

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 October 2009 (15.10.2009)

PCT

(10) International Publication Number
WO 2009/125434 A2

(51) International Patent Classification:

C07D 413/14 (2006.01) C07D 405/14 (2006.01)
C07D 401/14 (2006.01) A61K 31/4523 (2006.01)
C07D 401/12 (2006.01) A61P 9/00 (2006.01)
C07D 409/14 (2006.01) A61P 3/00 (2006.01)

(21) International Application Number:

PCT/IN2009/000227

(22) International Filing Date:

6 April 2009 (06.04.2009)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

802/mum/2008 7 April 2008 (07.04.2008) IN
2693/MUM/2008 24 December 2008 (24.12.2008) IN

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, 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, ST, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

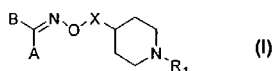
Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))



WO 2009/125434 A2

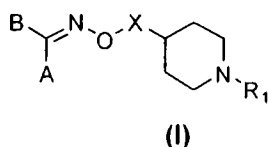
(54) Title: OXIME DERIVATIVES



(57) Abstract: The present invention relates to novel oxime derivatives of the general formula (I), their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, pharmaceutical compositions containing them, methods for their preparation, use of these compounds in medicine and the intermediates involved in their preparation.

OXIME DERIVATIVES**FIELD OF INVENTION**

The present invention relates to novel oxime derivatives of the general formula (I), their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, pharmaceutical compositions containing them, methods for their preparation, use of these compounds in medicine and the intermediates involved in their preparation.



The present invention is directed to G-protein coupled receptor (GPCR) agonists that are useful for the treatment of obesity, diabetes and related metabolic disorders.

The compounds of the general formula (I) lower blood glucose, regulate peripheral satiety, lower or modulate triglyceride levels and/or cholesterol levels and/or low-density lipoproteins (LDL) and raises the high-density lipoproteins (HDL) plasma levels and hence are useful in combating different medical conditions, where such lowering (and raising) is beneficial. Thus, it could be used in the treatment and/or prophylaxis of obesity, hyperlipidemia, hypercholesteremia, hypertension, atherosclerotic disease events, vascular restenosis, diabetes and many other related conditions.

The compounds of general formula (I) are useful to prevent or reduce the risk of developing atherosclerosis, which leads to diseases and conditions such as arteriosclerotic cardiovascular diseases, stroke, coronary heart diseases, cerebrovascular diseases, peripheral vessel diseases and related disorders.

These compounds of general formula (I) are useful for the treatment and/or prophylaxis of metabolic disorders loosely defined as Syndrome X. The characteristic features of Syndrome X include initial insulin resistance followed by hyperinsulinemia, dyslipidemia and impaired glucose tolerance. The glucose intolerance can lead to non-insulin dependent diabetes mellitus (NIDDM, Type 2 diabetes), which is characterized by hyperglycemia, which if not controlled may lead to diabetic complications or metabolic disorders caused by insulin resistance. Diabetes is no longer considered to be associated only with glucose metabolism, but it affects anatomical and physiological

parameters, the intensity of which vary depending upon stages/duration and severity of the diabetic state.

BACKGROUND OF THE INVENTION

Diabetes mellitus is a serious disease afflicting over 100 million people
5 worldwide. In the United States, there are more than 12 million diabetics, with 600,000 new cases diagnosed each year.

Diabetes mellitus is a diagnostic term for a group of disorders characterized by abnormal glucose homeostasis resulting in elevated blood sugar. There are many types of diabetes, but the two most common are Type I (also referred to as insulin-dependent
10 diabetes mellitus or IDDM) and Type II (also referred to as non-insulin-dependent diabetes mellitus or NIDDM).

The etiology of the different types of diabetes is not the same; however, everyone with diabetes has two things in common: overproduction of glucose by the liver and little or no ability to move glucose out of the blood into the cells where it
15 becomes the body's primary fuel.

People who do not have diabetes rely on insulin, a hormone made in the pancreas, to move glucose from the blood into the cells of the body. However, people who have diabetes either don't produce insulin or can't efficiently use the insulin they produce; therefore, they can't move glucose into their cells. Glucose accumulates in the
20 blood creating a condition called hyperglycemia, and over time, can cause serious health problems.

Diabetes is a syndrome with interrelated metabolic, vascular, and neuropathic components. The metabolic syndrome, generally characterized by hyperglycemia, comprises alterations in carbohydrate, fat and protein metabolism caused by absent or
25 markedly reduced insulin secretion and/or ineffective insulin action. The vascular syndrome consists of abnormalities in the blood vessels leading to cardiovascular, retinal and renal complications. Abnormalities in the peripheral and autonomic nervous systems are also part of the diabetic syndrome.

About 5% to 10% of the people who have diabetes have IDDM. These
30 individuals don't produce insulin and therefore must inject insulin to keep their blood glucose levels normal. IDDM is characterized by low or undetectable levels of endogenous insulin production caused by destruction of the insulin-producing β cells of the pancreas, the characteristic that most readily distinguishes IDDM from NIDDM. IDDM, once termed juvenile-onset diabetes, strikes young and older adults alike.

Approximately 90 to 95% of people with diabetes have Type II (or NIDDM). NIDDM subjects produce insulin, but the cells in their bodies are insulin resistant: the cells don't respond properly to the hormone, so glucose accumulates in their blood. NIDDM is characterized by a relative disparity between endogenous insulin production and insulin requirements, leading to elevated blood glucose levels. In contrast to IDDM, there is always some endogenous insulin production in NIDDM; many NIDDM patients have normal or even elevated blood insulin levels, while other NIDDM patients have inadequate insulin production (Rotwein, R. et al. N. Engl. J. Med. 308, 65-71 (1983)). Most people diagnosed with IDDM are age 30 or older, and half of all new cases are age 55 and older. Compared with whites and Asians, IDDM is more common among Native Americans, African-Americans, Latinos, and Hispanics. In addition, the onset can be insidious or even clinically inapparent, making diagnosis difficult.

The primary pathogenic lesion on NIDDM has remained elusive. Many have suggested that primary insulin resistance of the peripheral tissues is the initial event. Genetic epidemiological studies have supported this view. Similarly, insulin secretion abnormalities have been argued as the primary defect in NIDDM. It is likely that both phenomena are important contributors to the disease process (Rimoin, D. L., et. al. Emery and Rimoin's Principles and Practice of Medical Genetics 3rd Ed. 1:1401-1402 (1996)).

Many people with NIDDM have sedentary lifestyles and are obese; they weigh approximately 20% more than the recommended weight for their height and build. Furthermore, obesity is characterized by hyperinsulinemia and insulin resistance, a feature shared with NIDDM, hypertension and atherosclerosis.

Obesity and diabetes are among the most common human health problems in industrialized societies. In industrialized countries a third of the population is at least 20% overweight. In the United States, the percentage of obese people has increased from 25% at the end of the 1970s, to 33% at the beginning the 1990s. Obesity is one of the most important risk factors for NIDDM. Definitions of obesity differ, but in general, a subject weighing at least 20% more than the recommended weight for his/her height and build is considered obese. The risk of developing NIDDM is tripled in subjects 30% overweight, and three-quarters with NIDDM are overweight.

Obesity, which is the result of an imbalance between caloric intake and energy expenditure, is highly correlated with insulin resistance and diabetes in experimental

animals and human. However, the molecular mechanisms that are involved in obesity-diabetes syndromes are not clear. During early development of obesity, increase insulin secretion balances insulin resistance and protects patients from hyperglycemia (Le Stunff, et al. *Diabetes* 43, 696-702 (1989)). However, after several decades, β cell
5 function deteriorates and non-insulin-dependent diabetes develops in about 20% of the obese population (Pederson, P. *Diab. Metab. Rev.* 5, 505-509 (1989)) and (Brancati, F. L., et al., *Arch. Intern. Med.* 159, 957-963 (1999)). Given its high prevalence in modern societies, obesity has thus become the leading risk factor for NEDDM (Hill, J. O., et al., *Science* 280, 1371-1374 (1998)). The present invention is directed to G-protein coupled
10 receptor (GPCR) agonists. In particular, the present invention is directed to agonists of GPR 119 that are useful for the treatment of obesity, e.g. as regulators of satiety, and for the treatment of diabetes.

Obesity is characterized by an excessive adipose tissue mass relative to body size. Clinically, body fat mass is estimated by the body mass index (BMI; $\text{weight}(\text{kg})/\text{height}(\text{m})^2$), or waist circumference. Individuals are considered obese when
15 the BMI is greater than 30 and there are established medical consequences of being overweight. It has been an accepted medical view for some time that an increased body weight, especially as a result of abdominal body fat, is associated with an increased risk for diabetes, hypertension, heart disease, and numerous other health complications,
20 such as arthritis, stroke, gallbladder disease, muscular and respiratory problems, back pain and even certain cancers. However, the factors which predispose a fraction of patients to alteration of insulin secretion in response to fat accumulation remain unknown.

Pharmacological approaches to the treatment of obesity have been mainly
25 concerned with reducing fat mass by altering the balance between energy intake and expenditure. Many studies have clearly established the link between adiposity and the brain circuitry involved in the regulation of energy homeostasis. Direct and indirect evidence suggest that serotonergic, dopaminergic, adrenergic, cholinergic, endocannabinoid, opioid, and histaminergic pathways in addition to many neuropeptide
30 pathways (e.g. neuropeptide Y and melanocortins) are implicated in the central control of energy intake and expenditure. Hypothalamic centres are also able to sense peripheral hormones involved in the maintenance of body weight and degree of adiposity, such as insulin and leptin, and fat tissue derived peptides.

Drugs aimed at the pathophysiology associated with insulin dependent Type I diabetes and non-insulin dependent Type II diabetes have many potential side effects and do not adequately address the dyslipidaemia and hyperglycaemia in a high proportion of patients. Treatment is often focused at individual patient needs using diet, exercise, hypoglycaemic agents and insulin, but there is a continuing need for novel antidiabetic agents, particularly ones that may be better tolerated with fewer adverse effects.

Similarly, metabolic syndrome (syndrome X) which is characterized by hypertension and its associated pathologies including atherosclerosis, lipidemia, hyperlipidemia and hypercholesterolemia have been associated with decreased insulin sensitivity which can lead to abnormal blood sugar levels when challenged. Myocardial ischemia and microvascular disease is an established morbidity associated with untreated or poorly controlled metabolic syndrome.

There is a continuing need for novel antiobesity and antidiabetic agents, particularly ones that are well tolerated with few adverse effects.

The present invention is directed to G-protein coupled receptor agonists of GPR 119 that are useful for the treatment of obesity, e.g. as regulators of satiety, and for the treatment of diabetes. GPR 119 is a GPCR identified as SNORF25 in WO00/50562 which discloses both the human and rat receptors, US 6,468,756 also discloses the mouse receptor (accession numbers: AAN95194 (human), AAN95195 (rat) and ANN95196 (mouse)).

In humans, GPR 119 is expressed in the pancreas, small intestine, colon and adipose tissue. A Role of G Protein-Coupled Receptor 119 Expressed in β -Cell- in Glycemic Control by Enhancing Glucose Dependent Insulin Release was demonstrated by using an agonist of GPR-119 (Endocrinology 148(6):2601–2609). Further the anti obesity effects of GPR-119 agonist which suppress food intake in rats and reduce body weight gain and white adipose tissue deposition upon subchronic oral administration to high-fat-fed rats was also demonstrated (CELL METABOLISM 3, 167–175). GPR119 therefore represents a novel and attractive potential target for the therapy of obesity and related metabolic disorders.

International patent applications WO2005/061489, WO2007116230, WO2007116229, WO2007003964, WO2007003962, WO2007003961, WO2006070208 discloses heterocyclic derivatives as GPR 119 receptor agonists. However, the therapeutic potential of these compounds to treat diseases has not yet

been proved and so there remains the need to develop newer medicines which are better or of comparable efficacy with the present treatment regimes, have lesser side effects and require a lower dosage regime

We herein disclose novel compounds of formula (I) useful as antidiabetic, anti-obesity, hypolipidaemic, hypolipoproteinemic, and antihyperglycemic agents which may have additional body weight lowering effect and beneficial effect in the treatment and/or prophylaxis of diseases caused by hyperlipidaemia, diseases classified under Syndrome X and atherosclerosis, and methods for their preparation.

PREFERRED EMBODIMENTS OF THE INVENTION

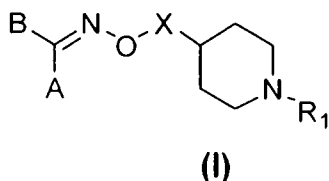
The main objective of the present invention is to provide novel substituted oximes and their derivatives represented by the general formula (I), their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, and pharmaceutical compositions containing them or their mixtures thereof.

In an embodiment of the present invention is provided a process for the preparation of novel substituted oximes and their derivatives represented by the general formula (I), their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts.

In a further embodiment of the present invention is provided pharmaceutical compositions containing compounds of the general formula (I), their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, or their mixtures in combination with suitable carriers, solvents, diluents and other media normally employed in preparing such compositions.

DETAILED DESCRIPTION OF THE INVENTION

Accordingly, the present invention relates to compounds of the general formula (I),



their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, and pharmaceutical compositions containing them wherein

each of 'A' and 'B' independently represents H, optionally substituted linear or branched (C₁-C₆)alkyl or an optionally substituted single or fused group selected from aryl, heteroaryl, heterocyclyl, cycloalkyl groups; 'X' represents either a bond or a group represented by Y-Z, wherein Z represents O, NH or a further bond and Y represents linear or branched optionally substituted (C₁-C₆)alkyl or an optionally substituted single or fused group selected from aryl, heteroaryl, cycloalkyl groups; R₁ represents optionally substituted groups selected from linear or branched (C₁-C₆)alkyl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl or C(O)OR₂ wherein R₂ represents optionally substituted groups selected from linear or branched (C₁-C₆)alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroaralkyl groups.

In a preferred embodiment, the alkyl groups may be selected from methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *tert*-butyl, amyl, *t*-amyl, *n*-pentyl, *n*-hexyl, *iso*-hexyl groups;

The aryl group may be an aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be fused; in a preferred embodiment such aryl group may be selected from phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl groups;

The heteroaryl group represents 5 to 8 membered aromatic radicals, which may be single or fused containing one or more hetero atoms selected from O, N or S; in a preferred embodiment such groups may be selected from pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, isothiazolyl, imidazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzothienyl, indolinyl, indolyl, azaindolyl, azaindolonyl, benzodihydrofuranyl, Benzo[1,3]dioxole, benzodihydrothienyl, pyrazolopyrimidinyl, pyrazolopyrimidonyl, azaquinazoliny, azaquinazolinoyl, pyridofuranyl, pyridothienyl, thienopyrimidyl, thienopyrimidonyl, quinolinyl, pyrimidinyl, pyrazolyl, quinazoliny, quinazolonyl, pyrimidonyl, pyridazinyl, triazinyl, benzoxazinyl, benzoxazinonyl, benzothiazinyl, benzothiazinonyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, benzotriazolyl, phthalazynyl, naphthylidinyl, purinyl, carbazolyl, phenothiazinyl, phenoxazinyl groups;

The term "heterocyclyl" represents saturated, partially saturated and unsaturated ring-shaped radicals, the heteroatoms selected from nitrogen, sulfur and oxygen; in a preferred embodiment such groups may be selected from aziridinyl, azetidiny, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, 2-oxopiperidinyl, 4-

oxopiperidinyl, 2-oxopiperazinyl, 3-oxopiperazinyl, morpholinyl, thiomorpholinyl, 2-oxomorpholinyl, azepinyl, diazepinyl, oxapinyl, thiazepinyl, oxazolidinyl, thiazolidinyl, and the like; examples of partially saturated heterocyclic radicals include dihydrothiophene, dihydropyran, dihydrofuran, dihydrothiazole groups;

5 When any of 'A', 'B' 'Y' 'R₁' or 'R₂' is substituted with one or more groups, the substituents may be independently selected from groups hydroxyl, oxo, halo, thio, nitro, amino, cyano, formyl, or substituted or unsubstituted groups selected from amidino, alkyl, haloalkyl, perhaloalkyl, alkoxy, haloalkoxy, perhaloalkoxy, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, bicycloalkenyl, alkenoxy, cycloalkoxy,
10 aryl, aryloxy, aralkyl, aralkoxy, heterocylyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, heterocyclylalkoxyacyl, acyl, acyloxy, acylamino, monosubstituted or disubstituted amino, arylamino, aralkylamino, carboxylic acid and its derivatives such as esters and amides, carbonylamino, hydroxyalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl,
15 aralkoxyalkyl, alkylthio, thioalkyl, arylthio, alkylsulfonylamino, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkoxyamino, hydroxyl amino, sulfenyl derivatives, sulfonyl derivatives, sulfonyloxy derivatives, sulfonic acid and its derivatives.

 Preferred substituents on any of 'A', 'B' 'Y' 'R₁' or 'R₂' may be selected from
20 hydroxyl, oxo, halo, thio, nitro alkyl, alkenyl, haloalkyl alkoxy, haloalkoxy aryl, aryloxy, aralkyl, aralkoxy, heterocylyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy hydroxyalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl alkylthio, thioalkyl, arylthio sulfenyl derivatives, sulfonyl derivatives, sulfonyloxy derivatives, sulfonic acid and its derivatives, carboxylic acid and its
25 derivatives such as esters and amides.

 When the substituents on any of 'A', 'B' 'Y' 'R₁' or R₂ are further substituted, those substituents are independently selected from hydroxyl, oxo, halo, thio, nitro, amino, cyano, formyl, or substituted or unsubstituted groups selected from amidino, alkyl, haloalkyl, perhaloalkyl, alkoxy, haloalkoxy, perhaloalkoxy, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, bicycloalkenyl, alkoxy, alkenoxy, cycloalkoxy,
30 aryl, aryloxy, aralkyl, aralkoxy, heterocylyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, heterocyclylalkoxy, heterocyclylalkoxyacyl, acyl, acyloxy, acylamino, monosubstituted or disubstituted amino, arylamino, aralkylamino, carboxylic acid and its derivatives such as esters and

amides, carbonylamino, hydroxyalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, arylthio, alkylsulfonylamino, alkoxy carbonylamino, aryloxy carbonylamino, aralkyloxy carbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkoxyamino, hydroxyl amino, sulfenyl derivatives, sulfonyl derivatives, sulfonyloxy derivatives, sulfonic acid and its derivatives.

In a preferred embodiment, when the substituents on any of 'A', 'B' 'Y' 'R₁' or R₂ are further substituted, those substituents are selected from hydroxyl, oxo, halo, thio, nitro, amino, alkoxy, carboxylic acid and its derivatives such as esters and amides, acyl, sulfenyl derivatives, sulfonyl derivatives, sulfonyloxy derivatives, sulfonic acid and its derivatives.

In a still further preferred embodiment, when any of A, B, R₁ or Y independently represents an aryl group, the aryl groups are selected from phenyl, naphthyl, tetrahydronaphthyl groups;

When any of A or B independently represents a heteroaryl, the preferred groups are selected from pyridyl, thienyl, benzofuranyl, Benzo[1,3]dioxole, benzimidazolyl, benzothiazinonyl, benzothiazinonyl, phenothiazinyl, phenoxazinyl isoxazolyl, furyl, oxazolyl, thiazolyl, indolyl groups;

When any of A or B independently represents a heterocyclyl group, the preferred groups are selected from pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, oxazolidinyl, thiazolidinyl groups;

When 'Y' represents a heteroaryl group, the preferred groups are selected from pyrimidinyl, pyridyl, pyridazinyl, phthalazynil, benzoxazinyl, benzimidazolyl, benzotriazolyl groups;

When R₁ represents a heteroaryl group, the preferred groups selected from oxadiazolyl, pyridyl, pyrimidinyl, triazinyl, triazolyl, tetrazolyl, purinyl groups; When R₁ represents a heterocyclyl group, the preferred groups selected from pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl groups;

The various groups, radicals and substituents used anywhere in the specification are further described in the following paragraphs.

- the "alkyl" group used either alone or in combination with other radicals, denotes a linear or branched radical containing one to six carbons, selected from methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *tert*-butyl, amyl, *t*-amyl, *n*-pentyl, *n*-hexyl, and the like;

- the "alkenyl" group used either alone or in combination with other radicals, is selected from a radical containing from two to six carbons, more preferably groups selected from vinyl, allyl, 2-butenyl, 3-butenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl and the like; the "alkenyl" group includes dienes and trienes of straight and branched chains wherever applicable;
- 5 - the "alkynyl" group used either alone or in combination with other radicals, is selected from a linear or branched radical containing two to six carbon atoms, more preferably thynyl, 1-propynyl, 2-propynyl, 1-butylnyl, 2-butylnyl, 3-butylnyl, 1-pentylnyl, 2-pentylnyl, 3-pentylnyl, 4-pentylnyl, 1-hexynyl, and the like. The term
10 "alkynyl" includes di- and tri-yne wherever applicable;
- the "cycloalkyl", or "alicyclic" group used either alone or in combination with other radicals, is selected from a cyclic radical containing three to six carbons, more preferably cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like; The terms "bicycloalkyl" means more than one cycloalkyl groups fused together;
- 15 - the "cycloalkenyl" group used either alone or in combination with other radicals, are preferably selected from cyclopropenyl, 1-cyclobutenyl, 2-cyclobutenyl, 1-cyclopentenyl, 2-cyclopentenyl, 3-cyclopentenyl, 1-cyclohexenyl, 2-cyclohexenyl, 3-cyclohexenyl and the like. The terms "bicycloalkenyl" means more than one cycloalkenyl groups fused together;
- 20 - the "alkoxy" group used either alone or in combination with other radicals, is selected from groups containing an alkyl radical, as defined above, attached directly to an oxygen atom, more preferably groups selected from methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *t*-butoxy, *iso*-butoxy, pentyloxy, hexyloxy, and the like;
- 25 - the "cycloalkoxy" group used either alone or in combination with other radicals, is selected from groups containing an cycloalkyl radical, as defined above, attached directly to an oxygen atom, more preferably groups selected from cyclopropoxy, cyclobutoxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy and the like;
- the "aryloxy" group used either alone or in combination with other radicals, is
30 selected from groups containing an aryl radical, as defined above, attached directly to an oxygen atom, more preferably groups selected from phenoxy, naphthyloxy, tetrahydronaphthyloxy, biphenyloxy, and the like;
- the "aralkyl" group used either alone or in combination with other radicals, is selected from groups containing an aryl radical, as defined above, attached directly

- to an alkyl radical, as define above, more preferably groups selected from benzyl, phenethyl, and the like;
- the "aralkoxy" group used either alone or in combination with other radicals, is selected from groups containing an aralkyl radical, as defined above, attached directly to an oxygen atom, more preferably groups selected from benzyloxy, phenethyloxy, and the like;
 - the "heteroaralkyl" group used either alone or in combination with other radicals, is selected from groups containing an heteroaryl radical, as defined above, attached directly to an alkyl radicals, as define above, more preferably groups selected from pyridinealkyl, thiophenealkyl, quinolinealkyl, and the like;
 - the "alkenoxy" group used either alone or in combination with other radicals, is selected from groups containing an alkenyl radical, as defined above, attached to an oxygen atom, more preferably selected from vinyloxy, allyloxy, butenoxy, pentenoxy, hexenoxy, and the like;
 - the "haloalkyl" group is selected from an alkyl radical, as defined above, suitably substituted with one or more halogens; such as perhaloalkyl, more preferably, perfluoro (C₁-C₆)alkyl such as fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, mono or polyhalo substituted methyl, ethyl, propyl, butyl, pentyl or hexyl groups;
 - the "haloalkoxy" group is selected from suitable haloalkyl, as defined above, directly attached to an oxygen atom, more preferably groups selected from fluoromethoxy, chloromethoxy, fluoroethoxy, chloroethoxy and the like;
 - the "perhaloalkoxy" group is selected from a suitable perhaloalkyl radical, as defined above, directly attached to an oxygen atom, more preferably groups selected from trifluoromethoxy, trifluoroethoxy, and the like;
 - the groups "heteroaryloxy", "heteroaralkoxy", "heterocycloxy", "heterocylylalkoxy" are selected from suitable heteroaryl, heteroarylalkyl, heterocyclyl, heterocylylalkyl groups respectively, as defined above, attached to an oxygen atom;
 - the "acyl" group used either alone or in combination with other radicals, is selected from a radical containing one to eight carbons, more preferably selected from formyl, acetyl, propanoyl, butanoyl, *iso*-butanoyl, pentanoyl, hexanoyl, heptanoyl, benzoyl and the like, which may be substituted;

- the “acyloxy” group used either alone or in combination with other radicals, is selected from a suitable acyl group, as defined above, directly attached to an oxygen atom, more preferably such groups are selected from acetyloxy, propionyloxy, butanoyloxy, *iso*-butanoyloxy, benzoyloxy and the like;
- 5 - the “acylamino” group used either alone or in combination with other radicals, is selected from a suitable acyl group as defined earlier, attached to an amino radical, more preferably such groups are selected from CH₃CONH, C₂H₅CONH, C₃H₇CONH, C₄H₉CONH, C₆H₅CONH and the like, which may be substituted;
- the “mono-substituted amino” group used either alone or in combination with other
10 radicals, represents an amino group substituted with one group selected from (C₁-C₆)alkyl, substituted alkyl, aryl, substituted aryl or arylalkyl groups as defined earlier, more preferably such groups are selected from methylamine, ethylamine, *n*-propylamine, *n*-butylamine, *n*-pentylamine and the like;
- the “disubstituted amino” group used either alone or in combination with other
15 radicals, represents an amino group, substituted with two radicals that may be same or different selected from (C₁-C₆)alkyl, substituted alkyl, aryl, substituted aryl, or arylalkyl groups, as defined above, more preferably the groups are selected from dimethylamino, methylethylamino, diethylamino, phenylmethyl amino and the like;
- the “arylamino” used either alone or in combination with other radicals, represents
20 an aryl group, as defined above, linked through amino having a free valence bond from the nitrogen atom, more preferably the groups are selected from phenylamino, naphthylamino, N-methyl anilino and the like;
- the “oxo” or “carbonyl” group used either alone (-C=O-) or in combination with other radicals such as alkyl described above, for e.g. “alkylcarbonyl”, denotes a
25 carbonyl radical (-C=O-) substituted with an alkyl radical described above such as acyl or alkanoyl;
- the “carboxylic acid” group, used alone or in combination with other radicals, denotes a -COOH group, and includes derivatives of carboxylic acid such as esters and amides;
- 30 - the “ester” group used alone or in combination with other radicals, denotes -COO- group, and includes carboxylic acid derivatives, more preferably the ester moieties are selected from alkoxycarbonyl, such as methoxycarbonyl, ethoxycarbonyl, and the like, which may optionally be substituted; aryloxycarbonyl group such as phenoxycarbonyl, naphthyloxycarbonyl, and the like, which may optionally be

substituted; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethyloxycarbonyl, naphthylmethoxycarbonyl, and the like, which may optionally be substituted; heteroaryloxycarbonyl, heteroaralkoxycarbonyl, wherein the heteroaryl group, is as defined above, which may optionally be substituted;
5 heterocyclyloxycarbonyl, where the heterocyclic group, as defined earlier, which may optionally be substituted;

- the "amide" group used alone or in combination with other radicals, represents an aminocarbonyl radical ($\text{H}_2\text{N}-\text{C}=\text{O}$), wherein the amino group is mono- or di-substituted or unsubstituted, more preferably the groups are selected from methyl
10 amide, dimethyl amide, ethyl amide, diethyl amide, and the like;

- the "aminocarbonyl" group used either alone or in combination with other radicals, may be selected from 'aminocarbonyl', 'aminocarbonylalkyl', "n-alkylaminocarbonyl", "N-arylaminocarbonyl", "N,N-dialkylaminocarbonyl", "N-alkyl-N-arylaminocarbonyl", "N-alkyl-N-hydroxyaminocarbonyl", and "N-alkyl-
15 N-hydroxyaminocarbonylalkyl", each of them being optionally substituted. The terms "N-alkylaminocarbonyl" and "N,N-dialkylaminocarbonyl" denotes aminocarbonyl radicals, as defined above, which have been substituted with one alkyl radical and with two alkyl radicals, respectively. Preferred are "lower alkylaminocarbonyl" having lower alkyl radicals as described above attached to
20 aminocarbonyl radical. The terms "N-arylaminocarbonyl" and "N-alkyl-N-arylaminocarbonyl" denote aminocarbonyl radicals substituted, respectively, with one aryl radical, or one alkyl, and one aryl radical. The term "aminocarbonylalkyl" includes alkyl radicals substituted with aminocarbonyl radicals;

- the "hydroxyalkyl" group used either alone or in combination with other radicals, is
25 selected from an alkyl group, as defined above, substituted with one or more hydroxy radicals, more preferably the groups are selected from hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, hydroxypentyl, hydroxyhexyl and the like;

- the "aminoalkyl" group used alone or in combination with other radicals, denotes
30 an amino ($-\text{NH}_2$) moiety attached to an alkyl radical, as defined above, which may be substituted, such as mono- and di-substituted aminoalkyl. The term "alkylamino" used herein, alone or in combination with other radicals, denotes an alkyl radical, as defined above, attached to an amino group, which may be substituted, such as mono- and di-substituted alkylamino;

- the “alkoxyalkyl” group used alone or in combination with other radicals, denotes an alkoxy group, as defined above, attached to an alkyl group as defined above, more preferably the groups may be selected from methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl and the like;
- 5 - the “alkylthio” group used either alone or in combination with other radicals, denotes a straight or branched or cyclic monovalent substituent comprising an alkyl group as defined above, linked through a divalent sulfur atom having a free valence bond from the sulfur atom, more preferably the groups may be selected from methylthio, ethylthio, propylthio, butylthio, pentylthio and the like or cyclic
10 alkylthio selected from cyclopropylthio, cyclobutylthio, cyclopentylthio, cyclohexylthio and the like, which may be optionally substituted;
- the “thioalkyl” group used either alone or in combination with other radicals, denotes an alkyl group, as defined above, attached to a group of formula $-SR'$, where R' represents hydrogen, alkyl or aryl group, e.g. thiomethyl,
15 methylthiomethyl, phenylthiomethyl and the like, which may be optionally substituted.
- the “alkoxycarbonylamino” group used alone or in combination with other radicals, is selected from a suitable alkoxycarbonyl group, as defined above, attached to an amino group, more preferably methoxycarbonylamino, ethoxycarbonylamino, and
20 the like;
- the “aminocarbonylamino”, “alkylaminocarbonylamino”, “dialkylaminocarbonylamino” groups used alone or in combination with other radicals, is a carbonylamino ($-CONH_2$) group, attached to amino(NH_2), alkylamino group or dialkylamino group respectively, where alkyl group is as defined above;
- 25 - the “amidino” group used either alone or in combination with other radicals, represents a $-C(=NH)-NH_2$ radical; the “alkylamidino” group represents an alkyl radical, as described above, attached to an amidino group;
- the “alkoxyamino” group used either alone or in combination with other radicals, represents a suitable alkoxy group as defined above, attached to an amino group;
- 30 - the “hydroxyamino” group used either alone or in combination with other radicals, represents a $-NHOH$ moiety, and may be optionally substituted with suitable groups selected from those described above;
- the “sulfenyl” group or “sulfenyl derivatives” used alone or in combination with other radicals, represents a bivalent group, $-SO-$ or R_xSO , where R_x is an optionally

substituted alkyl, aryl, heteroaryl, heterocyclyl, group selected from those described above;

- the "sulfonyl" group or "sulfones derivatives" used either alone or in combination with other radicals, with other terms such as alkylsulfonyl, represents a divalent radical $-\text{SO}_2-$, or R_xSO_2- , where R_x is as defined above. More preferably, the groups may be selected from "alkylsulfonyl" wherein suitable alkyl radicals, selected from those defined above, is attached to a sulfonyl radical, such as methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like, "arylsulfonyl" wherein an aryl radical, as defined above, is attached to a sulfonyl radical, such as phenylsulfonyl and the like.
- the "sulfonyloxy" group used either alone or in combination with other radicals, with other terms such as alkylsulfonyloxy, represents a divalent radical $-\text{SO}_3-$, or R_xSO_3- , where R_x is as defined above. More preferably, the groups may be selected from "alkylsulfonyl" wherein suitable alkyl radicals, selected from those defined above, is attached to a sulfonyloxy radical, such as methanesulfonyloxy, ethanesulfonyloxy, propanesulfonyloxy and the like, "arylsulfonyl" wherein an aryl radical, as defined above, is attached to a sulfonyl radical, such as benzenesulfonyloxy and the like

Suitable groups and substituents on the groups may be selected from those described anywhere in the specification.

Particularly useful compounds may be selected from

1-(4-(Methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

1-(4-(Methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime;

tert-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate;

1-(4-(Methylsulfonyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

iso-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;

iso-propyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;

- iso*-propyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-
- 5 carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-
- carboxylate;
- iso*-propyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-
- 10 yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(4-nitrophenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-*p*-tolylethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 15 *iso*-propyl 4-(6-(1-(4-fluorophenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(4-methoxyphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(naphthalen-2-yl)ethylideneaminoxy)pyrimidin-4-
- 20 yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(benzofuran-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(4-butylphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 25 *iso*-propyl 4-(6-(1-(4-methoxy-3-methylphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(pyridin-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(3,4-dimethoxyphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-
- 30 yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;

- iso*-propyl 4-(6-(1-(4-methoxyphenyl)hexylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(diphenylmethyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 5 *iso*-propyl 4-(5-methyl-6-(phenyl(pyridin-2-yl)methyleneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(bis(4-fluorophenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-((3,4-difluorophenyl)(phenyl)methyleneaminoxy)-5-methylpyrimidin-10 4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(bis(4-methoxyphenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 15 *tert*-butyl 4-(6-(1-(2-fluoro-4-(methylsulfonyl)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-methyl-6-(1-(4-
- 20 (trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-
- 25 yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(benzyloxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-nitro-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 30 *iso*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-butyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;

- iso*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-butyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 5 Ethyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Ethyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Ethyl 4-(6-(1-(4-(allyloxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 10 Phenyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Phenyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 15 Phenyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Benzyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Benzyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 20 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-Methoxyphenyl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 25 1-p-tolyethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(Pyridin-3-yl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-Fluorophenyl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 30 1-(Benzo[d][1,3]dioxol-5-yl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

- 1-(Benzo[d][1,3]dioxol-5-yl)ethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-(2-Fluoro-4-(methylsulfonyl)phenyl)ethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 5 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(Benzo[d][1,3]dioxol-5-yl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Methylsulfonyl)phenyl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 10 1-(Pyridin-3-yl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-6-(1-benzylpiperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 15 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-5-methyl-6-(1-(3-nitropyridin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- (1-(4-(Methylsulfonyl)phenyl)ethanone-O-5-methyl-6-(1-(3-nitropyridin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- tert*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)-1,4'-bipiperidine-1'-carboxylate;
- 20 *tert*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 25 *tert*-butyl 4-(6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 30 *tert*-butyl 4-(6-(1-p-tolylethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-fluorophenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;

- tert*-butyl 4-(6-(1-(pyridin-3-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 5 *tert*-butyl 4-(6-(1-(benzofuran-2-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-methoxyphenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 10 1-(4-(Trifluoromethoxy)phenyl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime;
- tert*-butyl 4-(2-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 15 *tert*-butyl 4-(2-(1-(pyridin-3-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(biphenyl-4-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(pyridin-4-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 20 *tert*-butyl 4-(2-(1-(pyridin-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(benzofuran-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-p-tolylethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-fluorophenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 25 *tert*-butyl 4-(2-(1-(naphthalen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 30 *tert*-butyl 4-(2-(1-(5-chlorothiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(thiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;

- tert*-butyl 4-(2-(1-(4-methoxyphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(3,4-dimethoxyphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 5 *tert*-butyl 4-(2-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(5-methylthiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-methoxy-3-methylphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 10 *tert*-butyl 4-(2-(1-(4-nitrophenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(3,4-
- 15 bis(trifluoromethyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-butylphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(2-fluoro-4-
- (methylsulfonyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(diphenylmethyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- 20 *tert*-butyl 4-(2-(phenyl(pyridin-2-yl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-((4-methoxyphenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(bis(4-methoxyphenyl)methyleneaminoxy)ethoxy)piperidine-1-
- 25 carboxylate;
- tert*-butyl 4-(2-((4-chlorophenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-((3,4-difluorophenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- 30 *tert*-butyl 4-(3-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)propyl)piperidine-1-carboxylate;
- 1-(4-(Methylsulfonyl)phenyl)ethanone O-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yl oxime;

tert-butyl 4-((1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate;

tert-butyl 4-((1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate;

5 *tert*-butyl 4-((1-(2-fluoro-4-(methylsulfonyl)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate;

tert-butyl 4-(3-(diphenylmethyleneaminoxy)propyl)piperidine-1-carboxylate;

tert-butyl 4-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)piperidine-1-carboxylate;

10 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yl oxime;...

The following compounds can be prepared according to the processes of the invention including their suitable variations, as disclosed elsewhere in the specification.

Benzaldehyde-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

15 Acetophenone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

1-(4-Methoxyphenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

20 1-p-tolyethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

1-(4-Fluorophenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

25 1-(4-(Trifluoromethyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

1-(Naphthalen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

1-(Thiophen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

30 1-(Benzofuran-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

Benzophenone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

Bis(4-fluorophenyl)methanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

5 Benzaldehyde O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

Acetophenone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

10 1-(4-Methoxyphenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

1-p-tolyloethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

1-(4-Fluorophenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

15 1-(4-(Trifluoromethyl)phenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

1-(Naphthalen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

20 1-(Thiophen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

1-(Benzofuran-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

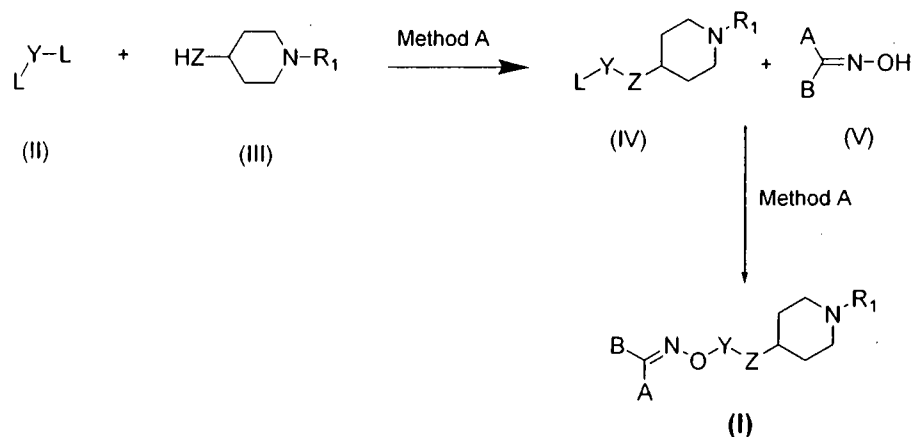
25 Benzophenone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

Bis(4-fluorophenyl)methanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

The novel compounds of this invention may be prepared using the reactions and techniques described in this section. The reactions are performed in solvents appropriate to the reagents and materials employed and are suitable for the transformations being effected. It is understood by those skilled in the art that the nature and order of the synthetic steps presented may be varied for the purpose of optimizing the formation of the compounds of the present invention and also that

certain steps may be modified, altered, obvious steps added or deleted in order to optimize as well as required for preparing the compounds of the present invention. Such, obvious changes should also be considered as being part of the present invention.

Scheme 1: Compounds of general formula (I) where A, B, Z and R₁ are as defined earlier and Y represents aryl, heteroaryl, heterocyclyl, cycloalkyl may be prepared according to the scheme described here

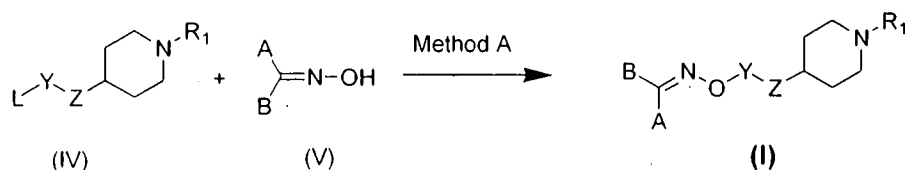


Scheme 1

The process of synthesizing the compounds of general formula (I) comprises the steps of

- 10 i. reacting compounds of general formula (II), Where L represents a suitable leaving group such as halogen, mesylate, tosylate, triflate & the like and Y is as defined earlier with compounds of general formula (III), where Z and R₁ are as defined earlier to yield compound of general formula (IV) where all symbols are as defined earlier;
- 15 ii. Reacting compound of general formula (IV) where all symbols are as defined earlier, with compounds of general formula (V) where all symbols are as defined earlier to yield the compound of general formula (I).

Scheme 2: Compounds of general formula (I) where A, B, Z and R₁ are defined earlier and Y represents linear or branched C₍₁₋₆₎alkyl may be prepared according to the following scheme



Scheme 2

The following examples further illustrate the processes of preparing compounds of formula (I) according to the present invention and are provided for illustration only. Such disclosure should not be construed as limiting the scope of the present invention in any way.

5 *¹H NMR spectral data given in the examples (vide infra) are recorded using a 400 MHz spectrometer (Bruker AVANCE-400) and reported in δ scale. Until and otherwise mentioned the solvent used for NMR is CDCl₃.*

Example 1

1-(4-(methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

10 Step I: Preparation of 5-(4-(6-chloro-5-methylpyrimidin-4-yloxy)piperidin-1-yl)-3-isopropyl-1,2,4-oxadiazole.

Pottasium *tert*-butoxide (478 mg, 0.00426 moles) was added to a solution of 1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-ol (0.9 gm, 0.00426 moles) and 4,6-
15 dichloro-5-methylpyrimidine (690 mg, 0.00426 moles) in dry THF (30 ml) at 0 °C and the reaction mixture was stirred for 20 hours at 30 °C. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extract was washed with water and brine, dried over sodium sulfate and evaporated under reduced pressure to yield 900 mg off white solid product.

20 ¹HNMR: 1.29 (6H, d, *J*=7.2 Hz), 1.89-1.97 (2H, m), 2.07-2.24 (2H, m), 2.24 (3H, s), 2.86-2.93 (1H, m), 3.60-3.66 (2H, m), 3.81-3.87 (2H, m), 5.40-5.45 (1H, m), 8.40 (1H, m).

Step II: Preparation of 1-(4-(methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

25 Cesium carbonate (1.29 gm, 0.00397 moles) was added to a solution of 5-(4-(6-chloro-5-methylpyrimidin-4-yloxy)piperidin-1-yl)-3-isopropyl-1,2,4-oxadiazole (900 mg, 0.00266 moles) and 1-(4-(methylsulfonyl)phenyl)ethanone oxime (567 mg, 0.00266 moles) in dry DMF (10 ml) and reaction mixture was stirred for 6 hours at 30 °C. Then reaction mixture was poured into ice cold water and extracted with ethyl acetate.

30 Organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure to obtain 900 mg of product.

¹HNMR: 1.29 (6H, d, *J*=6.8 Hz), 1.30 (3H, s), 1.92-1.97 (2H, m), 2.08-2.14 (2H, m), 2.15 (3H, s), 2.54 (3H, s), 2.88-2.92 (1H, m), 3.06 (3H, s), 3.61-3.68 (2H, m), 3.82-3.88 (2H, m), 5.43-5.44 (1H, m), 7.97-8.02 (4H, m), 8.43 (1H, s).

Example 2

1-(4-(Methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime

Step I: Preparation of 5-(4-(6-chloropyridazin-3-yloxy)piperidin-1-yl)-3-*iso*-propyl-1,2,4-oxadiazole.

Pottasium *tert*-butoxide (1.1 gm, 0.00994 moles) was added to a solution of 1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-ol (2.1 gm, 0.00994 moles) and 3,6-dichloropyridazine (1.5 gm, 0.00994 moles) in dry THF (30 ml) at 0 °C and then reaction mixture was stirred for 4 hours at 30 °C. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extract was washed with water and brine, dried over sodium sulfate and evaporated under reduced pressure to give 1.2 gm product.

¹HNMR: 1.29 (6H, d, *J*=6.8 Hz), 1.90-1.98 (2H, m), 2.15-2.22 (2H, m), 2.86-2.93 (1H, m), 3.53-3.59 (2H, m), 3.89-3.94 (2H, m), 5.49-5.55 (1H, m), 6.95 (1H, d, *J*=9.2 Hz), 7.40 (1H, d, *J*=9.2 Hz).

Step II: Preparation of 1-(4-(methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime.

Cesium carbonate (755 mg, 0.002317 moles) was added to a solution to 5-(4-(6-chloropyridazin-3-yloxy)piperidin-1-yl)-3-*iso*-propyl-1,2,4-oxadiazole (500 mg, 0.001545 moles) and 1-(4-(methylsulfonyl)phenyl)ethanone oxime (329.0 mg, 0.001545 moles) in dry DMF (10 ml) and the reaction mixture was stirred at 60 °C for 4 hours. Then reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure. The crude product obtained was purified by flash column chromatography (silica gel) using 40% ethyl acetate in hexane as eluent to obtain 1 gm of product.

¹HNMR: 1.29 (6H, d, *J*=4.4 Hz), 1.93-1.98 (2H, m), 2.17-2.22 (2H, m), 2.58 (3H, s), 2.86-2.93 (1H, m), 3.08 (3H, s), 3.54-3.60 (2H, m), 3.88-3.94 (2H, m), 5.50-5.52 (1H, m), 7.00 (1H, d, *J*=9.6 Hz), 7.55 (1H, d, *J*=9.6 Hz), 7.96 (2H, dd, *J*=6.8 & 2.4 Hz), 8.00 (2H, dd, *J*=6.2 & 2.4 Hz).

Example 3

tert-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate

Step I: Preparation of *tert*-butyl 4-(6-chloro-5-methylpyrimidin-4-ylamino)piperidine-1-carboxylate

Pottasium carbonate (437.7 mg, 0.00317 moles) was added to a solution of *tert*-butyl 4-aminopiperidine-1-carboxylate (317.6 mg, 0.001586 moles) and 4,6-dichloro-5-methylpyrimidine (200 mg, 0.001586 moles) in dry THF (10 ml) at 30 °C and the reaction mixture was stirred for 24 hours at 30 °C. The reaction mixture was poured into ice cold water and solid product was filtered and dried over P₂O₅ to obtain 140 mg of product.

¹HNMR: 1.36-1.47 (11H, m), 1.74-1.79 (2H, m), 2.07 (3H, s), 2.70-2.92 (2H, m), 3.90-3.93 (2H, m), 4.13-4.17 (1H, m), 6.82 (1H, d, *J*=7.6 Hz, NH), 8.14 (1H, s).

Step II: Preparation of *tert*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate

Cesium carbonate (151 mg, 0.00046 moles) was added to a solution of *tert*-butyl 4-(6-chloro-5-methylpyrimidin-4-ylamino)piperidine-1-carboxylate (100 mg, 0.000309 moles) and 1-(4-(methylsulfonyl)phenyl)ethanone oxime (67 mg, 0.000309 moles) in dry DMF (2 ml) and reaction mixture was stirred for 4 hours at 70 °C. Then reaction mixture was poured into ice cold water and extracted with ethyl acetate. Organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure. The crude product obtained was purified by flash column chromatography (silica gel) using 60% ethyl acetate in hexane as eluent to yield 70 mg of product.

¹HNMR: 1.39 (2H, m), 1.47 (9H, s), 2.03 (3H, s), 2.04-2.09 (2H, m), 2.52 (3H, s), 2.93-2.95 (2H, m), 3.06 (3H, s), 4.09-4.13 (2H, m), 4.21-4.23 (1H, m), 4.39 (1H, d, *J*=7.6Hz), 7.96-7.97 (4H, m), 8.36 (1H, s).

Example 4

1-(4-(methylsulfonyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Step I: Preparation of 4-chloro-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidine

Pottasium *tert*-butoxide (2.86 gm, 0.01397 moles) was added to a solution of 1-(pyrimidin-2-yl)piperidin-4-ol (2.50 gm, 0.01397 moles) and 4,6-dichloro-5-methylpyrimidine (2.27 mg, 0.01397 moles) in dry THF (15 ml) at 0 °C and the reaction mixture was stirred for 5 hours at 30 °C. The reaction mixture was poured into

ice cold water, solid precipitated was filtered and dried over P₂O₅ to obtain 140 mg of product.

¹HNMR: 1.79-1.87 (2H, m), 2.04-2.11 (2H, m), 2.23 (3H, s), 3.69-3.76 (2H, m), 4.16-4.22 (2H, m), 5.41-5.46 (1H, m), 6.49 (1H, t, *J*=4.48 Hz), 8.31 (2H, d, *J*=4.8 Hz), 8.40 (1H, s).

Step II: Preparation of 1-(4-(methylsulfonyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime..

Cesium carbonate (640 mg, 0.001963 moles) was added to a solution of 4-chloro-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidine (400 mg, 0.001309 moles) and 1-(4-(methylsulfonyl)phenyl)ethanone oxime (278 mg, 0.001309 moles) in dry DMF (2.5 ml) and reaction mixture was stirred for an 12 hours at 60 °C. The reaction mixture was poured into ice cold water, solid separated was filtered and dried over P₂O₅ to obtain 400 mg of product.

¹HNMR: 1.83-1.89 (2H, m), 2.05-2.12 (2H, m), 2.15 (3H, s), 2.54 (3H, s), 3.06 (3H, s), 3.71-3.77 (2H, m), 4.17- 4.23 (2H, m), 5.43-5.49 (1H, m), 6.47 (1H, t, *J* = 4.8 Hz), 7.96-8.01 (4H, m), 8.31 (2H, d, *J* = 4.8 Hz), 8.44 (1H, s).

Example 5

iso-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

Step I: Preparation of *iso*-butyl 4-(6-chloro-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

Pottasium *tert*-butoxide (1.95 gm, 0.0174 moles) was added to a solution of *iso*-butyl 4-hydroxypiperidine-1-carboxylate (3.50 gm, 0.0174 moles) and 4,6-dichloro-5-methylpyrimidine (2.84 mg, 0.0174 moles) in dry THF (25 ml) at 0 °C and the reaction mixture was stirred for 1 hour at 30 °C. Then reaction mixture was poured into ice cold water and extracted with ethyl acetate. Organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure. The crude product obtained was purified by flash column chromatography (silica gel) using 8% ethyl acetate in hexane as eluent to yield 3.7 gm of product.

¹HNMR: 0.95 (6H, d, *J*=6.8 Hz), 1.74-1.82 (2H, m), 1.89-2.08 (3H, m), 2.23 (3H, s), 3.40-3.46 (2H, m), 3.73-3.79 (2H, m), 3.88 (2H, d, *J*=6.8 Hz), 5.30-5.38 (1H, m), 8.38 (1H, s).

Step II: Preparation of *iso*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate.

Cesium carbonate (746 mg, 0.002285 moles) was added to a solution of *iso*-butyl 4-(6-chloro-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate (500 mg, 0.001526 moles) and 1-(4-(methylsulfonyl)phenyl)ethanone oxime (325 mg, 0.001526 moles) in dry DMF (10 ml) and reaction mixture was stirred for an 3 hours at 30 °C. Then reaction mixture was poured into ice cold water and extracted with ethyl acetate. Organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure to yield 670 mg of product.

¹HNMR: 0.95 (6H, d, *J*= 6.8 Hz), 1.76-1.84 (2H, m), 1.92-2.04 (3H, m), 2.14 (3H,s) 2.54 (3H, s), 3.06 (3H, s), 3.41-3.48 (2H, m), 3.75-3.81 (2H, m),3.88 (2H,d, *J*=6.8Hz), 5.35-5.39 (1H, m), 7.96-8.01 (4H, m), 8.42 (1H, s).

The following compounds are prepared by procedure similar to those described in example 1-5 with appropriate variations of reactants, reaction conditions and quantities of reagents.

Example 6

iso-Propyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.74-1.82 (2H, m), 1.97-2.02 (2H, m), 2.14 (3H, s), 2.53 (3H, s), 3.39-3.45 (2H, m), 3.74-3.78 (2H, m), 4.91-4.97 (1H, m), 5.34-5.39 (1H, m), 7.39 (1H, dd, *J*=8 & 4.8 Hz), 8.15-8.18 (1H, m), 8.42 (1H, s), 8.68 (1H, dd, *J*=4.8 & 1.6 Hz), 8.97 (1H, d, *J*=2.0 Hz).

Example 7

iso-Propyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.74-1.82 (2H, m), 1.97-2.02 (2H, m), 2.14 (3H, s), 2.54 (3H, s), 3.06 (3H, s), 3.38-3.45 (2H, m), 3.74-3.78 (2H, m), 4.91-4.97 (1H, m), 5.34-5.39 (1H, m), 7.96-8.01 (4H, m), 8.42 (1H, s).

Example 8

iso-Propyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.74-1.81 (2H, m), 1.96-2.01 (2H, m), 2.13 (3H, s), 2.49 (3H, s), 3.38-3.45 (2H, m), 3.74-3.78 (2H, m), 4.90-4.97 (1H, m), 5.33-5.38 (1H, m), 7.20-7.27 (2H, m), 7.79-7.83 (2H, m), 8.41 (1H, s).

Example 9

5 *iso*-propyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.74-1.82 (2H, m), 1.97-2.02 (2H, m), 2.13 (3H, s), 2.52 (3H, s), 3.38-3.45 (2H, m), 3.75-3.77 (2H, m), 4.91-4.97 (1H, m), 5.33-5.39 (1H, m), 7.66 (2H, d, *J*=8.0 Hz), 7.90 (2H, d, *J*=8.0 Hz), 8.42 (1H, s).

Example 10

iso-propyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

15 ¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.80-1.84 (2H, m), 1.97-2.01 (2H, m), 2.27 (3H, s), 2.53 (3H, s), 3.39-3.45 (2H, m), 3.75 (2H, t, *J*= 8.0 Hz), 4.91-4.97 (1H, m), 5.34-5.39 (1H, m), 7.13 (1H, d, *J*=4.0 Hz), 7.31 (1H, d, *J*=4.0 Hz), 8.44 (1H, s).

Example 11

iso-propyl 4-(5-methyl-6-(1-(4-nitrophenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

20 ¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.77-1.80 (2H, m), 1.97-2.01 (2H, m), 2.14 (3H, s), 2.54 (3H, s), 3.38-3.45 (2H, m), 3.75-3.76 (2H, m), 4.91-4.97 (1H, m), 5.34-5.39 (1H, m), 7.97 (2H, d, *J*=8.4 Hz), 8.26 (2H, d, *J*=8.8 Hz), 8.43 (1H, s).

Example 12

25 *iso*-Propyl 4-(5-methyl-6-(1-*p*-tolylethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.75-1.81 (2H, m), 1.96-2.01 (2H, m), 2.12 (3H, s), 2.38 (3H, s), 2.47 (3H, s), 3.38-3.45 (2H, m), 3.74-3.76 (2H, m), 4.90-4.97 (1H, m), 5.33-5.37 (1H, m), 7.21 (2H, d, *J*=8.0 Hz), 8.26 (2H, d, *J*=8.4 Hz), 8.41 (1H, s).

Example 13

30 *iso*-propyl 4-(6-(1-(4-fluorophenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.76-1.82 (2H, m), 1.96-2.04 (2H, m), 2.12 (3H, s), 2.53 (3H, s), 3.38-3.45 (2H, m), 3.75 (2H, m), 4.90-4.97 (1H, m), 5.33-5.38 (1H, m), 7.07-7.12 (2H, m), 7.75-7.80 (2H, m), 8.42 (1H, s).

Example 14

iso-propyl 4-(6-(1-(4-methoxyphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.73-1.82 (2H, m), 1.97-2.04 (2H, m), 2.12 (3H, s),
5 2.46 (3H, s), 3.38-3.45 (2H, m), 3.74-3.75 (2H, m), 3.84 (3H, s), 4.90-4.97 (1H, m),
5.32-5.38 (1H, m), 6.90-6.94 (2H, m), 7.72-7.76 (2H, m), 8.41 (1H, s).

Example 15

iso-propyl 4-(5-methyl-6-(1-(naphthalen-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.75-1.83 (2H, m), 1.97-2.02 (2H, m), 2.15 (3H, s),
10 2.61 (3H, s), 3.39-3.45 (2H, m), 3.75-3.78 (2H, m), 4.91-4.97 (1H, m), 5.34-5.39 (1H,
m), 7.49-7.55 (2H, m), 7.84-7.91 (3H, m), 8.00 (1H, dd, *J*=8.8 & 2.0 Hz), 8.19 (1H, s),
8.44 (1H, s).

Example 16

15 *iso*-Propyl 4-(6-(1-(benzofuran-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.76-1.82 (2H, m), 1.97-2.02 (2H, m), 2.13 (3H, s),
2.52 (3H, s), 3.38-3.45 (2H, m), 3.75-3.77 (2H, m), 4.91-4.97 (1H, m), 5.34-5.39 (1H,
m), 7.23-7.28 (2H, m), 7.35-7.39 (1H, m), 7.57 (1H, dd, *J*=8.0 & 0.4 Hz), 7.62 (1H, d,
20 *J*=8.0 Hz), 8.46 (1H, s)

Example 17

iso-propyl 4-(6-(1-(4-butylphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 0.943 (3H, s), 1.26 (6H, d, *J*=6.4 Hz), 1.29-1.39 (2H, m), 1.56-1.63 (2H, m),
25 1.77-1.80 (2H, m), 1.96-2.01 (2H, m), 2.12 (3H, s), 2.48 (3H, s), 2.63 (2H, t,
J=15.6Hz), 3.38-3.45 (2H, m), 3.74-3.76 (2H, m), 4.90-4.97 (1H, m), 5.23-5.38 (1H,
m), 7.22 (2H, d, *J*=8.0 Hz), 7.68 (2H, d, *J*=8.4 Hz), 8.41 (1H, s)

Example 18

30 *iso*-propyl 4-(6-(1-(4-methoxy-3-methylphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.4 Hz), 1.75-1.80 (2H, m), 1.96-2.04 (2H, m), 2.12 (3H, s),
2.24 (3H, s), 2.46 (3H, s), 3.38-3.45 (2H, m), 3.74-3.76 (2H, m), 3.86 (3H, s), 4.90-4.97
(1H, m, 1H), 5.33-5.37 (1H, m), 6.83 (1H, d, *J*=8.0 Hz), 7.56 (1H, dd, *J*=8.4 Hz &
J=2.4 Hz), 7.62 (1H, d, *J*= 1.6 Hz), 8.41 (1H, s).

Example 19

iso-propyl 4-(5-methyl-6-(1-(pyridin-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=4.0 Hz), 1.79-1.81 (2H, m), 1.97-2.02 (2H, m), 2.14 (3H, s),
 5 2.61 (3H, s), 3.39-3.45 (2H, m), 3.74-3.76 (2H, m), 4.91-4.97 (1H, m), 5.34-5.39 (1H, m),
 7.32-7.35 (1H, dd; *J*=12.0 Hz & *J*=8.0 Hz), 7.70-7.75 (1H, m), 8.12 (1H, d, *J*=8.0 Hz),
 8.43 (1H, s), 8.658 (1H, d, *J*=5.2 Hz).

Example 20

iso-propyl 4-(6-(1-(3,4-dimethoxyphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.74-1.80 (2H, m), 1.96-2.04 (2H, m), 2.12 (3H, s),
 2.47 (3H, s), 3.38-3.45 (2H, m), 3.73-3.77 (2H, m), 3.92 (3H, s), 3.95 (3H, s), 4.90-4.97
 (1H, m), 5.32-5.38 (1H, m), 6.87 (1H, d, *J*=8.4 Hz), 7.28-7.31 (1H, dd, *J*=8.0 Hz &
J=8.0 Hz), 7.38 (1H, d, *J*=4.0 Hz), 8.41 (1H, s).

Example 21

iso-propyl 4-(6-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.75-1.82 (2H, m), 1.96-2.01 (2H, m), 2.12 (3H, s),
 2.46 (3H, s), 3.38-3.45 (2H, m), 3.48 (3H, s), 3.73-3.76 (2H, m), 4.90-4.97 (1H, m),
 20 5.20 (2H, s), 5.32-5.38 (1H, m), 7.04-7.07 (2H, m), 7.71-7.75 (2H, m), 8.41 (1H, s)

Example 22

iso-propyl 4-(5-methyl-6-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.26 (6H, d, *J*=6.0 Hz), 1.75-1.81 (6H, m), 1.96-2.05 (2H, m), 2.12 (3H, s),
 25 2.46 (3H, s), 2.79 (4H, d, *J*=5.6 Hz), 3.38-3.44 (2H, m), 3.75-3.77 (2H, m), 4.90-4.97
 (1H, m), 5.32-5.38 (1H, m), 7.09 (1H, d, *J*=8.0 Hz), 7.45-7.49 (2H, m), 8.41 (1H, s).

Example 23

iso-propyl 4-(6-(1-(4-methoxyphenyl)hexylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 0.84-0.91 (3H, m), 1.27 (6H, d, *J*=6.4 Hz), 1.31-1.42 (4H, m), 1.59-1.67 (2H, m),
 30 1.72-1.79 (2H, m), 2.00 (2H, s), 2.11 (3H, s), 2.91 (2H, t, *J*=16.0 Hz), 3.38-3.44
 (2H, m), 3.73-3.78 (2H, m), 3.84 (3H, s), 4.90-4.95 (1H, m), 5.34-5.36 (1H, m), 6.90
 (2H, d, *J*=7.2 Hz), 7.70 (2H, d, *J*=7.2 Hz), 8.41 (1H, s).

Example 24

iso-propyl 4-(6-(diphenylmethyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.25 (6H, d, *J*=6.4 Hz), 1.72-1.76 (2H, m), 1.78 (3H, s), 1.93-1.98 (2H, m),
5 3.36-3.42 (2H, m), 3.70-3.73 (2H, m), 4.90-4.94 (1H, m), 5.30-5.34 (1H, m), 7.35-7.47
(8H, m), 7.62-7.64 (2H, m), 8.45 (1H, s).

Example 25

iso-propyl 4-(5-methyl-6-(phenyl(pyridin-2-yl)methyleneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.24 (6H, d, *J*=6.4 Hz), 1.71-1.79 (2H, m), 1.84 (3H, s), 1.94-1.99 (2H, m),
10 3.36-3.43 (2H, m), 3.70-3.73 (2H, m), 4.89-4.95 (1H, m), 5.30-5.36 (1H, m), 7.32-7.35
(1H, m), 7.47 (5H, s), 7.75-7.79 (1H, m), 7.99 (1H, d, *J* = 8.0 Hz), 8.43 (1H, s), 8.64-
8.66 (1H, m).

Example 26

15 *iso*-propyl 4-(6-(bis(4-fluorophenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.24 (6H, d, *J* = 6.4 Hz), 1.74-1.77 (2H, m), 1.81 (3H, s), 1.94-1.98 (2H, m),
3.36-3.42 (2H, m), 3.72-3.74 (2H, m), 4.91-4.94 (1H, m), 5.32-5.34 (1H, m), 7.05-7.09
(2H, m), 7.15-7.19 (2H, m), 7.39-7.43 (2H, m), 7.59-7.63 (2H, m), 8.42 (1H, s).

Example 27

20 *iso*-propyl 4-(6-((3,4-difluorophenyl)(phenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.24 (6H, d, *J*=6.0 Hz), 1.73-1.79 (2H, m), 1.84 (3H, s), 1.95-1.98 (2H, m),
3.36-3.42 (2H, m), 3.72-3.74 (2H, m), 4.89-4.96 (1H, m), 5.31-5.35 (1H, m), 7.17-7.19
25 (1H, m), 7.28-7.33 (2H, m), 7.36-7.41 (2H, m), 7.45-7.51 (1H, m), 7.59-7.61 (2H, m),
7.61 (1H, s).

Example 28

iso-propyl 4-(6-(bis(4-methoxyphenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.24 (6H, d, *J*=6.0 Hz), 1.76-1.84 (2H, m), 1.84 (3H, s), 1.93-1.98 (2H, m),
30 3.36-3.43 (2H, m), 3.71-3.76 (2H, m), 3.83 (3H, s), 3.87 (3H, s), 4.89-4.94 (1H, m),
5.30-5.35 (1H, m), 6.86-6.89 (2H, m), 6.94-6.97 (2H, m), 7.36-7.39 (2H, m), 7.54-7.58
(2H, m), 8.42 (1H, s).

Example 29

tert-butyl 4-(6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.72-1.77 (2H, m), 1.96-2.00 (2H, m), 2.51 (3H, s), 3.27-3.33 (2H, m), 3.75-3.79 (2H, m), 5.30-5.34 (1H, m), 6.70 (1H, s), 7.26-7.29 (2H, m), 7.80-7.83 (2H, m); 8.46 (1H, s).

Example 30

tert-butyl 4-(6-(1-(2-fluoro-4-(methylsulfonyl)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.48 (9H, s), 1.63-1.68 (2H, m), 1.76-1.78 (2H, m), 2.13 (3H, s), 2.53 (3H, s), 3.06 (3H, s), 3.34-3.40 (2H, m), 3.71-3.75 (2H, m), 5.32-5.34 (1H, m), 7.71-7.78 (2H, m), 7.85-7.89 (1H, m), 8.40 (1H, s).

Example 31

tert-butyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.48 (9H, s), 1.74-1.81 (2H, m), 1.96-2.01 (2H, m), 2.13 (3H, s), 2.52 (3H, s), 3.34-3.40 (2H, m), 3.70-3.74 (2H, m), 5.33-5.36 (1H, m), 7.67 (2H, d, *J*=8.4 Hz), 7.89 (2H, d, *J*=8.0 Hz), 8.42 (1H, s).

Example 32

tert-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.73-1.81 (2H, m), 1.95-2.01 (2H, m), 2.12 (3H, s), 2.49 (3H, s), 3.34-3.40 (2H, m), 3.70-3.74 (2H, m), 5.32-5.36 (1H, m), 7.25-7.27 (2H, m), 7.80-7.83 (2H, m), 8.41 (1H, s).

Example 33

tert-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.48 (9H, s), 1.75-1.80 (2H, m), 1.96-2.01 (2H, m), 2.14 (3H, s), 2.54 (3H, s), 3.05 (3H, s), 3.34-3.40 (2H, m), 3.70-3.76 (2H, m), 5.33-5.37 (1H, m), 7.96-8.01 (4H, m), 8.42 (1H, s).

Example 34

tert-butyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate.

¹HNMR: 1.48 (9H,s), 1.73-1.81 (2H,m), 1.96-2.01 (2H, m), 2.13 (3H,s), 2.53 (3H, s), 3.34-3.40 (2H, m), 3.71-3.75 (2H, m), 5.33-5.37 (1H, m), 7.34 (1H, dd, *J*=8.0 & 4.8 Hz), 8.11-8.14 (1H,m), 8.42 (1H,s), 8.67 (1H, dd, *J*=4.8 &1.6 Hz), 8.96 (1H,d, *J* = 1.6Hz).

5 **Example 35**

tert-butyl 4-(6-(1-(4-(benzyloxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.74-1.79 (2H, m), 1.95-2.00 (2H, m), 2.12 (3H, s), 2.46 (3H, s), 3.34-3.40 (2H, s), 3.70-3.73 (2H, s), 5.10 (2H, s), 5.31-5.35 (1H, m), 6.97-7.01 (2H, m), 7.33-7.44 (5H, m); 7.72-7.76 (2H, m), 8.41 (1H, s).

Example 36

tert-butyl 4-(5-nitro-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.82-1.87 (2H, m), 2.04 (2H, m), 2.63 (3H, s), 3.24-3.31 (2H, m), 3.81-3.84 (2H, m), 5.28-5.32 (1H, m), 7.72 (2H, d, *J*=8.0 Hz), 7.90 (2H, d, *J*=6.8 Hz), 9.19 (1H, s)

Example 37

iso-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 0.95 (6H, d, *J* = 6.8 Hz), 1.79-1.81 (2H, m), 1.90-2.00 (3H, m), 2.14 (3H, s), 2.50 (3H, s), 3.41-3.47 (2H, m), 3.76-3.80 (2H, m), 3.88 (2H, d, *J* = 6.8 Hz), 5.35-5.39 (1H, m), 7.27 (2H, d, *J* = 8.0 Hz), 7.87 (2H, d, *J* = 8.0 Hz), 8.47 (1H, s).

Example 38

iso-butyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 0.95 (6H, d, *J* = 6.8 Hz), 1.76-1.84 (2H, m), 1.90-2.03 (3H, m), 2.14 (3H, s), 2.53 (3H, s), 3.41-3.48 (2H, m), 3.76-3.80 (2H, m), 3.88 (2H, d, *J* = 6.4 Hz), 5.34-5.40 (1H, m), 7.34-7.37 (1H, m), 8.11-8.14 (1H, m), 8.42 (1H, s), 8.67-8.69 (1H, m), 8.97 (1H, d, *J* = 2.0 Hz).

Example 39

iso-butyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 0.95 (6H, d, *J* = 6.8 Hz), 1.76-1.84 (2H, m), 1.90-2.03 (3H, m), 2.13 (3H,s) 2.52 (3H, s), 3.41-3.48 (2H, m), 3.75-3.81 (2H, m), 3.88 (2H, d, *J*=6.4 Hz), 5.34-5.39 (1H, m), 7.67 (2H,d, *J* = 8.4 Hz), 7.90 (2H, d, *J*= 8.4Hz), 8.42 (1H, s).

Example 40

5 *iso*-butyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 0.94 (6H, d, *J*= 6.8Hz), 1.77-1.85 (2H, m), 1.90-2.06 (3H, m), 2.27 (3H,s) 2.54 (3H, s), 3.42-3.48 (2H, m), 3.73-3.81 (2H, m), 3.88 (2H, d, *J*=6.8Hz), 5.33-5.40 (1H, m), 7.13 (1H, d, *J*=4.4Hz), 7.32 (1H, d, *J*=4Hz), 8.44 (1H, s).

Example 41

10 Ethyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.27 (3H, t, *J* = 7.2 Hz), 1.77-1.83 (2H, m), 1.96-2.02 (2H, m), 2.12 (3H, s), 2.49 (3H, s), 3.40-3.47 (2H, m), 3.75-3.77 (2H, m), 4.13-4.18 (2H, q, *J*= 7.0 Hz), 5.34-5.38 (1H, m), 7.26 (2H, d, *J* = 8.0 Hz), 7.80-7.83 (2H, m), 8.41 (1H, s).

Example 42

Ethyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

20 ¹HNMR: 1.28 (3H, t, *J*=7.2 Hz), 1.77-1.83 (2H, m), 1.98-2.04 (2H, m), 2.14 (3H, s), 2.54 (3H, s), 3.06 (3H, s), 3.40-3.47 (2H, m), 3.75-3.77 (2H, m), 4.15 (2H, q, *J*=7.2 Hz), 5.34-5.39 (1H, m), 7.96-8.01 (4H, m), 8.42 (1H, s).

Example 43

Ethyl 4-(6-(1-(4-(allyloxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate

25 ¹HNMR: 1.27 (3H, t, *J*=7.2 Hz), 1.75-1.83 (2H, m), 1.97-2.02 (2H, m), 2.24 (3H, s), 2.46 (3H, s), 3.40-3.47 (2H, m), 3.74-3.76 (2H, m), 4.12 (2H, q, *J*=7.2 Hz), 4.56-4.58 (2H,m), 5.29-5.31 (1H, m), 5.32-5.38 (1H, m), 5.39-5.44 (1H, m), 6.00-6.10 (1H, m), 6.91-6.95 (2H, m), 7.71-7.75 (2H, m), 8.41 (1H, s).

Example 44

30 Phenyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.90-1.93 (2H, m), 2.09 (2H, bs), 2.16 (3H, s), 2.50 (3H, s), 3.58-3.67 (2H, m), 3.85-3.9. (2H, m), 5.41-5.46 (1H, m), 7.10-7.13 (2H, m), 7.18-7.22 (3H, m), 7.34-7.39 (2H, m), 7.80-7.84 (2H, m), 8.43 (1H, m).

Example 45

Phenyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.91-1.93 (2H, m), 2.10 (2H, bs), 2.17 (3H, s), 2.55 (3H, s) 3.06 (3H, s), 3.59-
5 3.67 (2H, m), 3.89-3.95 (2H, m), 5.42-5.47 (1H, m), 7.11-7.14 (2H, m), 7.19-7.22 (1H, m), 7.35-7.39 (2H, m), 7.97-8.02 (4H, m), 8.44 (1H, s).

Example 46

Phenyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

10 ¹HNMR: 1.91-1.93 (2H, m), 2.09 (2H, bs), 2.16 (3H, s), 2.54 (3H, s), 3.58-3.67 (2H, m), 3.85-3.89 (2H, m), 5.42-5.46 (1H, m), 7.12 (2H, d, *J*=8.0 Hz), 7.19-7.22 (1H, m), 7.35-7.39 (3H, m), 8.13 (1H, d, *J*= 8Hz), 8.44 (1H, s), 8.67-8.69 (1H, m), 8.97 (1H, d, *J*= 2Hz).

Example 47

15 Benzyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.79-1.82 (2H, m), 1.94-1.96 (2H, m) 2.04 (3H, s), 2.54 (3H, s), 3.06 (3H, s), 3.45-3.51 (2H, m), 3.76-3.82 (2H, m), 5.15 (2H, s), 5.34-5.40 (1H, m), 7.30-7.38 (5H, m), 7.96-8.01 (4H, m), 8.42 (1H, s).

Example 48

20 Benzyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate

¹HNMR: 1.79-1.82 (2H, m), 1.94-1.96 (2H, m), 2.12 (3H, s), 2.50 (3H, s), 3.45-3.51 (2H, m), 3.77-3.81 (2H, m), 5.15 (2H, s), 5.34-5.39 (1H, m), 7.24-7.26 (2H, m), 7.30-
25 7.38 (5H, m), 7.82 (2H, d, *J*=8.8 Hz), 8.41 (1H, s).

Example 49

1-(4-(Trifluoromethoxy)phenyl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

30 ¹HNMR: 1.27 (6H, d, *J*=6.0 Hz), 1.29 (3H, s), 1.90-1.98 (2H, m), 2.08-2.12 (2H, m), 2.14 (3H, s), 2.50 (3H, s), 2.87-2.94 (1H, m), 3.61-3.67 (2H, m), 3.82-3.88 (2H, m), 5.41-5.46 (1H, m), 7.25-7.27 (2H, m), 7.80-7.83 (2H, m), 8.42 (1H, s).

Example 50

1-(4-Methoxyphenyl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

¹HNMR: 1.29 (6H, d, *J*=6.8 Hz), 1.90-1.98 (2H, m), 2.04-2.11 (2H, m), 2.13 (3H, s), 2.47 (3H, s), 2.86-2.93 (1H, m), 3.61-3.67 (2H, m), 3.83-3.88 (5H, m), 5.40-5.46 (1H, m), 6.91-3.94 (2H, dd, *J*=4.8 & 2.8 Hz), 7.73-7.75 (2H, m), 8.42 (1H, s).

Example 51

5 1-p-tolylethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

¹HNMR: 1.29 (6H, d, *J*=7.2 Hz), 1.90-1.98 (2H, m), 2.06-2.1 (2H, m), 2.13 (3H, s), 2.38 (3H, s), 2.48 (3H, s), 2.87-2.96 (1H, m), 3.61-3.67 (2H, m), 3.81-3.88 (2H, m), 5.40-5.46 (1H, m), 7.21 (2H, d, *J*=8.0 Hz), 7.67 (2H, d, *J*=8.4 Hz), 8.43 (1H, s)

10 Example 52

1-(Pyridin-3-yl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

¹HNMR: 1.28 (6H, d, *J*=6.8Hz), 1.90-1.98 (2H, m), 2.07-2.12 (2H, m), 2.14 (3H, s), 2.53 (3H, s), 2.87-2.94 (1H, m), 3.61-3.68 (2H, m), 3.82-3.88 (2H, m), 5.41-5.47 (1H, m), 7.34-7.38 (1H, m), 8.12-8.15 (1H, m), 8.43 (1H, s), 8.67-8.69 (1H, dd, *J*=4.8 & 1.8 Hz), 8.97 (1H, d, *J*=1.6Hz)

Example 53

1-(4-Fluorophenyl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

20 ¹HNMR: 1.29 (6H, d, *J*=6.8 Hz), 1.92-1.98 (2H, m), 2.06-2.12 (2H, m), 2.13 (3H, s), 2.86-2.93 (1H, m), 2.49 (3H, s), 3.61-3.67 (2H, m), 3.82-3.88 (2H, m), 5.41-5.45 (1H, m), 7.08-7.12 (2H, m), 7.76-7.80 (2H, m), 8.42 (1H, s).

Example 54

1-(Benzo[d][1,3]dioxol-5-yl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

25 ¹HNMR: 1.29 (6H, d, *J* = 6.8 Hz), 1.90-1.98 (2H, m), 2.04-2.10 (2H, m), 2.12 (3H, s), 2.45 (3H, s), 2.87-2.93 (1H, m), 3.61-3.67 (2H, m), 3.81-3.88 (2H, m), 5.41-5.45 (1H, m), 6.01 (2H, s), 6.83 (1H, d, *J* = 8.0 Hz), 7.24-7.27 (1H, m), 7.34-7.36 (1H, m), 8.42 (1H, s).

30 Example 55

1-(4-(Trifluoromethoxy)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime

¹HNMR: 1.81-1.89 (2H, m), 2.04-2.12 (2H, m), 2.13 (3H, s), 2.50 (3H, s), 3.71-3.77 (2H, m), 4.17-4.23 (2H, m), 5.43-5.47 (1H, m), 6.47 (1H, t, *J* = 4.8 Hz), 7.25 (1H, s), 7.27 (1H, s), 7.80-7.84 (2H, m), 8.31 (2H, d, *J* = 4.8 Hz), 8.44 (1H, s).

Example 56

5 1-(Benzo[d][1,3]dioxol-5-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

¹HNMR: 1.80-1.88 (2H, m), 2.04-2.10 (2H, m), 2.12 (3H, s), 2.45 (3H, s), 3.71-3.77 (2H, m), 4.16-4.22 (2H, m), 5.41-5.46 (1H, m), 6.00 (2H, s), 6.47 (1H, t, *J* = 4.8 Hz), 6.82 (1H, d, *J* = 8.0 Hz), 7.24-7.27 (1H, m), 7.34 (1H, s), 8.31 (2H, d, *J* = 4.4 Hz), 8.43 (1H, s).

Example 57

1-(2-Fluoro-4-(methylsulfonyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

¹HNMR: 1.81-1.89 (2H, m), 2.04-2.12 (2H, m), 2.14 (3H, s), 2.50 (3H, s), 3.06 (3H, s), 3.71-3.77 (2H, m), 4.17-4.23 (2H, m), 5.43-5.48 (1H, m), 6.48 (1H, t, *J* = 4.6 Hz), 7.71 (1H, dd, *J* = 9.4 & 1.4 Hz), 7.76 (1H, dd, *J* = 8.0 & 1.6 Hz), 7.85 (1H, t, *J* = 7.4 Hz), 8.32 (2H, d, *J* = 4.8 Hz), 8.42 (1H, s).

Example 58

1-(4-(Trifluoromethoxy)phenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

¹HNMR: 1.18 (3H, t, *J* = 7.4 Hz), 1.80-1.88 (2H, m), 2.04-2.11 (2H, m), 2.13 (3H, s), 2.44-2.48 (2H, m), 2.49 (3H, s), 3.66-3.73 (2H, m), 4.15-4.21 (2H, m), 5.41-5.47 (1H, m), 7.24-7.26 (2H, m), 7.81 (2H, d, *J* = 8.4 Hz), 8.19 (2H, s), 8.43 (1H, s).

Example 59

25 1-(Benzo[d][1,3]dioxol-5-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

¹HNMR: 1.18 (3H, t, *J* = 7.6 Hz), 1.79-1.87 (2H, m), 2.04-2.10 (2H, m), 2.12 (3H, s), 2.45 (3H, s), 2.46-2.50 (2H, m), 3.66-3.73 (2H, m), 4.14-4.20 (2H, m), 5.40-5.46 (1H, m), 6.00 (2H, s), 6.82 (1H, d, *J* = 8.0 Hz), 7.24-7.27 (1H, s), 7.34-7.34 (1H, m), 8.19 (2H, s), 8.43 (1H, s).

Example 60**C-156-DRP-103**

1-(4-(Methylsulfonyl)phenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

¹HNMR: 1.19 (3H, t, *J*= 6.0 Hz), 1.80-1.88 (2H, m), 2.05-2.12 (2H, m), 2.14 (3H, s), 2.45-2.50 (2H, q, *J*=7.6 Hz), 2.54 (3H, s), 3.06 (3H, s), 3.66-3.73 (2H, m), 4.15-4.21 (2H, m), 5.43-5.46 (1H, m), 7.96-8.01 (4H, m), 8.19 (2H, s), 8.44 (1H, s).

Example 61

5 1-(Pyridin-3-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

¹HNMR: 1.18 (3H, t, *J*=6.0 Hz), 1.80-1.88 (2H, m), 2.05-2.11 (2H, m), 2.14 (3H, s), 2.44-2.50 (2H, q, *J*=7.6 Hz), 2.53 (3H, s), 3.66-3.73 (2H, m), 4.15-4.21 (2H, m), 5.41-5.47 (1H, m), 7.34-7.37 (1H, m), 8.12-8.15 (1H, m), 8.19 (2H, s), 8.44 (1H, s), 8.67-10 8.68 (1H, m), 8.96 (1H, d, *J*=2.0 Hz).

Example 62

1-(4-(Trifluoromethoxy)phenyl)ethanone O-6-(1-benzylpiperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

¹HNMR: 1.81-1.89 (2H, m), 2.02 (2H, bs), 2.12 (3H, s), 2.35-2.37 (2H, m), 2.49 (3H, 15 s), 2.73 (2H, bs), 3.54 (2H, s), 5.18-5.22 (1H, m), 7.24-7.28 (2H, m), 7.32-7.35 (5H, m), 7.79-7.83 (2H, m), 8.40 (1H, s).

Example 63

1-(4-(Trifluoromethoxy)phenyl)ethanone O-5-methyl-6-(1-(3-nitropyridin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

20 ¹HNMR: 1.92 - 2.00 (2H, m), 2.12 - 2.18 (5H, m), 2.50 (3H, s), 3.42-3.48 (2H, m), 3.67-3.73 (2H, m), 5.44-5.49 (1H, m), 6.74-6.79 (1H, m), 7.25-7.27 (2H, m), 7.82 (2H, d, *J* = 8.4Hz), 8.14-8.16 (1H, dd, *J*=8.0 & 1.6 Hz), 8.34-8.35 (1H, dd, *J*=4.8 & 2.0 Hz), 8.43 (1H, s).

Example 64

25 (1-(4-(Methylsulfonyl)phenyl)ethanone O-5-methyl-6-(1-(3-nitropyridin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

¹HNMR: 1.93-2.01 (2H, m), 2.12-2.19 (5H, m), 2.54 (3H, s), 3.06 (3H, s), 3.42-3.48 (2H, m), 3.67-3.73 (2H, m), 5.45 - 5.50 (1H, m), 6.74 (1H, dd, *J*=8.0 & 4.4 Hz), 7.96-8.01 (4H, m), 8.15 (1H, dd, *J*=8.0 & 2.0 Hz), 8.34 (1H, dd, *J*=4.4 & 1.6 Hz), 8.43 (1H, 30 s).

Example 65

tert-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)-1,4'-bipiperidine-1'-carboxylate

¹HNMR: 1.44-1.47 (9H, m), 1.72-1.74 (4H, m), 1.83-1.85 (4H, m), 2.10-2.13 (5H, m), 2.54 (5H, s), 2.70 (2H, bs), 2.85 (2H, bs), 3.06 (3H, s), 4.11-4.18 (1H, m), 5.19-5.21 (1H, m), 7.96-8.01 (4H, m), 8.42 (1H, s).

Example 66

5 *tert*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate

¹HNMR: 1.39 (2H, m), 1.47 (9H, s), 2.02 (3H, s), 2.04-2.09 (2H, m), 2.48 (3H, s), 2.91-2.93 (2H, m), 4.09-4.11 (2H, m), 4.20-4.23 (1H, m), 4.36 (1H, d, *J*= 7.6Hz), 7.23-7.26 (2H, m), 7.79-7.82 (2H, m), 8.36 (1H, s).

Example 67

tert-butyl 4-(6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

15 ¹HNMR: 1.47 (9H, s), 1.72-1.80 (2H, m), 2.05-2.11 (2H, m), 2.53 (3H, s), 3.20-3.29 (2H, m), 3.79-3.82 (2H, m), 5.39-5.43 (1H, m), 7.02 (1H, d, *J*=9.2 Hz), 7.26-7.28 (2H, m), 7.55 (1H, d, *J*=9.2 Hz), 7.78-7.81 (2H, m).

Example 68

tert-butyl 4-(6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

20 ¹HNMR: 1.47 (9H, s), 1.75-1.77 (2H, m), 2.06-2.11 (2H, m), 2.57 (3H, s), 3.08 (3H, s), 3.23-3.29 (2H, m), 3.78-3.81 (2H, m), 5.40-5.44 (1H, m), 7.04 (1H, d, *J*=9.6 Hz), 7.53 (1H, d, *J*=9.6 Hz), 7.95-8.01 (4H, m).

Example 69

25 *tert*-butyl 4-(6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.74-1.79 (2H, m), 2.05-2.10 (2H, m), 2.56 (3H, s), 3.23-3.30 (2H, m), 3.79-3.82 (2H, m), 5.40-5.44 (1H, m), 7.03 (1H, d, *J* = 8.0 Hz), 7.54 (1H, d, *J* = 8.6 Hz), 7.68 (2H, d, *J* = 9.2 Hz), 7.87 (2H, d, *J* = 8.0 Hz).

Example 70

30 *tert*-butyl 4-(6-(1-*p*-tolylethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.73-1.77 (2H, m), 2.04-2.10 (2H, m), 2.39 (3H, s), 2.51 (3H, s), 3.23-3.29 (2H, m), 3.79-3.82 (2H, m), 5.39-5.43 (1H, m), 7.00 (1H, d, *J*= 8.0 Hz), 7.22 (2H, d, *J*= 8.0 Hz), 7.59 (1H, d, *J*= 9.2 Hz), 7.64 (2H, d, *J*= 8.0 Hz).

Example 71

tert-butyl 4-(6-(1-(4-fluorophenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.75-1.78 (2H, m), 2.05-2.10 (2H, m), 2.52 (3H, s), 3.23-3.29 (2H, m), 3.79-3.82 (2H, m), 5.40-5.42 (1H, m), 7.01 (1H, d, *J* = 9.6 Hz), 7.09-7.13 (2H, m), 7.55 (1H, d, *J* = 9.6 Hz), 7.73-7.77 (2H, m).

Example 72

tert-butyl 4-(6-(1-(pyridin-3-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.75-1.77 (2H, m), 2.06-2.10 (2H, m), 2.56 (3H, s), 3.23-3.30 (2H, m), 3.76-3.79 (2H, m), 5.40-5.44 (1H, m), 7.03 (1H, d, *J* = 9.6 Hz), 7.35-7.38 (1H, m), 7.55 (1H, d, *J* = 10.8 Hz), 8.07 (1H, d, *J* = 8 Hz), 8.69 (1H, s), 8.99 (1H, s).

Example 73

tert-Butyl 4-(6-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.73-1.79 (2H, m), 2.04-2.10 (2H, m), 2.50 (3H, s), 3.23-3.29 (2H, m), 3.48 (3H, s), 3.79-3.82 (2H, m), 5.21 (2H, s), 5.39-5.43 (1H, m), 7.00 (1H, d, *J* = 9.6 Hz), 7.05-7.09 (2H, m), 7.57 (1H, d, *J* = 9.6 Hz), 7.68-7.72 (2H, m).

Example 74

tert-butyl 4-(6-(1-(benzofuran-2-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.72-1.81 (2H, m), 2.04-2.12 (2H, m), 2.56 (3H, s), 3.23-3.30 (2H, m), 3.78-3.80 (2H, m), 5.39-5.45 (1H, m), 7.06 (1H, d, *J* = 9.2 Hz), 7.20 (1H, d, *J* = 0.8 Hz), 7.26-7.29 (1H, m), 7.36-7.40 (1H, m), 7.52-7.56 (1H, m), 7.62-7.66 (2H, m).

Example 75

tert-Butyl 4-(6-(1-(4-methoxyphenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.72-1.77 (2H, m), 2.04-2.12 (2H, m), 2.50 (3H, s), 3.23-3.29 (2H, m), 3.79-3.82 (2H, m), 3.85 (3H, s), 5.39-5.43 (1H, m), 6.93 (2H, d, *J* = 8.8 Hz), 7.00 (1H, d, *J* = 9.2 Hz), 7.58 (1H, d, *J* = 9.6 Hz), 7.71 (2H, d, *J* = 8.4 Hz).

Example 76

tert-Butyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate

¹HNMR: 1.47 (9H, s), 1.74-1.77 (2H, m), 2.04-2.10 (2H, m), 2.48 (3H, s), 3.23-3.29 (2H, m), 3.76-3.79 (2H, m), 5.39-5.43 (1H, m), 7.03-7.04 (2H, m), 7.13 (1H, d, *J*=4Hz), 7.54 (1H, d, *J*=9.6Hz).

Example 77

5 1-(4-(Trifluoromethoxy)phenyl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime

¹HNMR: 1.29 (6H, d, *J*=7.2Hz), 1.93-1.97 (2H, m), 2.17-2.21 (2H, m), 2.54 (3H, s), 2.88-2.92 (1H, m), 3.54-3.60 (2H, m), 3.88-3.93 (2H, m), 5.50-5.55 (1H, m), 7.04 (1H, d, *J*=9.2 Hz), 7.28 (2H, m), 7.57 (1H, d, *J*=9.6 Hz), 7.79-7.81 (2H, m).

10 Example 78

tert-Butyl 4-(2-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate.

Cesium carbonate (2 gm, 0.00200 moles) was added to a solution of 1-(4-(methylsulfonyl)phenyl)ethanone oxime (513 mg, 0.00241 moles) and *tert*-butyl 4-(2-(methylsulfonyloxy)ethoxy)piperidine-1-carboxylate (650 mg, 0.00241 moles) in dry
15 DMF (20 ml) and reaction mixture was stirred at 80 °C for 2 hours. The reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure. The crude product obtained was purified by flash column
20 chromatography (silica gel) using 25% ethyl acetate in hexane as eluent to yield 560 mg of product.

¹HNMR: 1.46 (9H,s), 1.50-1.58 (2H, m), 1.80-1.84 (2H, m), 2.27 (3H, s), 3.04 (3H, s), 3.06-3.13 (2H, m), 3.49-3.53 (1H, m), 3.74-3.79 (4H, m), 4.35 (2H, t, *J*=4.8 Hz), 7.84 (2H, d, *J*=8.4 Hz), 7.92 (2H, d, *J*=8.0 Hz).

25 The following compounds are prepared by procedure similar to those described in example 78 with appropriate variations of reactants, reaction conditions and quantities of reagents.

Example 79

tert-butyl 4-(2-(1-(pyridin-3-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

30 ¹HNMR: 1.45 (9H, s), 1.52-1.57 (2H, m), 1.82-1.84 (2H, m), 2.26 (3H, s), 3.05-3.11 (2H, m), 3.49-3.53 (1H, m), 3.74-3.79 (4H, m), 4.35 (2H, t, *J*=4.8 Hz), 7.27-7.31 (1H, m), 7.93-7.96 (1H, m), 8.58 (1H, d, *J*=4.8 & 1.2 Hz), 8.87 (1H, d, *J*=1.6 Hz).

Example 80

tert-butyl 4-(2-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.49-1.57 (2H, m), 1.77-1.81 (6H, m), 2.21 (3H, s), 2.76-2.77 (4H, m), 3.04-3.10 (2H, m), 3.49-3.53 (1H, m), 3.75 (4H, t, *J* = 5.2 Hz), 4.31 (2H, t, *J*=4.8 Hz); 7.05 (1H, d, *J*=6.4 Hz), 7.33 (2H, dd, *J*=9.6 & 1.6 Hz).

Example 81

tert-butyl 4-(2-(1-(biphenyl-4-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.51-1.59 (2H, m), 1.83 (2H, m), 2.28 (3H, s), 3.05-3.11 (2H, m), 3.50-3.54 (1H, m), 3.78-3.81 (4H, m), 4.35 (2H, t, *J*= 4.8 Hz), 7.34-7.38 (1H, m), 7.43-7.47 (2H, m), 7.58-7.61 (4H, m), 7.70-7.74 (2H, m).

Example 82

tert-butyl 4-(2-(1-(pyridin-4-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.52-1.57 (2H, m), 1.82 (2H, m), 2.23 (3H, s), 3.05-3.11 (2H, m), 3.48-3.53 (1H, m), 3.76-3.79 (4H, m), 4.36 (2H, t, *J*=4.8 Hz), 7.53 (2H, dd, *J*=4.8 & 1.6 Hz), 8.62 (2H, dd, *J*=4.8 & 1.6 Hz)

Example 83

tert-butyl 4-(2-(1-(pyridin-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.48 (9H, s), 1.56-1.59 (2H, m), 1.86 (2H, m), 2.37 (3H, s), 3.08-3.14 (2H, m), 3.54-3.56 (1H, m), 3.78-3.83 (4H, m), 4.40 (2H, t, *J*=4.8 Hz), 7.27-7.29 (1H, m), 7.67-7.72 (1H, m), 7.92 (1H, d, *J*=8.0 Hz), 8.63 (1H, dd, *J*=4.0 & 0.8 Hz).

Example 84

tert-butyl 4-(2-(1-(benzofuran-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.44 (9H, s), 1.53-1.56 (2H, m), 1.82 (2H, m), 2.27 (3H, s), 3.05-3.12 (2H, m), 3.52 (1H, m), 3.80 (4H, m), 4.42 (2H, t, *J*=4.8 Hz), 6.96 (1H, d, *J*=0.8 Hz), 7.21-7.25 (1H, m), 7.30-7.34 (1H, m), 7.53-7.59 (2H, m)

Example 85

tert-butyl 4-(2-(1-*p*-tolylethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.49-1.56 (2H, m), 1.82 (2H, m), 2.22 (3H, s), 2.36 (3H, s), 3.04-3.10 (2H, m), 3.49-3.53 (1H, m), 3.75-3.78 (4H, m), 4.31 (2H, t, *J*=4.8 Hz), 7.17 (2H, d, *J*=8.0 Hz), 7.53 (2H, d, *J*=8.0 Hz).

Example 86

tert-butyl 4-(2-(1-(4-fluorophenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.49-1.54 (2H, m), 1.82-1.84 (2H, m), 2.22 (3H, s), 3.05-3.11 (2H, m), 3.49-3.53 (1H, m), 3.72-3.78 (4H, m), 4.33 (2H, t, *J*=4.8 Hz), 7.02-7.06 (2H, m), 7.60-7.64 (2H, m).

Example 87

tert-butyl 4-(2-(1-(naphthalen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s); 1.53-1.57 (2H, m), 1.83 (2H, m), 2.36 (3H, s), 3.05-3.12 (2H, m), 3.51-3.55 (1H, m), 3.74-3.82 (4H, m), 4.38 (2H, t, *J*=4.8 Hz), 7.47-7.51 (2H, m), 7.79-7.92 (4H, m), 7.99 (1H, s).

Example 88

tert-butyl 4-(2-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.48-1.54 (2H, m), 1.81-1.84 (2H, m), 2.26 (3H, s), 3.05-3.11 (2H, m), 3.48-3.54 (1H, m), 3.74-3.79 (4H, m), 4.35 (2H, t, *J*=4.8 Hz), 7.61 (2H, d, *J*=8.0 Hz), 7.75 (2H, d, *J*=8.0 Hz).

Example 89

tert-butyl 4-(2-(1-(5-chlorothiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.44 (9H, s), 1.51-1.59 (2H, m), 1.80-1.84 (2H, m), 2.27 (3H, s), 3.07-3.13 (2H, m), 3.52-3.56 (1H, m), 3.71-3.80 (4H, m), 4.36 (2H, t, *J*=4.8 Hz), 6.91 (1H, d, *J*=4.4 Hz), 7.17 (1H, d, *J*=4.4 Hz).

Example 90

tert-butyl 4-(2-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.44 (9H, s), 1.53-1.60 (2H, m), 1.81-1.84 (2H, m), 2.28 (3H, s), 3.07-3.14 (2H, m), 3.52-3.56 (1H, m), 3.72-3.80 (4H, m), 4.36 (2H, t, *J* = 4.8 Hz), 7.04 (1H, d, *J* = 4.0 Hz), 7.13 (1H, d, *J* = 4.0 Hz).

Example 91

tert-butyl 4-(2-(1-(thiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.44 (9H, s), 1.52-1.57 (2H, m), 1.80-1.81 (2H, m), 2.33 (3H, s), 3.03-3.10 (2H, m), 3.52-3.56 (1H, m), 3.72-3.81 (4H, m), 4.37 (2H, t, *J* = 4.8 Hz), 7.09 (1H, dd, *J* = 8.0 & 4.0 Hz), 7.45 (1H, dd, *J* = 3.6 & 0.8 Hz), 7.52 (1H, dd, *J* = 5.2 & 1.2 Hz).

Example 92

5 *tert*-butyl 4-(2-(1-(4-methoxyphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.50-1.57 (2H, m), 1.82 (2H, s), 2.21 (3H, s), 3.04-3.11 (2H, m), 3.49-3.53 (1H, m), 3.75-3.78 (4H, m), 3.82 (3H, s), 4.30 (2H, t, *J* = 4.8 Hz), 6.86-6.90 (2H, m), 7.56-7.60 (2H, m).

10 **Example 93**

tert-butyl 4-(2-(1-(3,4-dimethoxyphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.44 (9H, s), 1.52-1.57 (2H, m), 1.81-1.84 (2H, m), 2.22 (3H, s), 3.05-3.11 (2H, m), 3.49-3.53 (1H, m), 3.75-3.77 (4H, m), 3.89 (3H, s), 3.91 (3H, s), 4.32 (2H, t, *J* = 12.0 Hz), 6.84 (1H, d, *J* = 8.4 Hz), 7.12-7.15 (1H, dd, *J* = 8.4 & 2.0 Hz), 7.27 (1H, d, *J* = 2.0 Hz).

15 **Example 94**

tert-butyl 4-(2-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

20 ¹HNMR: 1.45 (9H, s), 1.51-1.55 (2H, m), 1.82 (2H, m), 2.21 (3H, s), 3.04-3.11 (2H, m), 3.47 (3H, s), 3.49-3.53 (1H, m), 3.75-3.78 (4H, m), 4.30 (2H, t, *J* = 4.8 Hz), 5.18 (2H, s), (7.00-7.04 (2H, m), 7.56-7.59 (2H, m).

Example 95

25 *tert*-butyl 4-(2-(1-(5-methylthiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.44 (9H, s), 1.51-1.60 (2H, m), 1.81 (2H, s), 2.28 (3H, s), 2.49 (3H, s), 3.06-3.12 (2H, m), 3.52-3.58 (1H, m), 3.72 (2H, t, *J* = 12.0 Hz), 3.79 (2H, t, *J* = 4.8 Hz), 4.34 (2H, t, *J* = 4.8 Hz), 6.74-6.75 (1H, m), 7.24-7.26 (1H, d, *J* = 3.6 Hz).

Example 96

30 *tert*-butyl 4-(2-(1-(4-methoxy-3-methylphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.49-1.55 (2H, m), 1.82-1.84 (2H, m), 2.21 (3H, s), 2.22 (3H, s), 3.04-3.11 (2H, m), 3.48-3.54 (1H, m), 3.76-3.78 (4H, m), 3.84 (3H, s), 4.30 (2H, t,

$J=4.8$ Hz), 6.78 (1H, d, $J=8.4$ Hz), 7.40-7.43 (1H, dd, $J=8.6$ & 2.2 Hz), 7.45-7.46 (1H, d, $J=1.6$ Hz).

Example 97

tert-butyl 4-(2-(1-(4-nitrophenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

5 $^1\text{HNMR}$: 1.45 (9H, s), 1.55 (2H, m), 1.84 (2H, m), 2.27 (3H, s), 3.09 (2H, m), 3.53 (1H, m), 3.77-3.79 (4H, m), 4.38 (2H, t, $J=4.8$ Hz), 7.82 (2H, d, $J=8.8$ Hz), 8.21 (2H, d, $J=9.2$ Hz).

Example 98

tert-butyl 4-(2-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)ethoxy)piperidine-

10 1-carboxylate

$^1\text{HNMR}$: 1.45 (9H, s), 1.49-1.55 (2H, m), 1.82 (2H, m), 2.23 (3H, s), 3.05-3.11 (2H, m), 3.49-3.53 (1H, m), 3.74-3.78 (4H, m), 4.33 (2H, t, $J=4.8$ Hz), 7.20 (2H, d, $J=8.4$ Hz), 7.65-7.69 (2H, m).

Example 99

15 *tert*-butyl 4-(2-(1-(3,4-bis(trifluoromethyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

$^1\text{HNMR}$: 1.45 (9H, s), 1.50-1.54 (2H, m), 1.82-1.84 (2H, m), 2.28 (3H, s), 3.05-3.12 (2H, m), 3.49-3.53 (1H, m), 3.74-3.79 (4H, m), 4.38 (2H, t, $J=4.8$ Hz), 7.85 (1H, s), 8.09 (2H, s).

Example 100

tert-butyl 4-(2-(1-(4-butylphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

20 $^1\text{HNMR}$: 0.929 (3H, s), 1.31-1.37 (2H, m), 1.45 (9H, s), 1.51-1.62 (4H, m), 1.81-1.84 (2H, m), 2.22 (3H, s), 2.61 (2H, t, $J=7.6$ Hz), 3.04-3.11 (2H, m), 3.49-3.53 (1H, m), 3.75-3.77 (4H, m), 4.31 (2H, t, $J=5.2$ Hz), 7.17 (2H, d, $J=8.0$ Hz), 7.53-7.55 (2H, dd, $J=6.4$ Hz & $J=6.4$ Hz).

Example 101

tert-butyl 4-(2-(1-(2-fluoro-4-(methylsulfonyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate

30 $^1\text{HNMR}$: 1.45 (9H, s), 1.50-1.55 (2H, m), 1.83 (2H, s), 2.27 (3H, s), 3.05 (3H, s), 3.08-3.12 (2H, m), 3.49-3.53 (1H, m), 3.76-3.78 (4H, m), 4.35 (2H, t, $J=4.8$ Hz), 7.72 - 7.66 (3H, m).

Example 102

tert-butyl 4-(2-(diphenylmethyleneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.47-1.49 (2H, m), 1.74 (2H, m), 3.00-3.06 (2H, m), 3.42-3.46 (1H, m), 3.65-3.68 (2H, m), 3.74 (2H, t, *J*=5.4 Hz), 4.31 (2H, t, *J*=4.8 Hz), 7.25-7.46 (8H, m), 7.46-7.48 (2H, m).

Example 103

5 *tert*-butyl 4-(2-(phenyl(pyridin-2-yl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45-1.51 (11H, m), 1.74 (2H, m), 3.00-3.07 (2H, m), 3.43-3.47 (1H, m), 3.66-3.69 (2H, m), 3.75 (2H, t, *J*=5.2 Hz), 4.38 (2H, t, *J*=4.8 Hz), 7.24-7.27 (1H, m), 7.39-7.43 (5H, m), 7.68-7.70 (2H, m), 8.61-8.63 (1H, m).

Example 104

10 *tert*-butyl 4-(2-((4-methoxyphenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45-1.55 (11H, m), 1.74-1.76 (2H, m), 2.99-3.08 (2H, m), 3.43-3.48 (1H, m), 3.66-3.77 (4H, m), 3.88 (3H, s), 4.27-4.33 (2H, m), 6.83-6.92 (1H, m), 7.32-7.48 (8H, m).

Example 105

tert-butyl 4-(2-(bis(4-methoxyphenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate

20 ¹HNMR: 1.45 (9H, s), 1.47-1.54 (2H, m), 1.76-1.79 (2H, m), 3.01-3.08 (2H, m), 3.45-3.49 (1H, m), 3.69-3.72 (2H, m), 3.75 (2H, t, *J*=5.2 Hz), 3.81 (3H, s), 3.84 (3H, s), 4.29 (2H, t, *J*=5.2 Hz), 6.83-6.87 (2H, m), 6.89-6.93 (2H, m), 7.33-7.37 (2H, m), 7.39-7.42 (2H, m).

Example 106

25 *tert*-butyl 4-(2-((4-chlorophenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45-1.50 (11H, m), 1.74-1.76 (2H, m), 3.00-3.09 (2H, m), 3.42-3.47 (1H, m), 3.68-3.75 (4H, m), 4.29-4.31 (2H, m), 7.26-7.46 (9H, m).

Example 107

30 *tert*-butyl 4-(2-((3,4-difluorophenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate

¹HNMR: 1.45 (9H, s), 1.48-1.55 (2H, m), 1.73-1.75 (2H, m), 3.02-3.10 (2H, m), 3.44-3.49 (1H, m), 3.69-3.75 (4H, m), 4.29-4.34 (2H, m), 7.10 (1H, s), 7.15 (1H, s), 7.20 (1H, s), 7.26-7.45 (5H, m).

Example 108

tert-butyl 4-(3-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)propyl)piperidine-1-carboxylate

Cesium carbonate (1.59 gm, 0.00492 moles) was added to a solution of 1-(4-(methylsulfonyl)phenyl)ethanone oxime (498.5 mg, 0.00234 moles) and *tert*-butyl 4-(3-(methylsulfonyloxy)propyl)piperidine-1-carboxylate (791 mg, 0.00246 moles) in dry DMF (10 ml) and the reaction mixture was stirred at 80 °C for 2 hours. Then reaction mixture was poured into ice cold water and extracted with ethyl acetate. The organic extract was washed with water and brine, dried over sodium sulfate and concentrated under reduced pressure to collect crude product. The crude product was purified by flash column chromatography (silica gel, 28 % ethyl acetate in hexane) to collect 967 mg of product as yellow oil.

¹HNMR: 1.08-1.25 (2H, m), 1.32-1.37 (2H, m), 1.41-1.43 (1H, m), 1.45 (9H, s), 1.68 (2H, d, *J*=12.4 Hz), 1.72-1.77 (2H, m), 2.25 (3H, s), 2.67 (2H, m), 3.05 (3H, s), 4.07-1.09 (2H, m), 4.21 (2H, t, *J*=6.8 Hz), 7.82-7.85 (2H, m), 7.91-7.94 (2H, m).

15 **Example 109**

1-(4-(methylsulfonyl)phenyl)ethanone O-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yl oxime

Cesium carbonate (1.7 gm, 0.00519 moles) was added to solution to 1-(4-(methylsulfonyl)phenyl)ethanone oxime (736 mg, 0.00346 moles) and 1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yl methanesulfonate (1.0 gm, 0.00346 moles) in dry DMF (20 ml) and the reaction mixture was stirred at 80 °C for 4 hours. Then reaction mixture was poured into ice cold water and solid separated was filtered and dried to yield 800 mg of product.

¹HNMR: 1.29 (6H, d, *J*=6.8Hz), 1.88-1.96 (2H, m), 2.05-2.12 (2H, m), 2.28 (3H, s), 2.86-2.96 (1H, m), 3.06 (3H, s), 3.53-3.59 (2H, m), 3.79-3.85 (2H, m), 4.48-4.53 (1H, m), 7.86 (2H, dd, *J*=8.8 & 2.0 Hz), 7.93 (2H, dd, *J*=7.2 & 1.6 Hz).

The following compounds are prepared by procedure similar to those described in example 109 with appropriate variations of reactants, reaction conditions and quantities of reagents.

30 **Example 110**

tert-butyl 4-((1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate

¹HNMR: 1.20-1.27 (2H, m), 1.46 (9H, s), 1.73 (2H, d, $J = 12.8$ Hz), 1.92-1.94 (1H, m), 2.22 (3H, s), 2.72-2.75 (2H, m), 4.52 (2H, d, $J = 6.8$ Hz), 4.09-4.12 (2H, m), 7.20 (2H, d, $J = 8.0$ Hz), 7.65-7.69 (2H, m).

Example 111

5 *tert*-butyl 4-((1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate

¹HNMR: 1.20-1.27 (2H, m), 1.46 (9H, s), 1.74 (2H, d, $J = 16.0$ Hz), 1.90-1.97 (1H, m), 2.25 (3H, s), 2.67-2.78 (2H, m), 3.05 (3H, s), 4.06-4.10 (4H, m), 7.83 - 7.85 (2H, m), 7.92-7.96 (2H, m).

Example 112

10 *tert*-butyl 4-((1-(2-fluoro-4-(methylsulfonyl)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate

¹HNMR: 1.20-1.27 (2H, m), 1.46 (9H, s), 1.74 (2H, d, $J = 12.4$ Hz), 1.90-1.95 (1H, m), 2.25 (3H, s), 2.69-2.75 (2H, m), 3.06 (3H, s), 4.08 (2H, d, $J = 6.4$ Hz), 4.12-4.14 (2H, m), 7.66-7.73 (3H, m).

Example 113

tert-butyl 4-(3-(diphenylmethyleneaminoxy)propyl)piperidine-1-carboxylate

15 ¹HNMR: 1.03-1.07 (2H, m), 1.24-1.30 (2H, m), 1.36-1.37 (1H, m), 1.45 (9H, s), 1.62 (2H, d, $J = 12.4$ Hz), 1.70-1.75 (2H, m), 2.63-2.65 (2H, m), 4.05 (2H, m), 4.16 (2H, t, $J = 16.0$ Hz), 7.29-7.35 (5H, m), 7.39-7.45 (3H, m), 7.46-7.48 (2H, m).

Example 114

tert-butyl 4-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)piperidine-1-carboxylate

25 ¹HNMR: 1.47 (9H, s), 1.72-1.77 (2H, m), 1.94-2.00 (2H, m), 2.27 (3H, s), 3.05 (3H, s), 3.23-3.30 (2H, m), 3.69-3.75 (2H, m), 4.39-4.43 (1H, m), 7.84 (2H, dd, $J = 7.2$ & 2.0 Hz), 7.93 (2H, dd, $J = 6.8$ & 1.6 Hz).

Example 115

1-(4-(Trifluoromethoxy)phenyl)ethanone O-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yl oxime

30 ¹HNMR: 1.29 (6H, d, $J = 6.8$ Hz), 1.87-1.95 (2H, m), 2.03-2.10 (2H, m), 2.25 (3H, s), 2.86-2.93 (1H, m), 3.52-3.59 (2H, m), 3.79-3.85 (2H, m), 4.44-4.48 (1H, m), 7.20 (2H, dd, $J = 8.8$ & 0.8 Hz), 7.66-7.69 (2H, m).

The following compounds can be prepared by procedure similar to those described in example 1-5 with appropriate variations of reactants, reaction conditions and quantities of reagents

Example: 116

5 Benzaldehyde O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime

Example: 117

Acetophenone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

10 **Example: 118**

1-(4-Methoxyphenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime

Example: 119

15 1-p-tolyethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 120

1-(4-Fluorophenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 121

20 1-(4-(Trifluoromethyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 122

25 1-(Naphthalen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 123

1-(Thiophen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 124

30 1-(Benzofuran-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 125

1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 126

Benzophenone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime

Example: 127

5 Bis(4-fluorophenyl)methanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime.

Example: 128

Benzaldehyde O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 129

10 Acetophenone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 130

15 1-(4-Methoxyphenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 131

1-p-tolyloethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 132

20 1-(4-Fluorophenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 133

1-(4-(Trifluoromethyl)phenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 134

25 1-(Naphthalen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

Example: 135

30 1-(Thiophen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

Example: 136

1-(Benzofuran-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime

Example: 137

1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 138

Benzophenone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Example: 139

Bis(4-fluorophenyl)methanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.

Biological Activity:

The biological activity of the compounds of the present invention were tested in the following in vitro and in vivo models mentioned here.

cAMP assay: A stable cell line expressing recombinant human GPR 119 receptor was established and used to investigate the efficacy of the compounds of the invention based on the intracellular levels of cyclic AMP (cAMP) using commercially available cAMP kits. Compounds of the invention produced a concentration dependent increase in cAMP level and EC₅₀ values of representative compounds were provided in table 1.

Table 1

Example	EC ₅₀
45	70 nM
32	83 nM
49	110 nM
48	324 nM
44	221 nM
41	74 nM
37	247 nM
8	149 nM
31	86.3 nM
33	35.8 nM
7	109 nM

In Vivo efficacy studies:

Feed Intake in Sprague Dawley rats:

Sprague Dawley rats of 6-8 week age were be used for this experiment they were be kept for acclimatization in reversed light / dark cycle for 15 days. Animals will have free access to a standard chow diet and water during acclimatization period. After 15 days reversed light / dark cycle acclimatization animals were trained for fasting induced feed intake for 5 days till they show consistent feed intake. Grouping was done based on the monitored feed intake the training days. On treatment day each group of animals were dosed with test compound or vehicle by appropriate routes of administration (orally or intraperitoneally). Exactly 30 min. after treatment, measured amount of standard chow diet was provided and recorded as 0-min feed offered. Then subsequently 2, 4, 6 and 24 hour after 0-min, feed intake was measured and the cumulative feed intakes were calculated. The change in cumulative feed intake as compare to vehicle treated control at each time point was calculated for test compound and results were provided in table 2

Table 2

Example	Dose (mg/kg)	% reduction in food in take			
		2hour	4 hour	6 hour	24 hour
45	25	40	36	40	12
32	25	39	41	39	22
49	30	40	25	20	11
48	100	61	47	26	20
44	100	54	43	36	8
41	100	71	40	39	19
37	100	58	36	33	28
8	100	93	77	72	33
31	100	42	36	39	15
33	100	49	38	32	14
7	100	69	50	47	22

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Oral Glucose Tolerance Tests (OGTT) in C57/BL6 mice:

C57/BL6 mice of 6-8 week age were used for this experiment. Animals were grouped based on non-fasting serum glucose levels and kept on fasting for overnight (day before OGTT). On the experiment day, each animal received a single dose of vehicle/test compounds (30 mg/kg) were administered orally, 30 min post dosing animals were bled

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for basal glucose level estimation and at same time glucose load (3gm/kg) will be administered per orally. Blood was collected at time points corresponding to 20, 40, 60 and 120 min after glucose load administration. Serum was separated for determination of glucose levels and change in area under curve for glucose was calculated and provided in table 3 as % reduction in AUC.

Table 3

Example	% reduction in AUC at 30 mg/kg
8	21
32	26
49	25
55	27

Thus, the compounds of the present invention are selective to the GPR-119 receptor and shows potential to reduce food intake and thereby has potential to help control/reduce obesity. Additionally, they have potential glucose reducing effects in various degrees. Thus, these compounds may be useful as potential treatments of diabetes &/or obesity.

The novel compounds of the present invention (I) may be formulated into suitable pharmaceutically acceptable compositions by combining with suitable excipients by techniques and processes and concentrations as are well known.

The compounds of formula (I) or pharmaceutical compositions containing them are suitable for humans and other warm blooded animals, and may be administered either by oral, topical or parenteral administration for the treatment of various disease conditions associated with dyslipidemia, obesity etc.

The pharmaceutical composition is provided by employing conventional techniques. Preferably the composition is in unit dosage form containing an effective amount of the active component, that is, the compounds of formula (I) according to this invention.

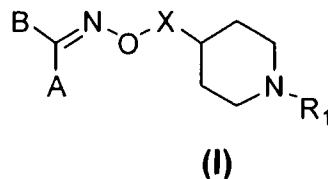
The quantity of active component, that is, the compounds of formula (I) according to this invention, in the pharmaceutical composition and unit dosage form thereof may be varied or adjusted widely depending upon the particular application method, the potency of the particular compound and the desired concentration.

Generally, the quantity of active component will range between 0.5% to 90% by weight of the composition.

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We claim:

1. Compounds of the general formula (I),



- 5 their tautomeric forms, their stereoisomers, their pharmaceutically acceptable salts, and pharmaceutical compositions containing them wherein each of 'A' and 'B' independently represents H, optionally substituted linear or branched (C₁-C₆)alkyl or an optionally substituted single or fused group selected from aryl, heteroaryl, heterocyclyl, cycloalkyl groups; 'X' represents either a bond or a group represented by Y-Z, wherein 'Z' represents O, NH or a further bond and 'Y' represents optionally substituted linear or branched (C₁-C₆)alkyl or an optionally substituted single or fused group selected from aryl, heteroaryl, cycloalkyl groups; R₁ represents optionally substituted groups selected from linear or branched (C₁-C₆)alkyl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, hererocyclylalkyl, heteroaryl, heteroaralkyl or the group C(O)OR₂ wherein R₂ represents, optionally substituted linear or branched (C₁-C₆)alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, hererocyclylalkyl, heteroaryl, heteroaralkyl groups.
- 10 2. The compounds as claimed in claim 1, wherein the groups representing R₁ and Y are selected independently from aryl or heteroaryl groups.
- 15 3. The compounds as claimed in claim 1 wherein, when any of A, B, R₁ or Y independently represents an aryl group, the aryl groups are selected from phenyl, naphthyl, tetrahydronaphthyl groups.
- 20 4. The compounds as claimed in claim 1 wherein, when any of A, B independently represents a heteroaryl, group, the heteroaryl groups are selected from pyridyl, thienyl, benzofuranyl, Benzo[1,3]dioxole, benzimidazolyl, benzothiazinonyl, benzothiazinonyl, phenothiazinyl, phenoxazinyl isoxazolyl, furyl, oxazolyl, thiazolyl, indolinyl groups.
- 25 5. The compounds as claimed in claim 1 wherein, when any of A or B independently represents a heterocyclyl group, the heterocyclyl groups are selected from

pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, oxazolidinyl, thiazolidinyl groups.

6. The compounds as claimed in claim 1 wherein, when 'Y' represents a heteroaryl group, the groups are selected from pyrimidinyl, pyridyl, pyridazinyl, phthalazynil, benzoxazinyl, benzimidazolyl, benzotriazolyl groups.
7. The compounds as claimed in claim 1 wherein, when R₁ represents a heteroaryl group, the groups are selected from oxadiazolyl, pyridyl, pyrimidinyl, triazinyl, triazolyl, tetrazolyl, purinyl groups.
8. The compounds as claimed in claim 1 wherein, when R₁ represents a heterocyclyl group, the groups are selected from pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl groups.
9. The compounds of any of the preceding claims wherein the substituents on any of 'A', 'B' 'Y' 'R₁' or 'R₂' are selected from hydroxyl, oxo, halo, thio, nitro optionally substituted groups selected from alkyl, alkenyl, haloalkyl alkoxy, haloalkoxy aryl, aryloxy, aralkyl, aralkoxy, heterocyllyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclyoxy hydroxyalkyl, aminoalkyl, alkoxyalkyl, aryloxyalkyl alkylthio, thioalkyl, arylthio sulfenyl derivatives, sulfonyl derivatives, sulfonyloxy derivatives, sulfonic acid and its derivatives, carboxylic acid and its derivatives.
10. The compounds as claimed any preceding claim wherein, when the substituents on any of 'A', 'B' 'Y' 'R₁' or R₂ are further substituted, those substituents are selected from hydroxyl, oxo, halo, thio, nitro, amino, alkoxy, carboxylic acid and its derivatives such as esters and amides, acyl, sulfenyl derivatives, sulfonyl derivatives, sulfonyloxy derivatives, sulfonic acid and its derivatives.
11. The compounds as claimed in claim 1, selected from
- 1-(4-(Methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Methylsulfonyl)phenyl)ethanone O-6-(1-(3-*iso*-propyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime;
- tert*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate;
- 1-(4-(Methylsulfonyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

- iso*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 5 *iso*-propyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 10 *iso*-propyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 15 *iso*-propyl 4-(5-methyl-6-(1-(4-nitrophenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-*p*-tolylethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(4-fluorophenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 20 *iso*-propyl 4-(6-(1-(4-methoxyphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(naphthalen-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 25 *iso*-propyl 4-(6-(1-(benzofuran-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(4-butylphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(4-methoxy-3-methylphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 30 *iso*-propyl 4-(5-methyl-6-(1-(pyridin-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(1-(3,4-dimethoxyphenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;

- iso*-propyl 4-(6-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 5 *iso*-propyl 4-(6-(1-(4-methoxyphenyl)hexylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-(diphenylmethyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(5-methyl-6-(phenyl(pyridin-2-yl)methyleneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 10 *iso*-propyl 4-(6-(bis(4-fluorophenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-propyl 4-(6-((3,4-difluorophenyl)(phenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 15 *iso*-propyl 4-(6-(bis(4-methoxyphenyl)methyleneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(2-fluoro-4-(methylsulfonyl)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 20 *tert*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 25 *tert*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 30 *tert*-butyl 4-(6-(1-(4-(benzyloxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(5-nitro-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-butyl 4-(5-methyl-6-(1-(4-

- (trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-butyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 5 *iso*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- iso*-butyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- Ethyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 10 Ethyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Ethyl 4-(6-(1-(4-(allyloxy)phenyl)ethylideneaminoxy)-5-methylpyrimidin-4-yloxy)piperidine-1-carboxylate;
- 15 Phenyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Phenyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Phenyl 4-(5-methyl-6-(1-(pyridin-3-yl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 20 Benzyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- Benzyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)piperidine-1-carboxylate;
- 25 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-Methoxyphenyl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-*p*-tolylethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 30 1-(Pyridin-3-yl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-Fluorophenyl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;

- 1-(Benzo[d][1,3]dioxol-5-yl)ethanone-O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 5 1-(Benzo[d][1,3]dioxol-5-yl)ethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-(2-Fluoro-4-(methylsulfonyl)phenyl)ethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 10 1-(Benzo[d][1,3]dioxol-5-yl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Methylsulfonyl)phenyl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 15 1-(Pyridin-3-yl)ethanone-O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-6-(1-benzylpiperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-5-methyl-6-(1-(3-nitropyridin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 20 (1-(4-(Methylsulfonyl)phenyl)ethanone-O-5-methyl-6-(1-(3-nitropyridin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- tert*-butyl 4-(5-methyl-6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyrimidin-4-yloxy)-1,4'-bipiperidine-1'-carboxylate;
- 25 *tert*-butyl 4-(5-methyl-6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyrimidin-4-ylamino)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 30 *tert*-butyl 4-(6-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;

- tert*-butyl 4-(6-(1-*p*-tolylethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-fluorophenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 5 *tert*-butyl 4-(6-(1-(pyridin-3-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(benzofuran-2-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 10 *tert*-butyl 4-(6-(1-(4-methoxyphenyl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- tert*-butyl 4-(6-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)pyridazin-3-yloxy)piperidine-1-carboxylate;
- 15 1-(4-(Trifluoromethoxy)phenyl)ethanone O-6-(1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yloxy)pyridazin-3-yl oxime;
- tert*-butyl 4-(2-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(pyridin-3-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 20 *tert*-butyl 4-(2-(1-(5,6,7,8-tetrahydronaphthalen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(biphenyl-4-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(pyridin-4-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(pyridin-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 25 *tert*-butyl 4-(2-(1-(benzofuran-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-*p*-tolylethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-fluorophenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 30 *tert*-butyl 4-(2-(1-(naphthalen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-(trifluoromethyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;

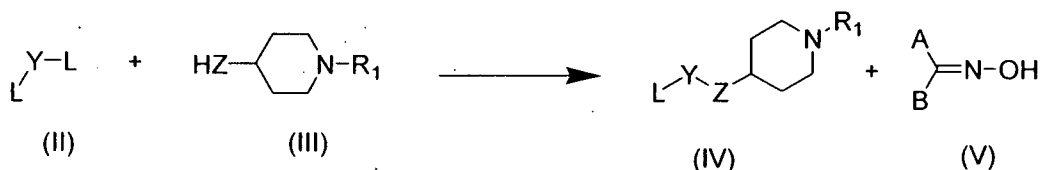
- tert*-butyl 4-(2-(1-(5-chlorothiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(5-bromothiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 5 *tert*-butyl 4-(2-(1-(thiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-methoxyphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(3,4-dimethoxyphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- 10 *tert*-butyl 4-(2-(1-(4-(methoxymethoxy)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(5-methylthiophen-2-yl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-methoxy-3-methylphenyl)ethylideneaminoxy)ethoxy)piperidine-
- 15 1-carboxylate;
- tert*-butyl 4-(2-(1-(4-nitrophenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(3,4-
- 20 bis(trifluoromethyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(4-butylphenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(1-(2-fluoro-4-
- (methylsulfonyl)phenyl)ethylideneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(diphenylmethyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- 25 *tert*-butyl 4-(2-(phenyl(pyridin-2-yl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-((4-methoxyphenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-(bis(4-methoxyphenyl)methyleneaminoxy)ethoxy)piperidine-1-
- 30 carboxylate;
- tert*-butyl 4-(2-((4-chlorophenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;
- tert*-butyl 4-(2-((3,4-difluorophenyl)(phenyl)methyleneaminoxy)ethoxy)piperidine-1-carboxylate;

- tert*-butyl 4-(3-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)propyl)piperidine-1-carboxylate;
- 1-(4-(Methylsulfonyl)phenyl)ethanone O-1-(3-isopropyl-1,2,4-oxadiazol-5-yl)piperidin-4-yl oxime;
- 5 *tert*-butyl 4-((1-(4-(trifluoromethoxy)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate;
- tert*-butyl 4-((1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate;
- tert*-butyl 4-((1-(2-fluoro-4-
- 10 (methylsulfonyl)phenyl)ethylideneaminoxy)methyl)piperidine-1-carboxylate;
- tert*-butyl 4-(3-(diphenylmethyleneaminoxy)propyl)piperidine-1-carboxylate;
- tert*-butyl 4-(1-(4-(methylsulfonyl)phenyl)ethylideneaminoxy)piperidine-1-carboxylate;
- 1-(4-(Trifluoromethoxy)phenyl)ethanone-O-1-(3-isopropyl-1,2,4-oxadiazol-5-
- 15 yl)piperidin-4-yl oxime;
- Benzaldehyde-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- Acetophenone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 20 1-(4-Methoxyphenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-p-tolyethanone-O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-(4-Fluorophenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-
- 25 yloxy)pyrimidin-4-yl oxime;
- 1-(4-(Trifluoromethyl)phenyl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-(Naphthalen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 30 1-(Thiophen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 1-(Benzofuran-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;

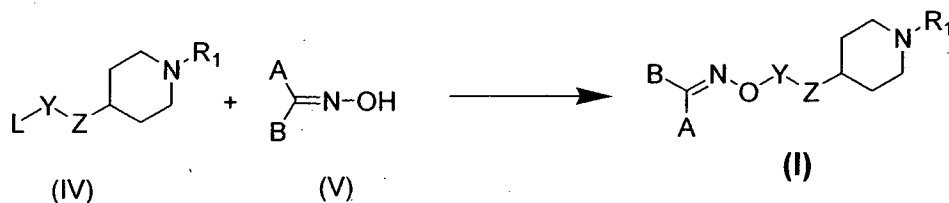
- 1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
Benzophenone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
- 5 Bis(4-fluorophenyl)methanone O-5-methyl-6-(1-(pyrimidin-2-yl)piperidin-4-yloxy)pyrimidin-4-yl oxime;
Benzaldehyde O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
Acetophenone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-
- 10 yl oxime;
1-(4-Methoxyphenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
1-p-tolyloethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 15 1-(4-Fluorophenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
1-(4-(Trifluoromethyl)phenyl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 20 1-(Naphthalen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
1-(Thiophen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 1-(Benzofuran-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 25 1-(5,6,7,8-Tetrahydronaphthalen-2-yl)ethanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
Benzophenone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime;
- 30 Bis(4-fluorophenyl)methanone O-6-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yloxy)-5-methylpyrimidin-4-yl oxime.
11. A pharmaceutical composition which comprises compounds of formula (I), as claimed in any preceding claims and a pharmaceutically acceptable carrier, diluent or excipients.

12. The compounds as claimed any preceding claims suitable as modulators of GPR-119 receptors.
13. The compounds as claimed in claim 12 suitable as a glucose lowering agent suitable for humans and other warm blooded animals.
- 5 14. The compounds as claimed in claim 12 suitable as an anti-obesity agent for humans and other warm blooded animals.
15. A medicine suitable as a glucose lowering agent comprising a compound of formula (I), as defined in any preceding claims and a pharmaceutically acceptable carrier, diluent or excipients to a patient in need thereof.
- 10 16. A medicine suitable as an anti-obesity agent comprising a compound of formula (I), as defined in any preceding claims and a pharmaceutically acceptable carrier, diluent or excipients to a patient in need thereof.
17. Use of compounds of formula (I), their pharmaceutical compositions and medicines containing them as defined in any previous claims as a medicament suitable for the
- 15 treatment of diseases mentioned in any of the aforesaid claims.
18. Modulators of GPR-119 receptors as described in the aforesaid description and claims.
19. A process for preparing compounds of formula (I) wherein A, B, Z and R₁ are as defined in claim 1 and Y represents aryl, heteroaryl, heterocyclyl, cycloalkyl
- 20 groups, comprising the steps of

- i. reacting compounds of general formula (II), Where L represents a suitable leaving group and Y is as defined in claim 1 with compounds of general formula (III), where Z and R₁ are as defined in claim 1 to yield compound of general formula (IV) where all symbols are as defined earlier;

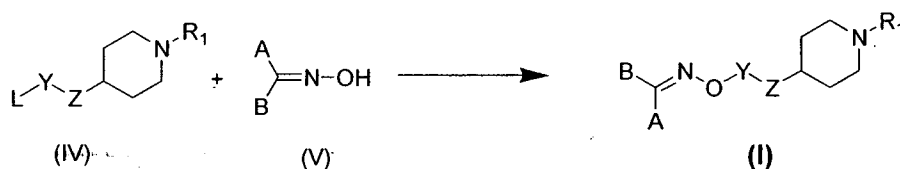


- 25 ii. reacting compound of general formula (IV) where all symbols are as defined in claim 1, with compounds of general formula (V) where all symbols are as defined in claim 1 to yield the compound of general formula (I).



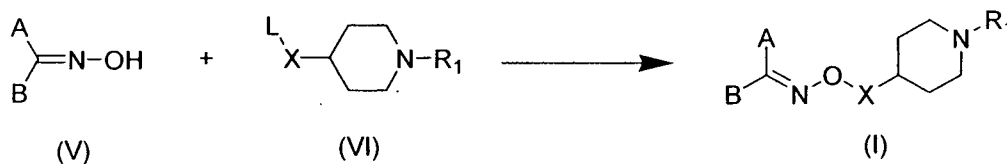
20. A process for preparing compounds of formula (I) wherein A, B, Z and R₁ are defined in claim 1 and Y represents linear or branched C₍₁₋₆₎alkyl comprising the steps of

- 5 i. reacting compound of general formula (IV) where all symbols are as defined in claim 1 and Y represents linear or branched C₍₁₋₆₎alkyl with compound of general formula (V) where all symbols are as defined in claim 1 to yield the compound of general formula (I).



21. A process for preparing compounds of formula (I) wherein X represents linear or branched C₍₁₋₆₎alkyl or a bond and A, B and R₁ are defined in claim 1 comprising the steps of

- 15 i. reacting compounds of general formula (V) where all symbols are as defined in claim 1 with compounds of general formula (VI), where all symbols are as defined in claim 1, and 'L' represents a suitable leaving group to yield compound of general formula (I) where all symbols are as defined earlier.



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