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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 June 2009 (25.06.2009)

PCT

(10) International Publication Number
WO 2009/078498 A1

(51) International Patent Classification:
C07D 417/04 (2006.01) ***C07D 285/02*** (2006.01)
C07D 413/04 (2006.01) ***A61K 31/415*** (2006.01)
C07D 419/04 (2006.01) ***A61K 31/4155*** (2006.01)
C07D 249/08 (2006.01) ***A61P 3/04*** (2006.01)
C07D 269/02 (2006.01)

(21) International Application Number:
PCT/KR2007/006590

(22) International Filing Date:
17 December 2007 (17.12.2007)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant *(for all designated States except US)*: **GREEN CROSS CORPORATION** [KR/KR]; #303, Bojeong-dong, Giheung-gu, Yongin-si, Gyeonggi-do 446-770 (KR).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **LEE, Sung-Han** [KR/KR]; 676-5 ho, Ilwon-dong, Gangnam-gu, Seoul 135-230 (KR). **SEO, Hee Jeong** [KR/KR]; Woojeong Apt. 104-1902, Sangbong-dong, Chungnang-gu, Seoul 131-780 (KR). **LEE, Jinhwa** [KR/KR]; #341, Bojeong-dong, Giheung-gu, Yongin-si, Gyeonggi-do 446-913 (KR). **KIM, Min-ah** [KR/KR]; Duyoung Officetel 508-ho, #145-3, Gumi-dong Bundang-gu, Seongnam-si, Gyeonggi-do 463-810 (KR). **KIM, Jeong Min** [KR/KR]; Banpo Hanyang Apt. 5-703, Jamwon-dong, Seocho-gu, Seoul 137-799 (KR). **KANG, Suk Youn** [KR/KR]; Hundai Sungwoo Apt. 802-1206, Pungdeokcheon 2-dong-Suji-gu, Yongin-si, Gyeonggi-do 448-992 (KR). **AHN, Kwang-Woo** [KR/KR]; Sindo Branew 101-202, #821, Chang 3-dong, Dobong-gu, Seoul 132-916 (KR). **LEE, Suk Ho** [KR/KR]; Doosan We've Apt. 107-502, Bandalmaeul, #880, Banwol-dong, Hwaseong-si, Gyeonggi-do 445-738 (KR).

(74) Agents: JANG, Seongku et al.; 19th Fl., Trust Tower, #275-7, Yangjae-dong Seocho-ku, Seoul 137-130 (KR).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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

Published:
— *with international search report*

(54) Title: BIARYLPYRAZOLE 4-CARBOXAMIDES AS CANNABINOID CB1 RECEPTOR LIGANDS

(57) Abstract: A novel biarylpyrazole 4-carboxamide compound of formula (I) or a pharmaceutically acceptable salt thereof is effective as a cannabinoid CB1 receptor ligand, which is useful for preventing or treating obesity and obesity-related metabolic disorders. The present invention also provide a method for preparing same, a pharmaceutical composition containing same, and a method for preventing or treating obesity and obesity-related metabolic disorders.

BIARYLPYRAZOLE 4-CARBOXAMIDES AS CANNABINOID CB_1 RECEPTOR LIGANDS

FIELD OF THE INVENTION

The present invention relates to a novel biarylpyrazole 4-carboxamide compound which is effective as a cannabinoid CB_1 receptor ligand.

BACKGROUND OF THE INVENTION

The World Health Organization (WHO) recently reported that obesity has become a global epidemic, posing a serious threat to public health because of the increased risk of associated health problems (*see Report of a WHO Consultation on Obesity: Obesity-Preventing and Managing a Global Epidemic*; World Health Organization: Geneva, 1997). Obesity is characterized by excess body fat, especially visceral fat, and constitutes a pro-inflammatory state eventually leading to serious health consequences. There are growing evidences that obesity as a chronic disease cannot be cured by short-term dieting or exercise alone, but additional pharmacological treatments would lead to higher success rates.

CB_1 cannabinoid receptor belongs to G-protein-coupled receptor (GPCR) type and is coupled to inhibitory G proteins (G(i/o)) to inhibit certain adenylyl cyclase isozymes, leading to decreased cAMP production, decreased Ca^{2+} conductance, increased K^+ conductance, and increased mitogen-activated protein kinase activity (*see* Di Marzo et al., *Nat. Rev. Drug Discovery* **2004**, *3*, 771-784; Rhee, M. H. et al., *J. Neurochem.* **1998**, *71*, 1525-1534). The major physiological effect of cannabinoids (in the central nervous system (CNS) and neuronal tissues) is the modulation of neurotransmitter release via activation of presynaptic CB_1 receptors located on distinct types of axon terminals throughout the brain (*see* Howlett, A. C. et al., *Neuropharmacology* **2004**, *47* (Suppl. 1), 345-358).

The CB_1 receptor is mainly expressed in several brain areas including the limbic system (amygdala, hippocampus), hypothalamus, cerebral cortex, cerebellum, and basal ganglia. In the cerebellum and basal ganglia cannabinoids modulate the locomotor activity. In the limbic system, cannabinoids influence learning, memory, emotion, and motivation, and through activation of CB_1 receptors in the limbic system-hypothalamus axis, cannabinoids have an important role in the control of appetite. Moreover, lower levels of CB_1 receptors can also be found in peripheral tissues including urinary bladder, testis, prostate, GI tract, heart, lung, adrenal gland, parotid gland, bone marrow, uterus, ovary, and adipose tissue (*see* Cota, D. et al., *J. Clin. Invest.* **2003**, *112*, 423-431; Ravinet Trillou, C. et al., *Int. J. Obes. Relat. Metab. Disord.* **2004**, *28*, 640-648; Galiegue, S. et al., *Eur. J. Biochem.* **1995**, *232*, 54-61; Howlett, A. C. et al., *Pharmacol. Rev.* **2002**, *54*, 161-202).

Many preclinical *in vitro* and *in vivo* experiments have been shown that CB_1 receptor antagonists can influence energy homeostasis by central and peripheral mechanisms and may represent promising targets to treat diseases that are characterized by impaired energy balance. Already the first published studies with rimonabant (SR141716) in both rodents (*see* Arnone, M. et al., *Psychopharmacology (Berlin)* **1997**, *132*, 104-106) and primates (*see* Simiand, J.; Keane, M.; Keane, P. E.; Soubrie, P. *Behav. Pharmacol.* 1998, *9*, 179-181) showed clear differentiation, i.e., marked effects on sweet food intake versus marginal effects on regular chow intake or water drinking. Many other preclinical "proof of concept" studies have been performed in the meantime with several CB agonists and antagonists to further uncover the amount and mode of contribution of cannabinergic system modulators to energy homeostasis. Almost all of those studies have been recently reviewed (*see* Smith, R. A. et al., *IDrugs* **2005**, *8*, 53-66).

Considering the important impact of obesity on public health and the lack of any efficient and viable drug to cure it, it is no surprise that CB_1 antagonists are currently the subject of intense studies, which were published in several reviews (*see* Adam, J. et al., *Expert Opin.Ther.Patents,* **2002**, 12(10), 1475-1489; Hertzog, D. L. *Expert Opin.Ther.Patents,* **2004**, 14(10), 1435-1452; Lange, J. H. M. et al., *Drug Discov. Today*, **2005**, 10, 693-702; Bishop, M. J. *J Med. Chem.,* **2006,** 49(14), 4008-4016).

On the other hand, CB_1/CB_2 agonists have been clinically used as an antiemetic agent to stimulate appetite. Potential therapeutic uses of cannabinoid receptor agonists include the management of multiple sclerosis, spinal cord injury, pain, inflammatory disorders, glaucoma, bronchial asthma, vasodilatation that accompanies advanced cirrhosis and cancer (*see* Singh, J., *Exp. Clin. Pharmacol.,* **2006**, 28(3): 177).

SUMMARY OF THE INVENTION

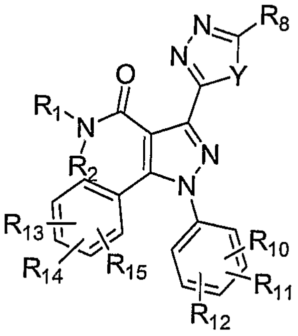
It is a primary object of the present invention to provide a novel biarylpyrazole 4-carboxamide compound or a pharmaceutically acceptable salt thereof, which is effective as a cannabinoid CB_1 receptor ligand, useful for preventing or treating obesity and obesity-related metabolic disorders.

It is another object of the present invention to provide a method for preparing the inventive compound.

It is another object of the present invention to provide a pharmaceutical composition for preventing or treating obesity and obesity-related metabolic disorders, comprising the inventive compound as an active ingredient.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with one aspect of the present invention, there is provided a compound of formula (I) or a pharmaceutically acceptable salt thereof and a method for preparing same:



(I)

wherein,

Y is O or S;

R_1 and R_2 are each independently hydrogen, C_{1-6} alkyl, substituted C_{1-6} alkyl, C_{3-12} carbocycle, substituted C_{3-12} carbocycle, NR_3R_4, $-CHR_5(CO)OR_7$, $-CHR_5(CO)\ NR_3R_4$, or

R_1 and R_2 are fused to each other together with the nitrogen atom to which they are bonded to form a 4- to 10-membered saturated or unsaturated heterocyclic ring which is optionally substituted by one or more substituents selected from the group consisting of C_{1-3} alkyl, benzyl, phenyl, C_{1-3} alkoxy or halogen;

R_3 and R_4 are each independently selected from the group consisting of hydrogen, C_{1-7} alkyl, C_{3-8} carbocycle, substituted C_{3-8} carbocycle, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle and acyl; or are fused to each other together with the nitrogen atom to which they are bonded to form a 5- to 10-membered heterocycle which is unsubstituted or substituted by one or more substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy and fluoride;

R_5 is hydrogen, C_{1-4} alkyl, substituted C_{1-4} alkyl, C_{3-6} carbocycle, substituted C_{3-6} carbocycle, $(CH_2)_n$-C_{3-6} carbocycle or $(CH_2)_n$-R_6, n being 1, 2 or 3;

R_6 is phenyl, furan, thiophene, tetrahydrofuran, tetrahydropyran or dioxane;

R_7 is C_{1-4} alkyl, substituted C_{1-4} alkyl, C_{3-8} carbocycle, substituted C_{3-8} carbocycle, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle or substituted heterocycle;

R_8 is hydrogen, NR_3R_4, C_{3-8} carbocycle, substituted C_{3-8} carbocycle, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, C_{1-8} alkyl optionally substituted by alkoxy or halogen, C_{2-6} alkenyl optionally substituted by alkoxy or halogen, $(CH_2)_m$-C_{3-6} carbocycle optionally substituted by alkoxy or halogen, or $(CH_2)_m$-R_9, m being 1 or 2;

R_9 is phenyl, furanyl, benzofuranyl, thienyl, benzothienyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridizinyl, tetrahydrofuranyl, tetrahydropyranyl, dioxanyl, 1,4-benzodioxanyl or benzo[1,3]dioxolyl, each having one or more optional substituents selected from the group consisting of halogen, C_{1-3} alkyl and C_{1-2} alkoxy, each having one to three optional fluorine substituents; and

R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, halogen, cyano, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} sulfanyl or trifluoromethyl.

In accordance with another aspect of the present invention, there is provided a method for preparing the compound of formula (I) of claim 1, which comprises the steps of:

(i) subjecting a compound of formula (II) to bromination using NBS (N-bromosuccinimide) to obtain a compound of formula (III);

(ii) subjecting the compound of formula (III) to a substitution reaction with sodium acetate in an organic solvent to obtain an acetate compound of formula (IV);

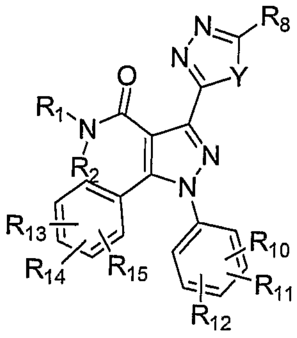
(iii) hydrolyzing the compound of formula (IV) to obtain an alcohol compound of formual (V);

(iv) oxidizing the compound of formual (V) in the presence of an oxidant to obtain an aldehyde compound of formula (VI);

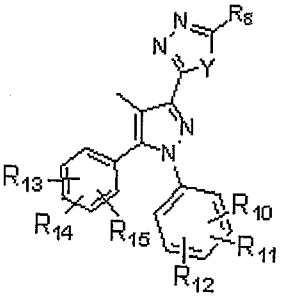
(v) further oxidizing the compound of formual (VI) in the presence of sodium chlorite and monobasic potassium phosphate to obtain a carboxylic acid compound of formula (VII);

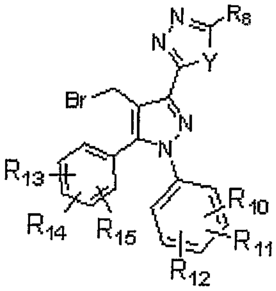
(vi) chlorinating the compound of formula (VII) with a chlorinating agent to obtain an acid chloride compound of formula (VIII), and

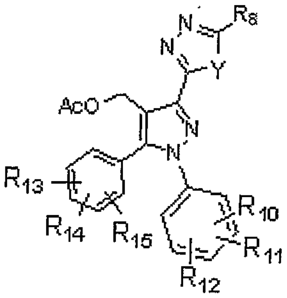
(vii) treating the compound of formula (VIII) with an amine in the presence of a base to obtain the compound of formula (I):

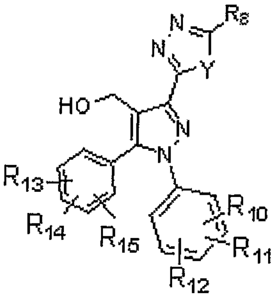


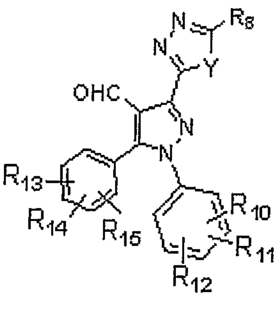
(I)

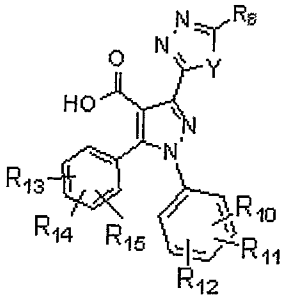

(II)


(III)

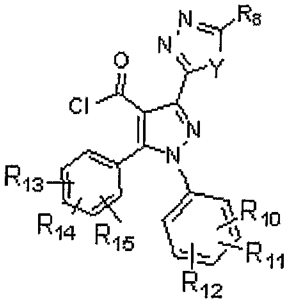

(IV)


(V)


(VI)



(VII)



(VIII)

wherein, R_1, R_2, R_8 and R_{10} to R_{15} have the same meanings as defined above.

As used herein, the term "alkyl" refers to a straight or branched chain saturated hydrocarbon radical. Examples of "alkyl" as used herein include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, n-pentyl, isopentyl and hexyl.

As used herein, the term "substituted alkyl" refers to a straight or branched chain saturated hydrocarbon radical, which is optionally substituted by one or more substituents selected from the group consisting of C_{1-3} alkyl optionally having one to three fluorine substituents, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-2} alkoxy optionally having one to three fluorine substituents, sulfanyl, sulfinyl, sulfonyl, oxo, hydroxy, mercapto, amino, guanidino, carboxy, aminocarbonyl, aryl, aryloxy, heteroaryl, heteroaryloxy, heterocyclic, aminosulfonyl, sulfonylamino, carboxyamide, ureido, nitro, cyano and halogen.

As used herein, the term "alkenyl" refers to a straight or branched chain hydrocarbon radical having at least one carbon-carbon double bond. Examples of "alkenyl" as used herein include, but are not limited to, ethenyl and propenyl.

As used herein, the term "substituted alkenyl" refers to a straight or branched chain hydrocarbon radical having at least one carbon-carbon double bond, which has optional substituents selected from the group consisting of C_{1-3}

alkyl optionally having one to three fluorine substituents, amino, aryl, cyano and halogen.

As used herein, the term "alkynyl" refers to a straight or branched chain hydrocarbon radical having at least one carbon-carbon triple bond. Examples of "alkynyl" as used herein include, but are not limited to, acetylenyl and 1-propynyl.

As used herein, the term "substituted alkynyl “refers to a straight or branched chain hydrocarbon radical having at least one carbon-carbon triple bond, optionally having one or more substituents selected from the group consisting of C_{1-3} alkyl optionally having one to three fluorine substituents, amino, aryl and halogen.

As used herein, the term "halogen" refers to fluorine (F), chlorine (Cl), bromine (Br), or iodine (I).

As used herein, the term "carbocycle" refers to a non-aromatic cyclic hydrocarbon radical composed of three to seven carbon atoms. Five-to seven-membered rings may contain a double bond in the ring structure. Exemplary "carbocycle" groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, and cycloheptyl.

As used herein, the term "substituted carbocycle" refers to a non-aromatic cyclic hydrocarbon radical composed by three to seven carbon atoms, which is optionally substituted with one or more substituents selected from the group consisting of C_{1-3} alkyl optionally having one to three fluorine substituents, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-2} alkoxy optionally having one to three fluorine substituents, sulfanyl, sulfinyl, sulfonyl, oxo, hydroxy, mercapto, amino, guanidino, carboxy, aminocarbonyl, aryl, aryloxy, heteroaryl, heterocyclic, aminosulfonyl, sulfonylamino, carboxyamide, nitro, ureido, cyano and halogen.

As used herein, the term "aryl" refers to an optionally substituted benzene ring or refers to a ring system which may result by fusing one or more optional substituents. Exemplary optional substituents include substituted C_{1-3} alkyl, substituted C_{2-3} alkenyl, substituted C_{2-3} alkynyl, heteroaryl, heterocyclic, aryl, alkoxy optionally having one to three fluorine substituents, aryloxy, aralkoxy, acyl, aroyl, heteroaroyl, acyloxy, aroyloxy, heteroaroyloxy, sulfanyl, sulfinyl, sulfonyl, aminosulfonyl, sulfonylamino, carboxyamide, aminocarbonyl, carboxy, oxo, hydroxy, mercapto, amino, nitro, cyano, halogen, or ureido. Such a ring or ring system may be optionally fused to aryl rings (including benzene rings) optionally having one or more substituents, carbocycle rings or heterocyclic rings. Examples of "aryl" groups include, but are not limited to, phenyl, naphthyl, tetrahydronaphthyl, biphenyl, indanyl, anthracyl or phenanthryl, as well as substituted derivatives thereof.

As used herein, the term "heteroaryl" refers to an optionally substituted monocyclic five to six-membered aromatic ring containing one or more heteroatomic substitutions selected from S, SO, SO_2, O, N, or N-oxide, or refers to such an aromatic ring fused to one or more rings such as heteroaryl rings, aryl rings, heterocyclic rings, or carbocycle rings (e. g., a bicyclic or tricyclic ring system), each having optional subsituents.

Examples of optional substituents are selected from the group consisting of substituted C_{1-3} alkyl, substituted C_{2-3} alkenyl, substituted C_{2-3} alkynyl, heteroaryl, heterocyclic, aryl, C_{1-3} alkoxy optionally having one to three fluorine substituents, aryloxy, aralkoxy, acyl, aroyl, heteroaroyl, acyloxy, aroyloxy, heteroaroyloxy, sulfanyl, sulfinyl, sulfonyl, aminosulfonyl, sulfonylamino, carboxyamide, aminocarbonyl, carboxy, oxo, hydroxy, mercapto, amino, nitro, cyano, halogen or ureido. Examples of "heteroaryl" groups used herein include, but are not limited to, benzoimidazolyl, benzothiazolyl, benzoisothiazolyl, benzothiophenyl, benzopyrazinyl, benzotriazolyl, benzo[1,4]dioxanyl, benzofuranyl, 9H-a-carbolinyl, cinnolinyl, furanyl, furo[2,3-b]pyridinyl, imidazolyl, imidazolidinyl, imidazopyridinyl, isoxazolyl, isothiazolyl, isoquinolinyl, indolyl, indazolyl, indolizinyl, naphthyridinyl, oxazolyl, oxothiadiazolyl, oxadiazolyl, phthalazinyl, pyridyl, pyrrolyl, purinyl, pteridinyl, phenazinyl, pyrazolyl, pyridyl, pyrazolopyrimidinyl, pyrrolizinyl, pyridazyl, pyrazinyl, pyrimidyl, 4-oxo-1, 2-dihydro-4H-pyrrolo[3,2,1-ij]-quinolin-4-yl, quinoxalinyl, quinazolinyl, quinolinyl, quinolizinyl, thiophenyl, triazolyl, triazinyl, tetrazolopyrimidinyl, triazolopyrimidinyl, tetrazolyl, thiazolyl, thiazolidinyl, and substituted versions thereof.

As used herein, the term "heterocyclic" refers to a three to seven-membered ring containing one or more heteroatomic moieties selected from S, SO, SO_2, O, N, or N-oxide, optionally substituted with one or more substituents selected from the group which includes substituted C_{1-3} alkyl, substituted C_{2-3} alkenyl, substituted C_{2-3} alkynyl, heteroaryl, heterocyclic, aryl, C_{1-3} alkoxy optionally having one to three fluorine substituents, aryloxy, aralkoxy, acyl, aroyl, heteroaroyl, acyloxy, aroyloxy, heteroaroyloxy, sulfanyl, sulfinyl, sulfonyl, aminosulfonyl, sulfonylamino, carboxyamide, aminocarbonyl, carboxy, oxo, hydroxy, mercapto, amino, nitro, cyano, halogen, and ureido. Such a ring can be saturated or have one or more degrees of unsaturation. Such a ring may be optionally fused to one or more "heterocyclic" ring(s), aryl ring(s), heteroaryl ring(s) or carbocycle ring(s), each having optional substituents.

Examples of "heterocyclic" moieties include, but are not limited to, 1,4-dioxanyl, 1,3-dioxanyl, pyrrolidinyl, pyrrolidin-2-onyl, piperidinyl, imidazolidine-2,4-dionepiperidinyl, piperazinyl, piperazine-2,5-dionyl, morpholinyl, dihydropyranyl, dihydrocinnolinyl, 2,3-dihydrobenzo [1,4] -dioxinyl, 3,4-dihydro-2H-benzo[b][1,4]-dioxepinyl, tetrahydropyranyl, 2,3-dihydrofuranyl, 2,3-dihydrobenzofuranyl, dihydroisoxazolyl, tetrahydrobenzodiazepinyl, tetrahydroquinolinyl, tetrahydrofuranyl, tetrahydronaphthyridinyl, tetrahydropurinyl, tetrahydrothiopyranyl, tetrahydrothiophenyl, tetrahydroquinoxalinyl, tetrahydropyridinyl, tetrahydrocarbolinyl, 4H-benzo[1,3]-dioxinyl, benzo[1,3]dioxonyl, 2,2-difluorobenzo-[1,3]-dioxonyl, 2,3-dihydro-phthalazine-1, 4-dionyl, and isoindole-1,3-dionyl.

As used herein, the term "alkoxy" refers to the group $-OR_a$, where R_a is alkyl as defined above. Exemplary alkoxy groups useful in the present invention include, but are not limited to, methoxy, difluoromethoxy, trifluoromethoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy and t-butoxy.

As used herein the term "aralkoxy" refers to the group $-OR_aR_b$, wherein R_a is alkyl and R_b is aryl as defined above.

As used herein the term "aryloxy" refers to the group -OR$_b$, wherein R$_b$ is aryl as defined above.

As used herein, the term "mercapto" refers to the group -SH.

As used herein, the term "sulfanyl" refers to the group -SR$_c$, wherein R$_c$ is substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "sulfinyl" refers to the group –S-(O)R$_c$, wherein R$_c$ is substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "sulfonyl" refers to the group –S(O)$_2$R$_c$, wherein R$_c$ is substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "oxo" refers to the group =O.

As used herein, the term "hydroxy" refers to the group -OH.

As used herein, the term "amino" refers to the group -NH$_2$. The amino group is optionally substituted by substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "cyano" refers to the group -CN.

As used herein, the term "aminosulfonyl" refers to the group -S(O)$_2$NH$_2$. The aminosulfonyl group is optionally substituted by substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "sulfonylamino" refers to the group -NHS(O)$_2$R$_c$ wherein R$_c$ is substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "carboxyamide" refers to the group -NHC(O)R$_c$ wherein R$_c$ is substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "carboxy" refers to the group -C(O)OH. The carboxy group is optionally substituted by substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "aminocarbonyl" refers to the group -C(O)NH$_2$. The aminocarbonyl group is optionally substituted by substituted alkyl, substituted carbocycle, aryl, heteroaryl or heterocyclic, as defined above.

As used herein, the term "ureido" refers to the group -NHC(O)NHR$_d$ wherein R$_d$ is hydrogen, alkyl, carbocycle or aryl as defined above.

As used herein, the term "guanidino" refers to the group -NHC(=NH)NH$_2$.

As used herein, the term "acyl" refers to the group -C(O)R$_e$, wherein R$_e$ is alkyl, carbocycle, or heterocyclic as defined herein.

As used herein, the term "aroyl" refers to the group -C(O)R$_b$, wherein R$_b$ is aryl as defined herein.

As used herein, the term "heteroaroyl" refers to the group -C(O)R$_f$, wherein R$_f$ is heteroaryl as defined herein.

As used herein, the term "acyloxy" refers to the group -OC(O)R$_e$, wherein R$_e$ is alkyl, carbocycle, or heterocyclic as defined herein.

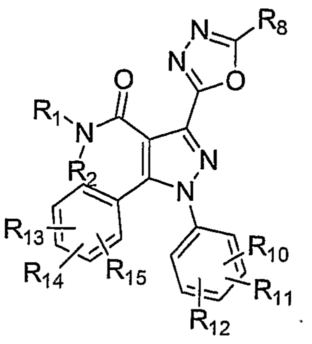
As used herein, the term "aroyloxy" refers to the group -OC(O)R$_b$, wherein R$_b$ is aryl as defined herein.

As used herein, the term "heteroaroyloxy" refers to the group -OC(O)R$_f$, wherein R$_f$ is heteroaryl as defined herein.

It is to be understood that the present invention also includes a pharmaceutically acceptable salt and an addition salt of the inventive compound, such as a hydrochloride, hydrobromide or trifluoroacetate addition salt and a sodium, potassium and magnesium salt.

The compounds of the present invention may contain one or more asymmetric carbon atoms and may exist in racemic and optically active forms. All of these compounds and diastereomers are incorporated within the scope of the present invention.

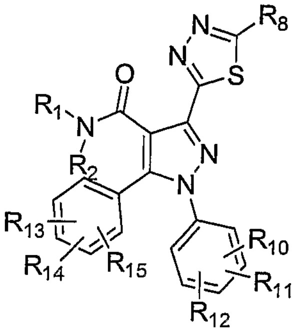
One embodiment of the present invention is to provide a compound of formula (**Ia**) or a pharmaceutically acceptable salt thereof:



(Ia)

wherein, R_1, R_2, R_8, R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} have the same meanings as defined above.

Another embodiment of the present invention is provide a compound of formula **(Ib)** or a pharmaceutically acceptable salt thereof:



(Ib)

wherein, R_1, R_2, R_8, R_{10}, R_{11}, R_{12}, R_{13}, R_{14}, and R_{15} have the same meanings as defined above.

Preferred compounds useful in the present invention are selected from the group consisting of:

(3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)-morpholino-methanone;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

N-tert-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-methyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N,N-diethyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-ethyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-ethyl-N-methyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

(3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)(pyrrolidin-1-yl)methanone;

(3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)(piperidin-1-yl)methanone;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

N'-acetyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carbohydrazide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N'-phenyl-1H-pyrazole-4-carbohydrazide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(2-oxopropyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-methyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-ethyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-ethyl-N-methyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N,N-diethyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-N-tert-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-propyl-1H-pyrazole-4-carboxamide;

N-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cycloheptyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-fluorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-oxopropyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-hydroxypropyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

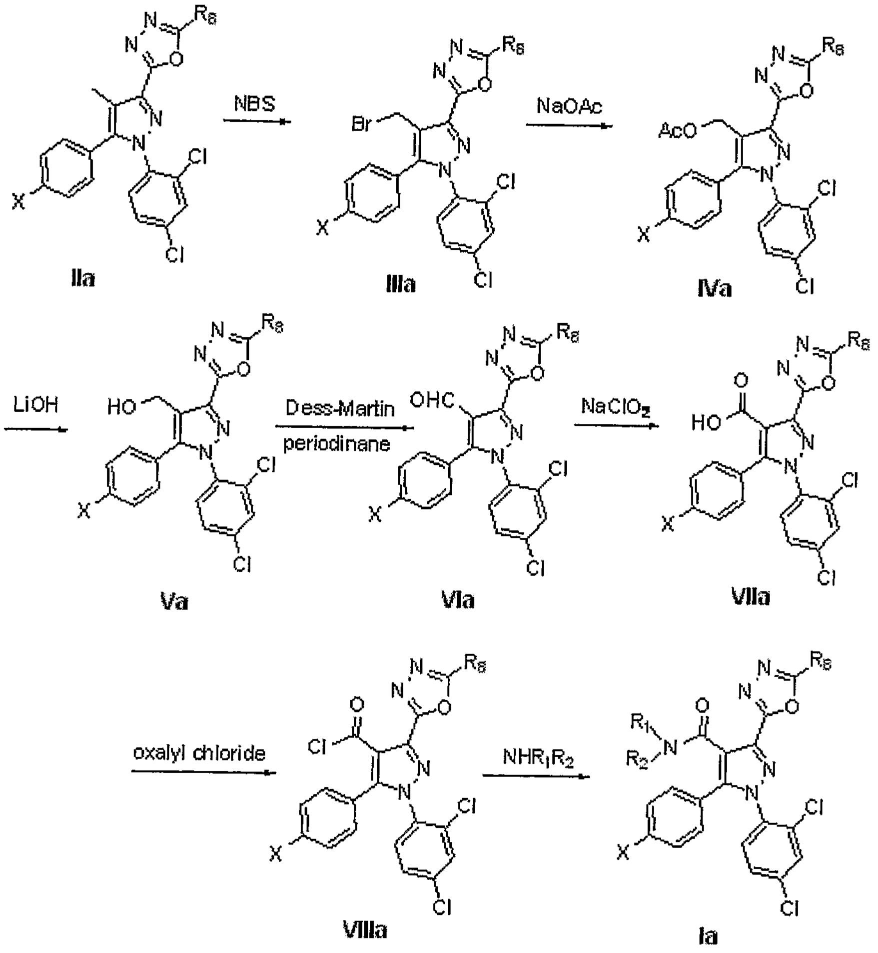
5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide; and
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide.

The compound of formula (**Ia**) may be illustratively prepared by the synthetic rout shown in Reaction Scheme 1.

Reaction Scheme 1



wherein, R_1, R_2 and R_8 have the same meanings as defined above.

Specifically, Reaction Scheme 1 comprises the steps of:

(i) subjecting an 1,3,4-oxadiazole compound of formula (IIa) to bromination using NBS (N-bromosuccinimide) to obtain an activated 4-pyrazole intermediate such as the bromomethyl derivative of formula (IIIa);

(ii) subjecting the compound of formula (IIIa) to a substitution reaction with sodium acetate in an organic solvent such as DMF to obtain an acetate compound of formula (IVa);

(iii) hydrolyzing the compound of formula (IVa) to obtain an alcohol compound of formual (Va);

(iv) oxidizing the compound of formual (Va) in the presence of an oxidant such as Dess-Martin periodinane to obtain an aldehyde compound of formula (VIa);

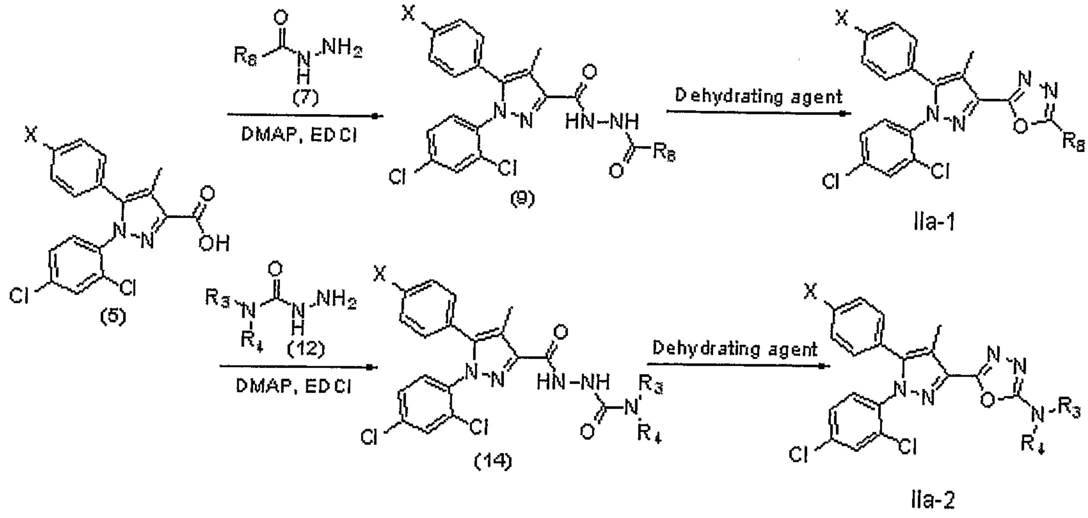
(v) further oxidizing the compound of formual (VIa) in the presence of sodium chlorite and monobasic potassium phosphate to obtain a carboxylic acid compound of formula (VIIa);

(vi) chlorinating the compound of formula (VIIa) with a chlorinating agent such as oxalyl chloride to obtain an acid chloride compound of formula (VIIIa), and

(vii) treating the compound of formula (VIIIa) with an amine in the presence of a suitable base such as triethylamine to obtain a compound of formula (**Ia**).

The 1,3,4-oxadiazole compound of formula (IIa) used as a starting material in preparing the compound of formula (**Ia**) may be prepared by reacting a carboxylic acid derivative (5) with a hydrazide compound (7) or a semicarbazide compound (12) in the presence of a coupling agent, e.g., EDCI, DMAP; and cyclizing the resulting acyl hydrazide intermediate (9 or 14) using a dehydrating agent, as shown in Reaction Scheme 2.

Reaction Scheme 2

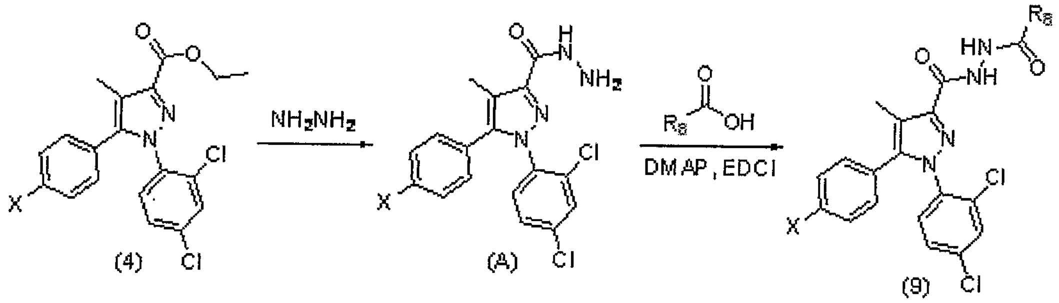


wherein, R_3, R_4 and R_8 have the same meanings as defined above.

The cyclization may be conducted using Burgess reagent as a dehydrating agent while applying microwave irradiation thereon (*see* Leber, J. D. et al., WO 2005/032550), or using triphenylphosphine with carbon tetrachloride and a base such triethylamine in a suitable solvent such as acetonitrile and THF or using phosphorus(III) oxychloride in refluxing 1,4-dioxane.

The acyl hydrazide intermediate (9) used in Reaction Scheme 2 may be also prepared by treating an ester compound of formula (4) with hydrazine in refluxing EtOH and coupling the resulting hydrazide compound (A) with a corresponding acid in the presence of coupling reagents such as DMAP and EDCI, as shown in Reaction Scheme 3.

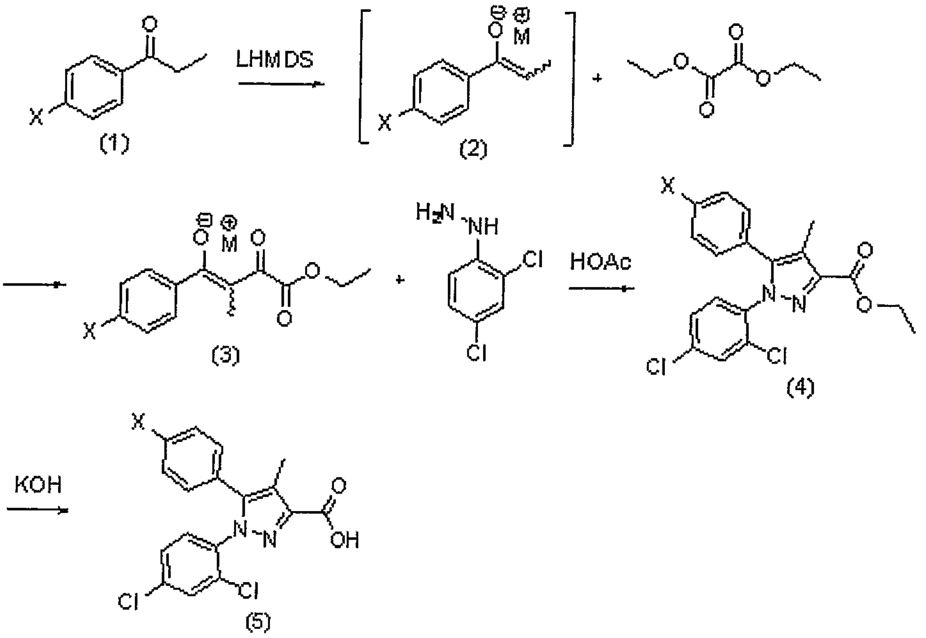
Reaction Scheme 3



wherein, R_8 has the same meanings as defined above.

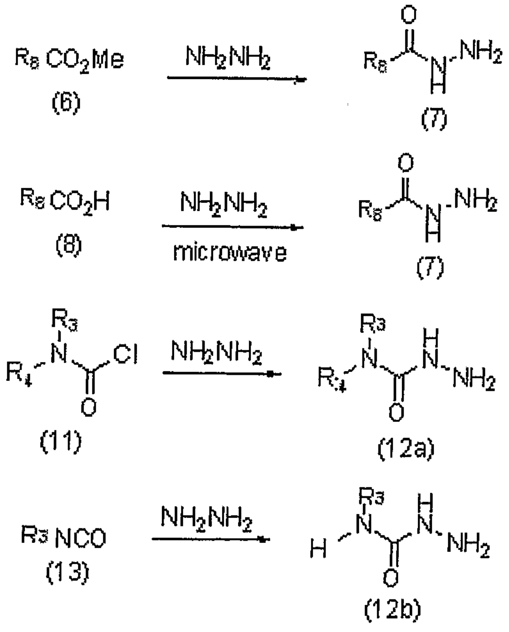
The carboxylic acid derivative (5) used in Reaction Scheme 2 may be prepared by a conventional method, e.g., by treating an acetophenone derivative (1) with an organic base such as lithium hexamethyldisilazide (LHMDS) to produce a corresponding alkali metal salt (2); reacting the resulting salt with an equimolar amount of diethyl oxalate to provide a ketoester salt (3); reacting the salt (3) with a hydrazine derivative in refluxing acetic acid to obtain a pyrazole-3-carboxylic ester (4); and transforming the ester (4) into an acid form (5) using an alkaline agent such as potassium hydroxide or lithium hydroxide, followed by acidification (*see* Barth, F. et al., US Patent No 5,462,960), as shown in Reaction Scheme 4.

Reaction Scheme 4



The hydrazide compound (7) used in Reaction Scheme 2 may be prepared by treating an ester or a carboxylic acid with hydrazine, and also, the semicarbazide compound (12) may be prepared by treating carbamyl chloride or isocynate with hydrazine, as shown in Reaction Scheme 5.

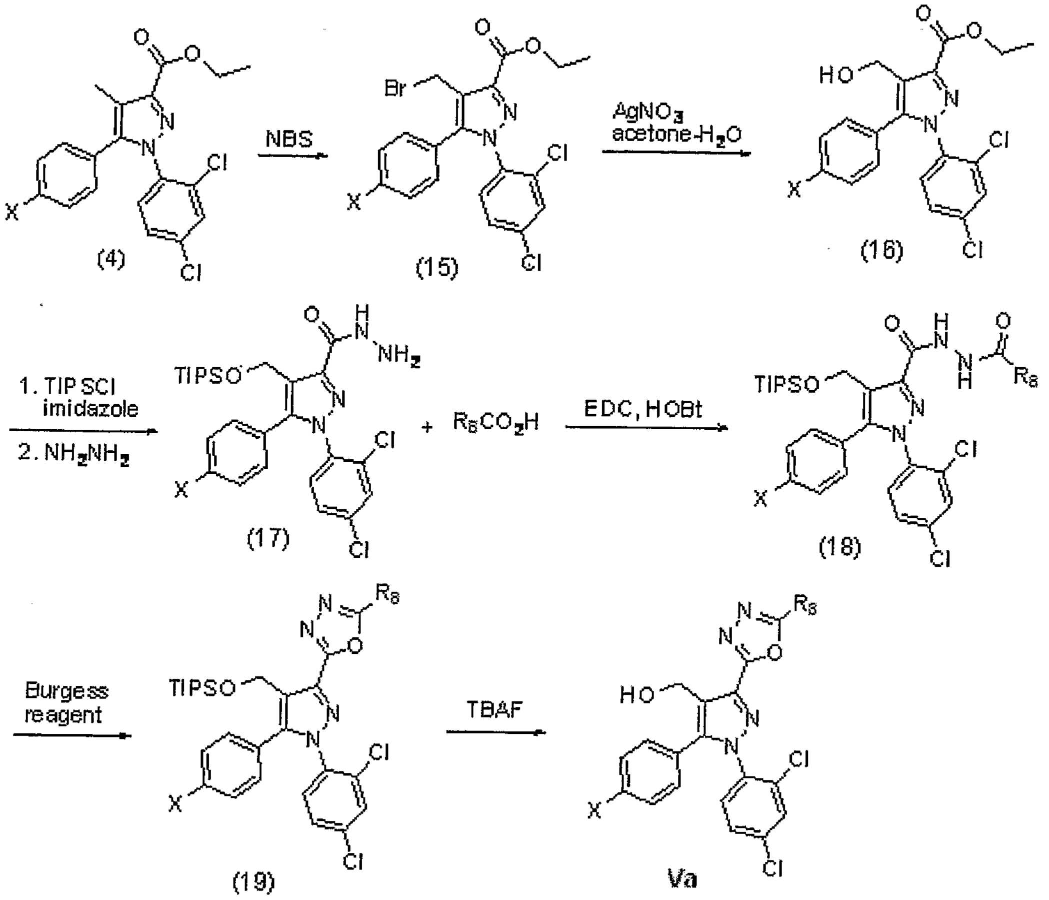
Reaction Scheme 5



wherein, R_3, R_4 and R_8 have the same meanings as defined above.

In Reaction Scheme 1, the compound of formula (Va) may be also prepared by converting a pyrazole-3-carboxylic ester (4) to a bromide compound (15) using NBS in the presence of a catalytic amount of benzoyl peroxide or AIBN; subjecting the bromide compound (15) to transformation into an alcohol compound (16) by the action of silver nitrate in aqueous acetone; protecting the alcohol compound (16) with TIPSCl (triisopropylsilyl chloride) in the presence of a suitable base such as imidazole and subsequently treating the intermediate with hydrazine to produce a hydrazide compound (17); coupling the hydrazide compound (17) with carboxylic acid in the presence of appropriate coupling reagents such as EDC and HOBt to produce a corresponding acyl hydrazide compound (18); and cyclizing the acyl hydrazide compound (18) using Burgess reagent, followed by deprotecting the silyl group of the resulting compound (19) with TBAF, as shown in Reaction Scheme 6.

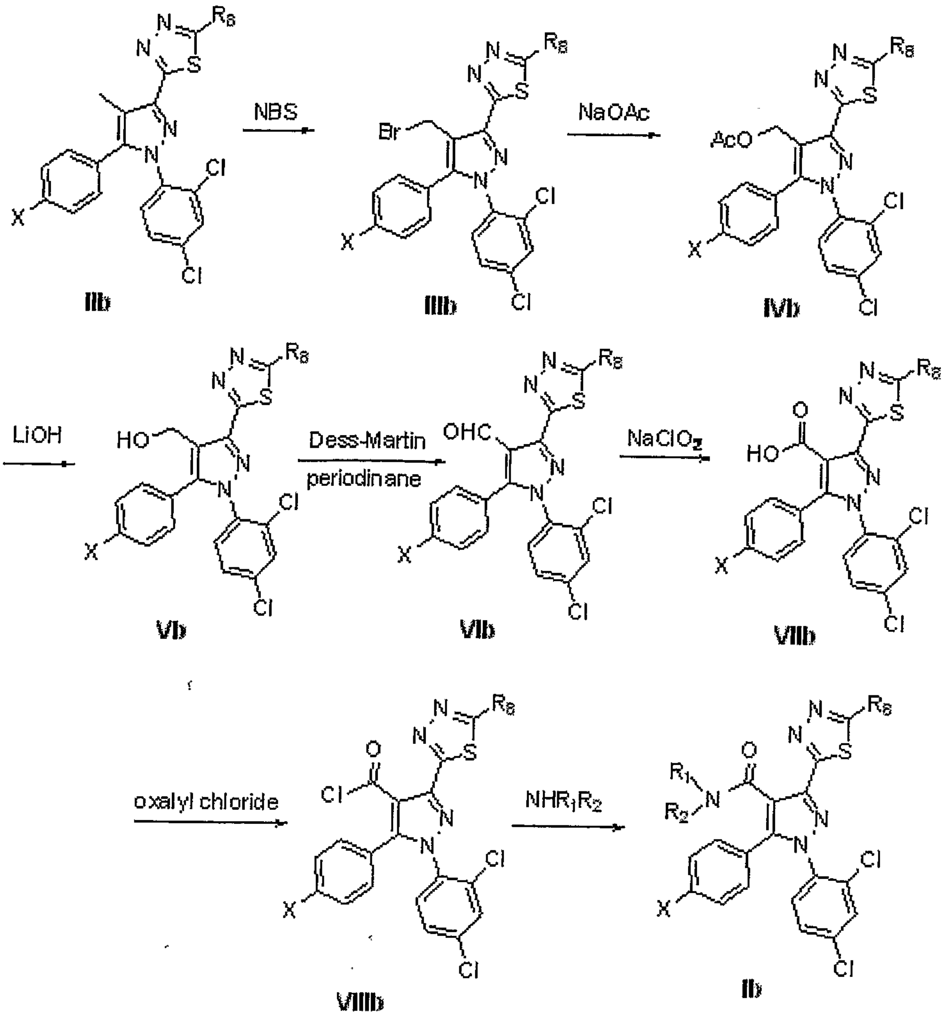
Reaction Scheme 6



wherein, R_8 has the same meaning as defined above.

The compound of formula **(Ib)** may be illustratively prepared by the synthetic rout shown in Reaction Scheme 7.

Reaction Scheme 7



wherein, R_1, R_2 and R_8 have the same meanings as defined above.

Specifically, Reaction Scheme 7 comprises the steps of:

(i) subjecting a thiadiazole compound of formula (IIb) to bromination using NBS (N-bromosuccinimide) to obtain an activated 4-pyrazole intermediate such as the bromomethyl derivative of formula (IIIb);

(ii) subjecting the compound of formula (IIIb) to reaction with sodium acetate in an organic solvent such as DMF to obtain an acetate compound of formula (IVb);

(iii) hydrolyzing the compound of formula (IVb) to obtain an alcohol compound of formual (Vb);

(iv) oxidizing the compound of formual (Vb) in the presence of an oxidant such as Dess-Martin periodinane to obtain an aldehyde compound of formula (VIb);

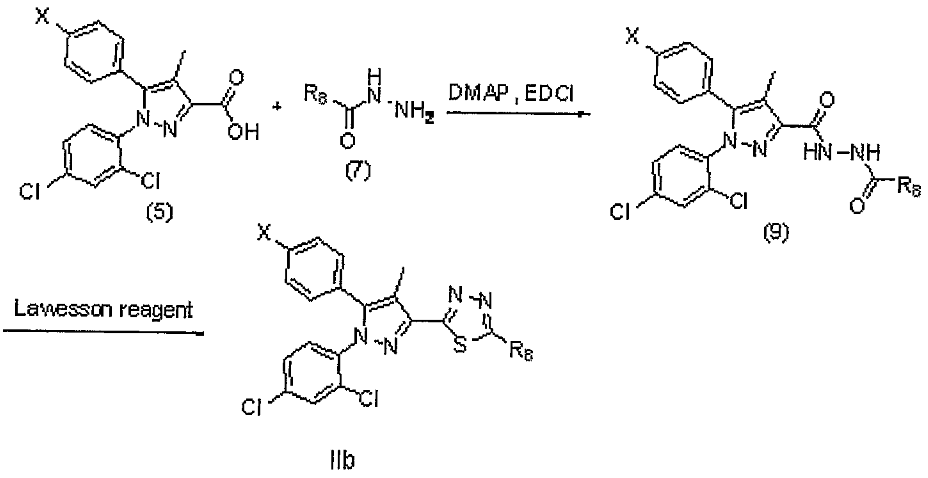
(v) further oxidizing the compound of formual (VIb) in the presence of sodium chlorite and monobasic potassium phosphate to obtain a carboxylic acid compound of formula (VIIb);

(vi) chlorinating the compound of formula (VIIb) with a chlorinating agent such as oxalyl chloride to obtain an acid chloride compound of formula (VIIIb), and

(vii) treating the compound of formula (VIIIb) with an amine in the presence of a suitable base such as triethylamine to obtain a compound of formula **(Ib)**.

The thiadiazole compound of formula (IIb) used as a starting material in preparing the compound of formula **(Ib)** may be prepared by reacting a carboxylic acid derivative (5) with a hydrazide compound (7) in the presence of coupling agents, e.g., EDCI, DMAP; and cyclizing the resulting product using a Lawesson's reagent, which can be conducted with microwave irradiation (*see* Kiryanov, A. A., Sampson, P., Seed, A. J., *J. Org. Chem.* **2001**, *665*, 7925-7929), as shown in Reaction Scheme 8.

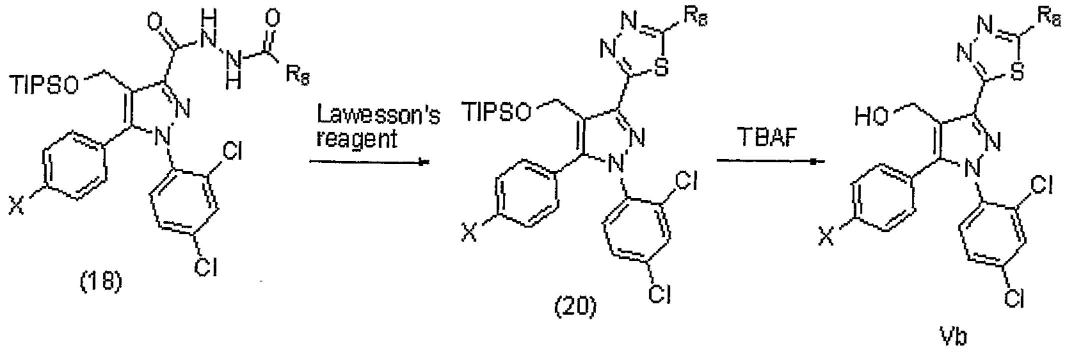
Reaction Scheme 8



wherein, R_8 has the same meaning as defined above.

In Reaction Scheme 7, the compound of formula (Vb) may be also prepared by cyclizing an acyl hydrazide compound (18) using Lawesson's reagent, followed by deprotecting the silyl group of the resulting compound (20) with TBAF, as shown in Reaction Scheme 9.

Reaction Scheme 9



wherein, R_8 has the same meaning as defined above.

The inventive biarylpyrazole 4-carboxamide compound, i.e., pyrazole-3-azole-4-carboxamide compound of formula (I) is effective as a cannabinoid CB_1 receptor ligand, thereby preventing or treating obesity and obesity-related metabolic disorders.

Accordingly, the present invention provides a pharmaceutical composition for preventing or treating obesity and obesity-related metabolic disorders, which comprises the compound of formula (I) or a pharmaceutically acceptable salt thereof as an active ingredient and a pharmaceutically acceptable carrier.

Further, the present invention provides a method for preventing or treating obesity and obesity-related metabolic disorders in a mammal, which comprises administering the compound of formula (I) to the mammal.

Also, the present invention provides a method for inhibiting cannabinoid CB_1 receptor in a mammal, which comprises administering the compound of formula (I) to the mammal.

As used herein, the term "obesity-related metabolic disorders" refers to chronic diseases that require treatment to reduce the excessive health risks associated with obesity and exemplary disorders include type 2 diabetes mellitus, cardiovascular and hypertension, hyperlipidaemia, fibrinolytic abnormalities.

The pharmaceutical composition may be administered orally, intramuscularly or subcutaneously. The formulation for oral administration may take various forms such as a syrup, tablet, capsule, cream and lozenge. A syrup formulation will generally contain a suspension or solution of the compound or its salt in a liquid carrier, e.g., ethanol, peanut oil, olive oil, glycerine or water, optionally with a flavoring or coloring agent. When the composition is in the form of a tablet, any one of pharmaceutical carriers routinely used for preparing solid formulations may be used. Examples of such carriers include magnesium stearate, terra alba, talc, gelatin, acacia, stearic acid, starch, lactose and sucrose. When the composition is in the form of a capsule, any of the routine encapsulation procedures may be employed, e.g., using the aforementioned carriers in a hard gelatin capsule shell. When the composition is formulated in the form of a soft gelatin shell capsule, any of the pharmaceutical carrier routinely used for preparing dispersions or suspensions may be prepared using an aqueous gum, cellulose, silicate or oil. The formulation for intramuscular or subcutaneous administration may take a liquid form such as a solution, suspension and emulsion which includes aqueous solvents such as water, physiological saline and Ringer's solution; or lipophilic solvents such as fatty oil, sesame oil, corn oil and synthetic fatty acid ester.

Preferably the composition is formulated in a specific dosage form for a particular patient.

Each dosage unit for oral administration contains suitably from 0.1 mg to 500 mg/Kg, and preferably from 1 mg to 100 mg/Kg of the compound of formula (I) or its pharmaceutically acceptable salt.

The suitable daily dosage for oral administration is about 0.01 mg/Kg to 40 mg/Kg of the compound of formula (I) or its pharmaceutically acceptable salt, may be administered 1 to 6 times a day, depending on the patient's condition.

The present invention is further described and illustrated in Examples provided below, which are, however, not intended to limit the scope of the present invention.

EXAMPLES

As used herein the symbols and conventions used describing the processes, schemes and examples of the present invention are consistent with those used in the contemporary scientific literature, for example, the *Journal of the American Chemical Society* or the *Journal of Biological Chemistry*. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification.

Hz (Hertz)
T_r (retention time)
MeOH (methanol)
TFA (trifluoroacetic acid)
EtOH (ethanol)
DMSO (dimethylsulfoxide)
DCM (dichloromethane)
DMF (*N,N*-dimethylformamide)
CDI (1,1-carbonyldiimidazole)
HOSu (*N*-hydroxysuccinimide)
HOBT (1-hydroxybenzotriazole)
Boc (*tert*-butyloxycarbonyl)
mCPBA (meta-chloroperbenzoic acid)
FMOC (9-fluorenylmethoxycarbonyl)
DCC (dicyclohexylcarbodiimide)
Cbz (benzyloxycarbonyl)
NMM (N-methyl morpholine)
HOAt (1-hydroxy-7-azabenzotriazole)
TBAF (tetra-*n*-butylammonium fluoride)
THP (tetrahydro-2H-pyran-2-yl)
DMAP (4-dimethylaminopyridine)
HPLC (high pressure liquid chromatography)
BOP (bis(2-oxo-3-oxazolidinyl)phosphinic chloride);

TLC (thin layer chromatography)
RP (reverse phase)
i-PrOH (isopropanol)
TEA (triethylamine)
THF (tetrahydrofuran)
EtOAc (ethyl acetate)
HOAc (acetic acid)
Ac (acetyl)
Bn (benzyl)

EDCI (1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride)

HBTU (O-Benzotriazole1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate)

AIBN (2,2'-Azobis(2-methylpropionitrile))

All references to ether are to diethyl ether; brine refers to a saturated aqueous solution of NaCl. Unless otherwise indicated, all temperatures are expressed in ℃ (degrees Centigrade). All reactions are conducted under an inert atmosphere at room temperature unless otherwise noted, and all solvents are of the highest available purity unless otherwise indicated.

Microwave reaction was conducted with a Biotage microwave reactor.

^{1}H NMR spectra were recorded on either a Jeol ECX-400, or a Jeol JNM-LA300 spectrometer. Chemical shifts were expressed in parts per million (ppm, δ units). Coupling constants are in units of hertz (Hz). Splitting patterns describe apparent multiplicities and are designated as s (singlet), d(doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), br (broad).

Mass spectra were obtained with either a Micromass, Quattro LC Triple Quadruple Tandem Mass Spectometer, ESI or Agilent, 1100LC/MSD, ESI.

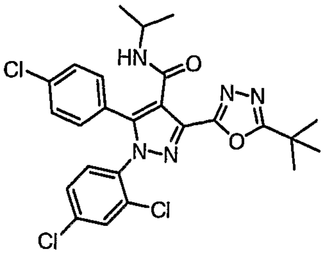
For preparative HPLC, *ca* 100 mg of a product was injected in 1 ml of DMSO onto a SunFire^{TM} Prep C18 OBD 5 μm 19x100mm Column with a 10 min gradient from 10% CH_3CN to 90% CH_3CN in H_2O. Flash chromatography was carried using Merck silica gel 60 (230-400 mesh). Most of the reactions were monitored by thin-layer chromatography on 0.25 mm E. Merck silica gel plates (60F-254), visualized with UV light using a 5% ethanolic phosphomolybdic acid or p-anisaldehyde solution.

The following synthetic schemes are merely illustrative of the methods by which the compounds of the invention may be prepared and are not intended to limit the scope of the invention as defined in the appended claims.

Preparation of pyrazole-3-azole-4-carboxamide compound (formula (I))

Example 1

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide



Step 1: 2-(4-(Bromomethyl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-3-yl)-5-tert-butyl-1,3,4-oxadiazole (IIIa)

2-tert-Butyl-5-(5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazol-3-yl)-1,3,4-oxadiazole (IIa) (1 g, 2.17 mmol) was dissolved in CCl_4 (50 mL), to which N-bromosuccinimide (422 mg, 2.38 mmol) and catalytic amounts of AIBN. The mixture was heated for 12 hours at 90℃, cooled to room temperature and filtered off to remove the salts. The filtrate was diluted with CH_2Cl_2 and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in *vacuo* to obtain the desired compound as a solid (1.2 g, 100 %), which was used without further purification.

Step 2: 5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)methyl acetate (IVa)

2-(4-(Bromomethyl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-3-yl)-5-tert-butyl-1,3,4-oxadiazole (2.7g, 4.614 mmol) obtained in Step 1 above was dissolved in DMF (20 ml), to which sodiumacetate (1.13 mg, 13.842 mmol) was added. The mixture was heated for 12 hours at 60℃, was diluted with EtOAc and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (Eluent : Hexane/EtOAc=3/1) to obtain the desired compound as a solid (1.75 g, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.47 (m, 2H), 7.44-7.39 (m, 1H), 7.40-7.38 (m, 1H), 7.35-7.32 (m, 1H), 7.25-7.06 (m, 2H), 5.30 (s, 2H), 2.03 (s, 3H), 1.49 (s, 9H).

MH+ 563.

Step 3: (3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)methanol (Va)

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichloro phenyl)-1H-pyrazol-4-yl)methyl acetate (1.57 g, 3.020 mmol) obtained in Step 2 above was dissolved in THF (9ml)/MeOH (9ml)/H_2O (2ml). Thereto, LiOH monohydrate (380 mg, 9.060 mmol) was added. The mixture was stirred for 12 hours at room temperature, diluted with EtOAc and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in *vacuo* to obtain the desired compound as a solid (1.37g, 95 %), which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.44 (m, 1H), 7.34-7.32 (m, 4H), 7.16-7.14 (m, 2H), 4.82-4.78 (m, 1H), 4.72-4.70 (m, 2H), 1.51 (s, 9H).

MH+ 478.

Step 4: 3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carbaldehyde (VIa)

(3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichloro phenyl)-1H-pyrazol-4-yl)methanol (100 mg, 0.209 mmol) obtained in Step 3 above and Dess-Martin periodinane (132mg, 0.313 mmol) were dissolved in CH_2Cl_2 (5 ml) and stirred at room temperature. The mixture was filtered off. The filtered white solid was diluted with CH_2Cl_2 (50ml) and washed with brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (Eluent : Hexane/EtOAc=3/1) to obtain the desired compound as a solid (78 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.65 (s, 1H), 7.46-7.45 (m, 1H), 7.38-7.31 (m, 4H), 7.36-7.23 (m, 2H), 1.52 (s, 9H).
MH+ 475.

Step 5: 3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxylic acid (VIIa)

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichloro phenyl)-1H-pyrazole-4-carbaldehyde (1.0 g, 2.10 mmol) obtained in Step 4 above was dissolved in t-BuOH (60 ml). Thereto, 2-methyl-2-butene (12.0 ml, 99.0 mmol), KH_2PO_4 (2.2 g, 14.7 mmol) and $NaClO_2$ (2.4 g, 18.9 mmol in H_2O (35ml)) were added. The mixture was stirred for 12 hours at room temperature. The resultant was acidified with AcOH and extracted with EtOAc. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in *vacuo* to obtain the desired compound as a solide (981 mg, 95 %), which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.45 (m, 1H), 7.38-7.31 (m, 4H), 7.36-7.23 (m, 2H), 1.52 (s, 9H).
MH+ 491.

Step 6: 3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide (Ia)

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichloro phenyl)-1H-pyrazole-4-carboxylic (150 mg, 0.31 mmol) obtained in Step 5 above was dissolved in CH_2Cl_2 (5 ml). Thereto, oxalyl chloride (35 μL, 0.37 mmol) and the catalytic amount of DMF were added. The mixture was stirred for 1 hour and concentrated in *vacuo*. The residue (crude acyl chloride) was diluted with CH_2Cl_2 (10 ml), to which isopropylamine (40 μL, 0.46 mmol) and triethylamine (0.13 ml, 0.93 mmol) were added and stirred for 2 hours at room temperature. The resultant was concentrated in *vacuo* and diluted with EtOAc.

The organic layer was washed with aq. saturated $NaHCO_3$ solution, dried over anhydrous $MgSO_4$, filtered and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (Biotage) to obtain the title compound as a solid (103mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (d, J = 7.2 Hz, 1H), 7.42 (dd, J = 2.0 Hz, 0.4 Hz, 1H), 7.30-7.24 (m, 4H), 7.23-7.19 (m, 2H), 4.18 (septet, J = 7.2 Hz, 1H), 1.51 (s, 9H), 1.26 (d, J = 6.4 Hz, 6H).
MH+ 532.

The following compounds of Examples 2 to 82 were obtained by using corresponding starting materials and repeating the procedure of Example 1.

Example 2

(3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)-morpholino-methanone

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.47 (m, 1H), 7.39-7.25 (m, 5H), 7.23-7.18 (m, 2H), 3.85-3.13 (m, 8H), 1.48 (s, 9H).
MH+ 560.

Example 3

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.43 (dd, J = 2.0 Hz, 0.4 Hz, 1H), 7.30-7.25 (m, 4H), 7.23-7.18 (m, 2H), 5.65 (s, 1H), 1.51 (s, 9H).
MH+ 491.

Example 4

N-tert-Butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.41 (dd, J = 2.0 Hz, 0.4 Hz, 1H), 7.31-7.23 (m, 4H), 7.21-7.17 (m, 2H), 1.51 (s, 9H), 1.44 (s, 9H).
MH+ 546.

Example 5

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ ~10.95 (br s, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.31-7.19 (m, 6H), 3.10 (br s, 4H), 1.79 (br s, 4H), 1.52-1.48 (m, 11H).
MH+ 575.

Example 6

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.44 (m, 1H), 7.37-7.33 (m, 2H), 7.31-7.26 (m, 2H), 7.22-7.17 (m, 2H), 3.10 (s, 3H), 2.92 (s, 3H), 1.48 (s, 9H).
MH+ 518.

Example 7

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-methyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.42 (dd, J = 2.0 Hz, 0.8 Hz, 1H), 7.29-7.24 (m, 4H), 7.23-7.19 (m, 2H), 2.93 (d, J = 4.4 Hz, 3H), 1.51 (s, 9H).
MH+ 506.

Example 8

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N,N-diethyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.46 (m, 1H), 7.37-7.31 (m, 1H), 7.29-7.20 (m, 5H), 3.52 (quartet, J = 7.2 Hz, 2H), 3.21 (quartet, J = 6.4 Hz, 2H), 1.47 (s, 9H), 1.21 (t, J = 7.2 Hz, 3H), 0.85 (t, J = 7.2 Hz, 3H).
MH+ 546.

Example 9

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-ethyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.43-7.41 (m, 1H), 7.30-7.19 (m, 6H), 3.47-3.38 (m, 2H), 1.50 (s, 9H), 1.25 (t, J = 7.2 Hz, 3H).
MH+ 518.

Example 10

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-ethyl-N-methyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.25 (m, 5H), 7.23-7.17 (m, 2H), 3.57 (quartet, J = 7.2 Hz, 2H), 2.86 (s, 3H), 1.45 (s, 9H), 1.18 (t, J = 7.2 Hz, 3H).
MH+ 532.

Example 11

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.42 (dd, J = 2.0 Hz, 0.8 Hz, 1H), 7.30-7.24 (m, 4H), 7.23-7.19 (m, 2H), 2.87 (m, 1H), 1.46 (s, 9H), 0.81-0.75 (m, 2H), 0.70-0.64 (m, 2H).
MH+ 530.

Example 12

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ ¯10.07 (d, J = 7.2 Hz, 1H), 7.43-7.41 (m, 1H), 7.29-7.23 (m, 4H), 7.22-7.18 (m, 2H), 4.51-4.49 (m, 1H), 2.39-2.30 (m, 2H), 2.15-2.04 (m, 2H), 1.81-1.65 (m, 2H), 1.47 (s, 9H).
MH+ 544.

Example 13

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (d, J = 6.0 Hz, 1H), 7.42 (d, J = 2.0 Hz, J = 0.8 Hz, 1H), 7.31-7.24 (m, 4H), 7.23-7.19 (m, 2H), 4.35-4.27 (m, 1H), 2.05-1.95 (m, 2H), 1.85-1.70 (m, 2H), 1.69-1.52 (m, 4H), 1.51 (s, 9H).
MH+ 560.

Example 14

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (d, J = 8.0 Hz, 1H), 7.43-7.41 (m, 1H), 7.30-7.24 (m, 4H), 7.22-7.19 (m, 2H), 3.94-3.83 (m, 1H), 2.03-1.91 (m, 2H), 1.75-1.70 (m, 2H), 1.63-1.53 (m, 2H), 1.43 (s, 9H), 1.42-1.21 (m, 4H).
MH+ 574.

Example 15

(3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)(pyrrolidin-1-yl)methanone

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.46 (m, 1H), 7.37-7.33 (m, 2H), 7.28-7.21 (m, 4H), 3.66-3.59 (m, 2H), 3.29-3.19 (m, 2H), 1.95-1.79 (m, 4H), 1.45 (s, 9H).

MH+ 546.

Example 16

(3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)(piperidin-1-yl)methanone

^{1}H NMR (400 MHz, CDCl$_3$) δ ~7.48-7.44 (m, 1H), 7.37-7.24 (m, 4H), 7.22-7.17 (m, 2H), 3.37-3.21 (m, 2H), 1.81-1.45 (m, 6H), 1.46 (s, 9H).
MH+ 560.

Example 17

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 11.90 (s, 1H), 7.78-7.73 (m, 2H), 7.45-7.43 (m, 1H), 7.32-7.22 (m, 8H), 7.11-7.05 (m, 1H), 1.51 (s, 9H).
MH+ 566.

Example 18

N'-Acetyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carbohydrazide

^{1}H NMR (400 MHz, CDCl$_3$) δ 12.70 (s, 1H), 8.03 (s, 1H), 7.46-7.42 (m, 1H), 7.31-7.19 (m, 6H), 2.01 (s, 3H), 1.52 (s, 9H).
MH+ 547.

Example 19

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N'-phenyl-1H-pyrazole-4-carbohydrazide

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.76 (s, 1H), 7.58-7.53 (m, 2H), 7.49-7.46 (m, 1H), 7.42-7.21 (m, 9H), 2.05-1.81 (m, 1H), 1.25 (s, 9H).

MH+ 581.

Example 20

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(2-oxopropyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.46-7.41 (m, 1H), 7.31-7.15 (m, 6H), 4.24 (d, J = 5.2 Hz, 2H), 2.16 (s, 3H), 1.51 (s, 9H).
MH+ 548.

Example 21

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.32 (s, 1H), 8.61 (d, J = 8.8 Hz, 1H), 8.27-8.21 (m, 1H), 8.10-8.03 (m, 1H), 7.47-7.40 (m, 1H), 7.38-7.25 (7H), 1.52 (s, 9H).
MH+ 567.

Example 22

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.42 (m, 3H), 7.39-7.32 (m, 2H), 7.21-7.11 (m, 2H), 3.11 (s, 3H), 2.92 (s, 3H), 1.47 (s, 9H).
MH+ 562.

Example 23

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-methyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 7.47-7.40 (m, 3H), 7.32-7.24 (m, 2H), 7.19-7.13 (m, 2H), 2.94 (d, J = 4.0 Hz, 3H), 1.52 (s, 9H).

MH+ 548.

Example 24

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-ethyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.45-7.41 (m, 3H), 7.29-7.26 (m, 2H), 7.19-7.13 (m, 2H), 3.48-3.37 (m, 2H), 1.52 (s, 9H), 1.25 (t, J = 7.2 Hz, 3H).
MH+ 562.

Example 25

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-ethyl-N-methyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.27 (m, 5H), 7.19-7.09 (m, 2H), 3.57 (quartet, J = 7.2 Hz, 2H), 3.05 (s, 3H), 1.45 (s, 9H), 1.19 (t, J = 7.2 Hz, 3H).
MH+ 576.

Example 26

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N,N-diethyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.26 (m, 5H), 7.18-7.12 (m, 2H), 3.52 (quartet, J = 7.2 Hz, 2H), 3.19 (quartet, J = 7.2 Hz, 2H), 1.48 (s, 9H), 1.20 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.2 Hz, 3H).
MH+ 590.

Example 27

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide

^1H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, J = 6.4 Hz, 1H), 7.44-7.39 (m, 2H), 7.32-7.21 (m, 3H), 7.18-7.10 (m, 2H), 4.18 (m, 1H), 1.48 (s, 9H), 1.26 (d, J = 6.8 Hz, 6H).

MH+ 576.

Example 28

5-(4-Bromophenyl)-N-tert-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^1H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.45-7.38 (m, 2H), 7.32-7.19 (m, 3H), 7.16-7.09 (m, 2H), 1.51 (s, 9H), 1.44 (s, 9H).

MH+ 590.

Example 29

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^1H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.44-7..6 (m, 2H), 7.31-7.21 (m, 3H), 7.20-7.11 (m, 2H), 2.87 (m, 1H), 1.51 (s, 9H), 0.81-0.72 (m, 2H), 0.70-0.62 (m, 2H).

MH+ 574.

Example 30

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^1H NMR (400 MHz, $CDCl_3$) δ 10.07 (d, J = 6.8 Hz, 1H), 7.45-7.36 (m, 2H), 7.32-7.23 (m, 3H), 7.16-7.10 (m, 2H), 4.53-4.43 (m, 1H), 2.40-2.29 (m, 2H), 2.17-2.02 (m, 2H), 1.84-1.63 (m, 2H), 1.47 (s, 9H).

MH+ 588.

Example 31

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.78 (d, J = 6.0 Hz, 1H), 7.45-7.39 (m, 2H), 7.31-7.19 (m, 3H), 7.18-7.11 (m, 2H), 4.36-4.25 (m, 1H), 2.05-1.95 (m, 2H), 1.89-1.71 (m, 2H), 1.69-1.53 (m, 4H), 1.51 (s, 9H).
MH+ 602.

Example 32

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.72 (d, J = 7.2 Hz, 1H), 7.46-7.39 (m, 2H), 7.31-7.21 (m, 3H), 7.22-7.11 (m, 2H), 3.94-3.82 (m, 1H), 2.03-1.91 (m, 2H), 1.79-1.69 (m, 2H), 1.63-1.53 (m, 2H), 1.43 (s, 9H), 1.45-1.19 (m, 4H).
MH+ 616.

Example 33

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 11.89 (s, 1H), 7.79-7.70 (m, 2H), 7.49-7.41 (m, 3H), 7.32-7.22 (m, 4H), 7.21-7.13 (m, 2H), 7.11-7.05 (m, 1H), 1.51 (s, 9H).
MH+ 610.

Example 34

3-(5-tert-Butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-propyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.84 (s, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.31-7.17 (m, 6H), 3.38-3.29 (m, 2H), 1.87-1.78 (m, 2H), 1.51 (s, 9H), 0.97 (t, J = 7.2 Hz, 3H).

MH+ 532.

Example 35

N-Butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (br s, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.32-7.18 (m, 6H), 3.42-3.35 (m, 2H), 1.67-1.55 (m, 2H), 1.53 (s, 9H), 1.47-1.35 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H).
MH+ 546.

Example 36

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.32 (br s, 1H), 8.59 (d, J = 8.8 Hz, 1H), 8.24 (d, J = 4.8 Hz, 1H), 8.01 (t, J = 7.6 Hz, 1H), 7.49-7.40 (m, 3H), 7.37-7.32 (m, 1H), 7.30-7.23 (m, 4H), 1.51 (s, 9H).
MH+ 611.

Example 37

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.46 (s, 1H), 7.80-7.75 (m, 2H), 7.45-7.42 (m, 2H), 7.34-7.7.26 (m, 3H), 7.25-7.22 (m, 2H), 7.20-7.17 (m, 2H), 7.09-7.06 (m, 1H), 1.55 (s, 9H).
MH+ 626.

Example 38

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (s, 1H), 7.44-7.39 (m, 2H), 7.28-7.25 (m, 2H), 7.22-7.21 (m, 1H), 7.17-7.14 (m, 2H), 2.89-2.83 (m, 1H), 1.53 (s, 9H), 0.85-0.78 (m, 2H), 0.70-0.66 (m, 2H).
MH+ 590.

Example 39

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 7.43-7.38 (m, 2H), 7.29-7.25 (m, 2H), 7.22-7.21 (m, 1H), 7.16-7.12 (m, 2H), 4.52-4.44 (m, 1H), 2.40-2.32 (m, 2H), 2.18-2.08 (m, 2H), 1.83-1.64 (m, 2H), 1.54 (s, 9H).
MH+ 604.

Example 40

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 7.42-7.40 (m, 2H), 7.27-7.24 (m, 2H), 7.23-7.21 (m, 1H), 7.17-7.14 (m, 2H), 4.34-4.28 (m, 1H), 2.02-1.96 (m, 2H), 1.81-1.79 (m, 2H), 1.69-1.59 (m, 4H), 1.53 (s, 9H).
MH+ 618.

Example 41

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.43-7.40 (m, 2H), 7.27-7.24 (m, 2H), 7.23-7.20 (m, 1H), 7.19-7.13 (m, 2H), 3.89 (bs, 1H), 1.99-1.95 (m, 2H), 1.77-1.74 (m, 2H), 1.53 (s, 9H), 1.47-1.24 (m, 6H).
MH+ 632.

Example 42

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cycloheptyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.21 (s, 1H), 7.43-7.39 (m, 2H), 7.27-7.24 (m, 2H), 7.20-7.18 (m, 1H), 7.17-7.13 (m, 2H), 4.07-4.02 (m, 1H), 2.07-1.96 (m, 2H), 1.88-1.37 (m, 10H), 1.55 (s, 9H).
MH+ 646.

Example 43

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-fluorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.42 (s, 1H), 8.19-8.14 (m, 1H), 7.45-7.42 (m, 2H), 7.30-7.09 (m, 6H), 7.07-7.02 (m, 2H), 1.55 (s, 9H).
MH+ 644.

Example 44

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-oxopropyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 7.49-7.19 (m, 5H), 7.17-7.09 (m, 2H), 4.24 (s, 2H), 2.16 (s, 3H), 1.47 (s, 9H).
MH+ 590.

Example 45

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-hydroxypropyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.90 (s, 1H), 7.44-7.41 (m, 2H), 7.29-7.20 (m, 3H), 7.16-7.13 (m, 2H), 4.08-4.04 (m, 1H), 3.60-3.55 (m, 1H), 3.36-3.30 (m,

1H), 1.55 (s, 9H), 1.23-1.20 (m, 3H).
MH+ 608.

Example 46

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (d, J = 7.6 Hz, 1H), 7.45-7.21 (m, 9H), 7.15-7.08 (m, 2H), 4.21-4.07 (m, 1H), 1.84-1.77 (m, 2H), 1.55-1.43 (m, 2H), 1.21 (d, J = 6.4 Hz, 6H).
MH+ 670.

Example 47

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.45-7.37 (m, 4H), 7.35-7.30 (m, 2H), 7.29-7.20 (m, 3H), 7.17-7.10 (m, 2H), 2.86-2.77 (m, 1H), 1.88-1.78 (m, 2H), 1.55-1.46 (m, 2H), 0.79-0.72 (m, 2H), 0.64-0.58 (m, 2H).
MH+ 668.

Example 48

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (br d, J = 7.2 Hz, 1H), 7.45-7.37 (m, 4H), 7.36-7.31 (m, 2H), 7.29-7.20 (m, 3H), 7.15-7.09 (m, 2H), 4.55-4.40 (m, 1H), 2.36-2.25 (m, 2H), 2.10-1.97 (m, 2H), 1.87-1.80 (m, 2H), 1.79-1.61 (m, 2H), 1.59-1.47 (m, 2H).
MH+ 682.

Example 49

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.67 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.47-7.40 (m, 4H), 7.35-7.22 (m, 7H), 7.19-7.13 (m, 2H), 7.07 (t, J = 7.2 Hz, 1H), 1.90-1.79 (m, 2H), 1.60-1.45 (m, 2H).
MH+ 704.

Example 50

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.25 (s, 1H), 8.64 (d, J = 8.8 Hz, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.12 (t, J = 8.0 Hz, 1H), 7.70-7.33 (m, 13H), 2.11-1.98 (m, 2H), 1.73-1.60 (m, 2H).
MH+ 705.

Example 51

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (d, J = 7.2 Hz, 1H), 7.45-7.41 (m, 2H), 7.37-7.33 (m, 1H), 7.31-7.24 (m, 6H), 7.22-7.18 (m, 2H), 4.21-4.09 (m, 1H), 1.85-1.80 (m, 2H), 1.53-1.47 (m, 2H), 1.22 (d, J = 6.4 Hz, 6H).
MH+ 626.

Example 52

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.44-7.40 (m, 3H), 7.37-7.33 (m, 2H), 7.30-7.23 (m, 4H), 7.22-7.19 (m, 2H), 2.87-2.79 (m, 1H), 1.85-1.78 (m,

2H), 1.53-1.47 (m, 2H), 0.79-0.71 (m, 2H), 0.65-0.58 (m, 2H).
MH+ 624.

Example 53

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.88 (br d, J = 7.2 Hz, 1H), 7.46-7.41 (m, 3H), 7.38-7.33 (m, 2H), 7.30-7.22 (m, 4H), 7.21-7.17 (m, 2H), 4.53-4.48 (m, 1H), 2.38-2.27 (m, 2H), 2.11-1.98 (m, 2H), 1.85-1.80 (m, 2H), 1.78-1.63 (m, 2H), 1.57-1.49 (m, 2H).
MH+ 638.

Example 54

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 11.69 (s, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.45-7.40 (m, 3H), 7.38-7.34 (m 2H), 7.32-7.21 (m, 8H), 7.07 (t, J = 7.6 Hz, 1H), 1.88-1.72 (m, 2H), 1.57-1.49 (m, 2H).
MH+ 660.

Example 55

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 11.83 (s, 1H), 8.38-8.34 (m, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.64-7.57 (m, 1H), 7.45-7.38 (m, 3H), 7.34-7.21 (m, 8H), 7.03-6.97 (m, 1H), 1.88-1.80 (m, 2H), 1.56-1.47 (m, 2H).
MH+ 661.

Example 56

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.35 (s, 1H), 7.44-7.39 (m, 5H), 7.36-7.32 (m, 2H), 7.25-7.22 (m, 1H), 7.15-7.12 (m, 3H), 2.88-2.83 (m, 1H), 1.97-1.94 (m, 2H), 1.60-1.53 (m, 2H), 0.82-0.77 (m, 2H), 0.69-0.65 (m, 2H).
MH+ 684.

Example 57

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.47 (s, 1H), 7.45-7.38 (m, 5H), 7.36-7.33 (m, 2H), 7.25-7.21 (m, 1H), 7.16-7.10 (m, 3H), 4.53-4.43 (m, 1H), 2.40-2.32 (m, 2H), 2.17-2.08 (m, 2H), 2.07-1.83 (m, 2H), 1.79-1.67 (m, 2H), 1.61-1.54 (m, 2H).
MH+ 698.

Example 58

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 13.39 (s, 1H), 7.78-7.76 (m, 2H), 7.46-7.40 (m, 4H), 7.37-7.30 (m, 4H), 7.25-7.19 (m, 2H), 7.18-7.15 (m, 3H), 7.10-7.06 (m, 1H), 2.02-1.99 (m, 2H), 1.59-1.55 (m, 2H).
MH+ 720.

Example 59

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.07 (s, 1H), 7.45-7.41 (m, 5H), 7.40-7.32 (m, 2H), 7.25-7.22 (m, 1H), 7.16-7.11 (m, 3H), 4.21-4.13 (m, 1H), 2.08-1.95 (m, 2H), 1.56-1.53 (m, 2H), 1.28 (d, J = 6.8 Hz, 4H).

MH+ 686.

Example 60

5-(4-Bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.79 (s, 1H), 8.44-8.43 (m, 1H), 8.19-8.17 (m, 1H), 7.63-7.51 (m, 1H), 7.45-7.39 (m, 4H), 7.36-7.33 (m, 1H), 7.27-7.24 (m, 2H), 7.22-7.20 (m, 2H), 7.18-7.13 (m, 2H), 7.02-6.99 (m, 1H), 2.09-2.01 (m, 2H), 1.56-1.53 (m, 2H).

MH+ 721.

Example 61

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (s, 1H), 7.44-7.40 (m, 2H), 7.28-7.23 (m, 2H), 7.22-7.15 (m, 3H), 4.21-4.16 (m, 1H), 1.55 (s, 9H), 1.30 (d, J = 6.4 Hz, 4H).

MH+ 592.

Example 62

5-(4-Bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.89 (s, 1H), 8.45-8.43 (m, 1H), 8.20-8.18 (m, 1H), 7.64-7.59 (m, 1H), 7.47-7.44 (m, 2H), 7.31-7.18 (m, 5H), 7.02-6.99 (m, 1H), 1.56 (s, 9H).

MH+ 627.

Example 63

5-(4-Bromophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.54 (br s, 1H), 7.45-7.38 (m, 2H), 7.31-7.29 (m, 1H), 7.29-7.24 (m, 2H), 7.17-7.08 (m, 2H), 2.90-2.83 (m, 1H), 1.67-1.62 (m, 4H), 0.81-0.77 (m, 2H), 0.67-0.61 (m, 2H).
MH+ 626.

Example 64

5-(4-Bromophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.68 (br d, 1H), 7.42 (d, J = 10.8 Hz, 2H), 7.31-7.22 (m, 3H), 7.14 (d, J = 13.2 Hz, 2H), 5.30-4.38 (m, 1H), 2.39-2.32 (m, 3H), 2.14-2.05 (m, 3H), 1.88-1.72 (m, 4H).
MH+ 640.

Example 65

5-(4-Bromophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.68 (br d, J = 7.2 Hz, 1H), 7.45-7.40 (m, 2H), 7.30 (dd, J = 8.4, 2.4 Hz, 1H), 7.27-7.25 (m, 2H), 7.17-7.14 (m, 2H), 4.21-4.10 (m, 1H), 1.27 (s, 3H), 1.25 (s, 3H), 1.26-1.15 (m, 4H).
MH+ 630.

Example 66

5-(4-Bromophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 11.52 (br s, 1H), 7.74 (d, J = 7.6 Hz, 2H),

7.46-7.43 (m, 3H), 7.40-7.28 (m, 5H) 7.19 (d, J = 6.8 Hz, 2H), 7.10 (t, J = 7.2 Hz, 1H), 1.64-1.48 (m, 4H).
MH+ 664.

Example 67

5-(4-Bromophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.72 (br s, 1H), 7.77 (d, J = 7.4 Hz, 2H), 7.47-7.41 (m, 3H), 7.38-7.31 (m, 4H) 7.22 (d, J = 7.4 Hz, 2H), 7.10 (t, J = 7.1 Hz, 1H), 1.63-1.53 (m, 4H).
MH+ 665.

Example 68

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.74 (s, 1H), 8.39-8.33 (m, 2H)˜, 7.82-7.78 (m, 1H), 7.45-7.38 (m, 3H), 7.35-7.32 (m, 2H), 7.29-7.23 (m, 6H), 7.14-7.11 (m, 1H), 2.05-2.02 (m, 2H), 1.58-1.51 (m, 2H)
MH+ 677.

Example 69

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.39 (s, 1H), 7.76 (d, *J*=7.6, 2H)˜, 7.45-7.40 (m, 3H), 7.37-7.29 (m, 4H), 7.29-7.16 (m, 6H), 7.10-7.06 (m, 1H), 2.01-1.98 (m, 2H), 1.58-1.55 (m, 2H).
MH+ 676.

Example 70

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.71 (b, 1H), 7.44-7.38 (m, 2H)˜, 7.35-7.31 (m, 2H), 7.25-7.21 (m, 4H), 7.19-7.10 (m, 2H), 4.51-4.44 (m, 1H), 2.39-2.34 (m, 2H), 2.20-2.10 (m, 2H), 2.00-1.92 (m, 2H), 1.83-1.66 (m, 2H), 1.55-1.52 (m, 2H).
MH+ 654.

Example 71

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (b, 1H), 7.43-7.38 (m, 2H)˜, 7.35-7.33 (m, 2H), 7.25-7.14 (m, 7H), 2.87-2.84 (m, 1H), 1.97-1.94 (m, 2H), 1.56-1.53 (m, 2H), 0.81-0.77 (m, 2H), 0.68-0.64 (m, 2H).
MH+ 640.

Example 72

5-(4-Chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (b, 1H), 7.43-7.38 (m, 2H)˜, 7.35-7.33 (m, 2H), 7.25-7.10 (m, 7H), 4.18-4.12 (m, 1H), 1.98-1.91 (m, 2H), 1.55-1.50 (m, 2H), 1.27 (d, *J*=6.4, 6H).
MH+ 642.

Example 73

5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.02 (s, 1H), 8.58 (d, *J*=4.4, 1H)˜, 8.22-8.20 (m,

1H), 8.04-8.00 (m, 1H), 7.44-7.42 (m, 1H), 7.40-7.24 (m, 7H), 1.84-1.77 (m, 2H), 1.68-1.60 (m, 2H).
MH+ 619.

Example 74

5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 7.73 (d, *J*=7.6, 2H)˜, 7.44 (d, *J*=2.0, 1H), 7.33-7.23 (m, 8H), 7.11-7.07 (m, 1H), 1.70 (s, 4H).
MH+ 618.

Example 75

5-(4-Chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (m, 1H), 7.42 (d, *J*=2.4, 1H)˜, 7.30-7.24 (m, 5H), 7.21-7.19 (m, 1H), 4.53-4.43 (m, 1H), 2.39-2.31 (m, 2H), 2.16-2.02 (m, 2H), 1.81-1.66 (m, 2H), 1.83-1.66 (m, 4H), 1.55-1.52 (m, 2H).
MH+ 596.

Example 76

5-(4-Chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (b, 1H), 7.42 (d, J=2.4, 1H)˜, 7.30-7.24 (m, 4H), 7.23-7.20 (m, 2H), 2.88-2.82 (m, 1H), 1.67 (m, 4H), 0.81-0.76 (m, 2H), 0.67-0.63 (m, 2H).
MH+ 582.

Example 77

5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluorom

ethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 9.20 (b, 1H), 7.42 (d, *J*=1.6, 1H)˜, 7.31-7.24 (m, 4H), 7.22-7.20 (m, 2H), 4.22-4.10 (m, 1H), 1.67 (s, 4H), 1.25 (d, *J*=6.4, 6H). MH+ 584.

Example 78

5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 12.49 (s, 1H), 8.44 (d, *J*=8.8, 1H)˜, 8.32 (d, 1H, *J*=5.6), 7.91-7.86 (m, 1H), 7.45-7.42 (m, 1H), 7.32-7.24 (m, 6H), 7.20-7.16 (m, 1H), 1.85-1.78 (m, 2H), 1.68-1.60 (m, 2H).
MH+ 635.

Example 79

5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 12.42 (s, 1H), 7.74 (d, *J*=8.8, 2H)˜, 7.45 (d, *J*=2.0, 1H), 7.34-7.23 (m, 8H), 7.10-7.07 (m, 1H), 1.80-1.73 (m, 2H), 1.69-1.64 (m, 2H).
MH+ 634.

Example 80

5-(4-Chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, CDCl$_3$) δ 10.33 (b, 1H), 7.43 (d, J=2.4, 1H)˜, 7.28-7.25 (m, 4H), 7.22-7.19 (m, 2H), 4.49-4.47 (m, 1H), 2.40-2.31 (m, 2H), 2.14-2.06 (m, 2H), 1.83-1.64 (m, 6H).
MH+ 612.

Example 81

5-(4-Chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.22 (b, 1H), 7.43 (m, 1H)˘, 7.29-7.25 (m, 4H), 7.23-7.20 (m, 2H), 2.88-2.86 (m, 1H), 1.74-1.71 (m, 2H), 1.70-1.65 (m, 2H), 0.82-0.77 (m, 2H), 0.68-0.64 (m, 2H).
MH+ 598.

Example 82

5-(4-Chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (b, 1H), 7.43 (d, J=2.0, 1H)˘, 7.29-7.25 (m, 4H), 7.23-7.20 (m, 2H), 4.19-4.10 (m, 1H), 1.76-1.74 (m, 2H), 1.67-1.64 (m, 2H), 1.27 (d, *J*=6.8, 6H).
MH+ 600.

Pharmacological Test: *In vitro* Activity Analysis

The compounds of the present invention were analyzed for their binding characteristics for CB_1 and CB_2 and the pharmacological activity thereof in accordance with the method disclosed in [Devane WA, Dysarz FA 3rd, Johnson MR, Melvin LS and Howlett AC, Determination and characterization of a cannabinoid receptor in rat brain, *Mol. Pharmacol.*, 34(5): 605-13(1998)]. The analysis was performed using [^{3}H]CP-55940 which is a selectively radioactivity-labeled 5-(1,1-dimethyheptyl)-2[5-hydroxy-2-(3-hydroxypropyl)-cyclohexyl]-phenol, purchased from PerkinElmer Life Sciences, Inc. (Boston, Massachusetts, U.S.A.), through a rat CB-1 receptor binding protocol as follows.

The tissue obtained from the brain of SD rats was homogenized with a

Dounce homogenate system in TME(50 mM Tris, 3 mM $MgCl_2$ and 1 mM EDTA, pH 7.4) at 4℃, and the homogenate was centrifuged at 48,000g for 30 min. at 4 ℃. The pellet was resuspended in 5 mℓ of TME and the suspension was divided into aliquots and stored at -70 ℃ until its use in the following assay.

2 μℓ of the test compound was diluted in dimethylsulphoxide and was added to a deep well of a polypropylene plate, to which 50 μℓ of $[^3H]$CP-55940 diluted in a ligand buffer solution (0.1 % bovine serum albumin(BAS)+TME) was added. The tissue concentrations were determined by Bradford protein analysis, and 148 μℓ of brain tissue of the required concentration was added to the plate. The plate was covered and placed in a 30 ℃ incubator for 60 min, and then transformed on GF/B filtermat pretreated in polyethylenimine (PEI) using a cell harvester. Each filter was washed five times and dried at 60 ℃ for 1 hr. Then, the degree of radioactivity retained by the filter was measured using Wallac Microbeta™ (PerkinElmer Life Sciences, Inc., Massachusetts, U.S.A.) and the activity of the compound for inhibiting CB_1 receptor was determined there from and compared with that of the control, rimonabant which is known as a cannabinoid CB_1 receptor antagonist. The results are shown in Table 1.

Table 1

Example	IC_{50} (nM)	Example	IC_{50} (nM)
1	9.31	27	7.37
2	68.5	29	2.58
3	23.8	30	3.98
5	17.2	31	5.84
6	13.4	32	11.4
7	18.3	33	1.35
8	62.1	34	5.72
9	12.7	35	17.8
10	11.5	36	1.46
11	3.27	37	3.09

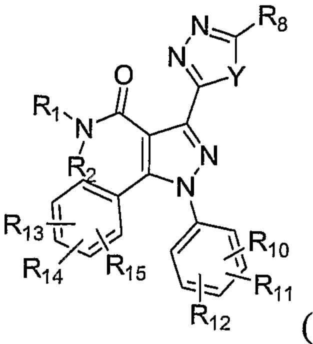
13	7.25	38	1.64
15	93.4	39	7.13
17	1.66	40	8.28
18	37.9	44	7.41
19	76.2	45	6.83
20	3.51	46	4.19
21	1.47	47	4.90
22	10.1	48	4.89
23	11.9	49	1.96
24	6.37	50	1.73
25	7.97	rimonabant	5.0

As shown in Table 1, the inventive compounds are effective as a cannabinoid CB_1 receptor ligand.

While the invention has been described with respect to the specific embodiments, it should be recognized that various modifications and changes may be made by those skilled in the art to the invention which also fall within the scope of the invention as defined as the appended claims.

WHAT IS CLAIMED IS:

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein:

Y is O or S;

R_1 and R_2 are each independently hydrogen, C_{1-6} alkyl, substituted C_{1-6} alkyl, C_{3-12} carbocycle, substituted C_{3-12} carbocycle, NR_3R_4, $-CHR_5(CO)OR_7$, $-CHR_5(CO)\ NR_3R_4$, or

R_1 and R_2 are fused to each other together with the nitrogen atom to which they are bonded to form a 4- to 10-membered saturated or unsaturated heterocyclic ring which is optionally substituted by one or more substituents selected from the group consisting of C_{1-3} alkyl, benzyl, phenyl, C_{1-3} alkoxy or halogen;

R_3 and R_4 are each independently selected from the group consisting of hydrogen, C_{1-7} alkyl, C_{3-8} carbocycle, substituted C_{3-8} carbocycle, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle and acyl; or are fused to each other together with the nitrogen atom to which they are bonded to form a 5- to 10-membered heterocycle which is unsubstituted or substituted by one or more substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy and fluoride;

R_5 is hydrogen, C_{1-4} alkyl, substituted C_{1-4} alkyl, C_{3-6} carbocycle, substituted C_{3-6} carbocycle, $(CH_2)_n$-C_{3-6} carbocycle or $(CH_2)_n$-R_6, n being 1, 2 or 3;

R_6 is phenyl, furan, thiophene, tetrahydrofuran, tetrahydropyran or dioxane;

R_7 is C_{1-4} alkyl, substituted C_{1-4} alkyl, C_{3-8} carbocycle, substituted C_{3-8} carbocycle, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle or substituted heterocycle;

R_8 is hydrogen, NR_3R_4, C_{3-8} carbocycle, substituted C_{3-8} carbocycle, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, C_{1-8} alkyl optionally substituted by alkoxy or halogen, C_{2-6} alkenyl optionally substituted by alkoxy or halogen, $(CH_2)_m$-C_{3-6} carbocycle optionally substituted by alkoxy or halogen, or $(CH_2)_m$-R_9, m being 1 or 2;

R_9 is phenyl, furanyl, benzofuranyl, thienyl, benzothienyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridizinyl, tetrahydrofuranyl, tetrahydropyranyl, dioxanyl, 1,4-benzodioxanyl or benzo[1,3]dioxolyl, each having one or more optional substituents selected from the group consisting of halogen, C_{1-3} alkyl and C_{1-2} alkoxy, each having one to three optional fluorine substituents; and

R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, halogen, cyano, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} sulfanyl or trifluoromethyl.

2. The compound or pharmaceutically acceptable salt of claim 1, which is selected from the group consisting of:

(3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)-morpholino-methanone;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

N-tert-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(piperidin-1-yl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)

-N-methyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N,N-diethyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-ethyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-ethyl-N-methyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

(3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)(pyrrolidin-1-yl)methanone;

(3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazol-4-yl)(piperidin-1-yl)methanone;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

N'-acetyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carbohydrazide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N'-phenyl-1H-pyrazole-4-carbohydrazide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(2-oxopropyl)-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N,N-dimethyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)

-N-methyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-ethyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-ethyl-N-methyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N,N-diethyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-N-tert-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-propyl-1H-pyrazole-4-carboxamide;

N-butyl-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-di chlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclopentyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cyclohexyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-N-cycloheptyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-fluorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-oxopropyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(2-hydroxypropyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-

1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-3-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-phenyl-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;

5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)

-N-cyclopropyl-1-(2,4-dichlorophenyl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-3-(5-(1-(4-chlorophenyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1-(2,4-dichlorophenyl)-N-isopropyl-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-oxadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-(pyridin-2-yl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-phenyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclobutyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide;
5-(4-chlorophenyl)-N-cyclopropyl-1-(2,4-dichlorophenyl)-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide; and
5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-N-isopropyl-3-(5-(1-(trifluoromethyl)cyclopropyl)-1,3,4-thiadiazol-2-yl)-1H-pyrazole-4-carboxamide.

3. A method for preparing the compound of formula (I) of claim 1, which comprises the steps of:

(i) subjecting a compound of formula (II) to bromination using NBS (N-bromosuccinimide) to obtain a compound of formula (III);

(ii) subjecting the compound of formula (III) to a substitution reaction with sodium acetate in an organic solvent to obtain an acetate compound of formula (IV);

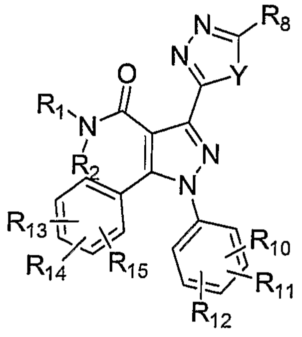
(iii) hydrolyzing the compound of formula (IV) to obtain an alcohol compound of formual (V);

(iv) oxidizing the compound of formual (V) in the presence of an oxidant to obtain an aldehyde compound of formula (VI);

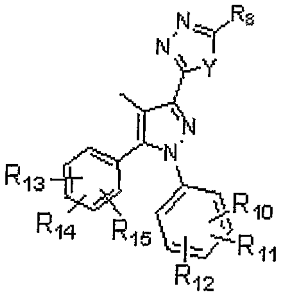
(v) further oxidizing the compound of formual (VI) in the presence of sodium chlorite and monobasic potassium phosphate to obtain a carboxylic acid compound of formula (VII);

(vi) chlorinating the compound of formula (VII) with a chlorinating agent to obtain an acid chloride compound of formula (VIII), and

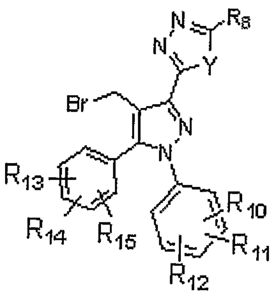
(vii) treating the compound of formula (VIII) with an amine in the presence of a base to obtain the compound of formula (**I**):



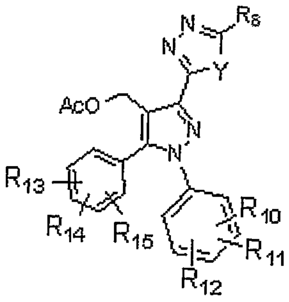
(I)



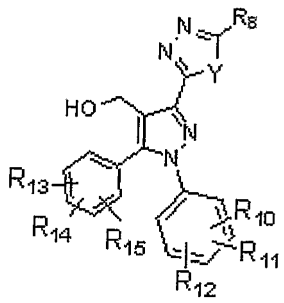
(II)



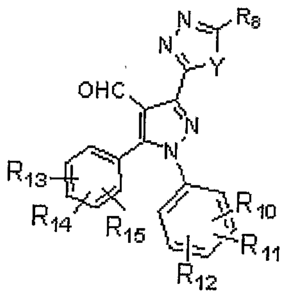
(III)



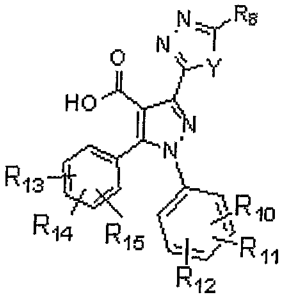
(IV)



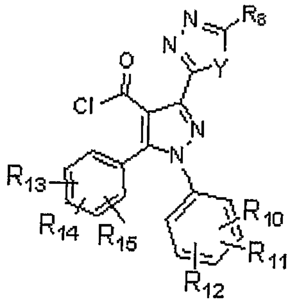
(V)



(VI)



(VII)



(VIII)

wherein, R_1, R_2, R_8 and R_{10} to R_{15} have the same meanings as defined in claim 1.

4. A pharmaceutical composition comprising the compound of formula (I) of claim 1 as an active ingredient and a pharmaceutically acceptable carrier.

5. A method for preventing or treating obesity and obesity-related metabolic disorders in a mammal, which comprises administering the compound of formula (I) of claim 1 to the mammal.

6. A method for inhibiting cannabinoid CB_1 receptor in a mammal, which comprises administering the compound of formula (I) of claim 1 to the mammal.

INTERNATIONAL SEARCH REPORT

International application No.
PCPCT/KR2007/006590

A. CLASSIFICATION OF SUBJECT MATTER

C07D 417/04(2006.01)i, C07D 413/04(2006.01)i, C07D 419/04(2006.01)i, C07D 249/08(2006.01)i, C07D 269/02(2006.01)i, C07D 285/02(2006.01)i, A61K 31/415(2006.01)i, A61K 31/4155(2006.01)i, A61P 3/04(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 8 as above

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN(REGISTRY, CAPLUS)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/087480 A1 (Sanofi-Aventis) 24 August 2006 See the whole document	1-4
A	WO 2004/035566 A1 (Pfizer Production Inc.) 29 April 2004 See the whole document	1-4
A	EP 418845 A (Fujisawa Pharmaceutical Co., Ltd.) 27 March 1991 See the whole document	1-4
A	DE 2906252 A (Merck Patent GMBH) 28 August 1980 See the whole document	1-4
A	Elkholy, Y. M. et al "Studies with pyrazol-3-carboxylic acid hydrazide: the synthesis of new pyrazolyloxadiazole and pyrazolyltriazole derivatives", Phosphorus, Sulfur and Silicon and the Related Elements (2006), 181(9), 2037-2049, ISSN: 1042-6507 See the whole document	1-4
A	Sayed, H.H. et al "Conversion of 3-arylazo-5-phenyl-2(3H)-furanones into other heterocycles of anticipated biological activity", Archiv der Pharmazie (Weinheim, Germany) (2007), 340(6), 315-319, ISSN: 0365-6233 See the whole document	1-4

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

*	Special categories of cited documents:
"A"	document defining the general state of the art which is not considered to be of particular relevance
"E"	earlier application or patent but published on or after the international filing date
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)
"O"	document referring to an oral disclosure, use, exhibition or other means
"P"	document published prior to the international filing date but later than the priority date claimed
"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&"	document member of the same patent family

Date of the actual completion of the international search 16 SEPTEMBER 2008 (16.09.2008)	Date of mailing of the international search report **16 SEPTEMBER 2008 (16.09.2008)**
Name and mailing address of the ISA/KR Korean Intellectual Property Office Government Complex-Daejeon, 139 Seonsa-ro, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer LEE, MIN JUNG Telephone No. 82-42-481-5603

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2007/006590

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 5, 6
   because they relate to subject matter not required to be searched by this Authority, namely:
   Claims 5 and 6 pertain to methods for treatment of the human or animal body by therapy, as well as diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

2. ☐ Claims Nos.:
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required addtional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/KR2007/006590

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006/087480 A1	24.08.2006.	FR 2882365 A1	25.08.2006
		FR 2882365 B1	07.09.2007
		AU 2006215443 A1	24.08.2006
		CA 2597359 A1	24.08.2006
		EP 1853595 A1	14.11.2007
WO 2004/035566 A1	29.04.2004	AU 2003267728 A1	04.05.2004
		BR 200314872 A	02.08.2005
		CA 2502511 A1	29.05.2004
		EP 1556373 A1	27.07.2005
		JP 18506366 A	23.02.2006
		US 2004077650 A1	22.04.2004
EP 418845 A1	27.03.1991	DE 69021472 C0	14.09.1995
		EP 418845 B1	09.08.1995
		GB 9008399 A0	13.06.1990
		JP 3141261 A2	17.06.1991
		RU 2021990 C1	30.10.1994
		RU 2059622 C1	10.05.1996
		US 5134142 A	28.07.1992
DE 2906252 A	28.08.1980	AU 5556280 A1	28.08.1980
		EP 14847 A1	03.09.1980
		ES 488717 A1	16.12.1980
		IL 59410 A0	30.05.1980
		JP 55120583 A2	17.09.1980
		US 4258047 A	24.03.1981