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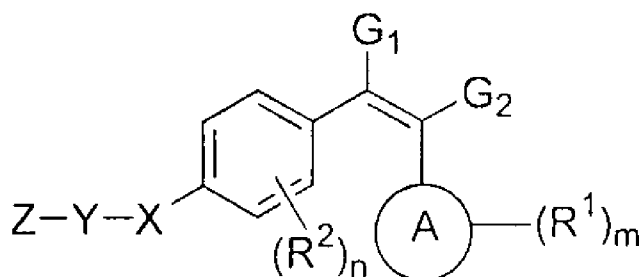
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(54) Title: ARYL SUBSTITUTED OLEFINIC COMPOUNDS AS PDE10A INHIBITORS



(I)

(57) Abstract: The present invention provides aryl substituted olefinic compounds as Phosphodiesterase 1 0A (PDE 1 0A) inhibitors. In particular, compounds described herein are useful for treating or preventing diseases, conditions and/or disorders by inhibiting Phosphodiesterase 1 0A enzyme. Also provided herein are processes for preparing compounds described herein, intermediates used in their synthesis, pharmaceutical compositions thereof.



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ARYL SUBSTITUTED OLEFINIC COMPOUNDS AS PDE10A INHIBITORSRelated applications

This application claims the benefit of Indian Provisional Application Nos. 1418/MUM/2010 filed on May 04, 2010; 3006/MUM/2010 filed on October 29, 2010; and US Provisional application Nos. 61/334,903 filed on May 14, 2010; 61/416,498 filed on November 23, 2010 and all of which are hereby incorporated by reference.

Technical Field

The present invention relates to aryl substituted olefinic compounds and their use in treating or preventing diseases, conditions and/or disorders by inhibiting phosphodiesterase 10A (PDE10A) enzyme.

Background of the Invention

The cyclic nucleotide phosphodiesterases (PDEs) are a class of intracellular enzymes related to a family of phosphohydrolases that selectively catalyze the hydrolysis of the 3' cyclic phosphate bonds of adenosine and/or guanosine 3',5' cyclic monophosphates (cAMP/cGMP) into their respective 5' monophosphates (5'-AMP/GMP). The cyclic nucleotides cAMP and cGMP act as second messengers of intracellular signal transduction in response to extracellular stimuli and are synthesized from ATP and GTP by the catalytic cyclization activity of enzymes adenylyl and guanylyl cyclases, respectively. PDEs play a very important role in signal transduction by regulating the cellular levels of these second messengers (cAMP/cGMP) in the way of controlling their rates of degradation.

Mammalian PDEs are composed of 21 genes and are categorized into 11 families (PDE1 to PDE11), with each family typically having several different isoforms and splice variants, based on sequence homology, enzymatic properties, biochemical characteristics and sensitivity to inhibitors. These unique PDEs differ in their three-dimensional structures, kinetic properties, modes of regulation, intracellular localization, cellular expression patterns with different individual isozymes modulating distinct regulatory pathways in the cell. Furthermore, PDEs are differentially expressed throughout the body, including in the central nervous system, serving

distinct physiological functions. Thus PDEs provide an unique opportunity of selective drug targets for the potential treatment of specific disease states.

PDEs are also subclassified based on different substrate specificities into cAMP selective (PDE4, 7 and 8), cGMP selective (PDE5, 6 and 9) and cAMP and cGMP dual selective (PDE1, 2, 3, 10 and 11). The human PDE10A family enzyme was reported essentially at the same time by two different groups (Fujishige K et al., *J. Biol. Chem.* vol. 274, p.18438-18445, (1999); Loughney K et al., *Gene* vol. 234, p. 109-117, (1999); Loughney K et al., WO 99/42596) based on the identification of cDNA fragments published in the National Center for Biotechnology Information (NCBI) Expressed Sequence Tags (EST) database. To till date there is only one gene in this family, PDE10A, although four variants PDE10A1-4 have been described. While PDE10A was found to share homology with known PDEs, no function could be identified for PDE10. PDE10 has been identified as a unique family based on primary amino acid sequence and distinct enzymatic activity. The murine homologue has also been cloned [(Soderling, S. et al., *Proc. Natl. Acad. Sci. USA* vol. 96 p. 7071-7076, (1999)] and N-terminal splice variants of both the rat and human genes have been identified [Kotera, J. et al., *Biochem. Biophys. Res. Comm.* vol. 261, p. 551-557, (1999); Fujishige, K. et al., *Eur. J. Biochem.* vol. 266, p. 1118-1127, (1999)]. There is a high degree of homology across species. The mouse PDE10A1 is a 779 amino acid protein that hydrolyzes both cAMP and cGMP to AMP and GMP, respectively. PDE10A hydrolyzes cAMP with a K_m of 0.05 μ M and cGMP with a K_m of 3 μ M, suggesting that the affinity of PDE10A for cAMP is higher than for cGMP. However, approximately 5-fold greater V_{max} for cGMP over cAMP (V_{max} ratio of cGMP/cAMP is 4.7) has lead to the suggestion that PDE 10A is a unique cAMP-inhibited cGMP phosphodiesterase [Soderling, SH et al., *Proc. Natl. Acad. Sci. USA* vol. 96 p. 7071-7076, (1999); Fujishige et al., *J. Biol. Chem.* vol. 274, p. 18438-18445, (1999)].

The PDE10A family of polypeptides shows a lower degree of sequence homology to previously identified PDE families. These low degrees of sequence homology of PDE10A family of polypeptide make them insensitive to certain inhibitors that are known to be specific for other known PDE families (US 6,350,603, incorporated herein by reference).

Regarding PDE10A which is one of the PDE subtypes, the expression of its mRNA has been identified in many tissues and organs such as striatum, testis, kidney, thyroid gland,

pituitary gland, thalamus, cerebellum, heart, lungs and placenta, cells such as aortic smooth muscle cells and aortic endothelial cells, cells of cancers such as lung small cell carcinoma, breast cancer and large bowel cancer. Accordingly, the possibility that PDE10A is involved in diseases related to these cells, tissues and organs has been demonstrated [*J. Biol. Chem.* vol. 274, p. 18438 (1999), *Gene*, vol. 234, p. 109 (1999) and WO 01/29199].

From the view points of strong expression of mRNA of PDE10A and its enzymatic activity in the striatum, medium spiny striatal neuronal projections, nucleus accumbens, thalamus, pineal & pituitary glands of [Lakics V et al., *Neuropharmacology*, vol 59, p. 367-374, (2011)] this enzyme is suggested to be involved in, for example, onset or progression of various disorders and diseases related to striatal, basal ganglia related dysfunctions/disorders such as schizophrenia (positive, negative & cognitive symptoms), parkinson's disease, Huntington disease, obsessive compulsive disorders, sleep disorders and disorders of changed circadian rhythm [Siuciak JA et al., *Neuropharmacology*, vol 51, p. 374-385, (2006); Threlfell S et al., *JPET*, vol 328, p. 785-795, (2009); Grauer SM et al., *JPET*, vol.331, p.574-590, (2009); Szwed-Berger I et al., *Neuroendocrinology*, (2011)DOI:10.1159/000327138]. It has been reported that PDE10A mRNA expression in the striatum of Huntington disease mouse model is different from that in the striatum of normal mice (WO 01/24781) and chronic suppression of PDE10A alters striatal expression of genes responsible for neurotransmitter synthesis, neurotransmission and signaling pathways implicated in Huntington's disease [Kleiman RJ et al., *JPET*, vol.336, p.64-76, (2011)].

There are very few effective treatments for neurological disorders characterized by progressive cell loss, known as neurodegenerative diseases, as well as those involving acute cell loss, such as stroke and trauma. In addition, few effective treatments exist for neurological disorders such as psychosis which has been linked to altered striatal function relating to changes in expression of the enzyme PDE10A [J. A. Siuciak, et al. *Neuropharmacology*, vol. 51, p. 374-385, (2006)]. Striatal dysfunction is implicated in a number of CNS disorders including psychosis, schizophrenia, obsessive-compulsive disorders, Parkinson's disease and Huntington's disease. The results with PDE10A knock-out mice provide evidence that PDE10A functions to inhibit striatal output by reducing spiny medium neuron excitability. PDE10A is selectively expressed in dopamine receptive medium spiny neurons, and considerable data suggests that

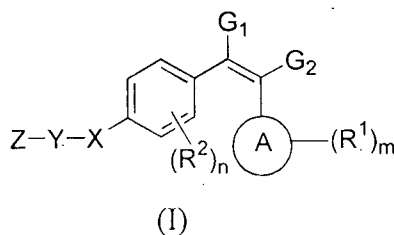
cAMP and cGMP signalling pathways play significant roles in the regulation of medium spiny neuron excitability. Additional studies with papaverine, a potent inhibitor of PDE10A, confirm that PDE10A regulates both cAMP and cGMP in vivo in rats [J. A. Siuciak, et al. *Neuropharmacology*. vol. 51, p. 386-396, (2006)].

In view of the foregoing, PDE10A inhibitors are useful for treating and/or preventing various diseases caused by enhanced activity of PDE10A, possibly with reduced side effects (for example, a neural disease such as Parkinson's disease, Huntington disease or Alzheimer's disease, dyskinesia, hypogonadism, diabetes, an ischemic heart disease, hypertension, an inflammatory disease, a disease of the digestive system, an allergic disease, osteoporosis, pain or a malignant tumor).

WO 2003/000269, WO 2003/014115, WO 2003/014116, WO 2003/014117, WO 2003/051877, WO 2006/034491 and WO 2006/034512 describe PDE10 inhibitors for treatment of neurodegenerative diseases, cancer, diabetes and its related disorders. Also WO 2006/072828, WO 2008/084299, WO 2003/093499, WO 2005/082883, WO 2005/120514, WO 2006/011040, WO 2006/070284, WO 2007/077490, WO 2007/085954, WO 2007/096743, WO 2007/129183, WO 2008/001182, WO 2008/004117, WO 2008/020302, WO 2009/070584, WO 2009/068320, WO 2009/068246 and WO 2009/036766 describe PDE10 inhibitors for treatment of obesity, diabetes, certain central nervous system disorders, neurodegenerative and psychiatric disorders. Also WO 2009/029214, WO 2009/025839 and WO 2009/025823 describe PDE10 inhibitors for treatment of obesity, non-insulin dependent diabetes, schizophrenia, bipolar disorder and obsessive-compulsive disorder. WO 2009/143178, WO 2009/152825, WO 2009/158393, WO 2009/158467, WO 2009/158473, WO 2010/006130, WO 2010/017236, WO 2010/027097 and WO 2010/030027 describe PDE10 inhibitors for treatment of anxiety, schizophrenia, drug addiction, movement disorder, certain central nervous system disorders, neurodegenerative and psychiatric disorders.

Summary of the Invention

The present invention relates to compounds of the formula (I):



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from -O-, -S-, -NR³-, -S(O)-, -SO₂-, -(CR⁴R⁵)_pO-, -(CR⁴R⁵)_pN(R³)-, -C≡C-, -(CR⁴R⁵)_pC≡C-, -(R⁶)C=C(R⁷)- and -(CR⁴R⁵)_p(R⁶)C=C(R⁷)-;

Y is a bond, or is selected from -(CR⁴R⁵)_p- and -SO₂-;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

G₁ and G₂, are independently selected from, hydrogen, cyano, nitro, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, haloalkyl, haloalkoxy, cycloalkyl, aryl, heteroaryl, heterocyclyl, -(CR⁴R⁵)_pR⁸, -(CR⁴R⁵)_pC(O)R⁸, -(CR⁴R⁵)_p-NR⁹R¹⁰, -(CR⁴R⁵)_p-OR¹¹, -C(O)R⁸, -C(O)(CR⁴R⁵)_pR⁸, -C(O)NR⁹R¹⁰, -NR⁹R¹⁰, -NR³C(O)R⁸, -NR³C(O)NR⁹R¹⁰, -N(R³)SO₂R⁸, -OC(O)R⁸ and -OC(O)NR⁹R¹⁰; with the proviso that at least one of G₁ or G₂ is not hydrogen;

at each occurrence, R¹ and R², which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -C(O)R^a, -C(O)NR^bR^c, -C(O)OR^a, -NR^bR^c, -NR^bC(O)R^a, -NR^bC(O)NR^bR^c, -N(R^b)SO₂R^a, -OC(O)R^a, -OC(O)NR^bR^c, -S(O)R^a, -SO₂R^a, -SONR^bR^c, -SO₂NR^bR^c and -SR^a;

R³ is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and -C(O)OR^a;

at each occurrence, R⁴, R⁵, R⁶ and R⁷, which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy,

cycloalkyl, aryl, heterocyclyl, heteroaryl, $-C(O)OR^a$, $-NR^bR^c$ and $-SR^a$; or R^4 and R^5 , at each occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

R^8 is selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-NR^bR^c$, $-NR^bC(O)R^a$, $-NR^bC(O)NR^bR^c$, $-N(R^b)SO_2R^a$, $-OC(O)R^a$, $-OC(O)NR^bR^c$, $-S(O)R^a$, $-SO_2R^a$, $-SONR^bR^c$, $-SO_2NR^bR^c$ and $-SR^a$;

R^9 and R^{10} , which may be the same or different, are independently selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-S(O)R^a$, $-SO_2R^a$, $-S(O)NR^bR^c$ and $-SO_2NR^bR^c$; or R^9 and R^{10} together with the nitrogen atom to which they are attached, may form an optionally substituted heterocyclyl or heteroaryl ring, wherein said heterocyclic or heteroaryl ring may contain 1, 2, 3 or 4 hetero atom(s) selected from O, S or N;

R^{11} is selected from hydrogen, nitro, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-NR^bR^c$, $-NR^bC(O)R^a$, $-NR^bC(O)NR^bR^c$, $-N(R^b)SO_2R^a$, $-S(O)R^a$, $-SO_2R^a$, $-S(O)NR^bR^c$ and $-SO_2NR^bR^c$;

at each occurrence, R^a , R^d and R^e , which may be the same or different, are independently selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive;

'p' is an integer ranging from 1 to 3, both inclusive;

'q' is an integer ranging from 1 to 3, both inclusive;

with the proviso that the compound of formula (I) is not

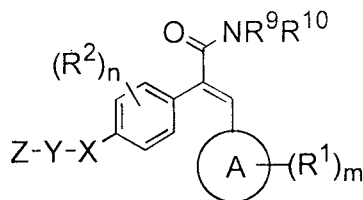
4-Hydroxy-*N*-methyl-3-(pyridine-4-yl)-2-(4-(quinoline-2-ylmethoxy)phenyl)but-2-enamide;

4-{4-[(Quinolin-2-yl)methoxy]phenyl}-3-(phenyl)but-3-en-2-one; and

4-{4-[(Quinolin-2-yl)methoxy]phenyl}-3-(pyridine-4-yl)but-3-en-2-one.

The compounds of formula (I) may involve one or more embodiments. It is to be understood that the embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, there is provided a compound of the formula (Ia):



(Ia)

or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from $-O-$, $-S-$, $-NR^3-$, $-S(O)-$, $-SO_2-$, $-(CR^4R^5)_pO-$, $-(CR^4R^5)_pN(R^3)-$, $-C\equiv C-$, $-(CR^4R^5)_pC\equiv C-$, $-(R^6)C=C(R^7)-$ and $-(CR^4R^5)_p(R^6)C=C(R^7)-$;

Y is a bond, or is selected from $-(CR^4R^5)_p-$ and $-SO_2-$;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl,

alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-NR^bR^c$, $-NR^bC(O)R^a$, $-NR^bC(O)NR^bR^c$, $-N(R^b)SO_2R^a$, $-OC(O)R^a$, $-OC(O)NR^bR^c$, $-S(O)R^a$, $-SO_2R^a$, $-SONR^bR^c$, $-SO_2NR^bR^c$ and $-SR^a$;

R^3 is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and $-C(O)OR^a$;

at each occurrence, R^4 , R^5 , R^6 and R^7 , which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, $-C(O)OR^a$, $-NR^bR^c$ and $-SR^a$; or R^4 and R^5 , at each occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

R^9 and R^{10} , which may be the same or different, are independently selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-S(O)R^a$, $-SO_2R^a$, $-S(O)NR^bR^c$ and $-SO_2NR^bR^c$; or R^9 and R^{10} together with the nitrogen atom to which they are attached, may form an optionally substituted heterocyclyl or heteroaryl ring, wherein said heterocyclic or heteroaryl ring may contain 1, 2, 3 or 4 hetero atom(s) selected from O, S or N;

at each occurrence, R^a , R^d and R^e , which may be the same or different, are independently selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive;

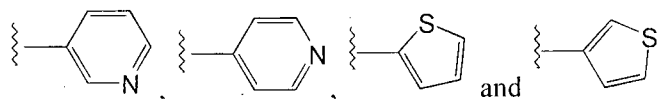
'p' is an integer ranging from 1 to 3, both inclusive; and

'q' is an integer ranging from 1 to 3, both inclusive.

The embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (Ia) in which A is selected aryl, preferably phenyl.

According to another embodiment, specifically provided are compounds of the formula (Ia) in which A is heteroaryl selected from a group consisting of



According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^1 is halogen (e.g., fluorine or chlorine), haloalkyl (e.g., trifluoromethyl), alkoxy (e.g., methoxy) or haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy); and 'm' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which 'm' is 0.

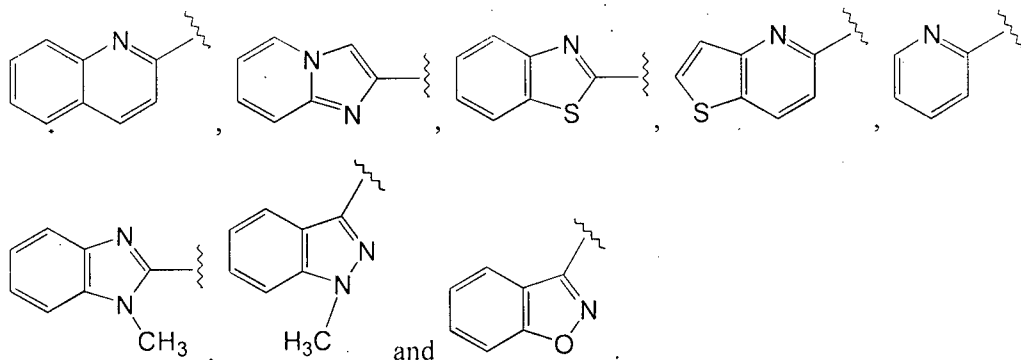
According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which 'n' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which X is $-O-$.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which X is bond.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which Y is $-(CR^4R^5)_p-$; wherein both R^4 and R^5 are hydrogen and 'p' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which Z is substituted or unsubstituted heteroaryl selected from a group consisting of



According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^9 is hydrogen.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^{10} is hydrogen, alkyl (e.g., methyl or ethyl), cyanoalkyl (e.g., cyanoethyl), haloalkyl (e.g., trifluoromethyl, trifluoroethyl), hydroxyalkyl (e.g., hydroxyethyl), cycloalkyl (e.g., cyclopropyl), heterocyclyl (e.g., piperidinyl) or heteroaryl (e.g., thiazole).

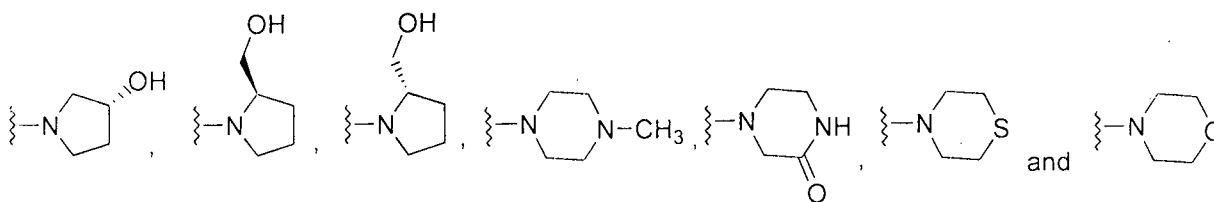
According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^{10} is $-(CR^dR^e)_qR^a$; wherein R^d and R^e are independently alkyl (e.g., methyl or ethyl), hydroxyalkyl (e.g., hydroxymethyl) or phenyl and R^a is hydrogen. In this embodiment 'q' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^{10} is $-(CR^dR^e)_qR^a$; wherein both R^d and R^e are hydrogen and R^a is $-NR^fR^g$ or $-C(O)NR^fR^g$. In this embodiment R^f and R^g are independently hydrogen, alkyl (e.g., methyl or ethyl) or $-C(O)$ alkyl (e.g., $-C(O)$ methyl); and 'q' is 1 or 2.

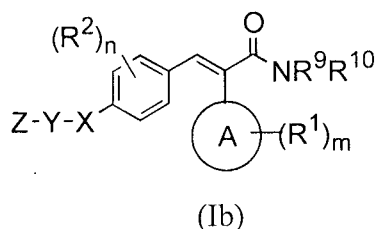
According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^{10} is $-(CR^dR^e)_qR^a$; wherein both R^d and R^e are hydrogen or alkoxy (e.g., methoxy) and R^a is hydrogen. In this embodiment 'q' is 2.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^{10} is $-(CR^dR^e)_qR^a$; wherein R^a is hydrogen; R^d is alkyl (e.g., methyl) and R^e is $-C(O)OR^f$. In this embodiment R^f is hydrogen or alkyl (e.g., ethyl); and 'q' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ia) in which R^9 and R^{10} together with the nitrogen atom to which they are attached, forms an heterocyclic ring selected from a group consisting of



According to one embodiment, there is provided a compound of the formula (Ib):



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from -O-, -S-, -NR³-, -S(O)-, -SO₂-, -(CR⁴R⁵)_pO-, -(CR⁴R⁵)_pN(R³)-, -C≡C-, -(CR⁴R⁵)_pC≡C-, -(R⁶)C=C(R⁷)- and -(CR⁴R⁵)_p(R⁶)C=C(R⁷)-;

Y is a bond, or is selected from -(CR⁴R⁵)_p- and -SO₂-;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

at each occurrence, R¹ and R², which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -C(O)R^a, -C(O)NR^bR^c, -C(O)OR^a, -NR^bR^c, -NR^bC(O)R^a, -NR^bC(O)NR^bR^c, -N(R^b)SO₂R^a, -OC(O)R^a, -OC(O)NR^bR^c, -S(O)R^a, -SO₂R^a, -SONR^bR^c, -SO₂NR^bR^c and -SR^a;

R³ is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and -C(O)OR^a;

at each occurrence, R⁴, R⁵, R⁶ and R⁷, which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or

unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, $-C(O)OR^a$, $-NR^bR^c$ and $-SR^a$; or R^4 and R^5 , at each occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

R^9 and R^{10} , which may be the same or different, are independently selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-S(O)R^a$, $-SO_2R^a$, $-S(O)NR^bR^c$ and $-SO_2NR^bR^c$; or R^9 and R^{10} together with the nitrogen atom to which they are attached, may form an optionally substituted heterocyclyl or heteroaryl ring, wherein said heterocyclic or heteroaryl ring may contain 1, 2, 3 or 4 hetero atom(s) selected from O, S or N;

at each occurrence, R^a , R^d and R^e , which may be the same or different, are independently selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive;

'p' is an integer ranging from 1 to 3, both inclusive; and

'q' is an integer ranging from 1 to 3, both inclusive.

The embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (1b) in which A is aryl, preferably phenyl.

According to another embodiment, specifically provided are compounds of the formula (Ib) in which R^1 is halogen (e.g., fluorine or chlorine); and 'm' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ib) in which 'n' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (Ib) in which X is -O-.

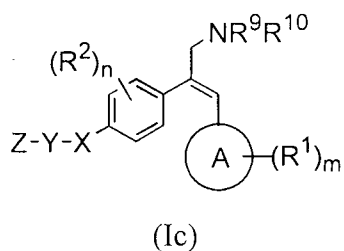
According to yet another embodiment, specifically provided are compounds of the formula (Ib) in which Y is $-(CR^4R^5)_p-$; wherein both R^4 and R^5 are hydrogen and 'p' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ib) in which Z is heteroaryl, preferably quinolinyl.

According to yet another embodiment, specifically provided are compounds of the formula (Ib) in which R^9 is hydrogen.

According to yet another embodiment, specifically provided are compounds of the formula (Ib) in which R^{10} is alkyl (e.g., methyl), cyanoalkyl (e.g., cyanoethyl) or $-(CR^dR^e)_qR^a$; wherein R^d and R^e are independently alkyl (e.g., methyl or ethyl) or hydroxyalkyl (e.g., hydroxymethyl) and R^a is hydrogen. In this embodiment 'q' is 1.

According to one embodiment, there is provided a compound of the formula (Ic):



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from -O-, -S-, $-NR^3-$, $-S(O)-$, $-SO_2-$, $-(CR^4R^5)_pO-$, $-(CR^4R^5)_pN(R^3)-$, $-C\equiv C-$, $-(CR^4R^5)_pC\equiv C-$, $-(R^6)C=C(R^7)-$ and $-(CR^4R^5)_p(R^6)C=C(R^7)-$;

Y is a bond, or is selected from $-(CR^4R^5)_p-$ and $-SO_2-$;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-NR^bR^c$, $-NR^bC(O)R^a$, $-NR^bC(O)NR^bR^c$, $-N(R^b)SO_2R^a$, $-OC(O)R^a$, $-OC(O)NR^bR^c$, $-S(O)R^a$, $-SO_2R^a$, $-SONR^bR^c$, $-SO_2NR^bR^c$ and $-SR^a$;

R^3 is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and $-C(O)OR^a$;

at each occurrence, R^4 , R^5 , R^6 and R^7 , which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, $-C(O)OR^a$, $-NR^bR^c$ and $-SR^a$; or R^4 and R^5 , at each occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

R^9 and R^{10} , which may be the same or different, are independently selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-S(O)R^a$, $-SO_2R^a$, $-S(O)NR^bR^c$ and $-SO_2NR^bR^c$; or R^9 and R^{10} together with the nitrogen atom to which they are attached, may form an optionally substituted heterocyclyl or heteroaryl ring, wherein said heterocyclic or heteroaryl ring may contain 1, 2, 3 or 4 hetero atom(s) selected from O, S or N;

at each occurrence, R^a , R^d and R^e , which may be the same or different, are independently selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive;

'p' is an integer ranging from 1 to 3, both inclusive; and

'q' is an integer ranging from 1 to 3, both inclusive.

The embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (Ic) in which A is aryl, preferably phenyl.

According to another embodiment, specifically provided are compounds of the formula (Ic) in which R^1 is halogen (e.g., fluorine or chlorine); and 'm' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which 'm' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which 'n' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which X is $-O-$.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which Y is $-(CR^4R^5)_p-$; wherein both R^4 and R^5 are hydrogen and 'p' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which Z is quinolinyl.

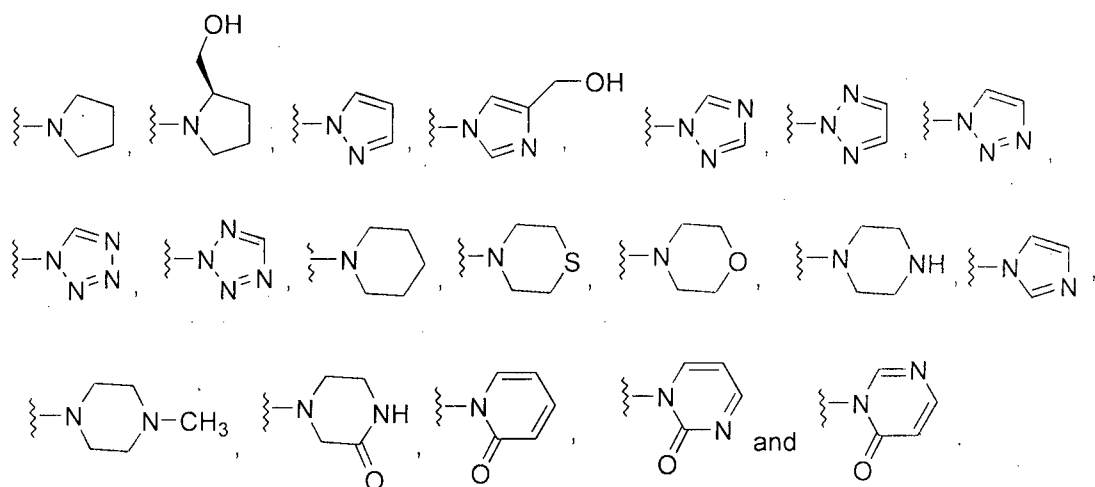
According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which R^9 is hydrogen or alkyl, preferably methyl.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which R^{10} is alkyl (e.g., methyl), alkynyl (e.g., prop-2-ynyl), $-C(O)R^a$, cyanoalkyl (e.g., cyanoethyl) or heterocyclyl (e.g., pyrrolidinyl, pyrrolidin-2-one, piperidinyl, piperidin-2-

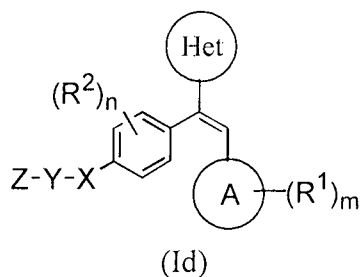
one or ethyl piperidine-1-carboxylate). In this embodiment R^a is alkyl (e.g., methyl) or alkoxyalkyl (e.g., -CH₂-OCH₃).

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which R^{10} is $-(CR^dR^e)_qR^a$; wherein both R^d and R^e are hydrogen and R^a is alkoxy (e.g., methoxy) or $-NR^fR^g$. In this embodiment, R^f and R^g are independently hydrogen, alkyl (e.g., methyl) or $-C(O)alkyl$, preferably $-C(O)methyl$; and 'q' is 2.

According to yet another embodiment, specifically provided are compounds of the formula (Ic) in which R⁹ and R¹⁰ together with the nitrogen atom to which they are attached, forms heterocyclyl or heteroaryl ring selected from,



According to one embodiment, there is provided a compound of the formula (Id):



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from -O-, -S-, -NR³-, -S(O)-, -SO₂-, -(CR⁴R⁵)_pO-, -(CR⁴R⁵)_pN(R³)-, -C≡C-, -(CR⁴R⁵)_pC≡C-, -(R⁶)C=C(R⁷)- and -(CR⁴R⁵)_p(R⁶)C=C(R⁷)-;

Y is a bond, or is selected from $-(CR^4R^5)_p-$ and $-SO_2-$;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

Het is selected from heteroaryl and heterocyclyl; wherein said heteroaryl and heterocyclyl may optionally be substituted with at least one R^{12} ;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-NR^bR^c$, $-NR^bC(O)R^a$, $-NR^bC(O)NR^bR^c$, $-N(R^b)SO_2R^a$, $-OC(O)R^a$, $-OC(O)NR^bR^c$, $-S(O)R^a$, $-SO_2R^a$, $-SONR^bR^c$, $-SO_2NR^bR^c$ and $-SR^a$;

R^3 is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and $-C(O)OR^a$;

at each occurrence, R^4 , R^5 , R^6 and R^7 , which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, $-C(O)OR^a$, $-NR^bR^c$ and $-SR^a$; or R^4 and R^5 , at each occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

at each occurrence, R^{12} is selected from hydrogen, halogen, hydroxyl, cyano, substituted or unsubstituted alkyl, hydroxyalkyl, haloalkyl and alkoxy;

R^a is selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

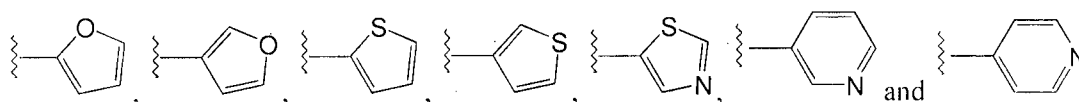
'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

The embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (Id) in which ring A is aryl, preferably phenyl.

According to another embodiment, specifically provided are compounds of the formula (Id) in which A is heteroaryl selected from a group consisting of



According to yet another embodiment, specifically provided are compounds of the formula (Id) in which R^1 is halogen (e.g., fluorine or chlorine), haloalkyl (e.g., trifluoromethyl), alkoxy (e.g., methoxy or ethoxy) or haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy); and 'm' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of the formula (Id) in which 'm' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (Id) in which 'n' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (Id) in which R^2 is halogen (e.g., fluorine or chlorine) or alkoxy (e.g., methoxy or ethoxy); and 'n' is 1.

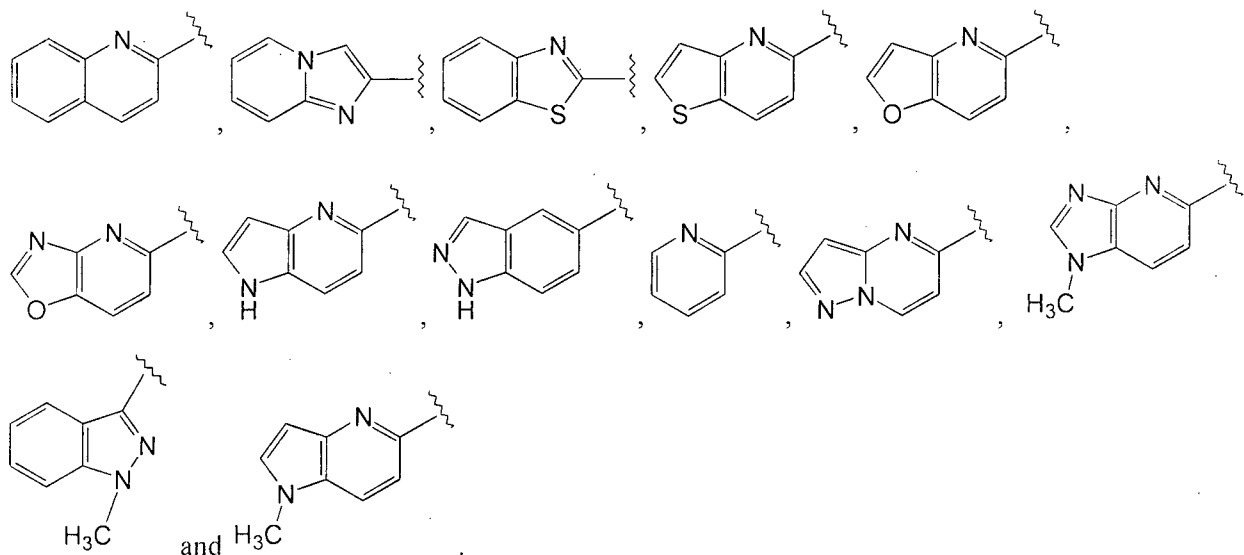
According to yet another embodiment, specifically provided are compounds of the formula (Id) in which X is $-O-$.

According to yet another embodiment, specifically provided are compounds of the formula (Id) in which X is bond.

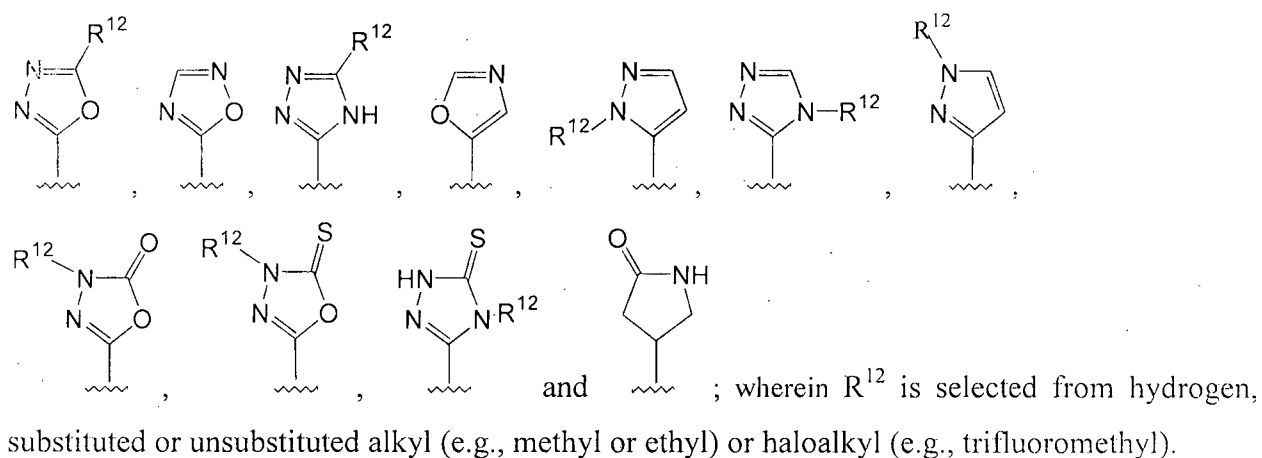
According to yet another embodiment, specifically provided are compounds of the formula (Id) in which Y is $-(CR^4R^5)_p-$; wherein R^4 and R^5 are hydrogen and 'p' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of the formula (Id) in which Z is aryl, preferably quinolinyl.

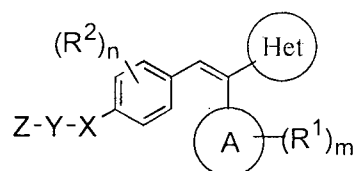
According to yet another embodiment, specifically provided are compounds of the formula (Id) in which Z is heteroaryl selected from a group consisting of



According to yet another embodiment, specifically provided are compounds of the formula (Id) in which Het is selected from a group consisting of



According to one embodiment, there is provided a compound of the formula (Ie):



(Ie)

or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from -O-, -S-, -NR³-, -S(O)-, -SO₂-, -(CR⁴R⁵)_pO-, -(CR⁴R⁵)_pN(R³)-, -C≡C-, -(CR⁴R⁵)_pC≡C-, -(R⁶)C=C(R⁷)- and -(CR⁴R⁵)_p(R⁶)C=C(R⁷)-;

Y is a bond, or is selected from -(CR⁴R⁵)_p- and -SO₂-;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

Het is selected from heteroaryl and heterocyclyl; wherein said heteroaryl and heterocyclyl may optionally be substituted with at least one R¹²;

at each occurrence, R¹ and R², which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -C(O)R^a, -C(O)NR^bR^c, -C(O)OR^a, -NR^bR^c, -NR^bC(O)R^a, -NR^bC(O)NR^bR^c, -N(R^b)SO₂R^a, -OC(O)R^a, -OC(O)NR^bR^c, -S(O)R^a, -SO₂R^a, -SONR^bR^c, -SO₂NR^bR^c and -SR^a;

R³ is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and -C(O)OR^a;

at each occurrence, R⁴, R⁵, R⁶ and R⁷, which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, -C(O)OR^a, -NR^bR^c and -SR^a; or R⁴ and R⁵, at each occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

at each occurrence, R¹² is selected from hydrogen, halogen, hydroxyl, cyano, substituted or unsubstituted alkyl, hydroxyalkyl, haloalkyl and alkoxy;

R^a is selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

The embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (Ie) in which A is aryl preferably phenyl.

According to another embodiment, specifically provided are compounds of the formula (Ie) in which R^1 is halogen, preferably chlorine; and 'm' is 1.

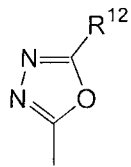
According to yet another embodiment, specifically provided are compounds of the formula (Ie) in which X is $-O-$.

According to yet another embodiment, specifically provided are compounds of the formula (Ie) in which Y is $-(CR^4R^5)_p-$; wherein R^4 and R^5 are hydrogen and 'p' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (Ie) in which Z is heteroaryl, preferably quinolinyl.

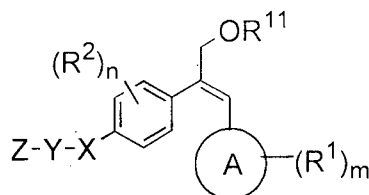
According to yet another embodiment, specifically provided are compounds of the formula (Ie) in which 'n' is 0.

According to yet another embodiment, specifically provided are compounds of the



formula (Ie) in which Het is ; wherein R^{12} is hydrogen or substituted or unsubstituted alkyl, preferably unsubstituted alkyl, more preferably methyl.

According to one embodiment, there is provided a compound of the formula (If):



(If)

or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is selected from cycloalkyl, aryl, heteroaryl and heterocyclyl;

X is a bond, or is selected from -O-, -S-, -NR³-, -S(O)-, -SO₂-, -(CR⁴R⁵)_pO-, -(CR⁴R⁵)_pN(R³)-, -C≡C-, -(CR⁴R⁵)_pC≡C-, -(R⁶)C=C(R⁷)- and -(CR⁴R⁵)_p(R⁶)C=C(R⁷)-;

Y is a bond, or is selected from -(CR⁴R⁵)_p- and -SO₂-;

Z is selected from substituted or unsubstituted alkyl, cycloalkyl, aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

at each occurrence, R¹ and R², which may be the same or different, are independently selected from halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -C(O)R^a, -C(O)NR^bR^c, -C(O)OR^a, -NR^bR^c, -NR^bC(O)R^a, -NR^bC(O)NR^bR^c, -N(R^b)SO₂R^a, -OC(O)R^a, -OC(O)NR^bR^c, -S(O)R^a, -SO₂R^a, -SONR^bR^c, -SO₂NR^bR^c and -SR^a;

R³ is selected from hydrogen, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl and -C(O)OR^a;

at each occurrence, R⁴, R⁵, R⁶ and R⁷, which may be the same or different, are independently selected from hydrogen, halogen, nitro, cyano, hydroxyl, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, hydroxyalkyl, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, -C(O)OR^a, -NR^bR^c and -SR^a; or R⁴ and R⁵, at each

occurrence, together with the carbon atom to which they are attached, may form an optionally substituted cycloalkyl or heterocyclyl ring;

R^1 is selected from hydrogen, nitro, substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxyalkyl, hydroxyalkyl, haloalkyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-(CR^dR^e)_qR^a$, $-C(O)R^a$, $-C(O)NR^bR^c$, $-C(O)OR^a$, $-NR^bR^c$, $-NR^bC(O)R^a$, $-NR^bC(O)NR^bR^c$, $-N(R^b)SO_2R^a$, $-S(O)R^a$, $-SO_2R^a$, $-S(O)NR^bR^c$ and $-SO_2NR^bR^c$;

at each occurrence, R^a , R^d and R^e , which may be the same or different, are independently selected from hydrogen, halogen, cyano, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, alkoxyalkyl, $-C(O)OR^f$, $-NR^fR^g$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^b and R^c , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, haloalkyl, hydroxyalkyl, cyanoalkyl, alkoxy, $-C(O)OR^f$, $-C(O)NR^fR^g$, cycloalkyl, aryl, heteroaryl and heterocyclyl;

at each occurrence, R^f and R^g are independently selected from hydrogen, alkyl, alkenyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive;

'p' is an integer ranging from 1 to 3, both inclusive; and

'q' is an integer ranging from 1 to 3, both inclusive.

The embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (If) in which A is aryl, preferably phenyl.

According to another embodiment, specifically provided are compounds of the formula (If) in which A is heteroaryl, preferably 4-pyridyl.

According to yet another embodiment, specifically provided are compounds of the formula (If) in which R^1 is halogen, preferably fluorine or chlorine; and 'm' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (If) in which 'm' is 0.

According to yet another embodiment, specifically provided are compounds of the formula (If) in which 'n' is 0.

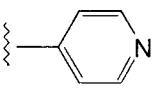
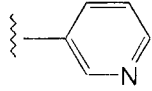
According to yet another embodiment, specifically provided are compounds of the formula (If) in which X is -O-.

According to yet another embodiment, specifically provided are compounds of the formula (If) in which Y is $-(CR^4R^5)_p$; wherein R^4 and R^5 are hydrogen and 'p' is 1.

According to yet another embodiment, specifically provided are compounds of the formula (If) in which Z is heteroaryl, preferably quinoliny.

According to yet another embodiment, specifically provided are compounds of the formula (If) in which R^{11} is aryl, preferably phenyl.

According to yet another embodiment, specifically provided are compounds of the

formula (If) in which R^{11} is heteroaryl, preferably  or .

It should be understood that the formulas (I), (Ia), (Ib), (Ic), (Id), (Ie) and (If) structurally encompasses esters, *N*-oxide, all tautomers, stereoisomers, including enantiomers and diastereomers, geometrical isomers and pharmaceutically acceptable salts that may be contemplated from the chemical structure of the genera described herein.

The present invention also provides a pharmaceutical composition that includes at least one compound described herein and at least one pharmaceutically acceptable excipient, such as a pharmaceutically acceptable carrier or diluent. Preferably, the pharmaceutical composition comprises a therapeutically effective amount of at least one compound described herein. The compounds described in the present patent application may be associated with a pharmaceutically acceptable excipient, such as a carrier or a diluent or be diluted by a carrier, or enclosed within a carrier which can be in the form of a capsule, sachet, paper or other container.

The compounds and pharmaceutical compositions of the present invention are useful for inhibiting PDE10A, which is related to a variety of disease states.

The present invention further provides a method of treating a disease, condition or disorder modulated by a PDE10A, in a subject by administering to the subject in need thereof a therapeutically effective amount of a compound of formulas (I) to (If) or a pharmaceutical composition described herein.

Drawings:

The illustrative examples of the present invention are screened for 'in vivo' PDE10A based efficacy in a rat model of Dizocilpine (MK-801) – induced psychotic behavior.

The effect of Example 91 on MK-801 – induced psychosis behavior in female SD rats as shown in Figure 1 and the effect of Example 177 on MK-801 – induced psychosis behavior in female SD rats as shown in Figure 2.

Detailed Description of the Invention

Definitions

The terms “halogen” or “halo” means fluorine, chlorine, bromine or iodine.

The term “alkyl” refers to a hydrocarbon chain radical that includes solely carbon and hydrogen atoms in the backbone, containing no unsaturation, having from one to eight carbon atoms, and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, n-propyl, 1-methylethyl (isopropyl), n-butyl, n-pentyl and 1,1-dimethylethyl (t-butyl). Unless set forth or recited to the contrary, all alkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term “alkenyl” refers to a hydrocarbon chain containing from 2 to 10 carbon atoms and including at least one carbon-carbon double bond. Examples of such alkenyl moiety includes, but are not limited to, ethenyl, 1-propenyl, 2-propenyl (allyl), *iso*-propenyl, 2-methyl-1-propenyl, 1-butenyl and 2-butenyl. Unless set forth or recited to the contrary, all alkenyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term “alkynyl” refers to a hydrocarbyl radical having at least one carbon-carbon triple bond, and having 2 to about 12 carbon atoms (with radicals having 2 to about 10 carbon atoms being preferred). Examples of such alkynyl moiety include, but are not limited to, ethynyl, propynyl and butynyl. Unless set forth or recited to the contrary, all alkynyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term “alkoxy” refers an alkyl group attached via an oxygen linkage to the rest of the molecule. Examples of such alkoxy moiety include, but are not limited to, -OCH₃ and -OC₂H₅. Unless set forth or recited to the contrary, all alkoxy groups described herein may be straight chain or branched, substituted or unsubstituted.

The term "alkoxyalkyl" or "alkyloxyalkyl" refers to an alkoxy or alkyloxy group as defined above directly bonded to an alkyl group as defined above. Example of such alkoxyalkyl moiety includes, but are not limited to, $-\text{CH}_2\text{OCH}_3$ and $-\text{CH}_2\text{OC}_2\text{H}_5$. Unless set forth or recited to the contrary, all alkoxyalkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term "haloalkyl" refers to at least one halo group (selected from F, Cl, Br or I), linked to an alkyl group as defined above. Examples of such haloalkyl moiety include, but are not limited to, trifluoromethyl, difluoromethyl, 2,2,2-trifluoroethyl and fluoromethyl groups. Unless set forth or recited to the contrary, all haloalkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term "haloalkoxy" refers to an alkoxy group substituted with one or more halogen atoms. Examples of "haloalkoxy" include but are not limited to fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, pentafluoroethoxy, pentachloroethoxy, chloromethoxy, dichloromethoxy, trichloromethoxy and 1-bromoethoxy. Unless set forth or recited to the contrary, all haloalkoxy groups described herein may be straight chain or branched, substituted or unsubstituted.

The term "hydroxyalkyl" refers to an alkyl group as defined above wherein one to three hydrogen atoms on different carbon atoms is/are replaced by hydroxyl groups. Examples of hydroxyalkyl moiety include, but are not limited to $-\text{CH}_2\text{OH}$ and $-\text{C}_2\text{H}_4\text{OH}$. Unless set forth or recited to the contrary, all hydroxyalkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term "cyanoalkyl" refers to an alkyl group as defined above wherein one to three hydrogen atoms on different carbon atoms is/are replaced by cyano groups. Examples of cyanoalkyl moiety include, but are not limited to $-\text{CH}_2\text{CN}$ and $-\text{C}_2\text{H}_4\text{CN}$. Unless set forth or recited to the contrary, all cyanoalkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

The term "cycloalkyl" denotes a non-aromatic mono or multicyclic ring system of 3 to about 12 carbon atoms, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. Examples of multicyclic cycloalkyl groups include, but are not limited to, perhydronaphthyl, adamantyl and norbornyl groups, bridged cyclic groups or spirobicyclic groups, e.g., spiro(4,4)non-2-yl,

spiro[3,3]heptanyl, spiro[3,4]octanyl and spiro[4,4]heptanyl. Unless set forth or recited to the contrary, all cycloalkyl groups described herein may be substituted or unsubstituted.

The term “cycloalkylalkyl” refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms directly attached to an alkyl group. The cycloalkylalkyl group may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Examples of cycloalkylalkyl moiety include, but are not limited to cyclopropylmethyl, cyclobutylethyl, and cyclopentylethyl. Unless set forth or recited to the contrary, all cycloalkylalkyl groups described or claimed herein may be substituted or unsubstituted.

The term “cycloalkenyl” refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms with at least one carbon-carbon double bond, such as cyclopropenyl, cyclobutenyl, and cyclopentenyl. Unless set forth or recited to the contrary, all cycloalkenyl groups described or claimed herein may be substituted or unsubstituted.

The term “cycloalkenylalkyl” refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms with at least one carbon-carbon double bond, directly attached to an alkyl group. The cycloalkenylalkyl group may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Unless set forth or recited to the contrary, all cycloalkenylalkyl groups described or claimed herein may be substituted or unsubstituted.

The term “aryl” refers to an aromatic radical having 6 to 14 carbon atoms, including monocyclic, bicyclic and tricyclic aromatic systems, such as phenyl, naphthyl, tetrahydronaphthyl, indanyl and biphenyl. Unless set forth or recited to the contrary, all aryl groups described herein may be substituted or unsubstituted.

The term “aryloxy” refers to an aryl group as defined above attached via an oxygen linkage to the rest of the molecule. Examples of aryloxy moiety include, but are not limited to phenoxy and naphthoxy. Unless set forth or recited to the contrary, all aryloxy groups described herein may be substituted or unsubstituted.

The term “arylalkyl” refers to an aryl group as defined above directly bonded to an alkyl group as defined above. Examples of arylalkyl moiety include, but are not limited to $-\text{CH}_2\text{C}_6\text{H}_5$ and $-\text{C}_2\text{H}_4\text{C}_6\text{H}_5$. Unless set forth or recited to the contrary, all arylalkyl groups described herein may be substituted or unsubstituted.

The term "heterocyclic ring" or "heterocyclyl" unless otherwise specified refers to substituted or unsubstituted non-aromatic 3 to 15 membered ring radical which consists of carbon atoms and from one to five heteroatoms selected from nitrogen, phosphorus, oxygen and sulfur. The heterocyclic ring radical may be a mono-, bi- or tricyclic ring system, which may include fused, bridged or spiro ring systems, and the nitrogen, phosphorus, carbon, oxygen or sulfur atoms in the heterocyclic ring radical may be optionally oxidized to various oxidation states. In addition, the nitrogen atom may be optionally quaternized; also, unless otherwise constrained by the definition the heterocyclic ring or heterocyclyl may optionally contain one or more olefinic bond(s). Examples of such heterocyclic ring radicals include, but are not limited to azepinyl, azetidiny, benzodioxolyl, benzodioxanyl, chromanyl, dioxolanyl, dioxaphospholanyl, decahydroisoquinolyl, indanyl, indoliny, isoindoliny, isochromanyl, isothiazolidinyl, isoxazolidinyl, morpholiny, oxazoliny, oxazolidinyl, oxadiazolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, octahydroindolyl, octahydroisoindolyl, perhydroazepinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, piperidinyl, phenothiazinyl, phenoxazinyl, quinuclidinyl, tetrahydroisquinolyl, tetrahydrofuryl, tetrahydropyranyl, thiazoliny, thiazolidinyl, thiamorpholiny, thiamorpholiny sulfoxide, thiamorpholiny sulfone, 1,4 azathianyl, 7-aza-spiro[3,3]heptanyl, 7-spiro[3,4]octanyl, and 7-aza- spiro[3,4]octanyl. The heterocyclic ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure. Unless set forth or recited to the contrary, all heterocyclyl groups described herein may be substituted or unsubstituted.

The term "heterocyclylalkyl" refers to a heterocyclic ring radical directly bonded to an alkyl group. The heterocyclylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Unless set forth or recited to the contrary, all heterocyclylalkyl groups described herein may be substituted or unsubstituted.

The term "heteroaryl" unless otherwise specified refers to substituted or unsubstituted 5 to 14 membered aromatic heterocyclic ring radical with one or more heteroatom(s) independently selected from N, O or S. The heteroaryl may be a mono-, bi- or tricyclic ring system. The heteroaryl ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure. Examples of such heteroaryl ring radicals include, but are not limited to oxazolyl, isoxazolyl, imidazolyl, furyl, indolyl, isoindolyl,

pyrrolyl, triazolyl, triazinyl, tetrazolyl, thienyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzofuranyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, benzothienyl, benzopyranyl, carbazolyl, quinolynyl, isoquinolynyl, quinazolynyl, cinnolynyl, naphthyridinyl, pteridinyl, purinyl, quinoxalynyl, quinolyl, isoquinolyl, thiadiazolyl, indolizynyl, acridinyl, phenazinyl, phthalazinyl, furo[3,2-*b*]pyridinyl, pyrrolo[3,2-*b*]pyridinyl, thieno[3,2-*b*]pyridinyl, indazolyl and imidazo[1,2-*a*]pyridinyl. Unless set forth or recited to the contrary, all heteroaryl groups described herein may be substituted or unsubstituted.

The term “heteroarylalkyl” refers to a heteroaryl ring radical directly bonded to an alkyl group. The heteroarylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Unless set forth or recited to the contrary, all heteroarylalkyl groups described herein may be substituted or unsubstituted.

Unless otherwise specified, the term “substituted” as used herein refers to a group or moiety having one or more of the substituents attached to the structural skeleton of the group or moiety, including, but not limited to such substituents as hydroxy, halogen, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted haloalkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstituted guanidine, -COOR^x, -C(O)R^x, -C(S)R^x, -C(O)NR^xR^y, -C(O)ONR^xR^y, -NR^xCONR^yR^z, -N(R^x)SOR^y, -N(R^x)SO₂R^y, -(=N-N(R^x)R^y), -NR^xC(O)OR^y, -NR^xR^y, -NR^xC(O)R^y, -NR^xC(S)R^y, -NR^xC(S)NR^yR^z, -SONR^xR^y, -SO₂NR^xR^y, -OR^x, -OC(O)OR^y, -OC(O)R^x, -OC(O)NR^xR^y, -SR^x, -SOR^x, -SO₂R^x, and -ONO₂, wherein R^x, R^y and R^z are independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl,

substituted heterocyclalkyl ring, substituted or unsubstituted heteroarylalkyl, or substituted or unsubstituted heterocyclic ring. The substituents in the aforementioned “substituted” groups cannot be further substituted. For example, when the substituent on “substituted alkyl” is “substituted aryl”, the substituent on “substituted aryl” cannot be “substituted alkenyl”.

The term “treating” or “treatment” of a state, disorder or condition includes: (a) preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a subject that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder or condition; (b) inhibiting the state, disorder or condition, i.e., arresting or reducing the development of the disease or at least one clinical or subclinical symptom thereof; or (c) relieving the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms.

The term “subject” includes mammals (especially humans). Other mammals include domestic animals (e.g., household pets including cats and dogs) and non-domestic animals (such as wildlife).

A “therapeutically effective amount” means the amount of a compound that, when administered to a subject for treating a state, disorder or condition, is sufficient to effect such treatment. The “therapeutically effective amount” will vary depending on the compound, the disease and its severity and the age, weight, physical condition and responsiveness of the subject to be treated.

Pharmaceutically acceptable salts forming part of this patent application include salts derived from inorganic bases (such as Li, Na, K, Ca, Mg, Fe, Cu, Zn, and Mn), salts of organic bases (such as *N,N'*-diacetylenediamine, glucamine, triethylamine, choline, hydroxide, dicyclohexylamine, metformin, benzylamine, trialkylamine, and thiamine), salts of chiral bases (such as alkylphenylamine, glycinol, and phenyl glycinol), salts of natural amino acids (such as glycine, alanine, valine, leucine, isoleucine, norleucine, tyrosine, cystine, cysteine, methionine, proline, hydroxy proline, histidine, ornithine, lysine, arginine, and serine), salts of non-natural amino acids (such as D-isomers or substituted amino acids), salts of guanidine, salts of substituted guanidine (wherein the substituents are selected from nitro, amino, alkyl, alkenyl or alkynyl), ammonium salts, substituted ammonium salts and aluminum salts. Other

pharmaceutically acceptable salts include acid addition salts (where appropriate) such as sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates (such as trifluoroacetate), tartrates, maleates, citrates, fumarates, succinates, palmoates, methanesulphonates, benzoates, salicylates, benzenesulfonates, ascorbates, glycerophosphates and ketoglutarates. Yet other pharmaceutically acceptable salts include, but are not limited to, quaternary ammonium salts of the compounds of invention with alkyl halides or alkyl sulphates (such as MeI or Me₂SO₄).

Compounds described herein can comprise one or more asymmetric carbon atoms and thus can occur as racemic mixtures, enantiomers and diastereomers. These compounds can also exist as conformers/rotamers. All such isomeric forms of these compounds are expressly included in the present patent application. Although the specific compounds exemplified in this application may be depicted in a particular stereochemical configuration, compounds having either the opposite stereochemistry at any given chiral centre are envisioned as a part thereof. In addition, compounds of Formulas (I) to (If) can exist in different geometrical isomeric forms. Unless otherwise stated a reference to a particular compound includes all such isomeric forms, including racemic and other mixtures thereof. The various isomeric forms of the compounds of the present invention may be separated from one another by methods known in the art or a given isomer may be obtained by stereospecific or asymmetric synthesis. Tautomeric forms and mixtures of compounds described herein are also contemplated.

Pharmaceutical Compositions

The pharmaceutical composition of the present patent application comprises one or more compounds described herein and one or more pharmaceutically acceptable excipients, carriers, diluents or mixture thereof. The compounds described herein may be associated with one or more pharmaceutically acceptable excipients, carriers, diluents or mixture thereof in the form of capsule, sachet, paper or other container.

Examples of suitable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, polyhydroxyethoxylated castor oil, peanut oil, olive oil, gelatin, lactose, terra alba, sucrose, dextrin, magnesium carbonate, sugar, cyclodextrin, amylose, magnesium stearate, talc, gelatin, agar, pectin, acacia, stearic acid or lower alkyl ethers of

cellulose, silicic acid, fatty acids, fatty acid amines, fatty acid monoglycerides and diglycerides, pentaerythritol fatty acid esters, polyoxyethylene, hydroxymethyl cellulose and polyvinylpyrrolidone.

The carrier or diluent may include a sustained release material, such as glyceryl monostearate or glyceryl distearate, alone or mixed with a wax.

The pharmaceutical composition may also include one or more pharmaceutically acceptable auxiliary agents, wetting agents, emulsifying agents, suspending agents, preserving agents, salts for influencing osmotic pressure, buffers, sweetening agents, flavoring agents, colorants or any combination of the foregoing. The pharmaceutical composition of the patent application may be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the subject by employing methods known in the art.

The pharmaceutical compositions of the present patent application may be prepared by conventional techniques, e.g., as described in *Remington: The Science and Practice of Pharmacy*, 20th Ed., 2003 (Lippincott Williams & Wilkins). For example, the active compound is mixed with a carrier, or diluted by a carrier, or enclosed within a carrier, which may be in the form of an ampoule, capsule, sachet, paper or other container. When the carrier serves as a diluent, it may be a solid, semi-solid or liquid material that acts as a vehicle, excipient or medium for the active compound. The active compound is adsorbed on a granular solid container, for example, in a sachet.

The pharmaceutical compositions may be in conventional forms, for example, capsules, tablets, aerosols, solutions, suspensions or products for topical application.

The route of administration may be any route which effectively transports the active compound of the patent application to the appropriate or desired site of action. Suitable routes of administration include, but are not limited to, oral, nasal, pulmonary, buccal, subdermal, intradermal, transdermal, parenteral, rectal, depot, subcutaneous, intravenous, intraurethral, intramuscular, intranasal, ophthalmic (such as with an ophthalmic solution) or topical (such as with a topical ointment). The oral route is preferred.

Solid oral formulations include, but are not limited to, tablets, capsules (soft or hard gelatin), dragees (containing the active ingredient in powder or pellet form), troches and lozenges. Tablets, dragees, or capsules having talc and/or a carbohydrate carrier or binder or the

like are particularly suitable for oral application. Preferable carriers for tablets, dragees, or capsules include lactose, cornstarch and/or potato starch. A syrup or elixir is used in cases where a sweetened vehicle is employed.

Liquid formulations include, but are not limited to, syrups, emulsions, soft gelatin and sterile injectable liquids, such as aqueous or non-aqueous liquid suspensions or solutions.

For parenteral application, particularly suitable are injectable solutions or suspensions, preferably aqueous solutions with the active compound dissolved in polyhydroxylated castor oil.

Suitable doses of the compounds for use in treating the diseases and disorders described herein can be determined by those skilled in the relevant art. Therapeutic doses are generally identified through a dose ranging study in humans based on preliminary evidence derived from the animal studies. Doses must be sufficient to result in a desired therapeutic benefit without causing unwanted side effects. For example, the daily dosage of the PDE10A inhibitors can range from about 0.1 to about 30.0 mg/Kg. Mode of administration, dosage forms, suitable pharmaceutical excipients, diluents or carriers can also be well used and adjusted by those skilled in the art. All changes and modifications are envisioned within the scope of the present patent application.

Methods of Treatment

The present patent application provides a method of treating a disease, condition or disorder modulated by a PDE10A, in a subject by administering to the subject in need thereof a therapeutically effective amount of a compound or a pharmaceutical composition described herein.

The present patent application further provides a method of treating diseases, disorders or conditions, modulated by a PDE10A in mammals including human, of neuropsychiatric, neurodegenerative, neurological, neuroendocrinological nature such as, but not limiting to, schizophrenia, psychoses, schizoaffective disorders, positive symptoms of schizophrenia including delusions, disordered thoughts and speech, and tactile, auditory, visual, olfactory and gustatory hallucinations, paranoia, paranormal behaviors, negative symptoms of schizophrenia like deficits of normal emotional responses or of other thought processes including flat or blunted affect and emotion, poverty of speech (alogia), inability to experience pleasure

(anhedonia), lack of desire to form relationships (asociality), and lack of motivation (avolition) leading to poor quality of life, functional disabilities typically regarded as manifestations of psychosis and other comorbidities like cognitive, executive, attention, learning, memory, spatial memory and social cognitive functions, Tic disorders like Tourette's syndrome, autism, autism spectrum disorders, attention deficit hyperactivity disorders (ADHD), pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), mood disorders, anxiety, depression, major depressive disorders, bipolar disorders, manias, aggression, obsessive compulsive disorders, Huntington's disease, Alzheimer's disease, Parkinson's disease, rest-less leg syndrome, various other neurological disorders consisting of movement disorders, ataxias, sensation disorders, cognitive disorders related to multiple sclerosis, amyotrophic lateral sclerosis, abnormalities of brain, spinal cord, nerves leading to symptoms such as paralysis, seizures, catatonias, catalepsies, muscle rigidities, muscle weakness, poor coordination, loss of sensation, confusion, mental suffering, pain and altered levels of consciousness and various other diseases, disorders or conditions related to neuroendocrinological and metabolic manifestations like change of circadian rhythms, sleep disorders, insomnia, jet lags, eating disorders like anorexia nervosa, bulimia nervosa, exercise bulimia or binge eating disorder, aggressive behaviours, obsessive compulsive personality disorders, narcissistic personality disorders, sexual and gender identity disorders, various disorders related to central neurotransmission systems such as dopaminergic, glutamatergic, serotonergic, adrenergic, GABAergic, excitatory amino acid (EAA) mediated signal transduction dysfunctions and diseases related to brain, spinal cord regions, glands and hormones located in the central and peripheral nervous systems related to basal ganglia, limbic system, neostriatum, caudate putamen, striatum, striatal medium spiny neurons, globus pallidus, thalamus, prefrontal cortex, cortex, nucleus accumbens, ventral tegmental area, corpus striatum, substantia nigra, optic chiasm, vomeronasal organ, suprachiasmatic nucleus, hippocampus, amygdala, cerebellum, pineal gland, pituitary gland, hypothalamus, hypothalamo-pituitary-adrenal axis, thyroid, gonads and trinucleotide repeat expansion diseases of polyglutamine and non-polyglutamine nature.

This patent application also provides a method of treating a disorder or condition comprising as a symptom a deficiency in attention and/or cognition in a mammal, including a human, which method comprises administering to said mammal an amount of a compound of

formulas (I) to (If) effective in treating said disorder or condition. The phrase “deficiency in attention and/or cognition” as used in the phrase “disorder comprising as a symptom a deficiency in attention and/or cognition” refers to a subnormal functioning in one or more cognitive aspects such as memory, intellect, or learning and logic ability, in a particular individual relative to other individuals within the same general age population. “Deficiency in attention and/or cognition” also refers to a reduction in any particular individual’s functioning in one or more cognitive aspects, for example as occur in age-related cognitive decline.

Examples of disorders that comprise as a symptom a deficiency in attention and/or cognition that can be treated according to the present patent application are dementia, for example, Alzheimer’s disease, multi-infarct dementia, alcoholic dementia or other drug-related dementia, dementia associated with intracranial tumors or cerebral trauma, dementia associated with Huntington’s disease or Parkinson’s disease, Multiple sclerosis, Amyotrophic lateral sclerosis, Down’s syndrome or AIDS-related dementia; delirium, amnesic disorder, post-traumatic stress disorder, mental retardation, a learning disorder, for example reading disorder, mathematics disorder, or a disorder of written expression, attention-deficit/hyperactivity disorder and age-related cognitive decline. This patent application also provides a method of treating a mood disorder or mood episode in a mammal, including a human, comprising administering to said mammal an amount of a compound of formulas (I) to (If) effective in treating said disorder or episode. This patent application also provides a method of treating a mood disorder or mood episode in a mammal, including a human, comprising administering to said mammal a therapeutically effective amount of a compound of formulas (I) to (If) in inhibiting PDE10A.

Examples of mood disorders and mood episodes that can be treated according to the present patent application include, but are not limited to, major depressive episode of the mild, moderate or severe type, a manic or mixed mood episode, a hypomanic mood episode; a depressive episode with atypical features; a depressive episode with melancholic features; a depressive episode with catatonic features; a mood episode with postpartum onset; post-stroke depression; major depressive disorder; dysthymic disorder; minor depressive disorder; premenstrual dysphoric disorder; post-psychotic depressive disorder of schizophrenia; a major depressive disorder superimposed on a psychotic disorder such as delusional disorder or

schizophrenia; a bipolar disorder, for example bipolar I disorder, bipolar II disorder and cyclothymic disorder.

This patent application further provides a method of treating a neurodegenerative disorder or condition in a mammal, including a human, which method comprises administering to said mammal a therapeutically effective amount of a compound of the present invention in treating said disorder or condition.

This patent application further provides a method of treating a neurodegenerative disorder or condition in a mammal, including a human, which method comprises administering to said mammal a therapeutically effective amount of a compound of formulas (I) to (II) in inhibiting PDE10A. As used herein and unless otherwise indicated, a “neurodegenerative disorder or condition” refers to a disorder or condition that is caused by the dysfunction and/or death of neurons in the central nervous system. The treatment of these disorders and conditions can be facilitated by administration of an agent which prevents the dysfunction or death of neurons at risk in these disorders or conditions and/or enhances the function of damaged or healthy neurons in such a way as to compensate for the loss of function caused by the dysfunction or death of at-risk neurons. The term “neurotrophic agent” as used herein refers to a substance or agent that has some or all of these properties.

Examples of neurodegenerative disorders and conditions that can be treated according to the present patent application include, but are not limited to, Parkinson’s disease; Huntington’s disease; dementia, for example Alzheimer’s disease, multi-infarct dementia, AIDS-related dementia, and Fronto temporal Dementia; neurodegeneration associated with cerebral trauma; neurodegeneration associated with stroke, neurodegeneration associated with cerebral infarct; hypoglycemia-induced neurodegeneration; neurodegeneration associated with epileptic seizure; neurodegeneration associated with neurotoxin poisoning; and multi-system atrophy.

In one aspect of the present patent application, the neurodegenerative disorder or condition comprises neurodegeneration of striatal medium spiny neurons in a mammal, including a human.

In another aspect, this patent application provides a pharmaceutical composition for treating psychotic disorders, delusional disorders and drug induced psychosis, anxiety disorders, movement disorders, mood disorders, neurodegenerative disorders or drug addiction, comprising

a therapeutically effective amount of a compound of the present invention in treating said disorder or condition.

In another aspect, this patent application provides a method of treating a disorder selected from psychotic disorders, delusional disorders and drug induced psychosis, anxiety disorders, movement disorders, mood disorders, and neurodegenerative disorders, which method comprises administering a therapeutically effective amount of a compound of the present invention in treating said disorder.

In another aspect, this patent application provides a method of treating the disorders above, where the disorders are selected from the group consisting of: dementia, Alzheimer's disease, multi-infarct dementia, alcoholic dementia or other drug-related dementia, dementia associated with intracranial tumors or cerebral trauma, dementia associated with Huntington's disease or Parkinson's disease, or AIDS-related dementia; delirium; amnesic disorder; posttraumatic stress disorder; mental retardation; a learning disorder, for example reading disorder, mathematics disorder, or a disorder of written expression; attention-deficit/hyperactivity disorder; age-related cognitive decline, major depressive episode of the mild, moderate or severe type; a manic or mixed mood episode; a hypomanic mood episode; a depressive episode with atypical features; a depressive episode with melancholic features; a depressive episode with catatonic features; a mood episode with postpartum onset; post-stroke depression; major depressive disorder; dysthymic disorder; minor depressive disorder; premenstrual dysphoric disorder; post-psychotic depressive disorder of schizophrenia; a major depressive disorder superimposed on a psychotic disorder comprising a delusional disorder or schizophrenia; a bipolar disorder comprising bipolar I disorder, bipolar II disorder, cyclothymic disorder, Parkinson's disease; Huntington's disease; dementia, Alzheimer's disease, multi-infarct dementia, AIDS-related dementia, Frontotemporal Dementia; neurodegeneration associated with cerebral trauma; neurodegeneration associated with stroke; neurodegeneration associated with cerebral infarct; hypoglycemia-induced neurodegeneration; neurodegeneration associated with epileptic seizure; neurodegeneration associated with neurotoxin poisoning; multi-system atrophy, paranoid, disorganized, catatonic, undifferentiated or residual type; schizophreniform disorder; schizoaffective disorder of the delusional type or the depressive type; delusional disorder; substance-induced psychotic disorder, psychosis induced by alcohol, amphetamine, cannabis,

cocaine, hallucinogens, inhalants, opioids, or phencyclidine; personality disorder of the paranoid type; and personality disorder of the schizoid type.

In another aspect, there is provided a method for preventing, ameliorating or treating a disease or condition selected from obesity or related diseases, conditions; diabetes (including Type I and Type II diabetes); diabetic complications; glucose tolerance; hyperinsulinemia; insulin sensitivity or resistance; metabolic syndromes; cardiovascular diseases including, for example, atherosclerosis, lipidemia, dyslipidemia, elevated blood pressure, microalbuminemia, hyperuricaemia, hypercholesterolemia, hyperlipidemias, hypertriglyceridemias, arteriosclerosis or combination thereof; respiratory diseases or disorders including, for example, sinusitis, asthma, bronchitis or combination thereof; or any combination these diseases, disorders, conditions and/or syndromes thereof; the disease or condition related to serum levels of triglyceride, LDL, HDL, VLDL, total cholesterol, which method comprises administering to said mammal a therapeutically effective amount of a compound of formulas (I) to (If) in treating said disorder or condition.

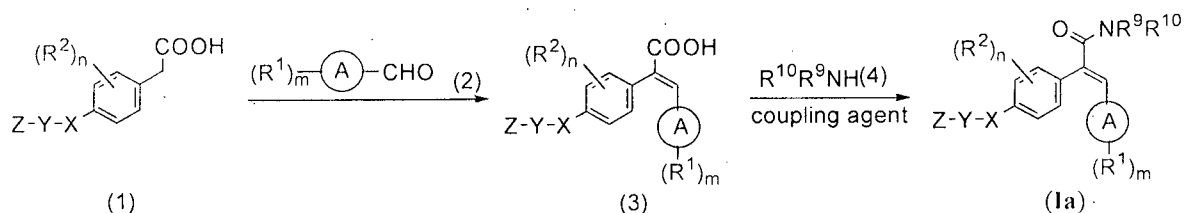
General Methods of Preparation

The compounds described herein, including compounds of general formulas (I), (Ia), (Ib), (Ic), (Id), (Ie), (If) and specific examples are prepared using techniques known to one skilled in the art through the reaction sequences depicted in schemes 1-15. Furthermore, in the following schemes, where specific acids, bases, reagents, coupling agents, solvents, etc. are mentioned, it is understood that other suitable acids, bases, reagents, coupling agents etc. may be used and are included within the scope of the present invention. Modifications to reaction conditions, for example, temperature, duration of the reaction or combinations thereof, are envisioned as part of the present invention. The compounds obtained by using the general reaction sequences may be of insufficient purity. These compounds can be purified by using any of the methods for purification of organic compounds known to persons skilled in the art, for example, crystallization or silica gel or alumina column chromatography using different solvents in suitable ratios. All possible geometrical isomers and stereoisomers are envisioned within the scope of this invention.

The starting materials for the below reaction schemes are commercially available or can be prepared according to methods known to one skilled in the art or by methods disclosed herein. In general, intermediates and compounds of the present invention may be prepared through the reaction scheme as follows, wherein all symbols are as defined in the description.

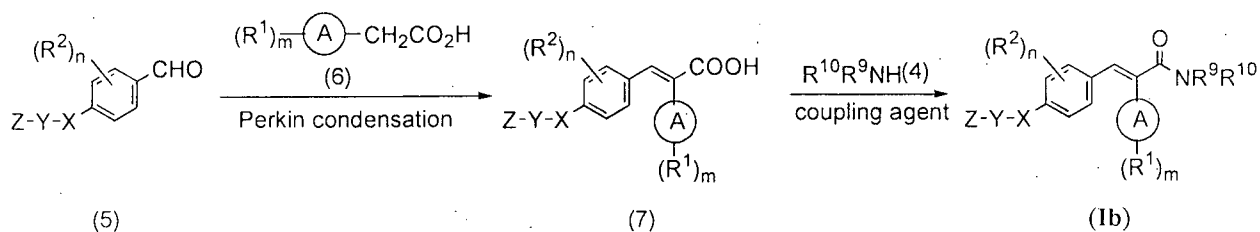
The compounds of formula **(1a)** can be prepared according to Synthetic scheme 1. The phenyl acetic acid derivative of formula (1) is condensed with aromatic aldehyde of formula (2) under suitable Perkin reaction conditions [*Journal of Medicinal Chemistry*, 13, (1970)] to give the acrylic acid of formula (3). Coupling reaction of the acid of formula (3) with amine of formula (4) using appropriate reagents such as dicyclohexyl carbodiimide (DCC) or *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide (EDCI) either alone or in combination with 1H-benzotriazol-1-ol (HOBT) gives compounds of formula **(1a)**.

Synthetic scheme 1



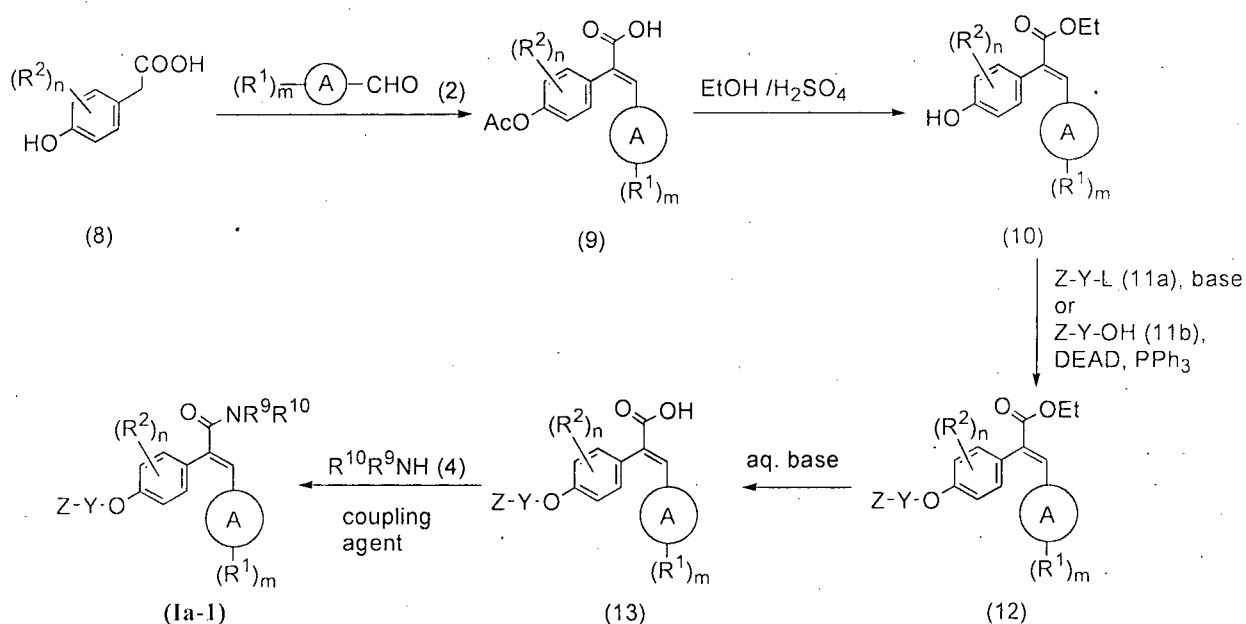
The regioisomeric amide of formula **(1b)** can be prepared according to Synthetic scheme 2. The acetic acid of formula (6) is condensed with benzaldehyde derivative of formula (5) under suitable Perkin reaction conditions to give the acrylic acid derivative of formula (7). Coupling of this acid (7) with amine of formula (4) as described above gives the final compound of formula **(1b)**.

Synthetic scheme 2



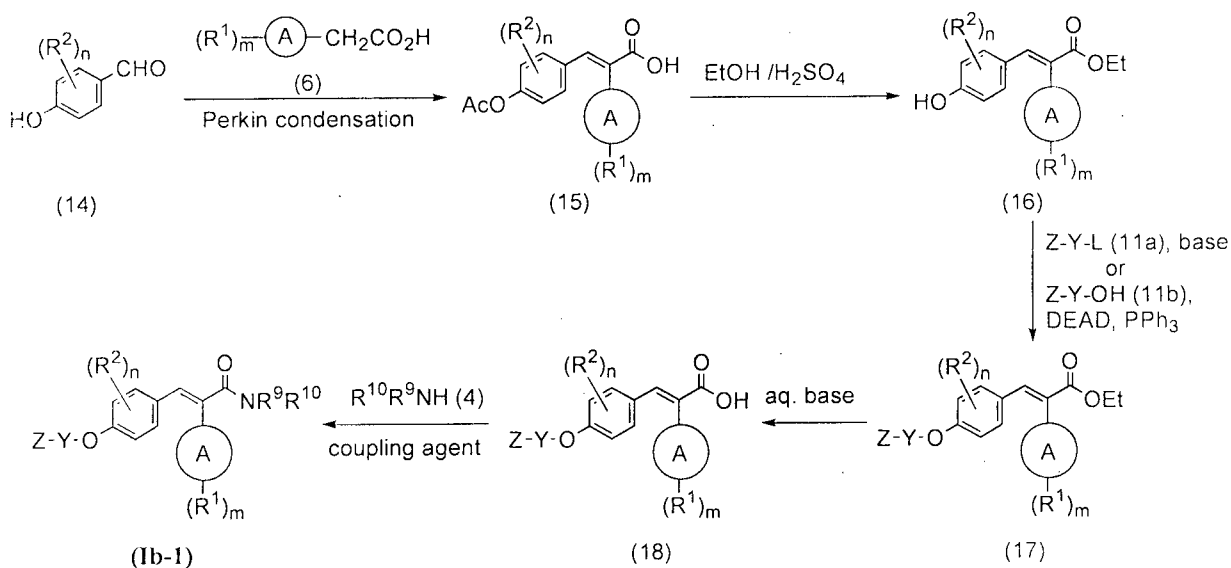
The synthesis of compounds of formula (Ia), where X is an oxygen atom, is shown in Synthetic scheme 3. Thus, 4-hydroxyphenylacetic acid of the formula (8) is condensed with an aldehyde of formula (2) in the presence of a base such as *N*-methylmorpholine, triethylamine or diisopropylethylamine in acetic anhydride to give acrylic acid of formula (9). Deacetylation followed by esterification in a one pot reaction under acidic conditions gives the phenolic ester of formula (10). Alkylation of compound of formula (10) with alkyl halide of formula (11a) (where L is halogen) under basic conditions or reaction of appropriate alcohol of formula (11b) under Mitsunobu reaction conditions gives intermediate (12). Base hydrolysis of the ester of formula (12) results in the formation of the corresponding acrylic acid derivative (13) which on coupling with amine (4), using suitable coupling agent such as EDCI or DCC gives the compound of formula (Ia-1).

Synthetic scheme 3



Similarly, the regioisomeric acrylamide of formula (**Ib-1**) where X is an oxygen atom can be prepared as shown in Synthetic scheme 4. Thus, 4-hydroxybenzaldehyde of the formula (14) is condensed with an aryl acetic acid derivative of formula (6) under Perkin reaction conditions in the presence of base such as N-methylmorpholine, triethylamine or diisopropylethylamine in acetic anhydride to give acrylic acid of formula (15). Deacetylation followed by esterification in a one pot reaction under acidic conditions gives the phenolic ester of formula (16). Alkylation of intermediate (16) with alkyl halide of formula (11a) (where L is halogen) under basic conditions or reaction with appropriate alcohol (11b) under Mitsunobu reaction conditions gives Intermediate (17). Base hydrolysis of ester group of (17) results in the formation of corresponding acid of formula (18) which on coupling with amines of formula (4) using suitable coupling agents such as EDCI or DCC gives compound of formula (**Ib-1**).

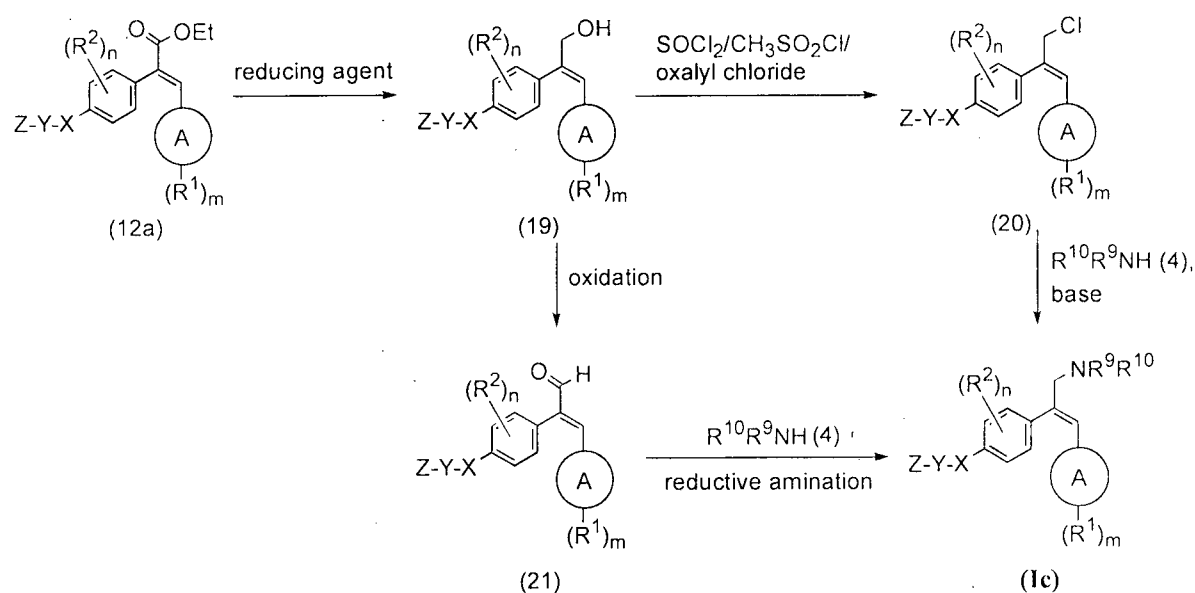
Synthetic scheme 4



The amine of formula (**Ic**) can be prepared according to Synthetic scheme 5. The ester of formula (12a) is reduced to corresponding alcohol of formula (19) using diisobutyl aluminium hydride, $LiAlH_4$ or $LiBH_4$ in a suitable solvent. The hydroxyl group of formula (19) is converted to an appropriate leaving group such as chloride using thionyl chloride or methane sulphonyl chloride or oxalyl chloride to give compound of formula (20). Reaction of Intermediate (20) with an amine of formula (4) in the presence of a base, gives the compound of general formula (**Ic**).

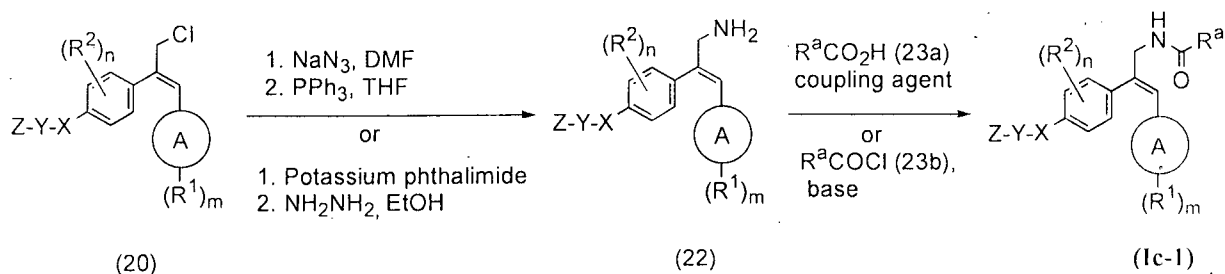
The compound of formula (**Ic**) can also be prepared from the alcohol of formula (19) by its oxidation to the corresponding aldehyde of formula (21) using an appropriate oxidizing agent such as manganese dioxide followed by reductive amination using an appropriate amine of formula (4) in presence of sodium triacetoxyborohydride in acetic acid.

Synthetic scheme 5



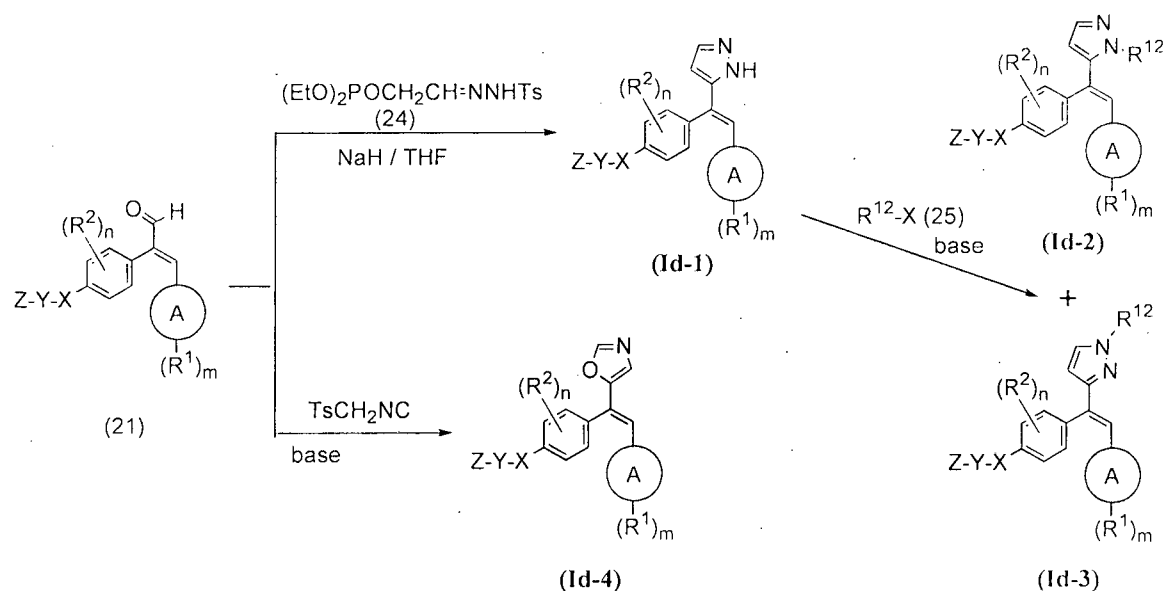
The compounds of formula (**Ic-1**) (wherein R^a is substituted or unsubstituted alkyl) can be prepared according to Synthetic scheme 6. Thus, the chloro compound of formula (20) is treated with sodium azide in the presence of suitable solvent to give azide derivative, which on reduction with the suitable reducing agent like triphenylphosphine gives amine derivative of formula (22) via an iminophosphinone intermediate [*Tetrahedron letters*, 39, p. 3287-3290, (1998)]. Alternatively, Intermediate (22) can also be synthesized directly from chloride of formula (20) by treating it with potassium phthalimide followed by hydrazine hydrate in presence of a suitable solvent such as ethanol. The amine derivative of formula (22) is then coupled with the carboxylic acid of formula (23a) using an appropriate coupling agent or acid chloride of formula (23b) in the presence of a base to give the amide of formula (**Ic-1**).

Synthetic scheme 6



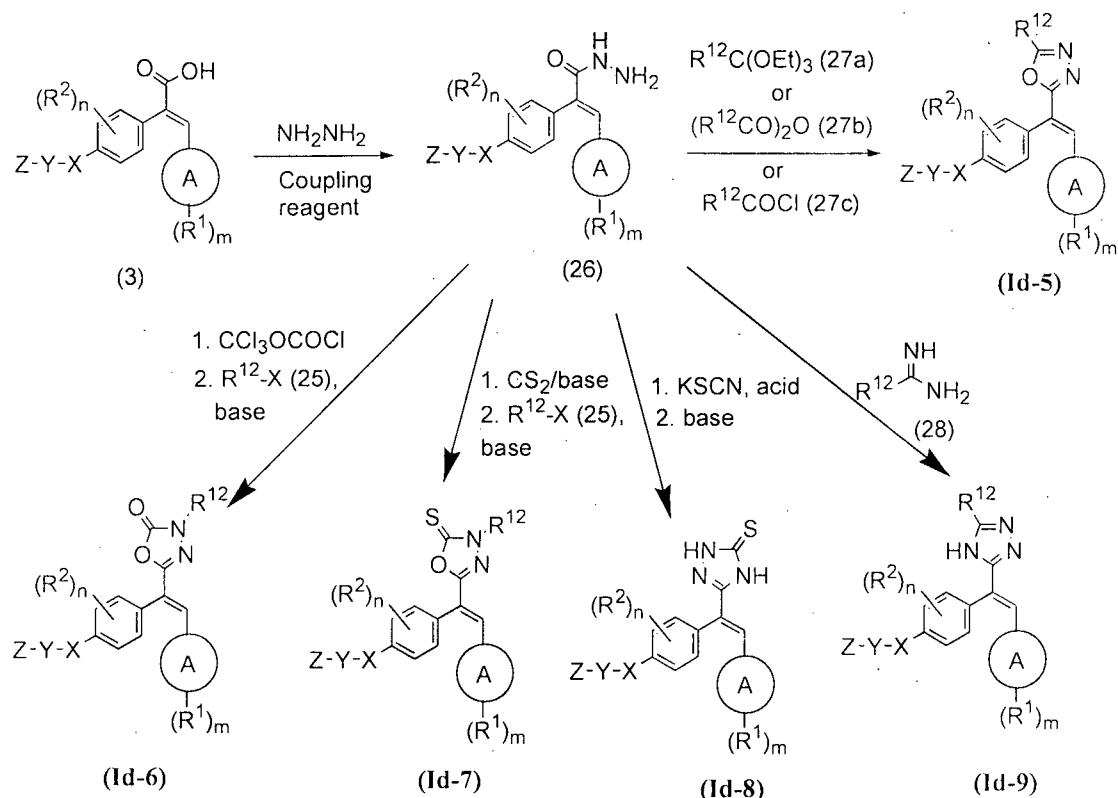
The compounds of formula (**Id-1**), (**Id-2**), (**Id-3**) and (**Id-4**) can be prepared from the aldehyde derivative (21) according to Synthetic scheme 7. Thus, pyrazole of the formula (**Id-1**) [*Tetrahedron letters*, 39, p. 3287-3290, (1998)] is synthesized from aldehyde of formula (21) by treating it with diethyl (2-{2-[(4-methylphenyl)sulfonyl]hydrazinylidene}ethyl)phosphonate (24) in the presence of a strong base such as sodium hydride. Further, alkylation of the pyrazole of formula (**Id-1**) with suitable alkyl halide of the formula (25) (where X is halogen) in the presence of suitable base such as K_2CO_3 gives easily separable regioisomeric mixture of products (**Id-2**) and (**Id-3**). The aldehyde of formula (21) is treated with p-toluenesulfonylmethyl isocyanide (TosMIC) in the presence of a suitable base like potassium carbonate in refluxing methanol to give the oxazole derivative of formula (**Id-4**).

Synthetic scheme 7



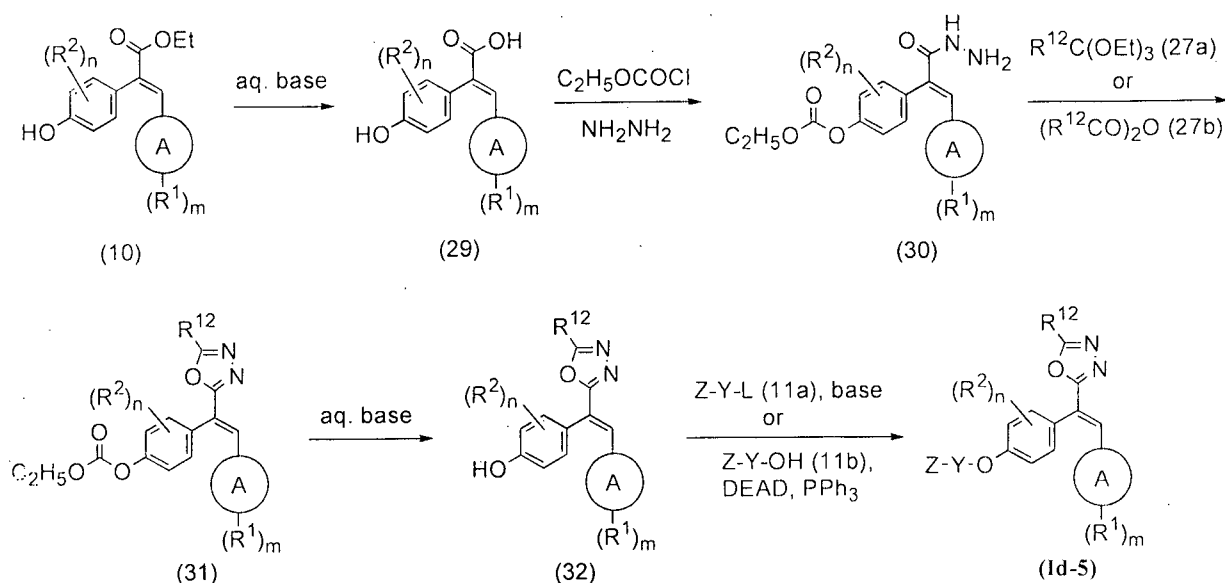
Compounds of the formula (**Id-5**), (**Id-6**), (**Id-7**), (**Id-8**) and (**Id-9**) can be prepared according to Synthetic scheme 8. Thus, the acrylic acid of formula (3) is coupled with hydrazine hydrate using ethyl chloroformate and base such as N-methylmorpholine, triethylamine or diisopropylethylamine in THF to give compound of formula (26). Hydrazide of formula (26) is treated with an ortho ester of formula (27a) in presence of an acid to give compound of formula (**Id-5**) [*J. Med.Chem.* 44, p. 1268-1285, (2001)]. Alternatively, compound of formula (**Id-5**) can also be prepared by treating compound of formula (26) with anhydride (27b) or an acid chloride (27c) under suitable conditions. Oxadiazolone of formula (**Id-6**) is synthesized, in good yields, from compound of formula (26) and trichloromethyl chloroformate in presence of a base followed by alkylation [*J. Heterocyclic.chem.* 19, p. 541, (1982)]. Compound of formula (26) is reacted with carbon disulfide under basic conditions followed by alkylation to give the thio oxadiazole of formula (**Id-7**) [*J. Heterocyclic.chem.* 19, p. 541, (1982)]. Triazolothione of formula (**Id-8**) is prepared from Intermediate (26) by its coupling with potassium thiocyanate followed by cyclization under basic conditions [*J. Med. Chem.* 37, p. 125-132, (1994)]. Substituted and unsubstituted 1,3,4-triazoles derivatives of formula (**Id-9**) is prepared by the reaction of hydrazide (26) with appropriate amidines of formula (28) under suitable conditions.

Synthetic scheme 8



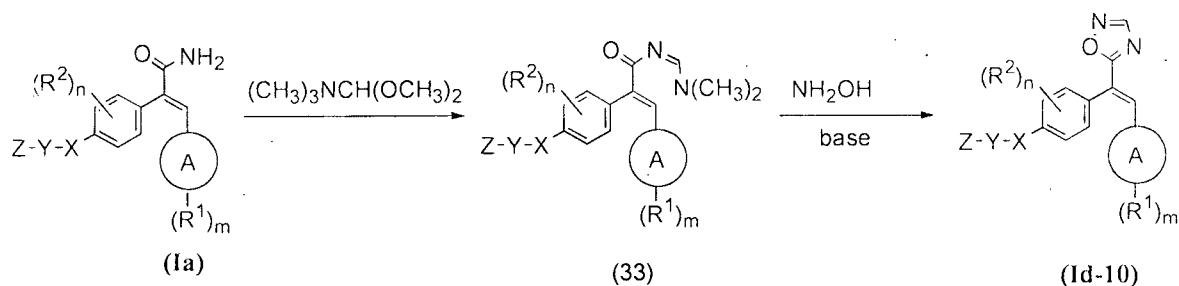
An alternate route for the synthesis of oxadiazole (Id-5) is depicted in Synthetic scheme 9. The ester of formula (10) is hydrolysed to the corresponding acid of formula (29) in presence of aqueous base. The acid group of formula (29) is converted to a hydrazide using hydrazine hydrate in the presence of ethyl chloroformate and a base such as triethylamine. The hydrazide of formula (30) is treated with an ortho ester of formula (27a) in presence of an acid to give compound of formula (31) [*J. Med. Chem.* 44, p.1268-1285, (2001)]. Alternatively, compound of formula (31) can also be prepared by treating compound of formula (30) with anhydride (27b) under suitable conditions. Deprotection of the carbonate group under basic conditions gives the phenol of formula (32), which on further coupling with alkyl halide of formula (11a) (where L is halogen) under basic conditions or with (11b) under Mitsunobu reaction conditions gives the final compound of formula (Id-5).

Synthetic scheme 9



The isomeric oxadiazole of formula (**Id-10**) can be prepared as described in Synthetic scheme (10). Thus, amide of formula (Ia), where R^9 and R^{10} are H, is condensed with *N,N*-dimethylformamide dimethyl acetal under reflux conditions to give the imine derivative (33). Intermediate (33) on reaction with hydroxyl amine in the presence of a suitable base such as sodium hydroxide gives compound of general formula (**Id-10**).

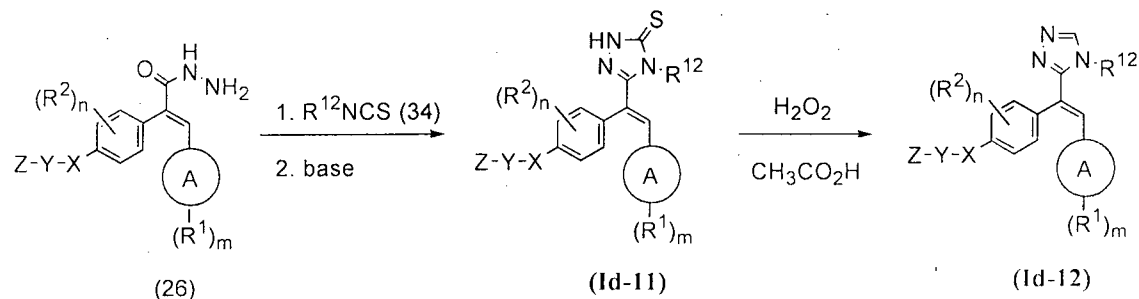
Synthetic scheme 10



The triazolothione compound of formula (**Id-11**) and its corresponding sulphur free aromatic compound of formula (**Id-12**) can be prepared as shown in Synthetic scheme 11. Thus, intermediate (26) is treated with alkylisothiocyanate of the formula (34) under reflux and the intermediate formed is cyclised under basic conditions to give the triazolothione (**Id-11**) [*J. Med.*

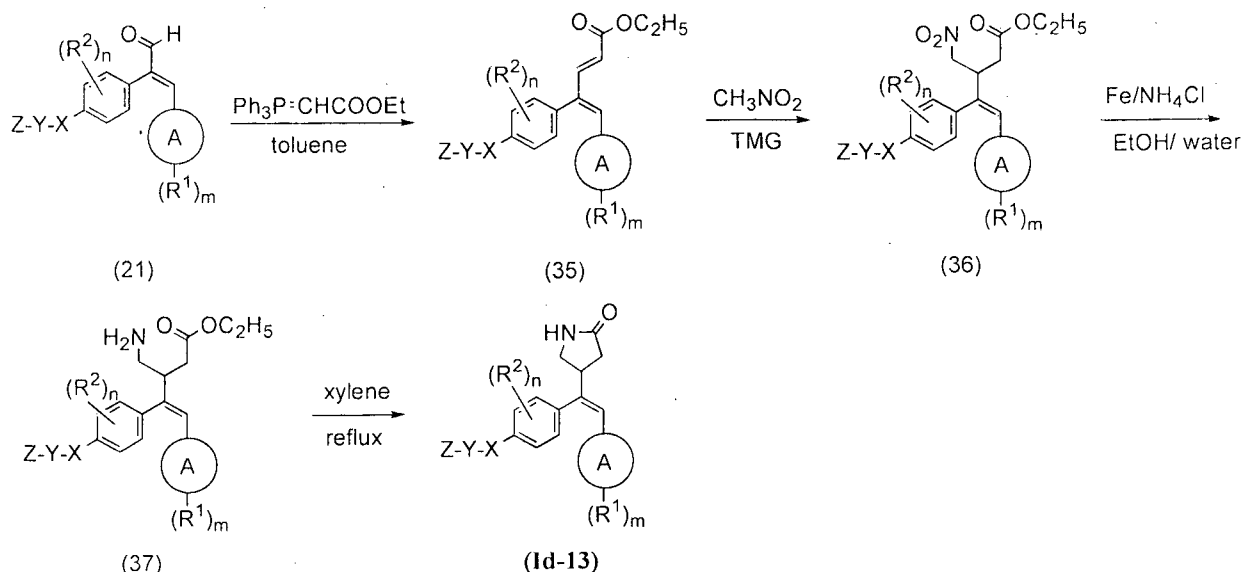
Chem. 37, p.125-132, (1994)]. Further oxidative desulphurization of (**Id-11**) by hydrogen peroxide in acetic acid gives the *N*-substituted triazole derivative (**Id-12**).

Synthetic scheme 11



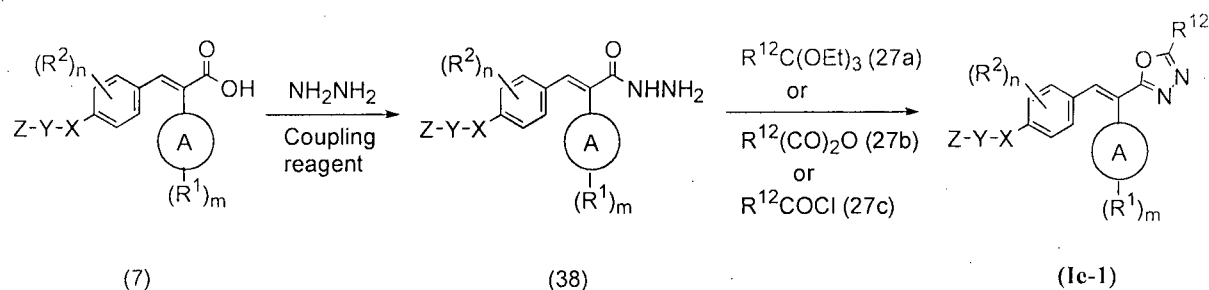
The lactam derivative of formula (**Id-13**) can be prepared according to Synthetic scheme 12. Thus, the aldehyde of formula (21) undergoes Wittig reaction with (carbethoxymethylene) triphenylphosphorane to give the diene ester of formula (35). Michael addition of nitromethane anion, generated by means of suitable base such as 1,1,2,2-tetramethylguanidine (TMG) gives the adduct of formula (36). Selective reduction of the nitro group using an appropriate reagent such as iron and ammonium chloride under aqueous conditions gives amine of the formula (37). Compound of formula (37) undergoes intramolecular cyclization in refluxing xylene to give compound of formula (**Id-13**).

Synthetic scheme 12



Similar to the approaches described in synthetic schemes 8 and 11, various regioisomeric olefins can be prepared from hydrazide of the isomeric acid (7). Preparation of one such derivative is shown in Synthetic scheme 13. Thus, the acrylic acid of formula (7) was coupled with hydrazine hydrate to give hydrazide of formula (38) using a suitable coupling agent such as EDCI. The oxadiazole derivative (1e-1) can be prepared as described in Synthetic scheme 13 using orthoester of formula (27a) or its equivalent (27b) or (27c) under suitable reaction conditions.

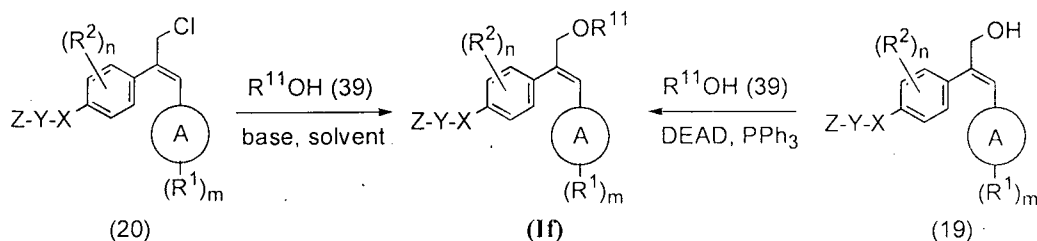
Synthetic scheme 13



The ether derivative of formula (If) can be prepared according to Synthetic scheme 14. Thus, chloro compound of formula (20) is coupled with alcohol of formula (39) under basic conditions to give ether of general formula (If). Alternatively, final compound of general

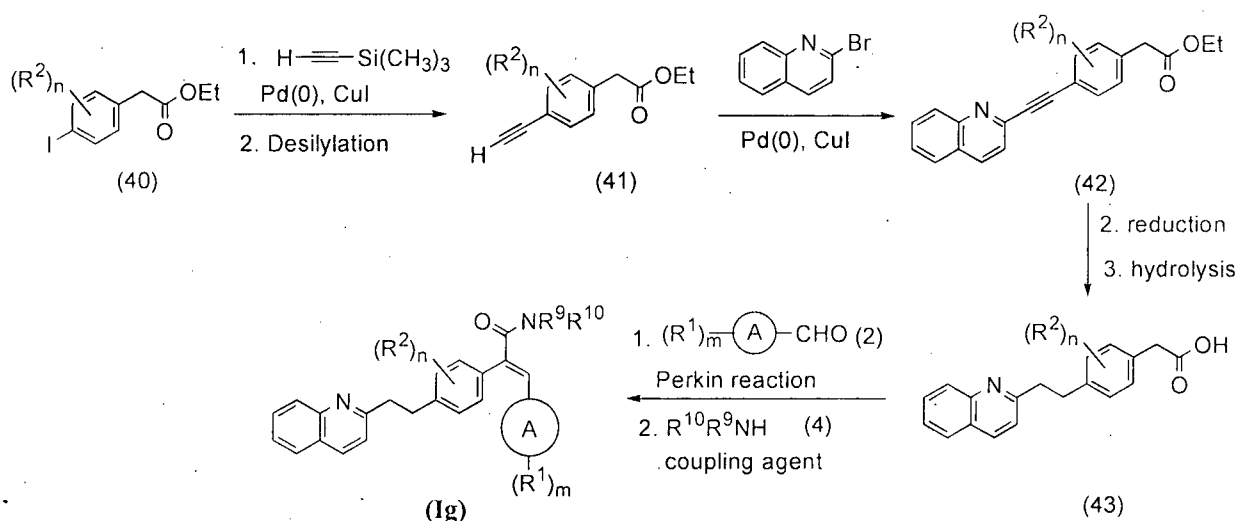
formula (If) can also be prepared by Mitsunobu coupling reaction of alcohol (19) with appropriate aromatic alcohol of formula (39).

Synthetic scheme 14



The compound of general formula (Ig) can be prepared as depicted in Synthetic scheme 15. Thus, ethyl (4-iodophenyl)acetate derivative (40) undergoes Sonagashira coupling reaction with ethynyltrimethyl silane followed by desilylation using appropriate reagent such as TBAF. H_2O , to give the acetylene compound of formula (41). The coupling reaction of compound of formula (41) with 2-bromoquinoline under Sonagashira coupling reaction gives the compound of formula (42). Catalytic reduction of the triple bond of compound of formula (42) followed by hydrolysis gives compound of formula (43). Perkin reaction of compound of formula (43) with aromatic aldehyde (2) gives acid derivative which on further amide coupling with amine of formula (4) gives the final compound of general formula (Ig).

Synthetic scheme 15



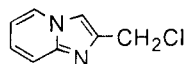
Experimental

Unless otherwise stated, work-up includes distribution of the reaction mixture between an organic and aqueous phase, separation of layers and drying the organic layer over sodium sulphate, filtration and evaporation of the solvent. Purification, unless otherwise mentioned, refers to purification by silica gel chromatographic techniques, in suitable solvents of a suitable polarity as the mobile phase or crystallization from an appropriate solvent or mixture of solvents. The following abbreviations are used in the text: DMSO- d_6 : hexadeuterodimethyl sulfoxide; $CDCl_3$: deuterated chloroform; J : coupling constant in units of Hz; RT or rt: room temperature (22-26°C). Aq.: aqueous; equiv. or eq.: equivalents.

The starting materials represented by the general formula Z-Y-X-, used for the preparation intermediates and compounds of invention are in some cases commercially available or can be prepared according to suitable literature procedure or as described below.

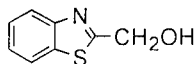
Preparation of Intermediates

Preparation of 2-(chloromethyl)imidazo[1,2- α]pyridine



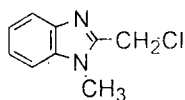
The title compound was prepared by condensation of 2-aminopyridine with 1,3-dichloroacetone in presence of dimethoxyethane as described in the literature (WO 2009/152825); ¹H NMR (300 MHz, $CDCl_3$) δ 4.77 (s, 2H), 6.79 (t, J = 6.9 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.57 (d, J = 9.3 Hz, 2H), 7.61 (s, 1H), 8.07 (d, J = 6.3 Hz, 1H).

Preparation of 1,3-benzothiazol-2-ylmethanol



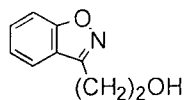
The title compound was synthesized by the reaction of 2-aminothiophenol with glycolic acid using 4N hydrochloric acid as described in the literature [*Journal of the Chemical Society*, p. 2395, (1928)]; ¹H NMR (300 MHz, $CDCl_3$) δ 5.08 (s, 2H), 7.39 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H).

Preparation of 2-(chloromethyl)-1-methyl-1H-benzimidazole



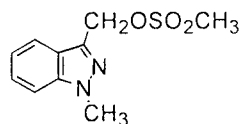
Synthesis of the title compound involves conversion of o-phenylenediamine to 1*H*-benzimidazol-2-ylmethanol using glycolic acid as described in the literature [*Journal of the Chemical Society*, p. 2395, (1928)], followed by alkylation and chlorination; ¹H NMR (300 MHz, CDCl₃) δ 4.14 (s, 3H), 5.42 (s, 2H), 7.47-7.52 (m, 1H), 7.56-7.64 (m, 2H), 7.75 (d, *J* = 8.4 Hz, 1H).

Preparation of 2-(1,2-benzoxazol-3-yl)ethanol



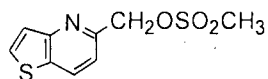
Reaction of 4-hydroxycoumarin with hydroxylamine hydrochloride in presence of triethylamine (TEA) gives 1,2-benzoxazol-3-ylacetic acid (WO 02/070495) which after esterification is reduced to the corresponding alcohol, using lithium aluminium hydride, to give the title compound; ¹H NMR (300 MHz, CDCl₃) δ 3.04 (br s, 1H), 3.24 (t, *J* = 6.0 Hz, 2H), 4.13 (t, *J* = 5.7 Hz, 2H), 7.30-7.35 (m, 2H), 7.57 (br s, 2H), 7.69 (d, *J* = 7.8 Hz, 1H).

Preparation of (1-methyl-1*H*-indazol-3-yl)methyl methanesulfonate



The title compound was synthesized by reduction of methyl 1-methyl-1*H*-indazole-3-carboxylate using lithium aluminium hydride followed by its reaction with methanesulfonyl chloride in the presence of TEA; ¹H NMR (300 MHz, CDCl₃) δ 3.03 (s, 3H), 4.06 (s, 3H), 4.97 (s, 2H), 7.19-7.24 (m, 1H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.82 (d, *J* = 8.1 Hz, 1H).

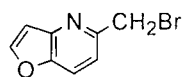
Preparation of thieno[3,2-*b*]pyridin-5-ylmethyl methanesulfonate



Reaction of 3-aminothiophene-2-carboxaldehyde with pyruvic acid in presence of sodium hydroxide gave thieno[3,2-*b*]pyridine-5-carboxylic acid, which was esterified using ethanol and catalytic amount of conc. sulphuric acid to give the corresponding ethyl ester. The ester group

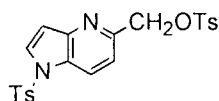
was reduced using lithium aluminium hydride and the alcohol thus obtained was treated with methanesulphonyl chloride to give the title compound (WO 94/22869); ^1H NMR (300 MHz, CDCl_3) δ 3.10 (s, 3H), 5.46 (s, 2H), 7.46 (d, $J = 8.1$ Hz, 1H), 7.55 (d, $J = 5.4$ Hz, 1H), 7.83 (d, $J = 5.4$ Hz, 1H), 8.26 (d, $J = 5.4$ Hz, 1H).

Preparation of 5-(bromomethyl)furo[3,2-*b*]pyridine



Reaction of 2-iodo-6-methylpyridin-3-ol with ethynyltrimethylsilane under Sonagashira coupling reaction conditions resulted in the formation of 5-methyl-2-(trimethylsilyl)furo[3,2-*b*]pyridine via C-C coupling and intramolecular cyclization. Desilylation using tetra-*n*-butyl ammonium fluoride followed by bromination of the methyl group using NBS gives the title compound (Synlett, 2002, 3, 453 – 457); ^1H NMR (300 MHz, CDCl_3) δ 5.12 (s, 2H), 6.93 (s, 1H), 7.10 (d, $J = 7.8$ Hz, 1H), 7.66 (d, $J = 7.8$ Hz, 1H), 7.81 (s, 1H).

Preparation of {1-[(4-Methylphenyl)sulfonyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}methyl-4-methyl benzenesulfonate



Step 1: Ethyl 5-amino-6-[2-(trimethylsilyl)ethynyl] pyridine-2-carboxylate:

To the well stirred solution of 5-amino-6-iodopyridine-2-carboxylate (7.5 g, 25.684 mmol) in TEA (40 ml) were added ethynyltrimethylsilane (10.16 ml, 71.915 mmol), bis(triphenylphosphine) palladium(II)chloride (180 mg, 0.256 mmol) and copper iodide (146 mg, 0.770 mmol) and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with water (100 ml) and extracted with ethyl acetate (300 ml x 3). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated to yield 7 g of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 0.27 (s, 9H), 1.28 (t, $J = 6.9$ Hz, 3H), 4.24 (q, $J = 6.9$ Hz, 2H), 6.24 (s, 1H), 6.62 (s, 1H), 7.09-7.14 (m, 1H), 7.74-7.79 (m, 1H).

Step 2: Ethyl 5-acetamido-6-[2-(trimethylsilyl)ethynyl]pyridine-2-carboxylate:

To the well stirred solution of Step 1 intermediate (5.5 g, 20.659 mmol) in DCM (100 ml) was added pyridine (3.3 ml) and the reaction mixture was cooled to 0 °C. Acetyl chloride (1.76 ml, 24.79 mmol) was then added to the reaction mixture drop wise and the reaction was stirred at room temperature for 2 h. The reaction mixture was quenched with water (100 ml) and extracted with chloroform (300 ml x 3). The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 5.56 g of product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 0.30 (s, 9H), 1.32 (t, *J* = 7.5 Hz, 3H), 2.16 (s, 3H), 4.33 (q, *J* = 6.9 Hz, 2H), 8.04 (d, *J* = 8.4 Hz, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 9.53 (s, 1H).

Step 3: Ethyl 1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylate:

To the well stirred solution of Step 2 intermediate (5.5 g, 17.84 mmol) in THF (50 ml) was added tetra-*n*-butyl ammonium fluoride (4.69 g, 17.59 mmol) and the reaction mixture was refluxed for 8 h. The reaction mixture was quenched with water (100 ml) and extracted with chloroform (300 ml x 3). The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 2.5 g of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 1.43 (t, *J* = 6.6 Hz, 3H), 4.51 (q, *J* = 6.6 Hz, 2H), 6.80 (br s, 1H), 7.58-7.62 (m, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 9.42 (s, 1H).

Step 4: 1*H*-Pyrrolo[3,2-*b*]pyridin-5-ylmethanol:

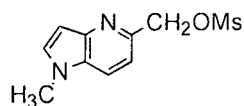
To the well stirred suspension of lithium aluminium hydride (359 g, 9.473 mmol) in dry THF (20 ml) was added a solution of Step 3 intermediate (300 g, 1.578 mmol) in THF at 0 °C and the reaction mixture was stirred at same temperature for 2 h. The reaction mixture was quenched with saturated solution of sodium sulphate, diluted with ethyl acetate and filtered. The filtrate was dried and concentrated under reduced pressure to yield 330 mg of the product; ¹H NMR (300 MHz, DMSO-*d*₆) δ 4.61 (s, 2H), 5.24 (br s, 1H), 6.46 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.59 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 11.21 (br s, 1H).

Step 5: [1-(Phenylsulfonyl)-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl]methyl benzenesulfonate:

To the well stirred suspension of sodium hydride (324 mg, 8.108 mmol) in dry THF (30 ml) was added Step 4 Intermediate (400 mg, 2.702 mmol) at 0 °C and the reaction mixture was stirred for 10 min. The solution of tosyl chloride (1.288 g, 6.755 mmol) in THF was added to the reaction mixture at 0 °C and it was further stirred overnight. The reaction mixture was quenched with water (50 ml) and extracted with chloroform (50 ml x 2). The combined organic layers were

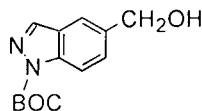
washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated to yield 290 mg of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.31 (s, 3H), 2.34 (s, 3H), 5.18 (br s, 2H), 6.91 (br s, 1H), 7.36-7.41 (m, 5H), 7.75 (d, $J = 7.8$ Hz, 2H), 7.91 (d, $J = 7.5$ Hz, 2H), 8.18 (br s, 1H), 8.31 (d, $J = 7.8$ Hz, 2H).

Preparation of (1-methyl-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl)methyl methanesulfonate



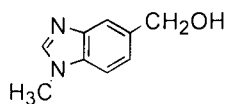
The title compound was synthesized by methylation of ethyl 1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylate using methyl iodide followed by its subsequent reduction and mesylation; ^1H NMR (300 MHz, CDCl_3) δ 3.03 (s, 3H), 4.02 (s, 3H), 5.09 (s, 2H), 7.05-7.11 (m, 1H), 7.61 (d, $J = 8.4$ Hz, 1H), 7.76 (s, 1H), 8.30 (d, $J = 8.4$ Hz, 1H).

Preparation of *tert*-butyl 5-(hydroxymethyl)-1*H*-indazole-1-carboxylate



The title compound was synthesized by esterification of indazole-6-carboxylic acid using methanol in presence of conc. sulphuric acid followed by reduction of the ester group using lithium aluminium hydride and its subsequent reaction with di-*tert*-butyl dicarbonate anhydride; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.64 (s, 9H), 4.67 (d, $J = 5.1$ Hz, 1H), 5.43 (br s, 1H), 7.29 (d, $J = 7.8$ Hz, 1H), 7.80 (d, $J = 8.1$ Hz, 1H), 8.12 (s, 1H), 8.36 (s, 1H).

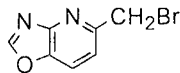
Preparation of (1-methyl-1*H*-benzimidazol-5-yl)methanol



The title compound was synthesized by esterification of 1*H*-benzimidazole-5-carboxylic acid using methanol in presence of conc. sulphuric acid followed by *N*-methylation using methyl iodide in presence of potassium carbonate and subsequent reduction of the ester group by lithium

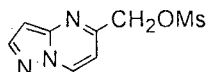
aluminium hydride; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 3.84 (s, 3H), 4.59 (s, 2H), 5.23 (br s, 1H), 7.26 (d, $J = 8.4$ Hz, 1H), 7.52-7.58 (m, 2H), 8.23-8.31 (m, 1H).

Preparation of 5-(bromomethyl)[1,3]oxazolo[4,5-*b*]pyridine



The title compound was prepared by reaction of 2-amino-6-methylpyridin-3-ol with triethyl orthoformate followed by bromination of methyl group with *N*-bromosuccinimide (NBS) in presence of azobisisobutyronitrile (AIBN); ^1H NMR (300 MHz, CDCl_3) δ 5.12 (s, 2H), 7.22 (d, $J = 8.4$ Hz, 1H), 7.78 (d, $J = 8.4$ Hz, 1H), 8.29 (s, 1H).

Preparation of pyrazolo[1,5-*a*]pyrimidin-5-ylmethyl methanesulfonate



Step 1: Ethyl 7-oxo-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylate:

To the well stirred solution of 1*H*-pyrazol-3-amine (5 g, 60.175 mmol) in THF (40 ml) was added diethyl acetylene dicarboxylate (7.70 ml, 48.14 mmol) and the reaction mixture was stirred at room temperature for 72 h. The precipitate obtained was filtered, washed with THF and dried to yield 4.5 g of the product; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.35 (t, $J = 7.2$ Hz, 3H), 4.41 (q, $J = 6.9$ Hz, 2H), 6.27 (s, 2H), 7.95 (s, 1H).

Step 2: Ethyl 7-chloro-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-5-carboxylate:

To the well stirred solution of Step 1 intermediate (1 g, 4.830 mmol) in phosphoryl chloride (POCl_3) (10 ml) was added *N,N*-dimethylaniline (1 ml, 4.83 mmol) and the reaction mixture was refluxed for 40 min. The excess of POCl_3 was distilled under reduced pressure and the residue obtained was poured into crushed ice and extracted with chloroform (2 x 100 ml). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated to yield 1.1 g of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.48 (t, $J = 7.2$ Hz, 3H), 4.54 (q, $J = 6.9$ Hz, 2H), 7.08 (s, 1H), 7.75 (s, 1H), 8.35 (s, 1H).

Step 3: 7-Chloropyrazolo[1,5-*a*]pyrimidine-5-carbaldehyde:

To the well stirred solution of Step 2 intermediate (1 g, 4.43 mmol) in dry THF (15 ml) was added 20 % Diisobutylaluminium hydride (DIBAL-H; 2.22 ml, 13.30 mmol) drop wise at 0°C

and the reaction mixture was stirred at the same temperature for 1 h. Water was added to the reaction mixture and it was further stirred for 15 min. The precipitate formed was filtered and the filtrate was concentrated to yield 1.3 g of the product; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.29 (s, 1H), 7.73 (s, 1H), 8.56 (s, 1H), 9.91 (s, 1H).

Step 4: (7-Chloropyrazolo[1,5-*a*]pyrimidin-5-yl)methanol:

To the well stirred solution of Step 3 intermediate (1.25 g, 5.449 mmol) in DCM (10 ml) was added sodium triacetoxyborohydride (1.154 g, 5.449 mmol) and the reaction was stirred at room temperature overnight. The reaction mixture was diluted with water and the pH was made neutral with sodium bicarbonate. The compound was extracted with chloroform and the organic layer was washed with water, brine, dried, filtered and concentrated to yield the 810 mg of the product; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 4.59 (s, 2H), 5.75 (br s, 1H), 6.79 (s, 1H), 7.38 (s, 1H), 8.31 (s, 1H).

Step 5: Pyrazolo[1,5-*a*]pyrimidin-5-ylmethanol:

To the well stirred solution of Step 4 Intermediate (800 mg, 4.312 mmol) in a mixture of ethanol (12 ml) and ethyl acetate (27 ml) was added sodium acetate (424 mg, 5.174 mmol) and palladium on activated carbon (20 mg) and the reaction mixture was stirred at room temperature under hydrogen atmosphere for 5 h. The reaction mixture was diluted with ethyl acetate filtered and washed with saturated solution of sodium bicarbonate, water and brine. The organic layer was dried and concentrated to yield 300 mg of the product; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 4.57 (s, 2H), 5.66 (br s, 1H), 6.59 (s, 1H), 7.09 (d, $J = 7.2$ Hz, 1H), 8.17 (s, 1H), 9.05 (d, $J = 7.2$ Hz, 1H).

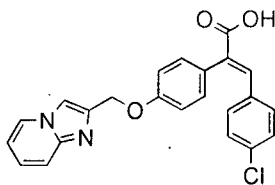
Step 6: Pyrazolo[1,5-*a*]pyrimidin-5-ylmethyl methanesulfonate:

To the well stirred solution of Step 5 intermediate (100 mg, 0.662 mmol) in DCM (10 ml) was added triethyl amine (TEA) (0.27 ml, 1.986 mmol) and the reaction mixture was cooled to 0°C . Methanesulphonyl chloride was added drop wise to the reaction mixture at this temperature and the reaction mixture was stirred for 30 min. The reaction mixture was diluted with water and was extracted with chloroform and the organic layer was washed with water, brine, dried, filtered and concentrated to yield the 150 mg of the product; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.37 (s, 3H), 5.37 (s, 2H), 6.75 (s, 1H), 7.11 (d, $J = 7.2$ Hz, 1H), 8.26 (s, 1H), 9.18 (d, $J = 7.5$ Hz, 1H).

The following intermediates were prepared using appropriate methods described in Synthetic schemes 1 to 13.

Intermediate 1

3-(4-Chlorophenyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]prop-2-enoic acid



Step 1: 2-[4-(Acetyloxy)phenyl]-3-(4-chlorophenyl)prop-2-enoic acid:

To a well stirred solution of 4-hydroxy phenyl acetic acid (10 g, 65.72 mmol) in acetic anhydride (100 ml), were added TEA (13.7 ml, 98.51 mmol) and 4-chloro benzaldehyde (9.23 g, 65.66 mmol) and the reaction mixture was refluxed for 3 h. The reaction mixture was quenched with water (100 ml) and was further refluxed for 30 mins. Mixture was cooled to room temperature and filtered. The solid obtained was titured with diethyl ether and dried to yield 12 g of off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.28 (s, 3H), 7.06 (d, $J = 9.0$ Hz, 2H), 7.11-7.21 (m, 4H), 7.27 (d, $J = 8.1$ Hz, 2H), 7.75 (s, 1H).

Step 2: Ethyl-3-(4-chlorophenyl)-2-(4-hydroxyphenyl)prop-2-enoate:

To a well stirred solution of the Step 1 Intermediate (11.5 g, 36.33 mmol) in ethanol (70 ml) was added concentrated sulphuric acid (9 ml) and the reaction mixture was refluxed for 16 h. The excess of ethanol was distilled off and the reaction mixture was diluted with ethyl acetate (500 ml). The organic layer was washed with water (50 ml x 2) and brine (50 ml), dried over anhydrous Na_2SO_4 and concentrated to yield the 10.5 g of off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.30 (t, $J = 7.5$ Hz, 3H), 4.27 (q, $J = 7.5$ Hz, 2H), 5.17 (br s, 1H), 6.80 (t, $J = 8.4$ Hz, 2H), 6.97-7.07 (m, 4H), 7.14 (d, $J = 8.1$ Hz, 2H), 7.72 (s, 1H).

Step 3: Ethyl-3-(4-chlorophenyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]prop-2-enoate:

To a well stirred solution of Step 2 Intermediate (10 g, 33.05 mmol) in dimethyl formamide (60 ml), were added potassium carbonate (6.85 g, 49.57 mmol) and 2-(chloromethyl)imidazo[1,2-*a*]pyridine (5.50 g, 33.05) and the reaction mixture was heated to 60 °C for 16 h. The reaction mixture was diluted with water (20 ml) and extracted with ethyl acetate (50 ml x 3). The combined organic layers were washed with water (25 ml x 2) and brine (25 ml), dried over

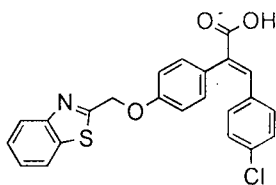
anhydrous Na_2SO_4 , filtered and concentrated to yield 9 g of off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.30 (t, $J = 6.9$ Hz, 3H), 4.26 (q, $J = 7.5$ Hz, 2H), 5.30 (s, 2H), 6.80 (t, $J = 6.9$ Hz, 1H), 6.96-7.05 (m, 4H), 7.12 (d, $J = 6.9$ Hz, 4H), 7.16-7.23 (m, 1H), 7.60 (d, $J = 9.3$ Hz, 1H), 7.66 (s, 1H), 7.72 (s, 1H), 8.11 (d, $J = 6.9$ Hz, 1H).

Step 4: 3-(4-Chlorophenyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]prop-2-enoic acid:

To a well stirred solution of Step 3 Intermediate (8.5 g, 19.63 mmol) in ethanol (60 ml) was added aqueous solution of 1 N sodium hydroxide and the reaction mixture was stirred for 16 h at room temperature. The excess of ethanol was distilled off and the reaction mass was diluted with water (50 ml). It was further acidified with 2N HCl solution and the solid so obtained was filtered and washed with water to yield 7.5 g of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.27 (s, 2H), 7.01- 7.10 (m, 7H), 7.27 (d, $J = 8.1$ Hz, 2H), 7.40 (t, $J = 7.5$ Hz, 1H), 7.63 (d, $J = 8.7$ Hz, 1H), 7.70 (s, 1H), 8.11 (s, 1H), 8.63 (d, $J = 6.3$ Hz, 1H), 13.58 (br s, 1H, D_2O exchangeable).

Intermediate 2

2-[4-(1,3-Benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)prop-2-enoic acid



Step 1: Ethyl-2-[4-(1,3-benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)prop-2-enoate:

To the well stirred solution of ethyl-3-(4-chlorophenyl)-2-(4-hydroxyphenyl)prop-2-enoate (Step 2 of intermediate 1, 1.5 g, 4.958 mmol) in dry tetrahydrofuran (30 ml), were added 1,3-benzothiazol-2-ylmethanol (819 mg, 4.958 mmol) and triphenyl phosphine (1.95 g, 7.438 mmol) followed by dropwise addition of diethyl azodicarboxylate (1.01 ml, 6.446 mmol). The reaction mixture was stirred at room temperature for 10 mins after which it was heated at 60 °C overnight. The reaction mixture was diluted with water (30 ml) and extracted with ethyl acetate (100 ml x 3). The combined organic layers were washed with water (50 ml x 2) and brine (50 ml), dried over anhydrous Na_2SO_4 , filtered and concentrated to yield 670 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.29 (t, $J = 7.5$ Hz, 3H), 4.26 (q, $J = 7.2$ Hz, 2H), 5.52 (s, 2H), 6.96 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.1$ Hz, 2H), 7.09-7.16 (m, 4H), 7.43 (t, $J =$

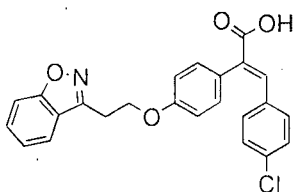
7.2 Hz, 1H), 7.52 (t, $J = 7.2$ Hz, 1H), 7.73 (s, 1H), 7.93 (d, $J = 7.8$ Hz, 1H), 8.04 (d, $J = 7.8$ Hz, 1H).

Step 2: 2-[4-(1,3-Benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)prop-2-enoic acid:

To a well stirred solution of the Step 1 Intermediate (650 mg, 1.445 mmol) in ethanol (15 ml) was added aqueous solution of 1N sodium hydroxide and the reaction mixture was stirred for 16 h at room temperature. The excess of ethanol was distilled off and the reaction mass was diluted with water (25 ml). It was further acidified with 2N HCl solution and the solid so obtained was filtered and washed with water to yield 560 mg of product as off-white solid; ^1H NMR (300 MHz, DMSO- d_6) δ 5.63 (s, 2H), 7.04-7.11 (m, 6H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.44-7.57 (m, 2H), 7.70 (s, 1H), 8.02 (d, $J = 8.4$ Hz, 1H), 8.14 (d, $J = 7.8$ Hz, 1H), 12.75 (br s, 1H).

Intermediate 3

2-{4-[2-(1,2-Benzoxazol-3-yl)ethoxy]phenyl}-3-(4-chlorophenyl)prop-2-enoic acid

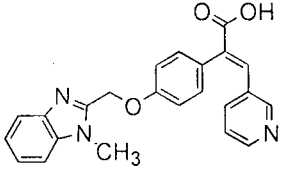
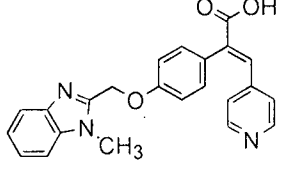
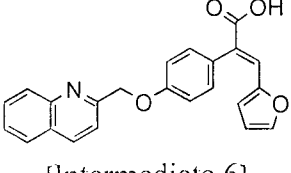
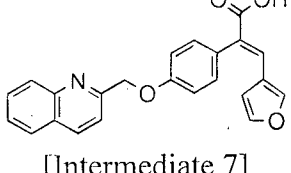
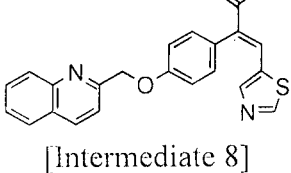
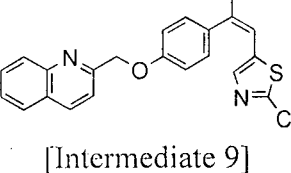
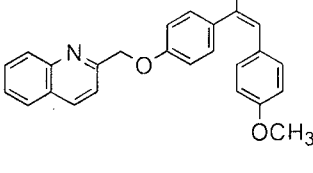


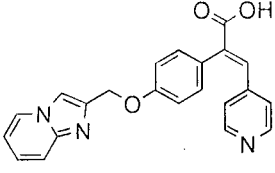
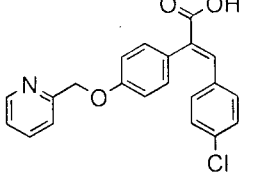
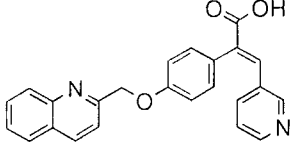
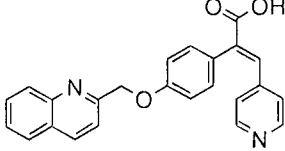
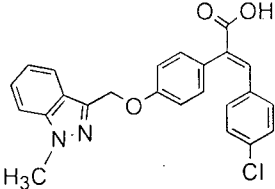
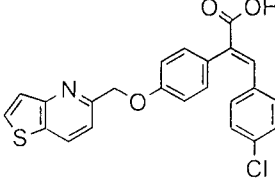
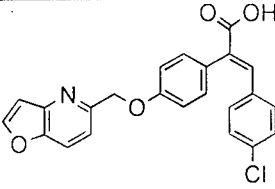
The title compound was prepared by Mitsunobu coupling of ethyl-3-(4-chlorophenyl)-2-(4-hydroxyphenyl)prop-2-enoate and 2-(1,2-benzoxazol-3-yl)ethanol as described in Intermediate 2; ^1H NMR (300 MHz, DMSO- d_6) δ 3.48-3.53 (m, 2H), 4.44 (t, $J = 6.3$ Hz, 2H), 6.92 (d, $J = 8.1$ Hz, 2H), 7.02-7.08 (m, 4H), 7.26 (d, $J = 8.1$ Hz, 2H), 7.41 (t, $J = 7.8$ Hz, 1H), 7.63-7.75 (m, 3H), 8.02 (d, $J = 7.8$ Hz, 1H), 12.85 (br s, 1H).

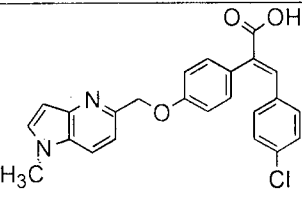
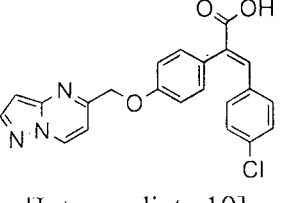
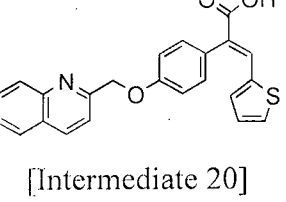
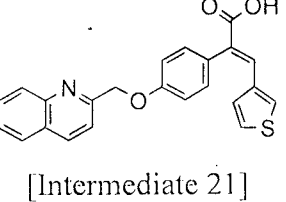
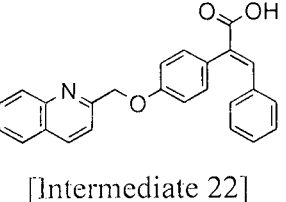
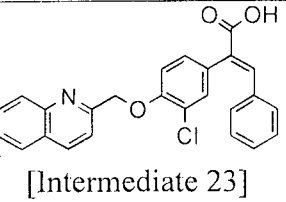
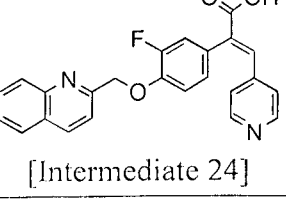
Intermediates 4 to 38 were prepared using appropriate starting materials as described in Intermediate 1. Their structure, names and ^1H NMR data are given in the Table 1.

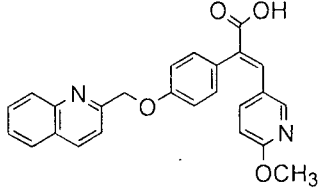
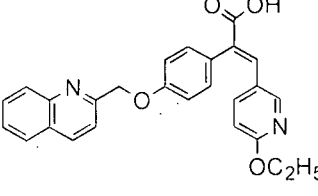
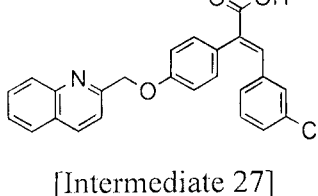
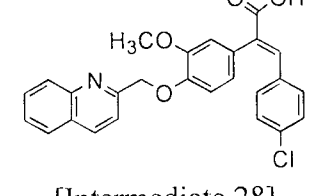
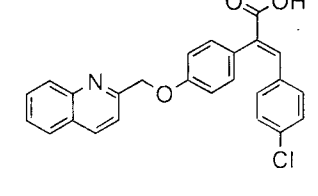
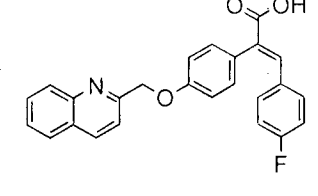
Table 1: Structure and characterization data for Intermediates 4 - 38

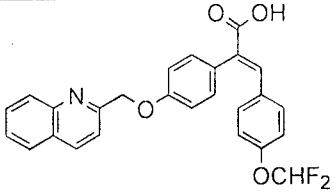
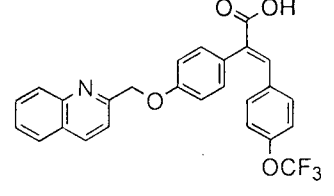
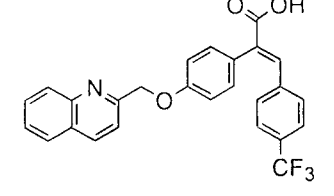
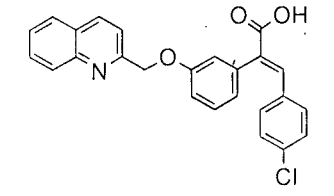
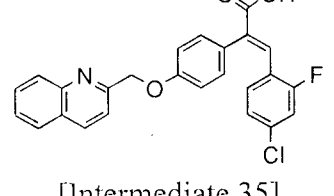
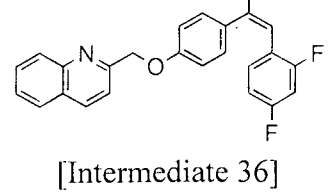
Molecular Structure and Intermediate No.	Chemical name and ^1H NMR data (δ ppm, 300 MHz)
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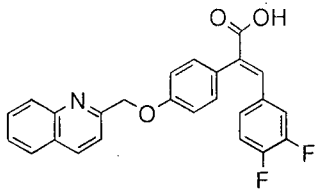
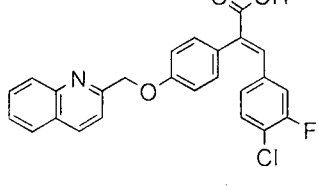
 [Intermediate 4]	2-{4-[(1-Methyl-1H-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-3-yl)prop-2-enoic acid: (CDCl₃) δ 3.90 (s, 3H), 5.45 (s, 2H), 7.03-7.08 (m, 1H), 7.18 (br s, 5H), 7.35-7.45 (m, 3H), 7.82 (br s, 2H), 8.31 (s, 1H), 8.32 (br s, 1H), 13.36 (br s, 1H, D₂O exchangeable); APCI-MS (<i>m/z</i>) 399 (M+H)⁺.
 [Intermediate 5]	2-{4-[(1-Methyl-1H-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-4-yl)prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 3.88 (s, 3H), 5.45 (s, 2H), 6.91 (d, <i>J</i> = 4.8 Hz, 2H), 7.11 (d, <i>J</i> = 8.1 Hz, 2H), 7.17 (d, <i>J</i> = 8.4 Hz, 2H), 7.23-7.33 (m, 2H), 7.51 (br s, 1H), 7.60 (d, <i>J</i> = 7.8 Hz, 1H), 7.66 (d, <i>J</i> = 7.8 Hz, 1H), 8.35 (d, <i>J</i> = 7.8 Hz, 2H), 13.45 (br s, 1H, D₂O exchangeable).
 [Intermediate 6]	3-(Furan-2-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 5.42 (s, 2H), 5.96 (s, 1H), 6.43 (s, 1H), 7.09-7.16 (m, 4H), 7.53 (s, 1H), 7.59-7.66 (m, 1H), 7.71-7.78 (m, 2H), 7.79-7.86 (m, 1H), 8.02 (t, <i>J</i> = 7.8 Hz, 2H), 8.45 (d, <i>J</i> = 8.7 Hz, 1H), 12.62 (br s, 1H).
 [Intermediate 7]	3-(Furan-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 5.42 (s, 2H), 5.44 (s, 1H), 7.08-7.14 (m, 4H), 7.45 (s, 1H), 7.59-7.63 (m, 2H), 7.71 (d, <i>J</i> = 9.0 Hz, 1H), 7.76-7.82 (m, 2H), 8.01 (t, <i>J</i> = 7.8 Hz, 2H), 8.43 (d, <i>J</i> = 8.4 Hz, 1H), 12.45 (br s, 1H).
 [Intermediate 8]	2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-(1,3-thiazol-5-yl)prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 5.43 (s, 2H), 7.10-7.18 (m, 4H), 7.63 (t, <i>J</i> = 7.5 Hz, 1H), 7.73 (d, <i>J</i> = 8.4 Hz, 1H), 7.80 (t, <i>J</i> = 7.5 Hz, 1H), 8.01-8.06 (m, 3H), 8.24 (s, 1H), 8.46 (d, <i>J</i> = 8.7 Hz, 1H), 8.89 (s, 1H), 12.60 (br s, 1H).
 [Intermediate 9]	3-(2-Chloro-1,3-thiazol-5-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 5.43 (s, 2H), 7.13-7.18 (m, 4H), 7.63 (t, <i>J</i> = 7.5 Hz, 1H), 7.76 (d, <i>J</i> = 8.1 Hz, 1H), 7.82 (t, <i>J</i> = 7.8 Hz, 1H), 7.87 (s, 1H), 8.00-8.05 (m, 2H), 8.45 (d, <i>J</i> = 8.1 Hz, 1H), 8.96 (s, 1H), 12.97 (br s, 1H).
 [Intermediate 10]	3-(4-Methoxyphenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 3.69 (s, 3H), 5.40 (s, 2H), 6.75 (d, <i>J</i> = 7.8 Hz, 2H), 7.01 (d, <i>J</i> = 8.1 Hz, 2H), 7.08 (s, 4H), 7.60-7.72 (m, 3H), 7.79 (t, <i>J</i> = 7.2 Hz, 1H), 8.01 (t, <i>J</i> = 7.5 Hz, 2H), 8.42 (d, <i>J</i> = 8.7 Hz, 1H), 12.86 (br s, 1H).

 [Intermediate 11]	2-[4-(Imidazo[1,2-a]pyridin-2-ylmethoxy)phenyl]-3-(pyridin-4-yl)prop-2-enoic acid: (CDCl₃) δ 5.21 (s, 2H), 6.80 (d, <i>J</i> = 5.1 Hz, 3H), 7.09 (s, 4H), 7.23 (br s, 1H), 7.60 (d, <i>J</i> = 8.7 Hz, 1H), 7.68 (s, 1H), 7.79 (s, 1H), 8.12 (d, <i>J</i> = 6.9 Hz, 1H), 8.38 (d, <i>J</i> = 5.4 Hz, 2H), 13.55 (br s, 1H, D₂O exchangeable).
 [Intermediate 12]	3-(4-Chlorophenyl)-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 5.18 (s, 2H), 6.98-7.06 (m, 6H), 7.24 (d, <i>J</i> = 8.1 Hz, 2H), 7.31-7.39 (m, 1H), 7.53 (d, <i>J</i> = 7.8 Hz, 1H), 7.59 (s, 1H), 7.82 (t, <i>J</i> = 7.2 Hz, 1H), 8.85 (br s, 1H), 12.82 (br s, 1H).
 [Intermediate 13]	3-(Pyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid: (CDCl₃) δ 5.40 (s, 2H), 7.10-7.15 (m, 6H), 7.58 (d, <i>J</i> = 6.9 Hz, 1H), 7.62-7.70 (m, 1H), 7.75-7.81 (m, 2H), 7.85 (d, <i>J</i> = 7.2 Hz, 1H), 8.15 (d, <i>J</i> = 8.4 Hz, 1H), 8.24 (d, <i>J</i> = 8.4 Hz, 1H), 8.35-8.41 (m, 2H), 13.42 (br s, 1H, D₂O exchangeable).
 [Intermediate 14]	3-(Pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid: (CDCl₃) δ 5.39 (s, 2H), 6.97 (br s, 2H), 7.08 (br s, 4H), 7.62 (br s, 2H), 7.70 (d, <i>J</i> = 8.1 Hz, 1H), 7.79 (d, <i>J</i> = 6.6 Hz, 1H), 8.01 (br s, 2H), 8.38-8.46 (m, 3H), 13.35 (br s, 1H).
 [Intermediate 15]	3-(4-Chlorophenyl)-2-{4-[(1-methyl-1H-indazol-3-yl) methoxy] phenyl}prop-2-enoic acid: (CDCl₃) δ 4.09 (s, 3H), 5.45 (s, 2H), 6.99 (d, <i>J</i> = 8.4 Hz, 2H), 7.04-7.10 (m, 4H), 7.13-7.22 (m, 4H), 7.39-7.45 (m, 2H), 7.82-7.88 (m, 1H), 13.32 (br s, 1H).
 [Intermediate 16]	3-(4-Chlorophenyl)-2-[4-(thieno[3,2-b]pyridin-5-yl methoxy) phenyl]prop-2-enoic acid: (DMSO-<i>d</i>₆) δ 5.32 (s, 2H), 7.06 (br s, 6H), 7.25 (d, <i>J</i> = 8.1 Hz, 2H), 7.51-7.60 (m, 2H), 7.65 (s, 1H), 8.19 (d, <i>J</i> = 5.7 Hz, 1H), 8.54 (d, <i>J</i> = 8.4 Hz, 1H), 12.78 (br s, 1H).
	3-(4-Chlorophenyl)-2-[4-(furo[3,2-b]pyridin-5-ylmethoxy) phenyl]prop-2-enoic acid: (CDCl₃) δ 5.32 (s, 2H), 6.99-7.05 (m, 5H), 7.12-7.18 (m, 4H), 7.52 (d, <i>J</i> = 7.8 Hz, 1H), 7.83 (br s, 2H), 7.89 (s, 1H), 12.35 (br s, 1H).

[Intermediate 17]  [Intermediate 18]	<u>3-(4-Chlorophenyl)-2-{4-[(1-methyl-1H-pyrrolo[3,2-b]pyridin-5-yl)methoxy]phenyl}prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 3.83 (s, 3H), 5.23 (s, 2H), 6.55 (s, 1H), 6.98-7.05 (m, 6H), 7.23 (d, <i>J</i> = 8.1 Hz, 2H), 7.31 (d, <i>J</i> = 8.4 Hz, 1H), 7.60-7.65 (m, 2H), 7.91 (d, <i>J</i> = 8.4 Hz, 1H), 12.43 (br s, 1H).
 [Intermediate 19]	<u>3-(4-Chlorophenyl)-2-[4-(pyrazolo[1,5-a]pyrimidin-5-yl)methoxy]phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.27 (s, 2H), 6.72 (s, 1H), 7.03-7.15 (m, 7H), 7.26 (d, <i>J</i> = 8.7 Hz, 2H), 7.69 (s, 1H), 8.24 (s, 1H), 9.14 (d, <i>J</i> = 6.9 Hz, 1H), 12.73 (br s, 1H).
 [Intermediate 20]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-(thiophen-2-yl)prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.43 (s, 2H), 7.00 (t, <i>J</i> = 4.8 Hz, 1H), 7.09-7.17 (m, 4H), 7.39 (br s, 1H), 7.48 (d, <i>J</i> = 4.8 Hz, 1H), 7.63 (t, <i>J</i> = 7.5 Hz, 1H), 7.71-7.82 (m, 2H), 7.96-8.06 (m, 3H), 8.45 (d, <i>J</i> = 9.0 Hz, 1H), 12.51 (br s, 1H).
 [Intermediate 21]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-(thiophen-3-yl)prop-2-enoic acid</u>: (CDCl₃) δ 5.45 (s, 2H), 6.54 (d, <i>J</i> = 5.4 Hz, 1H), 7.09 (d, <i>J</i> = 8.7 Hz, 3H), 7.15-7.22 (m, 2H), 7.86 (d, <i>J</i> = 7.8 Hz, 1H), 7.91 (s, 1H), 8.17 (d, <i>J</i> = 8.4 Hz, 1H), 8.25 (d, <i>J</i> = 8.4 Hz, 1H), 12.81 (br s, 1H).
 [Intermediate 22]	<u>3-Phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.36 (s, 2H), 6.95-7.05 (m, 6H), 7.09 (br s, 3H), 7.39 (s, 1H), 7.62 (t, <i>J</i> = 7.2 Hz, 1H), 7.70 (d, <i>J</i> = 8.7 Hz, 1H), 7.79 (t, <i>J</i> = 7.2 Hz, 1H), 8.01 (t, <i>J</i> = 7.8 Hz, 2H), 8.43 (d, <i>J</i> = 8.7 Hz, 1H), 12.86 (br s, 1H).
 [Intermediate 23]	<u>2-[3-Chloro-4-(quinolin-2-ylmethoxy)phenyl]-3-phenylprop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.50 (s, 2H), 7.03-7.10 (m, 3H), 7.21-7.29 (m, 5H), 7.63 (t, <i>J</i> = 7.8 Hz, 1H), 7.72-7.82 (m, 3H), 8.02 (d, <i>J</i> = 8.1 Hz, 2H), 8.47 (d, <i>J</i> = 8.7 Hz, 1H), 12.78 (br s, 1H).
 [Intermediate 24]	<u>2-[3-Fluoro-4-(quinolin-2-ylmethoxy)phenyl]-3-(pyridin-4-yl)prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.47 (s, 2H), 6.88 (d, <i>J</i> = 8.1 Hz, 1H), 6.99 (d, <i>J</i> = 5.4 Hz, 2H), 7.15 (d, <i>J</i> = 11.7 Hz, 1H), 7.25 (t, <i>J</i> = 9.0 Hz, 1H), 7.61-7.72 (m, 3H), 7.80 (t, <i>J</i> = 7.2 Hz, 1H), 8.02 (d, <i>J</i> = 8.4 Hz, 2H), 8.40-8.48 (m, 3H), 13.05 (br s, 1H).

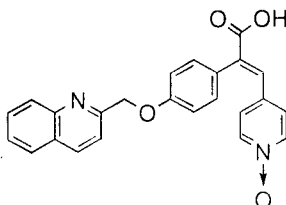
 [Intermediate 25]	<u>3-(6-Methoxypyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 3.80 (s, 3H), 5.40 (s, 2H), 6.61 (d, <i>J</i> = 9.0 Hz, 1H), 7.10-7.17 (m, 4H), 7.62-7.76 (m, 4H), 7.79 (t, <i>J</i> = 7.2 Hz, 1H), 7.99-8.02 (m, 3H), 8.44 (d, <i>J</i> = 9.0 Hz, 1H), 12.43 (br s, 1H).
 [Intermediate 26]	<u>3-(6-Ethoxypyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 1.26 (t, <i>J</i> = 6.6 Hz, 3H), 4.24 (q, <i>J</i> = 6.6 Hz, 2H), 5.40 (s, 2H), 6.57 (d, <i>J</i> = 8.7 Hz, 1H), 7.09-7.15 (m, 4H), 7.60-7.65 (m, 2H), 7.71 (d, <i>J</i> = 8.4 Hz, 1H), 7.79 (t, <i>J</i> = 7.8 Hz, 1H), 8.01 (br s, 3H), 8.44 (d, <i>J</i> = 9.0 Hz, 1H), 12.35 (br s, 1H).
 [Intermediate 27]	<u>3-(3-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.41 (s, 2H), 7.01-7.10 (m, 6H), 7.18-7.29 (m, 2H), 7.60-7.70 (m, 3H), 7.79 (t, <i>J</i> = 7.5 Hz, 1H), 8.01 (t, <i>J</i> = 7.5 Hz, 2H), 8.42 (d, <i>J</i> = 8.7 Hz, 1H), 12.86 (br s, 1H).
 [Intermediate 28]	<u>3-(4-Chlorophenyl)-2-[3-methoxy-4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 3.71 (s, 3H), 5.37 (s, 2H), 6.62 (d, <i>J</i> = 7.8 Hz, 1H), 6.80 (s, 1H), 7.04-7.09 (m, 3H), 7.25 (d, <i>J</i> = 7.8 Hz, 2H), 7.60-7.70 (m, 3H), 7.79 (t, <i>J</i> = 7.2 Hz, 1H), 8.00 (br s, 2H), 8.45 (d, <i>J</i> = 8.4 Hz, 1H), 12.68 (br s, 1H).
 [Intermediate 29]	<u>3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (CDCl₃) δ 5.39 (s, 2H), 7.07 (br s, 6H), 7.24 (d, <i>J</i> = 8.4 Hz, 2H), 7.60-7.71 (m, 3H), 7.79 (t, <i>J</i> = 7.2 Hz, 1H), 8.01 (t, <i>J</i> = 7.8 Hz, 2H), 8.44 (d, <i>J</i> = 8.4 Hz, 1H), 13.45 (br s, 1H, D₂O exchangeable).
 [Intermediate 30]	<u>3-(4-Fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (CDCl₃) δ 3.35 (br s, 1H, D₂O exchangeable), 5.41 (s, 2H), 6.84 (t, <i>J</i> = 8.7 Hz, 2H), 7.03-7.09 (m, 4H), 7.17 (d, <i>J</i> = 9.0 Hz, 2H), 7.56 (t, <i>J</i> = 7.5 Hz, 1H), 7.70-7.77 (m, 2H), 7.84 (d, <i>J</i> = 7.8 Hz, 2H), 8.15 (d, <i>J</i> = 8.4 Hz, 1H), 8.22 (d, <i>J</i> = 8.7 Hz, 1H).

 [Intermediate 31]	<u>3-[4-(Difluoromethoxy)phenyl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.42 (s, 2H), 6.46 (s, 1H), 6.89 (d, <i>J</i> = 8.1 Hz, 2H), 7.06 (t, <i>J</i> = 8.7 Hz, 4H), 7.18 (d, <i>J</i> = 8.1 Hz, 2H), 7.57 (t, <i>J</i> = 7.5 Hz, 1H), 7.70-7.79 (m, 2H), 7.85 (d, <i>J</i> = 8.4 Hz, 2H), 8.17 (d, <i>J</i> = 8.1 Hz, 1H), 8.24 (d, <i>J</i> = 8.1 Hz, 1H), 12.77 (br s, 1H).
 [Intermediate 32]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.40 (s, 2H), 7.12 (br s, 4H), 7.19 (s, 4H), 7.62 (t, <i>J</i> = 7.2 Hz, 1H), 7.64-7.74 (m, 3H), 8.01 (t, <i>J</i> = 7.8 Hz, 2H), 8.44 (d, <i>J</i> = 8.7 Hz, 1H), 12.76 (br s, 1H).
 [Intermediate 33]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.39 (s, 2H), 7.09 (br s, 4H), 7.26 (d, <i>J</i> = 7.8 Hz, 2H), 7.54-7.65 (m, 3H), 7.68-7.80 (m, 3H), 8.01 (t, <i>J</i> = 7.8 Hz, 2H), 8.44 (d, <i>J</i> = 8.4 Hz, 1H), 12.87 (br s, 1H).
 [Intermediate 34]	<u>3-(4-Chlorophenyl)-2-[3-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.44 (s, 2H), 6.76 (d, <i>J</i> = 7.8 Hz, 1H), 6.89 (s, 1H), 7.00 (d, <i>J</i> = 8.4 Hz, 2H), 7.10 (d, <i>J</i> = 8.1 Hz, 1H), 7.18 (d, <i>J</i> = 8.7 Hz, 2H), 7.33 (t, <i>J</i> = 7.8 Hz, 1H), 7.70-7.77 (m, 3H), 7.83-7.89 (m, 1H), 8.09 (br s, 2H), 8.59 (br s, 1H), 12.95 (s, 1H).
 [Intermediate 35]	<u>3-(4-Chloro-2-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.37 (s, 2H), 6.76 (t, <i>J</i> = 8.4 Hz, 1H), 7.02-7.14 (m, 5H), 7.44 (d, <i>J</i> = 10.2 Hz, 2H), 7.59-7.69 (m, 3H), 7.79 (t, <i>J</i> = 7.8 Hz, 1H), 8.01 (br s, 2H), 8.43 (d, <i>J</i> = 8.4 Hz, 1H).
 [Intermediate 36]	<u>3-(2,4-Difluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (CDCl₃) δ 5.40 (s, 2H), 6.54 (t, <i>J</i> = 8.4 Hz, 1H), 6.73-6.81 (m, 2H), 7.02 (d, <i>J</i> = 8.1 Hz, 2H), 7.17 (d, <i>J</i> = 9.0 Hz, 2H), 7.57 (t, <i>J</i> = 7.5 Hz, 1H), 7.70-7.78 (m, 2H), 7.85 (d, <i>J</i> = 7.8 Hz, 1H), 8.01 (s, 1H), 8.17 (d, <i>J</i> = 8.4 Hz, 1H), 8.24 (d, <i>J</i> = 8.4 Hz, 1H), 12.85 (br s, 1H).

 [Intermediate 37]	<u>3-(3,4-Difluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (CDCl₃) δ 5.44 (s, 2H), 6.78-6.88 (m, 2H), 6.93-6.99 (m, 1H), 7.05 (d, J = 8.7 Hz, 2H), 7.16 (d, J = 8.1 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.71-7.79 (m, 3H), 7.86 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 9.0 Hz, 1H), 12.45 (br s, 1H).
 [Intermediate 38]	<u>3-(4-Chloro-3-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid</u>: (DMSO-<i>d</i>₆) δ 5.41 (s, 2H), 6.92 (d, J = 9.0 Hz, 1H), 7.02-7.10 (m, 5H), 7.42 (t, J = 7.8 Hz, 1H), 7.60-7.66 (m, 1H), 7.70 (d, J = 8.7 Hz, 1H), 7.79 (t, J = 7.8 Hz, 1H), 8.01 (t, J = 7.5 Hz, 2H), 8.43 (d, J = 8.1 Hz, 1H), 12.95 (br s, 1H).

Intermediate 39

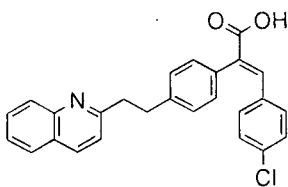
3-(1-Oxidopyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid



Ethyl-2-(4-hydroxyphenyl)-3-(pyridin-4-yl)prop-2-enoate was synthesized from 4-hydroxyphenylacetic acid and 4-pyridine carboxaldehyde as described in Steps 1 and 2 of Intermediate 1. *N*-oxidation of this intermediate by *m*-chloroperbenzoic acid gave ethyl-2-(4-hydroxyphenyl)-3-(1-oxidopyridin-4-yl)prop-2-enoate which was further coupled with 2-(chloromethyl)quinoline and hydrolysed as described in Steps 3 and 4 of Intermediate 1 to give the title compound; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.40 (s, 2H), 7.01 (d, J = 8.1 Hz, 2H), 7.08-7.17 (m, 4H), 7.59-7.65 (m, 2H), 7.71 (d, J = 8.4 Hz, 1H), 7.80 (t, J = 7.5 Hz, 1H), 7.99-8.06 (m, 4H), 8.45 (d, J = 8.4 Hz, 1H), 12.62 (br s, 1H).

Intermediate 40

3-(4-Chlorophenyl)-2-{4-[2-(quinolin-2-yl)ethyl]phenyl}prop-2-enoic acid



Step 1: Ethyl {4-[(trimethylsilyl)ethynyl]phenyl}acetate:

To a well stirred solution of ethyl (4-iodophenyl)acetate (5.5 g, 18.96 mmol) in DMSO (40 ml) were added dichlorobis(triphenylphosphine) palladium (II) (133 mg, 0.18 mmol), copper iodide (108 mg, 0.568 mmol), triethylamine (3.95 ml, 2.844 mmol) and ethynyltrimethyl silane (2.04 g, 20.85 mmol) and the reaction was stirred at room temperature overnight. The reaction mixture was diluted with water (100 ml) and ethyl acetate (300 ml), given charcoal treatment and filtered. The organic layer was washed with water (2 x 100 ml), brine (50 ml), dried and concentrated to yield 5 g of the product; ^1H NMR (300 MHz, CDCl_3) δ 0.24 (s, 9H), 1.21-1.27 (m, 3H), 3.59 (s, 2H), 4.14 (q, $J = 6.9$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 1H), 7.25 (d, $J = 7.8$ Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.64 (d, $J = 7.8$ Hz, 1H).

Step 2: Ethyl (4-ethynylphenyl)acetate:

To the well stirred solution of Step 1 intermediate (4.9 g, 18.82 mmol) in dichloromethane (30 ml) was added tetrabutylammonium fluoride hydrate (2.461 g, 9.413 mmol) and the reaction mixture was stirred at room temperature for 10 min. The reaction mixture was quenched with water (100 ml) and extracted with chloroform (2 x 250 ml). The combined organic layers were washed with water (2 x 50 ml) and brine (50 ml), dried over anhydrous Na_2SO_4 and concentrated to yield the crude product. The compound was purified by silica gel column chromatography to yield 2.9 g of the product; ^1H NMR (300 MHz, CDCl_3) δ 1.25 (t, $J = 7.2$ Hz, 3H), 3.06 (s, 1H), 3.61 (s, 2H), 4.15 (q, $J = 6.9$ Hz, 2H), 7.24 (d, $J = 8.1$ Hz, 2H), 7.45 (d, $J = 8.4$ Hz, 2H).

Step 3: Ethyl [4-(quinolin-2-ylethynyl)phenyl]acetate:

To a well stirred solution of Step 2 intermediate (1.44 g, 7.6 mmol) in TEA (20 ml) were added dichlorobis(triphenylphosphine) palladium (II) (54 mg, 0.076 mmol), copper iodide (44 mg, 0.23 mmol) and 2-bromoquinoline (1.6 g, 7.69 mmol) and the reaction was stirred at room temperature overnight. The reaction mixture was diluted with water (100 ml) and chloroform (300 ml), given charcoal treatment and filtered. The organic layer was washed with water (2 x 100 ml), brine (50 ml), dried and concentrated yield 1.45 g of the product; ^1H NMR (300 MHz,

CDCl₃) δ 1.26 (t, J = 7.2 Hz, 3H), 3.65 (s, 2H), 4.17 (q, J = 7.2 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 7.56-7.64 (m, 4H), 7.74 (t, J = 7.2 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 8.14 (t, J = 7.8 Hz, 2H).

Step 4: Ethyl {4-[2-(quinolin-2-yl)ethyl] phenyl}acetate:

To the well stirred solution of Step 3 intermediate (1.40 g, 4.44 mmol) in ethanol (30 ml) was added palladium on activated carbon (400 mg) and the reaction was carried for 4 h under 40 psi pressure of hydrogen gas. The reaction mixture was diluted with ethyl acetate and filtered. The organic layer was washed with water and concentrated to yield 1.35 g of the product; ¹H NMR (300 MHz, CDCl₃) δ 1.25 (t, J = 6.9 Hz, 3H), 3.12-3.17 (m, 2H), 3.29 (d, J = 8.1 Hz, 1H), 3.58 (m, 2H), 4.14 (q, J = 7.5 Hz, 2H), 7.21 (s, 4H), 7.23 (s, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.71 (t, J = 7.5 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H).

Step 5: {4-[2-(Quinolin-2-yl)ethyl]phenyl}acetic acid:

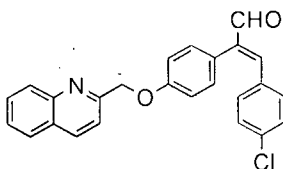
To the well stirred solution of Step 4 intermediate (500 mg, 1.566 mmol) in a mixture of ethanol (15 ml) and tetrahydrofuran (5 ml) was added aqueous solution of sodium hydroxide (313 mg, 7.83 mmol) and the reaction mixture was stirred at room temperature overnight. The solvent was distilled out and reaction mass was diluted with water and then neutralized with dil. HCl. The aqueous layer was extracted with ethyl acetate (2 x 100 ml). The combined organic layer was washed with water, brine, dried and concentrated under reduced pressure to yield 470 mg of the product; ¹H NMR (300 MHz, CDCl₃) δ 3.02-3.07 (m, 2H), 3.24-3.30 (m, 2H), 3.69 (s, 2H), 7.17 (d, J = 7.8 Hz, 2H), 7.29 (s, 2H), 7.35 (d, J = 8.1 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 8.1 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H).

Step 6: 3-(4-Chlorophenyl)-2-{4-[2-(quinolin-2-yl)ethyl]phenyl}prop-2-enoic acid:

To the well stirred solution of Step 5 intermediate (460 mg, 1.580 mmol) in acetic anhydride (15 ml), were added triethylamine (0.33 ml, 2.370 mmol) and 4-chlorobenzaldehyde (222 mg, 1.580 mmol) and the reaction mixture was refluxed for 5 h. The reaction mixture was quenched with water (50 ml) and was further refluxed for half hour after which the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water, brine, dried and concentrated under reduced pressure to yield 650 mg of the compound; ¹H NMR (300 MHz, CDCl₃) δ 0.88 (br s, 3H), 3.13 (br s, 2H), 6.98 (d, J = 8.1 Hz, 2H), 7.08 (d, J = 8.7 Hz, 2H), 7.14-7.22 (m, 4H), 7.35 (d, J = 8.1 Hz, 1H), 7.57 (t, J = 8.7 Hz, 1H), 7.76-7.88 (m, 3H), 8.18 (d, J = 8.4 Hz, 1H), 8.40 (d, J = 7.8 Hz, 1H), 13.78 (br s, 1H).

Intermediate 41

3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enal

Step 1: 3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-ol:

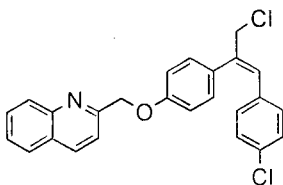
To a well stirred solution of the ester compound of Intermediate 29 (3.3 g, 7.440 mmol) in THF (40 ml) was added DIBAL (15.85 ml, 22.322 mmol) at -30 to -40 °C and stirred for 3 h at the same temperature. The reaction mixture was quenched with water (15 ml) and stirred for 20 mins after addition of ethyl acetate (200 ml). The precipitate obtained was filtered and the filtrate was dried and concentrated to yield 2.7 g of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.42 (s, 2H), 5.38 (s, 2H), 6.60 (s, 1H), 6.91 (d, $J = 8.4$ Hz, 2H), 6.98 (d, $J = 9.0$ Hz, 2H), 7.04-7.14 (m, 4H), 7.54-7.61 (m, 1H), 7.66-7.74 (m, 2H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H), 12.72 (br s, 1H).

Step 2: 3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enal:

Portion wise addition of MnO_2 (2.5 g, 28.737 mmol) to the well stirred solution of Step 1 intermediate (1.15 g, 2.287 mmol) in THF (40 ml) was carried out at room temperature and the reaction mixture was further stirred for 4 h. The reaction mixture was diluted with ethyl acetate (250 ml), filtered, dried and concentrated to yield the crude product which was purified by silica gel column chromatography to yield 1.3 g of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.42 (s, 2H), 7.05-7.16 (m, 3H), 7.18-7.25 (m, 4H), 7.27 (d, $J = 7.8$ Hz, 2H), 7.56 (d, $J = 7.5$ Hz, 1H), 7.68-7.77 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H), 9.73 (s, 1H).

Intermediate 42

2-({4-[3-Chloro-1-(4-chlorophenyl)prop-1-en-2-yl]phenoxy}methyl)quinoline



Step 1: 3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-ol:

To well stirred solution of the ester of Intermediate 29 (4 g, 9.36 mmol) in THF (60 ml) was added 20 % Diisobutylaluminium hydride (23.54 ml, 28.10 mmol) at -30 to -40 °C and stirred for 3 h at the same temperature. The reaction mixture was quenched with water (15 ml) and stirred for 20 mins after addition of ethyl acetate (200 ml). The precipitate obtained was filtered and the filtrate was dried and concentrated to yield 3.1 g of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.42 (s, 2H), 4.52 (br s, 1H), 5.38 (s, 2H), 6.60 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 7.05-7.13 (m, 4H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.67-7.74 (m, 2H), 7.84 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.7 Hz, 1H).

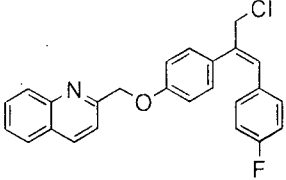
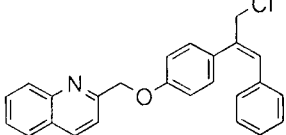
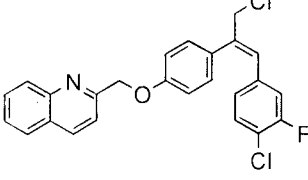
Step 2: 2-({4-[3-Chloro-1-(4-chlorophenyl)prop-1-en-2-yl]phenoxy}methyl)quinoline:

To a well stirred solution of the Step 1 intermediate (580 mg, 1.03 mmol) in DCM (10 ml) was added triethylamine (0.28 ml, 2.06 mmol) followed by methanesulfonylchloride (0.12 ml, 1.558 mmol) at 0 °C and was stirred overnight. The reaction mixture was quenched with water (20 ml), extracted with ethyl acetate (2 x 25 ml), washed with water (20 ml), brine (20 ml) and dried to yield 590 mg of the product; ¹H NMR (300 MHz, CDCl₃) δ 4.40 (s, 2H), 5.44 (s, 2H), 6.69 (s, 1H), 6.88-6.93 (m, 2H), 7.04-7.08 (m, 3H), 7.10-7.17 (m, 2H), 7.29 (s, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.72-7.81 (m, 2H), 7.87 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 8.4 Hz, 1H).

Intermediates 43-45 were prepared as described in Intermediate 42 by the reduction of appropriate ester followed by chlorination. Their structure, names and ¹H NMR data are given in the Table 2.

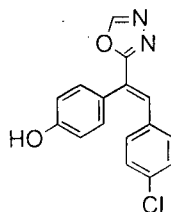
Table 2: Structure and characterization data for Intermediates 43 - 45

Molecular Structure and Intermediate No.	Chemical name and ¹ H NMR data (δ ppm, 300 MHz)
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Molecular Structure and Intermediate No.	Chemical name and ¹ H NMR data (δ ppm, 300 MHz)
 [Intermediate 43]	<u>2-({4-[3-Chloro-1-(4-fluorophenyl)prop-1-en-2-yl]phenoxy} methyl)quinoline</u>: (CDCl₃) δ 4.40 (s, 2H), 5.41 (s, 2H), 6.70 (s, 1H), 6.81 (t, <i>J</i> = 8.4 Hz, 2H), 6.94-7.03 (m, 4H), 7.16 (d, <i>J</i> = 8.7 Hz, 2H), 7.57 (t, <i>J</i> = 7.2 Hz, 1H), 7.70-7.87 (m, 2H), 7.86 (d, <i>J</i> = 7.8 Hz, 1H), 8.11 (d, <i>J</i> = 8.1 Hz, 1H), 8.24 (d, <i>J</i> = 8.4 Hz, 1H).
 [Intermediate 44]	<u>2-({4-[3-Chloro-1-phenylprop-1-en-2-yl]phenoxy} methyl)quinoline</u>: (CDCl₃) δ 4.42 (s, 2H), 5.38 (s, 2H), 6.74 (s, 1H), 7.00 (d, <i>J</i> = 8.1 Hz, 4H), 7.12 (br s, 3H), 7.18 (d, <i>J</i> = 8.4 Hz, 2H), 7.55 (t, <i>J</i> = 7.2 Hz, 1H), 7.68-7.76 (m, 2H), 7.84 (d, <i>J</i> = 7.8 Hz, 1H), 8.08 (d, <i>J</i> = 8.4 Hz, 1H), 8.21 (d, <i>J</i> = 8.1 Hz, 1H).
 [Intermediate 45]	<u>2-({4-[3-Chloro-1-(4-chloro-3-fluorophenyl)prop-1-en-2-yl]phenoxy}methyl)quinoline</u>: (CDCl₃) δ 4.38 (s, 2H), 5.42 (s, 2H), 6.65 (s, 1H), 6.72 (d, <i>J</i> = 9.3 Hz, 2H), 7.02 (d, <i>J</i> = 8.7 Hz, 2H), 7.10-7.16 (m, 3H), 7.57 (t, <i>J</i> = 7.2 Hz, 1H), 7.68-7.76 (m, 2H), 7.86 (d, <i>J</i> = 7.8 Hz, 1H), 8.11 (d, <i>J</i> = 9.0 Hz, 1H), 8.24 (d, <i>J</i> = 8.4 Hz, 1H).

Intermediate 46

4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenol

Step 1: 3-(4-Chlorophenyl)-2-(4-hydroxyphenyl)prop-2-enoic acid:

To the well stirred solution of ethyl-3-(4-chlorophenyl)-2-(4-hydroxyphenyl)prop-2-enoate (1 g, 3.30 mmol) in ethanol (20 ml) and THF (10 ml) was added aqueous solution of sodium hydroxide (661 mg, 16.52 mmol) and the reaction mixture was stirred at room temperature for 15 min. The reaction mixture was diluted with water (25 ml) and the pH was made acidic. The aqueous layer was then extracted with ethyl acetate (3 x 20 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 760 mg of the product as off-white solid;

¹H NMR (300 MHz, DMSO-*d*₆) δ 6.74 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.64 (s, 1H), 9.54 (br s, 1H), 12.63 (br s, 1H).

Step 2: 4-[1-(4-Chlorophenyl)-3-hydrazinyl-3-oxoprop-1-en-2-yl]phenyl ethyl carbonate:

To the well stirred solution of Step 1 intermediate (750 mg, 2.73 mmol) in THF (30 ml) was added TEA (1.14 ml, 8.19 mmol) and the reaction mixture was cooled to 0 °C after which ethyl chloroformate (0.78 ml, 8.19 mmol) was added to it and the reaction was stirred at the same temperature for 1 hour. Hydrazine hydrate (0.5 ml) was added to the reaction mixture and the reaction mixture was further stirred for 1h at 0 °C. The reaction mixture was diluted with water (25 ml) and extracted with ethyl acetate (3 x 20 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 710 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 1.42 (t, *J* = 7.5 Hz, 3H), 4.35 (q, *J* = 6.9 Hz, 2H), 6.81 (br s, 1H), 6.92 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.23-7.30 (m, 4H), 7.81 (s, 1H), 9.82 (br s, 2H).

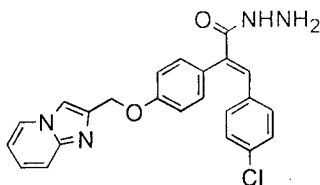
Step 3: 4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenyl ethyl carbonate:

To the well stirred solution of Step 2 intermediate (700 mg, 1.94 mmol) in triethyl orthoformate (15 ml) was added PTSA (74 mg, 0.388 mmol) and the reaction mixture was heated at 90-100 °C for 2 h. The reaction mixture was diluted with water (25 ml) and extracted with ethyl acetate (3 x 20 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 500 mg of the product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.30 (t, *J* = 6.9 Hz, 3H), 4.27 (q, *J* = 7.5 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.30-7.40 (m, 6H), 7.74 (s, 1H), 7.81 (s, 1H), 9.28 (s, 2H).

Step 4: 4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenol:

To the well stirred solution of Step 3 intermediate (320 mg, 0.863 mmol) in ethanol (10 ml) was added aqueous solution of sodium hydroxide (173 mg, 4.318 mmol) and the reaction mixture was stirred at room temperature for 15 min. The reaction mixture was diluted with water (25 ml) and the pH was made slightly acidic. The aqueous layer was then extracted with ethyl acetate (3 x 20 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 190 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 6.79 (d, *J* = 7.8 Hz, 2H), 7.06 (t, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 4H), 7.60 (s, 1H), 8.42 (s, 1H), 10.11 (br s, 1H).

Intermediate 47

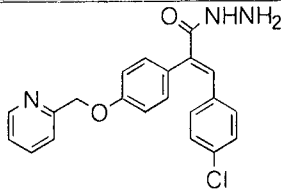
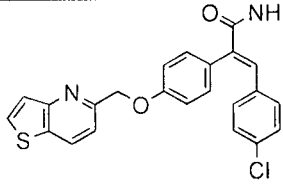
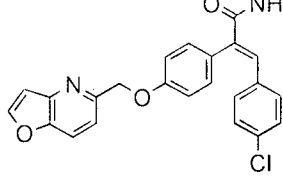
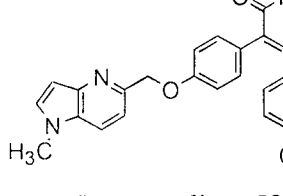
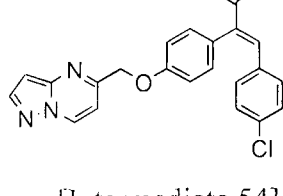
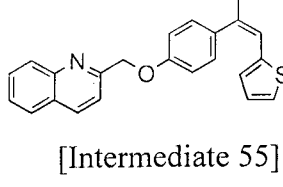
3-(4-Chlorophenyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]prop-2-enehydrazide

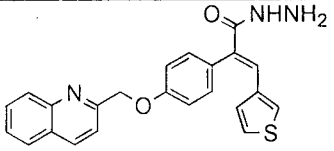
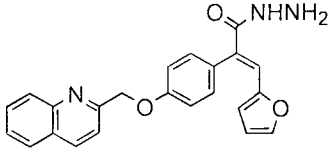
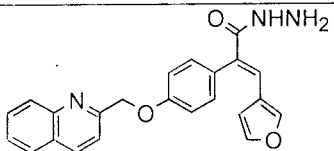
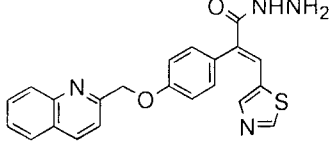
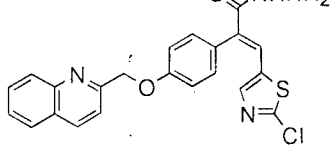
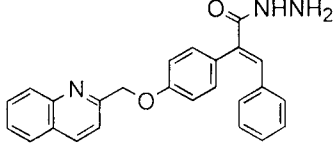
Ethyl chloroformate (0.35 ml, 3.70 mmol) was added drop wise to a well stirred solution of Intermediate 1 (1 g, 2.472 mmol) and TEA (0.52 ml, 3.70 mmol) in dry tetrahydrofuran (30 ml) at 0°C under nitrogen atmosphere and continued stirring for 30 min at same temperature. Excess of hydrazine hydrate (2 ml) was then added to the reaction mixture and stirred for further 1 h at 0-10 °C. The reaction mixture was quenched with water (50 ml) and extracted with ethyl acetate (100 ml x 2). The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 980 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.72 (br s, 3H), 5.21 (s, 2H), 6.89 (t, *J* = 6.3 Hz, 1H), 7.00-7.08 (m, 5H), 7.18-7.27 (m, 4H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.68 (s, 1H), 8.54 (d, *J* = 6.3 Hz, 1H), 8.87 (s, 1H).

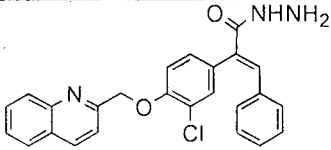
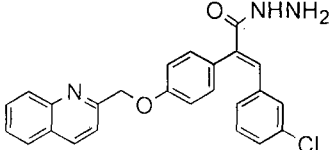
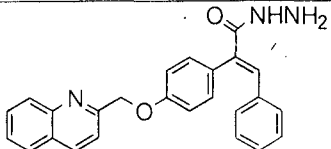
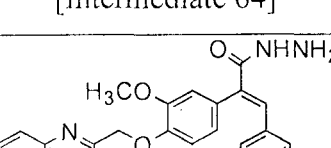
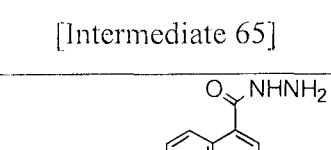
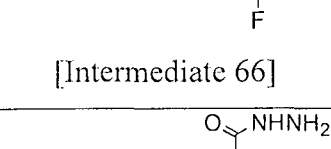
Intermediates 48 to 82 were prepared using appropriate propenoic acid and hydrazine hydrate as described in Intermediate 47. Their structure, names and ¹H NMR data are given in the Table 3.

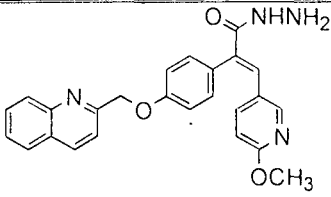
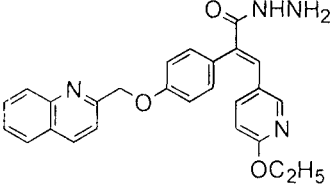
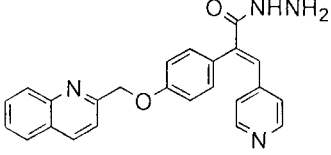
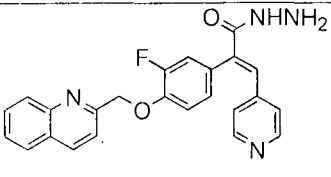
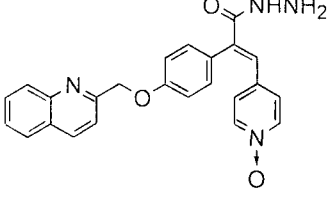
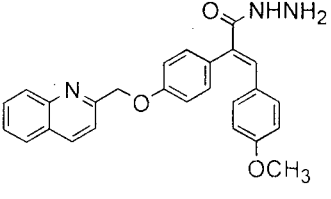
Table 3: Structure and characterization data for Intermediates 48 - 82

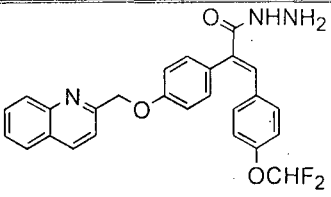
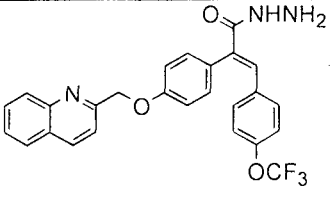
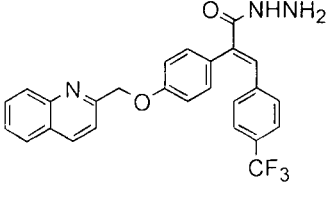
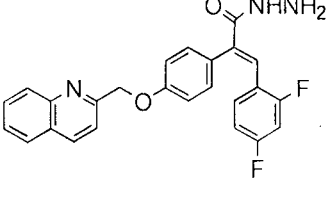
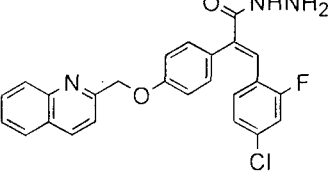
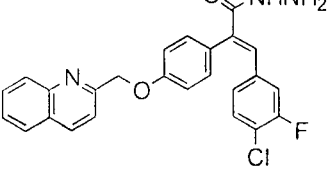
Molecular Structure and Intermediate No.	Chemical name and ¹ H NMR data (δ ppm, 300 MHz)
[Intermediate 48]	2-[4-(1,3-Benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)prop-2-ene hydrazide: (DMSO-<i>d</i>₆) δ 4.50 (br s, 2H), 5.62 (s, 2H), 6.99 (d, <i>J</i> = 9.0 Hz, 2H), 7.11 (s, 4H), 7.18-7.23 (m, 3H), 7.45-7.57 (m, 2H), 8.03 (d, <i>J</i> = 7.8 Hz, 1H), 8.14 (d, <i>J</i> = 7.8 Hz, 1H), 8.94 (br s, 1H).
[Intermediate 49]	3-(4-Chlorophenyl)-2-[4-[(1-methyl-1<i>H</i>-indazol-3-yl)methoxy]phenyl]prop-2-enehydrazide: (CDCl₃) δ 3.97 (br s, 2H), 4.10 (s, 4H), 5.48 (s, 2H), 6.74 (s, 1H), 6.91 (d, <i>J</i> = 8.1 Hz, 2H), 7.06-7.13 (m, 3H), 7.18-7.27 (m, 3H), 7.40-7.46 (m, 2H), 7.76 (s, 1H), 7.86 (d, <i>J</i> = 8.4 Hz, 1H), 8.29 (d, <i>J</i> = 8.7 Hz, 1H).

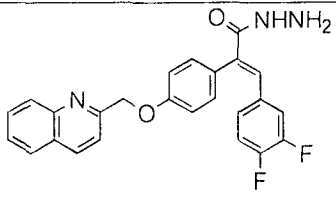
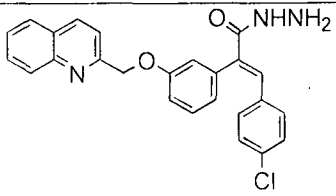
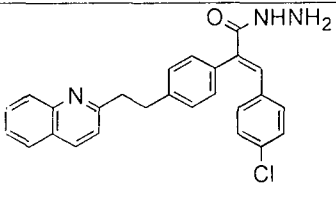
Molecular Structure and Intermediate No.	Chemical name and ¹ H NMR data (δ ppm, 300 MHz)
 [Intermediate 50]	<u>3-(4-Chlorophenyl)-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 4.52 (br s, 2H), 5.18 (s, 2H), 6.74 (s, 1H), 6.98-7.06 (m, 6H), 7.24 (d, <i>J</i> = 8.1 Hz, 2H), 7.31-7.39 (m, 1H), 7.53 (d, <i>J</i> = 7.8 Hz, 1H), 7.59 (s, 1H), 7.82 (t, <i>J</i> = 7.2 Hz, 1H), 8.85 (br s, 1H).
 [Intermediate 51]	<u>3-(4-Chlorophenyl)-2-[4-(thieno[3,2-<i>b</i>]pyridin-5-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 4.50 (br s, 2H), 5.32 (s, 2H), 6.52 (s, 1H), 7.06 (br s, 6H), 7.25 (d, <i>J</i> = 8.1 Hz, 2H), 7.51-7.60 (m, 2H), 7.65 (s, 1H), 8.19 (d, <i>J</i> = 5.7 Hz, 1H), 8.54 (d, <i>J</i> = 8.4 Hz, 1H).
 [Intermediate 52]	<u>3-(4-Chlorophenyl)-2-[4-(furo[3,2-<i>b</i>]pyridin-5-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 3.98-4.09 (m, 2H), 5.27 (s, 2H), 7.00-7.06 (m, 6H), 7.15-7.23 (m, 4H), 7.51 (d, <i>J</i> = 8.4 Hz, 1H), 8.09 (d, <i>J</i> = 8.7 Hz, 1H), 8.36 (s, 1H), 8.90 (br s, 1H).
 [Intermediate 53]	<u>3-(4-Chlorophenyl)-2-[4-[(1-methyl-1<i>H</i>-pyrrolo[3,2-<i>b</i>]pyridin-5-yl)methoxy]phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 3.83 (s, 3H), 4.54 (br s, 2H), 5.23 (s, 2H), 6.54 (s, 1H), 6.99-7.05 (m, 6H), 7.18 (s, 1H), 7.23 (d, <i>J</i> = 8.4 Hz, 2H), 7.32 (d, <i>J</i> = 9.0 Hz, 1H), 7.65 (br s, 1H), 7.91 (d, <i>J</i> = 8.4 Hz, 1H), 8.87 (s, 1H).
 [Intermediate 54]	<u>3-(4-Chlorophenyl)-2-[4-(pyrazolo[1,5-<i>a</i>]pyrimidin-5-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 4.01-4.06 (m, 2H), 5.27 (s, 2H), 6.71 (s, 1H), 6.99-7.15 (m, 6H), 7.18-7.27 (m, 3H), 8.24 (s, 1H), 8.92 (s, 1H), 9.15 (d, <i>J</i> = 7.2 Hz, 2H).
 [Intermediate 55]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-(thiophen-2-yl)prop-2-enehydrazide</u>: (CDCl₃) δ 3.97 (br s, 2H), 5.50 (s, 2H), 6.90-6.94 (m, 1H), 7.18-7.23 (m, 7H), 7.60 (t, <i>J</i> = 6.9 Hz, 1H), 7.76-7.81 (m, 2H), 7.88 (d, <i>J</i> = 7.8 Hz, 1H), 8.06 (s, 1H), 8.16 (d, <i>J</i> = 8.4 Hz, 1H), 8.29 (d, <i>J</i> = 8.4 Hz, 1H).

Molecular Structure and Intermediate No.	Chemical name and ^1H NMR data (δ ppm, 300 MHz)
 [Intermediate 56]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-(thiophen-3-yl)prop-2-enedihydrazide</u>: (CDCl_3) δ 3.97 (br s, 2H), 5.45 (s, 2H), 6.44 (br s, 1H), 6.66 (s, 1H), 7.05 (s, 2H), 7.12-7.17 (m, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.70-7.79 (m, 2H), 7.84-7.88 (m, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H).
 [Intermediate 57]	<u>3-(Furan-2-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enedihydrazide</u>: ($\text{DMSO}-d_6$) δ 4.48 (br s, 2H), 5.42 (s, 2H), 5.71 (d, $J = 3.3$ Hz, 1H), 6.36 (br s, 1H), 7.08-7.15 (m, 4H), 7.21 (s, 1H), 7.60-7.67 (m, 2H), 7.71-7.78 (m, 2H), 8.02 (t, $J = 7.8$ Hz, 2H), 8.45 (d, $J = 8.4$ Hz, 1H), 8.63 (s, 1H).
 [Intermediate 58]	<u>3-(Furan-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enedihydrazide</u>: ($\text{DMSO}-d_6$) δ 4.41 (br s, 2H), 5.42 (s, 2H), 7.08-7.16 (m, 4H), 7.28 (s, 1H), 7.42 (s, 1H), 7.60-7.73 (m, 3H), 7.79 (t, $J = 8.4$ Hz, 1H), 8.00-8.06 (m, 2H), 8.42-8.48 (m, 2H).
 [Intermediate 59]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-(1,3-thiazol-5-yl)prop-2-enedihydrazide</u>: ($\text{DMSO}-d_6$) δ 4.44 (br s, 2H), 5.43 (s, 2H), 7.10 (d, $J = 8.4$ Hz, 2H), 7.20 (d, $J = 8.1$ Hz, 2H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.71-7.82 (m, 3H), 8.01-8.06 (m, 2H), 8.11 (s, 1H), 8.46 (d, $J = 9.0$ Hz, 1H), 8.59 (s, 1H), 8.82 (s, 1H).
 [Intermediate 60]	<u>3-(2-Chloro-1,3-thiazol-5-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enedihydrazide</u>: ($\text{DMSO}-d_6$) δ 4.50 (m, 2H), 5.43 (s, 2H), 7.13 (d, $J = 8.7$ Hz, 2H), 7.21 (d, $J = 8.4$ Hz, 2H), 7.59-7.66 (m, 2H), 7.73 (d, $J = 8.4$ Hz, 1H), 7.80 (t, $J = 7.8$ Hz, 1H), 8.02-8.07 (m, 2H), 8.46 (d, $J = 8.7$ Hz, 1H), 8.79 (s, 1H), 8.89 (s, 1H).
 [Intermediate 61]	<u>3-Phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enedihydrazide</u>: ($\text{DMSO}-d_6$) δ 4.47 (s, 2H), 5.39 (s, 2H), 6.08-7.03 (m, 2H), 7.09 (s, 4H), 7.17 (br s, 2H), 7.23 (s, 2H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.79 (t, $J = 7.8$ Hz, 1H), 7.99-8.05 (m, 2H), 8.44 (d, $J = 8.4$ Hz, 1H), 8.84 (s, 1H).

Molecular Structure and Intermediate No.	Chemical name and ^1H NMR data (δ ppm, 300 MHz)
 [Intermediate 62]	<u>2-[3-Chloro-4-(quinolin-2-ylmethoxy)phenyl]-3-phenylprop-2-en-1-one hydrazide</u>: (DMSO-d_6) δ 4.59 (br s, 2H), 5.49 (s, 2H), 7.02-7.08 (m, 3H), 7.19-7.30 (m, 6H), 7.64 (t, J = 7.2 Hz, 1H), 7.71-7.83 (m, 2H), 8.02 (t, J = 7.8 Hz, 2H), 8.48 (d, J = 8.1 Hz, 1H), 9.01 (m, 1H).
 [Intermediate 63]	<u>3-(3-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one hydrazide</u>: (DMSO-d_6) δ 4.63 (br s, 2H), 5.41 (s, 2H), 7.02-7.13 (m, 4H), 7.16-7.27 (m, 5H), 7.60-7.69 (m, 2H), 7.79 (t, J = 7.5 Hz, 1H), 7.99-7.8.03 (m, 2H), 8.42 (d, J = 8.7 Hz, 1H), 9.58 (s, 1H).
 [Intermediate 64]	<u>3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one hydrazide</u>: (DMSO-d_6) δ 4.62 (br s, 2H), 5.39 (s, 2H), 7.00 (d, J = 8.4 Hz, 2H), 7.08 (br s, 4H), 7.18-7.25 (m, 2H), 7.60-7.71 (m, 3H), 7.79 (t, J = 7.5 Hz, 1H), 8.01 (br s, 2H), 8.44 (d, J = 8.1 Hz, 1H), 8.91 (s, 1H).
 [Intermediate 65]	<u>3-(4-Chlorophenyl)-2-[3-methoxy-4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one hydrazide</u>: (DMSO-d_6) δ 3.71 (s, 3H), 5.37 (s, 2H), 6.62 (d, J = 7.8 Hz, 1H), 6.80 (s, 1H), 7.03-7.10 (m, 3H), 7.25 (d, J = 7.8 Hz, 2H), 7.59-7.68 (m, 3H), 7.79 (t, J = 7.2 Hz, 1H), 8.00 (br s, 2H), 8.45 (d, J = 8.4 Hz, 1H), 12.68 (br s, 1H).
 [Intermediate 66]	<u>3-(4-Fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one hydrazide</u>: (DMSO-d_6) δ 4.75 (br s, 3H), 5.39 (s, 2H), 6.96-7.05 (m, 3H), 7.09 (br s, 4H), 7.22 (s, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.70 (d, J = 8.7 Hz, 1H), 7.79 (t, J = 7.2 Hz, 1H), 8.01 (br s, 2H), 8.44 (d, J = 8.1 Hz, 1H), 8.81 (s, 1H).
 [Intermediate 67]	<u>3-(Pyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one hydrazide</u>: (DMSO-d_6) δ 3.96-4.04 (m, 2H), 5.37 (s, 2H), 7.08 (br s, 4H), 7.17-7.27 (m, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.68 (d, J = 8.7 Hz, 1H), 7.77 (t, J = 6.9 Hz, 1H), 7.98-8.03 (m, 2H), 8.24-8.33 (m, 3H), 8.42 (d, J = 9.0 Hz, 1H), 8.93 (br s, 1H).

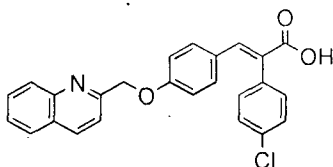
Molecular Structure and Intermediate No.	Chemical name and ¹ H NMR data (δ ppm, 300 MHz)
 [Intermediate 68]	<u>3-(6-Methoxypyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 3.78 (s, 3H), 4.40 (br s, 2H), 5.40 (s, 2H), 6.59 (d, <i>J</i> = 8.7 Hz, 1H), 7.11 (br s, 5H), 7.24 (s, 1H), 7.62 (t, <i>J</i> = 7.2 Hz, 1H), 7.71 (d, <i>J</i> = 8.4 Hz, 1H), 7.76 (t, <i>J</i> = 7.5 Hz, 1H), 7.93 (s, 1H), 7.98-8.05 (m, 2H), 8.44 (d, <i>J</i> = 8.1 Hz, 1H), 8.74 (s, 1H).
 [Intermediate 69]	<u>3-(6-Ethoxypyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 1.26 (t, <i>J</i> = 6.9 Hz, 3H), 3.95-4.03 (m, 2H), 4.19-4.26 (m, 2H), 5.40 (s, 2H), 6.56 (d, <i>J</i> = 8.7 Hz, 1H), 7.11 (br s, 5H), 7.23 (s, 1H), 7.62 (t, <i>J</i> = 7.8 Hz, 1H), 7.71 (d, <i>J</i> = 8.4 Hz, 1H), 7.79 (t, <i>J</i> = 7.5 Hz, 1H), 7.91 (s, 1H), 7.99-8.05 (m, 2H), 8.44 (d, <i>J</i> = 8.7 Hz, 1H), 8.72 (s, 1H).
 [Intermediate 70]	<u>3-(Pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 3.67 (br s, 2H), 5.41 (br s, 2H), 6.85 (br s, 3H), 7.11 (br s, 4H), 7.58 (t, <i>J</i> = 7.2 Hz, 1H), 7.67-7.78 (m, 2H), 7.86 (d, <i>J</i> = 7.8 Hz, 1H), 8.09 (d, <i>J</i> = 8.7 Hz, 1H), 8.25 (d, <i>J</i> = 8.4 Hz, 1H), 8.39 (br s, 2H), 8.74 (s, 1H).
 [Intermediate 71]	<u>2-[3-Fluoro-4-(quinolin-2-ylmethoxy)phenyl]-3-(pyridin-4-yl)prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 5.47 (s, 2H), 6.88 (d, <i>J</i> = 8.1 Hz, 1H), 6.99 (d, <i>J</i> = 6.3 Hz, 2H), 7.15 (d, <i>J</i> = 11.7 Hz, 1H), 7.25 (t, <i>J</i> = 9.0 Hz, 1H), 7.61-7.72 (m, 3H), 7.80 (t, <i>J</i> = 7.2 Hz, 1H), 8.02 (d, <i>J</i> = 8.4 Hz, 2H), 8.40-8.48 (m, 3H), 12.82 (br s, 1H).
 [Intermediate 72]	<u>3-(1-Oxidopyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 4.49 (br s, 1H), 5.40 (s, 2H), 6.45 (s, 1H), 7.01 (d, <i>J</i> = 8.1 Hz, 2H), 7.08-7.17 (m, 4H), 7.59-7.65 (m, 2H), 7.71 (d, <i>J</i> = 8.4 Hz, 1H), 7.80 (t, <i>J</i> = 7.5 Hz, 1H), 7.99-8.06 (m, 4H), 8.45 (d, <i>J</i> = 8.4 Hz, 1H).
 [Intermediate 73]	<u>3-(4-Methoxyphenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enehydrazide</u>: (DMSO-<i>d</i>₆) δ 3.68 (s, 3H), 3.78 (s, 2H), 5.39 (s, 2H), 6.73 (d, <i>J</i> = 8.4 Hz, 2H), 6.93 (d, <i>J</i> = 8.4 Hz, 2H), 7.08 (s, 4H), 7.22 (s, 1H), 7.60-7.65 (m, 1H), 7.71 (d, <i>J</i> = 8.7 Hz, 1H), 7.79 (t, <i>J</i> = 7.5 Hz, 1H), 7.99-8.05 (m, 2H), 8.44 (d, <i>J</i> = 8.7 Hz, 1H), 8.62 (s, 1H).

Molecular Structure and Intermediate No.	Chemical name and ^1H NMR data (δ ppm, 300 MHz)
 [Intermediate 74]	<u>3-[4-(Difluoromethoxy)phenyl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enhydrazide</u>: (DMSO-d_6) δ 4.59 (br s, 2H), 5.39 (s, 2H), 6.96-7.02 (m, 4H), 7.04-7.10 (m, 5H), 7.22 (s, 1H), 7.65 (t, $J = 7.5$ Hz, 1H), 7.71 (d, $J = 9.0$ Hz, 1H), 7.79 (t, $J = 7.5$ Hz, 1H), 8.00-8.04 (m, 2H), 8.45 (d, $J = 8.4$ Hz, 1H), 8.84 (s, 1H).
 [Intermediate 75]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoro-methoxy)phenyl]prop-2-enhydrazide</u>: (DMSO-d_6) δ 4.59 (br s, 2H), 5.39 (s, 2H), 7.07-7.15 (m, 4H), 7.18-7.23 (m, 5H), 7.62 (t, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 9.0$ Hz, 1H), 7.79 (t, $J = 7.2$ Hz, 1H), 7.99-8.04 (m, 2H), 8.44 (d, $J = 8.4$ Hz, 1H), 8.91 (s, 1H).
 [Intermediate 76]	<u>2-[4-(Quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enhydrazide</u>: (DMSO-d_6) δ 4.63 (br s, 2H), 5.39 (s, 2H), 7.09 (s, 3H), 7.17-7.29 (m, 3H), 7.52-7.60 (m, 3H), 7.63-7.71 (m, 2H), 7.79 (t, $J = 7.2$ Hz, 1H), 7.98-8.03 (m, 2H), 8.44 (d, $J = 8.4$ Hz, 1H), 9.06 (s, 1H).
 [Intermediate 77]	<u>3-(2,4-Difluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enhydrazide</u>: (CDCl$_3$) δ 4.01 (br s, 2H), 5.41 (s, 2H), 6.50 (t, $J = 8.4$ Hz, 1H), 6.63 (q, $J = 7.8$ Hz, 1H), 6.73-6.80 (m, 2H), 7.09 (d, $J = 8.7$ Hz, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.67-7.78 (m, 2H), 7.83-7.91 (m, 2H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H).
 [Intermediate 78]	<u>3-(4-Chloro-2-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enhydrazide</u>: (DMSO-d_6) δ 3.98-4.03 (m, 2H), 5.37 (s, 2H), 6.77 (t, $J = 8.1$ Hz, 1H), 7.00-7.06 (m, 4H), 7.13 (s, 1H), 7.40 (d, $J = 9.9$ Hz, 2H), 7.60-7.69 (m, 2H), 7.79 (t, $J = 7.8$ Hz, 1H), 8.01 (br s, 2H), 8.43 (d, $J = 8.7$ Hz, 1H), 9.05 (s, 1H).
	<u>3-(4-Chloro-3-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enhydrazide</u>: (DMSO-d_6) δ 4.63 (s, 2H), 5.40 (s, 2H), 6.86 (d, $J = 8.7$ Hz, 1H), 6.95 (d, $J = 11.1$ Hz, 1H), 7.10 (s, 4H), 7.19 (s, 1H), 7.39 (t, $J = 8.1$ Hz, 1H), 7.60-7.71 (m, 2H), 7.79 (t, $J = 7.5$ Hz, 1H), 7.99-8.05 (m, 2H), 8.43 (d, $J = 8.7$ Hz, 1H), 8.96 (s, 1H).

Molecular Structure and Intermediate No.	Chemical name and ^1H NMR data (δ ppm, 300 MHz)
[Intermediate 79]	
 [Intermediate 80]	<u>3-(3,4-Difluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enedihydrazide</u>: (CDCl_3) δ 4.01 (br s, 2H), 5.45 (s, 2H), 6.66-6.75 (m, 2H), 6.83 (br s, 1H), 6.95 (q, $J = 9.0$ Hz, 1H), 7.12 (br s, 4H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.66-7.73 (m, 3H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H).
 [Intermediate 81]	<u>3-(4-Chlorophenyl)-2-[3-(quinolin-2-ylmethoxy)phenyl]prop-2-enedihydrazide</u> ($\text{DMSO}-d_6$) δ 4.59 (br s, 2H), 5.44 (s, 2H), 6.51 (s, 1H), 6.76 (d, $J = 7.8$ Hz, 1H), 6.89 (s, 1H), 7.04 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.1$ Hz, 1H), 7.18 (d, $J = 8.7$ Hz, 2H), 7.33 (t, $J = 7.8$ Hz, 1H), 7.70-7.77 (m, 3H), 7.84-7.90 (m, 1H), 8.09 (br s, 2H), 8.59 (br s, 1H).
 [Intermediate 82]	<u>3-(4-Chlorophenyl)-2-{4-[2-(quinolin-2-yl)ethyl]phenyl}prop-2-enedihydrazide</u>: (CDCl_3) δ 3.20-3.26 (m, 2H), 3.32-3.36 (m, 2H), 3.96 (br s, 2H), 6.73 (s, 1H), 6.88 (d, $J = 8.4$ Hz, 2H), 7.04-7.11 (m, 4H), 7.27-7.32 (m, 3H), 7.53 (t, $J = 7.8$ Hz, 1H), 7.70-7.83 (m, 3H), 8.10 (d, $J = 8.4$ Hz, 2H).

Intermediate 83

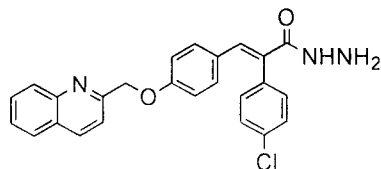
2-(4-Chlorophenyl)-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoic acid



The title compound was prepared from 4-hydroxybenzaldehyde, 4-chlorophenyl acetic acid and 2-(chloromethyl) quinoline in a 4 step procedure as described in Intermediate 1; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.31 (s, 2H), 6.91 (d, $J = 8.4$ Hz, 2H), 6.98 (d, $J = 8.7$ Hz, 2H), 7.15 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.62 (d, $J = 8.7$ Hz, 3H), 7.77 (d, $J = 7.8$ Hz, 1H), 7.97-8.02 (m, 2H), 8.39 (d, $J = 8.4$ Hz, 1H), 12.72 (br s, 1H).

Intermediate 84

2-(4-Chlorophenyl)-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enehydrazide

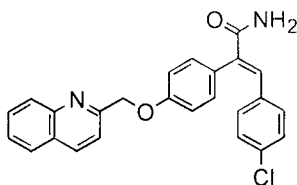


The title compound was prepared using Intermediate 83 and hydrazine hydrate as described in Intermediate 47; ^1H NMR (300 MHz DMSO- d_6) δ 4.59 (s, 2H), 5.31 (s, 2H), 6.90-6.97 (m, 4H), 7.16 (d, J = 7.8 Hz, 2H), 7.29 (s, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.77 (t, J = 7.2 Hz, 1H), 7.97-8.02 (br s, 2H), 8.40 (d, J = 8.4 Hz, 1H), 8.87 (s, 1H).

Examples

Example 1

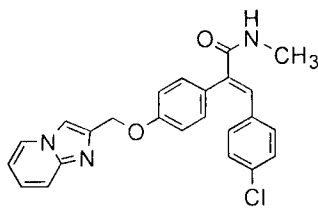
3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by reaction of aqueous ammonia (5 ml) with the mixed anhydride which was prepared from Intermediate 29 (1 g, 2.406 mmol) and ethyl chloroformate (0.39 ml, 3.609 mmol) in presence of TEA (0.5 ml, 3.609 mmol) to yield 50 mg of the product as off-white solid as described in Intermediate 47; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 5.50 (br s, 1H), 5.61 (br s, 1H), 6.93 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 9.0 Hz, 4H), 7.18 (d, J = 9.0 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.71-7.78 (m, 3H), 7.86 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 9.0 Hz, 1H), 8.24 (d, J = 8.1 Hz, 1H); ESI-MS (m/z) 415 (M) $^+$.

Example 2

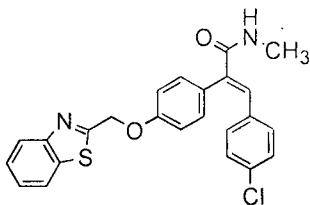
3-(4-Chlorophenyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]-*N*-methyl-prop-2-enamide



To a well stirred solution of Intermediate 1 (150 mg, 0.37 mmol) in dichloromethane (10 ml) were added N-[3-(dimethylamino)propyl]-N'-ethylcarbodiimide hydrochloride (EDCI.HCl; 107 mg, 0.55 mmol), 1H-benzotriazol-1-ol (HOBT; 75 mg, 0.55 mmol), TEA (0.11 ml, 1.1 mmol) and methylamine hydrochloride (48 mg, 0.74 mmol) and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was quenched with water (5 ml) and extracted with ethyl acetate (25 ml x 2). The combined organic layers were washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 110 mg of product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 2.65 (d, *J* = 4.2 Hz, 3H), 5.22 (s, 2H), 6.90 (t, *J* = 6.3 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 2H), 7.05-7.12 (m, 4H), 7.24 (d, *J* = 9.0 Hz, 2H), 7.28-7.34 (m, 3H), 7.54 (d, *J* = 9.3 Hz, 1H), 7.56 (s, 1H), 8.55 (d, *J* = 6.6 Hz, 1H); APCI-MS (*m/z*) 418 (M+H)⁺.

Example 3

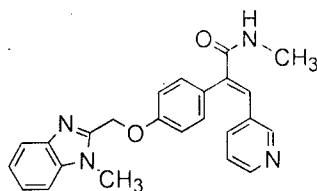
2-[4-(1,3-Benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)-*N*-methylprop-2-enamide



The title compound was prepared by coupling Intermediate 2 (150 mg, 0.372 mmol) with methylamine hydrochloride (30 mg, 0.446 mmol) as described in Example 2 to yield 95 mg of the product as off white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.84 (d, *J* = 4.5 Hz, 3H), 5.54 (br s, 3H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.06-7.18 (m, 6H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.77 (s, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H); ESI-MS (*m/z*) 435 (M+H)⁺.

Example 4

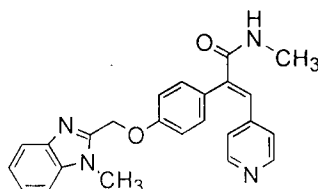
N-Methyl-2-{4-[(1-methyl-1*H*-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-3-yl)prop-2-enamide



The title compound was prepared by coupling Intermediate 4 (100 mg, 0.259 mmol) with methylamine hydrochloride (35 mg, 0.519 mmol) as described in Example 2 to yield 69 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.85 (d, $J = 4.8$ Hz, 3H), 3.95 (s, 3H), 5.44 (s, 2H), 5.56 (br s, 1H), 7.01-7.06 (m, 1H), 7.16 (br s, 5H), 7.31-7.40 (m, 3H), 7.79 (br s, 2H), 8.29 (s, 1H), 8.36 (br s, 1H); APCI-MS (m/z) 399 ($\text{M}+\text{H}$) $^+$.

Example 5

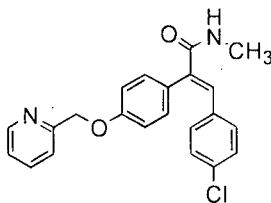
N-Methyl-2-{4-[(1-methyl-1*H*-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-4-yl)prop-2-enamide



The title compound was prepared by coupling Intermediate 5 (150 mg, 0.389 mmol) with methylamine hydrochloride (52 mg, 0.779 mmol) as described in Example 2 to yield 120 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.65 (d, $J = 4.2$ Hz, 3H), 3.88 (s, 3H), 5.45 (s, 2H), 6.91 (d, $J = 4.8$ Hz, 2H), 7.11 (d, $J = 8.1$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H), 7.23-7.33 (m, 3H), 7.51 (br s, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.66 (d, $J = 7.8$ Hz, 1H), 8.35 (d, $J = 7.8$ Hz, 2H); APCI-MS (m/z) 399 ($\text{M}+\text{H}$) $^+$.

Example 6

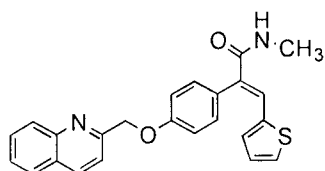
3-(4-Chlorophenyl)-*N*-methyl-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 12 (200 mg, 0.547 mmol) and methylamine hydrochloride (74 mg, 1.094 mmol) as described in Example 2 to yield 86 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.85 (d, $J = 4.8$ Hz, 3H), 5.24 (s, 2H), 5.56 (br s, 1H), 6.91 (d, $J = 8.7$ Hz, 2H), 7.05-7.15 (m, 6H), 7.27 (br s, 1H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.72-7.80 (m, 2H), 8.62 (d, $J = 3.9$ Hz, 1H); ESI (m/z) 379 ($\text{M}+\text{H}$) $^+$.

Example 7

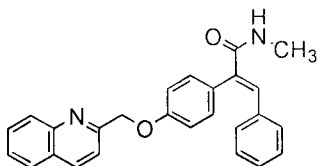
N-Methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-(thiophen-2-yl)prop-2-enamide



The title compound was prepared by coupling Intermediate 20 (150 mg, 0.387 mmol) with methylamine hydrochloride (31 mg, 0.464 mmol) as described in Example 2 to yield 85 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.83 (d, $J = 4.8$ Hz, 3H), 5.46 (s, 2H), 5.36 (s, 1H), 6.91 (t, $J = 4.5$ Hz, 1H), 7.12-7.19 (m, 6H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.74-7.88 (m, 2H), 7.87 (d, $J = 7.8$ Hz, 1H), 8.06 (s, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 401 ($\text{M}+\text{H}$) $^+$.

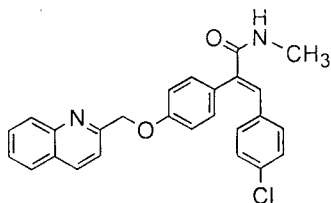
Example 8

N-Methyl-3-phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



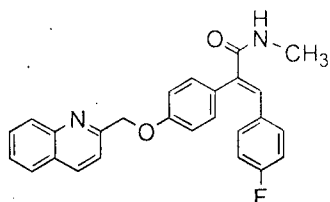
The title compound was prepared by coupling Intermediate 22 (200 mg, 0.524 mmol) with methylamine hydrochloride (53 mg, 0.787 mmol) as described in Example 2 to yield 70 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.84 (d, $J = 5.1$ Hz, 3H), 5.43 (s, 2H), 5.54 (br s, 1H), 6.99 (d, $J = 6.3$ Hz, 2H), 7.12-7.24 (m, 7H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.73-7.80 (m, 2H), 7.82-7.89 (m, 2H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 395 ($\text{M}+\text{H}$) $^+$.

Example 9

3-(4-Chlorophenyl)-*N*-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide

The title compound was prepared by coupling Intermediate 29 (100 mg, 0.24 mmol) with methylamine hydrochloride (32 mg, 0.48 mmol) as described in Example 2 to yield 60 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.85 (br s, 3H), 5.45 (s, 2H), 5.54 (br s, 1H), 6.90 (d, $J = 8.1$ Hz, 2H), 7.12 (br s, 6H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.72-7.78 (m, 3H), 7.88 (d, $J = 7.8$ Hz, 1H), 8.13 (d, $J = 8.4$ Hz, 1H), 8.27 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 429 ($\text{M}+\text{H}$) $^+$.

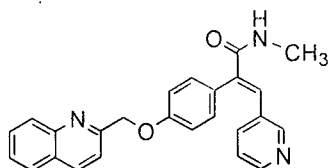
Example 10

3-(4-Fluorophenyl)-*N*-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide

The title compound was prepared by coupling Intermediate 30 (150 mg, 0.37 mmol) with methylamine hydrochloride (38 mg, 0.56 mmol) as described in Example 2 to yield 100 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.84 (d, $J = 4.5$ Hz, 3H), 5.43 (s, 2H), 5.55 (br s, 1H), 6.81 (t, $J = 8.7$ Hz, 2H), 6.96 (t, $J = 8.1$ Hz, 2H), 7.09-7.17 (m, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.69-7.80 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 9.0$ Hz, 1H); APCI-MS (m/z) 413 ($\text{M}+\text{H}$) $^+$.

Example 11

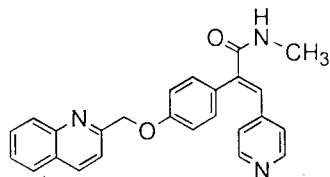
N-Methyl-3-(pyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 13 (100 mg, 0.261 mmol) with methylamine hydrochloride (35 mg, 0.523 mmol) as described in Example 2 to yield 60 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.86 (s, 3H), 5.42 (s, 2H), 5.58 (br s, 1H), 7.06-7.13 (m, 6H), 7.60 (d, $J = 6.9$ Hz, 1H), 7.59-7.71 (m, 1H), 7.71-7.80 (m, 2H), 7.87 (d, $J = 7.2$ Hz, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.26 (d, $J = 8.4$ Hz, 1H), 8.30-8.38 (m, 2H); ESI-MS (m/z) 396 ($\text{M}+\text{H}$) $^+$.

Example 12

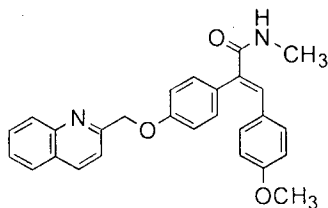
N-Methyl-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (150 mg, 0.392 mmol) with methylamine hydrochloride (26 mg, 0.74 mmol) as described in Example 2 to yield 89 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.66 (d, $J = 5.1$ Hz, 3H), 5.40 (s, 2H), 6.94 (d, $J = 5.1$ Hz, 2H), 7.11 (s, 3H), 7.28 (s, 1H), 7.53 (br s, 2H), 7.63 (t, $J = 6.9$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.80 (t, $J = 7.5$ Hz, 1H), 8.02 (d, $J = 8.4$ Hz, 2H), 8.37 (d, $J = 4.8$ Hz, 2H), 8.45 (d, $J = 8.7$ Hz, 1H); APCI-MS (m/z) 396 ($\text{M}+\text{H}$) $^+$.

Example 13

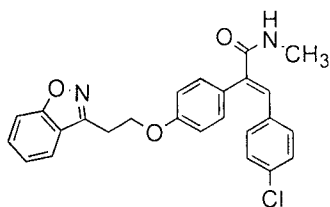
3-(4-Methoxyphenyl)-*N*-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 10 (180 mg, 0.437 mmol) with methylamine hydrochloride (44 mg, 0.656 mmol) as described in Example 2 to yield 140 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.83 (d, $J = 4.8$ Hz, 3H), 3.74 (s, 3H), 5.43 (s, 2H), 5.52 (s, 1H), 6.66 (d, $J = 9.0$ Hz, 2H), 6.93 (d, $J = 8.7$ Hz, 2H), 7.10-7.19 (m, 4H), 7.58 (t, $J = 8.4$ Hz, 1H), 7.72-7.79 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H); ESI (m/z) 425 ($\text{M}+\text{H}$) $^+$.

Example 14

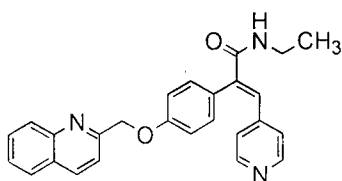
2-{4-[2-(1,2-Benzoxazol-3-yl)ethoxy]phenyl}-3-(4-chlorophenyl)-*N*-methylprop-2-enamide



The title compound was prepared by coupling Intermediate 3 (150 mg, 0.357 mmol) with methylamine hydrochloride (36 mg, 0.535 mmol) as described in Example 2 to yield 71 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.83 (d, $J = 4.8$ Hz, 3H), 3.53 (t, $J = 6.3$ Hz, 2H), 4.48 (t, $J = 6.3$ Hz, 2H), 5.50 (br s, 1H), 6.89-6.99 (m, 4H), 7.10 (d, $J = 8.4$ Hz, 4H), 7.36 (br s, 1H), 7.60 (br s, 2H), 7.76 (s, 1H), 7.82 (d, $J = 7.8$ Hz, 1H); ESI-MS (m/z) 433 (M) $^+$.

Example 15

N-Ethyl-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide

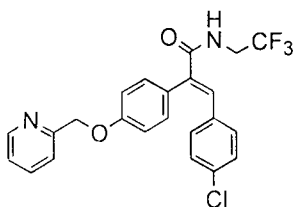


The title compound was prepared by coupling Intermediate 14 (150 mg, 0.392 mmol) with ethylamine hydrochloride (63 mg, 0.784 mmol) as described in Example 2 to yield 135 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.09 (d, $J = 6.9$ Hz, 3H), 3.29-3.40 (m, 2H), 5.43 (s, 2H), 5.60 (br s, 1H), 6.82 (d, $J = 4.8$ Hz, 2H), 7.12 (s, 4H), 7.58 (t, $J = 7.2$ Hz, 1H),

7.70-7.79 (m, 3H), 7.87 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H), 8.37 (d, $J = 5.1$ Hz, 2H); APCI-MS (m/z) 410 (M+H)⁺.

Example 16

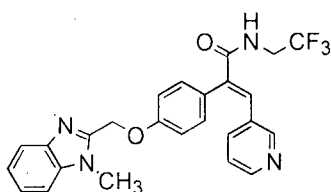
3-(4-Chlorophenyl)-2-[4-(pyridin-2-ylmethoxy)phenyl]-*N*-(2,2,2-trifluoroethyl)prop-2-enamide



The title compound was prepared by coupling Intermediate 12 (200 mg, 0.547 mmol) and 2,2,2-trifluoroethylamine hydrochloride (148 mg, 1.094 mmol) as described in Example 2 to yield 109 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 3.97 (t, $J = 7.8$ Hz, 2H), 5.25 (s, 2H), 5.78 (br s, 1H), 6.93 (d, $J = 7.8$ Hz, 2H), 7.07-7.18 (m, 6H), 7.27 (br s, 1H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.73-7.82 (m, 2H), 8.63 (d, $J = 3.6$ Hz, 1H); ESI (m/z) 447 (M)⁺.

Example 17

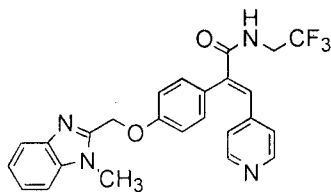
2-{4-[(1-Methyl-1*H*-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-3-yl)-*N*-(2,2,2-trifluoroethyl)prop-2-enamide



The title compound was prepared by coupling Intermediate 4 (100 mg, 0.259 mmol) with 2,2,2-trifluoroethylamine hydrochloride (70 mg, 0.518 mmol) as described in Example 2 to yield 75 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 3.89-4.00 (m, 5H), 5.48 (s, 2H), 5.79 (br s, 1H), 7.02-7.08 (m, 1H), 7.19 (br s, 5H), 7.34-7.44 (m, 3H), 7.78-7.85 (m, 2H), 8.31 (s, 1H), 8.39 (d, $J = 3.9$ Hz, 1H); APCI-MS (m/z) 467 (M+H)⁺.

Example 18

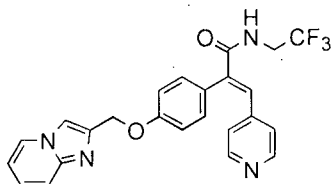
2-{4-[(1-Methyl-1*H*-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-4-yl)-*N*-(2,2,2-trifluoroethyl)prop-2-enamide



The title compound was prepared by coupling Intermediate 5 (150 mg, 0.389 mmol) with 2,2,2-trifluoroethylamine hydrochloride (105 mg, 0.778 mmol) as described in Example 2 to yield 110 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.95 (br s, 5H), 5.47 (s, 2H), 5.84 (br s, 1H), 6.83 (d, $J = 5.4$ Hz, 2H), 7.12-7.22 (m, 4H), 7.32-7.40 (m, 3H), 7.75 (s, 1H), 7.80 (d, $J = 7.8$ Hz, 1H), 8.38 (d, $J = 5.4$ Hz, 2H); ESI-MS (m/z) 467 ($\text{M}+\text{H}$) $^+$.

Example 19

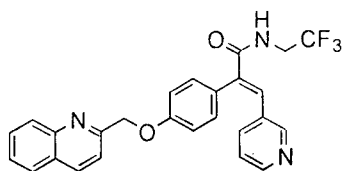
2-[4-(Imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]-3-(pyridin-4-yl)-*N*-(2,2,2-trifluoroethyl) prop-2-enamide



The title compound was prepared by coupling Intermediate 11 (150 mg, 0.40 mmol) with 2,2,2-trifluoroethylamine hydrochloride (108 mg, 0.80 mmol) as described in Example 2 to yield 80 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.94-4.04 (m, 2H), 5.33 (s, 2H), 5.90 (br s, 1H), 6.86 (d, $J = 5.1$ Hz, 3H), 7.15 (s, 4H), 7.28 (br s, 1H), 7.65 (d, $J = 8.7$ Hz, 1H), 7.70 (s, 1H), 7.76 (s, 1H), 8.14 (d, $J = 6.9$ Hz, 1H); 8.41 (d, $J = 5.4$ Hz, 2H); APCI-MS (m/z) 453 ($\text{M}+\text{H}$) $^+$.

Example 20

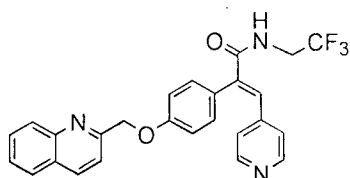
3-(Pyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-*N*-(2,2,2-trifluoroethyl)prop-2-enamide



The title compound was prepared by coupling Intermediate 13 (100 mg, 0.261 mmol) with 2,2,2-trifluoroethylamine hydrochloride (70 mg, 0.522 mmol) as described in Example 2 to yield 75 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.92-4.03 (m, 2H), 5.45 (s, 2H), 5.81 (br s, 1H), 7.13-7.23 (m, 6H), 7.60 (t, $J = 7.5$ Hz, 1H), 7.76- 7.81 (m, 1H), 7.83-7.9 (m, 3H), 8.13 (d, $J = 7.8$ Hz, 1H), 8.26-8.34 (m, 1H), 8.42 (br s, 2H); APCI-MS (m/z) 464 ($\text{M}+\text{H}$) $^+$.

Example 21

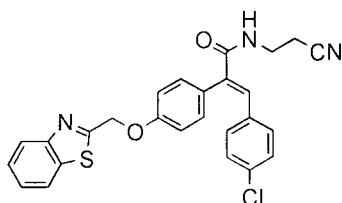
3-(Pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-*N*-(2,2,2-trifluoroethyl)prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (100 mg, 0.261 mmol) with 2,2,2-trifluoroethylamine hydrochloride (70 mg, 0.523 mmol) as described in Example 2 to yield 83 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.94 - 4.11 (m, 2H), 5.43 (s, 2H), 5.86 (br s, 1H), 6.84 (d, $J = 4.5$ Hz, 2H), 7.14 (br s, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.68-7.76 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H), 8.39 (d, $J = 4.5$ Hz, 2H); APCI-MS (m/z) 464 ($\text{M}+\text{H}$) $^+$.

Example 22

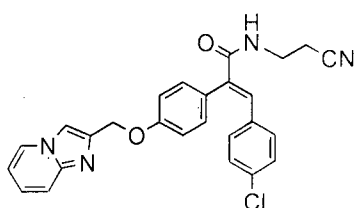
2-[4-(1,3-Benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)-*N*-(2-cyanoethyl)prop-2-enamide



The title compound was prepared by coupling Intermediate 2 (150 mg, 0.372 mmol) with 3-aminopropionitrile fumarate (114 mg, 0.446 mmol) as described in Example 2 to yield 90 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 6.3$ Hz, 2H), 3.53 (q, $J = 6.3$ Hz, 2H), 5.54 (s, 2H), 5.94 (br s, 1H), 6.90 (d, $J = 8.4$ Hz, 2H), 7.08-7.21 (m, 6H), 7.46 (t, $J = 7.8$ Hz, 1H), 7.53 (t, $J = 6.3$ Hz, 1H), 7.77 (s, 1H), 7.94 (d, $J = 7.8$ Hz, 1H), 8.05 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 474 ($\text{M}+\text{H}$) $^+$.

Example 23

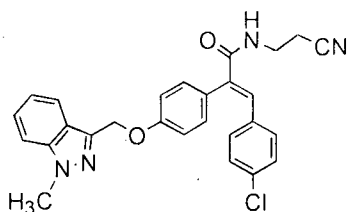
3-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy) phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 1 (150 mg, 0.37 mmol) with 3-aminopropionitrile fumarate (190 mg, 0.74 mmol) as described in Example 2 to yield 90 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.69 (t, $J = 6.3$ Hz, 2H), 3.34-3.39 (m, 2H), 4.20 (br s, 1H), 5.22 (s, 2H), 6.92 (t, $J = 6.3$ Hz, 1H), 7.02 (d, $J = 7.8$ Hz, 2H), 7.10 (br s, 4H), 7.25 (d, $J = 8.1$ Hz, 2H), 7.38 (s, 1H), 7.54 (d, $J = 9.3$ Hz, 1H), 7.73 (br s, 1H), 8.03 (s, 1H), 8.55 (d, $J = 6.3$ Hz, 1H); APCI-MS (m/z) 457 ($\text{M}+\text{H}$) $^+$.

Example 24

3-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-2-{4-[(1-methyl-1*H*-indazol-3-yl)methoxy]phenyl} prop-2-enamide

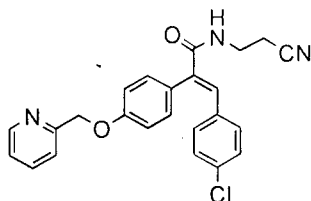


The title compound was prepared by coupling Intermediate 15 (150 mg, 0.358 mmol) with 3-aminopropionitrile fumarate (110 mg, 0.429 mmol) as described in Example 2 to yield 80 mg of

the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.67 (t, $J = 6.0$ Hz, 2H), 3.52 (br s, 2H), 4.09 (s, 3H), 5.48 (s, 2H), 6.00 (br s, 1H), 6.90 (d, $J = 8.1$ Hz, 2H), 7.07-7.15 (m, 3H), 7.17-7.23 (m, 4H), 7.43 (br s, 2H), 7.75 (s, 1H), 7.87 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 471 ($\text{M}+\text{H}$) $^+$.

Example 25

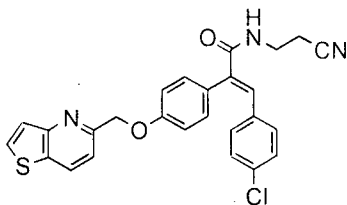
3-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 12 (200 mg, 0.547 mmol) with 3-aminopropionitrile fumarate (210 mg, 0.820 mmol) as described in Example 2 to yield 119 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (d, $J = 5.7$ Hz, 2H), 3.54 (q, $J = 6.3$ Hz, 2H), 5.25 (s, 2H), 5.98 (br s, 1H), 6.93 (d, $J = 8.7$ Hz, 2H), 7.07-7.19 (m, 6H), 7.29 (br s, 1H), 7.57 (d, $J = 7.8$ Hz, 1H), 7.74-7.81 (m, 2H), 8.63 (d, $J = 4.5$ Hz, 1H); ESI (m/z) 418 (M) $^+$.

Example 26

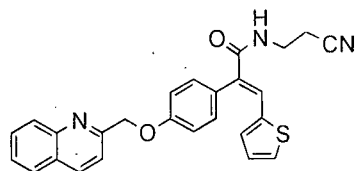
3-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(thieno[3,2-*b*]pyridin-5-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 16 (200 mg, 0.474 mmol) with 3-aminopropionitrile fumarate (243 mg, 0.948 mmol) as described in Example 2 to yield 58 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 5.7$ Hz, 2H), 3.53 (q, $J = 6.3$ Hz, 2H), 5.37 (s, 2H), 5.98 (br s, 1H), 6.92 (d, $J = 8.4$ Hz, 2H), 7.10-7.18 (m, 6H), 7.54-7.59 (m, 2H), 7.76 (s, 1H), 7.82 (d, $J = 5.4$ Hz, 1H), 8.27 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 474 ($\text{M}+\text{H}$) $^+$.

Example 27

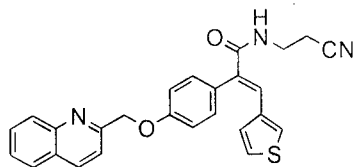
N-(2-Cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-(thiophen-2-yl)prop-2-enamide



The title compound was prepared by coupling Intermediate 20 (150 mg, 0.387 mmol) with 3-aminopropionitrile fumarate (119 mg, 0.464 mmol) as described in Example 2 to yield 90 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.66 (t, $J = 5.7$ Hz, 2H), 3.52 (q, $J = 6.3$ Hz, 2H), 5.47 (s, 2H), 5.87 (br s, 1H), 6.92 (t, $J = 4.5$ Hz, 1H), 7.14-7.21 (m, 6H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.74-7.79 (m, 2H), 7.87 (d, $J = 7.8$ Hz, 1H), 8.06 (s, 1H), 8.11 (d, $J = 9.0$ Hz, 1H), 8.26 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 28

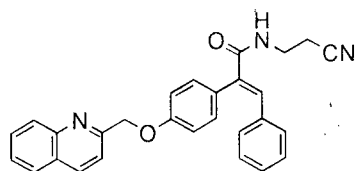
N-(2-Cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-(thiophen-3-yl)prop-2-enamide



The title compound was prepared by coupling Intermediate 21 (150 mg, 0.387 mmol) with 3-aminopropionitrile fumarate (119 mg, 0.464 mmol) as described in Example 2 to give 100 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.66 (t, $J = 6.3$ Hz, 2H), 3.49-3.54 (m, 2H), 5.45 (s, 2H), 5.92 (br s, 1H), 6.43 (br s, 1H), 7.05 (s, 2H), 7.15-7.21 (m, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.72-7.79 (m, 2H), 7.85 (br s, 2H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.7$ Hz, 1H); APCI-MS (m/z) 440 (M) $^+$.

Example 29

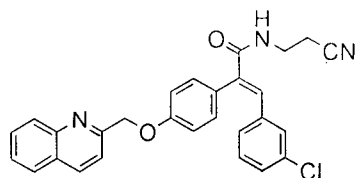
N-(2-Cyanoethyl)-3-phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 22 (200 mg, 0.524 mmol) with 3-aminopropionitrile fumarate (201 mg, 0.728 mmol) as described in Example 2 to yield 50 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 6.3$ Hz, 2H), 3.53 (d, $J = 6.6$ Hz, 2H), 5.43 (s, 2H), 5.97 (br s, 1H), 7.05 (d, $J = 6.9$ Hz, 2H), 7.14-7.26 (m, 7H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.71-7.72 (m, 4H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 434 ($\text{M}+\text{H}$) $^+$.

Example 30

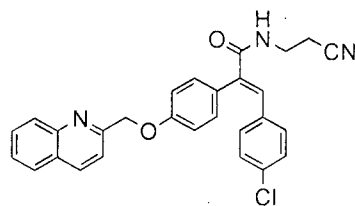
3-(3-Chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 27 (150 mg, 0.360 mmol) with 3-aminopropionitrile fumarate (130 mg, 0.540 mmol) as described in Example 2 to give 91 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 6.3$ Hz, 2H), 3.53 (q, $J = 6.3$ Hz, 2H), 5.44 (s, 2H), 5.99 (br s, 1H), 6.86 (d, $J = 7.8$ Hz, 1H), 6.94 (s, 1H), 7.04-7.11 (m, 3H), 7.12-7.18 (m, 3H), 7.57 (t, $J = 7.8$ Hz, 1H), 7.68-7.78 (m, 3H), 7.85 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 9.0$ Hz, 1H); ESI-MS (m/z) 468 (M) $^+$.

Example 31

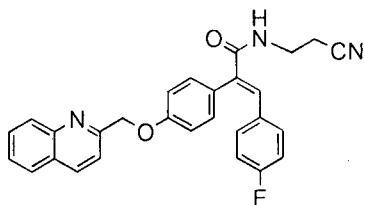
3-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.36 mmol) with 3-aminopropionitrile fumarate (138 mg, 0.54 mmol) as described in Example 2 to yield 96 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 2.69 (t, $J = 6.3$ Hz, 2H), 3.36-3.42 (m, 2H), 5.40 (s, 2H), 7.00 (d, $J = 8.1$ Hz, 2H), 7.08-7.15 (m, 4H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.38 (s, 1H), 7.63 (t, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 8.4$ Hz, 1H), 7.77-7.82 (m, 2H), 8.02 (d, $J = 5.7$ Hz, 2H), 8.45 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 468 ($\text{M}+\text{H}$) $^+$.

Example 32

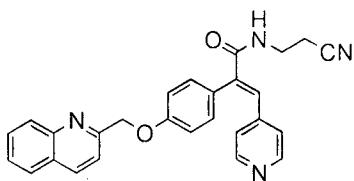
N-(2-Cyanoethyl)-3-(4-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 30 (150 mg, 0.37 mmol) with 3-aminopropionitrile fumarate (144 mg, 0.56 mmol) as described in Example 2 to yield 103 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.67 (t, $J = 6.3$ Hz, 2H), 3.53 (q, $J = 6.0$ Hz, 2H), 5.43 (s, 2H), 5.95 (br s, 1H), 6.82 (t, $J = 8.4$ Hz, 2H), 7.13-7.20 (m, 6H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.69-7.79 (m, 3H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 452 ($\text{M}+\text{H}$) $^+$.

Example 33

N-(2-Cyanoethyl)-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide

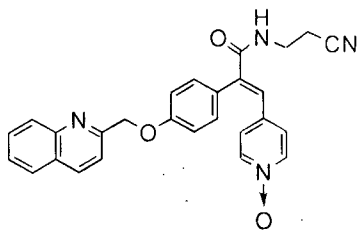


The title compound was prepared by coupling Intermediate 14 (130 mg, 0.340 mmol) with 3-aminopropionitrile fumarate (174 mg, 0.680 mmol) as described in Example 2 to yield 112 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.69 (t, $J = 6.6$ Hz, 2H), 3.49-3.59 (m, 2H), 5.42 (s, 2H), 6.07 (br s, 1H), 6.83 (d, $J = 4.5$ Hz, 2H), 7.14 (br s, 4H), 7.58 (t, $J = 7.5$

Hz, 1H), 7.69-7.79 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H), 8.38 (br s, 2H); APCI-MS (m/z) 435 (M+H)⁺.

Example 34

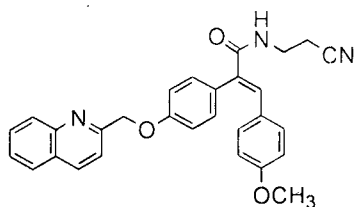
N-(2-Cyanoethyl)-3-(1-oxidopyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 39 (150 mg, 0.376 mmol) with 3-aminopropionitrile fumarate (116 mg, 0.565 mmol) as described in Example 2 to give 38 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.68 (t, $J = 6.9$ Hz, 2H), 3.55 (q, $J = 6.0$ Hz, 2H), 5.62 (s, 2H), 6.06 (br s, 1H), 6.84 (d, $J = 5.4$ Hz, 2H), 7.20 (s, 2H), 7.67 (s, 2H), 7.68-7.74 (m, 2H), 7.85-7.97 (m, 5H), 8.37 (d, $J = 7.8$ Hz, 1H), 8.46 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 451 (M+H)⁺.

Example 35

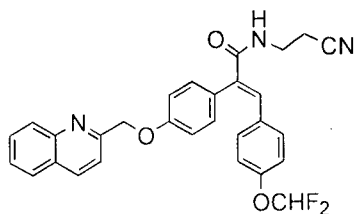
N-(2-Cyanoethyl)-3-(4-methoxyphenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 10 (180 mg, 0.437 mmol) with 3-aminopropionitrile fumarate (168 mg, 0.656 mmol) as described in Example 2 to yield 120 mg of the product as off white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.66 (t, $J = 6.3$ Hz, 2H), 3.52 (q, $J = 5.7$ Hz, 2H), 3.74 (s, 3H), 5.43 (s, 2H), 5.91 (br s, 1H), 6.67 (d, $J = 9.0$ Hz, 2H), 6.94 (d, $J = 8.1$ Hz, 2H), 7.12-7.21 (m, 4H), 7.60 (t, $J = 8.1$ Hz, 1H), 7.73-7.80 (m, 3H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H); ESI (m/z) 464 (M+H)⁺.

Example 36

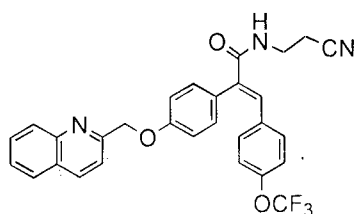
N-(2-Cyanoethyl)-3-[4-(difluoromethoxy)phenyl]-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide



The title compound was prepared by coupling Intermediate 31 (150 mg, 0.335 mmol) with 3-aminopropionitrile fumarate (112 mg, 0.435 mmol) as described in Example 2 to give 93 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 6.3$ Hz, 2H), 3.53 (q, $J = 6.3$ Hz, 2H), 5.43 (s, 2H), 5.96 (br s, 1H), 6.45 (t, $J = 73.8$ Hz, 1H), 6.87 (d, $J = 8.1$ Hz, 2H), 6.99 (d, $J = 8.4$ Hz, 2H), 7.12-7.19 (m, 4H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.70-7.78 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 500 ($\text{M}+\text{H}$) $^+$.

Example 37

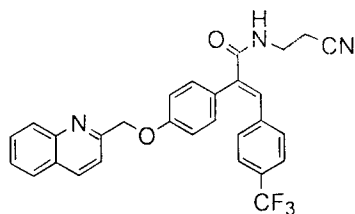
N-(2-Cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethoxy)phenyl] prop-2-enamide



The title compound was prepared by coupling Intermediate 32 (150 mg, 0.332 mmol) with 3-aminopropionitrile fumarate (111 mg, 0.432 mmol) as described in Example 2 to give 70 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 6.3$ Hz, 2H), 3.50-3.55 (m, 2H), 5.44 (s, 2H), 5.97 (br s, 1H), 6.95-7.03 (m, 4H), 7.15-7.20 (m, 4H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.71-7.79 (m, 3H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.11 (d, $J = 8.1$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 518 ($\text{M}+\text{H}$) $^+$.

Example 38

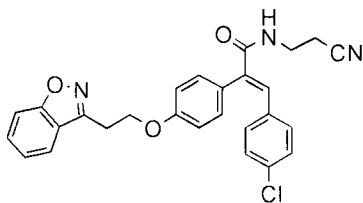
N-(2-Cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 33 (100 mg, 0.222 mmol) with 3-aminopropionitrile fumarate (86 mg, 0.333 mmol) as described in Example 2 to yield 50 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.68 (t, $J = 6.6$ Hz, 2H), 3.55 (q, $J = 6.3$ Hz, 2H), 5.43 (s, 2H), 6.02 (br s, 1H), 7.08-7.18 (m, 6H), 7.39 (d, $J = 8.4$ Hz, 2H), 7.58 (t, $J = 8.4$ Hz, 1H), 7.69-7.76 (m, 2H), 7.78-7.85 (m, 2H), 8.09 (d, $J = 9.0$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 502 ($\text{M}+\text{H}$) $^+$.

Example 39

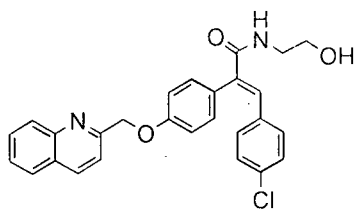
2-{4-[2-(1,2-Benzoxazol-3-yl)ethoxy]phenyl}-3-(4-chlorophenyl)-*N*-(2-cyanoethyl) prop-2-enamide



The title compound was prepared by coupling Intermediate 3 (150 mg, 0.352 mmol) with 3-aminopropionitrile fumarate (138 mg, 0.535 mmol) as described in Example 2 to yield 73 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.67 (t, $J = 5.7$ Hz, 2H), 3.48-3.56 (m, 4H), 4.48 (t, $J = 6.3$ Hz, 2H), 5.94 (br s, 1H), 6.91-7.00 (m, 4H), 7.13 (t, $J = 7.5$ Hz, 4H), 7.38 (br s, 1H), 7.60 (br s, 2H), 7.76 (s, 1H), 7.83 (d, $J = 7.8$ Hz, 1H); ESI-MS (m/z) 472 ($\text{M}+\text{H}$) $^+$.

Example 40

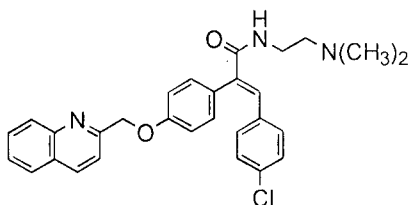
3-(4-Chlorophenyl)-*N*-(2-hydroxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (200 mg, 0.481 mmol) with 2-aminoethanol (0.04 ml, 0.722 mmol) as described in Example 2 to yield 70 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.84 (br s, 1H), 3.43-3.50 (m, 2H), 3.71 (br s, 2H), 5.42 (s, 2H), 5.99 (br s, 1H), 6.44 (d, $J = 8.1$ Hz, 2H), 7.08-7.17 (m, 6H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.68-7.79 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); APCI (m/z) 459 (M) $^+$.

Example 41

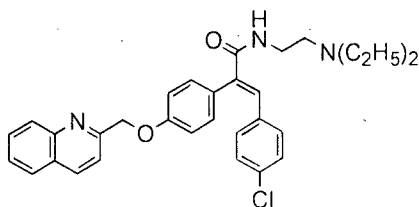
3-(4-Chlorophenyl)-*N*-[2-(dimethylamino)ethyl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (300 mg, 0.721 mmol) with *N,N*-dimethylethanamine (0.15 ml, 1.44 mmol) as described in Example 2 to give 52 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.12 (s, 6H), 2.36 (t, $J = 6.0$ Hz, 2H), 3.38 (q, $J = 5.7$ Hz, 2H), 5.42 (s, 2H), 6.13 (br s, 1H), 6.91 (d, $J = 8.7$ Hz, 2H), 7.07-7.15 (m, 6H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.69-7.78 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 486 ($\text{M}+\text{H}$) $^+$.

Example 42

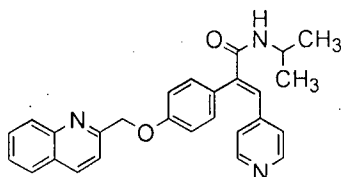
3-(4-Chlorophenyl)-*N*-[2-(diethylamino)ethyl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (300 mg, 0.721 mmol) with *N,N*-diethylethane-1,2-diamine (0.202 ml, 1.082 mmol) as described in Example 2 to give 48 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.78 (t, $J = 6.9$ Hz, 6H), 2.34 (d, $J = 6.9$ Hz, 4H), 2.48 (br s, 2H), 3.34 (d, $J = 4.8$ Hz, 2H), 5.42 (s, 2H), 6.39 (br s, 1H), 6.92 (d, $J = 8.4$ Hz, 2H), 7.07-7.15 (m, 6H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.68-7.78 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.7$ Hz, 1H), 8.23 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 515 ($\text{M}+\text{H}$) $^+$.

Example 43

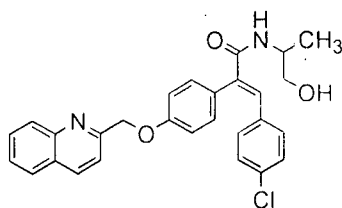
N-(Propan-2-yl)-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (150 mg, 0.392 mmol) with isopropylamine hydrochloride (46 mg, 0.784 mmol) as described in Example 2 to yield 90 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.10 (d, $J = 6.3$ Hz, 6H), 4.12-4.21 (m, 1H), 5.43 (br s, 3H), 6.81 (d, $J = 4.5$ Hz, 2H), 7.11 (br s, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.67-7.79 (m, 3H), 7.87 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H), 8.37 (d, $J = 4.5$ Hz, 2H); APCI-MS (m/z) 424 ($\text{M}+\text{H}$) $^+$.

Example 44

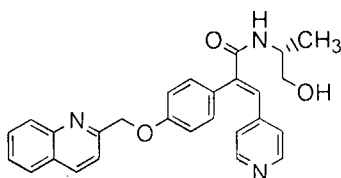
($\pm$)-3-(4-Chlorophenyl)-*N*-(1-hydroxypropan-2-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.360 mmol) with (±)-2-aminopropanol (0.03 ml, 0.397 mmol) as described in Example 2 to yield 120 mg of the product as white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.04 (d, $J = 6.6$ Hz, 3H), 2.96 (br s, 1H), 3.24-3.34 (m, 2H), 3.84-3.90 (m, 1H), 4.71 (t, $J = 5.4$ Hz, 1H), 5.39 (s, 2H), 7.00 (d, $J = 8.4$ Hz, 2H), 7.15 (s, 4H), 7.21-7.27 (m, 3H), 7.63 (t, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.80 (t, $J = 7.8$ Hz, 1H), 8.02 (d, $J = 6.9$ Hz, 2H), 8.45 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 473 ($\text{M}+\text{H}$) $^+$.

Example 45

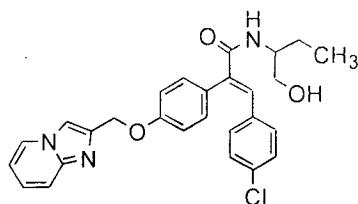
N-[(2*R*)-1-Hydroxypropan-2-yl]-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (100 mg, 0.260 mmol) with *R*-(-)-2-amino-1-propanol (0.02 ml, 0.280 mmol) as described in Example 2 to yield 71 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.11 (d, $J = 6.3$ Hz, 3H), 3.52 (br s, 2H), 3.65 (br s, 1H), 4.15 (br s, 1H), 5.43 (s, 2H), 5.72 (br s, 1H), 6.84 (br s, 2H), 7.12 (br s, 4H), 7.70 (br s, 1H), 7.72-7.78 (m, 3H), 7.87 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 7.8$ Hz, 1H), 8.25 (d, $J = 7.8$ Hz, 1H), 8.38 (br s, 2H); APCI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 46

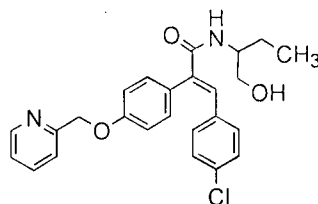
3-(4-Chlorophenyl)-*N*-(1-hydroxybutan-2-yl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 1 (150 mg, 0.370 mmol) with 2-aminobutan-1-ol (0.42 ml, 0.44 mmol) as described in Example 2 to yield 130 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.832 (t, $J = 7.5$ Hz, 3H), 1.29-1.40 (m, 1H), 1.49-1.61 (m, 1H), 2.54 (br s, 1H), 3.38 (br s, 2H), 3.76 (br s, 1H), 4.65 (br s, 1H), 5.21 (s, 2H), 6.90 (t, $J = 7.5$ Hz, 1H), 6.98-7.09 (m, 6H), 7.26 (d, $J = 11.7$ Hz, 4H), 7.53 (d, $J = 9.3$ Hz, 1H), 8.02 (s, 1H), 8.54 (d, $J = 6.9$ Hz, 1H); ESI (m/z) 476 ($\text{M}+\text{H}$) $^+$.

Example 47

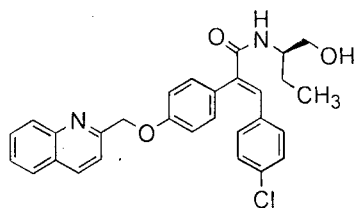
($\pm$)-3-(4-Chlorophenyl)-*N*-(1-hydroxybutan-2-yl)-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 12 (200 mg, 0.547 mmol) with 2-aminobutan-1-ol (0.77 ml, 0.820 mmol) as described in Example 2 to give 58 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.85 (t, $J = 7.5$ Hz, 3H), 1.25-1.37 (m, 1H), 1.50-1.59 (m, 1H), 1.69 (br s, 1H), 3.02 (br s, 1H), 3.50-3.58 (m, 1H), 3.70 (br s, 1H), 3.92 (br s, 1H), 5.24 (s, 2H), 5.62 (d, $J = 6.6$ Hz, 1H), 6.92 (d, $J = 8.1$ Hz, 2H), 7.05-7.13 (m, 3H), 7.15-7.26 (m, 3H), 7.30 (br s, 1H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.76 (br s, 1H), 8.63 (d, $J = 3.9$ Hz, 1H); ESI-MS (m/z) 437 ($\text{M}+\text{H}$) $^+$.

Example 48

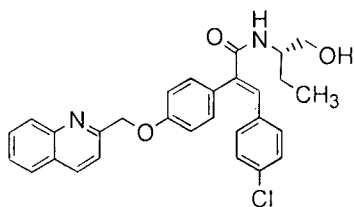
3-(4-Chlorophenyl)-*N*-[(2*R*)-1-hydroxybutan-2-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (200 mg, 0.481 mmol) with (*R*)-2-aminobutan-1-ol (47 mg, 0.520 mmol) as described in Example 2 to yield 50 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.84 (t, $J = 7.2$ Hz, 3H), 1.31-1.41 (m, 1H), 1.46-1.58 (m, 1H), 2.93 (br s, 1H), 3.50-3.56 (m, 1H), 3.64-3.71 (m, 1H), 3.91 (br s, 1H), 5.42 (s, 2H), 5.60 (d, $J = 7.5$ Hz, 1H), 6.91 (d, $J = 8.7$ Hz, 2H), 7.08-7.17 (m, 6H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.69-7.79 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.24 (d, $J = 9.0$ Hz, 1H); ESI (m/z) 487 ($\text{M}+\text{H}$) $^+$.

Example 49

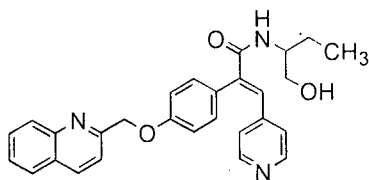
3-(4-Chlorophenyl)-*N*-[(2*S*)-1-hydroxybutan-2-yl]-2-[4-(quinolin-2-ylmethoxy) phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (200 mg, 0.481 mmol) with (*S*)-2-aminobutan-1-ol (47 mg, 0.520 mmol) as described in Example 2 to yield 50 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.84 (t, $J = 7.2$ Hz, 3H), 1.31-1.41 (m, 1H), 1.46-1.58 (m, 1H), 2.93 (br s, 1H), 3.50-3.56 (m, 1H), 3.64-3.71 (m, 1H), 3.91 (br s, 1H), 5.42 (s, 2H), 5.60 (d, $J = 7.5$ Hz, 1H), 6.91 (d, $J = 8.7$ Hz, 2H), 7.08-7.17 (m, 6H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.69-7.79 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.24 (d, $J = 9.0$ Hz, 1H); ESI (m/z) 487 ($\text{M}+\text{H}$) $^+$.

Example 50

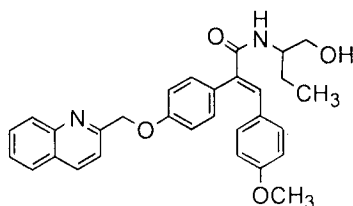
($\pm$)-*N*-(1-Hydroxybutan-2-yl)-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (100 mg, 0.260 mmol) with 2-amino-1-butanol (0.03 ml, 0.310 mmol) as described in Example 2 to yield 83 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.86 (t, $J = 7.2$ Hz, 3H), 1.34-1.42 (m, 1H), 1.51-1.60 (m, 1H), 3.54-3.58 (m, 1H), 3.65-3.71 (m, 1H), 3.94 (br s, 1H), 4.23 (br s, 1H), 5.42 (s, 2H), 5.69 (d, $J = 7.2$ Hz, 1H), 6.83 (d, $J = 5.1$ Hz, 2H), 7.09-7.17 (m, 4H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.70-7.79 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 9.0$ Hz, 1H), 8.25 (d, $J = 8.7$ Hz, 1H), 8.38 (d, $J = 4.5$ Hz, 2H); APCI-MS (m/z) 454 ($\text{M}+\text{H}$) $^+$.

Example 51

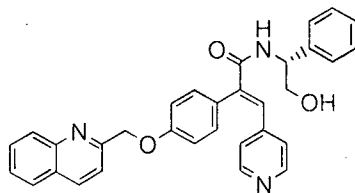
($\pm$)-*N*-(1-Hydroxybutan-2-yl)-3-(4-methoxyphenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide



The title compound was prepared by coupling Intermediate 10 (200 mg, 0.486 mmol) with 2-aminobutan-1-ol (47 mg, 0.535 mmol) as described in Example 2 to yield 120 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.83 (t, $J = 7.2$ Hz, 3H), 1.26-1.37 (m, 1H), 1.47-1.55 (m, 1H), 3.18 (br s, 1H), 3.54 (br s, 1H), 3.66 (br s, 1H), 3.74 (s, 3H), 3.89 (br s, 1H), 5.43 (s, 2H), 5.54 (d, $J = 6.9$ Hz, 1H), 6.67 (d, $J = 8.7$ Hz, 2H), 6.94 (d, $J = 9.0$ Hz, 2H), 7.12-7.22 (m, 4H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.70-7.79 (m, 3H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 9.0$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); ESI (m/z) 483 ($\text{M}+\text{H}$) $^+$.

Example 52

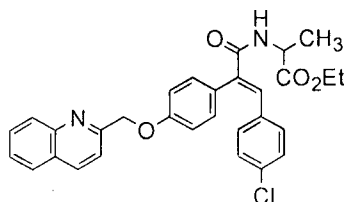
N-[(1*R*)-2-Hydroxy-1-phenylethyl]-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (95 mg, 0.240 mmol) with *R*-(-)-2-amino-2-phenylethanol (41 mg, 0.290 mmol) as described in Example 2 to yield 61 mg of the product as off-white; ^1H NMR (300 MHz, CDCl_3) δ 3.84 (br s, 3H), 4.26 (br s, 1H), 5.17 (d, $J = 6.3$ Hz, 1H), 5.43 (s, 2H), 6.34 (d, $J = 7.5$ Hz, 1H), 6.80 (d, $J = 4.8$ Hz, 2H), 7.10-7.20 (m, 5H), 7.28-7.33 (m, 4H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.69-7.79 (m, 2H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 8.7$ Hz, 1H), 8.24 (d, $J = 9.0$ Hz, 1H), 8.37 (d, $J = 4.8$ Hz, 2H); ESI (m/z) 502 ($\text{M}+\text{H}$) $^+$.

Example 53

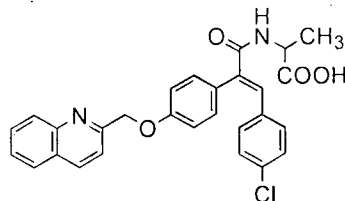
($\pm$)-Ethyl *N*-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl}alaninate



The title compound was prepared by coupling Intermediate 29 (250 mg, 0.601 mmol) with ethyl 2-aminopropanoate (120 mg, 0.783 mmol) as described in Example 2 to yield 170 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.24 (t, $J = 6.9$ Hz, 3H), 1.36 (d, $J = 7.2$ Hz, 3H), 4.15 (q, $J = 7.2$ Hz, 2H), 4.62-4.69 (m, 1H), 5.43 (s, 2H), 6.13 (br s, 1H), 6.91 (d, $J = 8.7$ Hz, 2H), 7.08-7.20 (m, 6H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.70-7.79 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 515 (M) $^+$.

Example 54

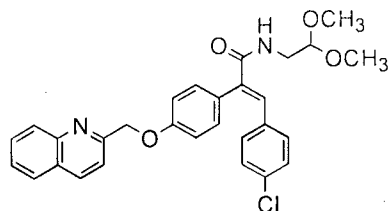
($\pm$)-*N*-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl}alanine



The title compound was prepared by base hydrolysis of Example 53 (100 mg, 0.194 mmol) to yield 75 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.46 (d, $J = 6.6$ Hz, 3H), 4.73 (t, $J = 6.9$ Hz, 1H), 5.49 (br s, 2H), 6.27 (d, $J = 6.0$ Hz, 1H), 6.91 (d, $J = 7.8$ Hz, 2H), 7.06-7.13 (m, 3H), 7.14-7.21 (m, 3H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.78 (br s, 3H), 7.87 (d, $J = 8.4$ Hz, 1H), 8.14 (d, $J = 7.8$ Hz, 1H), 8.30 (d, $J = 6.6$ Hz, 1H), 13.24 (br s, 1H); ESI-MS (m/z) 487 ($\text{M}+\text{H}$) $^+$.

Example 55

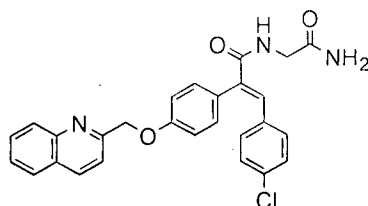
3-(4-Chlorophenyl)-*N*-(2,2-dimethoxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (1.0 g, 2.406 mmol) with aminoacetaldehyde dimethylacetal (0.38 ml, 3.610 mmol) as described in Example 2 to yield 900 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.31 (br s, 6H), 3.43 (t, $J = 5.7$ Hz, 2H), 4.35 (t, $J = 5.4$ Hz, 1H), 5.43 (s, 2H), 5.75 (br s, 1H), 6.91 (d, $J = 8.7$ Hz, 2H), 7.08-7.15 (m, 6H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.69-7.78 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.17 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 502 ($\text{M}+\text{H}$) $^+$.

Example 56

N-(2-Amino-2-oxoethyl)-3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide

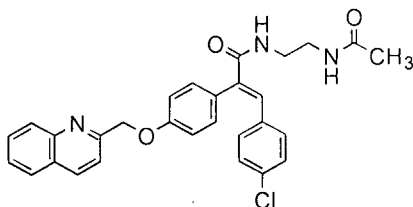


The title compound was prepared by coupling Intermediate 29 (200 mg, 0.480 mmol) and 2-aminoacetamide (80 mg, 0.720 mmol) as described in Example 2 to yield 100 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.98 (d, $J = 5.4$ Hz, 2H), 5.43 (s, 2H), 6.16 (br

s, 1H), 6.24 (br, 2H), 6.92 (d, $J = 8.4$ Hz, 2H), 7.08-7.19 (m, 6H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.70-7.79 (m, 3H), 7.87 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 8.1$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 472 ($M+H$)⁺.

Example 57

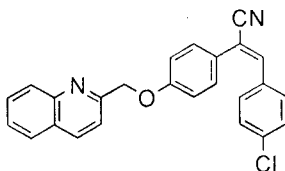
N-[2-(Acetylamino)ethyl]-3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.360 mmol) with *N*-(2-aminoethyl) acetamide (0.04 ml, 0.433 mmol) as described in Example 2 to yield 90 mg of the product as off white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.76 (s, 3H), 3.10-3.17 (m, 4H), 5.39 (s, 2H), 6.99 (d, $J = 8.4$ Hz, 2H), 7.10 (s, 4H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.33 (s, 1H), 7.49-7.54 (m, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.71 (d, $J = 8.4$ Hz, 1H), 7.80 (t, $J = 7.8$ Hz, 1H), 7.83-7.89 (m, 1H), 8.02 (d, $J = 7.5$ Hz, 2H), 8.45 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 500 ($M+H$)⁺.

Example 58

3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enenitrile

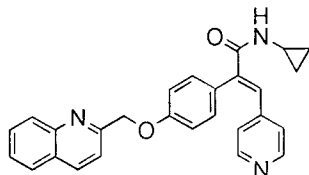


To the well stirred solution of Example 1 (500 mg, 1.206 mmol) in THF (15 ml) was added TEA (0.26 ml, 1.929 mmol) and the reaction mixture was cooled to 0 °C. Trifluoroacetic anhydride was added to this cooled reaction mixture and was further stirred at the same temperature for 2 h. The reaction mixture was diluted with water (50 ml) and extracted with ethyl acetate (3 x 50 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 50 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.40 (s, 2H), 7.00 (d, $J = 9.0$ Hz, 2H), 7.10 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 6.3$ Hz, 2H), 7.28 (d, $J = 8.7$ Hz, 3H), 7.57 (t, $J = 6.9$

Hz, 1H), 7.66 (d, $J = 9.0$ Hz, 1H), 7.75 (t, $J = 7.8$ Hz, 1H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 397 ($M+H$)⁺.

Example 59

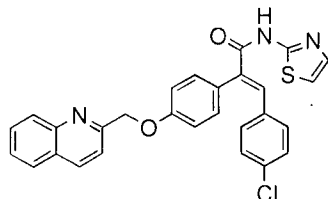
N-Cyclopropyl-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 14 (150 mg, 0.39 mmol) with cyclopropylamine hydrochloride (44 mg, 0.78 mmol) as described in Example 2 to yield 120 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 0.43 (br s, 2H), 0.79 (d, $J = 6.6$ Hz, 2H), 2.79 (br s, 1H), 5.42 (s, 2H), 5.65 (br s, 1H), 6.81 (d, $J = 5.1$ Hz, 2H), 7.09 (s, 4H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.71-7.79 (m, 3H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.7$ Hz, 1H), 8.37 (d, $J = 5.1$ Hz, 2H); APCI-MS (m/z) 422 ($M+H$)⁺.

Example 60

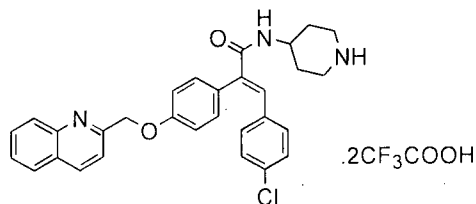
3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-*N*-(1,3-thiazol-2-yl)prop-2-enamide



The title compound was prepared by coupling Intermediate 29 (200 mg, 0.481 mmol) and 1,3-thiazol-2-amine as described (130 mg, 0.673 mmol) in Example 2 to yield 50 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.47 (s, 2H), 6.95 (d, $J = 8.4$ Hz, 2H), 7.00 (d, $J = 3.3$ Hz, 1H), 7.12-7.23 (m, 6H), 7.40 (d, $J = 3.6$ Hz, 1H), 7.58 (t, $J = 7.2$ Hz, 1H), 7.73-7.79 (m, 2H), 7.87 (d, $J = 7.8$ Hz, 1H), 7.95 (s, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.28 (d, $J = 8.4$ Hz, 1H), 8.72 (br s, 1H); APCI-MS (m/z) 498 ($M+H$)⁺.

Example 61

3-(4-Chlorophenyl)-*N*-(piperidin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide di (trifluoroacetic acid)



Step 1: *tert*-Butyl 4-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl} amino)piperidine-1-carboxylate:

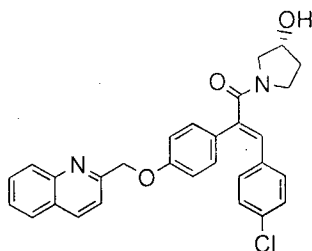
The title compound was prepared from Intermediate 29 and 4-amino-1-BOC piperidine as described in Example 2 to give 180 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.17-1.21 (m, 2H), 1.42 (s, 9H), 1.86 (br s, 2H), 2.87 (br s, 2H), 3.95 (br s, 3H), 5.38 (d, $J = 7.8$ Hz, 1H), 5.43 (s, 2H), 6.90 (d, $J = 8.1$ Hz, 2H), 7.07 (br s, 2H), 7.11 (s, 4H), 7.58 (t, $J = 7.5$ Hz, 1H), 7.70-7.79 (m, 3H), 7.87 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.7$ Hz, 1H).

Step 2: 3-(4-Chlorophenyl)-*N*-(piperidin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide di (trifluoroacetic acid):

To a well stirred solution of Step 1 Intermediate (170 mg, 0.284 mmol) in dichloromethane (4 ml) was added trifluoroacetic acid (0.5 ml) at 0 °C and the reaction was continued for 4 h. The reaction mixture was concentrated under reduced pressure and dried well under high vacuum. The product was recrystallized from diethyl ether to give 49 mg of an off-white salt; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.66 (br s, 2H), 1.95 (br s, 2H), 2.93-3.02 (m, 2H), 3.29 (br s, 2H), 3.68 (s, 1H), 3.92 (s, 1H), 4.31 (br s, 1H), 5.41 (s, 2H), 6.13 (br s, 2H), 7.01 (d, $J = 8.4$ Hz, 2H), 7.09 (s, 4H), 7.16 (s, 1H), 7.22 (d, $J = 7.8$ Hz, 1H), 7.74 (d, $J = 9.0$ Hz, 1H), 7.85 (t, $J = 6.9$ Hz, 1H), 8.05 (d, $J = 6.9$ Hz, 2H), 8.52 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 498 ($\text{M}+\text{H}$) $^+$.

Example 62

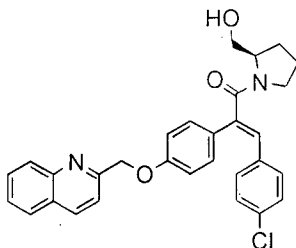
3-(4-Chlorophenyl)-1-[(3*R*)-3-hydroxypyrrolidin-1-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one



The title compound was prepared by coupling Intermediate 29 (200 mg, 0.481 mmol) with (*R*)-(+)-3-pyrrolidinol (50 mg, 0.570 mmol) as described in Example 2 to yield 70 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.81-1.93 (m, 3H), 3.24 (br s, 1H), 3.36-3.41 (m, 1H), 3.63-3.69 (m, 2H), 4.45 (d, $J = 32.7$ Hz, 1H), 5.37 (s, 2H), 6.77 (br s, 1H), 6.95 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.1$ Hz, 2H), 7.13 (d, $J = 8.4$ Hz, 2H), 7.20 (t, $J = 8.1$ Hz, 2H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.68 (d, $J = 8.7$ Hz, 1H), 7.53 (t, $J = 7.2$ Hz, 1H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); ESI (m/z) 485 ($\text{M}+\text{H}$) $^+$.

Example 63

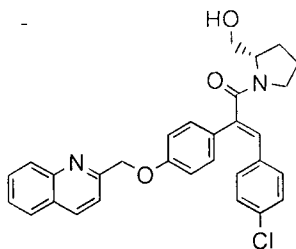
3-(4-Chlorophenyl)-1-[(2*R*)-2-(hydroxymethyl)pyrrolidin-1-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.361 mmol) with (2*R*)-pyrrolidin-2-ylmethanol (0.53 ml, 0.542 mmol) as described in Example 2 to yield 100 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.51-1.58 (m, 2H), 1.65-1.78 (m, 1H), 2.08 (br s, 1H), 3.13 (br s, 1H), 3.49 (br s, 1H), 3.64-3.73 (m, 2H), 4.28 (d, $J = 6.0$ Hz, 1H), 5.00 (br s, 1H), 5.38 (s, 2H), 6.74 (s, 1H), 6.97 (d, $J = 8.1$ Hz, 2H), 7.05 (d, $J = 7.8$ Hz, 2H), 7.14 (d, $J = 8.1$ Hz, 2H), 7.21 (d, $J = 8.1$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.66-7.78 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 499 ($\text{M}+\text{H}$) $^+$.

Example 64

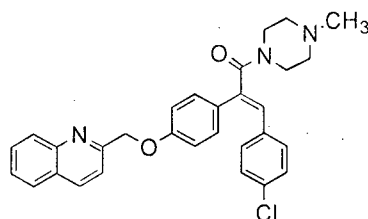
3-(4-Chlorophenyl)-1-[(2*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.360 mmol) with (2*S*)-pyrrolidin-2-ylmethanol (0.053 ml, 0.541 mmol) as described in Example 2 to yield 100 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.63-1.72 (m, 3H), 2.04-2.12 (m, 1H), 3.06-3.16 (m, 1H), 3.49 (br s, 1H), 3.61-3.72 (m, 2H), 4.28 (br s, 1H), 5.01 (br s, 1H), 5.38 (s, 2H), 6.74 (s, 1H), 6.97 (d, $J = 8.7$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.13-7.22 (m, 4H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.70-7.78 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.7$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 499 ($\text{M}+\text{H}$) $^+$.

Example 65

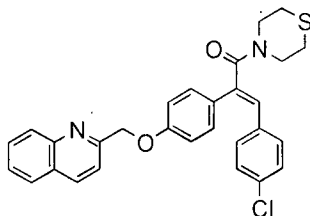
3-(4-Chlorophenyl)-1-(4-methylpiperazin-1-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.36 mmol) with N-methyl piperazine (0.06 ml, 0.541 mmol) as described in Example 2 to yield 70 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.18 (br s, 2H), 2.26 (br s, 3H), 2.41 (br s, 2H), 3.51 (br s, 2H), 3.71 (br s, 2H), 5.37 (s, 2H), 6.59 (s, 1H), 6.96 (d, $J = 8.4$ Hz, 2H), 7.06 (d, $J = 8.4$ Hz, 2H), 7.14 (d, $J = 8.4$ Hz, 2H), 7.21 (d, $J = 8.1$ Hz, 2H), 7.56 (d, $J = 7.2$ Hz, 1H), 7.67 (d, $J = 8.1$ Hz, 1H), 7.74 (t, $J = 7.2$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.07 (d, $J = 8.7$ Hz, 1H), 8.21 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 498 ($\text{M}+\text{H}$) $^+$.

Example 66

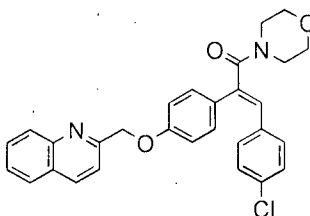
3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-1-(thiomorpholin-4-yl)prop-2-en-1-one



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.360 mmol) and thiomorpholine (0.041 ml, 0.433 mmol) as described in Example 2 to yield 140 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.22 (br s, 2H), 2.61 (br s, 2H), 3.71 (br s, 2H), 3.91 (br s, 2H), 5.39 (s, 2H), 6.58 (s, 1H), 6.97 (d, $J = 8.4$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.13-7.22 (m, 4H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.67 (d, $J = 9.0$ Hz, 1H), 7.75 (t, $J = 8.1$ Hz, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 501 ($\text{M}+\text{H}$) $^+$.

Example 67

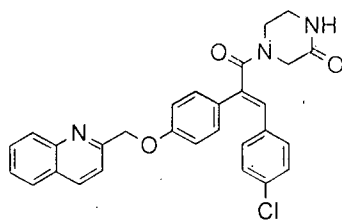
3-(4-Chlorophenyl)-1-(morpholin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one



The title compound was prepared by coupling Intermediate 29 (150 mg, 0.361 mmol) with morpholine (0.37 ml, 0.433 mmol) as described in Example 2 to yield 75 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.45 (br s, 4H), 3.67 (br s, 4H), 5.38 (s, 2H), 6.61 (s, 1H), 6.96 (d, $J = 8.7$ Hz, 2H), 7.05 (d, $J = 8.7$ Hz, 1H), 7.12-7.23 (m, 5H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.67 (d, $J = 8.7$ Hz, 1H), 7.75 (t, $J = 7.5$ Hz, 1H), 7.85 (d, $J = 8.1$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 485 ($\text{M}+\text{H}$) $^+$.

Example 68

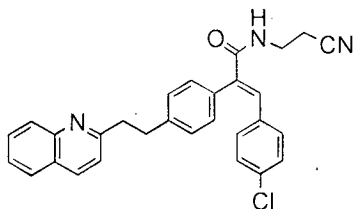
4-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl}piperazin-2-one



The title compound was prepared by coupling Intermediate 29 (200 mg, 0.481 mmol) with 2-oxopiperazine (72 mg, 0.721 mmol) as described in Example 2 to yield 60 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.01 (br s, 1H), 3.41 (br s, 1H), 3.64 (br s, 1H), 3.85 (br s, 1H), 4.06 (br s, 1H), 4.27 (br s, 1H), 5.37 (s, 2H), 6.09 (br s, 1H), 6.69 (s, 1H), 6.97 (d, $J = 8.7$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.13-7.22 (m, 4H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.67 (d, $J = 9.0$ Hz, 1H), 7.73 (t, $J = 7.5$ Hz, 1H), 7.85 (d, $J = 8.1$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 498 ($\text{M}+\text{H}$) $^+$.

Example 69

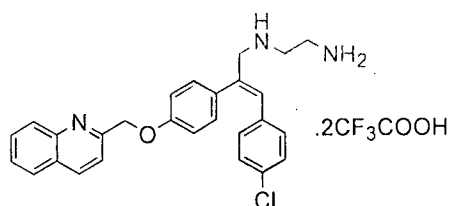
3-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-2-{4-[2-(quinolin-2-yl)ethyl]phenyl}prop-2-enamide



The title compound was prepared by coupling Intermediate 40 (100 mg, 0.241 mmol) with 3-aminopropionitrile fumarate (74 mg, 0.29 mmol) as described in Example 2 to give 65 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.67 (t, $J = 6.3$ Hz, 2H), 3.26 (d, $J = 7.8$ Hz, 2H), 3.35 (d, $J = 7.5$ Hz, 2H), 3.53 (q, $J = 6.3$ Hz, 2H), 5.98 (br s, 1H), 6.87 (d, $J = 8.4$ Hz, 2H), 7.05 (d, $J = 8.7$ Hz, 2H), 7.12 (d, $J = 7.8$ Hz, 2H), 7.29-7.35 (m, 3H), 7.54 (t, $J = 6.6$ Hz, 1H), 7.73-7.83 (m, 3H), 8.09 (br s, 2H); ESI-MS (m/z) 466 (M) $^+$.

Example 70

N-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}ethane-1,2-diamine di(trifluoro acetic acid) salt



Step 1: *tert*-butyl [2-({3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino)ethyl]carbamate:

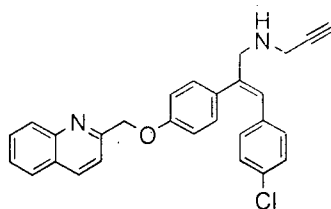
To the well stirred solution of Intermediate 41 (300 mg, 0.750 mmol) in dichloromethane (10 ml) were added N-BOC ethylenediamine (0.12 ml, 0.750 mmol) and sodium triacetoxy borohydride (318 mg, 1.501 mmol) and the reaction mixture was stirred for 30 mins after which acetic acid (0.04 ml, 0.7509) was added to it and it was further stirred overnight. The reaction mixture was quenched with sodium bicarbonate (25 ml), extracted with ethyl acetate (2 x 50ml), washed with water (2 x 25 ml) and dried. The crude product obtained was purified by silica gel column chromatography to yield 125 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.41 (s, 9H), 2.78 (br s, 2H), 3.22 (br s, 2H), 3.63 (s, 2H), 4.96 (br s, 1H), 5.38 (s, 2H), 6.20 (br s, 1H), 6.53 (s, 1H), 6.89 (d, $J = 9.0$ Hz, 2H), 6.98 (d, $J = 8.4$ Hz, 2H), 7.03-7.12 (m, 4H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.66-7.78 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H).

Step 2: *N*-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}ethane-1,2-diamine di(trifluoro acetic acid) salt:

To a well stirred solution of Step 1 Intermediate (115 mg, 0.211 mmol) in dichloromethane (4 ml) was added trifluoroacetic acid (0.5 ml) at 0°C and the reaction was continued for 4 h. The reaction mixture was concentrated under reduced pressure and dried well under high vacuum. The product was recrystallized from diethyl ether to give 56 mg of an off-white salt; ^1H NMR (300 MHz, CDCl_3) δ 3.10-3.18 (m, 4H), 4.06 (s, 2H), 4.32 (br, 2H), 5.40 (s, 2H), 6.80 (s, 1H), 6.95 (d, $J = 8.4$ Hz, 2H), 7.12 (d, $J = 7.8$ Hz, 2H), 7.19-7.25 (m, 5H), 7.65-7.71 (m, 2H), 7.82 (t, $J = 7.8$ Hz, 1H), 8.02 (d, $J = 8.1$ Hz, 2H), 8.46 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 444 ($\text{M}+\text{H}$) $^+$.

Example 71

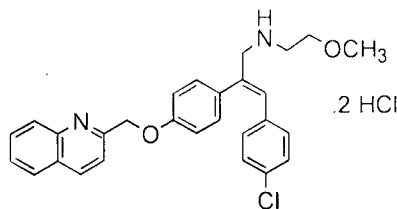
3-(4-Chlorophenyl)-*N*-(prop-2-yn-1-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and propargyl amine (0.51 ml, 0.750 mmol) as described in Step 1 of Example 70 to yield 50 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.24 (s, 1H), 3.45 (s, 2H), 3.68 (s, 2H), 5.38 (s, 2H), 6.55 (s, 1H), 6.71 (d, $J = 7.8$ Hz, 2H), 6.98 (d, $J = 8.1$ Hz, 2H), 7.04-7.14 (m, 5H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.67-7.78 (m, 2H), 7.80 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.21 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 439 ($\text{M}+\text{H}$) $^+$.

Example 72

3-(4-Chlorophenyl)-*N*-(2-methoxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine dihydrochloride



Step 1: 3-(4-Chlorophenyl)-*N*-(2-methoxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-en-1-amine:

The title compound was prepared from Intermediate 41 and 2-methoxyethylamine as described in Step 1 of Example 70.

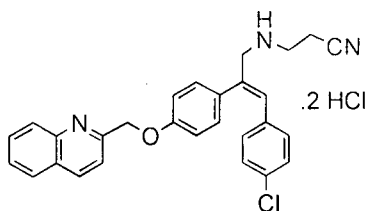
Step 2: 3-(4-Chlorophenyl)-*N*-(2-methoxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine dihydrochloride:

Excess of HCl gas in ethyl acetate was added to the Step 1 Intermediate (300 mg, 0.750 mmol) at 0°C and stirred for 2 h. Excess HCl was removed by bubbling nitrogen gas through the reaction mixture and the solid obtained was purified by silica gel column chromatography to yield 25 mg of off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.82 (t, $J = 4.8$ Hz, 2H), 3.31 (s, 3H), 3.47-3.51 (m, 2H), 3.61 (s, 2H), 5.38 (s, 2H), 6.52 (s, 1H), 6.88 (d, $J = 8.1$ Hz, 2H), 6.98 (d, $J = 8.1$ Hz, 2H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.1$ Hz, 2H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.68-7.77 (m,

3H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.21 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 459 (M+H)⁺.

Example 73

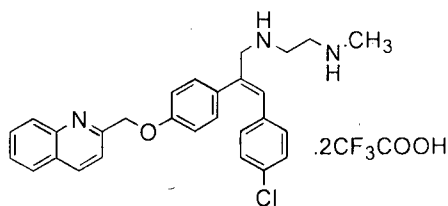
3-({3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) propanenitrile dihydrochloride



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and 3-aminopropionitrile (193 mg, 0.750 mmol) as described in Example 72 to yield 25 mg of off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) D₂O exchange δ 2.95 (t, $J = 6.9$ Hz, 2H), 3.27 (t, $J = 7.2$ Hz, 2H), 3.20 (br s, 1H), 4.03 (br s, 2H), 5.46 (s, 2H), 6.84 (s, 1H), 6.94 (d, $J = 8.1$ Hz, 2H), 7.12 (d, $J = 8.7$ Hz, 2H), 7.22 (d, $J = 8.4$ Hz, 4H), 7.72 (t, $J = 7.5$ Hz, 1H), 7.79 (d, $J = 8.4$ Hz, 1H), 7.88 (t, $J = 6.9$ Hz, 1H), 8.10 (t, $J = 7.8$ Hz, 2H), 8.60 (d, $J = 9.0$ Hz, 1H); ESI-MS (m/z) 454 (M+H)⁺.

Example 74

N-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}-*N*'-methyl ethane-1,2-diamine di(trifluoro acetic acid)

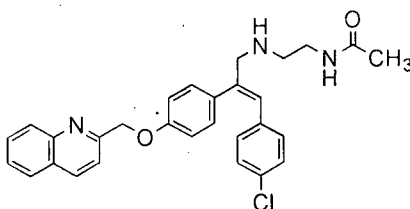


The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and *tert*-butyl (2-aminoethyl)methylcarbamate (0.13 ml, 0.750 mmol) as described in Example 70 to yield 56 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.63 (s, 3H), 3.33 (br s, 4H), 3.99 (s, 2H), 4.33 (br s, 1H), 5.40 (s, 2H), 6.74 (s, 1H), 6.89 (d, $J = 8.4$ Hz, 2H), 6.98 (d, $J = 7.8$ Hz, 2H), 7.01-7.13 (m, 5H), 7.61 (t, $J = 7.2$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 1H), 7.79 (t, $J = 7.8$ Hz, 1H).

7.88 (d, $J = 7.8$ Hz, 1H), 8.13 (d, $J = 7.8$ Hz, 1H), 8.31 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 458 ($M+H$)⁺.

Example 75

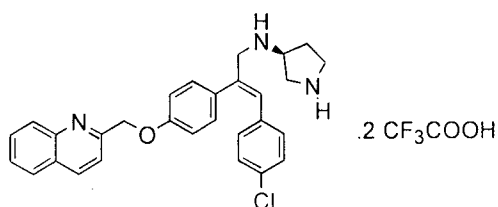
N-[2-({3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino)ethyl]acetamide



The title compound was prepared from Intermediate 41 (200 mg, 0.50 mmol) and *N*-(2-aminoethyl)acetamide (0.04 ml, 0.50 mmol) as described in Step 1 of example 70 to yield 20 mg of product as off white solid; ¹H NMR (300 MHz, CDCl₃) δ 1.86 (br s, 3H), 2.78 (br s, 2H), 3.30 (br s, 2H), 3.64 (s, 2H), 4.20 (br s, 1H), 5.38 (s, 2H), 6.04 (br s, 1H), 6.52 (s, 1H), 6.89 (d, $J = 7.8$ Hz, 2H), 6.95-7.02 (m, 2H), 7.04-7.12 (m, 4H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.66-7.77 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 9.0$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 486 ($M+H$)⁺.

Example 76

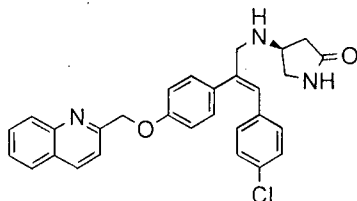
(3*S*)-*N*-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl} pyrrolidin-3-amine di(trifluoroacetic acid)



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and tert-butyl (3*S*)-3-aminopyrrolidine-1-carboxylate (0.13 ml, 0.750 mmol) as described in Example 70 to yield 57 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.07 (br s, 2H), 3.26 (br s, 4H), 3.54 (br s, 1H), 4.05 (br s, 2H), 5.39 (s, 2H), 6.82 (s, 1H), 6.95 (s, 3H), 7.12 (br s, 3H), 7.20 (br s, 4H), 7.69 (br s, 3H), 8.01 (br s, 2H), 8.45 (br s, 1H); ESI-MS (m/z) 470 ($M+H$)⁺.

Example 77

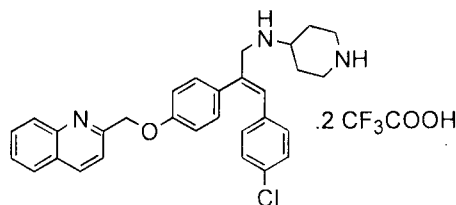
(4S)-4-({3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino)pyrrolidin-2-one



The title compound was prepared from Intermediate 41 (60 mg, 0.439 mmol) and (4S)-4-aminopyrrolidin-2-one hydrochloride (176 mg, 0.439 mmol) as described in Step 1 of Example 70 to yield 40 mg of product as white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.13-2.20 (m, 2H), 2.51-2.63 (m, 1H), 3.13-3.20 (m, 1H), 3.53-3.67 (m, 4H), 5.38 (m, 2H), 5.75 (br s, 1H), 6.52 (s, 1H), 6.88 (d, $J = 7.8$ Hz, 2H), 6.98 (d, $J = 8.1$ Hz, 2H), 7.04-7.13 (m, 4H), 7.56 (t, $J = 7.8$ Hz, 1H), 7.66-7.77 (m, 2H), 7.85 (d, $J = 8.1$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 484 ($\text{M}+\text{H}$) $^+$.

Example 78

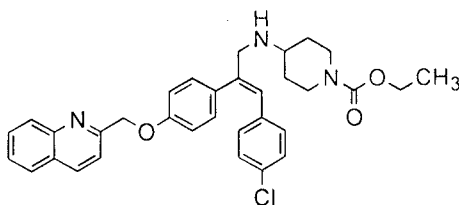
N-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}piperidin-4-amine di(trifluoroacetic acid) salt



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and *tert*-butyl 4-aminopiperidine-1-carboxylate (150 mg, 0.750 mmol) as described Example 70 to yield 52 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.76 (br s, 2H), 2.23 (br s, 3H), 2.67 (br s, 1H), 2.95 (br s, 2H), 3.40 (br s, 2H), 4.04 (s, 2H), 5.43 (s, 2H), 5.78 (br s, 1H), 6.81 (s, 1H), 6.93 (br s, 2H), 7.11 (br s, 4H), 7.18 (br s, 2H), 7.73 (br s, 2H), 7.88 (br s, 1H), 8.04 (br s, 2H), 8.51 (d, $J = 7.8$ Hz, 1H); APCI-MS (m/z) 484 ($\text{M}+\text{H}$) $^+$.

Example 79

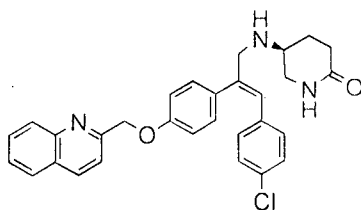
Ethyl 4-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) piperidine-1-carboxylate



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and ethyl-4-amino-piperidine carboxylate (0.12 ml, 0.750 mmol) as described in Step 1 of Example 70 to yield 24 mg of product as colourless oil; ^1H NMR (300 MHz, CDCl_3) δ 1.22-1.27 (m, 5H), 1.80 (br s, 2H), 2.69 (br s, 1H), 2.83 (t, $J = 11.1$ Hz, 2H), 3.62 (s, 2H), 4.08-4.15 (m, 4H), 4.35 (br s, 1H), 5.38 (s, 2H), 6.54 (s, 1H), 6.88 (d, $J = 8.4$ Hz, 2H), 6.98 (d, $J = 8.7$ Hz, 2H), 7.05 (d, $J = 8.7$ Hz, 2H), 7.10 (d, $J = 8.4$ Hz, 2H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.67-7.77 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 556 ($\text{M}+\text{H}$) $^+$.

Example 80

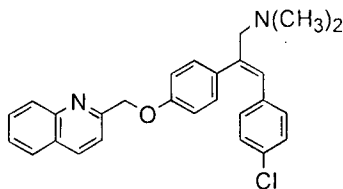
(5S)-5-({3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) piperidin-2-one



The title compound was prepared from Intermediate 41 (300 mg, 0.751 mmol) and (5S)-5-aminopiperidin-2-one (103 mg, 0.902 mmol) as described in Step 1 of Example 70 to yield 34 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.25 (s, 2H), 1.79 (br s, 1H), 2.28-2.39 (m, 1H), 2.40-2.53 (m, 1H), 3.06 (br s, 2H), 3.45 (br s, 1H), 3.62 (s, 2H), 5.38 (s, 2H), 5.82 (br s, 1H), 6.53 (s, 1H), 6.88 (d, $J = 8.4$ Hz, 2H), 6.98 (d, $J = 8.7$ Hz, 2H), 7.05-7.12 (m, 4H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.60-7.75 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 498 (M) $^+$.

Example 81

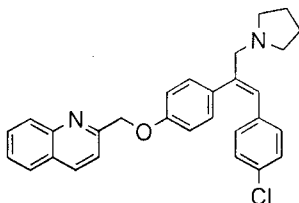
3-(4-Chlorophenyl)-*N,N*-dimethyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine



The title compound was prepared from Intermediate 41 (200 mg, 0.50 mmol) and dimethylamine (41 mg, 0.50 mmol) as described in Step 1 of Example 70 to yield 24 mg of product as white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.29 (s, 6H), 3.30 (br s, 2H), 5.37 (s, 2H), 6.54 (s, 1H), 6.89 (d, $J = 8.1$ Hz, 2H), 6.96 (d, $J = 8.7$ Hz, 2H), 7.06 (d, $J = 8.4$ Hz, 2H), 7.12 (d, $J = 8.7$ Hz, 2H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.67-7.77 (m, 2H), 7.84 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.7$ Hz, 1H), 8.21 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 429 ($\text{M}+\text{H}$) $^+$.

Example 82

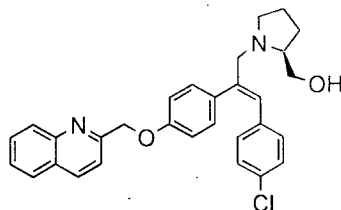
2-({4-[1-(4-Chlorophenyl)-3-(pyrrolidin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



To the well stirred solution of the Intermediate 42 (200 mg, 0.476 mmol) in DMF (10 ml) was added pyrrolidine (0.05 ml, 0.619 mmol) followed by potassium carbonate (164 mg, 1.19 mmol) and was stirred at room temperature overnight. The reaction mixture was quenched with water (20 ml), extracted with ethyl acetate (2 x 25 ml), washed with water (20 ml), brine (20 ml) and dried to yield 42 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.77 (br s, 4H), 2.56 (br s, 4H), 3.39 (s, 2H), 5.37 (s, 2H), 6.53 (s, 1H), 6.87 (d, $J = 8.1$ Hz, 2H), 6.95 (d, $J = 8.7$ Hz, 2H), 7.04 (d, $J = 8.7$ Hz, 2H), 7.13 (d, $J = 9.0$ Hz, 2H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.67-7.77 (m, 2H), 7.84 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.21 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 455 ($\text{M}+\text{H}$) $^+$.

Example 83

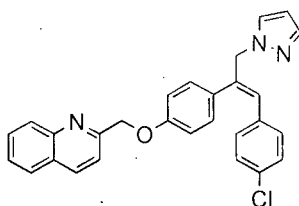
[(2*S*)-1-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrrolidin-2-yl]methanol



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and (2*S*)-pyrrolidin-2-ylmethanol (0.07 ml, 0.750 mmol) as described in Step 1 of Example 70 to yield 57 mg of product as off white solid; ¹H NMR (300 MHz, CDCl₃) δ 1.68 (br s, 2H), 1.85 (d, *J* = 8.4 Hz, 2H), 2.36 (d, *J* = 7.8 Hz, 1H), 2.69 (br s, 2H), 3.14 (br s, 2H), 3.32 (d, *J* = 10.8 Hz, 1H), 3.59 (d, *J* = 9.9 Hz, 1H), 3.81 (br s, 1H), 5.37 (s, 2H), 6.52 (s, 1H), 6.89 (d, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 8.1 Hz, 2H), 7.04-7.11 (m, 4H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.68-7.76 (m, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H); APCI-MS (*m/z*) 485 (M+H)⁺.

Example 84

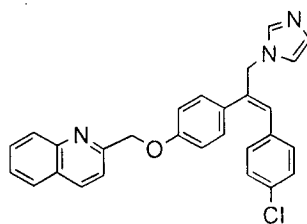
2-({4-[1-(4-Chlorophenyl)-3-(1*H*-pyrazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (150 mg, 0.352 mmol) and 1*H*-pyrazole (32 mg, 0.462 mmol) as described in Example 82 to yield 45 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.05 (s, 2H), 5.35 (s, 2H), 6.21 (s, 1H), 6.32 (s, 1H), 6.86-6.98 (m, 6H), 7.05 (d, *J* = 8.1 Hz, 2H), 7.31 (s, 1H), 7.51-7.60 (m, 2H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 6.9 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 8.21 (d, *J* = 8.7 Hz, 1H); APCI (*m/z*) 452 (M+H)⁺.

Example 85

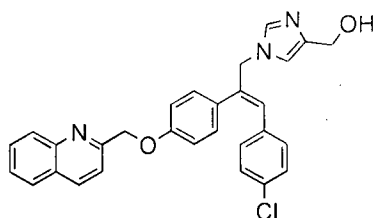
2-({4-[1-(4-Chlorophenyl)-3-(1*H*-imidazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (225 mg, 0.537 mmol) and 1*H*-imidazole (44 mg, 0.642 mmol) as described in Example 82 to yield 30 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.90 (s, 2H), 5.36 (s, 2H), 6.46 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.94 (br s, 5H), 7.08 (d, *J* = 7.8 Hz, 3H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.72-7.77 (m, 2H), 7.85 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H); ESI-MS (*m/z*) 452 (M+H)⁺.

Example 86

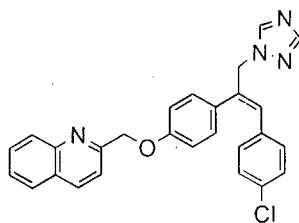
(1-({3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}-1*H*-imidazol-4-yl)methanol



The title compound was prepared from Intermediate 42 (500 mg, 1.190 mmol) and 1*H*-imidazol-4-ylmethanol (140 mg, 1.427 mmol) as described in Example 82 to yield 77 mg of the product as off white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.56 (s, 2H), 4.79 (s, 2H), 5.36 (s, 2H), 6.41 (s, 1H), 6.83-6.91 (m, 3H), 6.92-6.98 (m, 5H), 7.04-7.09 (m, 2H), 7.39 (s, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.74 (t, *J* = 6.9 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 9.0 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H); ESI-MS (*m/z*) 482 (M+H)⁺.

Example 87

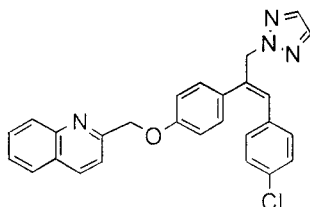
2-({4-[1-(4-Chlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (65 mg, 0.154 mmol) and 1*H*-1,2,4-triazole (13 mg, 0.185 mmol) as described in Example 82 to yield 20 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.23 (s, 2H), 5.32 (s, 2H), 6.61 (s, 1H), 6.94-7.05 (m, 6H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.62-7.69 (m, 2H), 7.79 (t, *J* = 8.1 Hz, 1H), 7.91 (s, 1H), 8.01 (d, *J* = 9.0 Hz, 2H), 8.36 (s, 1H), 8.43 (d, *J* = 8.4 Hz, 1H); ESI-MS (*m/z*) 453 (M+H)⁺.

Example 88

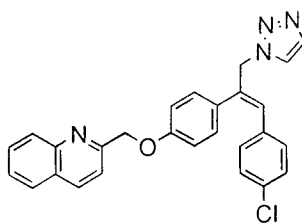
2-({4-[1-(4-Chlorophenyl)-3-(2*H*-1,2,3-triazol-2-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (350 mg, 0.833 mmol) and 2*H*-1,2,3-triazole (0.07 ml, 1.249 mmol) as described in Example 82 to yield regioisomeric mixture of products. These regioisomers were separated by silica gel column chromatography and 62 mg of the above less polar isomer was eluted out in 15 % acetone in petroleum ether solution as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.34 (s, 2H), 5.38 (s, 2H), 6.38 (s, 1H), 6.87-6.93 (m, 4H), 7.00-7.07 (m, 4H), 7.52-7.58 (m, 3H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H); ESI-MS (*m/z*) 453 (M+H)⁺.

Example 89

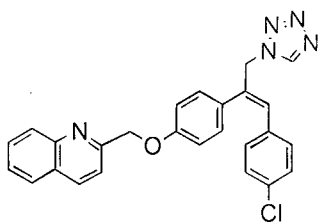
2-({4-[1-(4-Chlorophenyl)-3-(1*H*-1,2,3-triazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was the more polar isomer isolated from Example 88 and was eluted out in 20 % acetone in petroleum ether solution to give 70 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.33 (s, 2H), 5.35 (s, 2H), 6.51 (s, 1H), 6.89-7.00 (m, 6H), 7.08 (d, $J = 8.4$ Hz, 2H), 7.41 (s, 1H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.62-7.68 (m, 2H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.07 (d, $J = 8.4$ Hz, 1H), 8.21 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 453 ($\text{M}+\text{H}$) $^+$.

Example 90

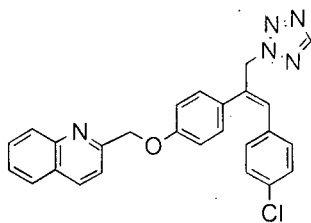
2-({4-[1-(4-Chlorophenyl)-3-(1*H*-tetrazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (400 mg, 0.952 mmol) and 1*H*-tetrazole (4.2 ml, 1.904 mmol) as described in Example 82 to yield regioisomeric mixture of products. These regioisomers were separated by silica gel column chromatography and 78 mg of the above less polar isomer was eluted out in 25 % acetone in petroleum ether solution as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.34 (s, 2H), 5.58 (s, 2H), 6.59 (s, 1H), 6.92 (d, $J = 8.1$ Hz, 4H), 7.02 (d, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.4$ Hz, 2H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.65 (d, $J = 8.4$ Hz, 1H), 7.74 (t, $J = 7.8$ Hz, 1H), 7.84 (d, $J = 8.1$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.21 (d, $J = 8.7$ Hz, 1H), 8.45 (s, 1H); ESI-MS (m/z) 454 ($\text{M}+\text{H}$) $^+$.

Example 91

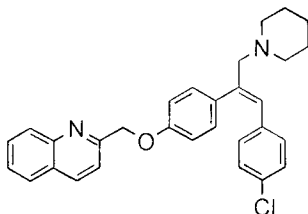
2-({4-[1-(4-Chlorophenyl)-3-(2*H*-tetrazol-2-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was the more polar isomer isolated from Example 90 and was eluted out in 28 % acetone in petroleum ether solution to give 92 mg of off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.36 (br s, 4H), 6.65 (s, 1H), 6.91-6.96 (m, 6H), 7.10 (d, $J = 8.4$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.65 (d, $J = 8.4$ Hz, 1H), 7.75 (t, $J = 7.2$ Hz, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H), 8.34 (s, 1H); ESI-MS (m/z) 454 ($\text{M}+\text{H}$) $^+$.

Example 92

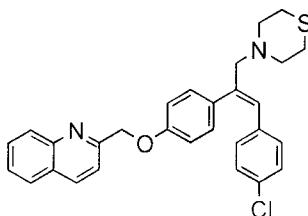
2-({4-[1-(4-Chlorophenyl)-3-(piperidin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (5 g, 11.26 mmol) and piperidine (0.52 ml, 0.5711 mmol) as described in Example 82 to yield 16 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.58 (br s, 6H), 3.35 (br s, 4H), 4.87 (s, 2H), 5.38 (s, 2H), 6.55 (s, 1H), 6.90-6.99 (m, 4H), 7.04-7.14 (m, 4H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.67-7.77 (m, 2H), 7.84 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.21 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 469 ($\text{M}+\text{H}$) $^+$.

Example 93

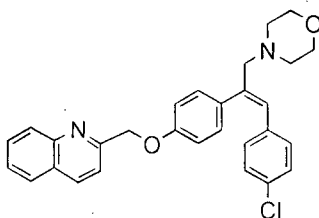
2-({4-[1-(4-Chlorophenyl)-3-(thiomorpholin-4-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (150 mg, 0.357 mmol) and thiomorpholine (0.04 ml, 0.428 mmol) as described in Example 82 to yield 55 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.65 (br s, 4H), 2.75 (br s, 4H), 3.26 (s, 2H), 5.38 (s, 2H), 6.49 (s, 1H), 6.87 (d, $J = 8.1$ Hz, 2H), 6.95 (d, $J = 8.1$ Hz, 2H), 7.04-7.12 (m, 4H), 7.56 (t, $J = 8.1$ Hz, 1H), 7.67-7.77 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.7$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); APCI-MS (m/z) 488 ($\text{M}+\text{H}$) $^+$.

Example 94

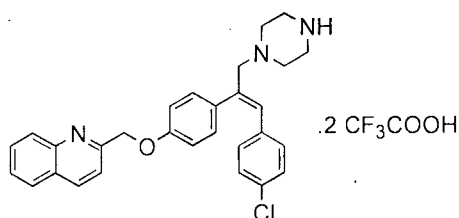
2-({4-[1-(4-Chlorophenyl)-3-(morpholin-4-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (240 mg, 0.571 mmol) and morpholine (0.09 ml, 1.142 mmol) as described in Example 82 to yield 103 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.51 (br s, 4H), 3.24 (s, 2H), 3.70 (br s, 4H), 5.38 (s, 2H), 6.51 (s, 1H), 6.88 (d, $J = 8.4$ Hz, 2H), 6.95 (d, $J = 8.7$ Hz, 2H), 7.05 (d, $J = 8.1$ Hz, 2H), 7.13 (d, $J = 8.7$ Hz, 2H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.68-7.77 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 471 ($\text{M}+\text{H}$) $^+$.

Example 95

2-({4-[1-(4-Chlorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline di(trifluoro acetic acid)

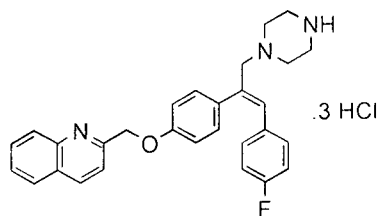


The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and 1-BOC piperazine (140 mg, 0.750 mmol) as described in Example 70 to yield 45 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.18 (br s, 4H), 3.33 (br s, 4H), 3.50 (br s, 1H), 3.75

(s, 2H), 5.51 (s, 2H), 6.65 (s, 1H), 6.89 (d, $J = 7.8$ Hz, 2H), 6.98 (d, $J = 8.1$ Hz, 2H), 7.06-7.12 (m, 4H), 7.67 (br s, 1H), 7.83-7.88 (m, 2H), 7.94 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H), 8.45 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 470 ($M+H$)⁺.

Example 96

2-({4-[1-(4-Fluorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline trihydrochloride



Step 1: 2-({4-[1-(4-Fluorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline:

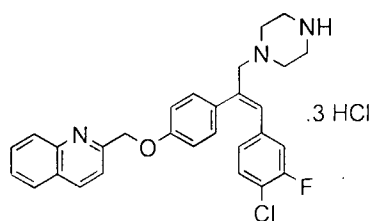
The title compound was prepared from Intermediate 43 (590 mg, 1.302 mmol) and N-BOC piperazine (485 mg, 2.604 mmol) as described in Example 82.

Step 2: 2-({4-[1-(4-Fluorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline trihydrochloride:

Excess of HCl gas in ethyl acetate was added to Step 1 BOC intermediate at 0°C and stirred for 2 h. HCl was removed by bubbling nitrogen gas through the reaction mixture and the solid obtained was purified by diethyl ether to yield 200 mg of off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 2.26 (br s, 1H), 3.35 (br s, 8H), 4.23 (br s, 2H), 5.43 (br s, 2H), 6.97 (d, $J = 5.4$ Hz, 5H), 7.09 (d, $J = 7.8$ Hz, 2H), 7.23 (d, $J = 8.1$ Hz, 2H), 7.69-7.79 (m, 2H), 7.87 (br s, 1H), 8.08 (br s, 2H), 8.59 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 454 ($M+H$)⁺.

Example 97

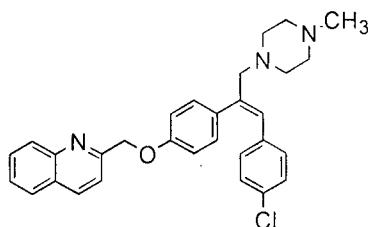
2-({4-[1-(4-Chloro-3-fluorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline trihydrochloride



The title compound was prepared from Intermediate 45 (350 mg, 0.799 mmol) and 1-BOC piperazine (298 mg, 1.598 mmol) as described in Example 96 to yield 252 mg of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.25 (br s, 1H), 3.39 (br s, 8H), 4.30 (s, 2H), 5.50 (s, 2H), 6.79-6.87 (m, 2H), 7.05 (s, 1H), 7.12 (d, $J = 8.4$ Hz, 2H), 7.26 (d, $J = 8.4$ Hz, 2H), 7.37 (t, $J = 7.8$ Hz, 1H), 7.73 (t, $J = 7.2$ Hz, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 7.91 (t, $J = 7.2$ Hz, 1H), 8.11-8.17 (m, 2H), 8.70 (d, $J = 9.0$ Hz, 1H); ESI-MS (m/z) 488 ($\text{M}+\text{H}$) $^+$.

Example 98

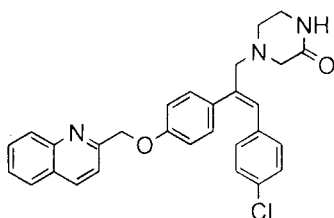
2-({4-[1-(4-Chlorophenyl)-3-(4-methylpiperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 41 (300 mg, 0.750 mmol) and 1-methyl piperazine (0.083 ml, 0.750 mmol) as described in Step 1 of Example 70 to yield 72 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.30 (s, 3H), 2.47 (br s, 4H), 2.56 (br s, 4H), 3.26 (s, 2H), 5.38 (s, 2H), 6.50 (s, 1H), 6.88 (d, $J = 8.1$ Hz, 2H), 6.95 (d, $J = 8.4$ Hz, 2H), 7.05 (d, $J = 8.7$ Hz, 2H), 7.12 (d, $J = 8.7$ Hz, 2H), 7.56 (t, $J = 7.8$ Hz, 1H), 7.68-7.77 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.7$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 484 ($\text{M}+\text{H}$) $^+$.

Example 99

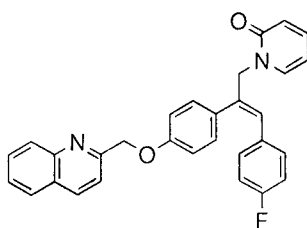
4-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}piperazin-2-one



The title compound was prepared from Intermediate 41 (200 mg, 0.500 mmol) and piperazin-2-one (50 mg, 0.500 mmol) as described in Step 1 of Example 70 to yield 52 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.71 (t, $J = 5.1$ Hz, 2H), 3.21 (s, 2H), 3.36 (br s, 4H), 5.38 (s, 2H), 6.02 (d, $J = 19.8$ Hz, 1H), 6.52 (s, 1H), 6.88 (d, $J = 9.0$ Hz, 2H), 6.95 (d, $J = 8.7$ Hz, 2H), 7.06 (d, $J = 8.4$ Hz, 2H), 7.11 (d, $J = 8.7$ Hz, 2H), 7.56 (t, $J = 7.8$ Hz, 1H), 7.67-7.77 (m, 2H), 7.84 (d, $J = 8.1$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 484 ($\text{M}+\text{H}$) $^+$.

Example 100

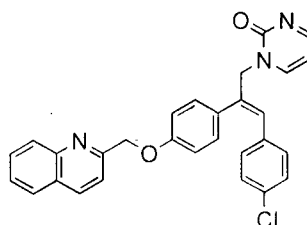
1-{3-(4-Fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyridin-2(1*H*)-one



The title compound was prepared from Intermediate 43 (200 mg, 0.491 mmol) and pyridin-2(1*H*)-one (70.70 mg, 0.743 mmol) as described in Example 82 to yield 39 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.91 (s, 2H), 5.35 (s, 2H), 6.06 (t, $J = 6.9$ Hz, 1H), 6.45 (s, 1H), 6.53 (d, $J = 9.3$ Hz, 1H), 6.76 (t, $J = 8.7$ Hz, 2H), 6.91-6.97 (m, 4H), 7.09 (d, $J = 8.7$ Hz, 2H), 7.17 (d, $J = 6.9$ Hz, 1H), 7.23 (s, 1H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.67 (d, $J = 8.1$ Hz, 1H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.84 (d, $J = 8.1$ Hz, 1H), 8.08 (d, $J = 9.0$ Hz, 1H), 8.21 (d, $J = 9.0$ Hz, 1H); ESI-MS (m/z) 463 ($\text{M}+\text{H}$) $^+$.

Example 101

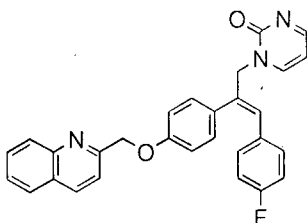
1-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-2(1*H*)-one



The title compound was prepared from Intermediate 41 (200 mg, 0.476 mmol) and pyrimidin-2(1*H*)-one hydrochloride (76 mg, 0.571 mmol) as described in Step 1 of Example 70 to yield 38 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.89 (s, 2H), 5.38 (s, 2H), 6.11-6.16 (m, 1H), 6.46 (s, 1H), 6.90-6.97 (m, 4H), 7.04-7.10 (m, 4H), 7.40-7.44 (m, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.77 (t, *J* = 8.1 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 8.49 (br s, 1H); APCI-MS (*m/z*) 480 (M+H)⁺.

Example 102

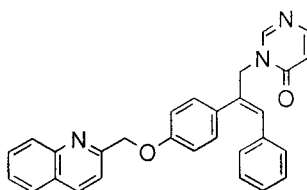
1-{3-(4-Fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-2(1*H*)-one



The title compound was prepared from Intermediate 43 (200 mg, 0.495 mmol) and pyrimidin-2(1*H*)-one hydrochloride (79 mg, 0.594 mmol) as described in Example 82 to yield 78 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.89 (s, 2H), 5.35 (s, 2H), 6.10-6.14 (m, 1H), 6.66 (s, 1H), 6.79 (t, *J* = 8.4 Hz, 2H), 6.91-6.97 (m, 4H), 7.06 (d, *J* = 8.7 Hz, 2H), 7.41-7.45 (m, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.7 Hz, 1H), 8.48 (br s, 1H); APCI-MS (*m/z*) 464 (M+H)⁺.

Example 103

3-{3-Phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-4(3*H*)-one

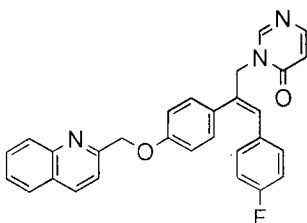


The title compound was prepared from Intermediate 44 (200 mg, 0.518 mmol) and pyrimidin-4(3*H*)-one (60 mg, 0.621 mmol) as described in Example 82 to yield 30 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.90 (s, 2H), 5.35 (s, 2H), 6.40 (d, *J* = 6.3 Hz, 1H),

6.63 (s, 1H), 6.90-6.97 (m, 4H), 7.11 (br s, 5H), 7.56 (t, $J = 7.8$ Hz, 1H), 7.68 (d, $J = 9.0$ Hz, 1H), 7.72-7.80 (m, 2H), 7.84 (d, $J = 8.1$ Hz, 1H), 7.94 (s, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 446 ($M+H$)⁺.

Example 104

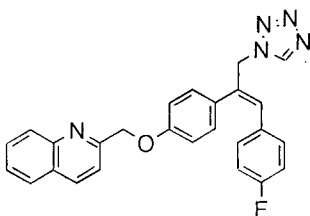
3-{3-(4-Fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-4(3H)-one



The title compound was prepared from Intermediate 43 (300 mg, 0.743 mmol) and pyrimidin-4(3H)-one (86 mg, 0.892 mmol) as described in Example 82 to yield 130 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.88 (s, 2H), 5.36 (s, 2H), 6.40 (d, $J = 6.9$ Hz, 1H), 6.59 (s, 1H), 6.79 (t, $J = 8.4$ Hz, 2H), 6.92-6.98 (m, 4H), 7.07 (d, $J = 8.7$ Hz, 2H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.67 (d, $J = 8.7$ Hz, 1H), 7.72-7.83 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 7.91 (s, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 464 ($M+H$)⁺.

Example 105

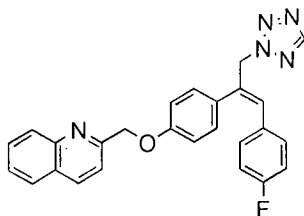
2-({4-[1-(4-Fluorophenyl)-3-(1H-tetrazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 43 (400 mg, 0.991 mmol) and 1H-tetrazole (4.5 ml, 1.982 mmol) as described in Example 82 to yield 119 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.34 (s, 2H), 5.58 (s, 2H), 6.62 (s, 1H), 6.81 (t, $J = 8.1$ Hz, 2H), 6.91-7.03 (m, 6H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.66 (d, $J = 8.4$ Hz, 1H), 7.74 (t, $J = 7.8$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.21 (d, $J = 8.4$ Hz, 1H), 8.45 (s, 1H); APCI-MS (m/z) 438 ($M+H$)⁺.

Example 106

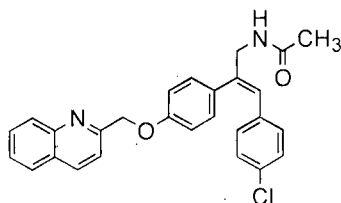
2-({4-[1-(4-Fluorophenyl)-3-(2*H*-tetrazol-2-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 43 (400 mg, 0.991 mmol) and 2*H*-tetrazole (4.5 ml, 1.982 mmol) as described in Example 82 to yield 148 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.35 (s, 4H), 6.68 (s, 1H), 6.83 (t, *J* = 8.4 Hz, 2H), 6.96 (br s, 6H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.75 (t, *J* = 7.2 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 8.33 (s, 1H); APCI-MS (*m/z*) 438 (M+H)⁺.

Example 107

N-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}acetamide



Step 1: 2-({4-[3-Azido-1-(4-chlorophenyl)prop-1-en-2-yl]phenoxy}methyl) quinoline:

To the well stirred solution of Intermediate 42 (1.7 g, 4.045 mmol) in dimethylformamide (25 ml) was added sodium azide (1.05 g, 16.18 mmol) and the reaction mixture was heated to 60°C and stirred at the same temperature overnight. The reaction mixture was diluted with water (250 ml) and extracted with ethyl acetate (250 ml x 2). The combined organic layers were washed with water (50 ml x 2) and brine (50 ml), dried over anhydrous Na₂SO₄ and concentrated to yield 1.35 g of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.31 (s, 2H), 5.43 (s, 2H), 6.92-7.01 (m, 4H), 7.05-7.15 (m, 4H), 7.47 (d, *J* = 8.7 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.67-7.83 (m, 2H), 7.84 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 8.21 (d, *J* = 8.7 Hz, 1H).

Step 2: 3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine:

To the well stirred solution of Step 1 Intermediate (500 mg, 1.171 mmol) in dry THF (10 ml) was added triphenylphosphine (338 mg, 1.288 mmol) and the reaction mixture was stirred for 3 h at room temperature. Water was then added to the reaction mixture and was further stirred overnight. The reaction mixture was diluted with water (100 ml) and extracted with ethyl acetate (150 ml x 2). The combined organic layers were washed with water (50 ml x 2) and brine (50 ml), dried (Na_2SO_4) and concentrated to yield 750 mg of product as off-white solid.

Step 3: 3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine hydrochloride:

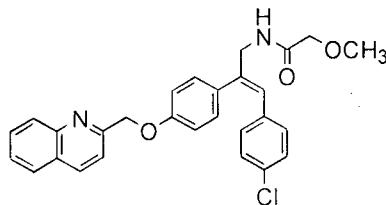
To the well stirred solution of Step 2 Intermediate (750 mg, 1.872 mmol) in acetonitrile (15 ml) was added TEA (0.52 ml, 3.745 mmol), water (0.5 ml) and BOC anhydride (450 mg, 2.059 mmol) and the reaction mixture was stirred at room temperature for 6 h. The reaction mixture was diluted with water (50 ml) and extracted with ethyl acetate (100 ml x 2). The combined organic layers were washed with water (50 ml x 2) and brine (50 ml), dried over anhydrous Na_2SO_4 and concentrated. The crude compound was purified by silica gel chromatography to yield 150 mg of product. The *tert*-butyl {3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl} carbamate so formed was deprotected using HCl gas in ethyl acetate to yield 200 mg of its hydrochloride salt.

Step 4: *N*-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}acetamide:

To the well stirred solution of Step 3 crude Intermediate (200 mg, 0.499 mmol) in dichloromethane (10 ml) were added triethylamine (0.27 ml, 1.997 mmol) and acetic acid (0.07 ml, 0.749 mmol) and the reaction was stirred at room temperature for 4 h. The reaction mixture was diluted with water (50 ml) and extracted with chloroform (100 ml x 2). The combined organic layers were washed with water (20 ml x 2) and brine (20 ml), dried over anhydrous Na_2SO_4 and concentrated to yield 90 mg of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.82 (s, 3H), 4.01 (br s, 2H), 5.36 (s, 2H), 6.43 (s, 1H), 6.91 (d, $J = 7.8$ Hz, 2H), 7.04-7.09 (m, 4H), 7.16 (d, $J = 7.8$ Hz, 2H), 7.62-7.70 (m, 2H), 7.75-7.81 (m, 1H), 8.00 (br s, 2H), 8.14 (br s, 1H), 8.43 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 443 ($\text{M}+\text{H}$) $^+$.

Example 108

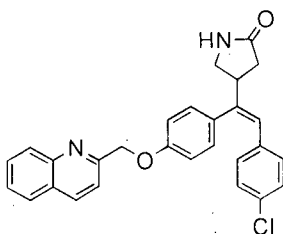
N-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}-2-methoxyacetamide



The title compound was prepared from 3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine hydrochloride (Step 3 of Example 107; 150 mg, 0.374 mmol) and methoxyacetyl chloride (0.05 ml, 5.617 mmol) as described in Example 107 to yield 51 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.28 (s, 3H), 3.86 (s, 2H), 4.28 (d, $J = 6.0$ Hz, 2H), 5.37 (s, 2H), 6.48 (s, 1H), 6.62 (br s, 1H), 6.89 (d, $J = 8.4$ Hz, 2H), 6.97 (d, $J = 8.7$ Hz, 2H), 7.05-7.12 (m, 4H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.68 (d, $J = 8.1$ Hz, 1H), 7.74 (t, $J = 7.2$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.21 (d, $J = 9.0$ Hz, 1H); ESI-MS (m/z) 473 ($\text{M}+\text{H}$) $^+$.

Example 109

4-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}pyrrolidin-2-one



Step 1: Ethyl-5-(4-chlorophenyl)-4-[4-(quinolin-2-ylmethoxy)phenyl]penta-2,4-dienoate:

To the well stirred solution of Intermediate 42 (1 g, 2.502 mmol) in toluene (30 ml) was added (carbethoxymethylene)triphenylphosphorane (1.04 g, 3.00 mmol) and the reaction mixture was heated overnight at 120 °C. The reaction mixture was quenched with water (50 ml), extracted with ethyl acetate (2 x 100 ml), washed with water (2 x 50 ml), brine (25 ml) and dried. The crude product obtained was purified by silica gel column chromatography to yield 900 mg of the product; ^1H NMR (300 MHz, CDCl_3) δ 1.26 (t, $J = 7.5$ Hz, 3H), 4.18 (q, $J = 7.2$ Hz, 2H), 5.42 (s, 2H), 5.54 (d, $J = 15.3$ Hz, 1H), 6.82-6.88 (m, 3H), 7.02-7.09 (m, 6H), 7.56 (d, $J = 7.2$ Hz, 1H),

7.63 (d, $J = 15.6$ Hz, 1H), 7.71-7.78 (m, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H).

Step 2: Ethyl-5-(4-chlorophenyl)-3-(nitromethyl)-4-[4-(quinolin-2-ylmethoxy)phenyl]pent-4-enoate:

To a well stirred solution of Step 2 Intermediate (900 mg, 1.916 mmol) in nitromethane (20 ml) was added 1,1,3,3-tetramethylguanidine (441 mg, 3.833 mmol) and the reaction was heated at 120 °C for 3h. The reaction mixture was quenched with water (50 ml), extracted with ethyl acetate (2 x 100 ml), washed with water (2 x 50 ml), brine (25 ml) and dried. The crude product obtained was purified by silica gel column chromatography to yield 520 mg of the product; ^1H NMR (300 MHz, CDCl_3) δ 1.23 (t, $J = 6.9$ Hz, 3H), 2.91 (d, $J = 6.9$ Hz, 2H), 4.07-4.18 (m, 2H), 4.60-4.68 (m, 1H), 4.77-4.86 (m, 1H), 5.39 (br s, 2H), 5.77 (t, $J = 6.9$ Hz, 1H), 6.73-6.82 (m, 1H), 6.93 (d, $J = 8.7$ Hz, 1H), 7.01-7.09 (m, 3H), 7.24 (br s, 4H), 7.56 (t, $J = 7.5$ Hz, 1H), 7.66 (d, $J = 9.0$ Hz, 1H), 7.75 (t, $J = 7.2$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 9.0$ Hz, 1H), 8.18-8.25 (m, 1H).

Step 3: Ethyl-3-(aminomethyl)-5-(4-chlorophenyl)-4-[4-(quinolin-2-ylmethoxy)phenyl] pent-4-enoate:

To the well stirred solution of Step 2 Intermediate (500 mg, 0.942 mmol) in ethanol (10 ml) was added aqueous solution of ammonium chloride (505 mg, 9.425 mmol) and the reaction was heated to reflux. At reflux temperature, iron powder (158 mg, 2.827 mmol) was added to the reaction mixture and it was further refluxed for 0.5 h. The reaction mixture was filtered and the filtrate was extracted with ethyl acetate (2 x 100 ml). The combined organic layer was washed with water (25 ml), brine (25 ml), dried over anhydrous Na_2SO_4 and concentrated to yield 100 mg of the crude product; ^1H NMR (300 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3H), 2.98 (t, $J = 7.5$ Hz, 2H), 3.98-4.10 (m, 5H), 5.33 (br s, 2H), 5.94 (br s, 2H), 7.10-7.21 (m, 4H), 7.51-7.63 (m, 3H), 7.68-7.80 (m, 4H), 8.05 (d, $J = 8.4$ Hz, 2H), 8.13-8.21 (m, 2H).

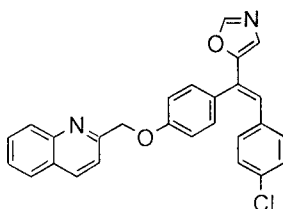
Step 4: 4-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}pyrrolidin-2-one:

The Step 3 Intermediate (100 mg, 0.199 mmol) was dissolved in xylene (20 ml) and refluxed for 2 h. The reaction mixture was dried and concentrated to yield the crude product which was purified by silica gel column chromatography to yield 30 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.44-2.50 (m, 2H), 3.45-3.56 (m, 3H), 5.39 (s, 2H), 5.52 (br s,

1H), 6.40 (s, 1H), 6.80 (d, $J = 8.4$ Hz, 2H), 6.99-7.06 (m, 6H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.66-7.74 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H), APCI (m/z) 455 ($M+H$)⁺.

Example 110

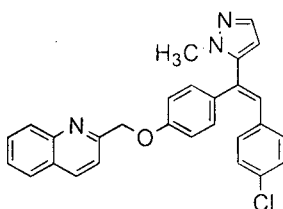
2-({4-[2-(4-Chlorophenyl)-1-(1,3-oxazol-5-yl)ethenyl]phenoxy}methyl)quinoline



To the well stirred solution of Intermediate 41 (100 mg, 0.250 mmol) in methanol (10 ml) was added p-toluenesulfonylmethyl isocyanide (54 mg, 0.275 mmol) followed by potassium carbonate (104 mg, 0.750 mmol) and the reaction mixture was refluxed for 2 h. Methanol was distilled out under reduced pressure and reaction mass was quenched with water. The compound was extracted with ethyl acetate (2 x 25 ml), washed with water (2 x 25 ml), brine (25 ml), dried and concentrated to yield the crude product. The compound was purified by silica gel column chromatography to yield 78 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.43 (s, 2H), 6.65 (s, 1H), 6.93 (d, $J = 8.1$ Hz, 2H), 7.05-7.10 (m, 5H), 7.20 (d, $J = 8.4$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.71-7.78 (m, 2H), 7.83-7.89 (m, 2H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 439 ($M+H$)⁺.

Example 111

2-({4-[2-(4-Chlorophenyl)-1-(1-methyl-1H-pyrazol-5-yl)ethenyl]phenoxy}methyl)quinoline



Step 1: 2-({4-[2-(4-chlorophenyl)-1-(1H-pyrazol-5-yl)ethenyl]phenoxy}methyl)quinoline: To the well stirred suspension of sodium hydride (100 mg, 2.503 mmol) in dry THF (15 ml) was added a solution of diethyl (2-{2-[(4-methylphenyl)sulfonyl]hydrazinylidene}ethyl)phosphonate

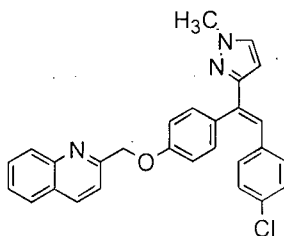
(653 mg, 1.877 mmol) in THF at 0 °C and the reaction mixture was stirred for 30 minutes at the same temperature. A solution of Intermediate 41 (500 mg, 1.251 mmol) in THF was added to the reaction mixture and it was stirred at room temperature for 1 h. The reaction was quenched with water, neutralized with dilute HCl and extracted with ethyl acetate. The combined organic layers were washed with water, brine, dried and concentrated to yield the crude product. The compound was purified by silica gel column chromatography to yield 595 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.52 (s, 2H), 6.35 (s, 1H), 6.93-7.01 (m, 2H), 7.05-7.11 (m, 5H), 7.20 (d, *J* = 8.4 Hz, 3H), 7.53 (br s, 1H), 7.62 (br s, 1H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 8.1 Hz, 3H), 8.23-8.35 (m, 2H).

Step 2: 2-({4-[2-(4-Chlorophenyl)-1-(1-methyl-1*H*-pyrazol-5-yl)ethenyl]phenoxy}methyl)quinoline:

To the well stirred solution of Step 1 Intermediate (590 mg, 1.348 mmol) in DMF (20 ml) were added cesium carbonate (527 mg, 1.618 mmol) followed by methyl iodide (0.21 ml, 3.371 mmol) and the reaction mixture was stirred at room temperature for 16 h. The reaction was quenched with water (50 ml) and extracted with ethyl acetate (2 x 50 ml). The combined organic layers were washed with water (2 x 50 ml), brine (50 ml), dried and concentrated to yield the regioisomeric mixture of products. These regioisomers were separated by silica gel column chromatography and 29 mg of the above less polar isomer was eluted out in 25 % ethyl acetate in petroleum ether solution as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 3.81 (s, 3H), 5.40 (s, 2H), 6.13 (s, 1H), 6.96 (d, *J* = 7.8 Hz, 2H), 7.10-7.18 (m, 6H), 7.64 (br s, 1H), 7.71-7.80 (m, 2H), 8.01 (br s, 2H), 8.46 (d, *J* = 7.8 Hz, 1H); ESI-MS (*m/z*) 452 (M+H)⁺.

Example 112

2-({4-[2-(4-Chlorophenyl)-1-(1-methyl-1*H*-pyrazol-3-yl)ethenyl]phenoxy}methyl)quinoline

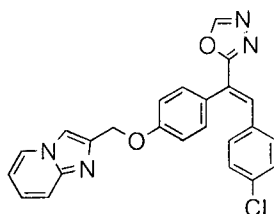


The title compound was the more polar isomer isolated from Example 111 and was eluted out in 30 % ethyl acetate in petroleum ether solution to give 15 mg of off-white solid; ¹H NMR (300

MHz, DMSO- d_6) δ 3.51 (s, 3H), 5.38 (s, 2H), 6.22 (s, 1H), 6.83 (s, 1H), 7.08 (s, 4H), 7.12 (s, 2H), 7.25 (d, $J = 8.4$ Hz, 2H), 7.40 (s, 1H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.79 (t, $J = 7.5$ Hz, 1H), 8.01 (d, $J = 8.4$ Hz, 2H), 8.44 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 452 ($M+H$)⁺.

Example 113

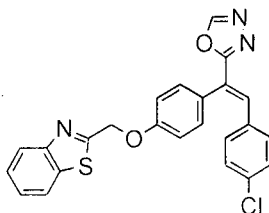
2-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)vinyl]phenoxy}methyl)imidazo[1,2-*a*]pyridine



To a well stirred solution of Intermediate 47 (200 mg, 0.477 mmol) in triethyl orthoformate (10 ml) was added p-toluenesulfonic acid (PTSA) (18 mg, 0.095 mmol) and the reaction mixture was heated to 90-100 °C for 3 h. The reaction mixture was diluted with water (10 ml) and extracted with ethyl acetate (25 ml x 2). The combined organic layers were washed with water (20 ml x 2) and brine (15 ml), dried over anhydrous Na₂SO₄ and concentrated to give crude product. The crude product was purified by silica gel column chromatography using 0.5 to 1% methanol in chloroform to yield 25 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.33 (s, 2H), 6.82 (t, $J = 6.3$ Hz, 1H), 7.07 (d, $J = 9.6$ Hz, 4H), 7.17 (d, $J = 8.7$ Hz, 2H), 7.21-7.28 (m, 3H), 7.59-7.68 (m, 3H), 8.12 (d, $J = 6.9$ Hz, 1H), 8.39 (s, 1H); ESI (m/z) 429 ($M+H$)⁺.

Example 114

2-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1,3-benzothiazole

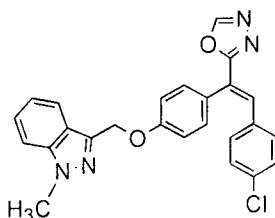


The title compound was prepared from Intermediate 48 (250 mg, 0.574 mmol) and excess of triethyl orthoformate (7 ml) as described in Example 113 to yield 70 mg of product as off-white

solid; ^1H NMR (300 MHz, CDCl_3) δ 5.53 (s, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 7.12 (q, $J = 8.4$ Hz, 4H), 7.30 (br s, 2H), 7.43 (t, $J = 7.5$ Hz, 1H), 7.54 (t, $J = 7.2$ Hz, 1H), 7.64 (s, 1H), 7.93 (d, $J = 8.1$ Hz, 1H), 8.05 (d, $J = 7.8$ Hz, 1H), 8.39 (s, 1H); ESI-MS (m/z) 446 ($\text{M}+\text{H}$) $^+$.

Example 115

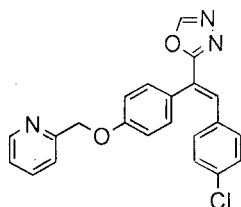
3-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-methyl-1*H*-indazole



The title compound was prepared from Intermediate 49 (300 mg, 0.693 mmol) and excess of triethyl orthoformate (7 ml) as described in Example 113 to yield 25 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.09 (s, 3H), 5.47 (s, 2H), 7.03 (d, $J = 8.1$ Hz, 2H), 7.11-7.16 (m, 4H), 7.19-7.25 (m, 3H), 7.42 (br s, 2H), 7.63 (s, 1H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.38 (s, 1H); APCI-MS (m/z) 443 ($\text{M}+\text{H}$).

Example 116

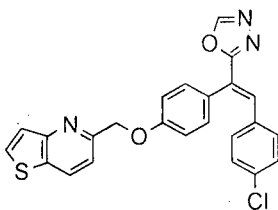
2-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)pyridine



The title compound was prepared from Intermediate 50 (200 mg, 0.527 mmol) and excess of triethyl orthoformate (7 ml) as described in Example 113 to give 56 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.25 (s, 2H), 7.05 (d, $J = 8.4$ Hz, 4H), 7.17 (d, $J = 8.1$ Hz, 2H), 7.24 (br s, 3H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.63 (s, 1H), 7.75 (t, $J = 7.2$ Hz, 1H), 8.39 (s, 1H), 8.61 (d, $J = 3.9$ Hz, 1H); APCI (m/z) 390 ($\text{M}+\text{H}$) $^+$.

Example 117

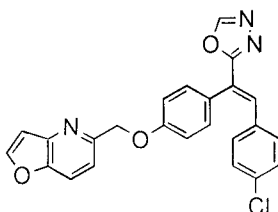
5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)thieno[3,2-*b*]pyridine



The title compound was prepared from Intermediate 51 (300 mg, 0.688 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 78 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.37 (s, 2H), 7.06 (t, $J = 8.7$ Hz, 4H), 7.16 (d, $J = 8.4$ Hz, 2H), 7.24 (br s, 2H), 7.53-7.59 (m, 2H), 7.63 (s, 1H), 7.81 (d, $J = 5.4$ Hz, 1H), 8.25 (d, $J = 8.4$ Hz, 1H), 8.39 (s, 1H); APCI-MS (m/z) 446 ($\text{M}+\text{H}$) $^+$.

Example 118

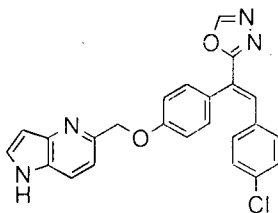
5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)furo[3,2-*b*]pyridine



The above compound was prepared from Intermediate 52 (400 mg, 0.953 mmol) and excess of triethyl orthoformate (10 ml) as described in Example 113 to yield 55 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.31 (s, 2H), 7.10-7.16 (m, 5H), 7.23-7.32 (m, 4H), 7.53 (d, $J = 8.1$ Hz, 1H), 7.66 (s, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.36 (s, 1H), 9.26 (s, 1H); APCI-MS (m/z) 430 ($\text{M}+\text{H}$) $^+$.

Example 119

5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1*H*-pyrrolo[3,2-*b*]pyridine



Step 1: 5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrolo[3,2-*b*]pyridine:

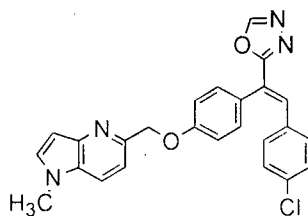
To the well stirred solution of Intermediate 46 (151 mg, 0.189 mmol) in DMF (20 ml) were added cesium carbonate (246 mg, 0.953 mmol) and {1-[(4-methylphenyl)sulfonyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}methyl 4-methyl benzenesulfonate (290 mg, 0.635 mmol) and the reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with water (20 ml) and extracted with ethyl acetate (2 x 20 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 150 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.36 (s, 3H), 5.28 (s, 2H), 6.87 (br s, 1H), 7.04 (d, *J* = 8.4 Hz, 4H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.22-7.28 (m, 4H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.63 (s, 1H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.83 (br s, 1H), 8.31 (d, *J* = 8.1 Hz, 1H), 8.39 (s, 1H).

Step 2: 5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1*H*-pyrrolo[3,2-*b*]pyridine:

To the well stirred solution of Step 1 Intermediate (150 mg, 0.349 mmol) in methanol (15 ml) was added aqueous sodium hydroxide (140 mg, 3.49 mmol) and the reaction mixture was stirred at room temperature for 15 min. The reaction mixture was diluted with water (20 ml) and extracted with ethyl acetate (2 x 20 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to yield 50 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.36 (s, 2H), 6.76 (s, 1H), 7.05 (t, *J* = 9 Hz, 4H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.22 (br s, 2H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.48 (br s, 1H), 7.62 (s, 1H), 7.72 (br s, 1H), 8.39 (s, 1H), 8.55 (br s, 1H); ESI-MS (*m/z*) 429 (M+H)⁺.

Example 120

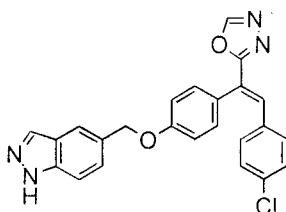
5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-methyl-1*H*-pyrrolo[3,2-*b*]pyridine



The title compound was prepared from Intermediate 53 (200 mg, 0.462 mmol) and excess of triethyl orthoformate (10 ml) as described in Example 113 to yield 70 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 3.83 (s, 3H), 5.28 (s, 2H), 6.55 (s, 1H), 7.09-7.16 (m, 4H), 7.22 (d, $J = 8.1$ Hz, 2H), 7.27-7.35 (m, 3H), 7.65 (s, 2H), 7.92 (d, $J = 8.4$ Hz, 1H), 9.22 (s, 1H); ESI-MS (m/z) 443 ($\text{M}+\text{H}$) $^+$.

Example 121

5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1*H*-indazole



Step 1: *tert*-Butyl 5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy} methyl)-1*H*-indazole-1-carboxylate:

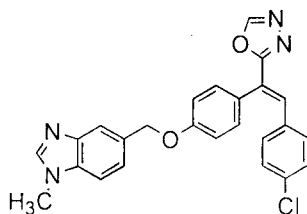
To the well stirred solution of Intermediate 46 (250 mg, 0.830 mmol) in THF (15 ml) were added triphenylphosphine (330 mg, 1.25 mmol) and *tert*-butyl 5-(hydroxymethyl)-1*H*-indazole-1-carboxylate (208 mg, 0.830 mmol). The reaction was stirred at room temperature for 15 mins followed by drop wise addition of diethylazodicarboxylate (0.19 ml, 1.25 mmol) and the reaction mixture was further stirred for 16 h. The excess solvent was distilled under reduced pressure and purified by silica gel column chromatography to yield 160 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.64 (s, 9H), 5.38 (s, 2H), 7.10-7.17 (m, 3H), 7.24-7.30 (m, 3H), 7.47 (d, $J = 7.8$ Hz, 1H), 7.66 (s, 1H), 7.91 (d, $J = 8.4$ Hz, 1H), 8.22 (s, 1H), 8.42 (s, 1H), 8.99 (s, 1H), 9.26 (s, 1H).

Step 2: 5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1*H*-indazole:

To a well stirred solution of the Step 1 Intermediate (180 mg, 0.340 mmol) in dichloromethane (3 ml) was added trifluoroacetic acid (3 ml) at 0 °C and the reaction was continued for 4 h. The reaction mixture was diluted with water and neutralized with sodium bicarbonate. The aqueous layer was extracted with ethyl acetate (3 x 50 ml), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to yield the crude product. The product was purified by silica gel column chromatography to yield 51 mg of an off-white salt; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.26 (s, 2H), 7.07-7.12 (m, 5H), 7.18-7.25 (m, 4H), 7.62 (s, 2H), 7.78 (d, *J* = 8.1 Hz, 1H), 8.06 (s, 1H), 9.13 (s, 1H); APCI-MS (*m/z*) 429 (M+H)⁺.

Example 122

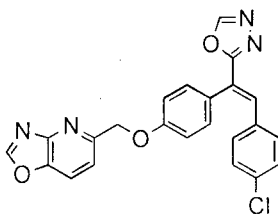
5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-methyl-1*H*-indazole



The title compound was prepared from Intermediate 46 (315 mg, 1.055 mmol) and (1-methyl-1*H*-benzimidazol-5-yl)methanol (190 mg, 1.172 mmol) as described in Step 1 of Example 121 to yield 39 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 3.88 (s, 3H), 5.24 (s, 2H), 7.02-7.07 (m, 4H), 7.12-7.18 (m, 2H), 7.22 (br s, 2H), 7.44 (s, 2H), 7.63 (s, 1H), 7.90 (d, *J* = 8.7 Hz, 2H), 8.38 (s, 1H); APCI-MS (*m/z*) 443 (M+H)⁺.

Example 123

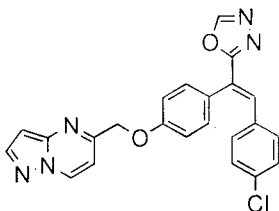
5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl] phenoxy} ethyl)[1,3]oxazolo [4,5-*b*]pyridine



The title compound was prepared from Intermediate 46 (148 mg, 0.492 mmol) and 5-(bromomethyl)[1,3]oxazolo[4,5-*b*]pyridine (700 mg, 3.286 mmol) as described in Example 82 to yield 31 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.39 (s, 2H), 7.06 (t, $J = 6.3$ Hz, 4H), 7.17 (d, $J = 8.1$ Hz, 2H), 7.24 (br s, 2H), 7.63 (s, 1H), 7.67 (d, $J = 8.1$ Hz, 1H), 7.97 (d, $J = 9.0$ Hz, 1H), 8.38 (d, $J = 4.8$ Hz, 2H); APCI-MS (m/z) 431 ($\text{M}+\text{H}$) $^+$.

Example 124

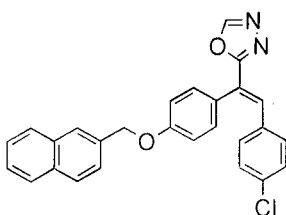
5-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)pyrazolo[1,5-*a*]pyrimidine



The title compound was prepared from Intermediate 54 (400 mg, 0.953 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to yield 40 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.25 (s, 2H), 6.68 (s, 1H), 7.05 (d, $J = 7.5$ Hz, 4H), 7.12-7.18 (m, 3H), 7.29 (br s, 2H), 7.64 (s, 1H), 8.16 (s, 1H), 8.39 (s, 1H), 8.72 (d, $J = 7.2$ Hz, 1H); APCI-MS (m/z) 430 ($\text{M}+\text{H}$) $^+$.

Example 125

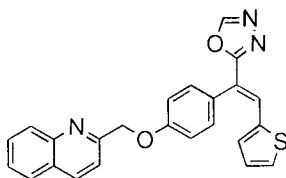
2-{2-(4-Chlorophenyl)-1-[4-(naphthalen-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazole



The title compound was prepared from Intermediate 46 (150 mg, 0.502 mmol) and 2-(chloromethyl)naphthalene (97 mg, 0.552 mmol) as described in Example 82 to yield 100 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.28 (s, 2H), 7.03-7.09 (m, 3H), 7.11-7.17 (m, 3H), 7.24 (br s, 2H), 7.49-7.58 (m, 3H), 7.64 (s, 1H), 7.85-7.91 (m, 4H), 8.39 (s, 1H); APCI-MS (m/z) 439 ($\text{M}+\text{H}$) $^+$.

Example 126

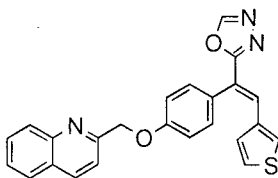
2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-(thiophen-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 55 (300 mg, 0.747 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 40 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.46 (s, 2H), 6.95 (br s, 1H), 7.17-7.22 (m, 4H), 7.29-7.32 (m, 2H), 7.57 (t, $J = 7.8$ Hz, 1H), 7.74 (d, $J = 8.4$ Hz, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 7.92 (s, 1H), 8.10 (d, $J = 8.1$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H), 8.35 (s, 1H); APCI-MS (m/z) 412 ($\text{M}+\text{H}$) $^+$.

Example 127

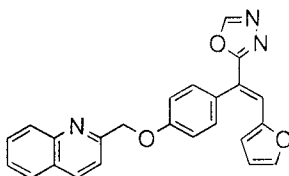
2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-(thiophen-3-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 56 (250 mg, 0.622 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 65 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.45 (s, 2H), 6.58 (d, $J = 5.1$ Hz, 1H), 7.10-7.15 (m, 4H), 7.29-7.35 (m, 3H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.72-7.78 (m, 2H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H), 8.36 (s, 1H); APCI-MS (m/z) 412 ($\text{M}+\text{H}$) $^+$.

Example 128

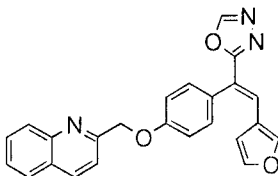
2-({4-[2-(Furan-2-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 57 (400 mg, 1.038 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 200 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.46 (s, 2H), 5.95 (d, $J = 3.3$ Hz, 1H), 6.30 (br s, 1H), 7.13 (d, $J = 8.4$ Hz, 2H), 7.31-7.38 (m, 3H), 7.54-7.60 (m, 2H), 7.72-7.78 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 9.0$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H), 8.36 (s, 1H); ESI-MS (m/z) 396 ($\text{M}+\text{H}$) $^+$.

Example 129

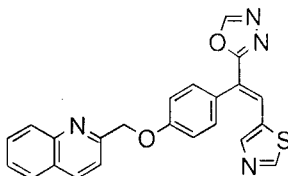
2-({4-[2-(Furan-3-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 58 (450 mg, 1.168 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 150 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.42 (s, 2H), 5.71 (s, 1H), 7.11-7.20 (m, 3H), 7.28 (t, $J = 8.7$ Hz, 2H), 7.40 (s, 1H), 7.53-7.60 (m, 2H), 7.69-7.78 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.7$ Hz, 1H), 8.23 (d, $J = 8.4$ Hz, 1H), 8.34 (s, 1H); APCI (m/z) 396 ($\text{M}+\text{H}$) $^+$.

Example 130

2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-(1,3-thiazol-5-yl)ethenyl]phenoxy}methyl)quinoline

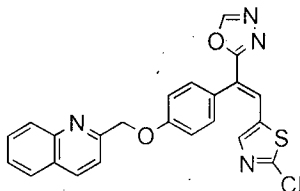


The title compound was prepared from Intermediate 59 (350 mg, 0.870 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 120 mg of the product as off-

white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.46 (s, 2H), 7.29 (q, $J = 9.0$ Hz, 4H), 7.63 (t, $J = 7.5$ Hz, 1H), 7.73-7.82 (m, 2H), 8.01-8.06 (m, 3H), 8.28 (s, 1H), 8.46 (d, $J = 8.4$ Hz, 1H), 8.91 (s, 1H), 9.24 (s, 1H); ESI-MS (m/z) 413 ($\text{M}+\text{H}$) $^+$.

Example 131

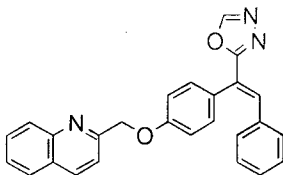
2-({4-[2-(2-Chloro-1,3-thiazol-5-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 60 (650 mg, 1.524 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 250 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.46 (s, 2H), 7.25 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.63 (t, $J = 7.5$ Hz, 1H), 7.72-7.82 (m, 3H), 8.02 (t, $J = 7.2$ Hz, 2H), 8.46 (d, $J = 8.1$ Hz, 1H), 8.98 (s, 1H), 8.27 (s, 1H); ESI-MS (m/z) 447 ($\text{M}+\text{H}$) $^+$.

Example 132

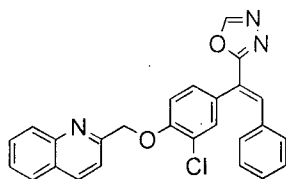
2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-phenylethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 61 (300 mg, 0.759 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 120 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.42 (s, 2H), 7.06-7.13 (m, 4H), 7.19-7.29 (m, 5H), 7.56 (t, $J = 7.8$ Hz, 1H), 7.68-7.77 (m, 3H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 9.0$ Hz, 1H), 8.38 (s, 1H); ESI-MS (m/z) 406 ($\text{M}+\text{H}$) $^+$.

Example 133

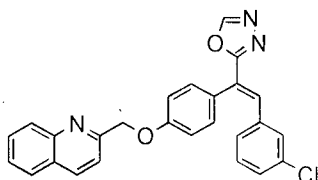
2-({2-Chloro-4-[1-(1,3,4-oxadiazol-2-yl)-2-phenylethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 62 (300 mg, 0.698 mmol) and excess of triethyl orthoformate as described in Example 113 to give 70 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.50 (s, 2H), 7.06-7.14 (m, 3H), 7.17-7.26 (m, 3H), 7.43 (s, 1H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.70 (s, 1H), 7.72-7.78 (m, 2H), 7.84 (d, $J = 8.7$ Hz, 2H), 8.07 (d, $J = 8.7$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H), 8.39 (s, 1H); APCI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 134

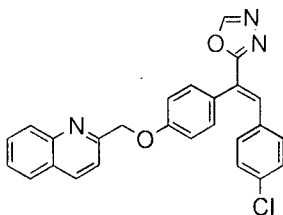
2-((4-[2-(3-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy)methyl)quinoline



The title compound was prepared from Intermediate 63 (300 mg, 0.698 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 26 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 6.97 (d, $J = 7.8$ Hz, 1H), 7.07-7.13 (m, 4H), 7.16-7.22 (m, 3H), 7.54-7.61 (m, 2H), 7.68-7.77 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 9.0$ Hz, 1H), 8.39 (s, 1H); APCI-MS (m/z) 440 (M) $^+$.

Example 135

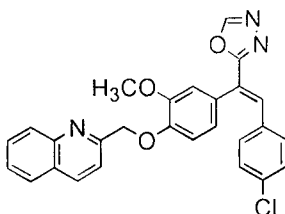
2-((4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy)methyl)quinoline



The title compound was prepared from Intermediate 64 (250 mg, 0.582 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 180 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.46 (s, 2H), 7.01-7.11 (m, 3H), 7.16 (d, $J = 9.0$ Hz, 2H), 7.24 (br s, 3H), 7.55-7.64 (m, 2H), 7.72-7.80 (m, 2H), 7.87 (d, $J = 8.4$ Hz, 1H), 8.13 (br s, 1H), 8.27 (d, $J = 8.1$ Hz, 1H), 8.38 (s, 1H); APCI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 136

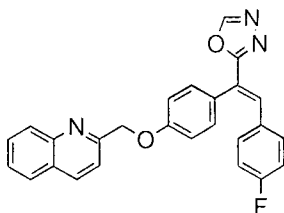
2-({4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]-2-methoxyphenoxy}methyl)quinoline



The title compound was prepared from Intermediate 65 (300 mg, 0.652 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 35 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.84 (s, 3H), 5.51 (s, 2H), 6.79-6.85 (m, 2H), 6.97-7.04 (m, 3H), 7.15 (d, $J = 8.4$ Hz, 2H), 7.53-7.62 (m, 2H), 7.74 (d, $J = 8.4$ Hz, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.07 (d, $J = 8.7$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H), 8.39 (s, 1H); ESI-MS (m/z) 470 ($\text{M}+\text{H}$) $^+$.

Example 137

2-({4-[2-(4-Fluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline

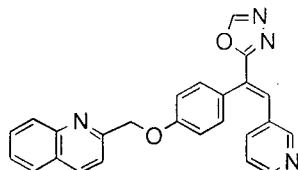


The title compound was prepared from Intermediate 66 (200 mg, 0.480 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to yield 152 mg of the product as white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 6.88 (d, $J = 8.4$ Hz, 2H), 7.09 (d, $J = 8.1$ Hz, 4H), 7.28 (br s, 2H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.65 (s, 1H), 7.69-7.77 (m, 2H), 7.85 (d, $J = 8.1$

Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.1$ Hz, 1H), 8.37 (s, 1H); APCI-MS (m/z) 424 (M+H)⁺.

Example 138

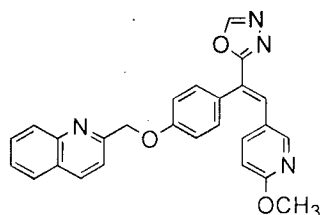
2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-(pyridin-3-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 67 (500 mg, 1.262 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 81 mg of the product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.42 (s, 2H), 7.19 (d, $J = 8.7$ Hz, 2H), 7.22-7.29 (m, 3H), 7.40 (d, $J = 8.4$ Hz, 1H), 7.65 (t, $J = 7.2$ Hz, 1H), 7.71-7.82 (m, 3H), 8.03 (t, $J = 7.8$ Hz, 2H), 8.41-8.47 (m, 3H), 9.28 (s, 1H); ESI-MS (m/z) 407 (M+H)⁺.

Example 139

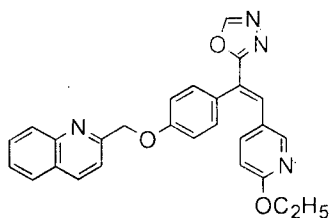
2-({4-[2-(6-Methoxypyridin-3-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 68 (180 mg, 0.422 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 80 mg of the product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 3.81 (s, 3H), 5.43 (s, 2H), 6.65 (d, $J = 8.7$ Hz, 1H), 7.16-7.29 (m, 5H), 7.60-7.66 (m, 2H), 7.71-7.82 (m, 2H), 8.02 (t, $J = 6.3$ Hz, 2H), 8.10 (s, 1H), 8.45 (d, $J = 8.4$ Hz, 1H), 9.23 (s, 1H); ESI-MS (m/z) 437 (M+H)⁺.

Example 140

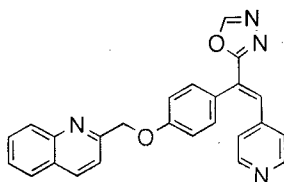
2-({4-[2-(6-Ethoxypyridin-3-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 69 (500 mg, 1.10 mmol) and excess of triethyl orthoformate (10 ml) as described in Example 113 to yield 105 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 1.36 (t, $J = 6.9$ Hz, 3H), 4.32 (q, $J = 6.9$ Hz, 2H), 5.42 (s, 2H), 6.47 (d, $J = 8.7$ Hz, 1H), 7.09-7.14 (m, 3H), 7.29 (br s, 2H), 7.54-7.60 (m, 2H), 7.69-7.77 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.04-8.10 (m, 2H), 8.23 (d, $J = 8.4$ Hz, 1H), 8.36 (s, 1H); ESI-MS (m/z) 451 ($\text{M}+\text{H}$) $^+$.

Example 141

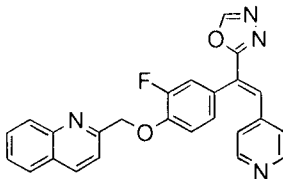
2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-(pyridin-4-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 70 (200 mg, 0.505 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to yield 163 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 6.96 (d, $J = 6$ Hz, 2H), 7.09 (d, $J = 6.9$ Hz, 2H), 7.24 (d, $J = 6.5$ Hz, 2H), 7.54-7.59 (m, 2H), 7.68-7.76 (m, 2H), 7.85 (d, $J = 7.5$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.4$ Hz, 1H), 8.40-8.46 (m, 3H); APCI-MS (m/z) 407 ($\text{M}+\text{H}$) $^+$.

Example 142

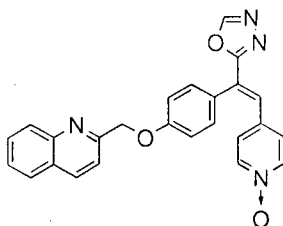
2-({2-Fluoro-4-[1-(1,3,4-oxadiazol-2-yl)-2-(pyridin-4-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 71 (250 mg, 0.603 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to yield 67 mg of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 5.51 (s, 2H), 7.07 (d, $J = 5.4$ Hz, 3H), 7.29-7.35 (m, 2H), 7.64-7.73 (m, 3H), 7.80 (t, $J = 7.2$ Hz, 1H), 8.02 (d, $J = 8.1$ Hz, 2H), 8.44-8.50 (m, 3H), 9.32 (s, 1H); APCI (m/z) 425 ($\text{M}+\text{H}$) $^+$.

Example 143

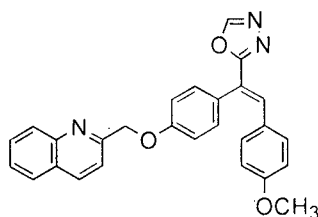
2-({4-[1-(1,3,4-Oxadiazol-2-yl)-2-(1-oxidopyridin-4-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 72 (300 mg, 0.724 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 40 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.47 (s, 2H), 6.95 (d, $J = 6.3$ Hz, 2H), 7.14 (d, $J = 8.4$ Hz, 2H), 7.29 (s, 2H), 7.53 (s, 1H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.71-7.80 (m, 2H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.97 (d, $J = 6.6$ Hz, 2H), 8.14 (d, $J = 7.8$ Hz, 1H), 8.27 (d, $J = 8.4$ Hz, 1H), 8.42 (s, 1H); APCI-MS (m/z) 423 ($\text{M}+\text{H}$) $^+$.

Example 144

2-({4-[2-(4-Methoxyphenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline

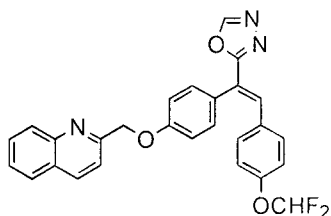


The title compound was prepared from Intermediate 73 (200 mg, 0.470 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to yield 15 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.77 (s, 3H), 5.43 (s, 2H), 6.72 (d, $J = 8.4$ Hz, 2H), 7.04-7.13 (m, 4H), 7.30 (br s, 2H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.70-7.78 (m, 2H), 7.85 (d, $J = 7.8$

Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H), 8.35 (s, 1H); ESI-MS (m/z) 436 ($M+H$)⁺.

Example 145

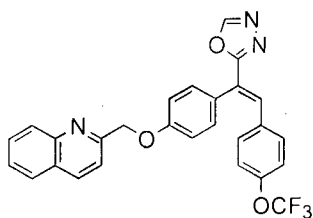
2-({4-[2-[4-(Difluoromethoxy)phenyl]-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from the Intermediate 74 (400 mg, 0.898 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 105 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 5.43 (s, 2H), 6.48 (t, $J = 73.2$ Hz, 1H), 6.93 (d, $J = 8.4$ Hz, 2H), 7.08-7.13 (m, 4H), 7.28 (br s, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.65 (s, 1H), 7.70-7.78 (m, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.4$ Hz, 1H), 8.38 (s, 1H); ESI-MS (m/z) 472 ($M+H$)⁺.

Example 146

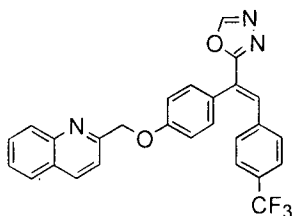
2-[(4-{1-(1,3,4-Oxadiazol-2-yl)-2-[4-(trifluoromethoxy)phenyl]ethenyl}phenoxy)methyl]quinoline



The title compound was prepared from Intermediate 75 (400 mg, 0.835 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 58 mg of the product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.43 (s, 2H), 7.16 (d, $J = 8.1$ Hz, 2H), 7.20-7.28 (m, 6H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.70-7.82 (m, 3H), 8.02 (t, $J = 7.2$ Hz, 2H), 8.45 (d, $J = 8.1$ Hz, 1H), 9.27 (s, 1H); ESI-MS (m/z) 490 ($M+H$)⁺.

Example 147

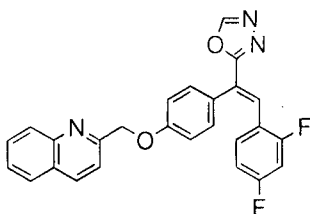
2-[(4-{1-(1,3,4-Oxadiazol-2-yl)-2-[4-(trifluoromethyl)phenyl]ethenyl}phenoxy)methyl]quinoline



The title compound was prepared from Intermediate 76 (300 mg, 0.647 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 40 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 7.09 (d, $J = 8.4$ Hz, 2H), 7.20-7.24 (m, 4H), 7.44 (d, $J = 7.8$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.69-7.77 (m, 3H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.7$ Hz, 1H), 8.41 (s, 1H); APCI-MS (m/z) 474 ($\text{M}+\text{H}$) $^+$.

Example 148

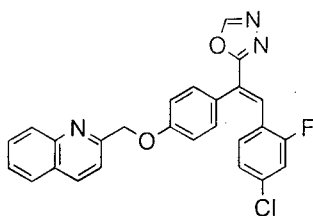
2-({4-[2-(2,4-Difluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 77 (280 mg, 0.640 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 40 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.41 (s, 2H), 6.57 (t, $J = 8.4$ Hz, 1H), 6.84 (q, $J = 9.0$ Hz, 2H), 7.07 (d, $J = 8.1$ Hz, 2H), 7.27 (br s, 2H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.67-7.78 (m, 3H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H), 8.40 (s, 1H); ESI-MS (m/z) 442 ($\text{M}+\text{H}$) $^+$.

Example 149

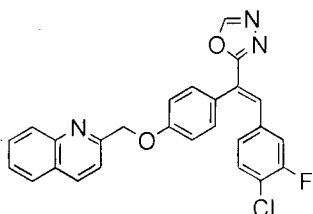
2-({4-[2-(4-Chloro-2-fluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 78 (350 mg, 0.780 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to yield 95 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.41 (s, 2H), 6.75-6.81 (m, 2H), 7.03-7.09 (m, 3H), 7.24 (br s, 2H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.68-7.77 (m, 3H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H), 8.41 (s, 1H); ESI-MS (m/z) 458 ($\text{M}+\text{H}$) $^+$.

Example 150

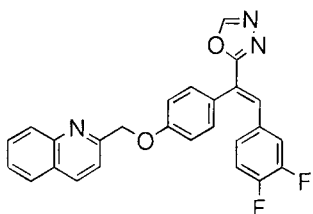
2-({4-[2-(4-Chloro-3-fluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 79 (300 mg, 0.670 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 75 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.45 (s, 2H), 6.83-6.89 (m, 2H), 7.10 (d, $J = 9.0$ Hz, 2H), 7.19-7.26 (m, 3H), 7.53-7.59 (m, 2H), 7.69-7.78 (m, 2H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H), 8.40 (s, 1H); ESI-MS (m/z) 458 ($\text{M}+\text{H}$) $^+$.

Example 151

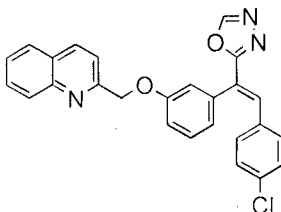
2-({4-[2-(3,4-Difluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 80 (280 mg, 0.649 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 46 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.44 (s, 2H), 6.82-6.91 (m, 2H), 6.94-7.05 (m, 1H), 7.10 (d, $J = 9.0$ Hz, 2H), 7.25 (d, $J = 8.1$ Hz, 2H), 7.53-7.59 (m, 2H), 7.67-7.78 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.4$ Hz, 1H), 8.39 (s, 1H); ESI-MS (m/z) 442 ($\text{M}+\text{H}$) $^+$.

Example 152

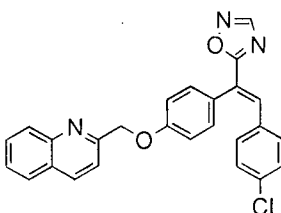
2-({3-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 81 (250 mg, 0.580 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 103 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.36 (s, 2H), 6.92-6.97 (m, 4H), 7.07-7.12 (m, 3H), 7.37 (t, $J = 7.8$ Hz, 1H), 7.53-7.65 (m, 3H), 7.73 (t, $J = 7.5$ Hz, 1H), 7.84 (d, $J = 8.4$ Hz, 1H), 8.03 (d, $J = 8.4$ Hz, 1H), 8.17 (d, $J = 8.4$ Hz, 1H), 8.31 (s, 1H); ESI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 153

2-({4-[2-(4-Chlorophenyl)-1-(1,2,4-oxadiazol-5-yl)ethenyl]phenoxy}methyl)quinoline



Step 1: 3-(4-Chlorophenyl)-*N*-[(*Z*)-(dimethylamino)methylidene]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide:

The solution of Example 1 (400 mg, 0.966 mmol) in *N,N*-dimethyl formamide dimethyl acetal (4 ml) was stirred at 120-130 °C for 3 h. The reaction mixture was concentrated to yield 456 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.11 (s, 3H), 3.14 (s, 3H), 5.40 (s, 2H),

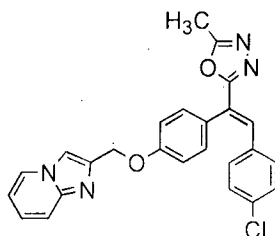
6.98-7.03 (m, 4H), 7.08-7.15 (m, 4H), 7.55 (t, $J = 6.9$ Hz, 1H), 7.70-7.76 (m, 2H), 7.84 (d, $J = 8.4$ Hz, 1H), 8.03 (s, 2H), 8.21 (d, $J = 8.4$ Hz, 1H), 8.46 (s, 1H).

Step 2: 2-({4-[2-(4-Chlorophenyl)-1-(1,2,4-oxadiazol-5-yl)ethenyl]phenoxy}methyl)quinoline:

To the well stirred solution of Step 1 Intermediate (450 mg, 0.958 mmol) in dioxane (5 ml) were added hydroxylamine hydrochloride (134 mg, 1.916 mmol), aqueous sodium hydroxide (5 ml) and acetic acid (4 ml) and the reaction mixture was stirred for 4 h at 110 °C. The reaction mixture was quenched with water (20 ml), neutralized by sodium bicarbonate and was extracted with ethyl acetate (50 ml x 2). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated to yield 24 mg of product as white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 7.05-7.18 (m, 6H), 7.23 (br s, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.70-7.78 (m, 2H), 7.82-7.87 (m, 2H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.1$ Hz, 1H), 8.39 (s, 1H); ESI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 154

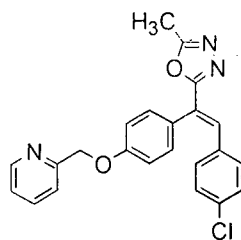
2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-(4-chlorophenyl)ethenyl]phenoxy}methyl)imidazo [1,2-*a*]pyridine



The title compound was prepared from Intermediate 47 (300 mg, 0.710 mmol) and triethyl orthoacetate (15 ml) as described in Example 113 to yield 183 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 2.53 (s, 3H), 5.24 (s, 2H), 6.09 (t, $J = 6.9$ Hz, 1H), 7.10-7.16 (m, 4H), 7.23 (d, $J = 8.7$ Hz, 3H), 7.30 (d, $J = 8.4$ Hz, 2H), 7.55 (d, $J = 9.6$ Hz, 2H), 8.03 (s, 1H), 8.55 (d, $J = 9.0$ Hz, 1H); APCI-MS (m/z) 443 ($\text{M}+\text{H}$) $^+$.

Example 155

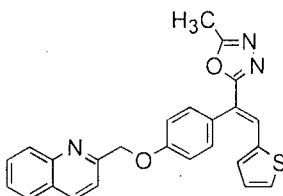
2-({4-[2-(4-Chlorophenyl)-1-(5-methyl-1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)pyridine



The title compound was prepared from Intermediate 50 (200 mg, 0.527 mmol) and triethyl orthoacetate (7 ml) as described in Example 113 to give 86 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.57 (s, 3H), 5.24 (s, 2H), 7.00-7.07 (m, 4H), 7.15 (d, $J = 8.1$ Hz, 2H), 7.23 (br s, 3H), 7.52-7.59 (m, 2H), 7.75 (t, $J = 7.5$ Hz, 1H), 8.67 (d, $J = 3.9$ Hz, 1H); APCI (m/z) 404 ($\text{M}+\text{H}$) $^+$.

Example 156

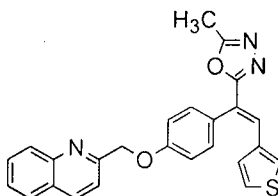
2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-(thiophen-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 55 (300 mg, 0.747 mmol) and triethyl orthoacetate (5 ml) as described in Example 113 to give 45 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.55 (s, 3H), 5.46 (s, 2H), 6.93 (br s, 1H), 7.12-7.19 (m, 4H), 7.27-7.32 (m, 2H), 7.56 (t, $J = 7.8$ Hz, 1H), 7.73-7.81 (m, 3H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 426 ($\text{M}+\text{H}$) $^+$.

Example 157

2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-(thiophen-3-yl)ethenyl]phenoxy}methyl)quinoline

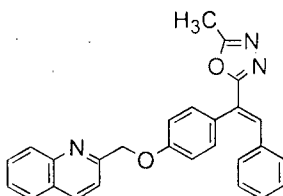


The title compound was prepared from Intermediate 56 (300 mg, 0.747 mmol) and triethyl orthoacetate (5 ml) as described in Example 113 to give 60 mg of the product as off-white solid;

^1H NMR (300 MHz, CDCl_3) δ 2.56 (s, 3H), 5.44 (s, 2H), 6.56 (d, $J = 4.5$ Hz, 1H), 7.13 (d, $J = 8.7$ Hz, 4H), 7.30 (br s, 2H), 7.54-7.61 (m, 2H), 7.72-7.78 (m, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.7$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 426 ($\text{M}+\text{H}$) $^+$.

Example 158

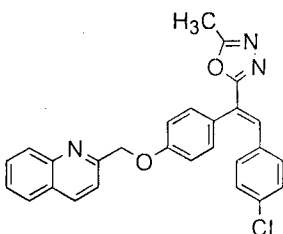
2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-phenylethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 61 (300 mg, 0.759 mmol) and triethyl orthoacetate (10 ml) as described in Example 113 to give 90 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.57 (s, 3H), 5.42 (s, 2H), 7.05-7.12 (m, 4H), 7.18 (d, $J = 6.0$ Hz, 3H), 7.28 (br s, 2H), 7.50-7.58 (m, 2H), 7.69-7.76 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H); ESI-MS (m/z) 420 ($\text{M}+\text{H}$).

Example 159

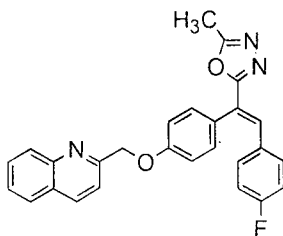
2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-(4-chlorophenyl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 64 (250 mg, 0.582 mmol) and triethyl orthoacetate (5 ml) as described in Example 113 to yield 170 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.56 (s, 3H), 5.44 (s, 2H), 7.01 (d, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.7$ Hz, 2H), 7.14 (d, $J = 8.4$ Hz, 2H), 7.24 (d, $J = 8.7$ Hz, 2H), 7.52 (s, 1H), 7.58 (t, $J = 7.8$ Hz, 1H), 7.71-7.78 (m, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.12 (d, $J = 8.4$ Hz, 1H), 8.25 (d, $J = 8.1$ Hz, 1H); APCI-MS (m/z) 454 ($\text{M}+\text{H}$) $^+$.

Example 160

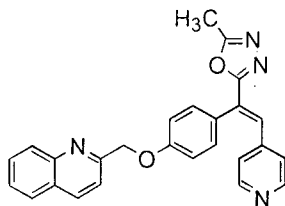
2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-(4-fluorophenyl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 66 (200 mg, 0.480 mmol) and triethyl orthoacetate (5 ml) as described in Example 113 to give 140 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.56 (s, 3H), 5.42 (s, 2H), 6.86 (t, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.7$ Hz, 4H), 7.25 (d, $J = 6.6$ Hz, 2H), 7.53-7.60 (m, 2H), 7.69-7.79 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.23 (d, $J = 8.7$ Hz, 1H); APCI-MS (m/z) 438 ($\text{M}+\text{H}$) $^+$.

Example 161

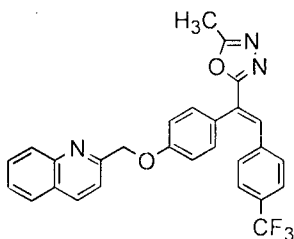
2-({4-[1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-pyridin-4-ylethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 70 (150 mg, 0.378 mmol) and triethyl orthoacetate (5 ml) as described in Example 113 to yield 63 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.59 (s, 3H), 5.43 (s, 2H), 6.93 (d, $J = 6.3$ Hz, 2H), 7.08 (d, $J = 8.7$ Hz, 2H), 7.24 (d, $J = 8.7$ Hz, 2H), 7.48 (s, 1H), 7.57 (t, $J = 6.9$ Hz, 1H), 7.68-7.78 (m, 2H), 7.85 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.1$ Hz, 1H), 8.23 (d, $J = 8.7$ Hz, 1H), 8.43 (d, $J = 5.7$ Hz, 2H); APCI-MS (m/z) 421 ($\text{M}+\text{H}$) $^+$.

Example 162

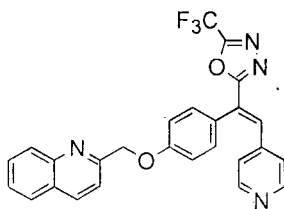
2-[(4-{1-(5-Methyl-1,3,4-oxadiazol-2-yl)-2-[4-(trifluoromethyl)phenyl]ethenyl}phenoxy)methyl]quinoline



The title compound was prepared from Intermediate 76 (300 mg, 0.647 mmol) and triethyl orthoacetate (10 ml) as described in Example 113 to give 150 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.58 (s, 3H), 5.44 (s, 2H), 7.08 (d, $J = 8.1$ Hz, 2H), 7.17-7.23 (m, 4H), 7.42 (d, $J = 8.1$ Hz, 2H), 7.59 (br s, 2H), 7.70-7.76 (m, 2H), 7.86 (d, $J = 7.8$ Hz, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 488 ($\text{M}+\text{H}$) $^+$.

Example 163

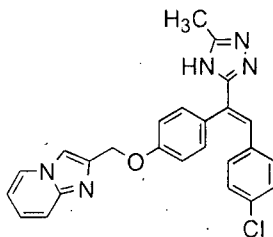
2-({4-[1-(5-{Trifluoromethyl}-1,3,4-oxadiazol-2-yl)-2-pyridin-4-ylethenyl]phenoxy}methyl)quinoline



Trifluoroacetic anhydride (0.1 ml, 0.757 mmol) was added drop wise to a cooled solution of Intermediate 70 (200 mg, 0.505 mmol) in dichloroethane (10 ml) and the reaction mixture was stirred at room temperature for 2 h after which it was further refluxed for 12 h. The reaction mixture was diluted with water (10 ml) and basified with saturated sodium bicarbonate solution. The aqueous layer was extracted with chloroform (25 ml x 2). The combined organic layers were washed with water (20 ml x 2) and brine (15 ml), dried over anhydrous Na_2SO_4 and concentrated to yield 45 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.43 (s, 2H), 6.97 (d, $J = 5.4$ Hz, 2H), 7.10 (d, $J = 8.7$ Hz, 2H), 7.24 (d, $J = 7.2$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.69-7.78 (m, 3H), 7.86 (d, $J = 8.1$ Hz, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 8.24 (d, $J = 8.4$ Hz, 1H), 8.47 (d, $J = 4.5$ Hz, 2H); APCI-MS (m/z) 475 ($\text{M}+\text{H}$) $^+$.

Example 164

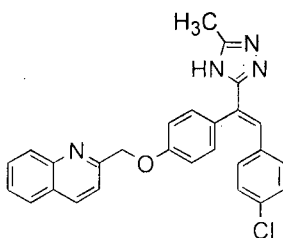
2-({4-[2-(4-Chlorophenyl)-1-(5-methyl-4*H*-1,2,4-triazol-3-yl)ethenyl]phenoxy}methyl)imidazo[1,2-*a*]pyridine



To a well stirred solution of Intermediate 47 (400 mg, 0.955 mmol) in ethanol (15 ml) were added sodium ethoxide (195 mg, 2.865 mmol) and acetamidine hydrochloride (271 mg, 2.865 mmol). The reaction was refluxed for 16 h after which excess of ethanol was distilled under reduced pressure and the reaction mass was diluted with water (15 ml). The aqueous layer was extracted with ethyl acetate (25 ml x 2) and the combined organic layers were washed with water (15 ml x 2) and brine (15 ml), dried over anhydrous Na₂SO₄ and concentrated to yield 43 mg of product as white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.36 (s, 3H), 5.22 (s, 2H), 6.90 (t, *J* = 6.9 Hz, 1H), 7.02-7.12 (m, 6H), 7.20-7.27 (m, 3H), 7.46-7.55 (m, 2H), 8.02 (s, 1H), 8.55 (d, *J* = 6.6 Hz, 1H), 13.46 (s, 1H); APCI (*m/z*) 442 (M+H)⁺.

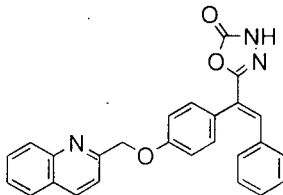
Example 165

2-({4-[2-(4-Chlorophenyl)-1-(5-methyl-4*H*-1,2,4-triazol-3-yl)ethenyl]phenoxy}methyl)quinoline



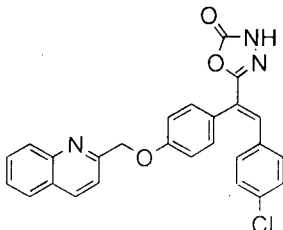
The title compound was prepared from Intermediate 64 (100 mg, 0.224 mmol) and acetamidine hydrochloride (42 mg, 0.448 mmol) as described in Example 164 to yield 68 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 2.57 (s, 3H), 5.42 (s, 2H), 7.01 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.23 (br s, 2H), 7.52-7.59 (m, 1H), 7.69-7.77 (m, 2H), 7.86 (d, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.30-8.38 (m, 2H); APCI-MS (*m/z*) 454 (M+H)⁺.

Example 166

5-{2-Phenyl-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazol-2(3*H*)-one

Trichloromethyl chloroformate (0.12 ml, 1.01 mmol) was added drop wise to a well stirred and cooled solution of Intermediate 61 (200 mg, 0.506 mmol) in dioxane (10 ml) and was refluxed for 12 h. The reaction mixture was diluted with water (15 ml) and extracted with ethyl acetate (20 ml x 3). The combined organic layers were washed with water (15 ml x 2) and brine (15 ml), dried over anhydrous Na₂SO₄, filtered and concentrated to yield 100 mg of off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.41 (s, 2H), 7.10-7.16 (m, 4H), 7.20-7.32 (m, 5H), 7.32 (s, 1H), 7.63 (t, *J* = 6.9 Hz, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.80 (t, *J* = 7.2 Hz, 1H), 8.00-8.06 (m, 2H), 8.45 (d, *J* = 8.4 Hz, 1H), 12.45 (s, 1H); ESI-MS (*m/z*) 422 (M+H)⁺.

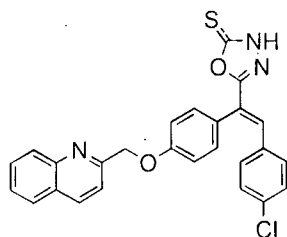
Example 167

5-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazol-2(3*H*)-one

The title compound was prepared from Intermediate 64 (200 mg, 0.505 mmol) as described in Example 166 to yield 68 mg of the product as off-white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.41 (s, 2H), 7.07-7.15 (m, 4H), 7.19-7.72 (m, 4H), 7.31 (s, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 7.8 Hz, 1H), 8.04 (br s, 2H), 8.45 (d, *J* = 8.7 Hz, 1H), 12.46 (s, 1H); APCI-MS (*m/z*) 456 (M+H)⁺.

Example 168

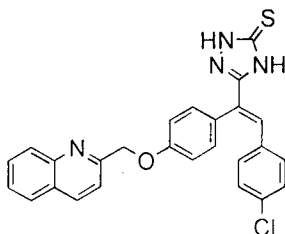
5-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazol-2(3*H*)-thione



To a well stirred solution of Intermediate 64 (200 mg, 0.465 mmol) in ethanol (10 ml) were added aqueous potassium hydroxide (52 mg, 2.931 mmol) followed by carbon bisulfide (107 mg, 1.396 mmol) and the reaction mixture was refluxed for 12 h. The excess of ethanol was distilled under reduced pressure and the reaction mass was diluted with water (15 ml). The solid so obtained was filtered, dissolved in ethyl acetate (30 ml), dried over anhydrous Na_2CO_3 and concentrated to yield 130 mg of the off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.42 (s, 2H), 7.14 (d, $J=7.5$ Hz, 4H), 7.23-7.30 (m, 5H), 7.49 (s, 1H), 7.63 (t, $J=5.1$ Hz, 1H), 7.71 (d, $J=8.7$ Hz, 1H), 7.80 (t, $J=7.8$ Hz, 1H), 8.01 (br s, 2H), 8.45 (d, $J=8.4$ Hz, 1H); APCI-MS (m/z) 472 ($\text{M}+\text{H}$) $^+$.

Example 169

5-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-2,4-dihydro-3H-1,2,4-triazole-3-thione

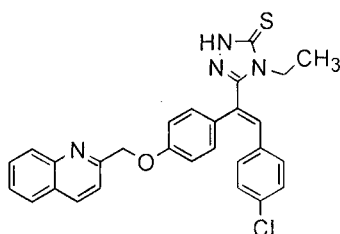


To the well stirred solution of Intermediate 64 (300 mg, 0.698 mmol) in dil.HCl (40 ml) was added potassium thiocyanate (340 mg, 3.505 mmol) and the reaction mixture was refluxed overnight. The crude product obtained was cyclized to give the title compound by refluxing it in 1M solution of sodium bicarbonate for 24 h. The compound thus obtained was purified by silica gel column chromatography to yield 200 mg of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.40 (s, 2H), 6.98 (d, $J=8.4$ Hz, 2H), 7.09 (d, $J=8.7$ Hz, 2H), 7.15 (d, $J=9.0$ Hz, 2H), 7.25 (d, $J=8.1$ Hz, 2H), 7.38 (s, 1H), 7.63 (t, $J=7.8$ Hz, 1H), 7.70 (d, $J=8.4$ Hz,

1H), 7.79 (t, $J = 7.8$ Hz, 1H), 8.02 (br s, 2H), 8.45 (d, $J = 8.7$ Hz, 1H), 13.52 (s, 1H), 13.60 (s, 1H); APCI-MS (m/z) 471 (M)⁺.

Example 170

5-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-4-ethyl-2,4-dihydro-3H-1,2,4-triazole-3-thione



Step 1: 2-{3-(4-Chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl}-*N*-ethylhydrazinecarbothioamide:

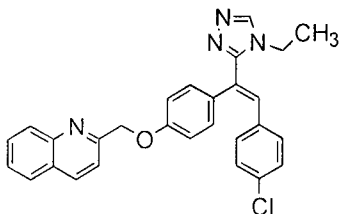
To a well stirred solution of Intermediate 64 (500 mg, 1.165 mmol) in dry THF (45 ml) was added ethyl isothiocyanate (0.09 ml, 1.04 mmol) and the reaction mixture was refluxed for 2 h and then stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure and recrystallized to give 500 mg of the product as off white solid; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.07 (t, $J = 6.9$ Hz, 3H), 2.50 (br s, 1H), 3.46 (br s, 2H), 5.32 (s, 2H), 6.92-7.00 (m, 4H), 7.26 (d, $J = 7.8$ Hz, 2H), 7.42-7.51 (m, 3H), 7.58-7.65 (m, 2H), 7.78 (t, $J = 7.2$ Hz, 1H), 7.99 (d, $J = 6.9$ Hz, 2H), 8.41 (d, $J = 9.0$ Hz, 1H), 9.19 (br s, 1H), 9.62 (br s, 1H).

Step 2: 5-{2-(4-Chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-4-ethyl-2,4-dihydro-3H-1,2,4-triazole-3-thione:

To the Step 1 Intermediate (500 mg, 0.967 mmol) was added saturated solution of sodium bicarbonate (40 ml) and was refluxed for 24 h after which it was filtered as it is. The precipitate obtained was dissolved in chloroform, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product thus obtained was purified by silica gel column chromatography to yield 300 mg of the product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 1.00 (t, $J = 6.9$ Hz, 3H), 3.69 (d, $J = 7.5$ Hz, 2H), 5.41 (s, 2H), 6.89 (d, $J = 8.4$ Hz, 2H), 7.06 (d, $J = 9.3$ Hz, 3H), 7.20 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.65 (d, $J = 9.0$ Hz, 1H), 7.76 (t, $J = 7.8$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.21 (d, $J = 8.4$ Hz, 2H), 11.07 (br s, 1H); APCI-MS (m/z) 499 (M)⁺.

Example 171

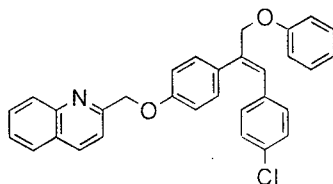
2-({4-[2-(4-Chlorophenyl)-1-(4-ethyl-4*H*-1,2,4-triazol-3-yl)ethenyl]phenoxy}methyl)quinoline



To a well stirred solution of Example 170 (100 mg, 0.2 mmol) in glacial acetic acid (5 ml) was added hydrogen peroxide (5 ml) drop wise and was stirred at room temperature for 12 h. The reaction mixture was neutralized with sodium bicarbonate (10 ml) and extracted with ethyl acetate (25 ml x 2). The combined organic layers were washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The product was purified by silica gel column chromatography to yield 50 mg of product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.10 (t, $J = 7.2$ Hz, 3H), 3.66 (q, $J = 6.9$ Hz, 2H), 5.34 (s, 2H), 6.97 (d, $J = 8.4$ Hz, 2H), 6.99-7.14 (m, 3H), 7.20 (d, $J = 8.4$ Hz, 2H), 7.44 (d, $J = 8.4$ Hz, 2H), 7.60-7.67 (m, 2H), 7.79 (t, $J = 7.2$ Hz, 1H), 8.00 (br s, 2H), 8.42 (d, $J = 8.7$ Hz, 1H), 8.57 (s, 1H); APCI-MS (m/z) 467 ($\text{M}+\text{H}$) $^+$.

Example 172

2-({4-[1-(4-Chlorophenyl)-3-phenoxyprop-1-en-2-yl]phenoxy}methyl)quinoline

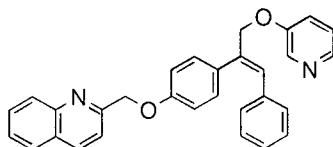


To the well stirred solution of the Intermediate 42 (200 mg, 0.476 mmol) in DMF (10 ml) was added phenol (54 mg, 0.571 mmol) followed by potassium carbonate (164 mg, 1.19 mmol) and was stirred at room temperature overnight. The reaction mixture was quenched with water (20 ml), extracted with ethyl acetate (2 x 25 ml), washed with water (20 ml), brine (20 ml) and dried to yield 69 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.76 (s, 2H), 5.39 (s, 2H), 6.71 (s, 1H), 6.92-7.01 (m, 7H), 7.07 (d, $J = 8.7$ Hz, 2H), 7.17 (d, $J = 8.1$ Hz, 2H), 7.30

(d, $J = 7.8$ Hz, 2H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.67-7.77 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.4$ Hz, 1H), 8.21 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 478.36 (M+H)⁺.

Example 173

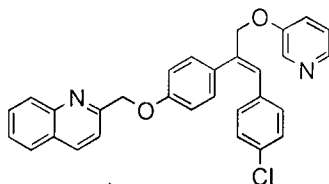
2-({4-[1-Phenyl-3-(pyridin-3-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 44 (200 mg, 0.518 mmol) and 3-hydroxypyridine (98 mg, 1.036 mmol) as described in Example 172 to yield 30 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.86 (s, 2H), 5.41 (s, 2H), 6.75 (s, 1H), 6.98-7.03 (m, 4H), 7.12-7.19 (m, 5H), 7.34 (br s, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.70-7.78 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.12 (d, $J = 9.0$ Hz, 1H), 8.24 (d, $J = 8.1$ Hz, 2H), 8.40 (br s, 1H); APCI-MS (m/z) 445 (M+H)⁺.

Example 174

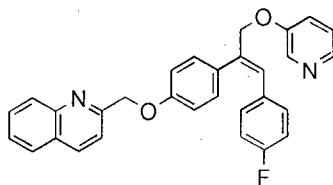
2-({4-[1-(4-Chlorophenyl)-3-(pyridin-3-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 42 (300 mg, 0.714 mmol) and 3-hydroxypyridine (102 mg, 1.071 mmol) as described in Example 172 to yield 26 mg of product as off-white solid; ¹H NMR (300 MHz, CDCl₃) δ 4.82 (s, 2H), 5.39 (s, 2H), 6.70 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 2H), 7.00 (d, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.4$ Hz, 2H), 7.16 (d, $J = 8.7$ Hz, 2H), 7.20-7.27 (m, 2H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.67-7.75 (m, 2H), 7.85 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 2H), 8.36 (br s, 1H); ESI-MS (m/z) 479 (M+H)⁺.

Example 175

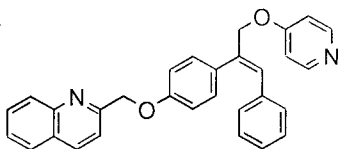
2-({4-[1-(4-Fluorophenyl)-3-(pyridin-3-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 43 (200 mg, 0.495 mmol) and 3-hydroxypyridine (71 mg, 0.743 mmol) as described in Example 172 to yield 38 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.09 (s, 2H), 5.30 (s, 2H), 6.76-6.82 (m, 4H), 6.90-6.96 (m, 6H), 7.06 (br s, 2H), 7.55 (t, $J = 7.2$ Hz, 1H), 7.62 (d, $J = 9.0$ Hz, 1H), 7.73 (t, $J = 7.5$ Hz, 1H), 7.83 (d, $J = 7.5$ Hz, 2H), 8.06 (d, $J = 8.4$ Hz, 1H), 8.19 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 463 ($\text{M}+\text{H}$) $^+$.

Example 176

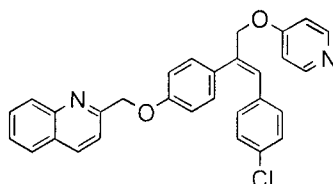
2-(4-[1-Phenyl-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy)methylquinoline



The title compound was prepared from Intermediate 44 (200 mg, 0.518 mmol) and 4-hydroxypyridine (59 mg, 0.621 mmol) as described in Example 172 to yield 91 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.66 (s, 2H), 5.36 (s, 2H), 6.34 (d, $J = 7.2$ Hz, 2H), 6.58 (s, 1H), 6.96 (br s, 5H), 7.10-7.16 (m, 3H), 7.23 (br s, 3H), 7.56 (t, $J = 7.2$ Hz, 1H), 7.66 (d, $J = 8.4$ Hz, 1H), 7.75 (t, $J = 7.2$ Hz, 1H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.7$ Hz, 1H); APCI-MS (m/z) 445 ($\text{M}+\text{H}$) $^+$.

Example 177

2-(4-[1-(4-Chlorophenyl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy)methylquinoline

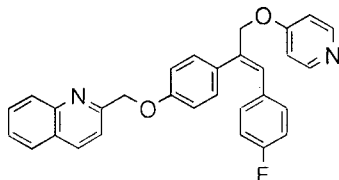


The title compound was prepared from Intermediate 42 (300 mg, 0.714 mmol) and 4-hydroxypyridine (102 mg, 1.071 mmol) as described in Example 172 to yield 156 mg of product

as white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.63 (s, 2H), 5.37 (s, 2H), 6.31 (d, $J = 7.5$ Hz, 2H), 6.49 (s, 1H), 6.88-6.99 (m, 6H), 7.09 (d, $J = 8.1$ Hz, 2H), 7.21 (d, $J = 7.2$ Hz, 2H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.66 (d, $J = 8.7$ Hz, 1H), 7.75 (t, $J = 7.2$ Hz, 1H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.22 (d, $J = 8.4$ Hz, 1H); ESI-MS (m/z) 479 ($\text{M}+\text{H}$) $^+$.

Example 178

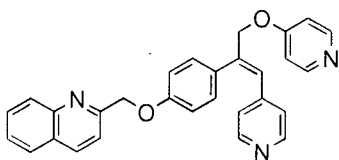
2-({4-[1-(4-Fluorophenyl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 43 (200 mg, 0.495 mmol) and 4-hydroxypyridine (71 mg, 0.743 mmol) as described in Example 172 to yield 107 mg of product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.64 (s, 2H), 5.37 (s, 2H), 6.34 (d, $J = 7.2$ Hz, 2H), 6.53 (s, 2H), 6.82 (t, $J = 9.0$ Hz, 2H), 6.92-7.00 (m, 5H), 7.23 (d, $J = 7.5$ Hz, 2H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.66 (d, $J = 9.0$ Hz, 1H), 7.75 (t, $J = 7.2$ Hz, 1H), 7.86 (d, $J = 8.4$ Hz, 1H), 8.08 (d, $J = 8.1$ Hz, 1H), 8.23 (d, $J = 8.4$ Hz, 1H); APCI-MS (m/z) 463 ($\text{M}+\text{H}$) $^+$.

Example 179

2-({4-[1-(Pyridin-4-yl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline



Step 1: 3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-ol;

To well stirred solution of the ester of Intermediate 14 (2 g, 4.878 mmol) in THF (30 ml) was added 20 % di-isobutylaluminium hydride (DIBAL-H; 13.50 ml, 29.26 mmol) at -30 to -40 $^{\circ}\text{C}$ and stirred for 3 h at the same temperature. The reaction mixture was quenched with water (150 ml) and stirred for 20 mins after addition of ethyl acetate (300 ml). The precipitate obtained was filtered and the filtrate was dried and concentrated to yield 1.1 g of the product as off-white solid; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 4.20 (d, $J = 5.1$ Hz, 2H), 5.38 (s, 2H), 6.60 (s, 1H), 6.86

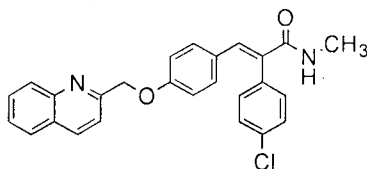
(d, $J = 5.7$ Hz, 2H), 7.05-7.13 (m, 4H), 7.60-7.70 (m, 2H), 7.79 (t, $J = 6.6$ Hz, 1H), 7.99-8.03 (m, 3H), 8.27-8.33 (m, 2H), 8.43 (d, $J = 8.7$ Hz, 1H).

Step 2: 2-({4-[1-(Pyridin-4-yl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline:

To the well stirred solution of Step 1 Intermediate (300 mg, 0.819 mmol) in THF (10 ml) were added triphenylphosphine (322 mg, 0.983 mmol) and 4-hydroxypyridine (86 mg, 0.737 mmol). The reaction was stirred at room temperature for 15 mins followed by drop wise addition of diethylazodicarboxylate (0.19 ml, 1.5 mmol) and the reaction mixture was further stirred for 16h. The excess solvent was distilled under reduced pressure and purified by silica gel column chromatography to yield 34 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 4.83 (s, 2H), 5.40 (s, 2H), 6.66 (s, 1H), 6.86 (br s, 4H), 7.02 (d, $J = 8.4$ Hz, 2H), 7.14 (d, $J = 7.8$ Hz, 2H), 7.57 (t, $J = 7.8$ Hz, 1H), 7.67-7.75 (m, 2H), 7.85 (d, $J = 7.8$ Hz, 1H), 8.08 (d, $J = 7.8$ Hz, 1H), 8.22 (d, $J = 8.1$ Hz, 1H), 8.35 (d, $J = 4.5$ Hz, 2H), 8.45 (d, $J = 4.8$ Hz, 2H); APCI-MS (m/z) 446 ($\text{M}+\text{H}$) $^+$.

Example 180

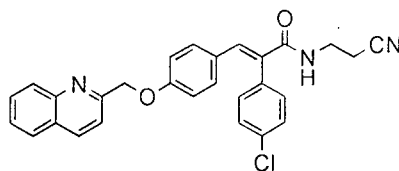
2-(4-Chlorophenyl)-*N*-methyl-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 83 (200 mg, 0.481 mmol) with methylamine hydrochloride (49 mg, 0.721 mmol) as described in Example 2 to yield 110 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.84 (d, $J = 4.8$ Hz, 3H), 5.32 (br s, 3H), 6.80 (d, $J = 8.7$ Hz, 2H), 6.93 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 8.1$ Hz, 2H), 7.43 (d, $J = 8.4$ Hz, 2H), 7.52-7.60 (m, 2H), 7.71-7.83 (m, 3H), 8.05 (d, $J = 8.4$ Hz, 1H), 8.16 (d, $J = 8.7$ Hz, 1H); ESI (m/z) 429 ($\text{M}+\text{H}$) $^+$.

Example 181

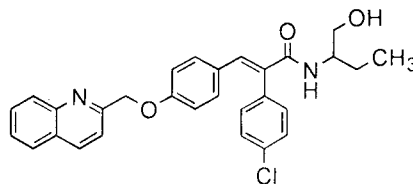
2-(4-Chlorophenyl)-*N*-(2-cyanoethyl)-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 83 (200 mg, 0.481 mmol) with 3-aminopropionitrile fumarate (247 mg, 0.962 mmol) as described in Example 2 to yield 120 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.67 (t, $J = 6.6$ Hz, 2H), 3.52 (q, $J = 6.3$ Hz, 2H), 5.33 (s, 2H), 5.78 (br s, 1H), 6.82 (d, $J = 8.7$ Hz, 2H), 6.94 (d, $J = 8.7$ Hz, 2H), 7.20-7.27 (m, 2H), 7.45 (d, $J = 8.4$ Hz, 2H), 7.51-7.61 (m, 2H), 7.71-7.83 (m, 3H), 8.06 (d, $J = 8.1$ Hz, 1H), 8.17 (d, $J = 8.1$ Hz, 1H); ESI (m/z) 468 ($\text{M}+\text{H}$) $^+$.

Example 182

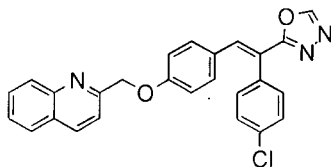
($\pm$)-2-(4-Chlorophenyl)-N-(1-hydroxybutan-2-yl)-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide



The title compound was prepared by coupling Intermediate 83 (150 mg, 0.360 mmol) with 2-aminobutan-1-ol (39 mg, 0.433 mmol) as described in Example 2 to yield 101 mg of the product as off white solid; ^1H NMR (300 MHz, CDCl_3) δ 0.85 (t, $J = 7.5$ Hz, 3H), 1.30-1.40 (m, 1H), 1.48-1.57 (m, 1H), 2.92 (br s, 1H), 3.55 (br s, 1H), 3.67 (br s, 1H), 3.92 (br s, 1H), 5.33 (s, 2H), 5.42 (d, $J = 6.9$ Hz, 1H), 6.81 (d, $J = 8.7$ Hz, 2H), 6.92 (d, $J = 8.7$ Hz, 2H), 7.19-7.27 (m, 2H), 7.44 (d, $J = 7.8$ Hz, 2H), 7.54-7.61 (m, 2H), 7.71-7.83 (m, 3H), 8.06 (d, $J = 8.4$ Hz, 1H), 8.17 (d, $J = 8.4$ Hz, 1H); ESI (m/z) 487 ($\text{M}+\text{H}$) $^+$.

Example 183

2-({4-[2-(4-Chlorophenyl)-2-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline

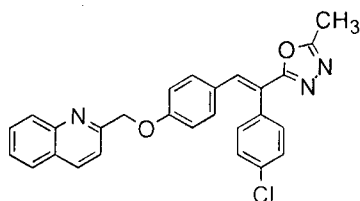


The title compound was prepared from Intermediate 84 (300 mg, 0.697 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 63 mg of the product as off-

white solid; ^1H NMR (300 MHz, CDCl_3) δ 5.36 (s, 2H), 6.86 (d, $J = 8.7$ Hz, 2H), 7.05 (d, $J = 8.7$ Hz, 2H), 7.25-7.32 (m, 2H), 7.41 (d, $J = 8.4$ Hz, 2H), 7.52-7.60 (m, 2H), 7.66 (s, 1H), 7.75 (t, $J = 7.8$ Hz, 1H), 7.83 (d, $J = 8.4$ Hz, 1H), 8.07 (d, $J = 9.0$ Hz, 1H), 8.19 (d, $J = 8.1$ Hz, 1H), 8.37 (s, 1H); ESI-MS (m/z) 440 ($\text{M}+\text{H}$) $^+$.

Example 184

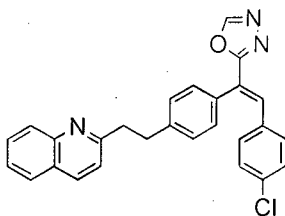
2-({4-[2-(4-Chlorophenyl)-2-(5-methyl-1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline



The title compound was prepared from Intermediate 84 (300 mg, 0.697 mmol) and triethyl orthoacetate (15 ml) as described in Example 113 to give 150 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 2.56 (s, 3H), 5.35 (s, 2H), 6.85 (d, $J = 9.0$ Hz, 2H), 7.03 (d, $J = 9.0$ Hz, 2H), 7.27 (d, $J = 9.6$ Hz, 2H), 7.40 (d, $J = 8.4$ Hz, 2H), 7.52-7.62 (m, 3H), 7.74 (t, $J = 7.5$ Hz, 1H), 7.83 (d, $J = 8.4$ Hz, 1H), 8.07 (d, $J = 7.8$ Hz, 1H), 8.18 (d, $J = 8.7$ Hz, 1H); ESI-MS (m/z) 454 ($\text{M}+\text{H}$) $^+$.

Example 185

2-(2-{4-[2-(4-Chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenyl}ethyl)quinoline



The title compound was prepared from Intermediate 82 (260 mg, 0.607 mmol) and excess of triethyl orthoformate (5 ml) as described in Example 113 to give 45 mg of the product as off-white solid; ^1H NMR (300 MHz, CDCl_3) δ 3.21-3.26 (m, 2H), 3.36 (d, $J = 7.8$ Hz, 2H), 6.99 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.7$ Hz, 2H), 7.21-7.32 (m, 5H), 7.53 (t, $J = 7.8$ Hz, 1H), 7.65 (s, 1H), 7.73 (t, $J = 7.8$ Hz, 1H), 7.82 (d, $J = 8.4$ Hz, 1H), 8.10 (d, $J = 7.2$ Hz, 2H), 8.39 (s, 1H); ESI-MS (m/z) 438 ($\text{M}+\text{H}$) $^+$.

Pharmacological activity

Phosphodiesterase 10 enzyme hydrolyses cAMP/cGMP to metabolically inactive 5'AMP/5'GMP. Inhibition of PDE10 enzyme activity can be quantitated by using a two step radiometric assay procedure (see Sette, C., Iona, S. and Conti, M., *J. Biol. Chem.*, 269 (12), 1994, pp 9245-9252). In this assay, PDE10 enzyme converts ^3H -cAMP/ ^3H -cGMP to ^3H -AMP/ ^3H -GMP which is then converted to ^3H -adenosine/ ^3H -guanosine using snake venom nucleotidase. The radioactivity released in the supernatant liquid is quantitated as an indicator of PDE10 enzyme activity.

In-vitro screening assay of PDE10A inhibitors

Test compounds or reference compounds such as Dipyridamole, IBMX (Calbiochem) and Papverine (Sigma) were dissolved in pure dimethylsulfoxide (DMSO) to prepare 1.0 mM stock solution and diluted suitably to afford the desired concentration. Final concentration of DMSO in the assay was 3 % (v/v). Substrate mixture was prepared by mixing ^3H -cAMP (GE Healthcare) and 1.0 mM cold cAMP (Sigma) in order to get 0.5 μCi / mL & 1 μM final concentrations of each respectively in the assay buffer. A 1.0 mg/mL of snake venom nucleotidase (Sigma) was prepared in D/w. Dowex (AG1-X8 from Biorad) slurry was mixed with water and ethanol at 1.0:1.0:1.0 ratios. The assay was carried out using suitably diluted PDE 10A enzyme preparation (BPS Biosciences) to get around 15-20% substrate hydrolysis to ensure linear reaction kinetics.

PDE10 assay was carried out in 200 μL reaction volume by addition of assay buffer containing 10.0 mM Tris-HCl (pH 7.4), 0.2 mM MgCl_2 , test compound at required concentration and diluted enzyme. Reaction mixture was incubated at 30 $^{\circ}\text{C}$ for 30 min. The reaction was stopped by heating the plate in boiling water bath for 5.0 min and then cooling on an ice bath for 15 min. This was followed by addition of 50 μL of *Crotalus atrox* snake venom 5'-nucleotidase and incubation at 30 $^{\circ}\text{C}$ for 30 min. Thereafter 400 μL of Dowex was added and incubated on ice bath for 15 min. Reaction mixture was centrifuged and supernatant liquid was used for quantifying radioactivity in the samples. Reaction was measured as counts per minute (cpm) using a Packard Biosciences plate reader. An enzyme control without test compounds was run to quantitate maximum PDE10 reaction. Inhibition of enzyme activity was calculated as a percent

of control reaction. The IC_{50} values were calculated from dose-response curve by nonlinear regression analysis using Graph Pad Prism software.

The compounds prepared were tested using the above assay procedure and the results obtained are given in Table 4. Percentage inhibition of human PDE10A enzyme at concentrations of 1.0 μ M and 10.0 μ M are given in the table 4 along with IC_{50} (nM) for selected examples. The IC_{50} (nM) values of the compounds are set forth in Table 4 wherein "A" refers to an IC_{50} value of less than 20 nM, "B" refers to an IC_{50} value in range of 20.01-50 nM, "C" refers to an IC_{50} value in range of 50.01-100 nM and "D" refers to an IC_{50} value of more than 100 nM.

Table 4: In-vitro screening results (hPDE10A activity) of compounds of invention

Example No.	Percentage inhibition of hPDE10A at		IC_{50} (nM)
	1 μ M	10 μ M	
1.	89.45	96.71	C
2.	84.60	98.37	C
3.	42.96	86.79	-
4.	35.21	73.51	--
5.	47.23	84.58	--
6.	22.09	67.39	-
7.	67.74	99.29	-
8.	55.51	88.00	-
9.	89.01	99.68	B
10.	65.82	95.80	D
11.	46.52	87.71	--
12.	78.07	96.24	D
13.	71.51	93.84	D
14.	17.03	17.22	-
15.	79.10	97.13	D
16.	14.08	67.09	-
17.	49.53	79.34	--
18.	55.67	87.74	D
19.	38.73	85.93	--

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
20.	55.07	90.54	D
21.	79.80	98.74	C
22.	58.29	91.58	-
23.	90.58	98.62	B
24.	17.31	51.94	-
25.	30.18	77.85	-
26.	94.79	99.49	A
27.	60.31	92.27	-
28.	75.11	97.60	D
29.	64.39	94.63	-
30.	45.71	81.87	-
31.	92.07	98.33	A
32.	72.13	95.68	D
33.	90.89	99.02	C
34.	38.63	73.09	-
35.	85.21	96.26	C
36.	70.38	92.15	D
37.	58.79	89.32	D
38.	72.70	95.36	D
39.	02.37	14.02	--
40.	91.18	98.08	C
41.	67.91	94.32	-
42.	44.79	86.43	-
43.	72.72	96.87	D
44.	90.96	98.97	C
45.	83.17	99.71	C
46.	87.83	98.46	D

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
47.	07.57	64.63	-
48.	92.74	98.03	B
49.	91.44	98.87	B
50.	86.05	101.33	C
51.	74.96	94.93	D
52.	67.97	93.82	D
53.	73.85	89.23	C
54.	91.42	97.06	C
55.	95.44	99.51	A
56.	90.79	97.93	C
57.	88.60	97.12	C
58.	95.19	97.88	A
59.	65.58	94.50	D
60.	73.01	88.11	-
61.	96.77	97.50	A
62.	66.93	95.44	D
63.	64.67	95.30	D
64.	87.62	97.18	D
65.	46.11	92.14	-
66.	43.03	54.21	-
67.	59.63	91.07	-
68.	83.03	100.78	D
69.	64.95	94.88	-
70.	94.45	99.90	B
71.	99.66	100.00	A
72.	92.99	99.29	C
73.	97.89	99.61	A

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
74.	94.01	99.21	B
75.	94.69	99.95	B
76.	95.68	99.56	A
77.	97.39	98.67	A
78.	95.65	97.55	A
79.	99.28	99.82	C
80.	97.82	99.94	A
81.	95.39	100.52	B
82.	94.52	100.00	A
83.	79.15	96.83	D
84.	97.44	97.36	A
85.	101.16	100.75	A
86.	99.14	98.92	A
87.	100.08	102.00	A
88.	96.67	97.08	A
89.	97.52	98.80	A
90.	97.18	97.87	A
91.	98.19	99.54	A
92.	86.49	89.58	A
93.	90.67	90.58	B
94.	97.23	99.29	A
95.	97.85	99.86	A
96.	86.80	99.94	C
97.	99.74	100.00	B
98.	96.64	98.26	A
99.	96.84	100.08	A
100.	90.93	98.61	C

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
101.	98.13	98.65	A
102.	94.70	98.68	B
103.	85.70	92.54	D
104.	96.99	100.36	B
105.	91.20	97.30	C
106.	95.17	96.21	A
107.	98.97	99.44	A
108.	99.27	98.44	A
109.	93.12	94.16	A
110.	98.11	99.51	A
111.	82.91	94.56	D
112.	84.25	97.65	B
113.	98.81	100.00	A
114.	83.11	96.09	D
115.	73.49	70.69	-
116.	70.96	96.25	D
117.	98.14	100.68	A
118.	96.81	99.76	A
119.	99.68	99.27	A
120.	99.61	99.40	A
121.	25.72	44.03	-
122.	13.07	37.48	-
123.	83.43	96.59	C
124.	93.40	97.34	A
125.	17.89	27.45	-
126.	86.51	98.14	B
127.	96.90	102.04	B

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
128.	94.30	99.94	B
129.	97.52	99.96	B
130.	97.87	102.30	A
131.	92.07	78.21	-
132.	88.70	98.80	D
133.	41.21	83.91	-
134.	85.98	96.78	B
135.	98.55	98.25	A
136.	85.86	95.78	C
137.	95.24	98.26	B
138.	95.31	101.76	B
139.	95.70	99.83	A
140.	87.92	94.96	C
141.	97.64	99.37	A
142.	89.68	98.38	C
143.	76.86	99.78	D
144.	95.18	98.72	A
145.	89.27	97.68	C
146.	05.58	14.63	-
147.	86.24	97.93	C
148.	89.03	97.51	C
149.	96.36	99.21	A
150.	100.54	102.21	A
151.	94.72	98.25	B
152.	25.97	57.87	-
153.	94.37	97.10	B
154.	97.75	98.84	A

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
155.	48.12	92.05	-
156.	72.89	95.20	D
157.	87.67	97.17	C
158.	81.40	98.40	D
159.	98.88	98.46	A
160.	93.80	99.07	B
161.	96.47	98.26	A
162.	78.61	93.38	D
163.	67.98	80.07	D
164.	84.09	98.62	C
165.	97.62	99.46	A
166.	68.68	93.30	-
167.	98.12	100.43	A
168.	99.91	100.57	A
169.	83.66	97.67	C
170.	13.80	05.78	-
171.	24.79	68.32	-
172.	60.35	65.29	-
173.	77.73	85.74	-
174.	99.64	99.14	A
175.	94.72	99.46	C
176.	98.03	99.06	A
177.	100.00	100.00	A
178.	96.02	97.68	A
179.	98.16	96.97	A
180.	08.38	54.94	-
181.	06.49	09.16	-

Example No.	Percentage inhibition of hPDE10A at		IC ₅₀ (nM)
	1 μ M	10 μ M	
182.	10.27	56.07	-
183.	09.07	11.65	-
184.	0.90	06.10	-
185.	89.69	97.62	B

In vivo efficacy screen for Psychoses:

The illustrative examples of the present invention are screened for 'in vivo' PDE10 based efficacy in a rat model of Dizocilpine (MK-801) – induced psychotic behaviour according to slightly modified procedures described in a [Andine, P et al., *JPET*, 290, p. 1393-1408. (1999)]. The screening of the compounds can also be carried out by some other methods and procedures known to persons skilled in the art.

Dizocilpine (MK-801) – induced model of Psychosis in female Sprague-Dawley rats:

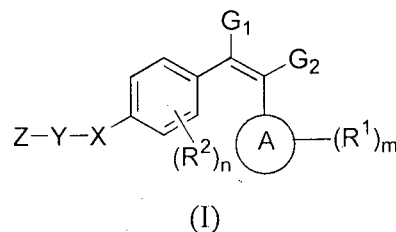
Dizocilpine (MK-801), a highly selective non-competitive antagonist of NMDA (N-methyl-d-aspartate) receptor [an excitatory amino acid (glutamate, EAA) receptor] is known to produce psychosis both in rodents and humans. A dysfunction in the main excitatory neurotransmitter system of the brain through the EAA receptors has been well documented in psychoses. On the day of the experiment, rats were acclimatized for 15 min before the administration of 0.2 mg/kg of MK-801 by subcutaneous route, followed by a behavioural observation (three behaviours: locomotion, stereotyped sniffing and ataxia) scoring that started 15 min after injection and continued for 1 h (i.e. 15-75 min post MK-801) [Andine, P et al., *JPET*, 290, p. 1393-1408, (1999)]. The test compounds were administered at appropriate time point prior to the MK-801 injection, based on the route of administration.

Example No. 91, at a dose of 30 mg/kg (p.o.), administered 60 min prior, potentially blocked the MK-801 - induced psychoses in female SD rats as shown in Figure 1.

Example No. 177, at a dose of 30 mg/kg (i.p.), administered 5 min prior, moderately blocked the MK-801 – induced psychoses in female SD rats as shown in Figure 2.

WE CLAIM:

1. A compound of the formula (I):



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

G_1 is selected from hydrogen, cyano, substituted or unsubstituted heteroaryl, heterocyclyl, $-(CR^4R^5)_p-NR^9R^{10}$, $-(CR^4R^5)_p-OR^{11}$ and $-C(O)NR^9R^{10}$;

G_2 is selected from hydrogen, substituted or unsubstituted heteroaryl, heterocyclyl and $-C(O)NR^9R^{10}$; with the proviso that at least one of G_1 or G_2 is not hydrogen;

A is aryl or heteroaryl;

X is a bond or $-O-$;

Y is $-(CR^4R^5)_p-$;

Z is selected from substituted or unsubstituted aryl, heterocyclyl and heteroaryl, wherein said cyclic ring may be monocyclic, bicyclic or spirocyclic;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

at each occurrence, both R^4 and R^5 are hydrogen;

R^9 and R^{10} , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, alkynyl, cyanoalkyl, hydroxyalkyl, haloalkyl, cycloalkyl, heterocyclyl, heteroaryl, $-(CR^dR^e)_qR^a$ and $-C(O)R^a$; or R^9 and R^{10} together with the nitrogen atom to which they are attached, may form an optionally substituted heterocyclyl or heteroaryl ring, wherein said heterocyclic or heteroaryl ring may contain 1, 2, 3 or 4 hetero atom(s) selected from O, S or N;

R^{11} is substituted or unsubstituted aryl or heteroaryl;

at each occurrence, R^a , R^d and R^e , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, aryl, $-C(O)NR^fR^g$, $-C(O)OR^f$ and $-NR^fR^g$;

at each occurrence, R^f and R^g , which may be the same or different, are independently selected from hydrogen, substituted or unsubstituted alkyl and $-C(O)alkyl$;

'm' is an integer ranging from 0 to 5, both inclusive;

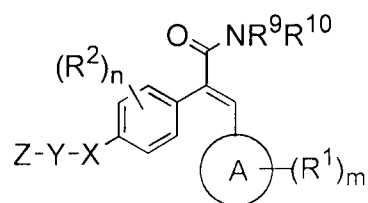
'n' is an integer ranging from 0 to 4, both inclusive;

'p' is an integer ranging from 1 to 3, both inclusive; and

'q' is an integer ranging from 1 to 3, both inclusive.

2. A compound selected from

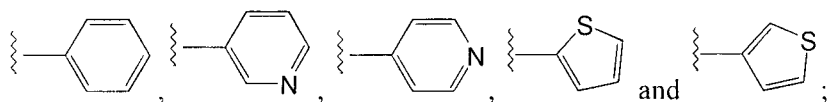
(a) a compound of formula (Ia)



(Ia)

or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

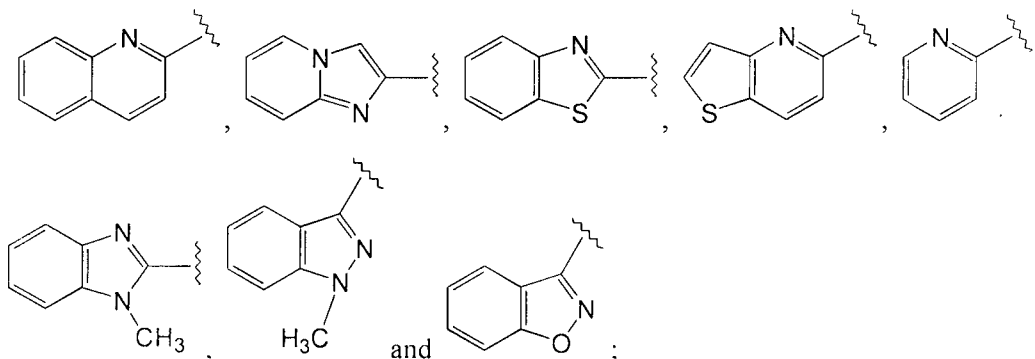
A is selected from a group consisting of



X is a bond or $-O-$;

Y is $-(CH_2)_p-$;

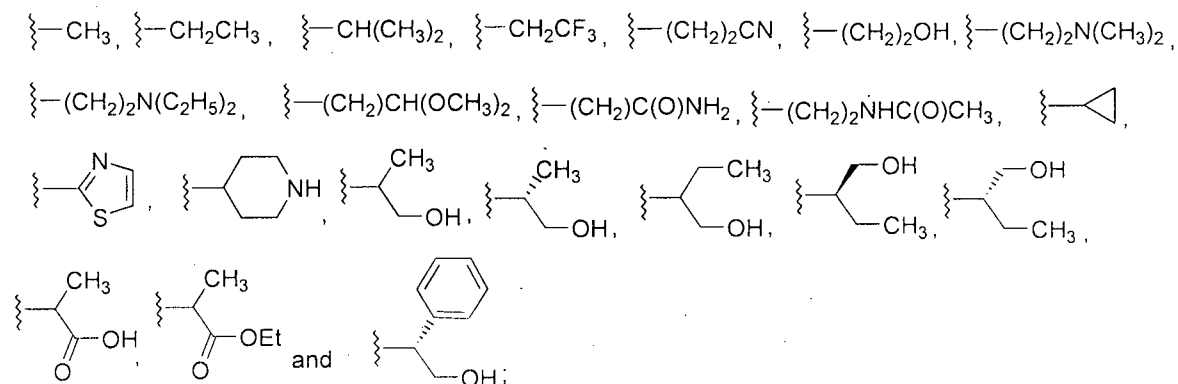
Z is independently selected from a group consisting of



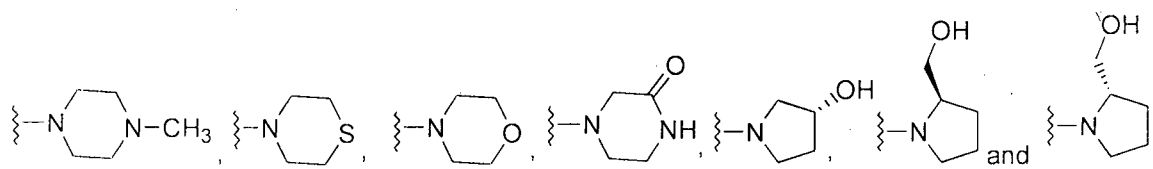
at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

R^9 is hydrogen or substituted or unsubstituted alkyl;

R^{10} is independently selected from a group consisting of hydrogen,



or R^9 and R^{10} together with the nitrogen atom to which they are attached, forms heterocyclic ring independently selected from a group consisting of

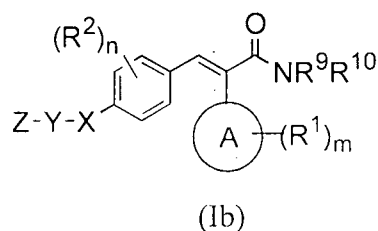


'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

(b) a compound of the formula (Ib)



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is aryl, preferably phenyl;

X is -O-;

Y is $-(CH_2)_p-$;

Z is heteroaryl, preferably quinolinyl;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

R^9 is hydrogen or substituted or unsubstituted alkyl;

R^{10} is independently selected from a group consisting of hydrogen,

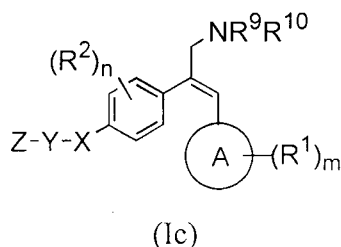
$\{ -CH_3, \{ -(CH_2)_2CN \}$ and $\{ \begin{array}{c} CH_3 \\ | \\ -C- \\ | \\ OH \end{array} \}$;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

(c) a compound of the formula (Ic)



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is aryl, preferably phenyl;

X is -O-;

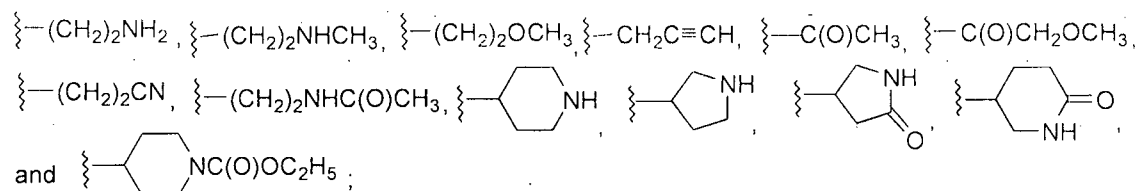
Y is $-(CH_2)_p-$;

Z is heteroaryl, preferably quinolinyl;

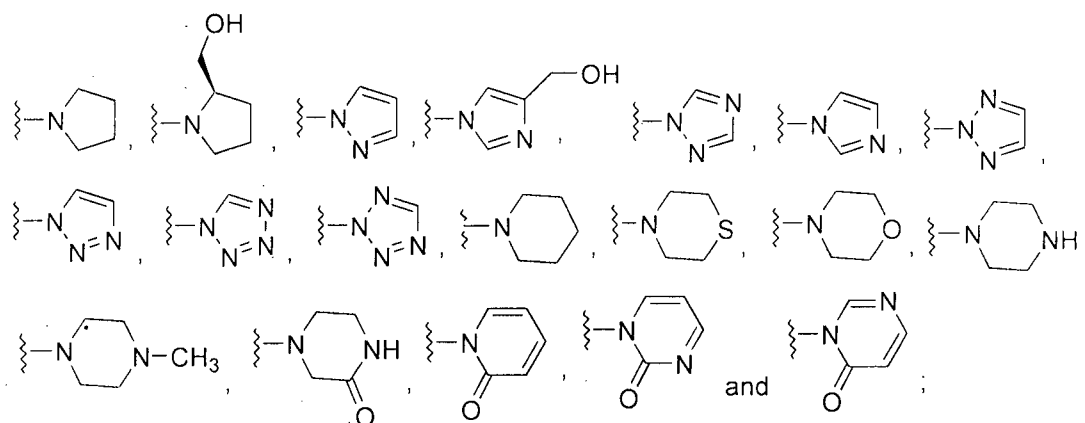
at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

R^9 is hydrogen or substituted or unsubstituted alkyl;

R^{10} is independently selected from a group consisting of hydrogen,



or R^9 and R^{10} together with the nitrogen atom to which they are attached, forms heterocyclic or heteroaryl ring independently selected from a group consisting of

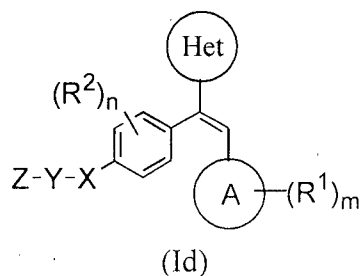


'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

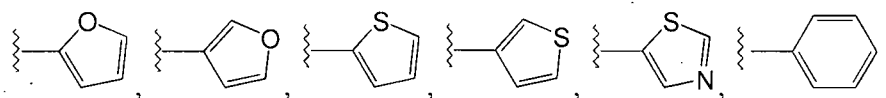
'p' is an integer ranging from 1 to 3, both inclusive.

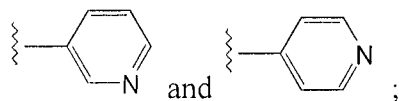
(d) a compound of the formula (Id)



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

ring A is selected from a group consisting of

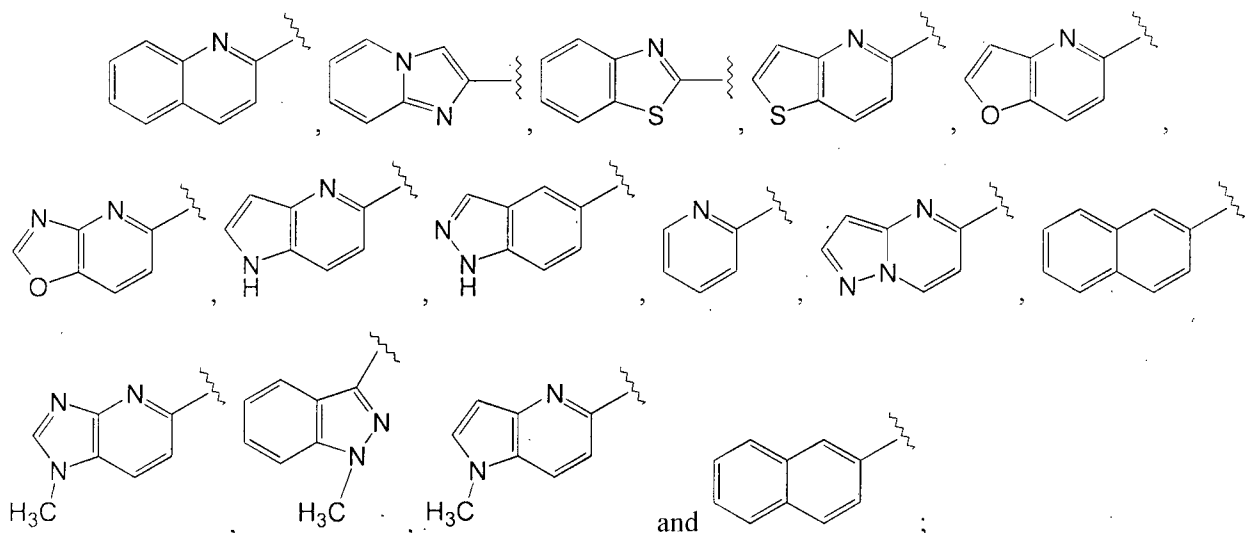




X is a bond or -O-;

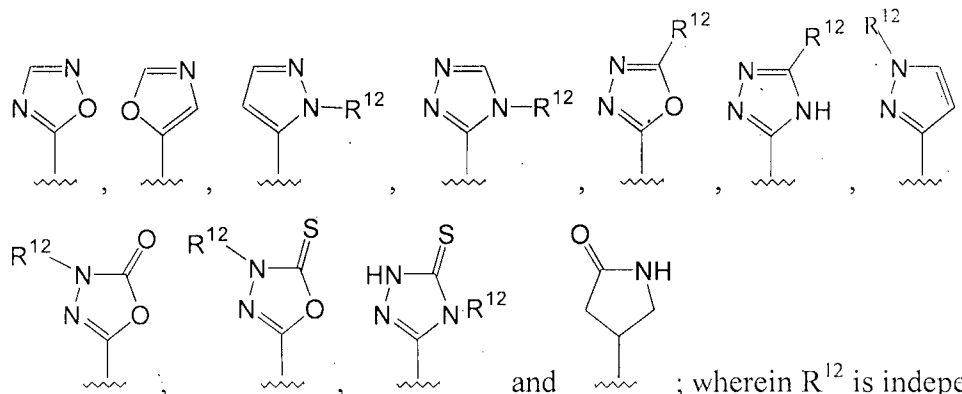
Y is $-(CH_2)_p$;

Z is independently selected from a group consisting of



at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

Het is heteroaryl or heterocyclyl independently selected from a group consisting of



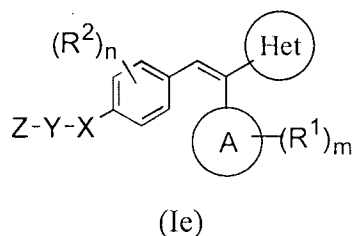
wherein R^{12} is independently selected from hydrogen, halogen, hydroxyl, cyano, substituted or unsubstituted alkyl, hydroxyalkyl, haloalkyl and alkoxy;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

(e) a compound of the formula (Ie)



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

A is aryl preferably phenyl;

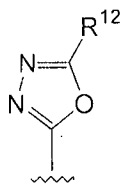
X is -O-;

Y is $-(CH_2)_p-$;

Z is heteroaryl, preferably quinolinyl;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

Het is heteroaryl selected from



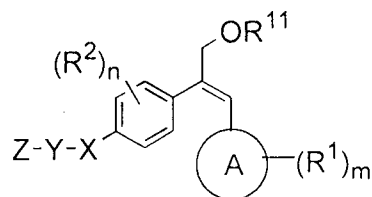
; wherein R^{12} is independently selected from hydrogen, halogen, hydroxyl, cyano, substituted or unsubstituted alkyl, hydroxyalkyl, haloalkyl and alkoxy;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

(f) a compound of the formula (If)



or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof or a *N*-oxide thereof, wherein,

ring A is aryl or heteroaryl selected from phenyl and 4-pyridyl;

X is -O-;

Y is $-(CH_2)_p$;

Z is heteroaryl, preferably quinolinyl;

at each occurrence, R^1 and R^2 , which may be the same or different, are independently selected from halogen, substituted or unsubstituted alkoxy, haloalkyl and haloalkoxy;

R^{11} is aryl or heteroaryl, selected from phenyl, 3-pyridyl and 4-pyridyl;

'm' is an integer ranging from 0 to 5, both inclusive;

'n' is an integer ranging from 0 to 4, both inclusive; and

'p' is an integer ranging from 1 to 3, both inclusive.

3. The compound of claim 1, wherein G_1 is cyano.
4. The compound of claim 2, wherein R^1 in formula (Ia) to (If) is haloalkyl.
5. The compound of claim 4, wherein haloalkyl is trifluoromethyl.
6. The compound of claim 2, wherein R^1 in formula (Ia) or (Id) is haloalkoxy.
7. The compound of claim 6, wherein haloalkoxy is difluoromethoxy or trifluoromethoxy.
8. The compound of claim 2, wherein R^1 in formula (Ia) or (Id) is alkoxy.
9. The compound of claim 8, wherein alkoxy is methoxy or ethoxy.
10. The compound of claim 2, wherein 'm' in formula (Ia) to (If) is 1.
11. The compound of claim 2, wherein 'm' in formula (Ic) or (Id) is 2.
12. The compound of claim 2, wherein 'm' in formula (Ia), (Ic), (Id) or (If) is 0.
13. The compound of claim 2, wherein 'n' in formula (Ia) to (If) is 0.
14. The compound of claim 2, wherein ' R^2 ' in formula (Id) is fluorine, chlorine or methoxy and 'n' is 1.

15. The compound of claim 2, wherein 'p' in formula (Ia) to (If) is 1.
16. The compound of claim 2, wherein 'p' in formula (Ia) or (Id) is 2
17. The compound of claim 2, wherein R¹² in formula (Id) or (Ie) is hydrogen.
18. The compound of claim 2, wherein R¹² in formula (Id) or (Ie) is alkyl.
19. The compound of claim 18, wherein alkyl is methyl or ethyl.
20. The compound of claim 2, wherein R¹² in formula (Id) or (Ie) is haloalkyl.
21. The compound of claim 20, wherein haloalkyl is trifluoromethyl.
22. The compound of claim 2, wherein
 - (a) the compound is selected from
 - 3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - 3-(4-chlorophenyl)-2-[4-(imidazo[1,2-a]pyridin-2-ylmethoxy)phenyl]-N-methyl-prop-2-enamide;
 - 2-[4-(1,3-benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)-N-methylprop-2-enamide;
 - N-methyl-2-{4-[(1-methyl-1H-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-3-yl)prop-2-enamide;
 - N-methyl-2-{4-[(1-methyl-1H-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-4-yl)prop-2-enamide;
 - 3-(4-chlorophenyl)-N-methyl-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enamide;
 - N-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-(thiophen-2-yl)prop-2-enamide;
 - N-methyl-3-phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - 3-(4-chlorophenyl)-N-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - 3-(4-fluorophenyl)-N-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - N-methyl-3-(pyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - N-methyl-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - 3-(4-methoxyphenyl)-N-methyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - 2-{4-[2-(1,2-benzoxazol-3-yl)ethoxy]phenyl}-3-(4-chlorophenyl)-N-methylprop-2-enamide;
 - N-ethyl-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 - 3-(4-chlorophenyl)-2-[4-(pyridin-2-ylmethoxy)phenyl]-N-(2,2,2-trifluoroethyl)prop-2-enamide;
 - 2-{4-[(1-methyl-1H-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-3-yl)-N-(2,2,2-trifluoroethyl)prop-2-enamide;

2-{4-[(1-methyl-1*H*-benzimidazol-2-yl)methoxy]phenyl}-3-(pyridin-4-yl)-*N*-(2,2,2-trifluoroethyl)prop-2-enamide;

2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]-3-(pyridin-4-yl)-*N*-(2,2,2-trifluoroethyl) prop-2-enamide;

3-(pyridin-3-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-*N*-(2,2,2-trifluoroethyl)prop-2-enamide;

3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-*N*-(2,2,2-trifluoroethyl)prop-2-enamide;

2-[4-(1,3-benzothiazol-2-ylmethoxy)phenyl]-3-(4-chlorophenyl)-*N*-(2-cyanoethyl)prop-2-enamide;

3-(4-chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy) phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-(2-cyanoethyl)-2-{4-[(1-methyl-1*H*-indazol-3-yl)methoxy]phenyl} prop-2-enamide;

3-(4-chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(thieno[3,2-*b*]pyridin-5-ylmethoxy)phenyl]prop-2-enamide;

N-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-(thiophen-2-yl)prop-2-enamide;

N-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-(thiophen-3-yl)prop-2-enamide;

N-(2-cyanoethyl)-3-phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(3-chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(2-cyanoethyl)-3-(4-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(2-cyanoethyl)-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(2-cyanoethyl)-3-(1-oxidopyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(2-cyanoethyl)-3-(4-methoxyphenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(2-cyanoethyl)-3-[4-(difluoromethoxy)phenyl]-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide;

N-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethoxy)phenyl] prop-2-enamide;

N-(2-cyanoethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide;

2-{4-[2-(1,2-benzoxazol-3-yl)ethoxy]phenyl}-3-(4-chlorophenyl)-*N*-(2-cyanoethyl) prop-2-enamide;

3-(4-chlorophenyl)-*N*-(2-hydroxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-[2-(dimethylamino)ethyl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-[2-(diethylamino)ethyl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(propan-2-yl)-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

(±)-3-(4-chlorophenyl)-*N*-(1-hydroxypropan-2-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide;

N-[(2*R*)-1-hydroxypropan-2-yl]-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-(1-hydroxybutan-2-yl)-2-[4-(imidazo[1,2-*a*]pyridin-2-ylmethoxy)phenyl]prop-2-enamide;

(±)-3-(4-chlorophenyl)-*N*-(1-hydroxybutan-2-yl)-2-[4-(pyridin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-[(2*R*)-1-hydroxybutan-2-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

3-(4-chlorophenyl)-*N*-[(2*S*)-1-hydroxybutan-2-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

(±)-*N*-(1-hydroxybutan-2-yl)-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

(±)-*N*-(1-hydroxybutan-2-yl)-3-(4-methoxyphenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide;

N-[(1*R*)-2-hydroxy-1-phenylethyl]-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl] prop-2-enamide;

(±)-ethyl *N*-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl} alaninate;

(±)-*N*-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl} alanine;

3-(4-chlorophenyl)-*N*-(2,2-dimethoxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

N-(2-amino-2-oxoethyl)-3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
N-[2-(acetylamino)ethyl]-3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
N-cyclopropyl-3-(pyridin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-*N*-(1,3-thiazol-2-yl)prop-2-enamide;
 3-(4-chlorophenyl)-*N*-(piperidin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide di(trifluoroacetic acid);
 3-(4-chlorophenyl)-1-[(3*R*)-3-hydroxypyrrolidin-1-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one;
 3-(4-chlorophenyl)-1-[(2*R*)-2-(hydroxymethyl)pyrrolidin-1-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one;
 3-(4-chlorophenyl)-1-[(2*S*)-2-(hydroxymethyl)pyrrolidin-1-yl]-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one;
 3-(4-chlorophenyl)-1-(4-methylpiperazin-1-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one;
 3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]-1-(thiomorpholin-4-yl)prop-2-en-1-one;
 3-(4-chlorophenyl)-1-(morpholin-4-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-one;
 4-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enoyl}piperazin-2-one;
 3-(4-chlorophenyl)-*N*-(2-cyanoethyl)-2-{4-[2-(quinolin-2-yl)ethyl]phenyl}prop-2-enamide;

(b) the compound is selected from

2-(4-chlorophenyl)-*N*-methyl-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 2-(4-chlorophenyl)-*N*-(2-cyanoethyl)-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;
 (±)-2-(4-chlorophenyl)-*N*-(1-hydroxybutan-2-yl)-3-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enamide;

(c) the compound is selected from

N-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}ethane-1,2-diamine di(trifluoroacetic acid) salt;
 3-(4-chlorophenyl)-*N*-(prop-2-yn-1-yl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine;

3-(4-chlorophenyl)-*N*-(2-methoxyethyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine dihydrochloride;

3-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) propanenitrile dihydrochloride;

N-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}-*N'*-methyl ethane-1,2-diamine di(trifluoro acetic acid);

N-[2-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino)ethyl] acetamide;

(3*S*)-*N*-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl} pyrrolidin-3-amine di(trifluoroacetic acid);

(4*S*)-4-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) pyrrolidin-2-one;

N-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl} piperidin-4-amine di(trifluoroacetic acid) salt;

ethyl 4-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) piperidine-1-carboxylate;

(5*S*)-5-({3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}amino) piperidin-2-one;

3-(4-chlorophenyl)-*N,N*-dimethyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-amine;

2-({4-[1-(4-chlorophenyl)-3-(pyrrolidin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

[(2*S*)-1-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrrolidin-2-yl]methanol;

2-({4-[1-(4-chlorophenyl)-3-(1*H*-pyrazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

2-({4-[1-(4-chlorophenyl)-3-(1*H*-imidazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

(1-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}-1*H*-imidazol-4-yl) methanol;

2-({4-[1-(4-chlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

2-({4-[1-(4-chlorophenyl)-3-(2*H*-1,2,3-triazol-2-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

2-({4-[1-(4-chlorophenyl)-3-(1*H*-1,2,3-triazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

2-({4-[1-(4-chlorophenyl)-3-(1*H*-tetrazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;

2-({4-[1-(4-chlorophenyl)-3-(2*H*-tetrazol-2-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;
 2-({4-[1-(4-chlorophenyl)-3-(piperidin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;
 2-({4-[1-(4-chlorophenyl)-3-(thiomorpholin-4-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;
 2-({4-[1-(4-chlorophenyl)-3-(morpholin-4-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;
 2-({4-[1-(4-chlorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline
 di(trifluoro acetic acid);
 2-({4-[1-(4-fluorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline
 trihydrochloride;
 2-({4-[1-(4-chloro-3-fluorophenyl)-3-(piperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl) quinoline
 trihydrochloride;
 2-({4-[1-(4-chlorophenyl)-3-(4-methylpiperazin-1-yl)prop-1-en-2-yl]phenoxy}methyl)
 quinoline;
 4-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}piperazin-2-one;
 1-{3-(4-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyridin-2(1*H*)-one;
 1-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-2(1*H*)-one;
 1-{3-(4-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-2(1*H*)-one;
 3-{3-phenyl-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-4(3*H*)-one;
 3-{3-(4-fluorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}pyrimidin-4(3*H*)-one;
 2-({4-[1-(4-fluorophenyl)-3-(1*H*-tetrazol-1-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;
 2-({4-[1-(4-fluorophenyl)-3-(2*H*-tetrazol-2-yl)prop-1-en-2-yl]phenoxy}methyl)quinoline;
N-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}acetamide;
N-{3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-en-1-yl}-2-methoxy
 acetamide;

(d) the compound is selected from

4-{2-(4-chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}pyrrolidin-2-one;
 2-({4-[2-(4-chlorophenyl)-1-(1,3-oxazol-5-yl)ethenyl]phenoxy}methyl)quinoline;
 2-({4-[2-(4-chlorophenyl)-1-(1-methyl-1*H*-pyrazol-5-yl)ethenyl]phenoxy}methyl)quinoline;
 2-({4-[2-(4-chlorophenyl)-1-(1-methyl-1*H*-pyrazol-3-yl)ethenyl]phenoxy}methyl)quinoline;
 2-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)vinyl]phenoxy}methyl)imidazo[1,2-*a*]
 pyridine;

2-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1,3-benzothiazole;
3-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-methyl-1*H*-indazole;
2-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)pyridine;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)thieno[3,2-*b*]pyridine;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)furo[3,2-*b*]pyridine;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1*H*-pyrrolo[3,2-*b*]pyridine;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-methyl-1*H*-pyrrolo[3,2-*b*]pyridine;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1*H*-indazole;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)-1-methyl-1*H*-indazole;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}ethyl)[1,3]oxazolo [4,5-*b*]pyridine;
5-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)pyrazolo[1,5-*a*]pyrimidine;
2-{2-(4-chlorophenyl)-1-[4-(naphthalen-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazole;
2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-(thiophen-2-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-(thiophen-3-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[2-(furan-2-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[2-(furan-3-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-(1,3-thiazol-5-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[2-(2-chloro-1,3-thiazol-5-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-phenylethenyl]phenoxy}methyl)quinoline;
2-({2-chloro-4-[1-(1,3,4-oxadiazol-2-yl)-2-phenylethenyl]phenoxy}methyl)quinoline;
2-({4-[2-(3-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;
2-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]-2-methoxyphenoxy}methyl)quinoline;

2-({4-[2-(4-fluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-(pyridin-3-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(6-methoxypyridin-3-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(6-ethoxypyridin-3-yl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-(pyridin-4-yl)ethenyl]phenoxy}methyl)quinoline;

2-({2-fluoro-4-[1-(1,3,4-oxadiazol-2-yl)-2-(pyridin-4-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(1,3,4-oxadiazol-2-yl)-2-(1-oxidopyridin-4-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(4-methoxyphenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-[4-(difluoromethoxy)phenyl]-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-[(4-{1-(1,3,4-Oxadiazol-2-yl)-2-[4-(trifluoromethoxy)phenyl]ethenyl}phenoxy)methyl]quinoline;

2-[(4-{1-(1,3,4-oxadiazol-2-yl)-2-[4-(trifluoromethyl)phenyl]ethenyl}phenoxy)methyl]quinoline;

2-({4-[2-(2,4-difluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(4-Chloro-2-fluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(4-chloro-3-fluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(3,4-difluorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[2-(4-chlorophenyl)-1-(1,2,4-oxadiazol-5-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(4-chlorophenyl)ethenyl]phenoxy}methyl)imidazo[1,2-*a*]pyridine;

2-({4-[2-(4-chlorophenyl)-1-(5-methyl-1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)pyridine;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(thiophen-2-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(thiophen-3-yl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-phenylethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(4-chlorophenyl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(4-fluorophenyl)ethenyl]phenoxy}methyl)quinoline;

2-({4-[1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-pyridin-4-ylethenyl]phenoxy}methyl)quinoline;

- 2-[(4-{1-(5-methyl-1,3,4-oxadiazol-2-yl)-2-[4-(trifluoromethyl)phenyl]ethenyl}phenoxy)methyl]quinoline;
- 2-({4-[1-(5-{trifluoromethyl}-1,3,4-oxadiazol-2-yl)-2-pyridin-4-ylethenyl]phenoxy}methyl)quinoline;
- 2-({4-[2-(4-chlorophenyl)-1-(5-methyl-4*H*-1,2,4-triazol-3-yl)ethenyl]phenoxy}methyl)imidazo[1,2-*a*]pyridine;
- 2-({4-[2-(4-chlorophenyl)-1-(5-methyl-4*H*-1,2,4-triazol-3-yl)ethenyl]phenoxy}methyl)quinoline;
- 5-{2-phenyl-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazol-2(3*H*)-one;
- 5-{2-(4-chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazol-2(3*H*)-one;
- 5-{2-(4-chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-1,3,4-oxadiazol-2(3*H*)-thione;
- 5-{2-(4-chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-2,4-dihydro-3*H*-1,2,4-triazole-3-thione;
- 5-{2-(4-chlorophenyl)-1-[4-(quinolin-2-ylmethoxy)phenyl]ethenyl}-4-ethyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione;
- 2-({4-[2-(4-chlorophenyl)-1-(4-ethyl-4*H*-1,2,4-triazol-3-yl)ethenyl]phenoxy}methyl)quinoline;
- 2-(2-{4-[2-(4-chlorophenyl)-1-(1,3,4-oxadiazol-2-yl)ethenyl]phenyl}ethyl)quinoline;
- (e) the compound is selected from
- 2-({4-[2-(4-chlorophenyl)-2-(1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;
- 2-({4-[2-(4-chlorophenyl)-2-(5-methyl-1,3,4-oxadiazol-2-yl)ethenyl]phenoxy}methyl)quinoline;
- (f) the compound is selected from
- 2-({4-[1-(4-chlorophenyl)-3-phenoxyprop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-phenyl-3-(pyridin-3-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-(4-chlorophenyl)-3-(pyridin-3-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-(4-fluorophenyl)-3-(pyridin-3-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-phenyl-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-(4-chlorophenyl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-(4-fluorophenyl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- 2-({4-[1-(pyridin-4-yl)-3-(pyridin-4-yloxy)prop-1-en-2-yl]phenoxy}methyl)quinoline;
- or a pharmaceutically acceptable salt thereof.

23. The compound of claim 1, wherein the compound is
3-(4-chlorophenyl)-2-[4-(quinolin-2-ylmethoxy)phenyl]prop-2-enenitrile or a
pharmaceutically acceptable salt thereof.
24. A pharmaceutical composition comprising a compound according to claims 1 to 23 either
as a free base or a pharmaceutically acceptable salt thereof and one or more pharmaceutically
acceptable excipients, carriers, diluents or mixture thereof.
25. A method for preventing, ameliorating or treating a phosphodiesterase 10A modulated
disease, disorder or syndrome in a subject in need thereof, the method comprising
administering to the subject a therapeutically effective amount of a compound according to
any one of claims 1 to 23.

Drawings:

Figure 1

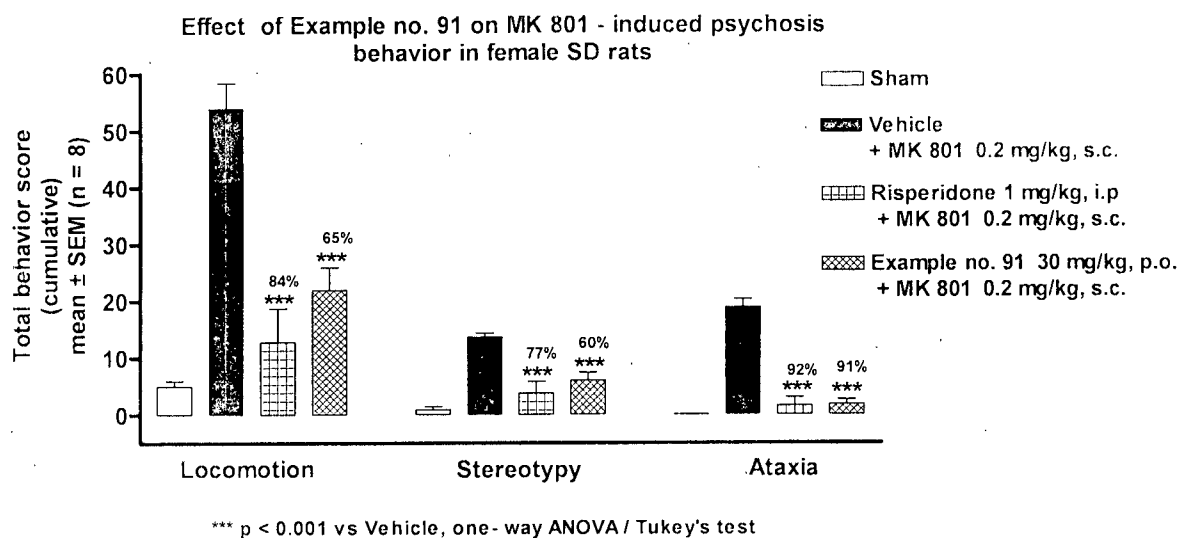
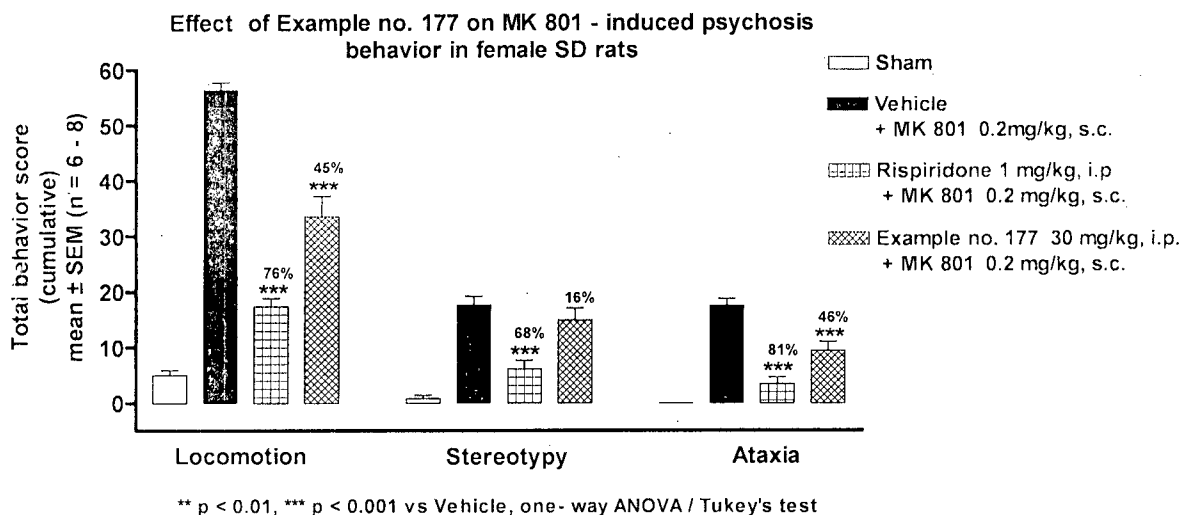


Figure 2



INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2011/000948

A. CLASSIFICATION OF SUBJECT MATTER

See extra sheet

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: C07D, A61P, A61K

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

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

CNABS; CNKI; DWPI; SIPOABS; REG; CAPLUS

quinoline+, +imidazole+, +thiazole+, psycho+, schizo+, delusion+, paranoia, depression+, anxiety, dementia, PDE10; structure search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP0669333A1(J. URIACH & CIA. S.A.), 30 August 1995(30.08.1995), see compounds 4 and 23 on pages 8 and 9 of the description	1, 24
X	CN1109057A(MERCK PATENT GMBH), 27 September 1995(27.09.1995), see example 2 on page 30 of the description	1, 3, 24-25
X	WO91/11999A1(MERCK & CO., INC.), 22 August 1991(22.08.1991), see paragraph 1 on page 4, scheme II-11 on page 156 of the description, claims	1, 3, 24-25
A	see the whole document	2, 4-23

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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

Date of the actual completion of the international search 31 August 2011(31.08.2011)	Date of mailing of the international search report 15 Sep. 2011 (15.09.2011)
Name and mailing address of the ISA/CN The State Intellectual Property Office, the P.R.China 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451	Authorized officer WU, Hao Telephone No. (86-10)62084369

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2011/000948

CLASSIFICATION OF SUBJECT MATTER

C07D215/14(2006.01) i
C07D471/04(2006.01) i
C07D277/64(2006.01) i
C07D235/12(2006.01) i
C07D213/30(2006.01) i
C07D417/12(2006.01) i
C07D401/12(2006.01) i
C07D495/04(2006.01) i
C07D261/20(2006.01) i
C07D413/12(2006.01) i
A61K31/47(2006.01) i
A61K31/4725(2006.01) i
A61K31/4184(2006.01) i
A61K31/428(2006.01) i
A61P25/28(2006.01) i
A61P25/18(2006.01) i
A61P25/22(2006.01) i

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2011/000948

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

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

1. ☒ Claims Nos.: 25

because they relate to subject matter not required to be searched by this Authority, namely:

Claim 25 is directed to a method of treatment of the human/animal body (Rule 39.1(iv) PCT).

Nonetheless, the search has been carried out based on the use of the compounds in the manufacture of medicaments for preventing, ameliorating or treating a phosphodiesterase 10A modulated disease, disorder or syndrome in a subject in need thereof.

2. ☐ Claims Nos.:

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

3. ☐ Claims Nos.:

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

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

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

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on protest

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

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2011/000948

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
EP0669333A1	30.08.1995	US5554624A	10.09.1996
		ES2079315B1	16.10.1996
		NO950684A	25.08.1995
		CA2143412A1	25.08.1995
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		MX9501084A	01.10.1997
		JP7267951A	17.10.1995
		MX197421B	11.07.2000
CN1109057A	27.09.1995	CZ9402873A3	14.06.1995
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		CA2136288A1	24.05.1995
		HU71113A2	28.11.1995
		SK140994A3	11.07.1995
		NO944469A	24.05.1995
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		ZA9409260A	25. 10.1995
		JP7267959A	17.10.1995
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		EP0517812A4	18.10.1995
		JP5504969T	29.07.1993
		EP0517812A1	16.12.1992