1H), 7.26 (d, 1H), 7.09 (d, 1H), 6.63 (s, 1H), 2.53 (s,
 3H)

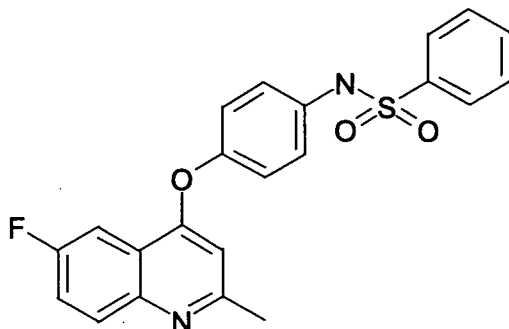
Melting point: 150-152 °C.

20 Yield: 47 %

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Example B9

N-[4-(6-Fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

 $C_{22}H_{17}FN_2O_3S$ Mw. 408.455 LC/MS purity: 95 %, m/z 407 [M-H]⁻ Rt. 2.90 min.¹H NMR (300 MHz, DMSO-d₆): 10.37 (s, 1H), 7.97 (m, 1H), 7.81 (m, 3H), 7.70-7.55 (m, 4H), 7.19 (dd, 4H), 6.40 (s, 1H), 2.54 (s, 3H)

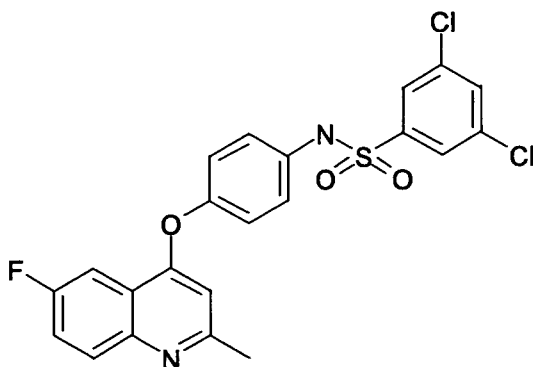
Melting point: 207-208 °C.

Yield: 65 %

10

Example B10

3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

15 $C_{22}H_{15}Cl_2FN_2O_3S$ Mw. 477.34LC/MS purity: 97 %, m/z 475 [M-H]⁻ Rt. 3.52 min.¹H NMR (300 MHz, DMSO-d₆): 10.52 (s, 1H), 7.98 (m, 2H), 7.85 (dd, 1H), 7.66 (m, 3H), 7.23 (dd, 4H), 6.45 (s, 1H), 2.54 (s, 3H)

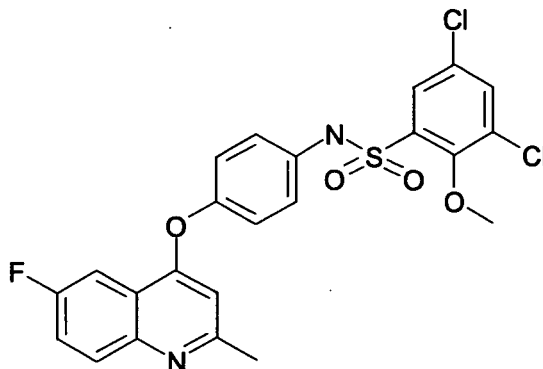
Melting point: 238-240 °C.

20 Yield: 73 %

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Example B11

3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-methoxybenzenesulfonamide



5 $C_{23}H_{17}Cl_2FN_2O_4S$ Mw. 507.37

LC/MS purity: 96 %, m/z 505 [M-H]⁻ Rt. 3.60 min.

¹H NMR (300 MHz, DMSO-d₆): 10.59 (s, 1H), 8.00 (m, 2H), 7.84 (dd, 1H), 7.73 (dd, 1H), 7.67 (m, 1H), 7.21 (dd, 4H), 6.42 (s, 1H), 3.96 (s, 3H), 2.54 (s, 3H)

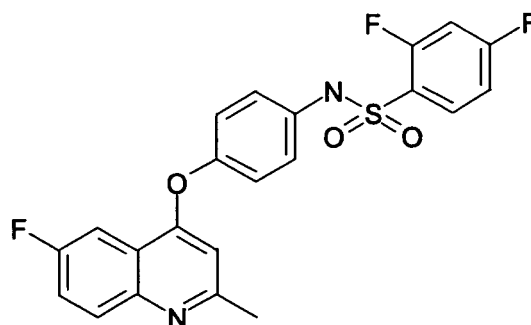
10 Melting point: 192-193 °C.

Yield: 78 %

Example B12

2,4-Difluoro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

15



$C_{22}H_{15}F_3N_2O_3S$ Mw. 444.44

LC/MS purity: 95 %, m/z 443 [M-H]⁻ Rt. 3.02 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.75 (s, 1H), 8.00-7.81 (m, 3H), 7.69 (m, 1H), 7.55 (m, 1H), 7.31-7.17 (m, 5H), 6.40 (s, 1H), 2.54 (s, 3H)

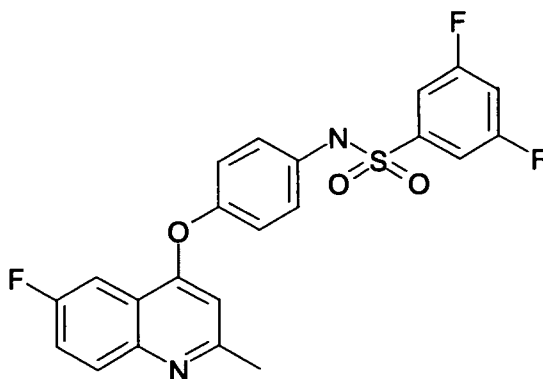
Melting point: 179-180 °C.

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Yield: 62 %

Example B13

3,5-Difluoro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-
benzenesulfonamid

 $C_{22}H_{15}F_3N_2O_3S$ Mw. 444.44LC/MS purity: 95 %, m/z 443 [M-H]⁻ Rt. 3.17 min.

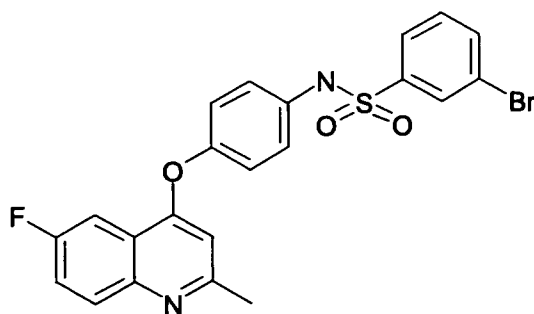
¹H NMR (300 MHz, DMSO-d₆): 10.54 (s, 1H), 7.99 (m, 1H), 7.85 (m, 1H),
7.67 (m, 2H), 7.44 (m, 2H), 7.23 (dd, 4H), 6.43 (s, 1H), 2.54 (s, 3H)

Melting point: 194-195 °C.

Yield: 54 %

Example B14

3-Bromo-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-
benzenesulfonamide

 $C_{22}H_{16}BrFN_2O_3S$ Mw. 487.35LC/MS purity: 96 %, m/z 485 [M-H]⁻ Rt. 3.25 min.

¹H NMR (300 MHz, DMSO-d₆): 10.45 (s, 1H), 7.98 (dd, 1H), 7.85 (m, 3H),
7.76 (d, 1H), 7.67 (m, 1H), 7.55 (t, 1H), 7.21 (dd, 4H), 6.43 (s, 1H), 2.54 (s,

- 122 -

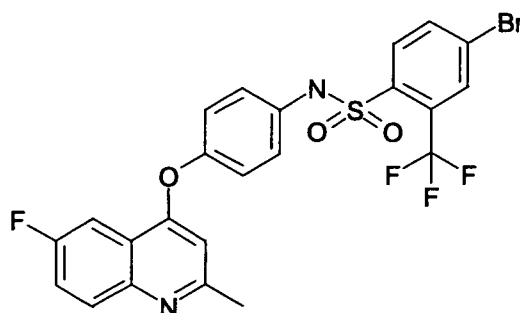
3H)

Melting point: 183-184 °C.

Yield: 73 %

5 Example B15

4-Bromo-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide

 $C_{23}H_{15}BrF_4N_2O_3S$ Mw. 555.3510 LC/MS purity: 96 %, m/z 553 [M-H]⁻ Rt. 3.52 min.¹H NMR (300 MHz, DMSO-d₆): 10.32 (s, 1H), 8.18 (dd, 1H), 8.00 (m, 1H), 7.85 (m, 2H), 7.70 (m, 5H), 6.44 (s, 1H), 2.54 (s, 3H)

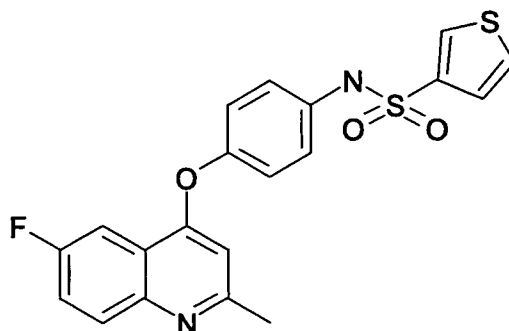
Melting point: 191-193 °C.

Yield: 63 %

15

Example B16

Thiophene-3-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

20 $C_{20}H_{15}FN_2O_3S_2$ Mw. 414.48LC/MS purity: 97 %, m/z 413 [M-H]⁻ Rt. 2.81 min.¹H NMR (300 MHz, DMSO-d₆): 10.31 (s, 1H), 8.18 (dd, 1H), 7.99 (dd, 1H),

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7.85 (dd, 1H), 7.73 (m, 1H), 7.67 (m, 1H), 7.30-7.18 (m, 5H), 6.44 (s, 1H),
2.54 (s, 3H)

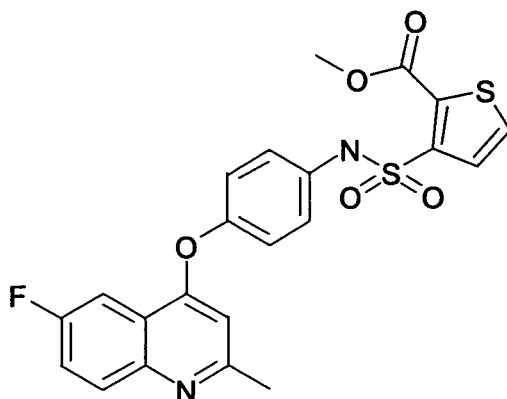
Melting point: 195-196 °C.

Yield: 66 %

5

Example B17

3-[4-(6-Fluoro-2-methyl-quinolin-4-yloxy)-phenylsulfamoyl]-thiophene-2-
carboxylic acid methyl ester



10 $C_{22}H_{17}FN_2O_5S_2$ Mw. 472.52

LC/MS purity: 96 %, m/z 471 [M-H]⁻ Rt. 3.02 min.

¹H NMR (300 MHz, DMSO-d₆): 10.20 (s, 1H), 7.99 (m, 2H), 7.84 (dd, 1H),
7.67 (m, 1H), 7.47 (d, 1H), 7.23 (d, 2H), 7.19 (d, 2H), 6.43 (s, 1H), 3.90 (s,
3H), 2.54 (s, 3H)

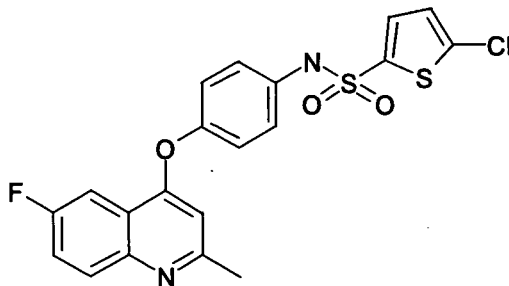
15 Melting point: 160-161 °C.

Yield: 72 %

Example B18

5-Chloro-thiophene-2-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-
phenyl]-amide

20



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$C_{20}H_{14}ClFN_2O_3S_2$ Mw. 448.93

LC/MS purity: 97 %, m/z 447 [M-H]⁻ Rt. 3.23 min.

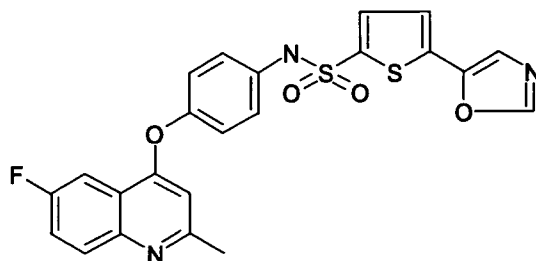
¹H NMR (300 MHz, DMSO-d₆): 10.64 (s, 1H), 7.99 (m, 1H), 7.85 (m, 1H), 7.67 (m, 1H), 7.46 (dd, 1H), 7.25 (m, 5H), 6.47 (s, 1H), 2.54 (s, 3H)

5 Melting point: 170-172 °C.

Yield: 44 %

Example B19

10 5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide



$C_{23}H_{16}FN_3O_4S_2$ Mw. 481.53

LC/MS purity: 95 %, m/z 480 [M-H]⁻ Rt.3.07 min.

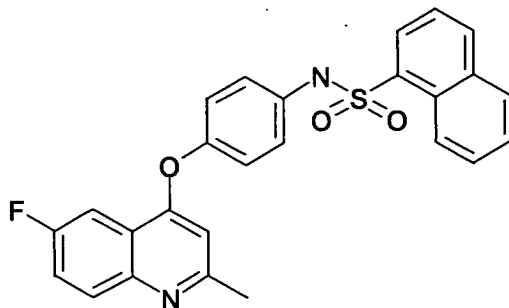
15 ¹H NMR (300 MHz, DMSO-d₆): 10.73 (s, 1H), 8.72 (d, 1H), 7.98 (dd, 1H), 7.85 (dd, 1H) 7.73-7.64 (m, 3H), 7.27 (m, 4H), 7.10 (d, 1H), 6.45 (s, 1H), 2.54 (s, 3H)

Melting point: 164-166 °C.

Yield: 35 %

20 Example B20

Naphthalene-1-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide



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$C_{26}H_{19}FN_2O_3S$ Mw. 458.52

LC/MS purity: 95 %, m/z 457 [M-H]⁻ Rt. 3.25 min.

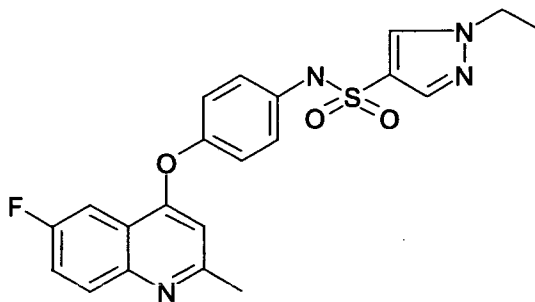
¹H NMR (300 MHz, DMSO-d₆): 10.8 (bs, 1H), 8.78 (d, 1H), 8.22 (d, 2H), 8.08 (d, 1H), 7.95 (dd, 1H), 7.81-7.60 (m, 5H), 7.12 (d, 2H), 7.05 (d, 2H), 6.33 (s, 1H), 2.55 (s, 3H)

Melting point: 223-225 °C.

Yield: 75 %

Example B21

1-Ethyl-1H-pyrazole-4-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide



$C_{21}H_{19}FN_4O_3S$ Mw. 426.47

LC/MS purity: 95 %, m/z 425 [M-H]⁻ Rt. 2.59 min.

¹H NMR (300 MHz, DMSO-d₆): 10.17 (s, 1H), 8.28 (s, 1H), 7.99 (dd, 1H), 7.86 (dd, 1H), 7.71 (s, 1H), 7.66 (dd, 1H), 7.25 (d, 4H), 6.47 (s, 1H), 4.16 (q, 2H), 2.48 (s, 3H), 1.33 (s, 3H)

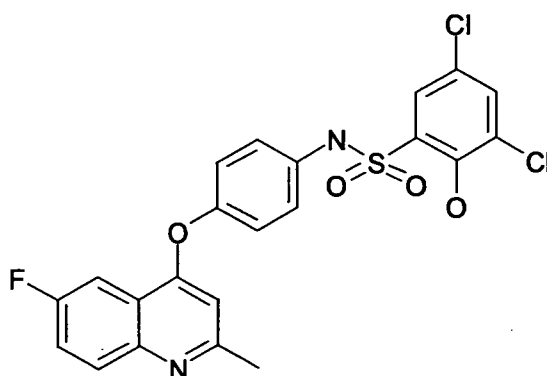
Melting point: 165-167 °C.

Yield: 42 %

Example B22

3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-hydroxy-benzenesulfonamide

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$C_{22}H_{15}Cl_2FN_2O_4S$ Mw. 493.34

LC/MS purity: 94 %, m/z 493 $[M+H]^+$ Rt. 3.24 min.

1H NMR (300 MHz, DMSO- d_6): 10.6 (bs, 2H), 7.99 (dd, 1H), 7.86 (m, 2H),

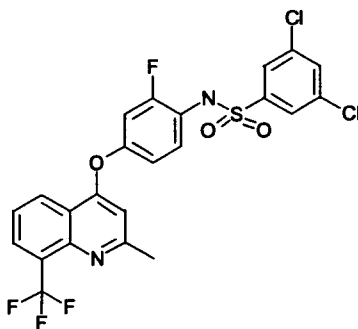
5 7.66 (m, 2H), 7.25 (d, 2H), 7.19 (d, 2H), 6.44 (s, 1H), 2.52 (s, 3H)

Melting point: 203-205 °C.

Yield: 56 %

10 Example C1

3,5-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide



$C_{23}H_{14}Cl_2F_4N_2O_3S$ Mw. 545.34

15 LC/MS purity: 95%, m/z 543 $[M-H]^-$, m/z 545 $[M-H]^+$ Rt. 5.39 min.

1H NMR (300 MHz, DMSO- d_6): 10.52 (s, 1H), 8.47 (d, 1H), 8.19 (d, 1H),
8.01 (s, 1H), 7.70 (m, 3H), 7.37 (m, 2H), 7.15 (dd, 1H), 6.76 (s, 1H), 2.59 (s,
3H)

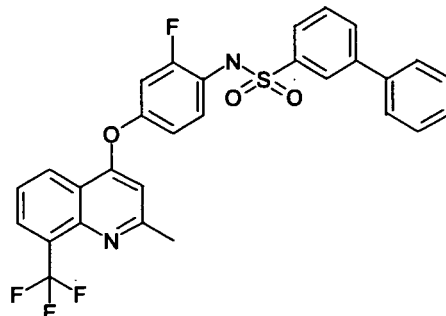
Melting point: 181-183 °C.

20 Yield: 44 %

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Example C2

Biphenyl-3-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide



5

$C_{29}H_{20}F_4N_2O_3S$ Mw. 552.55

LC/MS purity: 98 %, m/z 551 [M-H]⁻, m/z 553 [M-H]⁺ Rt. 5.34 min.

¹H NMR (300 MHz, DMSO-d₆): 10.30 (s, 1H), 8.45 (d, 1H), 8.18 (d, 1H), 8.02 (s, 1H), 7.97 (d, 1H), 7.69 (m, 5H), 7.54-7.29 (m, 5H), 7.14 (dd, 1H), 6.70 (s, 1H), 2.53 (s, 3H)

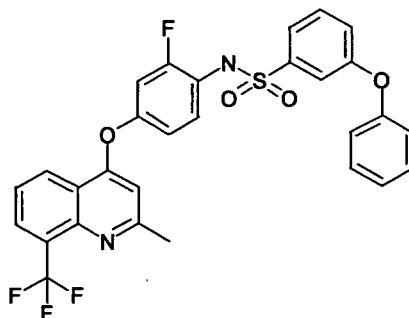
10

Melting point: 187-188 °C.

Yield: 57 %

Example C3

15 N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-3-phenoxy-benzenesulfonamide



$C_{29}H_{20}F_4N_2O_4S$ Mw. 568.55

LC/MS purity: 94 %, m/z 567 [M-H]⁻ Rt. 5.34 min.

20

¹H NMR (300 MHz, DMSO-d₆): 10.27 (s, 1H), 8.48 (d, 1H), 8.19 (d, 1H), 7.74-7.01 (m, 13H), 6.72 (s, 1H), 2.57 (s, 3H)

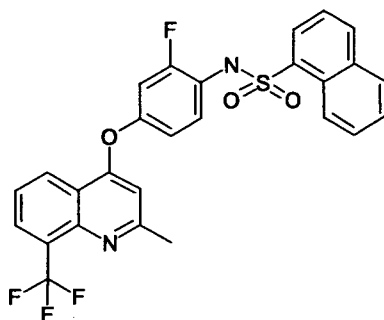
Melting point: 167-168 °C.

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Yield: 63 %

Example C4

Naphthalene-1-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

 $C_{27}H_{18}F_4N_2O_3S$ Mw. 526.51LC/MS purity: 95 %, m/z 525 [M-H]⁻, m/z 527 [M-H]⁺ Rt. 5.15 min.

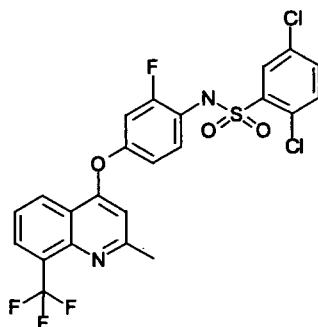
¹H NMR (300 MHz, DMSO-d₆): 10.53 (s, 1H), 8.72 (d, 1H), 8.43 (d, 1H), 8.26 (d, 1H), 8.14 (m, 3H), 7.67 (m, 4H), 7.31 (t, 1H), 7.19 (dd, 1H), 7.07 (dd, 1H), 6.94 (s, 1H), 2.57 (s, 3H)

Melting point: 232-234 °C.

Yield: 42 %

Example C5

2,5-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamid

 $C_{23}H_{14}Cl_2F_4N_2O_3S$ Mw. 545.34LC/MS purity: 95 %, m/z 543 [M-H]⁻, m/z 545 [M-H]⁺ Rt. 5.24 min.

¹H NMR (300 MHz, DMSO-d₆): 10.67 (s, 1H), 8.47 (d, 1H), 8.19 (d, 1H), 7.88 (s, 1H), 7.76 (s, 2H), 7.69 (m, 1H), 7.35 (m, 2H), 7.14 (dd, 1H), 6.72 (s,

- 129 -

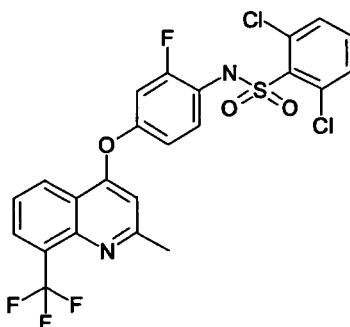
1H), 2.59 (s, 3H)

Melting point: 207-209 °C.

Yield: 73 %

5 Example C6

2,6-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide



$C_{23}H_{14}Cl_2F_4N_2O_3S$ Mw. 545.34

10 LC/MS purity: 95 %, m/z 543 [M-H]⁻, m/z 545 [M-H]⁺ Rt. 5.09 min.

¹H NMR (300 MHz, DMSO-d₆): 10.66 (s, 1H), 8.47 (d, 1H), 8.19 (d, 1H), 7.65 (m, 4H),

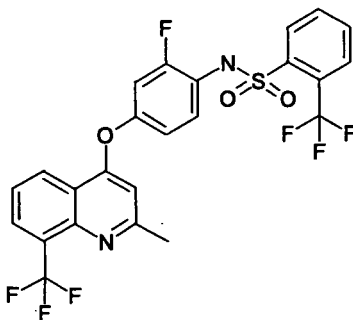
7.35 (m, 2H), 7.13 (dd, 1H), 6.68 (s, 1H), 2.57 (s, 3H)

Melting point: 171-173 °C.

15 Yield: 54 %

Example C7

N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamid



20

$C_{24}H_{15}F_7N_2O_3S$ Mw. 544.45

LC/MS purity: 95 %, m/z 543 [M-H]⁻ Rt. 5.05 min.

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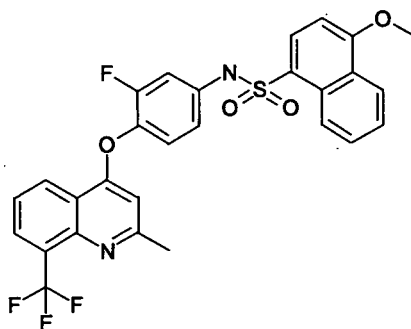
¹H NMR (300 MHz, DMSO-d₆): 10.43 (s, 1H), 8.47 (d, 1H), 8.19 (d, 1H), 8.05 (m, 2H), 7.88 (m, 2H), 7.72 (t, 1H), 7.33 (m, 2H), 7.12 (dd, 1H), 6.69 (s, 1H), 2.58 (s, 3H)

Melting point: 183-185 °C.

Yield: 56 %

Example C8

4-Methoxy-naphthalene-1-sulfonic acid [3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide



C₂₈H₂₀F₄N₂O₄S Mw. 556.54

LC/MS purity: 94 %, m/z 555 [M-H]⁻, m/z 557 [M-H]⁺ Rt. 5.25 min.

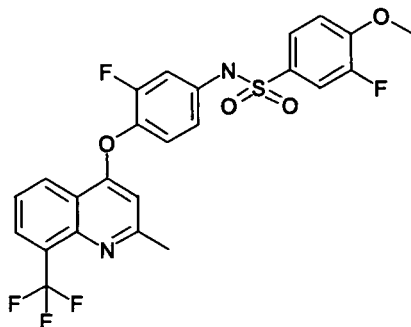
¹H NMR (300 MHz, DMSO-d₆): 10.97 (s, 1H), 8.68 (d, 1H), 8.47 (d, 1H), 8.30 (d, 2H), 8.17 (d, 1H), 7.79 (t, 1H), 7.67 (m, 2H), 7.31 (t, 1H), 7.11 (m, 2H), 6.95 (d, 1H), 6.51 (s, 2H), 4.06 (s, 3H), 2.56 (s, 3H)

Melting point: 242-244 °C.

Yield: 74 %

Example C9

3-Fluoro-N-[3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide



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$C_{24}H_{17}F_5N_2O_4S$ Mw. 524.47

LC/MS purity: 98 %, m/z 523 [M-H] Rt. 4.96 min.

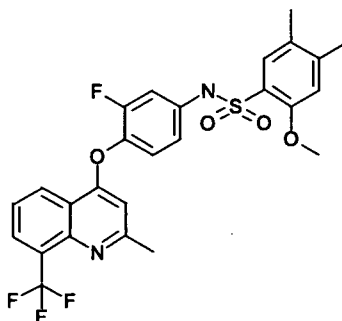
1H NMR (300 MHz, DMSO- d_6): 10.63 (bs, 1H), 8.53 (d, 1H), 8.20 (d, 1H), 7.65 (m, 3H), 7.40 (m, 2H), 7.19 (dd, 1H), 7.05 (dd, 1H), 6.58 (s, 1H), 3.92 (s, 3H), 2.55 (s, 3H)

Melting point: 128-130 °C.

Yield: 70 %

Example C10

N-[3-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-2-methoxy-4,5-dimethyl-benzenesulfonamide



$C_{26}H_{22}F_4N_2O_4S$ Mw. 534.53

LC/MS purity: 95 %, m/z 533 [M-H], m/z 535 [M-H]⁺ Rt. 5.19 min.

1H NMR (300 MHz, DMSO- d_6): 10.34 (s, 1H), 8.49 (d, 1H), 8.19 (d, 1H), 7.70 (t, 1H), 7.59 (s, 1H), 7.15 (dd, 1H), 7.03 (m, 2H), 6.54 (s, 1H), 3.86 (s, 3H), 2.58 (s, 3H), 2.26 (s, 3H), 2.19 (s, 3H)

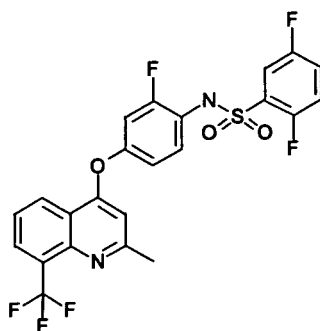
Melting point: 230-232 °C.

Yield: 62 %

Example C11

2,5-Difluoro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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$C_{23}H_{14}F_6N_2O_3S$ Mw. 512.43

LC/MS purity: 100 %, m/z 511 [M-H]⁻ Rt. 4.92 min.

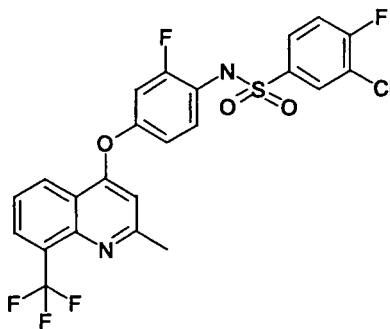
¹H NMR (300 MHz, DMSO-d₆): 10.70 (bs, 1H), 8.47 (d, 2H), 8.18 (d, 1H),
 5 7.69 (t, 1H), 7.53 (m, 3H), 7.37 (t, 1H), 7.27 (d, 1H), 7.07 (d, 1H), 6.71 (s,
 1H), 2.58 (s, 3H)

Melting point: 179-181 °C.

Yield: 52 %

10 Example C12

3-Chloro-4-fluoro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-
 phenyl]-benzenesulfonamide



$C_{23}H_{14}ClF_5N_2O_3S$ Mw. 528.89

15 LC/MS purity: 98 %, m/z 527 [M-H]⁻ Rt. 5.24 min.

¹H NMR (300 MHz, DMSO-d₆): 10.41 (bs, 1H), 8.47 (d, 1H), 8.19 (d, 1H),
 7.91 (dd, 1H), 7.71 (m, 3H), 7.33 (m, 2H), 7.12 (d, 1H), 6.75 (s, 1H), 2.58 (s,
 3H)

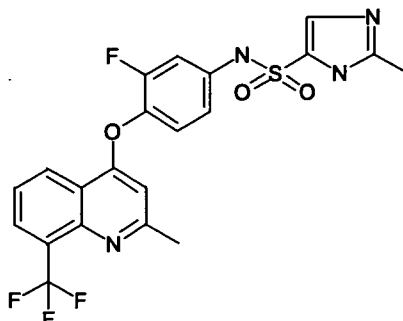
Melting point: 202-203 °C.

20 Yield: 57 %

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Example C13

2-Methyl-3H-imidazole-4-sulfonic acid [3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide



5 $C_{21}H_{16}F_4N_4O_3S$ Mw. 480.44

LC/MS purity: 98 %, m/z 479 [M-H]⁻ Rt. 4.07 min.

¹H NMR (300 MHz, DMSO-d₆): 12.5 (s, 1H), 10.6 (bs, 1H), 8.54 (d, 1H), 8.19 (d, 1H), 7.79 (s, 1H), 7.71 (t, 1H), 7.38 (t, 1H), 7.24 (d, 1H), 7.08 (d, 1H), 6.60 (s, 1H), 2.56 (s, 3H), 2.29 (s, 3H)

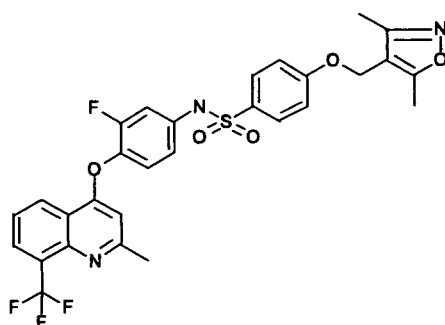
10 Melting point: 258-259 °C.

Yield: 57 %

Example C14

4-(3,5-Dimethyl-isoxazol-4-ylmethoxy)-N-[3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

15



$C_{29}H_{23}F_4N_3O_5S$ Mw. 601.58

LC/MS purity: 95 %, m/z 600 [M-H]⁻ Rt. 4.96 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 12.20 (bs, 1H), 8.52 (d, 1H), 8.19 (d, 1H), 7.80 (d, 2H), 7.71 (t, 1H), 7.40 (t, 1H), 7.18 (m, 3H), 7.04 (dd, 1H), 6.58 (s, 1H), 5.00 (s, 2H), 2.55 (s, 3H), 2.40 (s, 3H), 2.20 (s, 3H)

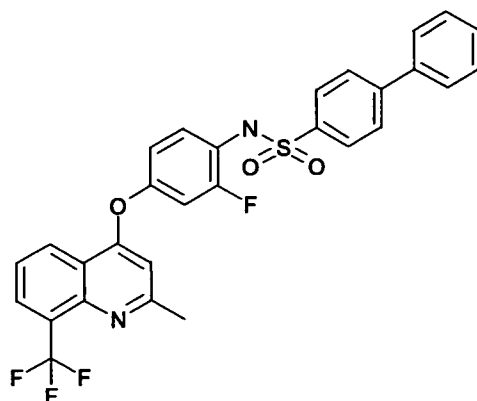
Melting point: 193-195 °C.

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Yield: 35 %

Example C15

Biphenyl-4-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

 $C_{29}H_{20}F_4N_2O_3S$ Mw. 552.55LC/MS purity: 96 %, m/z 551 [M-H]⁻, m/z 553 [M-H]⁺ Rt. 5.34 min.

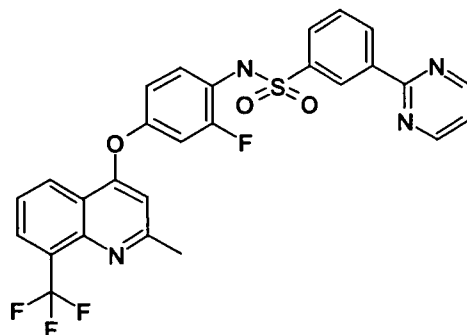
¹H NMR (300 MHz, DMSO-d₆): 10.32 (bs, 1H), 8.46 (d, 1H), 8.18 (d, 1H), 7.87 (dd, 4H), 7.72 (m, 3H), 7.53-7.36 (m, 4H), 7.29 (dd, 1H), 7.10 (d, 1H), 6.73 (s, 1H), 2.56 (s, 3H)

Melting point: 215-217 °C.

Yield: 63 %

Example C16

N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

 $C_{27}H_{18}F_4N_4O_3S$ Mw. 554.53

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LC/MS purity: 97 %, m/z 553 [M-H]⁻, m/z 555 [M-H]⁺ Rt. 4.92 min.

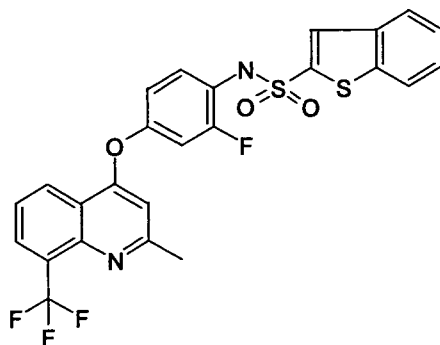
¹H NMR (300 MHz, DMSO-d₆): 10.39 (bs, 1H), 8.97 (s, 1H), 8.96 (s, 1H), 8.84 (t, 1H), 8.63 (d, 1H), 8.45 (d, 1H), 8.18 (d, 1H), 7.89 (d, 1H), 7.70 (m, 2H), 7.53 (t, 1H), 7.35 (t, 1H), 7.25 (dd, 1H), 7.07 (d, 1H), 6.68 (s, 1H), 2.58 (s, 3H)

Melting point: 219-220 °C.

Yield: 54 %

Example C17

Benzo[b]thiophene-2-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide



C₂₅H₁₆F₄N₂O₃S₂ Mw. 532.54

LC/MS purity: 96 %, m/z 531 [M-H]⁻, m/z 533 [M-H]⁺ Rt. 5.16 min.

¹H NMR (300 MHz, DMSO-d₆): 10.65 (s, 1H), 8.47 (d, 1H), 8.19 (d, 1H), 8.10 (d, 1H), 8.03 (d, 1H), 7.95 (s, 1H), 7.69 (t, 1H), 7.50 (m, 3H), 7.33 (dd, 1H), 7.15 (d, 1H), 6.75 (s, 1H), 2.58 (s, 3H)

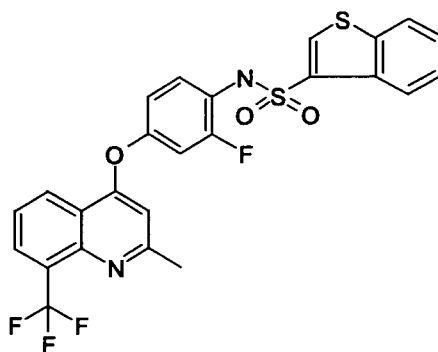
Melting point: 182-184 °C.

Yield: 51 %

Example C18

Benzo[b]thiophene-3-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)phenyl]-amide

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$C_{25}H_{16}F_4N_2O_3S_2$ Mw. 532.54

LC/MS purity: 96 %, m/z 531 [M-H]⁻, m/z 533 [M-H]⁺ Rt. 5.11 min.

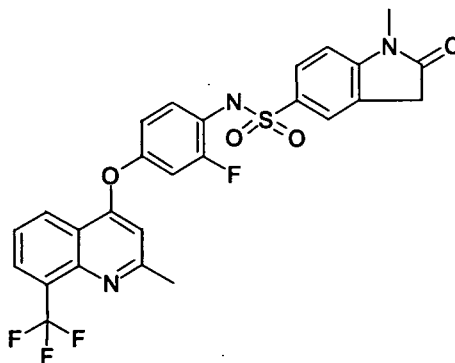
¹H NMR (300 MHz, DMSO-d₆): 10.46 (s, 1H), 8.49 (s, 1H), 8.45 (d, 1H), 8.14 (m, 3H), 7.69 (t, 1H), 7.52 (m, 2H), 7.37 (t, 1H), 7.23 (dd, 1H), 7.09 (d, 1H), 6.68 (s, 1H), 2.58 (s, 3H)

Melting point: 242-244 °C.

Yield: 75 %

Example C19

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoro-methyl-quinolin-4-yloxy)-phenyl]-amide



$C_{26}H_{19}F_4N_3O_4S$ Mw. 545.52

LC/MS purity: 90 %, m/z 544 [M-H]⁻, m/z 546 [M-H]⁺ Rt. 4.45 min.

¹H NMR (300 MHz, DMSO-d₆): 11.00 (bs, 1H), 8.47 (d, 1H), 8.18 (d, 1H), 7.69 (m, 2H), 7.63 (s, 1H), 7.34 (t, 1H), 7.25 (dd, 1H), 7.11 (d, 1H), 7.05 (d, 1H), 6.71 (s, 1H), 3.64 (s, 2H), 3.14 (s, 3H), 2.57 (s, 3H)

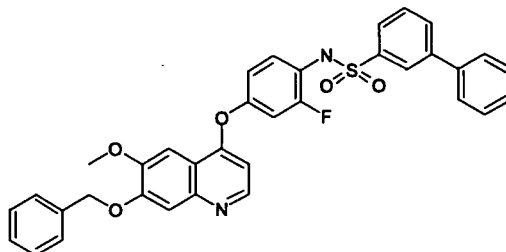
Melting point: 225-226 °C.

Yield: 35 %

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Example D1

Biphenyl-3-sulfonic acid [4-(7-benzyloxy-6-methoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide



5

$C_{35}H_{27}FN_2O_5S$ Mw. 606.68

LC/MS purity: 100 %, m/z 605 [M-H]⁻, m/z 607 [M-H]⁺ Rt. 3.71 min.

¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 8.43 (d, 1H), 7.96 (d, 2H), 7.72 (m, 4H), 7.68-7.25 (m, 11H), 7.18 (d, 1H), 7.23 (dd, 1H), 6.48 (d, 1H), 5.30 (s, 2H), 3.89 (s, 3H)

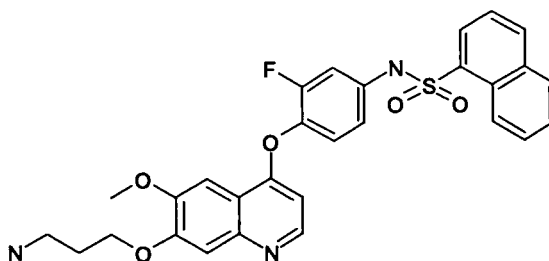
10

Melting point: 228-229 °C.

Yield: 72 %

Example D2

15 Naphthalene-1-sulfonic acid {4-[7-(3-amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-amide hydrochloride



$C_{29}H_{26}FN_3O_5S \cdot HCl$ Mw (base). 547.61

20

LC/MS purity: 100 %, m/z 546 [M-H]⁻, m/z 548 [M-H]⁺ Rt. 2.41 min.

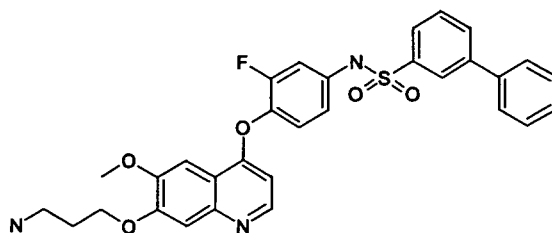
¹H NMR (300 MHz, DMSO-d₆): 11.28 (s, 1H), 8.72 (m, 2H), 8.30 (t, 2H), 8.12 (m, 3H), 7.77 (m, 5H), 7.38 (m, 1H), 7.16 (dd, 1H), 7.03 (d, 1H), .55 (s, 1H), 4.28 (t, 2H), 3.98 (s, 3H), 2.97 (t, 2H), 2.15 (t, 2H)

Melting point: °C.

Yield: 85 %

Example D3

Biphenyl-3-sulfonic acid {4-[7-(3-amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-amide hydrochloride



$C_{31}H_{28}FN_3O_5S \cdot HCl$ Mw (base). 573.65

LC/MS purity: 100 %, m/z 572 [M-H]⁻, m/z 574 [M-H]⁺ Rt. 2.58 min.

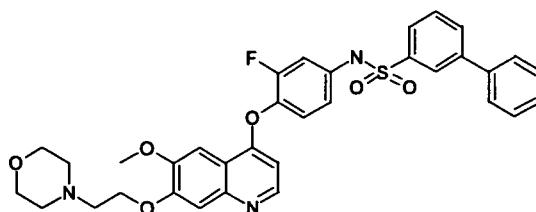
¹H NMR (300 MHz, DMSO-d₆): 10.96 (s, 1H), 8.72 (d, 1H), 8.05 (m, 5H), 7.83 (d, 1H), 7.69 (m, 5H), 7.50 (m, 4H), 7.31 (dd, 1H), 7.18 (dd, 1H), 6.81 (d, 1H), 4.33 (t, 2H), 4.00 (s, 3H), 3.00 (q, 2H), 2.18 (t, 2H)

Melting point: 198-202 °C.

Yield: 83 %

Example D4

Biphenyl-3-sulfonic acid {3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-amide



$C_{34}H_{32}FN_3O_6S$ Mw. 629.71

LC/MS purity: 99 %, m/z 628 [M-H]⁻, m/z 630 [M-H]⁺ Rt. 2.68 min.

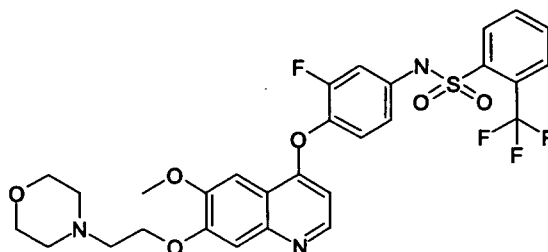
¹H NMR (300 MHz, DMSO-d₆): 10.50 (bs, 1H), 8.37 (d, 1H), 8.03 (s, 1H), 7.96 (d, 1H), 7.79 (d, 1H), 7.66 (m, 3H), 7.48 (m, 5H), 7.34 (t, 1H), 7.02 (d, 1H), 6.28 (d, 1H), 4.26 (t, 2H), 3.90 (s, 3H), 3.39 (m, 4H), 2.78 (t, 2H), 2.60 (m, 4H)

Melting point: 103-104 °C.

Yield: 36 %

Example D5

N-{3-Fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethyl-benzenesulfonamide



$C_{29}H_{27}F_4N_3O_6S$ Mw. 621.61

LC/MS purity: 100 %, m/z 620 [M-H], m/z 622 [M-H]⁺ Rt. 2.26 min.

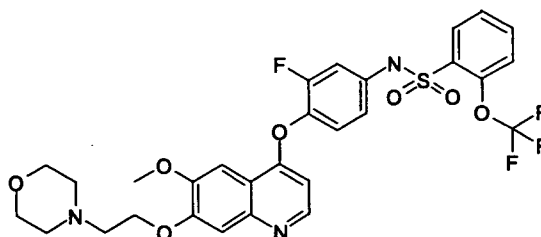
¹H NMR (300 MHz, DMSO-d₆): 11.00 (bs, 1H), 8.45 (d, 1H), 8.16 (d, 1H), 8.02 (d, 1H), 7.90 (m, 2H), 7.47 (s, 1H), 7.42 (s, 1H), 7.38 (t, 1H), 7.16 (t, 1H), 7.02 (d, 1H), 6.36 (d, 1H), 4.27 (t, 2H), 3.91 (s, 3H), 3.59 (t, 4H), 2.79 (t, 2H), 2.53 (m, 4H)

Melting point: 178-180 °C.

Yield: 43 %

Example D6

N-{3-Fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethoxy-benzenesulfonamide



$C_{29}H_{27}F_4N_3O_7S$ Mw. 637.61

LC/MS purity: 100 %, m/z 636 [M-H], m/z 638 [M-H]⁺ Rt. 2.45 min.

¹H NMR (300 MHz, DMSO-d₆): 11.00 (bs, 1H), 8.45 (d, 1H), 8.04 (dd, 1H), 7.79 (t, 1H), 7.59 (m, 2H), 7.47 (s, 1H), 7.42 (s, 1H), 7.36 (t, 1H), 7.16 (dd, 1H), 7.00 (d, 1H), 6.33 (d, 1H), 4.27 (t, 2H), 3.91 (s, 3H), 3.59 (t, 4H), 2.79 (t, 2H), 2.53 (m, 4H)

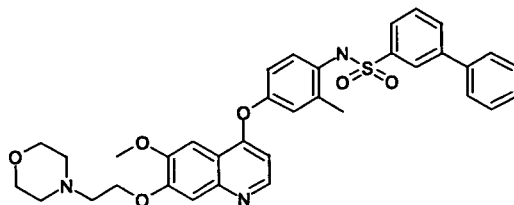
Melting point: 185-187 °C.

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Yield: 34 %

Example D7

Biphenyl-3-sulfonic acid {4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-amide



$C_{35}H_{35}N_3O_6S$ Mw. 625.75

LC/MS purity: 100 %, m/z 624 [M-H]⁻, m/z 626 [M-H]⁺ Rt. 2.59 min.

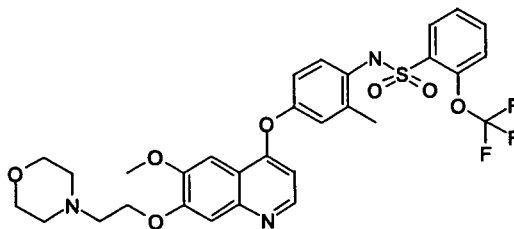
¹H NMR (300 MHz, DMSO-d₆): 9.82 (s, 1H), 8.40 (s, 1H), 8.01 (s, 1H), 7.86 (s, 1H), 7.67 (m, 4H), 7.48 (m, 3H), 7.46 (s, 1H), 7.44 (s, 1H), 7.07 (m, 3H), 6.37 (d, 1H), 4.26 (t, 2H), 3.90 (s, 3H), 3.59 (t, 4H), 2.78 (t, 2H), 2.53 (m, 4H), 199 (s, 3H)

Melting point: 105-107 °C.

Yield: 66 %

Example D8

N-{4-[6-Methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-2-trifluoromethoxy-benzenesulfonamide



$C_{30}H_{30}F_3N_3O_7S$ Mw. 633.65

LC/MS purity: 100 %, m/z 632 [M-H]⁻, m/z 634 [M-H]⁺ Rt. 2.44 min.

¹H NMR (300 MHz, DMSO-d₆): 9.25 (bs, 1H), 8.47 (d, 1H), 7.86 (d, 1H), 7.76 (t, 1H), 7.53 (m, 2H), 7.44 (s, 1H), 7.42 (s, 1H), 7.09 (d, 1H), 7.07 (s, 1H), 6.98 (d, 1H), 6.42 (d, 1H), 4.26 (t, 2H), 3.90 (s, 3H), 3.59 (t, 4H), 2.79 (t, 2H), 2.54 (t, 4H), 2.07 (m, 3H)

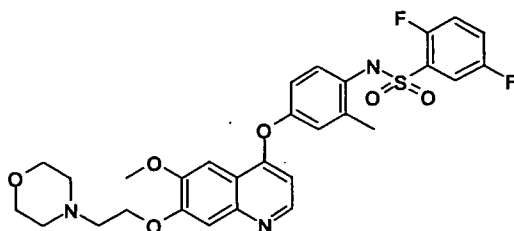
Melting point: 186-188 °C.

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Yield: 46 %

Example D9

2,5-Difluoro-N-{4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-benzenesulfonamide

 $C_{29}H_{29}F_2N_3O_6S$ Mw. 585.63LC/MS purity: 100 %, m/z 584 [M-H]⁻, m/z 586 [M-H]⁺ Rt. 2.09 min.

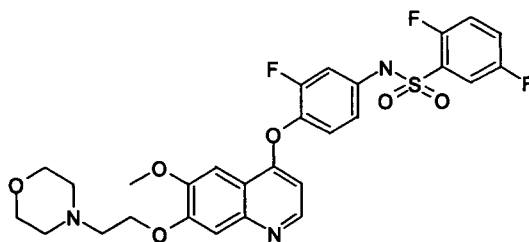
¹H NMR (300 MHz, DMSO-d₆): 10.18 (bs, 1H), 8.48 (d, 1H), 7.58 (m, 2H), 7.45 (m, 3H), 7.06 (m, 3H), 6.45 (d, 1H), 4.27 (t, 2H), 3.90 (s, 3H), 3.59 (t, 4H), 2.78 (t, 2H), 2.54 (t, 4H), 2.07 (m, 3H)

Melting point: 195-196 °C.

Yield: 41 %

Example D10

2,5-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

 $C_{28}H_{26}F_3N_3O_6S$ Mw. 589.60LC/MS purity: 100 %, m/z 588 [M-H]⁻, m/z 590 [M-H]⁺ Rt. 2.31 min.

¹H NMR (300 MHz, DMSO-d₆): 10.6 (bs, 1H), 8.46 (s, 1H), 7.61 (m, 1H), 7.43 (m, 4H), 7.21 (t, 1H), 7.04 (d, 1H), 6.89 (d, 1H), 6.35 (d, 1H), 4.26 (t, 2H), 3.92 (s, 3H), 3.60 (t, 4H), 2.78 (t, 2H), 2.53 (m, 4H)

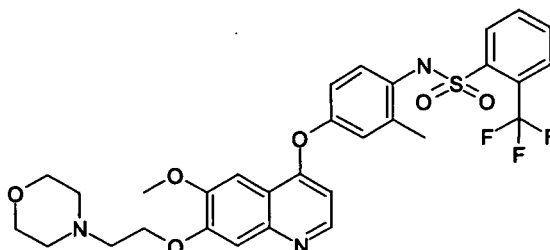
Melting point: 169-173 °C.

Yield: 26 %

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Example D11

N-{4-[6-Methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-2-trifluoromethyl-benzenesulfonamide



$C_{30}H_{30}F_3N_3O_6S$ Mw. 617.65

LC/MS purity: 100 %, m/z 616 [M-H]⁻, m/z 618 [M-H]⁺ Rt. 2.41 min.

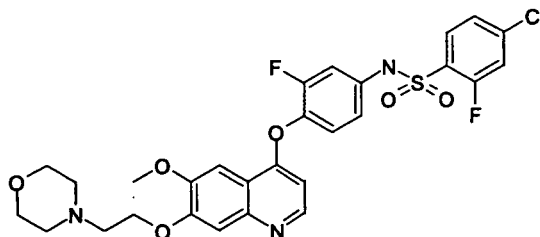
¹H NMR (300 MHz, DMSO-d₆): 9.89 (bs, 1H), 8.48 (d, 1H), 8.01 (m, 1H), 7.95 (m, 1H), 7.86 (m, 2H), 7.42 (d, 2H), 7.03 (m, 3H), 6.43 (d, 1H), 4.27 (t, 2H), 3.90 (s, 3H), 3.59 (t, 4H), 2.78 (t, 2H), 2.53 (m, 4H), 2.10 (s, 3H)

Melting point: 127-130 °C.

Yield: 31 %

Example D12

4-Chloro-2-fluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



$C_{28}H_{26}ClF_2N_3O_6S$ Mw. 606.05

LC/MS purity: 100 %, m/z 604 [M-H]⁻, m/z 606 [M-H]⁺ Rt. 2.42 min.

¹H NMR (300 MHz, DMSO-d₆): 11.2 (bs, 1H), 8.45 (d, 1H), 7.90 (t, 1H), 7.75 (d, 1H), 7.52-7.33 (m, 4H), 7.15 (d, 1H), 7.02 (d, 1H), 6.35 (d, 1H), 4.27 (t, 2H), 3.91 (s, 3H), 3.59 (t, 4H), 2.78 (t, 2H), 2.53 (m, 4H)

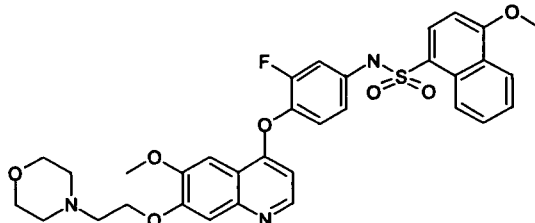
Melting point: 212-214 °C.

Yield: 42 %

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Example D13

4-Methoxy-naphthalene-1-sulfonic acid {3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-amide



5 $C_{33}H_{32}FN_3O_7S$ Mw. 633.70

LC/MS purity: 100 %, m/z 632 [M-H]⁻, m/z 634 [M-H]⁺ Rt. 2.53 min.

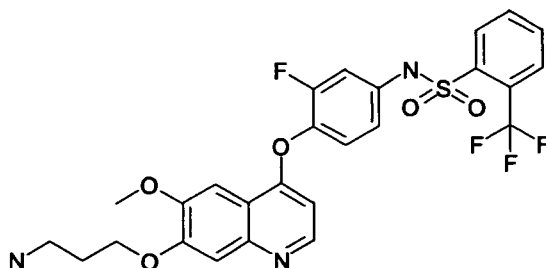
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.70 (d, 1H), 8.40 (d, 1H), 8.27 (t, 3H), 7.76 (t, 1H), 7.65 (t, 1H), 7.42 (s, 1H), 7.40 (s, 1H), 7.23 (t, 1H), 7.11 (d, 1H), 7.04 (d, 1H), 6.90 (d, 1H), 6.27 (d, 1H), 4.25 (t, 2H), 4.06 (s, 3H),
 10 3.58 (t, 4H), 2.77 (t, 2H), 2.54 (m, 4H)

Melting point: 189-190 °C.

Yield: 35 %

Example D14

15 N-{4-[7-(3-Amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-trifluoromethyl-benzenesulfonamide hydrochloride



$C_{26}H_{23}F_4N_3O_5S \cdot HCl$ Mw (base). 565.55

LC/MS purity: 100 %, m/z 564 [M-H]⁻, m/z 566 [M-H]⁺ Rt. 2.39 min.

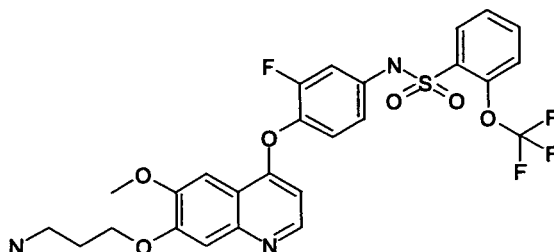
20 ¹H NMR (300 MHz, DMSO-d₆): 11.28 (s, 1H), 8.75 (d, 1H), 8.20 (d, 1H), 8.04 (m, 4H), 7.90 (m, 2H), 7.70 (s, 1H), 7.68 (s, 1H), 7.51 (t, 1H), 7.25 (dd, 1H), 7.12 (d, 1H), 6.82 (d, 1H), 4.32 (t, 2H), 4.00 (s, 3H), 3.00 (m, 2H), 2.17 (t, 2H)

Melting point: 197-199 °C.

25 Yield: 86 %

Example D15

N-{4-[7-(3-Amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-trifluoromethoxy-benzenesulfonamide hydrochloride



$C_{26}H_{23}F_4N_3O_6S$ Mw. 581.55

LC/MS purity: 100 %, m/z 580 [M-H]⁻, m/z 582 [M-H]⁺ Rt. 2.44 min.

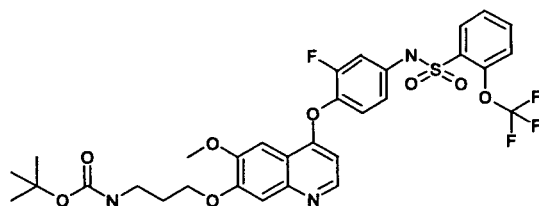
¹H NMR (300 MHz, DMSO-d₆): 11.16 (s, 1H), 8.76 (d, 1H), 8.07 (m, 6H), 7.82 (t, 1H), 7.69 (s, 2H), 7.50 (t, 1H), 7.23 (dd, 1H), 7.07 (d, 1H), 6.80 (d, 1H), 4.32 (t, 2H), 4.00 (s, 3H), 2.96 (m, 2H), 2.17 (t, 2H)

Melting point: 95-97 °C.

Yield: 90 %

Example D16

(3-{4-[2-Fluoro-4-(2-trifluoromethoxy-benzenesulfonylamino)-phenoxy]-6-methoxy-quinolin-7-yloxy}-propyl)-carbamic acid tert-butyl ester



$C_{31}H_{31}F_4N_3O_8S$ Mw. 681.67

LC/MS purity: 100 %, m/z 680 [M-H]⁻, m/z 682 [M-H]⁺ Rt. 3.48 min.

¹H NMR (300 MHz, DMSO-d₆): 10.94 (bs, 1H), 8.43 (d, 1H), 8.03 (d, 1H), 7.80 (t, 1H), 7.58 (m, 2H), 7.46 (s, 1H), 7.36 (dd, 2H), 7.14 (dd, 1H), 6.99 (d, 1H), 6.90 (t, 1H), 6.31 (d, 1H), 4.14 (t, 2H), 3.91 (s, 3H), 3.12 (m, 2H), 1.91 (t, 2H), 1.03 (s, 9H)

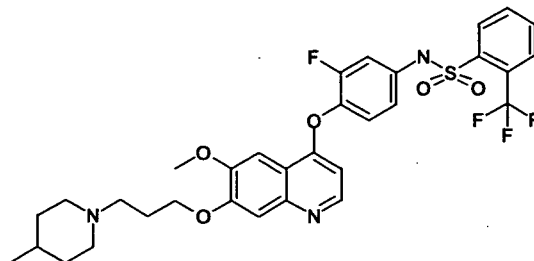
Melting point: 181-183 °C.

Yield: 76 %

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Example D17

N-(3-Fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-2-trifluoromethyl-benzenesulfonamide



5 $C_{32}H_{33}F_4N_3O_5S$ Mw. 647.69

LC/MS purity: 98 %, m/z 646 [M-H]⁻, m/z 648 [M-H]⁺ Rt. 2.78 min.

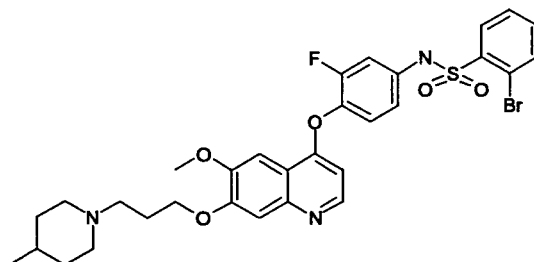
¹H NMR (300 MHz, DMSO-d₆): 12 (bs, 1H), 8.40 (d, 1H), 8.08 (d, 1H), 7.76 (d, 1H), 7.64 (t, 1H), 7.55 (t, 1H), 7.46 (s, 1H), 7.33 (s, 1H), 6.96 (t, 1H), 6.75 (d, 1H), 6.63 (d, 1H), 6.32 (d, 1H), 4.15 (t, 2H), 3.90 (s, 3H), 2.84 (m, 2H),
 10 2.55 (m, 2H), 2.42 (m, 1H), 1.92 (m, 2H), 1.56 (m, 2H), 1.29 (m, 2H), 1.14 (m, 2H), 0.87 (d, 3H)

Melting point: 110-112 °C.

Yield: 45 %

15 Example D18

2-Bromo-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide



$C_{31}H_{33}BrFN_3O_5S$ Mw. 658.59

20 LC/MS purity: 99 %, m/z 656 [M-H]⁻, m/z 658 [M-H]⁺ Rt. 2.76 min.

¹H NMR (300 MHz, DMSO-d₆): 11.5 (bs, 1H), 8.39 (d, 1H), 7.97 (d, 1H), 7.58 (d, 1H), 7.46 (s, 1H), 7.35 (m, 2H), 7.23 (t, 1H), 6.91 (t, 1H), 6.73 (d, 1H), 6.61 (d, 1H), 6.33 (d, 1H), 4.15 (t, 2H), 3.90 (s, 3H), 2.82 (m, 2H), 2.40 (m, 1H), 1.90 (m, 4H), 1.55 (m, 2H), 1.30 (m, 2H), 1.10 (m, 2H), 0.87 (d, 3H)

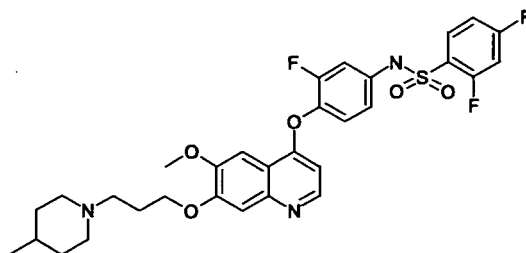
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Melting point: 184-186 °C.

Yield: 52 %

Example D19

- 5 2,4-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

 $C_{31}H_{32}F_3N_3O_5S$ Mw. 615.68LC/MS purity: 100 %, m/z 614 [M-H], m/z 616 [M-H]⁺ Rt. 2.73 min.

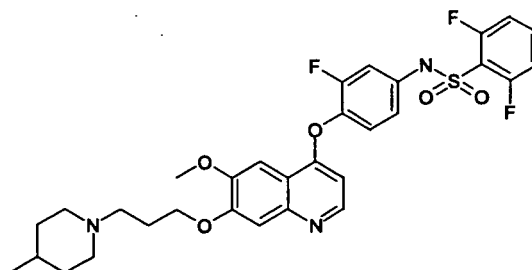
- 10 ¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 8.42 (d, 1H), 7.87 (d, 1H), 7.47 (s, 1H), 7.35 (bs, 2H), 7.15 (bs, 2H), 6.96 (d, 1H), 6.80 (bs, 1H), 6.33 (d, 1H), 4.16 (t, 2H), 3.90 (s, 3H), 2.91 (m, 2H), 2.53 (m, 1H), 1.98 (m, 4H), 1.59 (m, 2H), 1.34 (m, 2H), 1.17 (m, 2H), 0.87 (d, 3H)

Melting point: 135-137 °C.

- 15 Yield: 46 %

Example D20

2,6-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide



20

 $C_{31}H_{32}F_3N_3O_5S$ Mw. 615.68LC/MS purity: 94 %, m/z 614 [M-H], m/z 616 [M-H]⁺ Rt. 2.67 min.

¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 7.47 (bs, 2H), 7.35 (s, 1H), 7.08 (m, 3H), 6.94 (d, 1H), 6.76 (d, 1H), 6.33 (d, 1H), 4.16 (t, 2H), 3.90 (s,

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3H), 2.92 (m, 2H), 2.54 (m, 1H), 1.98 (m, 5H), 1.59 (m, 2H), 1.35 (m, 2H), 1.18 (m, 2H), 0.88 (d, 3H)

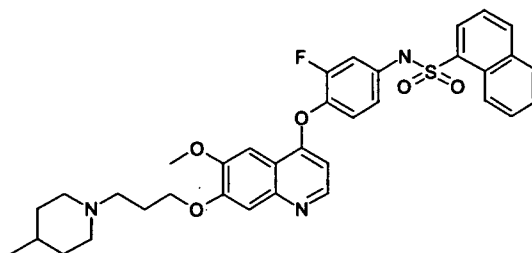
Melting point: 200-203 °C.

Yield: 37 %

5

Example D21

Naphthalene-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide



10 $C_{35}H_{36}FN_3O_5S$ Mw. 629.76

LC/MS purity: 95 %, m/z 628 [M-H]⁻, m/z 630 [M-H]⁺ Rt. 2.89 min.

¹H NMR (300 MHz, DMSO-d₆): 10.7 (bs, 1H), 8.78 (d, 1H), 8.38 (d, 1H), 8.22 (m, 2H), 8.06 (d, 1H), 7.66 (m, 3H), 7.41 (s, 1H), 7.31 (s, 1H), 7.15 (t, 1H), 7.00 (d, 1H), 6.86 (d, 1H), 6.24 (d, 1H), 4.15 (t, 2H), 3.87 (s, 3H), 2.92 (m, 2H), 2.54 (m, 1H), 1.99 (m, 4H), 1.59 (m, 2H), 1.21 (m, 2H), 1.17 (m, 2H), 0.87 (d, 3H)

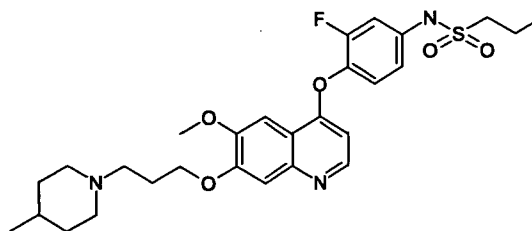
15

Melting point: 140-143 °C.

Yield: 35 %

20 Example D22

Propane-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide



$C_{28}H_{36}FN_3O_5S$ Mw. 545.68

25 LC/MS purity: 99 %, m/z 544 [M-H]⁻, m/z 546 [M-H]⁺ Rt. 2.50 min.

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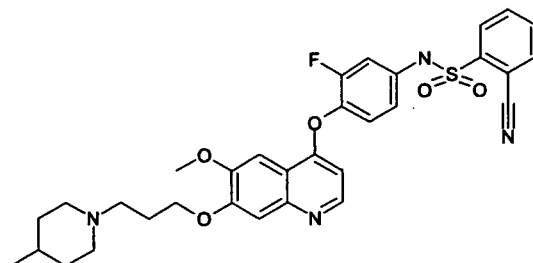
¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 8.45 (d, 1H), 7.49 (s, 1H), 7.36 (s, 1H), 7.34 (d, 1H), 7.16 (d, 1H), 7.03 (d, 1H), 6.44 (d, 1H), 4.26 (t, 1H), 3.93 (s, 3H), 3.07 (bs, 2H), 2.71 (m, 2H), 2.62 (m, 2H), 2.44 (m, 1H), 1.92 (m, 3H), 1.69 (m, 2H), 1.57 (m, 2H), 1.21 (m, 2H), 1.13 (m, 2H), 0.95 (t, 3H), 0.87 (d, 3H)

Melting point: 160-162 °C.

Yield: 16 %

Example D23

2-Cyano-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide



C₃₂H₃₃FN₄O₅S Mw. 604.71

LC/MS purity: 99 %, m/z 603 [M-H]⁻, m/z 605 [M-H]⁺ Rt. 2.52 min.

¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 8.44 (d, 1H), 7.99 (d, 1H), 7.77 (t, 1H), 7.63 (t, 2H), 7.49 (s, 1H), 7.38 (s, 1H), 7.09 (t, 1H), 6.94 (d, 1H), 6.77 (d, 1H), 6.37 (d, 1H), 4.20 (t, 2H), 3.92 (s, 3H), 3.14 (m, 2H), 2.77 (m, 2H), 2.33 (m, 1H), 2.07 (m, 2H), 2.07 (m, 2H), 1.69 (m, 2H), 1.45 (m, 2H), 1.24 (m, 2H), 0.90 (d, 3H)

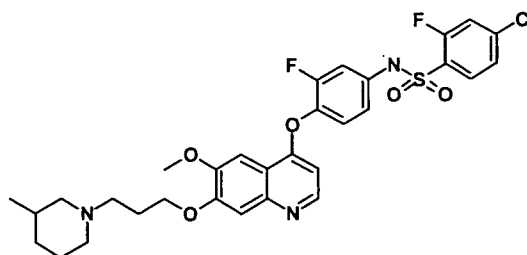
Melting point: 139-142 °C.

Yield: 19 %

Example D24

4-Chloro-2-fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

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$C_{31}H_{32}ClF_2N_3O_5S$ Mw. 632.13

LC/MS purity: 99 %, m/z 630 [M-H]⁻, m/z 632 [M-H]⁺ Rt. 2.58 min.

¹H NMR (300 MHz, DMSO-d₆): 10.8 (bs, 1H), 8.44 (d, 1H), 7.86 (t, 1H), 7.62 (d, 1H), 7.49 (s, 1H), 7.45 (d, 1H), 7.39 (s, 1H), 7.26 (m, 2H), 7.06 (d, 1H), 6.92 (d, 1H), 6.36 (d, 1H), 4.21 (t, 1H), 3.92 (s, 3H), 3.05 (m, 2H), 2.75 (m, 2H), 2.51 (m, 1H), 2.00 (m, 4H), 1.61 (m, 4H), 0.87 (d, 3H)

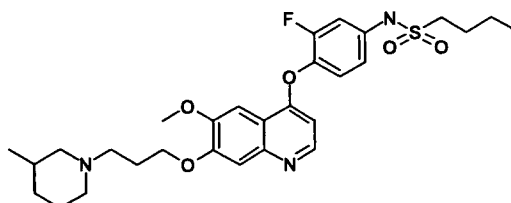
Melting point: 136-138 °C.

Yield: 24 %

10

Example D25

Butane-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide



$C_{29}H_{38}FN_3O_5S$ Mw. 559.71

LC/MS purity: 96 %, m/z 558 [M-H]⁻, m/z 560 [M-H]⁺ Rt. 2.68 min.

¹H NMR (300 MHz, DMSO-d₆): 10.24 (bs, 1H), 8.47 (d, 1H), 7.51 (s, 1H), 7.43 (s, 1H), 7.41 (s, 1H), 7.26 (d, 1H), 7.14 (d, 1H), 6.46 (d, 1H), 4.21 (t, 2H), 3.94 (s, 3H), 3.18 (m, 6H), 3.00 (m, 2H), 2.51 (t, 1H), 3.94 (s, 3H), 3.18 (m, 6H), 3.00 (m, 2H), 2.51 (m, 1H), 2.16 (m, 2H), 1.65 (m, 6H), 1.37 (m, 2H), 0.85 (m, 6H)

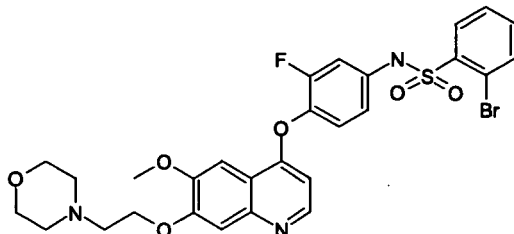
Melting point: 104-106 °C.

Yield: 23 %

25

Example D26

2-Bromo-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



5 $C_{28}H_{27}BrFN_3O_6S$ Mw. 632.51

LC/MS purity: 99 %, m/z 630 [M-H]⁻, m/z 632 [M-H]⁺ Rt. 2.53 min.

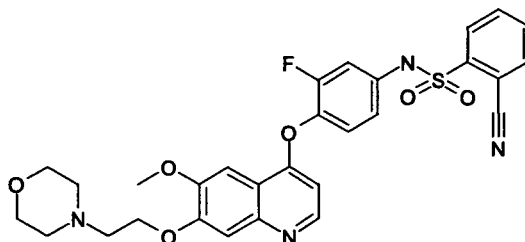
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.44 (d, 1H), 8.13 (d, 1H), 7.85 (d, 1H), 7.56 (m, 2H), 7.46 (s, 1H), 7.42 (s, 1H), 7.32 (t, 1H), 7.10 (dd, 1H), 6.99 (d, 1H), 6.34 (d, 1H), 4.26 (t, 2H), 3.93 (s, 3H), 3.59 (t, 4H), 2.78 (t, 2H),
10 2.53 (m, 4H)

Melting point: 175-177 °C.

Yield: 18 %

Example D27

15 2-Cyano-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



$C_{29}H_{27}FN_4O_6S$ Mw. 578.62

LC/MS purity: 99 %, m/z 577 [M-H]⁻, m/z 579 [M-H]⁺ Rt. 2.29 min.

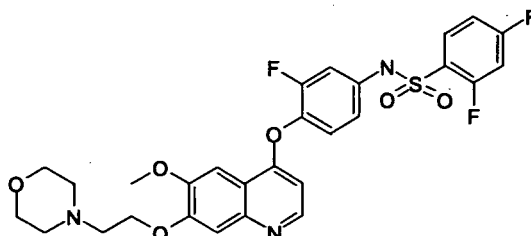
20 ¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.45 (d, 1H), 8.09 (m, 2H), 7.92 (t, 1H), 7.83 (t, 1H), 7.48 (s, 1H), 7.43 (s, 1H), 7.33 (t, 1H), 7.15 (d, 1H), 6.96 (d, 1H), 6.40 (d, 1H), 4.27 (t, 2H), 3.92 (s, 3H), 3.60 (m, 4H), 2.80 (t, 2H), 2.53 (m, 4H)

Melting point: 193-196 °C.

25 Yield: 23 %

Example D28

2,4-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



$C_{28}H_{26}F_3N_3O_6S$ Mw. 589.60

LC/MS purity: 99 %, m/z 588 [M-H]⁻, m/z 590 [M-H]⁺ Rt. 2.42 min.

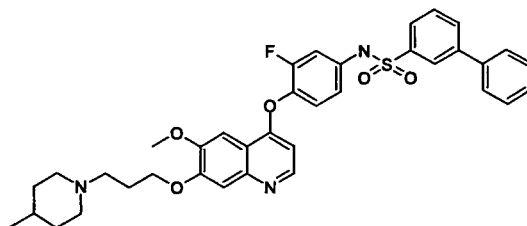
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.45 (d, 1H), 7.97 (q, 1H), 7.59-7.27 (m, 5H), 7.15 (dd, 1H), 7.02 (d, 1H), 6.35 (t, 1H), 3.91 (s, 3H), 3.59 (m, 4H), 2.78 (m, 4H), 2.53 (m, 4H)

Melting point: 189-191 °C.

Yield: 19 %

Example D29

Biphenyl-3-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide



$C_{37}H_{38}FN_3O_5S$ Mw. 655.79

LC/MS purity: 100 %, m/z 654 [M-H]⁻, m/z 656 [M-H]⁺ Rt. 2.93 min.

¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.36 (d, 1H), 8.02 (s, 1H), 7.94 (d, 1H), 7.79 (d, 1H), 7.70 (m, 3H), 7.52 (m, 4H), 7.36 (s, 1H), 7.30 (t, 1H), 7.14 (d, 1H), 7.00 (d, 1H), 6.28 (d, 1H), 4.17 (t, 2H), 3.90 (s, 3H), 2.88 (m, 2H), 2.50 (m, 1H), 1.98 (m, 4H), 1.58 (m, 2H), 1.34 (m, 2H), 1.15 (m, 2H), 0.88 (d, 3H)

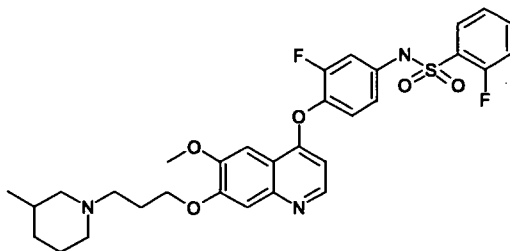
Melting point: 196-198 °C.

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Yield: 16 %

Example D30

2-Fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-
quinolin-4-yloxy}-phenyl)-benzenesulfonamide

 $C_{31}H_{33}F_2N_3O_5S$ Mw. 597.69LC/MS purity: 99 %, m/z 596 [M-H]⁻, m/z 598 [M-H]⁺ Rt. 2.55 min.

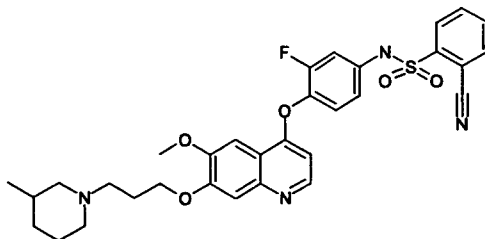
¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 8.43 (d, 1H), 7.87 (t, 1H), 7.66 (q, 1H), 7.47 (s, 1H), 7.35 (m, 3H), 7.26 (t, 1H), 7.08 (dd, 1H), 6.94 (d, 1H), 6.33 (d, 1H), 4.18 (t, 2H), 3.92 (s, 3H), 2.86 (m, 2H), 2.54 (m, 3H), 1.99 (m, 3H), 1.60 (m, 5H), 0.84 (d, 3H)

Melting point: 102-106 °C.

Yield: 25 %

Example D31

2-Cyano-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-
quinolin-4-yloxy}-phenyl)-benzenesulfonamide

 $C_{32}H_{33}FN_4O_5S$ Mw. 604.71LC/MS purity: 99 %, m/z 603 [M-H]⁻, m/z 605 [M-H]⁺ Rt. 2.50 min.

¹H NMR (300 MHz, DMSO-d₆): 10.8 (bs, 1H), 8.42 (d, 1H), 8.38 (d, 1H), 7.88 (d, 1H), 7.74 (t, 1H), 7.60 (t, 1H), 7.49 (s, 1H), 7.37 (s, 1H), 7.06 (t, 1H), 6.90 (dd, 1H), 6.74 (d, 1H), 6.37 (d, 1H), 4.19 (t, 2H), 3.92 (s, 3H), 3.07 (m, 2H), 2.63 (m, 2H), 2.50 (m, 1H), 2.03 (m, 3H), 1.66 (m, 5H), 0.87 (d, 3H)

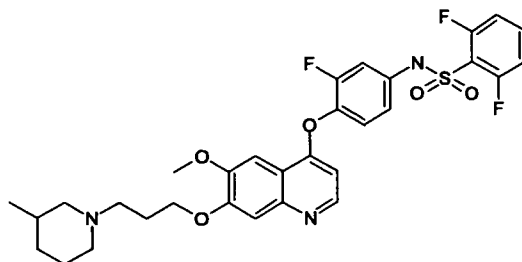
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Melting point: 131-132 °C.

Yield: 34 %

Example D32

- 5 2,6-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

 $C_{31}H_{32}F_3N_3O_5S$ Mw. 615.68LC/MS purity: 100 %, m/z 614 [M-H]⁻, m/z 616 [M-H]⁺ Rt. 2.71 min.

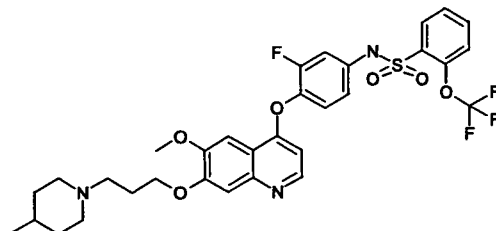
- 10 ¹H NMR (300 MHz, DMSO-d₆): 125 (bs, 1H), 8.44 (d, 1H), 7.59 (t, 1H), 7.49 (s, 1H), 7.33 (s, 1H), 7.20 (m, 3H), 7.04 (d, 1H), 6.88 (d, 1H), 6.35 (d, 1H), 4.20 (t, 2H), 3.92 (s, 3H), 2.98 (s, 2H), 2.67 (m, 2H), 2.04 (m, 3H), 1.86 (m, 1H), 1.60 (m, 5H), 0.86 (d, 3H)

Melting point: 117-119 °C.

- 15 Yield: 29 %

Example D33

N-(3-Fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-2-trifluoromethoxy-benzenesulfonamide



20

 $C_{32}H_{33}F_4N_3O_6S$ Mw. 663.69LC/MS purity: 99 %, m/z 662 [M-H]⁻, m/z 664 [M-H]⁺ Rt. 2.75 min.

- 25 ¹H NMR (300 MHz, DMSO-d₆): 11.5 (bs, 1H), 8.41 (d, 1H), 7.89 (d, 1H), 7.48 (s, 1H), 7.45 (d, 1H), 7.34 (m, 3H), 6.93 (t, 1H), 6.80 (d, 1H), 6.61 (d, 1H), 6.33 (d, 1H), 4.16 (t, 2H), 3.92 (s, 3H), 2.85 (m, 2H), 2.43 (m, 1H), 1.90

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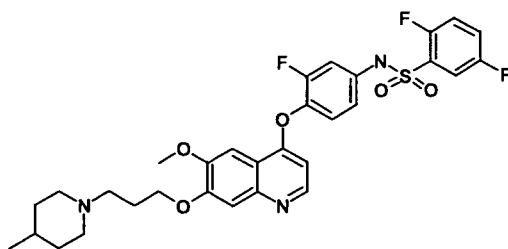
(m, 4H), 1.57 (m, 2H), 1.31 (m, 2H), 1.14 (m, 2H), 0.88 (d, 3H)

Melting point: 206-208 °C.

Yield: 32 %

5 Example D34

2,5-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

 $C_{31}H_{32}F_3N_3O_5S$ Mw. 615.6810 LC/MS purity: 100 %, m/z 614 [M-H]⁻, m/z 616 [M-H]⁺ Rt. 2.61 min.

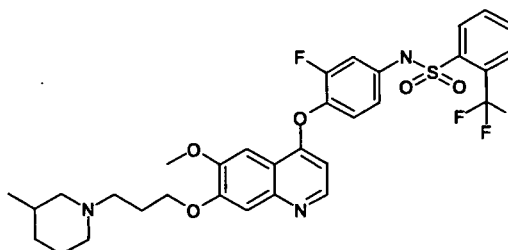
¹H NMR (300 MHz, DMSO-d₆): 10.2 (bs, 1H), 7.59 (m, 1H), 7.49 (s, 1H), 7.42 (s, 2H), 7.38 (s, 1H), 7.18 (t, 1H), 7.02 (dd, 1H), 6.86 (d, 1H), 6.36 (d, 1H), 4.20 (t, 1H), 3.93 (s, 3H), 3.08 (m, 2H), 2.73 (m, 2H), 2.63 (m, 1H), 2.27 (m, 2H), 2.04 (m, 2H), 1.66 (m, 2H), 1.44 (m, 1H), 1.21 (m, 2H), 0.90 (d, 3H)

15 Melting point: 223-225 °C.

Yield: 42 %

Example D35

20 N-(3-Fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}phenyl)-2-trifluoromethyl-benzenesulfonamide

 $C_{32}H_{33}F_4N_3O_5S$ Mw. 647.69LC/MS purity: 94 %, m/z 646 [M-H]⁻, m/z 648 [M-H]⁺ Rt. 2.86 min.

¹H NMR (300 MHz, DMSO-d₆): 10.6 (bs, 1H), 8.44 (d, 1H), 8.15 (d, 1H), 7.97 (d, 1H), 7.84 (m, 2H), 7.48 (s, 1H), 7.39 (s, 1H), 7.28 (t, 1H), 7.07 (d,

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1H), 6.94 (d, 1H), 6.36 (d, 1H), 4.21 (t, 2H), 3.92 (m, 3H), 2.89 (m, 2H), 2.76 (m, 2H), 2.26 (m, 1H), 1.99 (m, 3H), 1.68 (m, 4H), 1.02 (m, 1H), 0.86 (d, 3H)

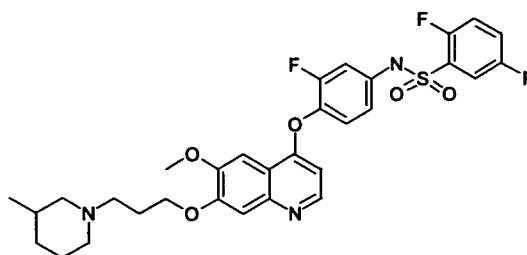
Melting point: 118-121 °C.

Yield: 38 %

5

Example D36

2,5-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide



10 $C_{31}H_{32}F_3N_3O_5S$ Mw. 615.68

LC/MS purity: 95 %, m/z 614 [M-H]⁻, m/z 616 [M-H]⁺ Rt. 2.83 min.

¹H NMR (300 MHz, DMSO-d₆): 10.3 (bs, 1H), 8.44 (d, 1H), 7.61 (bs, 1H), 7.44 (m, 4H), 7.22 (t, 1H), 7.05 (d, 1H), 6.90 (d, 1H), 6.36 (d, 1H), 4.21 (m, 2H), 3.93 (s, 3H), 3.07 (bs, 2H), 2.63 (bs, 2H), 2.39 (m, 1H), 2.25 (m, 3H),

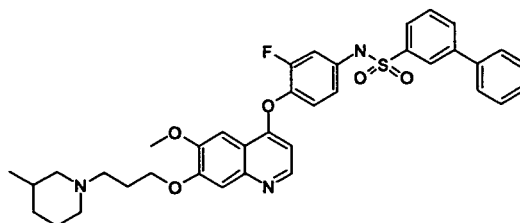
15 1.69 (m, 5H), 0.87 (d, 3H)

Melting point: 103-107 °C.

Yield: 45 %

Example D37

20 Biphenyl-3-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide



$C_{37}H_{38}FN_3O_5S$ Mw. 655.79

LC/MS purity: 97 %, m/z 654 [M-H]⁻, m/z 656 [M-H]⁺ Rt. 3.06 min.

25 ¹H NMR (300 MHz, DMSO-d₆): 10.5 (bs, 1H), 8.36 (d, 1H), 8.02 (s, 1H), 7.94

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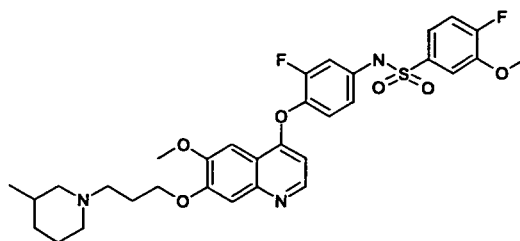
(d, 1H), 7.79 (d, 1H), 7.67 (m, 3H), 7.49 (m, 4H), 7.36 (s, 1H), 7.29 (t, 1H), 7.14 (d, 1H), 6.99 (d, 1H), 6.28 (d, 1H), 4.16 (t, 2H), 3.90 (s, 3H), 2.81 (m, 2H), 2.46 (m, 3H), 1.95 (m, 3H), 1.60 (m, 5H), 0.83 (d, 3H)

Melting point: 190-192 °C.

5 Yield: 39 %

Example D38

4-Fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-3-methoxy-benzenesulfonamide



10

$C_{32}H_{35}F_2N_3O_6S$ Mw. 627.71

LC/MS purity: 97 %, m/z 626 [M-H]⁻, m/z 628 [M-H]⁺ Rt. 2.88 min.

¹H NMR (300 MHz, DMSO-d₆): 10.4 (bs, 1H), 8.45 (d, 1H), 7.55-7.31 (m, 6H), 7.17 (dd, 1H), 7.01 (d, 1H), 6.35 (d, 1H), 4.19 (t, 2H), 3.92 (s, 3H), 3.89 (s, 3H), 2.90 (m, 2H), 2.60 (m, 3H), 2.02 (m, 3H), 1.65 (m, 5H), 0.85 (d, 3H)

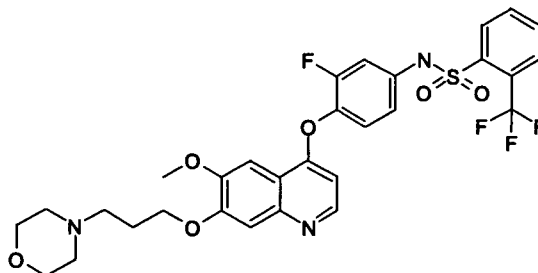
15

Melting point: 98-101 °C.

Yield: 34 %

Example D39

20 N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethyl-benzenesulfonamide



$C_{30}H_{29}F_4N_3O_6S$ Mw. 635.64

LC/MS purity: 99 %, m/z 634 [M-H]⁻, m/z 636 [M-H]⁺ Rt. 2.71 min.

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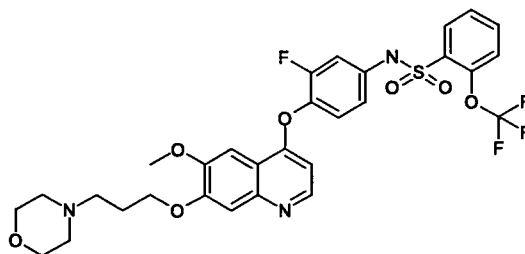
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.45 (d, 1H), 8.16 (d, 1H), 8.02 (d, 1H), 7.88 (m, 2H), 7.47 (s, 1H), 7.38 (s, 1H), 7.35 (t, 1H), 7.14 (d, 1H), 7.01 (d, 1H), 6.36 (d, 1H), 4.19 (t, 2H), 3.91 (s, 3H), 3.60 (t, 4H), 2.51 (m, 2H), 2.41 (m, 4H), 1.98 (t, 2H)

5 Melting point: 180-181 °C.

Yield: 29 %

Example D40

10 N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethoxy-benzenesulfonamide



C₃₀H₂₉F₄N₃O₇S Mw. 651.64

LC/MS purity: 98 %, m/z 650 [M-H]⁻, m/z 652 [M-H]⁺ Rt. 2.79 min.

15 ¹H NMR (300 MHz, DMSO-d₆): 10.9 (bs, 1H), 8.44 (d, 1H), 8.03 (d, 1H), 7.77 (m, 1H), 7.57 (m, 2H), 7.47 (s, 1H), 7.38 (s, 1H), 7.33 (t, 1H), 7.14 (d, 1H), 6.98 (d, 1H), 4.19 (t, 2H), 3.92 (s, 3H), 3.58 (bs, 4H), 2.51 (m, 2H), 2.40 (m, 6H), 1.98 (t, 1H)

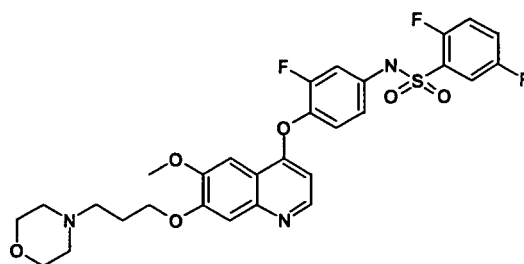
Melting point: 183-184 °C.

20 Yield: 40 %

Example D41

2,5-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

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$C_{29}H_{28}F_3N_3O_6S$ Mw. 603.62

LC/MS purity: 97 %, m/z 602 [M-H]⁻, m/z 604 [M-H]⁺ Rt. 2.59 min.

¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.44 (d, 1H), 7.70 (bs, 1H), 7.56 (m, 2H), 7.48 (s, 1H), 7.39 (s, 1H), 7.33 (d, 1H), 7.16 (dd, 1H), 7.04 (d, 1H), 6.35 (d, 1H), 4.19 (t, 2H), 3.92 (s, 3H), 3.60 (bs, 4H), 2.43 (m, 6H), 1.98 (t, 2H)

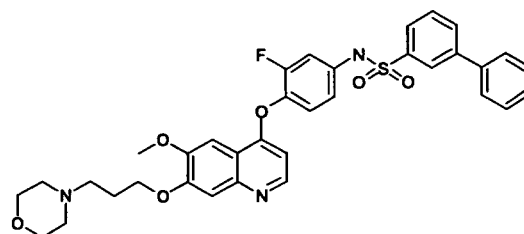
Melting point: 192-195 °C.

Yield: 43 %

10

Example D42

Biphenyl-3-sulfonic acid {3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-amide



$C_{35}H_{34}FN_3O_6S$ Mw. 643.74

LC/MS purity: 97 %, m/z 642 [M-H]⁻, m/z 644 [M-H]⁺ Rt. 2.97 min.

¹H NMR (300 MHz, DMSO-d₆): 10.7(bs, 1H), 8.37 (d, 1H), 8.03 (s, 1H), 7.97 (d, 1H), 7.80 (d, 1H), 7.69 (m, 3H), 7.52 (m, 4H), 7.45 (s, 1H), 7.32 (s, 1H), 7.18 (d, 1H), 7.05 (d, 1H), 6.28 (d, 1H), 4.18 (t, 2H), 3.90 (s, 3H), 3.58 (m, 4H), 2.46 (t, 2H), 2.38 (m, 4H), 1.96 (t, 2H)

Melting point: 210-212 °C.

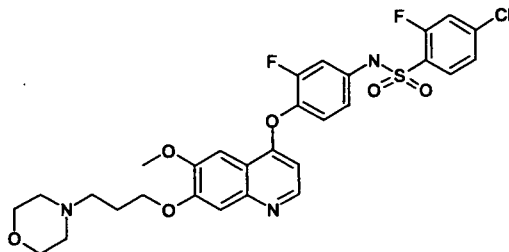
Yield: 39 %

25

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Example D43

4-Chloro-2-fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



5 $C_{29}H_{28}ClF_2N_3O_6S$ Mw. 620.08

LC/MS purity: 95 %, m/z 618 [M-H]⁻, m/z 620 [M-H]⁺ Rt. 2.73 min.

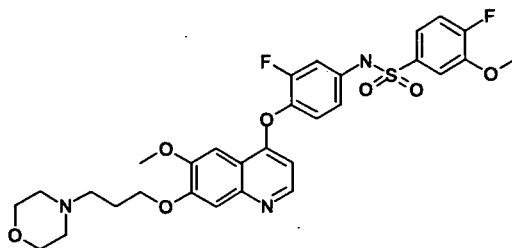
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.45 (d, 1H), 7.89 (t, 1H), 7.74 (d, 1H), 7.49 (d, 1H), 7.47 (s, 1H), 7.38 (s, 1H), 7.33 (d, 1H), 7.14 (d, 1H), 7.00 (d, 1H), 6.35 (d, 1H), 4.19 (t, 2H), 3.92 (s, 3H), 3.59 (bs, 4H), 2.48 (bs, 2H), 2.42 (bs, 4H), 1.98 (t, 2H)

Melting point: 200-203 °C.

Yield: 35 %

Example D44

15 4-Fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-3-methoxy-benzenesulfonamide



$C_{30}H_{31}F_2N_3O_7S$ Mw. 615.66

LC/MS purity: 96 %, m/z 614 [M-H]⁻, m/z 616 [M-H]⁺ Rt. 2.63 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 10.8 (bs, 1H), 8.44 (d, 1H), 7.54-7.32 (m, 6H), 7.17 (dd, 1H), 7.02 (d, 1H), 6.34 (d, 1H), 4.19 (t, 2H), 3.92 (s, 3H), 3.89 (s, 3H), 3.31 (m, 4H), 2.44 (t, 2H), 2.39 (m, 4H), 1.98 (t, 2H)

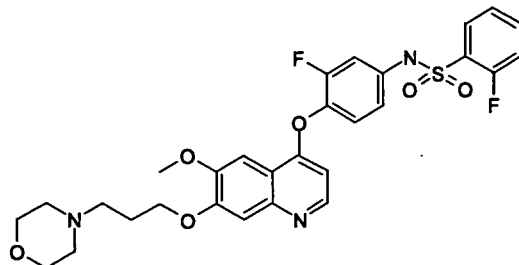
Melting point: 90-93 °C.

Yield: 58 %

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Example D45

2-Fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



5 $C_{29}H_{29}F_2N_3O_6S$ Mw. 585.63

LC/MS purity: 99 %, m/z 584 [M-H]⁻, m/z 586 [M-H]⁺ Rt. 2.49 min.

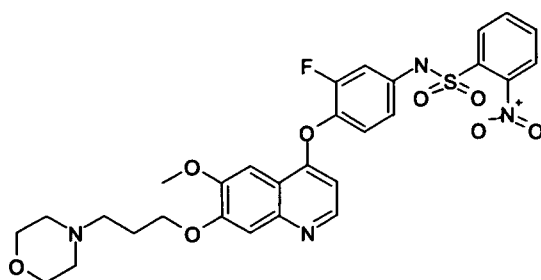
¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.44 (d, 1H), 7.90 (t, 1H), 7.73 (m, 1H), 7.46 (s, 1H), 7.40 (m, 3H), 7.38 (s, 1H), 7.15 (dd, 1H), 7.02 (d, 1H), 6.33 (d, 1H), 4.19 (t, 2H), 3.91 (s, 3H), 3.59 (m, 4H), 2.47 (t, 2H), 2.40 (m, 4H), 1.98 (t, 2H)

Melting point: 179-181 °C.

Yield: 59 %

Example D46

15 N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-nitro-benzenesulfonamide



$C_{29}H_{29}FN_4O_8S$ Mw. 612.64

LC/MS purity: 99 %, m/z 611 [M-H]⁻, m/z 613 [M-H]⁺ Rt. 2.58 min.

20 ¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.45 (d, 1H), 8.03 (m, 1H), 7.94 (m, 1H), 7.84 (m, 2H), 7.48 (s, 1H), 7.39 (s, 1H), 7.34 (t, 1H), 7.13 (d, 1H), 6.98 (d, 1H), 6.37 (d, 1H), 4.20 (t, 2H), 3.92 (s, 3H), 3.61 (bs, 4H), 2.56 (bs, 6H), 2.00 (m, 2H)

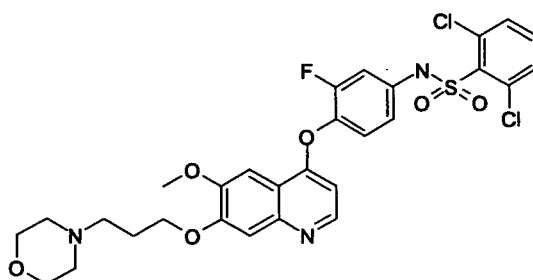
Melting point: 166-168 °C.

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Yield: 29 %

Example D47

2,6-Dichloro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-
5 quinolin-4-yloxy]-phenyl}-benzenesulfonamide



$C_{29}H_{28}Cl_2FN_3O_6S$ Mw. 636.53

LC/MS purity: 99 %, m/z 634 [M-H]⁻, m/z 636 [M-H]⁺ Rt. 2.71 min.

¹H NMR (300 MHz, DMSO-d₆): 11.1(bs, 1H), 8.44 (d, 1H), 7.60 (m, 2H),
10 7.47 (s, 1H), 7.38 (s, 1H), 7.34 (m, 2H), 7.13 (d, 1H), 6.99 (d, 1H), 6.33 (d,
1H), 4.19 (bs, 2H), 3.91 (s, 3H), 3.59 (bs, 4H), 3.17 (bs, 2H), 2.43 (m, 4H),
1.99 (bs, 2H)

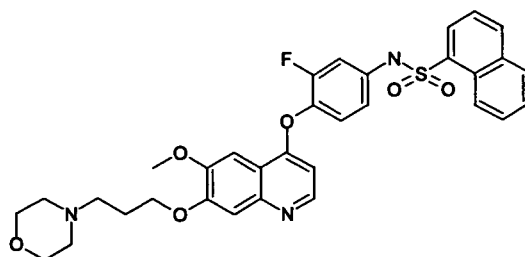
Melting point: 194-196 °C.

Yield: 16 %

15

Example D48

Naphthalene-1-sulfonic acid {3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-
propoxy)-quinolin-4-yloxy]-phenyl}-amide



20 $C_{33}H_{32}FN_3O_6S$ Mw. 617.70

LC/MS purity: 96 %, m/z 616 [M-H]⁻, m/z 618 [M-H]⁺ Rt. 2.62 min.

¹H NMR (300 MHz, DMSO-d₆): 11.1(bs, 1H), 8.75 (d, 1H), 8.40 (d, 1H), 8.28
(m, 2H), 8.11 (d, 1H), 7.71 (m, 3H), 7.42 (s, 1H), 7.36 (s, 1H), 7.24 (t, 1H),
7.05 (d, 1H), 6.91 (d, 1H), 6.31 (dd, 1H), 4.18 (t, 2H), 3.89 (s, 3H), 3.57 (bs,

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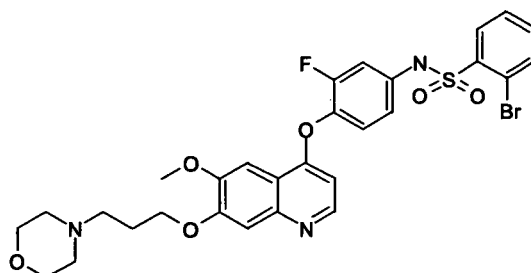
4H), 2.46 (m, 2H), 2.38 (bs, 4H), 1.96 (m, 2H)

Melting point: 108-111 °C.

Yield: 26 %

5 **Example D49**

2-Bromo-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide



$C_{29}H_{29}BrFN_3O_6S$ Mw. 646.54

10 LC/MS purity: 98 %, m/z 644 [M-H]⁻, m/z 646 [M-H]⁺ Rt. 2.63 min.

¹H NMR (300 MHz, DMSO-d₆): 11 (bs, 1H), 8.43 (d, 1H), 8.13 (d, 1H), 7.86 (d, 1H), 7.58 (m, 2H), 7.46 (s, 1H), 7.38 (s, 1H), 7.33 (t, 1H), 7.12 (dd, 1H), 7.00 (dd, 1H), 6.33 (d, 1H), 4.19 (t, 2H), 3.91 (s, 3H), 3.58 (bs, 4H), 2.45 (t, 2H), 2.39 (m, 4H), 1.97 (t, 2H)

15 Melting point: 185-188 °C.

Yield: 35 %

20 **3) Inhibitory Activity of Compounds on Axl Phosphorylation in NIH-3T3-AXL Cellular Tyrosine Kinase Assay**

Establishment of wild type AXL (wtAXL) receptor tyrosine kinase-overexpressing stable cell line NIH-3T3-AXL (Clone 22)

25 WtAXL cDNA was cloned into vector pLXSN(ESK) and transfected into Phoenix E packaging cells. The viral supernatant was collected and used to infect target cells NIH3T3 N7. Monoclonal NIH3T3-AXL cell lines stably expressing wtAXL were generated by selecting retrovirally infected cells in

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medium containing puromycin (2 μ g/ml) and subsequent clonal separation. NIH-3T3-AXL (clone 22) cells were used for further experiment because AXL was highly expressed and constitutively phosphorylated in these cells. In addition, these cells demonstrated aggressive behaviors on matrigel matrix (Matrigel™ Matrix, BD Biosciences, Bedford, MA, USA). Moreover, the inhibitory effects of compounds on AXL phosphorylation discovered by using NIH-3T3 AXL (clone 22) system have been confirmed in human breast cancer cells endogenously expressing AXL in our previous study (Zhang YX, et al. AXL is a potential target for therapeutic intervention in breast cancer progression. Cancer Res. 2008; 68:1905-15).

Determination of the morphology of cells grown on matrigel was carried out as described previously, with some modifications (Thompson EW, et al. Association of increased basement membrane invasiveness with absence of estrogen receptor and expression of vimentin in human breast cancer cell lines. J Cell Physiol 1992;150:534-44). Briefly, in a 96-well flat-bottomed plate, 10000 cells/100 μ l cell suspension was plated on the surface of precoated matrigel (3mg/ml). Colony outgrowth was visualized with a Zeiss Axiovert S100 microscope (Carl Zeiss UK, Welwyn Garden City, UK).

NIH-3T3-AXL Cellular Kinase Assay

NIH-3T3-AXL (Clone 22) cells were seeded onto 6-well plates (1.5 x 10⁵ cells/well) in 1.5ml culture medium and cultured overnight, followed by serum depletion in 0.1% heat inactivated FCS/DMEM for 24 h. Serial dilutions of compounds were added, and the cells were further incubated for 2 h. Cells were washed with PBS, and lysed on ice in 500 μ l lysis buffer (50 mM HEPES(pH 7.5), 150 mM NaCl, 1mM EGTA, 10% Glycerol, 1% Triton X-100, 100 mM NaF, 10 mM Na₄P₂O₇·10 H₂O, 1 mM Na₃VO₄, 1 mM phenylmethylsulfonyl fluoride, and 10 mg/ml aprotinin) for 15min. The clarified cell lysate (10min at 13000rpm at 4°C) were used for immunoprecipitation. Equal amounts of protein were mixed with 2 μ g anti-AXL polyclonal antibody (homemade) and 20 μ l Protein A sepharose beads,

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and rotated for 6hr at 4°C. After immunoprecipitation, the beads were washed three times with 1xHNTG (50 mM HEPES(pH 7.5), 150 mM NaCl, 10% Glycerol, 0.2% Triton X-100). The final pellet was suspended in 20 µl 2x Laemmli buffer, and boiled for 5min at 100°C. The immunoprecipitates were separated by 7.5% SDS-PAGE gel electrophoresis, and the proteins were transferred to a nitrocellulose membrane. Unspecific binding was blocked by incubating the membrane for 1hr in 0.25% gelatin in 1xNET buffer (50 mM Tris.HCl (pH7.5), 150 mM NaCl, 5mM EDTA, 0.1% Triton X-100). The membrane was then incubated with anti-phosphotyrosine antibody (4G10) overnight at 4°C followed by washing with 1xTBST buffer three times. After incubating membrane with HRP-conjugated anti-mouse secondary antibody for 1hour at room temperature followed by washing with 1xTBST buffer three times, the proteins were visualized by ECL. Afterwards, the membrane was stripped and reprobed with anti-AXL antibody (SC-1096, Santa Cruz Biotechnology, Santa Cruz, CA).

The results of the assay are described in Table 2.

A1-50	Cellular IC50 [µM]
A1	4.5
A2	3.01
A3	3.4
A4	6
A5	0.5
A6	4.3
A7	>10
A8	10
A9	3.7
A10	2.6
A11	2.26
A12	1.26
A13	2.9
A14	1.4
A15	2.265
A16	1.805
A17	0.89
A18	2.1

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A19	4.5
A20	5.05
A21	4.7
A22	9.6
A23	6
A24	2.4
A25	2.38
A26	4.73
A27	2.54
A28	3.9
A29	2.3
A30	0.63
A31	>10
A32	>10
A33	>10
A34	0.43
A35	3
A36	2.8
A37	>10
A38	>10
A39	6.4
A40	<1
A41	<1
A42	<1
A43	<1
A44	<1
A45	>10
A46	>10
A47	10
A48	1.5
A49	3,00
A50	< 1
A51	<3
A52	>3
A53	3
A54	>1
A55	>1
A56	>1
A57	>3
A58	>1
A59	>1
A60	0.8

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A61	0.7
A62	0.47
A63	>1
A64	>1
A65	>10
A66	>10
A67	>10
A68	>10
A69	>10
A70	>10
A71	>3
A72	0.58
A73	>3
A74	>1
A75	>3
A76	>10
A77	>10
A78	>3
A79	0.48
A80	>10
A81	>10
A82	>1
A83	>3
A84	>3
A85	>3
A86	>1
A87	3
A88	>1
A89	0.45
A90	>10
A91	>10
A92	>10
A93	>3
A94	>10
A95	>10
A96	0.077
A97	0.54
A98	0.74
A99	0.18
A100	0.74
A101	>1
A102	>1

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A103	0.35
A104	3
A105	10
A106	0.75
A107	>10
A108	>1
A109	>1
A110	1.18
A111	>3
A112	>3
A113	>3
A114	0.47
A115	1.26
A116	>3
A117	>10
A118	0.54
A119	>3
A120	>10
A121	>10
A122	>10
A123	1.96
A124	>3
A125	10
A126	0.13
A127	>3
A128	2.25
A129	>3
A130	>10
A131	1.68
A132	>10
A133	>10
A134	>1
A135	0.82
A136	>10
A137	>10
A138	>10
A139	2.2
A140	>10
A141	>10
A142	>10
A143	>10
A144	>10

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A145	>10
A146	0.89
A147	>3
A148	>10
A149	>3
A150	>10
A151	>10
A152	>10
A153	>10
A154	>10
A155	>3
A156	>1

B1-22	Cellular IC50 [μ M]
B1	> 10
B2	> 10
B3	8,00
B4	> 10
B5	> 10
B6	> 10
B7	> 10
B8	> 10
B9	> 10
B10	> 10
B11	< 1
B12	> 10
B13	< 1
B14	< 1
B15	> 10
B16	> 10
B17	> 10
B18	> 10
B19	8,00
B20	> 10
B21	> 10
B22	7,00

C01	>10
C02	>10
C03	>10
C04	>10
C05	>10

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C06	>10
C07	>10
C08	>10
C09	>10
C10	>10
C11	>10
C12	>10
C13	>1
C14	>10
C15	>10
C16	>10
C17	>10
C18	>10
C19	>10
D01	>10
D02	0.695
D03	0.837
D04	0.32
D05	0.049
D06	0.069
D07	0.35
D08	2.5
D09	2.46
D10	0.052
D11	>3
D12	0.3
D13	0.057
D14	0.238
D15	0.364
D16	0.271
D17	0.046
D18	0.151
D19	0.128
D20	0.029
D21	0.347
D22	0.477
D23	0.211
D24	0.181
D25	0.378
D26	0.15
D27	0.783
D28	>1

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D29	0.178
D30	0.082
D31	0.323
D32	0.042
D33	0.068
D34	0.016

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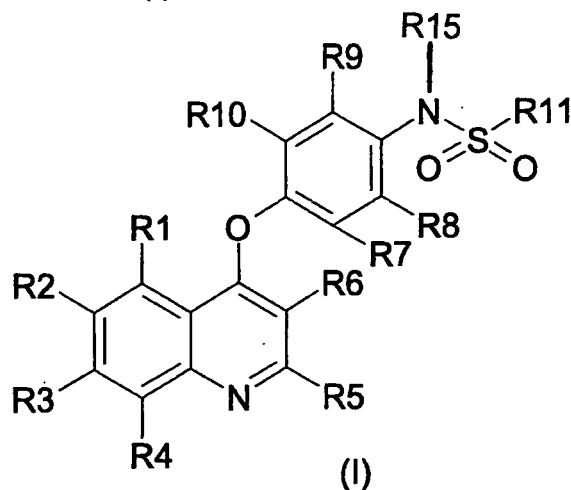
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Claims

1. Compounds of the formula (I):



wherein

- R¹, R², R³ and R⁴ which may be the same or different, represent hydrogen, hydroxyl, nitro, halogen, cyano, NR¹²R¹³, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, or C₁₋₆ alkoxy,

10 wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl; halogen, C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxy carbonyl; -(C=O)-NR¹²R¹³, and/or -NR¹²R¹³ wherein R¹² and R¹³, which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or alternatively R¹² and R¹³ may combine with the nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group; which is optionally mono- or polysubstituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy carbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system, wherein R² and/or R³ also may be -O-(CH₂)_n-R¹⁴ wherein n is an integer of 0 to 6, -

15

20

(CH₂)_n- is optionally substituted by C₁₋₆ alkyl, hydroxyl, or a halogen atom, and R¹⁴ represents a hydrogen atom; hydroxyl; a halogen atom; C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxycarbonyl; -(C=O)-NR¹²R¹³, -NR¹²R¹³ wherein R¹² or R¹³ which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or alternatively R¹² and R¹³ may combine with the nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group; in which the heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; amino in which one or two hydrogen atoms on the amino group are optionally substituted by C₁₋₆ alkyl or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system, and the C₁₋₆ alkyl group is optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; when the carbocyclic or heterocyclic group is substituted by two C₁₋₆ alkyl groups, the two alkyl groups may combine together to form an alkylene chain; and the carbocyclic or heterocyclic group may be condensed with another saturated or unsaturated five- to seven-membered carbocyclic or heterocyclic group to form a bicyclic group. When n = 0, -(CH₂)_n- represents a bond,

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- R⁵ and R⁶, which may be the same or different, represent a hydrogen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, halogen, cyano or nitro, wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl; halogen, C₁₋₆ alkoxy; C₁₋₆ alkylcarbonyl; carboxyl; C₁₋₆ alkoxycarbonyl; -(C=O)-NR¹²R¹³, and/or -NR¹²R¹³; wherein R¹² and R¹³, which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by hydroxyl, or alternatively R¹² and R¹³ may combine with the nitrogen atom attached thereto to form a saturated or unsaturated five- or six-membered heterocyclic group; in which the heterocyclic group is optionally substituted by hydroxyl, an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ alkoxycarbonyl, or a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl groups are optionally substituted by hydroxyl, C₁₋₆ alkoxy, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group,
- R⁷, R⁸, R⁹ and R¹⁰, which may be the same or different, represent a hydrogen atom, halogen, nitro, C₁₋₆ alkyl, C₁₋₆ alkoxy, wherein the C₁₋₆ alkyl or C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl and/or halogen, C₁₋₄ alkyl and/or C₁₋₄ alkoxy, wherein the C₁₋₆ alkyl, C₁₋₆ alkoxy, wherein the C₁₋₆ alkyl or C₁₋₆ alkoxy groups are optionally mono- or polysubstituted by hydroxyl and/or halogen,
- R¹¹ represents
- (i) a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally mono- or polysubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group,
- (ii) C₁₋₆ alkyl or C₁₋₆ alkoxy which is unsubstituted or substituted by a

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saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally mono- or polysubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group,

(iii) a nitrogen atom substituted with a saturated or unsaturated three- to twelve-membered or heterocyclic ring system which is optionally mono- or polysubstituted by an oxygen atom, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ alkoxy groups are optionally substituted by a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and

- R¹⁵ represents a hydrogen atom or C₁₋₆ alkyl and pharmaceutically acceptable salts thereof.

2. The compounds of claim 1, wherein R¹ is a hydrogen atom or C₁₋₄ alkyl, particularly a hydrogen atom.

3. The compounds of claim 1 or 2, wherein R² and/or R³ are selected from hydroxyl, optionally substituted C₁₋₆ alkoxy or C₁₋₆ alkyl, such as methoxy or trifluoromethyl, halogen such as fluorine, and cyano, and particularly R² is optionally substituted C₁₋₆ alkoxy, such as methoxy, and R³ is hydrogen, hydroxyl or optionally substituted C₁₋₆ alkoxy, such as methoxy.

4. The compounds of claim 3, wherein R² and R³ are both methoxy or R² is fluorine and R³ is hydrogen.

5. The compounds of claim 1, wherein R² is methoxy and R³ is selected

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from the group consisting of benzyloxy, 3-amino-propoxy, 2-morpholin-4-yl-ethoxy, 3-(4-methyl-piperidin-1-yl), 3-(3-methyl-piperidin-1-yl), 3-morpholin-4-yl-propoxy).

- 5 6. The compounds of any one of claims 1-3, wherein R^4 is a hydrogen atom or C_{1-6} alkyl optionally substituted, e.g. trifluoromethyl.
7. The compounds of any one of claims 1-6, wherein R^7 , R^8 , R^9 and R^{10} independently are selected from hydrogen, halogen, e.g. fluorine,
10 optionally substituted C_{1-6} alkoxy or alkyl such as methoxy or trifluoromethyl.
8. The compounds of any one of claims 1-7, wherein R^7 and R^{10} are hydrogen.
- 15 9. The compounds of any one of claims 1-8, wherein at least one of R^8 and R^9 is different from hydrogen, e.g. halogen such as fluorine.
- 10 10. The compounds of any one of claims 1-9, wherein R^{11} is selected from a saturated or unsaturated three- to twelve-membered carbocyclic or heterocyclic ring system which is optionally substituted, e.g. mono-, di- or trisubstituted by an oxygen atom, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, a halogen atom, or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group, and the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{1-6} alkoxy groups are optionally substituted by
25 a halogen atom or a saturated or unsaturated three- to eight-membered carbocyclic or heterocyclic group.
- 30 11. The compounds of any one of claims 1-10 wherein the substituents of the carbocyclic or heterocyclic ring system in R^{11} are selected from halogen, e.g. F, Cl or Br, C_{1-4} alkyl optionally halogenated, such as methyl, ethyl, or trifluoromethyl, C_{1-4} alkoxy, optionally halogenated such as methoxy, difluoromethoxy or trifluoromethoxy, hydroxyl, cyano, and

optionally substituted amino.

12. The compounds of claim 11, wherein the carbocyclic or heterocyclic group in R¹¹ comprises at least one halogen, e.g. fluorine or chlorine, trifluoromethyl or trifluoromethoxy substituent.

13. The compounds of any one of claims 1-12 selected from

3-Cyano-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3,4-difluoro-benzenesulfonamide

Thiophene-2-sulfonic acid 4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-hydroxy-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-4-methyl-benzenesulfonamide

N-{5-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenylsulfamoyl]-4-methyl-thiophen-2-yl}-acetamide

Quinoline-8-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

3-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenylsulfamoyl]-

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thiophene-2-carboxylic acid methyl ester

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

5

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-
fluoro-benzenesulfonamide

10

3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-
fluoro-benzenesulfonamide

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-
fluoro-benzenesulfonamide

15

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,6-difluoro-
benzenesulfonamide

3-Difluoromethoxy-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-
phenyl]-benzenesulfonamide

20

2-Phenyl-ethenesulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-
fluoro-phenyl]-amide

25

Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-
fluoro-phenyl]-amide

2,5-Dichloro-thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-
yloxy)-2-fluoro-phenyl]-amide

30

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-
methyl-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,3,4-trifluoro-

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benzenesulfonamide

5-Methyl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

5

Furan-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-trifluoromethyl-benzenesulfonamide

10

3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide

3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide

15

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methyl-benzenesulfonamide

20

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-methoxy-benzenesulfonamide

5-Chloro-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

25

5-Bromo-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-phenoxy-benzenesulfonamide

30

1-Ethyl-1H-pyrazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-

yloxy)-2-fluoro-phenyl]-amide

1-Methyl-1H-imidazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

5

Cyclopropanesulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

10

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-trifluoromethoxy-benzenesulfonamide

15

5-Phenyl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

20

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3,5-difluorobenzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,4-difluorobenzenesulfonamide

25

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2,5-difluorobenzenesulfonamide

30

2,6-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-benzenesulfonamide

2,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-

benzenesulfonamide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

5

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-
trifluoromethyl-benzenesulfonamide

10

2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-
trifluoromethyl-benzenesulfonamide

2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-5-
trifluoromethyl-benzenesulfonamide

15

3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-5-
trifluoromethyl-benzenesulfonamide

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-
trifluoromethyl-benzenesulfonamide

20

3,4-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-
methoxy-benzenesulfonamide

25

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methyl-
benzenesulfonamide

30

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-
benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-

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trifluoromethoxy-benzenesulfonamide

2-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

5

2-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-
benzenesulfonamide

10

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-ethyl-
benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-phenoxy-
benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-2-
methyl-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-fluoro-
benzenesulfonamide

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4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-
phenyl]-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-fluoro-3-
methoxy-benzenesulfonamide

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Butane-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-
phenyl]-amide

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2-Methyl-propane-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-
yloxy)-2-fluoro-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-C-phenyl-

methanesulfonamide

N-{2-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenylsulfamoyl]-4-methyl-phenyl}-acetamide

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N-{4-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenylsulfamoyl]-2,6-dimethyl-phenyl}-acetamide

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3-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide

5-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-methoxy-benzenesulfonamide

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5-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-methoxy-4-methyl-benzenesulfonamide

3-tert-Butyl-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-4-ethoxy-3-methyl-benzenesulfonamide

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4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-methoxy-4,5-dimethyl-benzenesulfonamide

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3-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-

phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-3-phenoxy-benzenesulfonamide

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Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-amide

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Isoquinoline-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-hydroxy-benzenesulfonamide

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2-Methyl-3H-imidazole-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

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Benzo[b]thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

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1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-

amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-4-(3,5-dimethyl-
isoxazol-4-ylmethoxy)-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-fluoro-4-
methoxy-benzenesulfonamide

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-
phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-3-phenoxy-
benzenesulfonamide

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Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-
methyl-phenyl]-amide

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-
phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-3-pyrimidin-2-
yl-benzenesulfonamide

Benzo[b]thiophene-2-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-
yloxy)-2-methyl-phenyl]-amide

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1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-
dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-
trifluoromethyl-benzenesulfonamide

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-

phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-3-phenoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2,5-difluoro-benzenesulfonamide

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Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide

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Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-4-hydroxy-benzenesulfonamide

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3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-methoxy-benzenesulfonamide

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Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide

Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-

yl oxy)-3-fluoro-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide

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4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-fluoro-benzenesulfonamide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-methoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-trifluoromethoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-trifluoromethyl-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-3-phenoxy-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide

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4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2,5-difluoro-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-

trifluoromethoxy-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-3-phenoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide

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4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-benzenesulfonamide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethyl-benzenesulfonamide

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4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-benzenesulfonamide

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-methoxy-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-trifluoromethyl-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2-trifluoromethoxy-benzenesulfonamide

4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-

yl oxy)-3-methyl-phenyl]-amide

N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-2,5-difluoro-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methyl-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

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4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-fluoro-benzenesulfonamide

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4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-amide

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

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1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

Biphenyl-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2,5-difluoro-benzenesulfonamide

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Naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-

fluoro-benzenesulfonamide

Biphenyl-4-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

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Benzo[b]thiophene-3-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-amide

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4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide

4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-2-trifluoromethoxy-benzenesulfonamide

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4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2-trifluoromethoxy-benzenesulfonamide

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4-Bromo-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-trifluoromethoxy-benzenesulfonamide

4-Methoxy-naphthalene-1-sulfonic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-amide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2,5-difluoro-benzenesulfonamide

4-Bromo-3-chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-

phenyl]-benzenesulfonamide

4-Chloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-2-fluoro-benzenesulfonamide

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N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-2-methyl-phenyl]-4-fluoro-3-methoxy-benzenesulfonamide

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3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-4-hydroxy-benzenesulfonamide

3,5-Dichloro-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-methoxy-phenyl]-2--hydroxy-benzenesulfonamide

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Thiophene-2-sulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

3-Cyano-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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N-[2-Fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-3-methoxy-benzenesulfonamide

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Cyclopropanesulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

3-Chloro-4-fluoro-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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2,6-Difluoro-N-[2-fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

5-Methyl-thiophene-2-sulfonic acid [2-fluoro-4-(6-fluoro-2-methyl-

quinolin-4-yloxy)-phenyl]-amide

N-[2-Fluoro-4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-3-trifluoromethyl-benzenesulfonamide

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N-[4-(6-Fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-methoxy-benzenesulfonamide

2,4-Difluoro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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3,5-Difluoro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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3-Bromo-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

4-Bromo-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-trifluoromethyl-benzenesulfonamide

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Thiophene-3-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

3-[4-(6-Fluoro-2-methyl-quinolin-4-yloxy)-phenylsulfamoyl]-thiophene-2-carboxylic acid methyl ester

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5-Chloro-thiophene-2-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-

yloxy)-phenyl]-amide

5-Oxazol-5-yl-thiophene-2-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

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Naphthalene-1-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

1-Ethyl-1H-pyrazole-4-sulfonic acid [4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-amide

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3,5-Dichloro-N-[4-(6-fluoro-2-methyl-quinolin-4-yloxy)-phenyl]-2-hydroxy-benzenesulfonamide

3,5-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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Biphenyl-3-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-3-phenoxy-benzenesulfonamide

Naphthalene-1-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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2,5-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

2,6-Dichloro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-2-

trifluoromethyl-benzenesulfonamide

4-Methoxy-naphthalene-1-sulfonic acid [3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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3-Fluoro-N-[3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-4-methoxy-benzenesulfonamide

N-[3-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-2-methoxy-4,5-dimethyl-benzenesulfonamide

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2,5-Difluoro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

3-Chloro-4-fluoro-N-[2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

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2-Methyl-3H-imidazole-4-sulfonic acid [3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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4-(3,5-Dimethyl-isoxazol-4-ylmethoxy)-N-[3-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-benzenesulfonamide

Biphenyl-4-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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N-[2-Fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-3-pyrimidin-2-yl-benzenesulfonamide

Benzo[b]thiophene-2-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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Benzo[b]thiophene-3-sulfonic acid [2-fluoro-4-(2-methyl-8-

trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

1-Methyl-2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid [2-fluoro-4-(2-methyl-8-trifluoromethyl-quinolin-4-yloxy)-phenyl]-amide

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Biphenyl-3-sulfonic acid [4-(7-benzyloxy-6-methoxy-quinolin-4-yloxy)-2-fluoro-phenyl]-amide

Naphthalene-1-sulfonic acid {4-[7-(3-amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-amide

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Biphenyl-3-sulfonic acid {4-[7-(3-amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-amide

Biphenyl-3-sulfonic acid {3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-amide

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N-{3-Fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethyl-benzenesulfonamide

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N-{3-Fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethoxy-benzenesulfonamide

Biphenyl-3-sulfonic acid {4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-amide

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N-{4-[6-Methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-2-trifluoromethoxy-benzenesulfonamide

2,5-Difluoro-N-{4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-benzenesulfonamide

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2,5-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-

quinolin-4-yloxy]-phenyl)-benzenesulfonamide

N-{4-[6-Methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-2-methyl-phenyl}-2-trifluoromethyl-benzenesulfonamide

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4-Chloro-2-fluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

4-Methoxy-naphthalene-1-sulfonic acid {3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-amide

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N-{4-[7-(3-Amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-trifluoromethyl-benzenesulfonamide

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N-{4-[7-(3-Amino-propoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-trifluoromethoxy-benzenesulfonamide

(3-{4-[2-Fluoro-4-(2-trifluoromethoxy-benzenesulfonylamino)-phenoxy]-6-methoxy-quinolin-7-yloxy}-propyl)-carbamic acid tert-butyl ester

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N-(3-Fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-2-trifluoromethyl-benzenesulfonamide

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2-Bromo-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

2,4-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

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2,6-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

Naphthalene-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide

5 Propane-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide

2-Cyano-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

10 4-Chloro-2-fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

Butane-1-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide

15 2-Bromo-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

20 2-Cyano-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

2,4-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(2-morpholin-4-yl-ethoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

25 Biphenyl-3-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide

2-Fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

30 2-Cyano-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

2,6-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

5 N-(3-Fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-2-trifluoromethoxy-benzenesulfonamide

2,5-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

10 N-(3-Fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}phenyl)-2-trifluoromethyl-benzenesulfonamide

2,5-Difluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-benzenesulfonamide

15 Biphenyl-3-sulfonic acid (3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-amide

20 4-Fluoro-N-(3-fluoro-4-{6-methoxy-7-[3-(3-methyl-piperidin-1-yl)-propoxy]-quinolin-4-yloxy}-phenyl)-3-methoxy-benzenesulfonamide

N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethyl-benzenesulfonamide

25 N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-trifluoromethoxy-benzenesulfonamide

2,5-Difluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

30 Biphenyl-3-sulfonic acid {3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-amide

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4-Chloro-2-fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

4-Fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-3-methoxy-benzenesulfonamide

2-Fluoro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

N-{3-Fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-2-nitro-benzenesulfonamide

2,6-Dichloro-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

Naphthalene-1-sulfonic acid {3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-amide

2-Bromo-N-{3-fluoro-4-[6-methoxy-7-(3-morpholin-4-yl-propoxy)-quinolin-4-yloxy]-phenyl}-benzenesulfonamide

14. The compounds of any one of claims 1-13 for use in medicine.

15. The compounds of claim 14 for the treatment and/or prevention of AXL receptor tyrosine kinase induced disorders.

16. The compounds of claim 15, wherein the AXL receptor tyrosine kinase induced disorders are disorders caused by, associated with and/or accompanied by AXL kinase hyperfunction.

17. The compounds of claim 16, wherein the AXL receptor tyrosine kinase induced disorders are selected from the group consisting of

hyperproliferative disorders.

- 5 18. The compounds of claim 17, wherein the AXL receptor tyrosine kinase induced disorders are selected from the group consisting of cancer and primary tumor metastases.
- 10 19. The compounds of claim 18, wherein the AXL receptor tyrosine kinase induced disorders are selected from breast, colon, prostate, lung, gastric, ovarian, endometrial, renal, hepatocellular, thyroid, uterine cancer, esophageal carcinoma, squamous cell carcinoma, leukemia, osteosarcoma, melanoma, glioblastoma, and neuroblastoma.
- 15 20. The compounds of claim 19, wherein the AXL receptor tyrosine kinase induced disorder is breast cancer.
21. The compounds of any one of claims 14-20 in combination with a further medicament.
- 20 22. The compounds of any one of claims 1-16 in a pharmaceutical composition further comprising pharmaceutically acceptable carriers, diluents and/or adjuvants.
- 25 23. The compounds of claim 22, wherein the composition is administered parenterally, topically, rectally, nasally, buccally, vaginally, transdermally, by inhalation, by injection or infusion, by spray or via implanted reservoir.
- 30 24. A method for the treatment and/or prevention of AXL receptor tyrosine kinase induced disorders comprising administering pharmaceutically effective amount of at least one compound of any one of claims 1-14 to a subject in need thereof.