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(71) Applicant *(for all designated States except US)*: **GLENMARK PHARMACEUTICALS S.A.** [CH/CH]; Chemin de la combeta 5, CH-2300 la chaux-de-fonds (CH).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GHARAT, Laxmikant Atmaram** [IN/IN]; Flat No-203, Tirupati Apartments, Pokhran road no - 2, Majiwada, Maharashtra, Thane 400 601 (IN). **GAJERA, Jitendra Maganbhai** [IN/IN]; Flat no. 12, Ideal Co-operative, Housing Society, Plot no: 24, Sector 2, Koparkhairane, Maharashtra, Navi Mumbai 400 709 (IN). **NARAYANA, Lakshminarayana** [IN/IN]; H. No: 13-29, Plot No: 27/B, Sai colony, Beeramguda Ameenpur Village, Patancheru Mandal, Medak, Maharashtra, Hyderabad 500 020 (IN). **KHAIRATKAR-JOSHI, Neelima** [IN/IN]; 101, Devprayag CHS, Bhakti Mandir Rd, Hari Niwas, Pachpakhadi, Maharashtra, Thane 400 602 (IN). **KATTIGE, Vidya Ganapati** [IN/IN]; 101, Eureka, Hiranandani Estate, Patlipada, Off Ghodbunder Road, Maharashtra, Thane 400 607 (IN).

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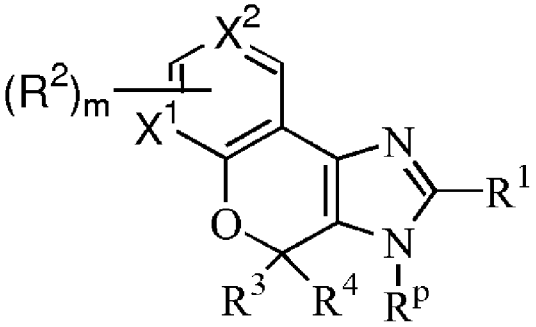
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[Continued on next page]

(54) **Title**: TRICYCLIC COMPOUNDS AS mPGES-1 INHIBITORS



(I)

(57) **Abstract**: The present invention relates to tricyclic compounds of formula (I) or pharmaceutically acceptable salt thereof as mPGES-1 inhibitors. These compounds are inhibitors of the microsomal prostaglandin E synthase- 1 (mPGES-1) enzyme and are therefore useful in the treatment of pain and/or inflammation from a variety of diseases or conditions, such as asthama, osteoarthritis, rheumatoid arthritis, acute or chronic pain and neurodegenerative diseases. (I).

WO 2012/110860 A1

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

TRICYCLIC COMPOUNDS AS mPGES-1 INHIBITORS

Related applications

This application claims benefit of Indian provisional application No 439/MUM/2011 filed on Feb 17, 2011 and US provisional application No 61/446,587 filed on Feb 25, 2011, all of which are hereby incorporated by reference in their entirely.

Technical Field

The present patent application relates to tricyclic compounds as mPGES-1 inhibitors.

Background

There are many diseases or disorders that are inflammatory in their nature. One of the major problems associated with existing treatments of inflammatory conditions is inadequate efficacy and/or the prevalence of side effects. Inflammatory diseases that affect the population include asthma, inflammatory bowel disease, rheumatoid arthritis, osteoarthritis, rhinitis, conjunctivitis and dermatitis. Inflammation is also a common cause of pain.

The enzyme cyclooxygenase (COX) converts arachidonic acid to an unstable intermediate, prostaglandin H_2 (PGH_2) which is further converted to other prostaglandins including PGE_2, PGF_{20}, PGD_2, prostacyclin and thromboxane A_2. These arachidonic acid metabolites are known to have pronounced physiological and pathophysiological activity including pro-inflammatory effects. The COX enzyme exists in two forms, one that is constitutively expressed in many cells and tissues (COX-1), and other that in most cells and tissues are induced by pro-inflammatory stimuli, such as cytokines, during an inflammatory response (COX-2).

Among all prostaglandin metabolites, PGE_2 is particularly known to be a strong pro-inflammatory mediator, and is also known to induce fever and pain. Consequently, numerous drugs have been developed with a view to inhibiting the formation of PGE_2, including "NSAIDs" (non-steroidal anti-inflammatory drugs) and "coxibs" (selective COX-2 inhibitors). These drugs act predominantly by inhibition of COX-1 and/or COX-2, thereby reducing the formation of PGE_2. However, the inhibition of COXs has the

disadvantage that it results in the reduction of the formation of all metabolites of PGH_2, thereby decreasing the beneficial properties of some of the metabolites. In view of this, drugs which act by inhibition of COXs are therefore known / suspected to cause adverse biological effects. For example, the non-selective inhibition of COXs by NSAIDs may give rise to gastrointestinal side-effects and affect platelet and renal function. Even the selective inhibition of COX-2 by coxibs, whilst reducing such gastrointestinal side-effects, is believed to give rise to cardiovascular problems.

A combination of pharmacological, genetic and neutralizing antibody approaches demonstrates the importance of PGE2 in inflammation. The conversion of PGH2 to PGE2 by prostaglandin E synthases (PGES) may therefore represent a pivotal step in the propagation of inflammatory stimuli. Microsomal prostaglandin E synthase-1 (mPGES-1) is an inducible PGES after exposure to pro-inflammatory stimuli. mPGES-1 is induced in the periphery and CNS by inflammation and represents therefore a target for acute and chronic inflammatory disorders. PGE2 is a major prostanoid, produced from arachidonic acid liberated by phospholipases (PLAs), which drives the inflammatory processes. Arachidonic acid is transformed by the action of prostaglandin H synthase (PGH synthase, cycloxygenase) into PGH2 which is a substrate for mPGES-1, which is the terminal enzyme transforming PGH2 to the pro-inflammatory PGE2.

PGH_2 may be transformed to PGE_2 by prostaglandin E synthases (PGES). There are two microsomal prostaglandin E synthases (mPGES-1 and mPGES-2), and one cytosolic prostaglandin E synthase (cPGES). Thus, agents that are capable of inhibiting the action of mPGES-1, and thus reducing the formation of the specific arachidonic acid metabolite PGE_2, are likely to be of benefit in the treatment of inflammation. Further, agents that are capable of inhibiting the action of the proteins involved in the synthesis of the leukotrienes are also likely to be of benefit in the treatment of asthma and COPD.

Blocking the formation of PGE2 in animal models of inflammatory pain results in reduced inflammation, pain and fever response (Kojima et. al, *The Journal of Immunology* **2008**, 180, 8361-6; Xu et. al., *The Journal of Pharmacology and Experimental Therapeutics* **2008**, 326, 754-63). In abdominal aortic aneurism, inflammation leads to connective tissue degradation and smooth muscle apoptosis

ultimately leading to aortic dilation and rupture. In animals lacking mPGES-1 a slower disease progression and disease severity has been demonstrated (Wang et. al., *Circulation*, **2008**, 117, 1302-1309).

Several lines of evidence indicate that PGE2 is involved in malignant growth. PGE2 facilitates tumor progression by stimulation of cellular proliferation and angiogenesis and by modulation of immunosupression. In support of a role for PGE2 in cancers, genetic deletion of mPGES-1 in mice suppress the intestinal tumourogenesis (Nakanishi et. al., *Cancer Research* **2008**, 68(9), 3251-9). In human beings, mPGES-1 is also upregulated in cancers such as colorectal cancer (*Schroder Journal of Lipid Research* **2006**, 47, 1071-80).

Myositis is chronic muscle disorder characterized by muscle weakness and fatigue. Proinflammatory cytokines and prostanoids have been implicated in the development of myositis. In skeletal muscle tissue from patients suffering from myositis an increase in cyclooxygenases and mPGES-1 has been demonstrated, implicating mPGES-1 as a target for treating this condition. (*Korotkova Annals of the Rheumatic Diseases* **2008**, 67, 1596- 1602).

In atherosclerosis inflammation of the vasculature leads to atheroma formation that eventually may progress into infarction. In patients with carotid atherosclerosis an increase in mPGES-1 in plauqe regions have been reported (Gomez-Hernandez *Atherosclerosis* **2006**,187, 139-49). In an animal model of atherosclerosis, mice lacking the mPGES-1 receptor was found to show a retarded atherogenesis and a concomitant reduction in macrophage-derived foam cells together with an increase in vascular smooth muscle cells (Wang, *Proceedings of National Academy of Sciences* **2006**, 103(39), 14507-12).

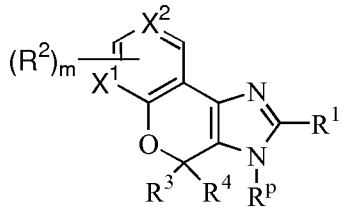
PCT publication numbers WO2006/063466, WO2007/059610, WO2010/034796, and WO2010/100249 disclose numerous heterocyclic compounds which are shown to be inhibitors of microsomal prostaglandin E synthase- 1 (mPGES-1) enzyme.

The present invention is directed to novel compounds that are inhibitors of the mPGES-1 enzyme and would therefore be useful for the treatment of pain and inflammation in a variety of diseases or conditions.

Summary of the Invention

The present patent application is directed to tricyclic compounds with mPGES-1 inhibition.

The present invention relates to compound of formula (I):



(I)

wherein,

X^1 and X^2 are independently selected from –CH- and –N-;

R^1 is selected from hydrogen, substituted or unsubstituted aryl and heteroaryl;

R^2, at each occurrence, is independently selected from halogen, $-C\equiv CR^a$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)R^b$, $-OR^a$, $-(CH_2)_nNR^aR^b$, substituted or unsubstituted alkyl, aryl, heteroaryl and heterocyclic ring;

R^3 and R^4 may be same or different, are independently selected from hydrogen and substituted or unsubstituted alkyl or R^3 and R^4 taken together with the carbon atom to which they are attached may form an optionally substituted 3 to 7 membered saturated or unsaturated cyclic ring, which may optionally include heteroatoms selected from O, N or S;

R^a and R^b, at each occurrence, are independently selected from hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclic ring, and heterocyclylalkyl; or R^a and R^b may be joined together to form an substituted or unsubstituted 3 to 7 membered saturated, unsaturated or partially saturated cyclic ring, which may optionally include at least two heteroatoms selected from O, N, and S;

R^p is hydrogen, substituted or unsubstituted alkyl or arylalkyl;

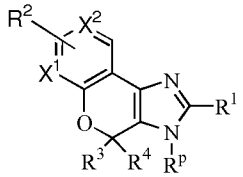
'm' is integer selected from 0 to 3, both inclusive;

and at each occurrence, 'n' is integer selected from 0 to 3, both inclusive;

or a pharmaceutically acceptable salt thereof.

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, the present application provides the compound of formula (Ia) or a pharmaceutically acceptable salt thereof:



(Ia)

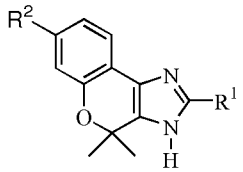
wherein,

X^1, X^2, R^1, R^3, R^4, and R^p are as defined for formula (I);

R^2 is selected from halogen, substituted or unsubstituted aryl, herteroaryl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

According to one embodiment, the present application provides compound of formula (Ia') or a pharmaceutically acceptable salt thereof:



(Ia')

wherein,

R^1 is substituted or unsubstituted aryl, wherein the substitution(s) on the substituted group are one or more selected from halogen and cyano;

R^2 is selected from halogen, substituted or unsubstituted aryl, herteroaryl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, cyano, $-OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl and cycloalkyl;

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

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, the compound of formula (Ia') wherein R^1 is substituted or unsubstituted aryl, preferably substituted aryl, more preferebly substituted phenyl, wherein substituents are halogen (for e.g. chloro, fluoro, bromo or iodo) and cyano.

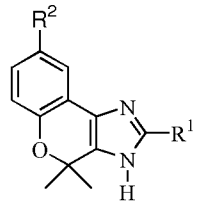
According to another embodiment, the compound of formula (Ia') wherein R^2 is halogen (for e.g. chloro, fluoro, bromo or iodo).

According to yet another embodiment, the compound of formula (Ia') wherein R^2 is unsubstituted or substituted aryl, preferably substituted aryl, more preferably substituted phenyl, wherein substituents are halogen (e.g. chloro, fluoro, bromo or iodo), haloalkyl (for e.g. trifluoromethyl), haloalkoxy (for e.g. trifluoromethoxy, trifluoroethoxy) and methylsulfonyl.

According to yet another embodiment, the compound of formula (Ia') wherein R^2 is unsubstituted or substituted heteroaryl, preferably unsubstituted heteroaryl, more preferably benzimidazole.

According to yet another embodiment, the compound of formula (Ia') wherein R^2 is unsubstituted or substituted heteroaryl, preferably substituted heteroaryl, more preferably oxadiazole, wherein substituent are alkyl (for e.g. propyl) and cycloalkyl (for e.g. cyclopropyl).

According to one embodiment, the present application provides the compound of formula (Ia'') or a pharmaceutically acceptable salt thereof:



(Ia'')

wherein,

R^1 is substituted or unsubstituted aryl, wherein the substitution(s) on the substituted group are one or more selected halogen and cyano; and

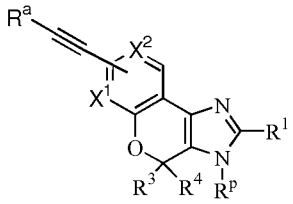
R^2 is halogen.

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, the compound of formula (Ia'') wherein R^1 is substituted or unsubstituted aryl, preferably substituted aryl, more preferebly substituted phenyl, wherein substituents are halogen (for e.g. chloro, fluoro, bromo or iodo) and cyano.

According to another embodiment, the compound of formula (Ia'') wherein R^2 is halogen (for e.g. chloro, fluoro, bromo or iodo).

According to one embodiment, the present application provides compound of formula (Ib) or a pharmaceutically acceptable salt thereof:



(Ib)

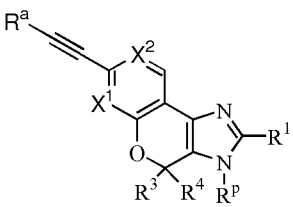
wherein,

X^1, X^2, R^1, R^3, R^4, and R^p are as defined for formula (I);

R^a is selected from hydrogen, substituted or unsubstituted alkyl, cycloalkyl, aryl, heteroaryl, heteroarylalkyl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

According to one embodiment, the present application provides compound of formula (Ib') or a pharmaceutically acceptable salt thereof:



(Ib')

wherein,

X^1, X^2, R^1, R^3, R^4, and R^p are as defined for formula (I);

R^a is selected from hydrogen, substituted or unsubstituted alkyl, cycloalkyl, aryl, heteroaryl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

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, the compound of formula (Ib') wherein R^1 is substituted or unsubstituted aryl, preferably substituted aryl, more preferebly substituted phenyl, wherein substituents are halogen (for e.g. chloro, fluoro, bromo or iodo) and cyano.

According to another embodiment, the compound of formula (Ib') wherein R^1 is substituted or unsubstituted heteroaryl, preferably substituted heteroaryl, more preferebly substituted thiazole, wherein substituent is alkyl, preferably methyl.

According to yet another embodiment, the compound of formula (Ib') wherein R^1 is substituted or unsubstituted heteroaryl, preferably substituted heteroaryl, more preferebly substituted pyridine, wherein substituents are alkyl (for e.g. methyl), cyano, or halogen (for e.g. chloro, fluoro, bromo or iodo).

According to yet another embodiment, the compound of formula (Ib') wherein X^1 and X^2 is –CH.

According to yet another embodiment, the compound of formula (Ib') wherein X^1 or X^2 is N.

According to yet another embodiment, the compound of formula (Ib') wherein R^P is hydrogen.

According to yet another embodiment, the compound of formula (Ib') wherein R^3 and R^4 are methyl.

According to yet another embodiment, the compound of formula (Ib') wherein R^3 and R^4 combines together to form substituted or unsubstituted cyclic ring, preferably unsubstituted cyclic ring, more preferably cyclobutyl.

According to yet another embodiment, the compound of formula (Ib') wherein R^a is 2-hydroxy-prop-2-yl.

According to yet another embodiment, the compound of formula (Ib') wherein R^a is unsubstituted aryl, preferably phenyl.

According to yet another embodiment, the compound of formula (Ib') wherein R^a is unsubstituted heteroaryl or heterocyclic ring, preferably pyrimidine, isoquinoline and pyridine.

According to yet another embodiment, the compound of formula (Ib') wherein R^a is substituted cycloalkyl, preferably substituted cyclohexyl and cyclopentyl, wherein substituent is hydroxy.

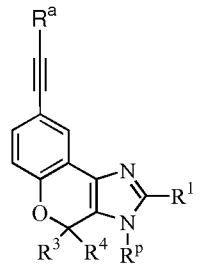
According to yet another embodiment, the compound of formula (Ib') wherein R^a is unsubstituted aryl, preferably phenyl

According to yet another embodiment, the compound of formula (Ib') wherein R^a is substituted aryl, preferably substituted phenyl, wherein substituents are halogen (for e.g. chloro, fluoro, bromo or iodo), cyano, alkyl (for e.g. methyl), nitro, C(O)OH, alkyl-C(O)O-, alkoxy (for e.g. methoxy, ethoxy), haloalkyl (for e.g. trifluoromethyl), haloalkoxy (for e.g. trifluoromethoxy, difluoromethoxy, trifluoroethoxy), alkylsulfinyl (for e.g. methylsulfinyl), aryl (for e.g. phenyl), heteroaryl (for e.g oxadiazole or methylated- oxadiazole) and heterocyclyl (for e.g. pyrrolidin-2-one).

According to yet another embodiment, the compound of formula (Ib') wherein R^a is unsubstituted heteroaryl, preferably pyridine, pyrimidine or isoquinoline.

According to yet another embodiment, the compound of formula (Ib') wherein R^a is substituted heteroaryl, preferably substituted thiazole, thiadiazole, pyridine or pyrimidine, wherein substituents are halogen (for e.g. chloro, fluoro, bromo or iodo), alkyl (for e.g. methyl) and haloalkyl (for e.g. trifluoromethyl).

According to one embodiment, the present application provides compound of formula (Ib'') or a pharmaceutically acceptable salt thereof:



(Ib'')

wherein,

R^1, R^3, R^4, and R^p are as defined for formula (I);

R^a is selected from hydrogen and substituted or unsubstituted aryl; whererin the substitution on the substituted groups are one or more selected from halogen, substituted or unsubstituted alkyl and haloalkyl;

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

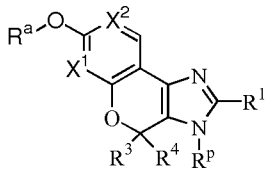
According to one embodiment, the compound of formula (Ib'') wherein R^1 is substituted or unsubstituted aryl, preferably substituted aryl, more preferebly substituted phenyl, wherein substituents are halo (for e.g. chloro, fluoro, bromo or iodo) and cyano.

According to another embodiment, the compound of formula (Ib'') wherein R^P is hydrogen.

According to yet another embodiment, the compound of formula (Ib'') wherein R^3 and R^4 both are methyl.

According to yet another embodiment, the compound of formula (Ib'') wherein R^a is substituted or unsubstituted aryl, preferably substituted aryl, more preferably substituted phenyl, wherein substituent is haloalkyl (for e.g. trifluoromethyl).

According to one embodiment, the present application provides the compound of formula (Ic) or a pharmaceutically acceptable salt thereof:



(Ic)

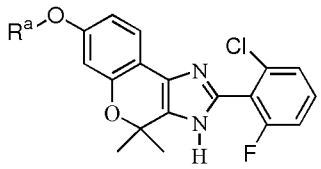
wherein,

X^1, X^2, R^1, R^3, R^4, and R^p are as defined for formula (I);

R^a is selected from hydrogen, substituted or unsubstituted cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl and heteroarylalkyl, whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, -OR_x, -$OC(O)R_x$, -$C(O)OR_x$, -SO_2R_x, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

According to one embodiment, the present application provides the compound of formula (Ic') or a pharmaceutically acceptable salt thereof:



(Ic')

wherein,

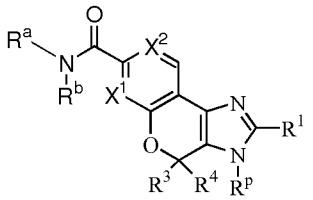
R^a is selected from substituted or unsubstituted cycloalkyl and arylalkyl, whererin the substitution on the substituted group is haloalkyl;

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, the compound of formula (Ic') wherein R^a is substituted arylalkyl, preferably substituted phenylalkyl, wherein substituent is haloalkyl (for e.g. trifluoromethyl).

According to yet another embodiment, the compound of formula (Ic') wherein R^a is unsubstituted or substituted cycloalkyl, preferably cyclopentyl.

According to one embodiment, the present application provides the compound of formula (Id) or a pharmaceutically acceptable salt thereof:



(Id)

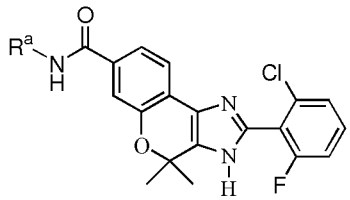
wherein,

X^1, X^2, R^1, R^3, R^4 and R^p are as defined for formula (I);

R^a and R^b are independently selected from hydrogen, substituted or unsubstituted alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclic ring, and heterocyclylalkyl; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

According to one embodiment, the present application provides the compound of formula (Id') or a pharmaceutically acceptable salt thereof:



(Id')

wherein,

R^a is selected from substituted or unsubstituted alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, whererin the substitution on the substituted groups are one or more selected from halogen, substituted or unsubstituted alkyl and haloalkyl;

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

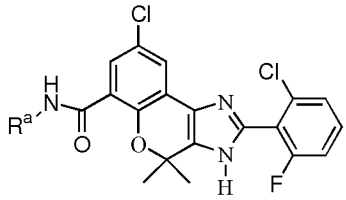
According to one embodiment, the compound of formula (Id') wherein R^a is substituted aryl, preferably substituted phenyl, wherein substituents are halogen (for e.g. fluoro, chloro, bromo or iodo) and haloalkyl (for e.g. trifluoromethyl).

According to another embodiment, the compound of formula (Id') wherein R^a is substituted arylalkyl, preferably benzyl, wherein substituent is haloalkyl (for e.g. trifluoromethyl).

According to another embodiment, the compound of formula (Id') wherein R^a is substituted heteroaryl, preferably thiazole and benzthiazole, wherein substituent is alkyl (for e.g. methyl).

According to yet another embodiment, the compound of formula (Id') wherein R^a is 6,6-dimethylbicyclo[3.1.1]hept-3-yl, 2,6,6-trimethylbicyclo[3.1.1]hept-3-yl, cyclohexyl, cyclohexylethyl, cyclopentyl, adamantan-1-yl or 3,3-dimethyl-2-butyl.

According to another embodiment, the present application provides the compound of formula (Ie) or a pharmaceutically acceptable salt thereof:



(Ie)

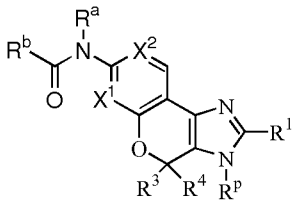
wherein,

R^a is substituted or unsubstituted aryl, whererin the substitution on the substituted group are one or more selected from halogen and haloalkyl;

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

According to one embodiment, the compound of formula (Ie) wherein R^a is substituted aryl, preferably substituted phenyl, wherein substituents are halogen (for e.g. fluoro, chloro, bromo or iodo) and haloalkyl (for e.g. trifluoromethyl).

According to one embodiment, the present application provides the compound of formula (If) or a pharmaceutically acceptable salt thereof:



(If)

wherein,

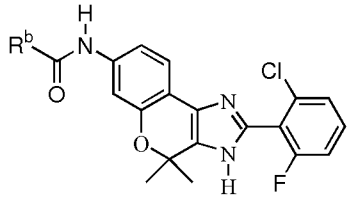
X^1, X^2, R^1, R^3, R^4, and R^p are as defined for formula (I);

R^b is selected from substituted or unsubstituted aryl and heteroaryl, whererin the substitution on the substituted groups are one or more selected from halogen, nitro,

cyano, hydroxyl, -OR_x, -$OC(O)R_x$, -$C(O)OR_x$, -SO_2R_x, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl;

R^a and R_x are independently selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl.

According to one embodiment, the present application provides the compound of formula (If') or pharmaceutically acceptable salt thereof:



(If')

wherein,

R^b is selected from substituted or unsubstituted aryl, whererin the substitution on the substituted group are one or more selected from halogen and haloalkyl.

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

According to one embodiment, the compound of formula (If') wherein R^b is substituted aryl, preferably substituted phenyl, wherein substituents are halogen (e.g. chloro, fluoro, bromo or iodo) and haloalkyl (for e.g. trifluoromethyl).

It should be understood that the formulas I, Ia, Ia', Ia'', Ib, Ib', Ib'', Ic, Ic', Id, Id' Ie, If and If' structurally encompasses *N*-oxide, all tautomers, geometrical isomers, stereoisomers, including enantiomers and diastereomers 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 the activity of mPGES-1, which is believed to be related to a variety of disease states.

The compounds of the present invention exhibit an IC_{50} value of less than 1000 nM, preferably, less than 500 nM, more preferably, less than 250 nM, with respect to mPGES-1 activity in cell based assay as measured by the method described in the present application.

The present patent application further provides a method of inhibiting mPGES-1 in a subject in need thereof by administering to the subject one or more compounds described herein in the amount effective to cause inhibition of such receptor.

Detailed Description of the Invention

Definitions

The invention is defined by the claims and not limited by the description provided herein below. The terms used in the appended claims are defined herein in this glossary section, with the proviso that the claim terms may be used in a different manner if so defined by express recitation.

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). The term "C_{1-6} alkyl" refers to an alkyl chain having 1 to 6 carbon atoms. Unless set forth or recited to the contrary, all alkyl groups described or claimed 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. Non-limiting examples of alkenyl groups include 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 or claimed 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). Non-limiting examples of alkynyl groups include ethynyl, propynyl, and butynyl. Unless set forth or recited to the contrary, all alkynyl groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

The term "alkoxy" denotes an alkyl group attached via an oxygen linkage to the rest of the molecule. Representative examples of such groups are $-OCH_3$ and $-OC_2H_5$. Unless set forth or recited to the contrary, all alkoxy groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

The term "haloalkyl" and "haloalkoxy" means alkyl or alkoxy, as the case may be, substituted with one or more halogen atoms, where alkyl and alkoxy groups are as defined above. The term "halo" is used herein interchangeably with the term "halogen" means F, Cl, Br, or I. Examples of "haloalkyl" include but are not limited to trifluoromethyl, difluoromethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, pentachloroethyl 4,4,4-trifluorobutyl, 4,4-difluorocyclohexyl, chloromethyl, dichloromethyl, trichloromethyl, 1-bromoethyl, and the like. Examples of "haloalkoxy" include but are not limited to fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, pentafluoroethoxy, pentachloroethoxy, chloromethoxy, dichlorormethoxy, trichloromethoxy, 1-bromoethoxy and the like.

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, perhydronaphththyl, adamantyl and norbornyl groups, bridged cyclic groups or spirobicyclic groups, e.g., spiro(4,4)non-2-yl. Unless set forth or recited to the contrary, all cycloalkyl groups described or claimed 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. Non-limiting examples of such groups include 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 "aryl" refers to an aromatic radical having 6 to 14 carbon atoms, including monocyclic, bicyclic and tricyclic aromatic systems, such as phenyl, naphthyl, tetrahydronapthyl, indanyl, and biphenyl. Unless set forth or recited to the contrary, all aryl groups described or claimed 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, e.g., $-CH_2C_6H_5$ and $-C_2H_4C_6H_5$. Unless set forth or recited to the contrary, all arylalkyl groups described or claimed 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,

azetidinyl, benzodioxolyl, benzodioxanyl, chromanyl, dioxolanyl, dioxaphospholanyl, decahydroisoquinolyl, indanyl, indolinyl, isoindolinyl, isochromanyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, oxazolinyl, oxazolidinyl, oxadiazolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, octahydroindolyl, octahydroisoindolyl, perhydroazepinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, piperidinyl, phenothiazinyl, phenoxazinyl, quinuclidinyl, tetrahydroisquinolyl, tetrahydrofuryl, tetrahydropyranyl, thiazolinyl, thiazolidinyl, thiamorpholinyl, thiamorpholinyl sulfoxide and thiamorpholinyl sulfone. 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 or claimed 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 or claimed 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, tetrazoyl, thienyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, benzofuranyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, benzothienyl, benzopyranyl, carbazolyl, quinolinyl, isoquinolinyl, quinazolinyl, cinnolinyl, naphthyridinyl, pteridinyl, purinyl, quinoxalinyl, quinolyl, isoquinolyl, thiadiazolyl, indolizinyl, acridinyl, phenazinyl and phthalazinyl. Unless set forth or recited to the contrary, all heteroaryl groups described or claimed 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 or claimed herein may be substituted or unsubstituted.

Unless otherwise specified, the term "substituted" as used herein refers to substitution with any one or any combination of the following substituents: hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted hydroxyl alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted haloalkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstituted guanidine, $-COOR^{x'}$, $-C(O)R^{x'}$, $-C(S)R^{x'}$, $-C(O)NR^{x'}R^{y'}$, $-C(O)ONR^{x'}R^{y'}$, $-NR^{x'}CONR^{y'}R^{z'}$, $-N(R^{x'})SOR^{y'}$, $-N(R^{x'})SO_2R^{y'}$, $-(=N-N(R^{x'})R^{y'})$, $-NR^{x'}C(O)OR^{y'}$, $-NR^{x'}R^{y'}$, $-NR^{x'}C(O)R^{y'}$, $-NR^{x'}C(S)R^{y'}$, $-NR^{x'}C(S)NR^{y'}R^{z'}$, $-SONR^{x'}R^{y'}$, $-SO_2NR^{x'}R^{y'}$, $-OR^{x'}$, $-OC(O)NR^{y'}R^{z'}$, $-OC(O)OR^{y'}$, $-OC(O)R^{x'}$, $-OC(O)NR^{x'}R^{y'}$, $-SR^{x'}$, $-SOR^{x'}$, $-SO_2R^{x'}$, NO_2, NO_2, and $-ONO_2$, 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 heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, or substituted or unsubstituted heterocyclic ring.

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) and other animals, such as 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.

The term "acute pain" is usually self-limiting. The sensation of pain can be triggered by any number of physical or chemical stimuli and the sensory neurons which mediate the response to this harmful stimulus are termed as "nociceptors". Nociceptors are primary sensory afferent (C and Aδ fibers) neurons that are activated by a wide variety of noxious stimuli including chemical, mechanical, thermal, and proton (pH<6) modalities. Nociceptors are the nerves which sense and respond to parts of the body which suffer from damage. They signal tissue irritation, impending injury, or actual injury. When activated, they transmit pain signals (via the peripheral nerves as well as the spinal cord) to the brain.

The term "chronic pain" usually refers to pain which persists for 3 months or longer and can lead to significant changes in a patient's personality; lifestyle, functional ability and overall quality of life. Chronic pain can be classified as either nociceptive or neuropathic. Nociceptive pain includes tissue injury-induced pain and inflammatory pain such as that associated with arthritis. Neuropathic pain is caused by damage to the sensory nerves of the peripheral or central nervous system and is maintained by aberrant somatosensory processing. The pain is typically well localized, constant, and often with an aching or throbbing quality. Visceral pain is the subtype of nociceptive pain that involves the internal organs. It tends to be episodic and poorly localized. Nociceptive

pain is usually time limited, meaning when the tissue damage heals, the pain typically resolves (arthritis is a notable exception in that it is not time limited).

The compound described in the present patent application may form salts. Non-limiting examples of pharmaceutically acceptable salts forming part of this patent application include salts derived from inorganic bases salts of organic bases salts of chiral bases, salts of natural amino acids and salts of non-natural amino acids. Certain compounds of present patent application are capable of existing in stereoisomeric forms (e.g. diastereomers and enantiomers). With respect to the overall compounds described by the general formula (I) the present patent application extends to these stereoisomeric forms and to mixtures thereof. To the extent prior art teaches synthesis or separation of particular stereoisomers, the different stereoisomeric forms of the present patent application may be separated from one another by the method 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.

Abbreviations used in the description of the chemistry and in the examples that follow are:

DMSO	- dimethyl sulphoxide
TEA	- triethyl amine
THF	- tetra hydro furan
HCl	– hydrochloric acid
DCM	- dichloro methane
DMF	- N,N-dimethyl formamide
PTSA	- p-Toluenesulfonic acid
$CDCl_3$	- duterated chlolroform
m-CPBA	- m-Chloro per benzoic acid
HBr	- hydrogen bromide
EDC	- 1-Ethyl-3-(3-dimethyllaminopropyl)carbodiimide
$MgCl_2$	- magnesium chloride
K_2CO_3	- potassium carbonate
EA	- ethyl acetate

$NaBH_4$ - sodium borohydrate
DME - dimethyl ether
HOBT - 1-hydroxybenzotriazole anhydrous
DMAP - N,N-dimethyl amino pyridine
T_3P - propyl phsophonic anhydride
$POCl_3$ - phosphorus oxychloride
RT - room temperature

Pharmaceutical Compositions

The compounds of the invention are typically administered in the form of a pharmaceutical composition. Such compositions can be prepared using procedures well known in the pharmaceutical art and comprise at least one compound of the invention. The pharmaceutical composition of the present patent application comprises one or more compounds described herein and one or more pharmaceutically acceptable excipients. . Typically, the pharmaceutically acceptable excipients are approved by regulatory authorities or are generally regarded as safe for human or animal use. The pharmaceutically acceptable excipients include, but are not limited to, carriers, diluents, glidants and lubricants, preservatives, buffering agents, chelating agents, polymers, gelling agents, viscosifying agents, solvents and the like.

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, ,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 polyvinyl pyrrolidone.

The pharmaceutical composition may also include one or more pharmaceutically acceptable auxiliary agents, wetting agents, emulsifying agents, suspending agents, preserving agents, , buffers, sweetening agents, flavoring agents, colorants or any combination of the foregoing.

The pharmaceutical compositions may be in conventional forms, for example, capsules, tablets, aerosols, solutions, suspensions, injectables or products for topical application. Further, the pharmaceutical composition of the present invention may be formulated so as to provide desired release profile.

Administration of the compounds of the invention, in pure form or in an appropriate pharmaceutical composition, can be carried out using any of the accepted routes of administration of pharmaceutical compositions. 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, dermal, intradermal, transdermal, parenteral, rectal, subcutaneous, intravenous, intraurethral, intramuscular, intranasal, ophthalmic (such as with an ophthalmic solution) or topical (such as with a topical ointment)..

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.

Topical dosage forms of the compounds include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants, eye ointments, eye or ear drops, impregnated dressings and aerosols, and may contain appropriate conventional additives such as preservatives, solvents to assist drug penetration and emollients in ointments and creams.

The pharmaceutical forms suitable for injectable or infusing use include sterile aqueous solutions, suspensions or dispersions, and sterile powders for the extemporaneous preparation of sterile injectable or infusing solutions, suspension or dispersions.

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).

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. Mode of administration, dosage forms, and suitable pharmaceutical excipients 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

Compounds of the present invention are particularly useful because they may selectively inhibit the activity of prostaglandin E synthases {and particularly microsomal prostaglandin E synthase-1 (mPGES-1)}, i.e. they prevent the action of mPGES-1 or a complex of which the mPGES-1 enzyme forms a part, and/or may elicit mPGES-1 modulating effect. Compounds of the invention may thus be useful in the treatment of those conditions in which inhibition of a PGES, and particularly mPGES-1, is required.

Compounds of the invention are thus expected to be useful in the treatment of inflammation. The term “inflammation” will be understood by those skilled in the art to include any condition characterized by a localized or a systemic protective response, which may be elicited by physical trauma, infection, chronic diseases, such as those mentioned hereinbefore, and/or chemical and/or physiological reactions to external stimuli (e.g. as part of an allergic response). Any such response, which may serve to destroy, dilute or sequester both the injurious agent and the injured tissue, may be manifest by, for example, heat, swelling, pain, redness, dilation of blood vessels and/or increased blood flow, invasion of the affected area by white.

The term “inflammation” is also understood to include any inflammatory disease, disorder or condition per se, any condition that has an inflammatory component associated with it, and/or any condition characterized by inflammation as a symptom, including inter alia acute, chronic, ulcerative, specific, allergic, infection by pathogens, immune reactions due to hypersensitivity, entering foreign bodies, physical injury, and necrotic inflammation, and other forms of inflammation known to those skilled in the art. The term thus also includes, for the purposes of this invention, inflammatory pain, pain generally and/or fever.

The compounds of the present invention may also be useful in the treatment of asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, inflammatory bowel disease, irritable bowel syndrome, pain, inflammatory pain, chronic pain, acute pain, fever, migraine, headache, low back pain, fibromyalgia, myofascial disorders, viral infections {e.g. influenza, common cold, herpes zoster, hepatitis C and AIDS), bacterial infections, fungal infections, dysmenorrhea, burns, surgical or dental procedures, malignancies {e.g. breast cancer, colon cancer, and prostate cancer), hyperprostaglandin E syndrome, classic Bartter syndrome, atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, juvenile onset rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, Hodgkin's disease, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes mellitus, neurodegenerative disorders such as Alzheimer's disease and multiple sclerosis, autoimmune diseases, allergic disorders, rhinitis, ulcers, mild to moderately active ulcerative colitis, familial adenomatous polyposis, coronary heart disease, sarcoidosis and any other disease with an inflammatory component.

Compounds of the invention may also have effects that are not linked to inflammatory mechanisms, such as in the reduction of bone loss in a subject. Conditions that may be mentioned in this regard include osteoporosis, osteoarthritis, Paget's disease and/or periodontal diseases.

By virtue of the mPGES-1 inhibitory activity of compounds of the present invention, the compounds of Formula I are useful for the relief of pain, fever and inflammation of a variety of conditions including rheumatic fever, symptoms associated

with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhea, headache, migraine (acute and prophylactic treatment), toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, including rheumatoid arthritis, juvenile rheumatoid arthritis, degenerative joint diseases (osteoarthritis), acute gout and ankylosing spondylitis, acute, subacute and chronic musculoskeletal pain syndromes such as bursitis, burns, injuries, and pain following surgical and dental procedures as well as the preemptive treatment of surgical pain. In addition, such a compound may inhibit cellular neoplastic transformations and metastic tumor growth and hence can be used in the treatment of cancer. Compounds of Formula I may also be useful for the treatment or prevention of endometriosis, hemophilic arthropathy and Parkinson's disease.

Compounds of Formula I will also inhibit prostanoid-induced smooth muscle contraction by preventing the synthesis of contractile prostanoids and hence may be of use in the treatment of dysmenorrhea, premature labor and asthma.

In addition, the compound of the present invention may inhibit cellular neoplastic transformations and metastic tumor growth and hence can be used in the treatment of cancer.

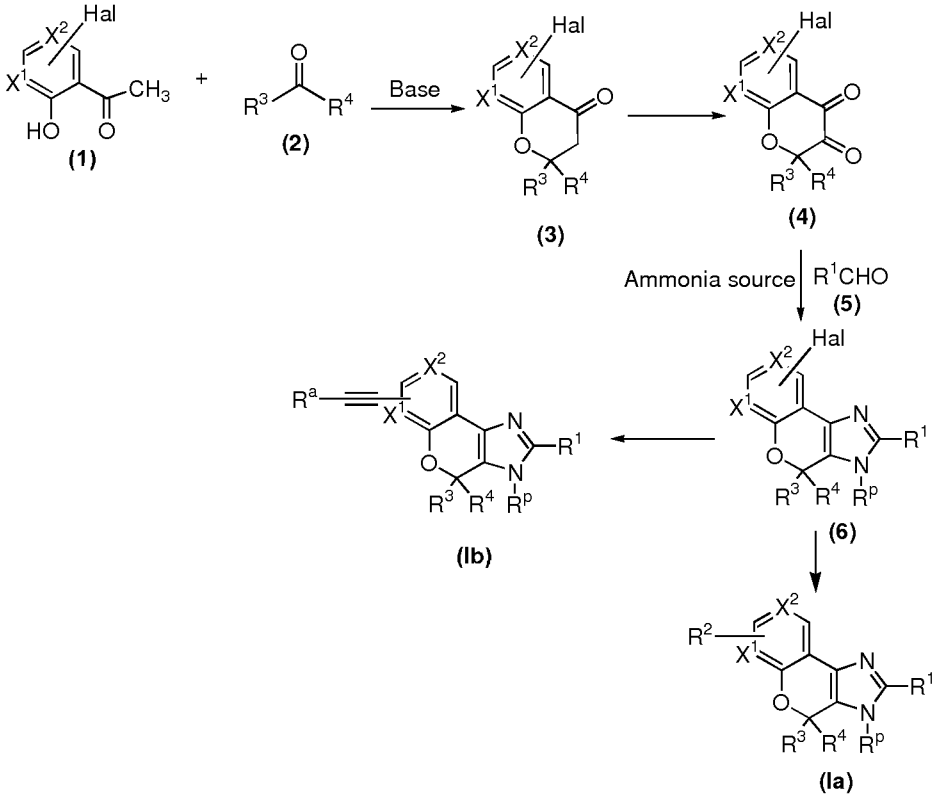
Compounds of the invention are indicated both in the therapeutic and/or prophylactic treatment of the above-mentioned conditions. For the above-mentioned therapeutic uses the dosage administered will, of course, vary with the compound employed, the mode of administration, the treatment desired and the disorder indicated. The daily dosage of the compound of the invention may be in the range from 0.05 mg/kg to 100 mg/kg.

General method of preparation

The compounds described herein, including compounds of general formula (I), (Ia), (Ib), (Ic), (Id), (If) and (Ib') and specific examples are prepared using techniques known to one skilled in the art through the reaction sequences depicted in scheme 1 as well as by other methods. 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. 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 stereoisomers are envisioned within the scope of this invention.

Scheme-1



The compounds of general formula (Ia) and (Ib), wherein X^1, X^2, R^P, R^1, R^2, R^3, R^4, and R^a are as defined above, while 'Hal' is halogen. The compounds of formula (Ia) and (Ib) are prepared according to the sequence depicted in Scheme 1. The compound of formula **(1)** can be converted to a compound of formula **(3)**, by reacting it with a compound of formula **(2)** in presence of an organic base (for e.g., piperidine, pyrrolidine, morpholine etc,) or inorganic base (for e.g., alkali metal carbonate, alkali metal hydroxide, alkali metal hydride etc). The compound of formula **(3)** can be converted to a compound of formula **(4)** in presence of oxidizing agent like isoamyl nitrite (*J. Heterocyclic chem.*, **1988**, 26, 1013-1021) or selenium dioxide by following procedure known in the art of organic synthesis. The compound of formula **(4)** can be converted to a

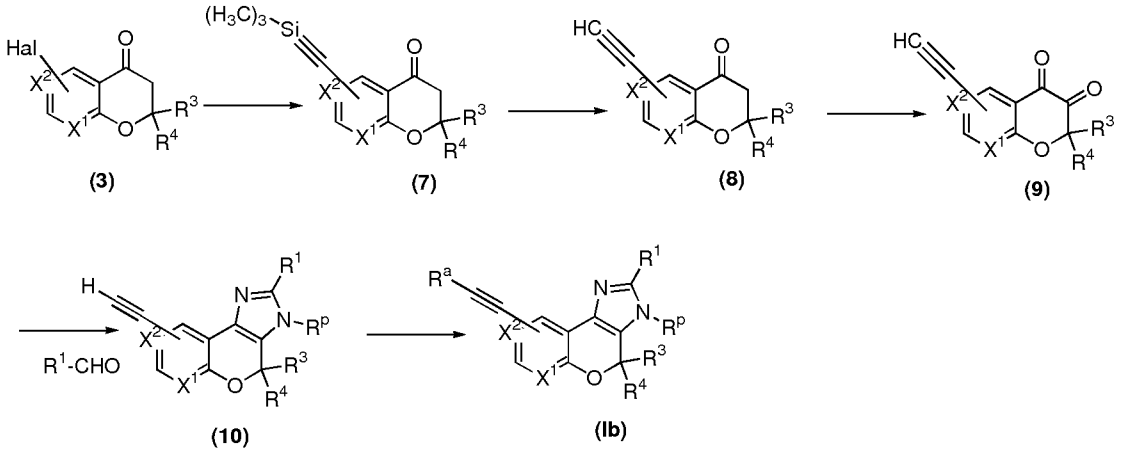
compound of formula **(6)** by reacting with a compound of formula **(5)** in presence of in situ generated ammonia using ammonium acetate or ammonium chloride in solvents such as acetic acid or propionic acid.

Compound of formula **(6)** can be converted to compound of formula **(Ia),** wherein substituted or unsubstituted monocyclic or bicyclic aryl, heteroaryl substituent, is introduced by a sequence of transformations such as transition metal catalyzed reactions.

Compound of formula **(6)** can be converted to compound of formula **(Ib),** which is a substituted or unsubstituted alkynyl derivative, by a sequence of transformations such as transition metal catalyzed reactions (for example Suzuki-Miyaura coupling or Sonogashira coupling).

In an alternate approach, the alkynyl or aryl/heteroaryl moiety may be introduced initially to the compound of formula **(3)** before converting it to compound of formula **(4)**. Ultimately the compound of formula **(4)** is converted to compound of formula **(Ia)** or **(Ib)**.

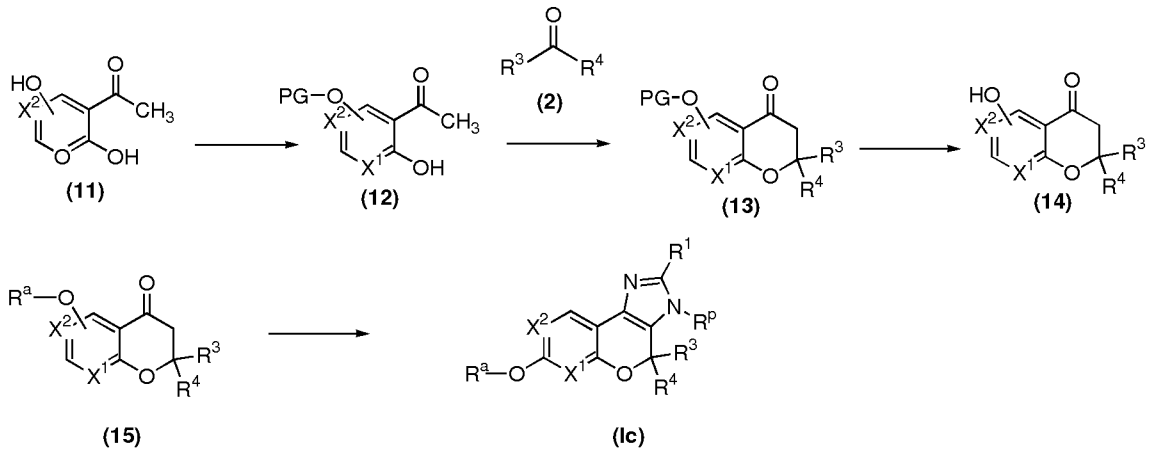
Scheme 2



Scheme 2 depicts another approach for the preparation of compound of formula **(Ia)**, wherein X^1, X^2, R^P, R^1, R^3, R^4, R^a are as defined above, while 'Hal' is halogen. The compound of formula **(3)** can be converted to alkyne derivative of formula **(7)** by reacting with trialkylacetylene compound, such as silyl acetylene derivative, in the presence of a catalyst (for example a palladium catalyst). The compound of formula **(7)** can be de-silylated for example in the presence of tertiary butyl ammnoum fluoride in the suitable solvent such as dichloromethane to get compound of formula **(8)**. The compound of formula **(8)** can be converted to a compound of formula **(9)** in presence of oxidizing

agent like isoamyl nitrite (*J. Heterocyclic chem.*, **1988**, 26, 1013-1021) or selenium dioxide following procedure known in the art of organic synthesis. The compound of formula **(9)** can be converted to a compound of formula **(10)** by reacting with an appropriate aldehyde in the presence of in situ generated ammonia using ammonium acetate or ammonium chloride in the presence of solvent such as acetic acid or propionic acid. The compound of formula **(10)** can be converted to compound of formula **(Ib)** wherein substituted or unsubstituted monocyclic or bicyclic aryl, heteroaryl substituent is introduced by a sequence of transformations such as transition metal catalyzed reactions.

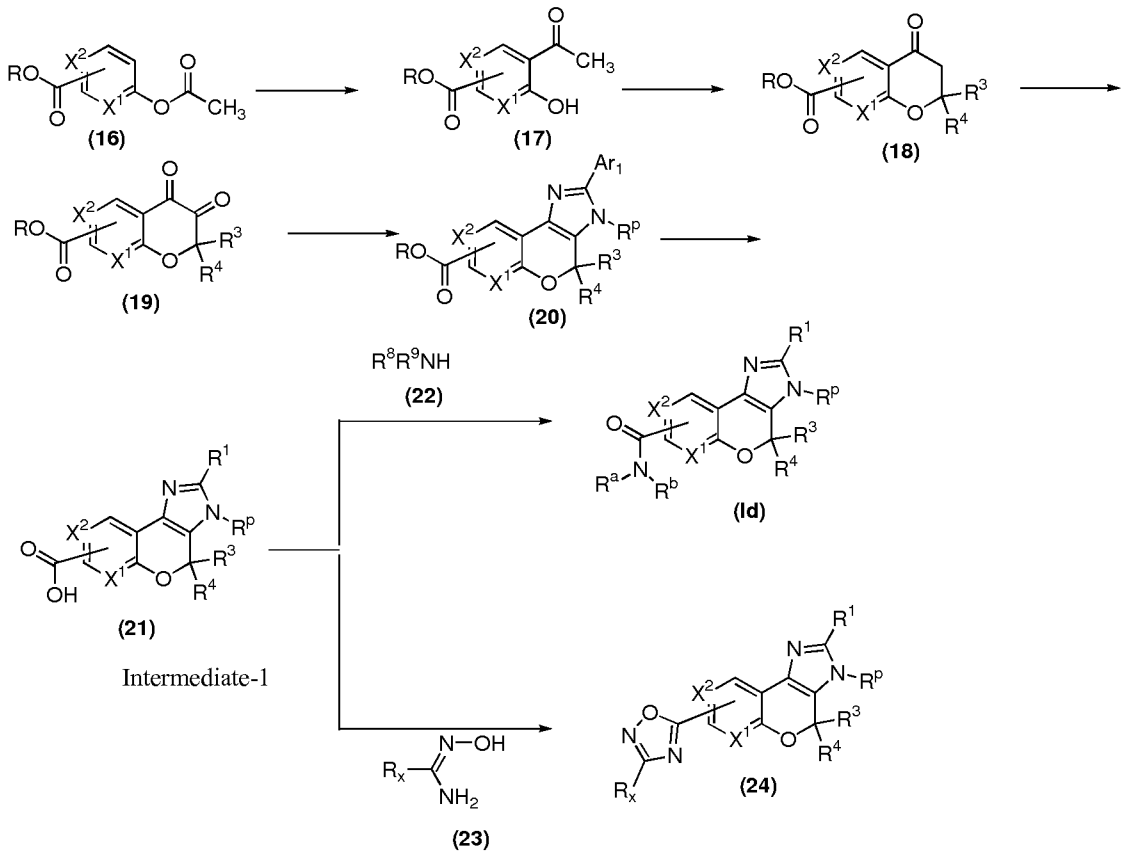
Scheme 3



The compound of formula **(Ic)** can be prepared following the synthetic route as depicted in scheme 3, wherein X^1, X^2, R^P, R^1, R^3, R^4, and R^a are as defined above and PG is a protecting group.

Scheme 3, primarily describes one of the ways to introduce the substituent $-OR^a$. The hydroxyl group of the compound of formula **(11)** can be masked using a suitable protecting group to obtain the compound of formula **(12)**. The compound of formula **(12)** can be converted to compound of formula **(13)** by reacting with compound of formula **(2)** in the presence of organic or inorganic base. The protection of the hydroxyl group may be removed under suitable conditions to obtain compound of formula **(14)** and desired OR^a substituent may be introduced under suitable condition, for example a halogen derivative may be reacted with compound of formula **(14)** in the presence of suitable solvent and suitable base to obtain the compound of formula **(15)**. The further transformations of compound of formula **(15)** to compound of formula **(1c)** can be achieved by following the reaction conditions/reagents described for similar steps in the scheme 1 or scheme 2.

Scheme 4

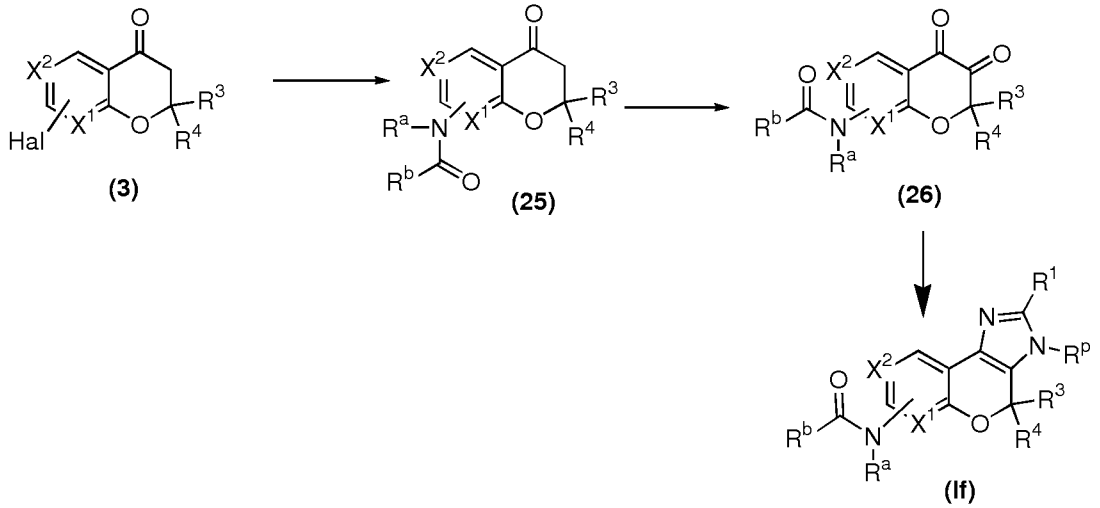


The compound of formula **(Id)** can be prepared following the synthetic route as depicted in scheme 4, wherein X^1, X^2, R^P, R^1, R^3, R^4, R^a, R^b and R_x are as defined above while R may be alkyl.

The scheme 4 primarily depicts the introduction of amide moiety to the basic scaffold of compound of formula **(I)**. The other transformations are previously described in the scheme 1 and scheme 2.

The compound of formula **(21)** which is a carboxylic acid derivative may be treated with an appropriate amine (compound of formula **22**) under suitable conditions to get compound of formula **(Id)** or compound of formula **(24)** depending on the nature of amine utilized for the reaction.

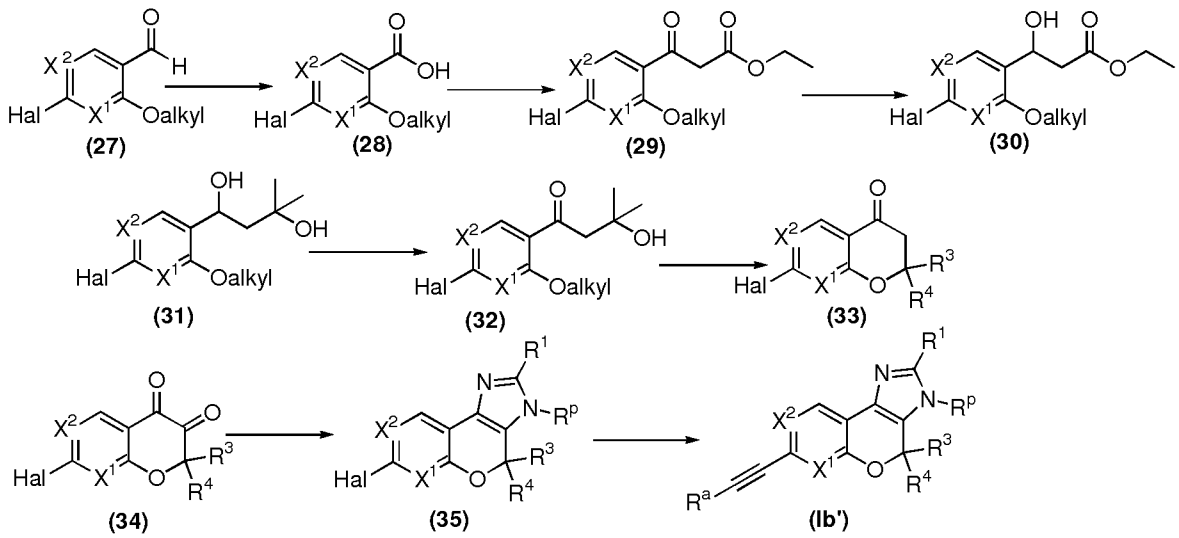
Scheme 5



The compound of formula **(If)** can be prepared following the synthetic route as depicted in scheme 5, wherein X^1, X^2, R^P, R^1, R^3, R^4, R^a and R^b are as defined above, while 'Hal' is halogen.

The compound of formula **(3)** can be converted to compound of formula **(25)** by treating it with amide derivative such as substituted or unsubstituted benzamides. The reaction may be catalyzed by transition metal catalyst such as palladium catalyst. The other transformations involving conversion of compound of formula **(25)** to compound of formula **(If)** via the preparation of compound of formula **(26)** are previously described in the scheme 1 and scheme 2.

Scheme 6



The compound of formula **(Ib')**, which is imidazolo-pyrano-pyridine derivative, may be prepared following the synthetic scheme depicted in scheme 6, wherein X^1, X^2, R^P, R^1, R^3, R^4, R^a are as defined above while 'Hal' is halogen.

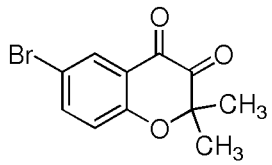
The pyridine aldehyde of formula **(27)** may be oxidized to its carboxylic acid derivative of formula **(28)** under standard acidic conditions in a suitable solvent. The acid derivative of formula **(28)** may be converted to compound of formula **(29)** by treating with a suitable ester derivative under suitable conditions. The keto group of compound of formula **(29)** may be selectively reduced to hydroxyl group using suitable reducing agent such as sodium borohydride to give compound of formula **(30)**. The compound of formula **(30)** may be further treated with methyl magnesium halide under Grignard reaction conditions to obtain tertiary alcohol of formula **(31)**. The secondary alcohol group of diol compound of formula **(31)** may be selectively oxidized to compound of formula **(32)** using suitable oxidizing reagent such as pyridinium chlorochromate. Other suitable oxidizing reagent may also be contemplated. The obtained compound of formula **(32)** may under go cyclization for example in the presence of hydrobromic acid in acetic acid under appropriate reaction conditions. The obtained compound of formula **(33)** may be converted to compound of formula **(35)** via preparation of intermediate compound of formula **(34)** following the reaction sequence described in the scheme 1 or scheme 2. The obtained compound of formula **(35)** may be converted to compound of formula **(Ib')** following the reaction sequence as described in the scheme 1.

Experimental

Unless otherwise stated, work-up implies the following operations: distribution of the reaction mixture between the organic and aqueous phase, separation of layers, drying the organic layer over sodium sulfate, filtration and evaporation of the organic solvent. Purification, unless otherwise mentioned, implies purification by silica gel chromatographic techniques, generally using ethyl acetate/petroleum ether mixture of a suitable polarity as the mobile phase. The following abbreviations are used in the text: DMSO-d_6: hexadeuterodimethyl sulfoxide; DMF: *N*,*N*-dimethylformamide, *J*: coupling constant in units of Hz; RT: room temperature (22-26°C). aq.: aqueous AcOEt: ethyl acetate; equiv.: equivalents.

Intermediate – 1

6-Bromo-2,2-dimethyl-2*H*-chromene-3,4-dione



Step-1:- Preparation of 6-bromo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-

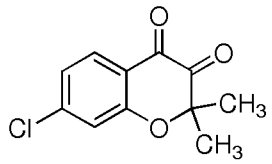
To a solution of 1-(5-bromo-2-hydroxyphenyl)ethanone (1.0 g, 0.0046 mmol) in methanol (4 mL) was added pyrrolidine (1 mL). The reaction mixture was cooled at 0-5°C and stirred for 20 mins and acetone (0.5 mL, 0.006 mmol) was added. The reaction mixtue was refluxed for 4 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over sodium sulphate and concentrated to afford 0.700 g of product. ^{1}HNMR (DMSO): δ 1.45 (s, 6H), 2.71 (s, 2H), 6.82 -6.84 (d, *J* = 8.7 Hz, 1H), 7.52–7.55 (dd, *J* = 2.4 Hz, *J* = 2.4 Hz, 1H), 7.96 (s,1H).

Step-2:- Preparation of 6-bromo-2,2-dimethyl-2*H*-chromene-3,4-dione:-

To the solution of 6-bromo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (0.5g, 0.0019 mmol) in ethanol (2 mL) was added hydrochloric acid (1 mL) and isoamyl nitrite (0.8 mL, 0.0059 mmol). The reaction mixture was stirred at room temperature for 12-16 hours. The reaction mixture was quenched in water and extracted with ethyl acetate. The organic layer was dried over sodium sulphate and concentrated to afford crude product which was further purified by column chromatography. ^{1}HNMR (DMSO): δ 1.46 (s, 6H), 6.88 (d, *J* = 8.7 Hz, 1H), 7.60-7.68 (m, 1H), 7.99 (m, 1H).

Intermediate – 2

7-Chloro-2,2-dimethyl-2*H*-chromene-3,4-dione



Step-1:- Preparation of 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-

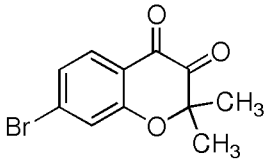
The title compound was prepared according the procedure described in step-1 of Intermediate-1 using 1-(4-chloro-2-hydroxy phenyl)ethanone. ^{1}HNMR (DMSO): δ 1.45 (s, 6H), 2.71 (s, 2H), 6.94-6.96 (m, 2H), 7.77-7.80 (d, *J* = 8.7 Hz, 1H).

Step-2:- Preparation of 7-chloro-2,2-dimethyl-2*H*-chromene-3,4-dione:-

The title compound was prepared according the procedure described in step-2 of Intermediate-1 using 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one.

Intermediate – 3

7-Bromo-2,2-dimethyl-2*H*-chromene-3,4-dione



Step-1:- Preparation of 7-bromo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-

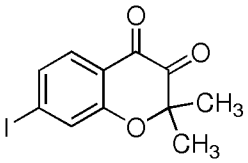
The title compound was prepared according to the procedure described in step-1 of Intermediate-1 using 1-(4-bromo-2-hydroxyphenyl) ethanone. ^{1}HNMR (DMSO): δ 1.45 (s, 6H), 2.71 (s, 2H), 7.10-7.12 (m, 2H), 7.71 (d, *J* = 8.4 Hz, 1H).

Step-2:- Preparation of 7-bromo-2,2-dimethyl-2*H*-chromene-3,4-dione:-

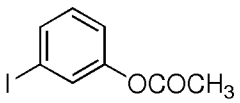
The title compound was prepared according to the procedure described in step-2 of Intermediate-1 using 7-bromo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one.

Intermediate –4

7-Iodo-2,2-dimethyl-chroman-3,4-dione

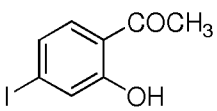


Step-1:- Preparation of 3-iodophenyl acetate:-



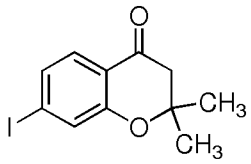
The mixture of 3-iodo phenol (10.0 g, 0.045 mol), pyridine (40 mL) and acetic anhydride (6.9 mL, 0.068 mol) was stirred at 50°C for 30 mins. The reaction mixture was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 10 g of desired product. ^{1}HNMR (DMSO): δ 2.50 (s, 3H), 7.15-7.24 (m, 2H), 7.56 (s, 1H), 7.62-7.64 (d, 1H, *J* = 7.2 Hz).

Step-2: Preparation of 1-(2-hydroxy-4-iodophenyl)ethanone:-



A mixture of 3-iodophenyl acetate (10 g, 0.030 mol) and anhydrous aluminium chloride (15.17 g, 0.114 mol) was stirred at 100°C. The reaction mixture was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 3 g of desired product. ^{1}HNMR ($CDCl_3$): δ 2.60 (s, 3H), 7.24-7.27 (m, 1H), 7.39-7.48 (m, 2H), 12.25 (s, 1H).

Step-3:- Preparation of 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-



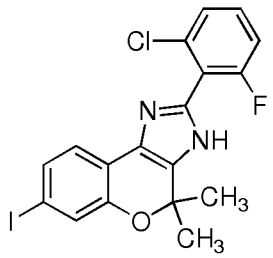
The title compound was prepared according to the procedure described in step-1 of Intermediate-1 using 1-(2-hydroxy-4-iodophenyl)ethanone (3 g, 0.114 mol), pyrrolidine (10 mL) and methanol (10 mL) to afford 2 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.44 (s, 6H), 2.70 (s, 2H), 7.31 (s, 1H), 7.36 (d, 1H, J = 8.7 Hz), 7.53 (d, 1H, J = 8.4 Hz).

Step-4:- Preparation of 7-Iodo-2,2-dimethyl-chroman-3,4-dione:-

The title compound was prepared according the procedure described in step-2 of Intermediate-1 using 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (2.5 g, mol), isoamyl nitrite (5 mL) and HCl (3mL) to afford 1.5 g of desired product.

Intermediate –5

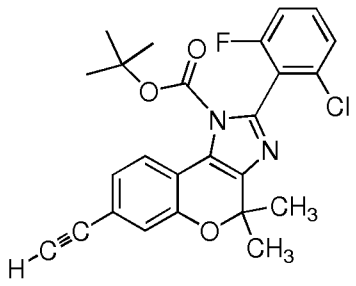
2-(2-Chloro-6-fluorophenyl)-7-iodo-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



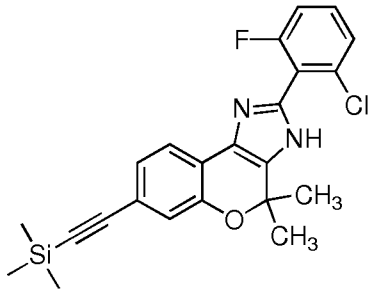
To a solution of 7-iodo-2,2-dimethyl-chroman-3,4-dione (0.300 g, 0.946 mmol) in acetic acid (10 mL) was added ammonium acetate (4.5 mmol) and 2-chloro-6-fluoro benzaldehyde (0.195 g, 1.22 mmol) and the reaction mixture was stirred at 100-120°C for 4-5 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford the desired product. ^{1}HNMR (DMSO): δ 1.62 (s, 6H), 7.17-7.62 (m, 6H), 13.09 (br s, 1H, d-exchangable); MS $[M+H]^+$:455.12.

Intermediate –6

2-(2-Chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-4H-chromeno[3,4-d]imidazole-1-carboxylic acid tert-butyl ester

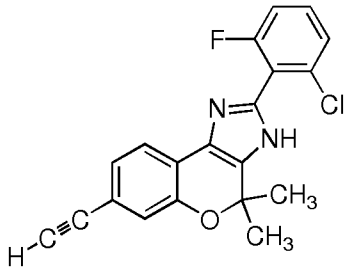


Step-1:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-trimethylsilanylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole:-



To a solution of 2-(2-chloro-6-fluorophenyl)-7-iodo-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole (0.100 g, 0.219 mmol) in DMSO (3 mL) was added copper iodide (catalytic amount), dichloro-bis(triphenylphosphine)palladium (II) (catalytic amount) and triethyl amine (0.5 mL). The reaction mixture was stirred under N_2 atmosphere for 20 mins at room temperature. Trimethylsilylacetylene (0.032 g, 0.329 mmol) was added to the reaction mixture and the reaction mixture was stirred at 90-100°C for 12 hours. The reaction mixture was filtered through celite bed. The filtrate was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 0.05 g of desired product. ^{1}HNMR (DMSO-d_6): δ 0.22 (s, 9H), 1.58 (s, 6H), 6.89-6.91 (m, 1H), 7.04-7.08 (m, 2H), 7.35-7.59 (m, 3H), 13.14 (s, 1H); MS $[M+H]^+$: 425.30.

Step-2:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole:-



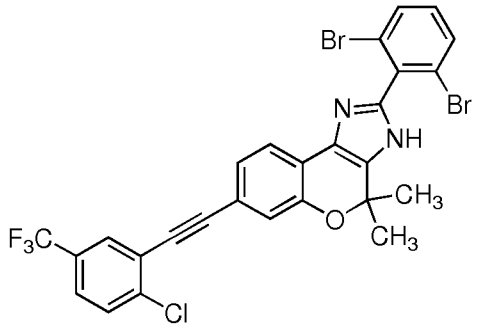
To a solution of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-trimethylsilanylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole (0.100 g, 0.235 mmol) in DCM was added tetra butyl ammonium fluoride (0.062 g, 0.237 mmol). The reaction mass was stirred at room temperature for 2-3 hours. The reaction mass was quenched in water, filtered through celite bed and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford 0.050 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 4.15-4.19 (m, 1H), 6.93-6.95 (m, 1H), 7.05-7.10 (m, 1H), 7.37-7.63 (m, 4H), 13.14 (s, 1H); MS $[M+H]^+$: 353.24.

Step-3:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-4H-chromeno[3,4-d]imidazole-1-carboxylic acid tert-butyl ester:-

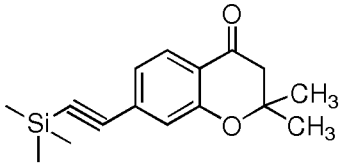
To a solution of 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (0.050 g, 0.142 mmol) in dry DMF was added (60%) sodium hydride (0.008 g, 0.213 mmol) at 0-5°C and the reaction mixture was stirred for 30 mins. BOC anhydride (0.046 ml, 0.213 mmol) was added at 0-5°C and the mixture was further stirred at 70-80°C for 6-7 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford 0.030 g desired product. ^{1}HNMR (DMSO-d_6): δ 1.22 (s, 9H), 1.59 (s, 6H), 4.28 (s, 1H), 7.01-7.05 (m, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 8.4 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.61-7.67 (m, 2H); MS $[M+H]^+$: 452.86.

Intermediate –7

7-(2-Chloro-5-trifluoromethyl-phenylethynyl)-2-(2,6-dibromo-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole

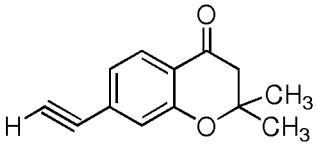


Step-1:- Preparation of 2,2-dimethyl-7-trimethylsilanylethynyl-chroman-4-one:-



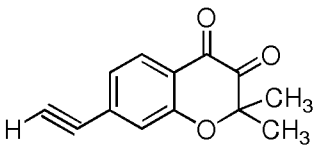
The title compound was prepared by following the same procedure as described for step-1 of intermediate-6 by using 7-iodo-2,2-dimethyl-chroman-4-one (step-3 of Intermediate-4 (25.0 g, 0.083 mol), copper iodide (0.630 g, 0.0033 mol), dichloro-bis(triphenylphosphine)palladium (II) (1.16 g, 0.0016 mol), triethyl amine (20.0 mL) and trimethylsilylacetylene (12.0 g, 0.124 mol) in DMSO (20 mL) to afford 22.0 g of desired product.

Step-2:- Preparation of 7-ethynyl-2,2-dimethyl-chroman-4-one:-



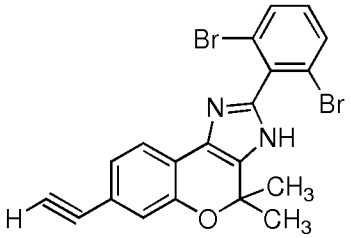
The title compound was prepared by following the same procedure as described for step-2 of Intermediate-6 by using 2,2-dimethyl-7-trimethylsilanylethynyl-chroman-4-one (22.0 g, 0.092 mol) and tetra butyl ammonium fluoride (24.0 g, 0.092 mol) in DCM (50 mL) to afford 10.0 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.27 (s, 6H), 2.82 (s, 2H), 4.49 (s, 1H), 7.08-7.17 (m, 2H), 7.72 (d, J = 7.8 Hz, 1H).

Step 3:- Preparation of 7-ethynyl-2,2-dimethyl-chroman-3,4-dione:-



The title compound was prepared by following the same procedure as described for step-2 of Intermediate-1 by using 7-ethynyl-2,2-dimethyl-chroman-4-one (10.0 g, 0.046 mol) and Isoamyl nitrite (10 mL) in HCl (6 mL) to afford 6.0 g of desired product.

Step 4:- Preparation of 2-(2,6-Dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole:-



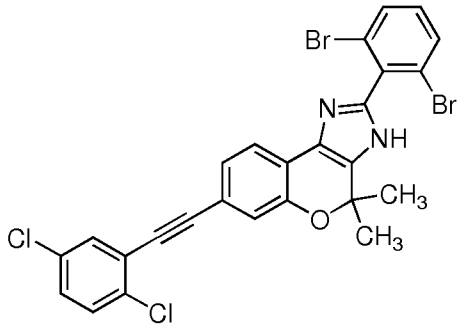
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (6.0 g, 0.028 mol), acetic acid (2 mL), ammonium acetate (10.78 g, 0.14 mol) and 2,6-dibromobenzaldehyde (8.8 g, 0.033 mol) to afford 4.5 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.59 (s, 6H), 4.09-4.17 (m, 1H), 6.93-6.94 (m, 1H), 7.05-7.09 (m, 1H), 7.31-7.46 (m, 2H), 7.82 (d, J = 7.8 Hz, 2H), 13.02 (s, 1H); MS $[M+H]^+$: 457.26.

Step 5:- Preparation of 7-(2-chloro-5-trifluoromethyl-phenylethynyl)-2-(2,6-dibromo-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole:-

The mixture of 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (0.500 g, 109 mol), dichloro bis (triphenyl phosphine)palladium (II) (0.022 g, 0.0327 mol), tetra butyl ammonium fluoride (0.855 g, 3.27 mol) and 1-chloro-2-iodo-4-trifluoromethyl-benzene (0.501 g, 1.63 mol) was heated at 80-90°C for 2-3 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford desired product (0.230 g). ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.09-7.11 (m, 1H), 7.21-7.24 (m, 1H), 7.38-7.44 (m, 1H), 7.52 (m, 1H), 7.77-7.87 (m, 4H), 8.08 (s, 1H), 13.09 (s, 1H).

Intermediate –8

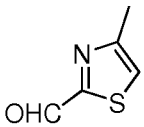
2-(2,6-Dibromo-phenyl)-7-(2,5-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (step-4 of Intermediate-7, 0.500 g, 109 mol), dichloro bis (triphenyl phosphine)palladium (II) (0.022 g, 0.032 mol), tetra butyl ammonium fluoride (0.855 g, 3.27 mol) and 2,5-dichloro-iodobenzene (0.447 g, 1.63 mol) to afford desired product (0.15 g).

Intermediate –9

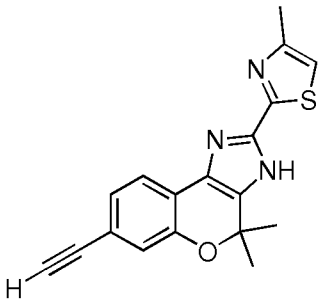
4-Methyl-thiazole-2-carbaldehyde



To a cold solution of 4-methyl thiazole (1.0 g, 0.010 mol) in THF was added n-BuLi (0.775 g, 0.012 mol) at -70°C. The reaction mass was stirred for 30-40 mins. DMF was added and the reaction mixture was stirred for 2-3 hours at -70°C. The reaction mass was quenched in cold water and acidified with dil acetic acid and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.800 g of desired product. ^{1}HNMR (DMSO-d_6): δ 2.58 (s, 3H), 7.35 (s, 1H), 9.96 (s, 1H); MS $[M+H]^+$: 127.20.

Intermediate –10

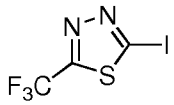
7-Ethynyl-4,4-dimethyl-2-(4-methyl-thiazol-2-yl)-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.150 g, 0.700 mmol), acetic acid (10 mL), ammonium acetate (0.270 g, 3.50 mmol mmol) and 4-methyl-thiazole-2-carbaldehyde (Intermediate-9, 0.106 g, 0.840 mmol) to afford 0.085 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 3.58-3.60 (m, 3H), 4.20-4.28 (m, 1H), 6.94 (s, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 7.51 (s, 1H), 7.72 (d, *J* = 7.8 Hz, 1H),13.76 (s, 1H); MS $[M+H]^+$: 322.38.

Intermediate –11

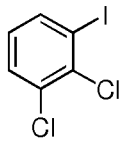
2-Iodo-5-trifluoromethyl-[1,3,4]thiadiazole



A solution of 5-trifluoromethyl-[1,3,4]thiadiazol-2-ylamine (0.250 g, 1.47 mmol) in 50% HCl was cooled at 0°C and sodium nitrite (0.255 g, 3.69 mmol) was added. The reaction mass was stirred for 15 mins. The aq. solution of potassium iodide (0.554 g, 3.69 mmol) was added and reaction was continued for 2-3 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.100 g of desired product. MS $[M+H]^+$: 279.24.

Intermediate –12

1,2-Dichloro-3-iodobenzene

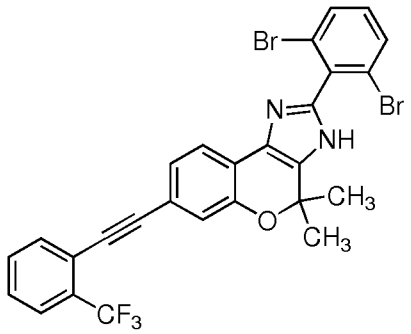


The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,3-dichloro phenyl amine (1.0 g, 5.23 mmol), sodium nitrite

(0.903 g, 13.08 mmol), potassium iodide (1.93 g, 12.95 mmol) and 50% HCl to afford 0.700 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.94 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.11(d, *J* = 7.8 Hz, 1H).

Intermediate –13

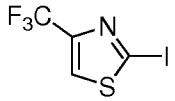
2-(2,6-Dibromo-phenyl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using (2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (step-4 of Intermediate-7, 0.500 g, 2.18 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), tetra butyl ammonium fluoride (2.06 g, 6.55 mmol) and 1-iodo-2-trifluoromethyl-benzene (0.890 g, 3.27 mmol) to afford 0.180 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.65 (s, 6 H), 7.00-7.01 (m, 1H), 7.15-7.17 (m, 1H), 7.38-7.43 (m, 2H), 7.52-7.54 (m, 1H), 7.58-7.61 (m, 1H), 7.63-7.84 (m, 4H), 13.09 (s, 1H); MS $[M+H]^+$: 603.22.

Intermediate –14

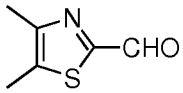
2-Iodo-4-trifluoromethyl-thiazole



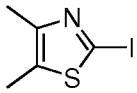
The title compound was prepared by following the same procedure as described for Intermediate-11 by using 4-trifluoromethyl-thiazol-2-ylamine (0.300 g, 1.78 mmol), sodium nitrite (0.314 g, 4.90 mmol), potassium iodide (0.665 g, 4.46 mmol) and 50% HCl to afford 0.100 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.30 (s, 1H).

Intermediate –15

4,5-Dimethyl-thiazole-2-carbaldehyde



Step-1:-Preperation of 2-iodo-4,5-dimethyl-thiazole:-



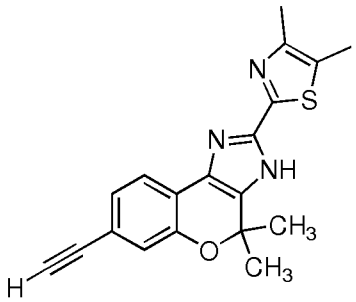
The title compound was prepared by following the same procedure as described for Intermediate-11 by using 4,5-dimethyl-thiazol-2-ylamine (2.0 g, 0.012 mol), sodium nitrite (1.25 g, 0.018 mol), potassium iodide (3.13 g, 0.018 mmol) and 50% HCl to afford 1.100 g of desired product. ^{1}HNMR (DMSO-d_6): δ 2.34 (s, 6H); MS $[M+H]^+$: 240.25.

Step-2:-Preperation of 4,5-dimethyl-thiazole-2-carbaldehyde:-

The title compound was prepared by following the same procedure as described for intermediate-9 by using 2-iodo-4,5-dimethyl-thiazole (0.800 g, 3.34 mmol), n-BuLi (3.13 mL, 5.02 mmol) in DMF (0.482 g, 6.69 mmol) to afford 0.400 g of desired product. ^{1}HNMR (DMSO-d_6): δ 2.45 (s, 3H), 2.48 (s, 3H), 9.85 (s, 1H).

Intermediate –16

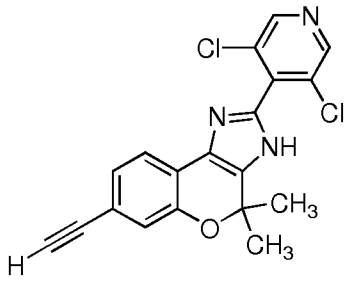
2-(4,5-Dimethyl-thiazol-2-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.300 g, 1.140 mmol), acetic acid (2 mL), ammonium acetate (0.540 g, 7.00 mmol) and 4,5-dimethyl-thiazole-2-carbaldehyde (Intermediate-15, 0.235 g, 1.68 mmol) to afford 0.120 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.59 (s, 6H), 2.34 (s, 3H), 2.39 (s, 3H), 4.17 (s, 1H), 6.92 (s, 1H), 7.06 (d, J = 7.2 Hz, 1H), 7.35-7.44 (m, 1H), 13.63 (s, 1H); MS $[M-H]^-$: 334.36.

Intermediate –17

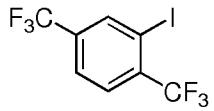
2-(3,5-Dichloro-pyridin-4-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.300 g, 1.140 mmol), 3,5-dichloro-pyridine-4-carbaldehyde (0.296 g, 1.68 mmol) and ammonium acetate (0.539 g, 7.00 mmol) to afford 0.200 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.60 (s, 6H), 4.20 (s, 1H), 6.39 (s, 1H), 7.08-7.11 (m, 1H), 7.40 (m, 1H), 8.80-8.82 (m, 2H), 13.33 (s, 1H); MS [M+] : 370.31.

Intermediate –18

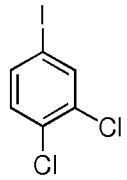
2-Iodo-1,4-bis-trifluoromethyl-benzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,5-bis-trifluoromethyl-phenylamine (0.500 g, 2.18 mmol), sodium nitrite (0.588 g, 6.54 mmol), potassium iodide (1.079 g, 6.5 mmol) and 50% HCl to afford 0.300 g of desired product. ^{1}HNMR (DMSO-d_6): δ 8.27 (s, 1H), 7.79-7.74 (m, 2H).

Intermediate –19

1.2-Dichloro-4-iodo-benzene

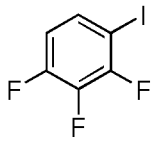


The title compound was prepared by following the same procedure as described for Intermediate-11 by using 3.4-dichloro aniline (1.0 g, 6.17 mmol), PTSA (1.76 g, 9.26 mmol), sodium nitrite (0.638 g, 9.25 mmol) and potassium iodide (1.53 g, 9.21 mmol) to

afford 0.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 8.27 (s, 1H), 7.79-7.74 (m, 2H), 7.42 (d, *J* = 8.4 Hz, 1H).

Intermediate –20

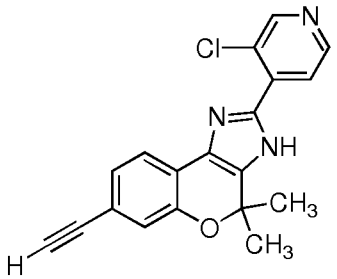
2,3,4-Trifluoro-1-iodo-benzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,3,4-trifluoro aniline (1.000 g, 6.800 mmol), conc. HCl:water (9.5mL :1mL), sodium nitrite (0.600 g, 6.66 mmol) and potassium iodide (1.7 g, 10.24 mmol) to afford 0.450 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.49-7.26 (m, 1H), 6.86-6.79 (m, 1H).

Intermediate –21

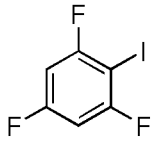
2-(3-Chloro-pyridin-4-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.800 g, 3.73 mmol), 3-chloro-pyridine-4-carbaldehyde (0.631 g, 4.47 mmol) and ammonium acetate (1.436 g, 18.65 mmol) to afford 0.400 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 3H), 1.67 (s, 3H), 4.22 (s, 1H), 6.95 (s, 1H), 6.97-7.14 (m, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.83 (s, 1H), 8.62 (s, 1H), 8.77 (s, 1H), 13.18 (s, 1H); MS $[M+H]^+$: 336.58.

Intermediate –22

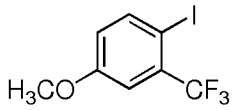
2,4,6-Trifluoro-1-iodo-benzene



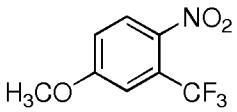
The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,4,6-trifluoro aniline (1.000 g, 6.800 mmol), conc HCl (0.877 g, 5.09 mmol), sodium nitrite (0.700 g, 7.77 mmol) and potassium iodide (1.50 g, 9.03 mmol) to afford 0.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 6.75-6.70 (m, 2H).

Intermediate –23

1-Iodo-4-methoxy-2-trifluoromethyl-benzene

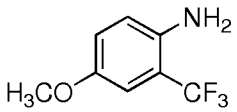


Step-1:-Preperation of 4-methoxy-1-nitro-2-trifluoromethyl-benzene:-



To a solution of 4-nitro-3-trifluoromethyl-phenol (1.0 g, 4.833 mmol) in DMF was added potassium carbonate (1.33 g, 9.65 mmol) and methyl iodide (1.37 g, 9.66 mmol). The reaction mass was stirred at 50-65°C for 2-3 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.560 g of desired product. ^{1}HNMR (DMSO-d_6): δ 3.95 (s, 3H), 7.10-7.14 (dd, 1H), 7.29-7.30 (m, 1H), 8.03 (d, J = 6.0 Hz, 1H).

Step-2:-Preperation of 4-methoxy-2-trifluoromethyl-phenylamine:-



To a solution of 4-methoxy-1-nitro-2-trifluoromethyl-benzene (1.0 g, 4.52 mmol) in methanol (5-7 mL) was drop wise added raney Ni (cat. amount) and hydrazine hydrate (1 mL). The reaction mass was stirred at RT for 2-3 hours. The reaction mass was quenched in water and the filtrate was concentrated to afford 0.400 g of desired product. ^{1}HNMR (DMSO-d_6): δ 3.67 (s, 3H), 5.09 (s, 2H), 6.79-6.85 (m, 2H), 6.96 (d, J = 6.9 Hz, 1H).

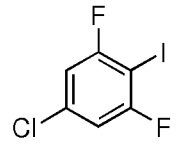
Step-3:- Preparation of 1-iodo-4-methoxy-2-trifluoromethyl-benzene:-

The title compound was prepared by following the same procedure as described for Intermediate-11 by using 4-methoxy-2-trifluoromethyl-phenylamine (0.400 g, 2.09 mmol), conc HCl (0.877 g, 5.09 mmol), sodium nitrite (0.213 g, 2.36 mmol) and

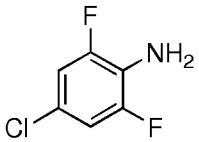
potassium iodide (0.416 g, 2.50 mmol) to afford 0.300 g of desired product. ^{1}HNMR (DMSO-d_6): δ 3.81 (s, 3H), 6.99-7.02 (dd, 1H), 7.28 (s, 1H), 7.98 (d, J = 8.1 Hz, 1H).

Intermediate –24

5-Chloro-1,3-difluoro-2-iodo-benzene



Step-1:- Preparation of 4-chloro-2,6-difluoro-phenylamine:-



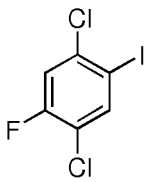
To a solution of 2,6-difluoro aniline (1.0 g, 7.75 mmol) in acetic acid (5 mL) was drop wise added solution of sulfuryl chloride (1.19 g, 8.82 mmol) in acetic acid at 80°C. The reaction mass was refluxed for 1-2 hours. The reaction mass was quenched in water and neutralized with potassium carbonate and the reaction mass was filtered. Filtrate was extracted with DCM. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.700 g of desired product. ^{1}HNMR (DMSO-d_6): δ 5.38 (s, 2H), 6.85-7.16 (s, 2H).

Step-2:- Preparation of 5-chloro-1,3-difluoro-2-iodo-benzene:-

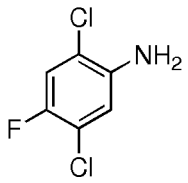
The title compound was prepared by following the same procedure as described for Intermediate-11 by using 4-chloro-2,6-difluoro-phenylamine (0.500 g, 3.060 mmol), conc HCl:water (9.5 mL:1 mL), sodium nitrite (0.700 g, 7.77 mmol) and potassium iodide (1.50 g, 9.03 mmol) to afford 0.400 g of desired product.

Intermediate –25

1,4-Dichloro-2-fluoro-5-iodo-benzene



Step-1:-Preperation of 2,5-dichloro-4-fluoro-phenylamine:-



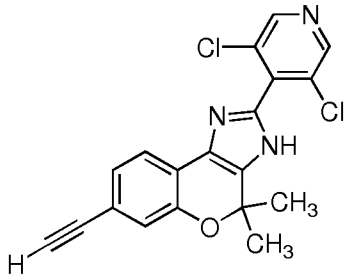
To a solution of 3-chloro-4-fluoro-phenylamine (1.0 g, 6.89 mmol) in THF (15 mL) was added N-chloro succinamide (0.917 g, 6.89 mmol). The reaction mass was stirred at RT for 16-18 hours. THF was removed and water was added and extracted with DCM. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.700 g of desired product. ^{1}HNMR (DMSO-d_6): δ 5.50 (s, 2H), 6.90 (d, J = 7.5 Hz, 1H), 7.41 (d, J = 9.3 Hz, 1H).

Step-2:- Preparation of 1,4-dichloro-2-fluoro-5-iodo-benzene:-

The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,5-dichloro-4-fluoro-phenylamine (0.500 g, 2.77 mmol), conc HCl:water (9.5 mL:1 mL), sodium nitrite (0.700 g, 7.77 mmol) and potassium iodide (1.50 g, 9.03 mmol) to afford 0.400 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.86 (d, J = 9.3 Hz, 1H), 8.21 (d, J = 7.8 Hz, 1H).

Intermediate –26

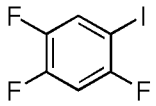
2-(3,5-Dichloro-pyridin-4-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.500 g, 2.33 mmol), 3,5-dichloro-pyridine-4-carbaldehyde (0.493 g, 2.86 mmol) and ammonium acetate (0.899 g, 11.68 mmol) to afford 0.300 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.59 (s, 6H), 4.16 (s, 1H), 6.95-6.97 (m, 1H), 7.06-7.12 (m, 1H), 7.38 (d, J = 7.8 Hz, 1H), 8.84 (s, 2H), 13.33 (s, 1H); MS $[M-H]^-$: 368.36.

Intermediate –27

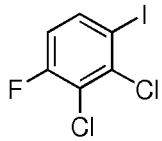
2,4,5-Trifluoro-1-iodo-benzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,4,5-trifluoro aniline (1.000 g, 6.800 mmol), conc. HCl (0.877 g, 5.09 mmol), sodium nitrite (0.700 g, 7.77 mmol) and potassium iodide (1.50 g, 9.03 mmol) to afford 0.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 6.93-7.01 (m, 1H), 7.53-7.60 (m, 1H).

Intermediate –28

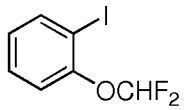
2,3-Dichloro-1-fluoro-4-iodo-benzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,3-dichloro-4-fluoro-phenylamine (0.500 g, 2.790 mmol), conc. HCl (0.877 g, 5.09 mmol), sodium nitrite (0.700 g, 7.77 mmol) and potassium iodide (1.50 g, 9.03 mmol) to afford 0.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.26-7.31 (m, 1H), 7.97-8.02 (m, 1H).

Intermediate –29

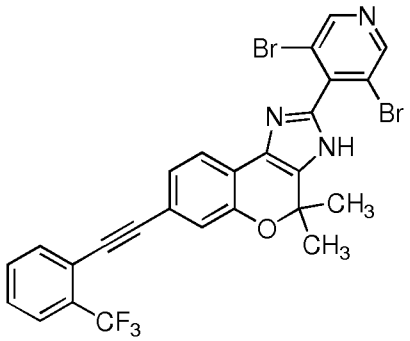
1-Difluoromethoxy-2-iodo-benzene



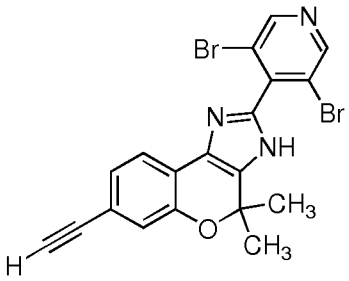
To a solution of 2-iodo phenol (1.0 g, 4.54 mmol) in DMF (10 mL) was added potassium carbonate (1.25 g, 9.08 mmol). The reaction mass was stirred at 60-70°C for 30 mins. The difluoro chloro methane gas was passed through reaction mixture for 4-5 hours and the reaction was stirred continuosly for 12 hours. The reaction mass was quenched in water and extracted with DCM and the organic layer was washed with dil HCl. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.750 g of desired product. ^{1}HNMR (DMSO-d_6): δ 6.27-6.70 (t, J = 12.8 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 7.28-7.35 (m, 1H), 7.37-7.86 (m, 1H).

Intermediate –30

2-(3,5-Dibromo-pyridin-4-yl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydrochromeno[3,4-d]imidazole



Step-1:- Preparation of 2-(3,5-dibromo-pyridin-4-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole:-



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 1.000 g, 4.67 mmol), 3,5-dibromo-pyridine-4-carbaldehyde (1.480 g, 5.60 mmol) and ammonium acetate (1.790 g, 23.360 mmol) to afford 0.700 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.60 (s, 6H), 4.20 (s, 1H), 6.96 (d, J = 5.7 Hz, 1H), 7.09 (t, J = 8.1 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 8.94 (s, 1H), 13.26 (s, 1H); MS $[M-H]^-$: 458..29.

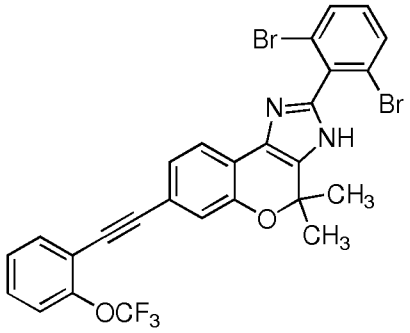
Step-2:- Preparation of 2-(3,5-dibromo-pyridin-4-yl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydrohromeno[3,4-d]imidazole:-

The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(3,5-dibromo-pyridin-4-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (0.300 g, 0.653 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-trifluoromethyl-benzene (0.213 g, 0.784 mmol) and tetra butyl ammonium fluoride (0.617 g, 1.96 mmol) to afford 0.120 g

of desired product. ^{1}HNMR (DMSO-d_6): δ 1.13 (s, 6H), 7.02 (s, 1H), 7.18 (d, J = 8.1 Hz, 1H), 7.70-7.85 (m, 4H), 8.31 (s, 1H), 8.94 (s, 2H), 13.32 (s, 1H); MS $[M-H]^-$: 603.27.

Intermediate –31

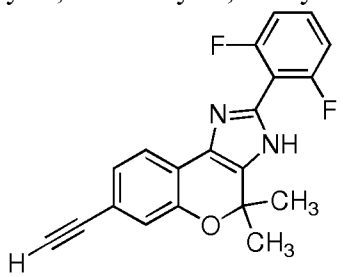
2-(2,6-Dibromo-phenyl)-4,4-dimethyl-7-(2-trifluoromethoxy-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (0.500 g, 109 mol), dichloro bis (triphenyl phosphine)palladium (II) (0.022 g, 0.0327 mol), 1-chloro-2-iodo-4-trifluoromethoxy-benzene (0.471 g, 1.63 mol) and tetra butyl ammonium fluoride (0.855 g, 3.27 mol) to afford 0.250 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 6.99 (s, 1H), 7.15 (d, J = 7.5 Hz, 1H), 7.41-7.67 (m, 5H), 7.72 (d, J = 6.9 Hz, 1H), 7.83 (d, J = 8.1 Hz, 2H), 13.09 (s, 1H).

Intermediate –32

2-(2,6-Difluorophenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole

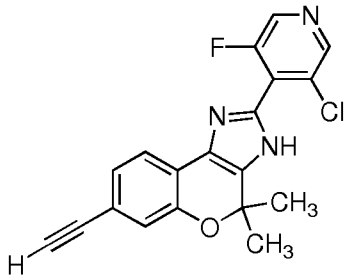


The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.400 g, 1.86 mmol), 2,6-difluoro benzaldehyde (0.318 g, 2.24 mmol) and ammonium acetate (0.719 g, 9.34 mmol) to afford 0.300 g of desired product.

^{1}HNMR (DMSO-d_6): δ 1.59 (s, 6H), 4.18 (s, 1H), 6.93-7.10 (m, 2H), 7.26-7.31 (m, 2H), 7.46-7.62 (m, 2H), 13.09 (br s, 1H); MS $[M+H]^+$: 337.47.

Intermediate –33

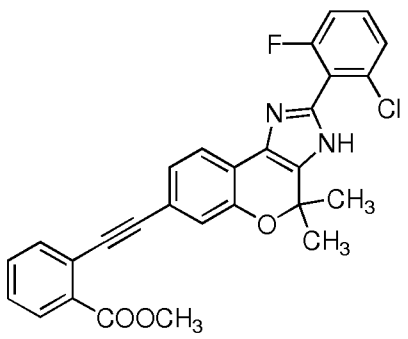
2-(3-Chloro-5-fluoropyridin-4-yl)-7-ethynyl-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-ethynyl-2,2-dimethyl-chroman-3,4-dione (step-3 of Intermediate-7, 0.350 g, 1.63 mmol), 3-chloro-5-fluoro pyridine-4-carbaldehyde (0.313 g, 1.96 mmol), ammonium acetate (0.629 g, 8.17 mmol) and acetic acid (5 mL) to afford 0.130 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.60 (s, 6H), 4.22 (s, 1H), 6.95-7.13 (m, 2H), 7.18 (d, *J* = 8.1 Hz, 1H), 8.74 (s, 1H), 8.80 (s, 1H), 13.39 (br s, 1H); MS $[M+H]^+$: 354.47.

Intermediate –34

Methyl 2-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}benzoate

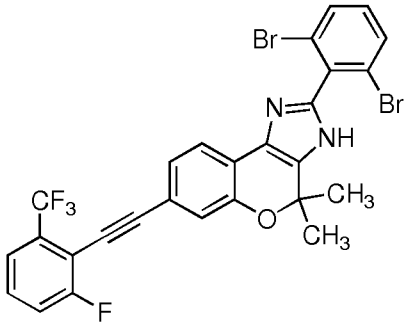


The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (step-2 of Intermediate-6, 0.150 g, 0.426 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.022 g, 0.0327 mol), methyl-2-iodo

benzoate (0.133 g, 0.511 mmol) and tetra butyl ammonium fluoride (0.402 g, 1.27 mmol) to afford 0.040 g of desired product.

Intermediate –35

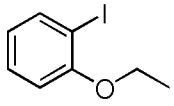
2-(2,6-Dibromophenyl)-7-{[2-fluoro-6-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-8 by using 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (step-4 of Intermediate-7, 1.000 g, 2.18 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.045 g, 0.065 mmol), 1-fluoro-2-iodo-3-(trifluoromethyl)benzene (0.949 g, 3.27 mmol) and tetra butyl ammonium fluoride (1.70 g, 6.51 mmol) to afford 0.550 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.60 (s, 6H), 6.97 (s, 1H), 7.17-7.36 (m, 1H), 7.39-7.51 (m, 3H), 7.68 (m, 2H), 7.79 (d, J = 8.1 Hz, 2H), 13.10 (s, 1H).

Intermediate –36

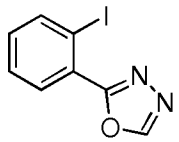
1-Ethoxy-2-iodobenzene



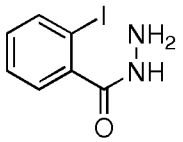
To a solution of 2-iodo phenol (1.0 g, 4.54 mmol) in DMF (10 mL) was added potassium carbonate (1.25 g, 9.08 mmol) and ethyl bromide (0.593 g, 5.44 mmol). The reaction mass was stirred at RT for 5 hours. The reaction mass was quenched in water and extracted with DCM and the organic layer was dried over anhydrous sodium sulphate and concentrated toafford 0.700 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.77 (d, J =7.8 Hz, 1H), 7.30-7.26 (m, 1H), 6.80 (d, J = 8.4 Hz, 1H), 6.69 (t, J = 7.5 Hz, 1H), 4.08 (q, J = 7.5 Hz, 2H), 1.48 (t, J = 7.5 Hz, 3H).

Intermediate –37

2-(2-Iodophenyl)-1,3,4-oxadiazole



Step-1:- Preperation of 2-iodobenzohydrazide:-



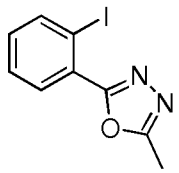
To the solution of 2-iodo bezoic acid (3.0 g, 12.09 mmol) in THF was added TEA (3.0 mL) and ethyl chloro formate (3.0 mL) at 0-5°C. The reaction mass was stirred at 0-5°C for 2 hours. Hydrazine hydrate (3.0 mL) was added to the reaction mass and stirrerd at RT for 4-5 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 2.0 g of desired product. ^{1}HNMR (DMSO-d_6): δ 4.45 (br s, 2H), 7.16 (t, J = 6.9 Hz, 1H), 7.27 (d, J = 6.6 Hz, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 9.51 (m, 1H); MS $[M+H]^+$: 263.18.

Step-2:- Preperation of 2-(2-iodophenyl)-1,3,4-oxadiazole:-

To the solution of 2-iodobenzohydrazide (0.500 g, 1.90 mmol) in trimethyl ortho formate (10 mL) was added PTSA (0.072 g, 0.380 mmol). The reaction mass was stirred at 80-90°C for 4-5 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.300 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.34 (t, 1H), 7.61 (t, J = 7.2 Hz, 1H), 7.80 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 9.46 (s, 1H).

Intermediate –38

2-(2-Iodophenyl)-5-methyl-1,3,4-oxadiazole

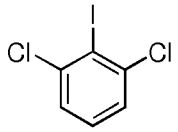


The title compound was prepared by following the same procedure as described for step-2 of Intermediate-37 by using 2-iodobenzohydrazide (step-1 of Intermediate-37, 0.500 g,

1.90 mmol), trimethyl ortho acetate (10 mL), PTSA (0.072 g, 0.380 mmol) to afford 0.200 g of desired product. ^{1}HNMR (DMSO-d_6): δ 2.59 (s, 3H), 7.34 (t, J = 7.8 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 7.75 (d, J = 6.6 Hz, 1H), 8.10 (d, J = 7.8 Hz, 1H); MS $[M+H]^+$: 287.16.

Intermediate –39

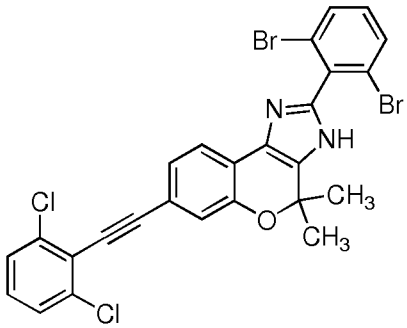
1,3-Dichloro-2-iodobenzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2,6-dichloro aniline (2.0 g, 12.3 mmol), PTSA (3.52 g, 18.52 mmol), sodium nitrite (1.02 g, 14.8 mmol) and potassium iodide (2.46 g, 14.8 mmol) to afford 1.200 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.38-7.43 (m, 1H), 7.53 (d, J = 8.4 Hz, 2H).

Intermediate –40

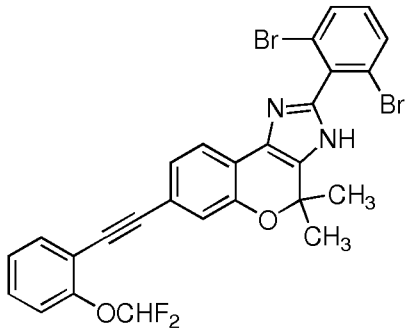
2-(2,6-Dibromophenyl)-7-[(2,6-dichlorophenyl)ethynyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



The title compound was prepared by following the same procedure as described for step-5 of intermediate-7 by using 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (step-4 of intermediate-7, 0.500 g, 1.09 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic acmount), 1,3-dichloro-2-iodobenzene (intermediate-39, 0.357 g, 1.31 mmol) and tetra butyl ammonium fluoride (1.03 g, 3.27 mmol) to afford 0.170 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.04 (s, 1H), 7.19 (m, 1H), 7.22-7.53 (m, 3H), 7.60 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 7.8 Hz, 2H), 13.10 (br s, 1H); MS $[M+]^+$:603.248.

Intermediate –41

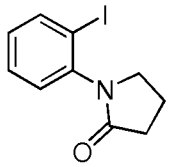
2-(2,6-Dibromophenyl)-7-{[2-(difluoromethoxy)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



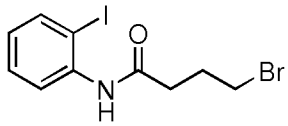
The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (step-4 of Inermediate-7, 0.500 g, 1.09 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic ampunt), 1-(difluoromethoxy)-2-iodobenzenedifluoromethyl 2-iodophenyl ether (0.353 g, 1.31 mmol) and tetra butyl ammonium fluoride (1.03 g, 3.27 mmol) to afford 0.140 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 6.56-7.06 (m, 1H), 7.62-7.00 (m, 6H), 7.82 (d, J = 6.0 Hz, 2H), 7.99 (d, J = 6.9 Hz, 1H), 8.12 (d, J = 8.7 Hz, 1H), 13.10 (br s, 1H).

Intermediate –42

1-(2-Iodophenyl)pyrrolidin-2-one



Step-1:- Preperation of 4-bromo-*N*-(2-iodophenyl)butanamide:-



To the solution of 2-iodoaniline (1.0 g, 4.56 mmol) in THF (20 mL) was added TEA (1.5 mL, 13.69 mmol) and the reaction mass was stirred at RT for 30 mins, and 4-bromo-butyryl chloride (1.27 g, 6.84 mmol) was added at 0-5 °C. The reaction mass was stirred at RT for 24 hours. The reaction mass was quenched in water and extracted with ethyl

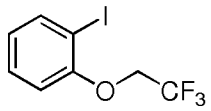
acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.350 g of desired product. ^{1}HNMR ($CDCl_3$): δ 2.28-2.35 (m, 2H), 2.64 (t, *J* = 6.9 Hz, 2H), 3.55 (t, *J* = 6.3 Hz, 2H), 6.86 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.46 (br s, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$: 369.85.

Step-2:- Preperation of 1-(2-iodophenyl)pyrrolidin-2-one:-

To the solution of 4-bromo-*N*-(2-iodophenyl)butanamide (0.500 g, 1.36 mmol) in THF (10 mL) was added sodium hydride (0.081 g, 2.0 mmol) at 5-10°C. The reaction mass was stirred at RT for 10 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.300 g of desired product. ^{1}HNMR ($CDCl_3$): δ 2.29 (m, 2H), 2.59 (t, *J* = 7.8 Hz, 2H), 3.76 (t, *J* = 6.9 Hz, 2H), 7.05 (t, *J* = 6.3 Hz, 1H), 7.25 (d, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$: 288.19.

Intermediate –43

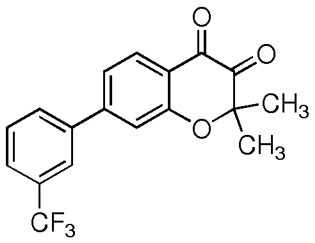
1-Iodo-2-(2,2,2-trifluoroethoxy)benzene



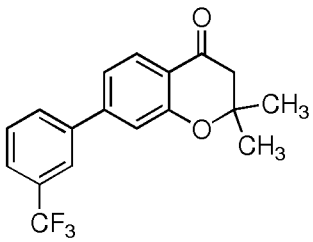
The title compound was prepared by following the same procedure as described for Intermediate-36 by using 2-iodo phenol (1.0 g, 4.54 mmol), potassium carbonate (1.25 g, 9.08 mmol), 1,1,1-trifluoro-2-iodoethane (1.43 g, 6.81 mmol) and DMF (10 mL) to afford 0.600 g of desired product. ^{1}HNMR (DMSO-d_6): δ 4.38 (q, *J* = 8.1 Hz, 2H), 6.76-6.86 (m, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H).

Intermediate –44

2,2-Dimethyl-7-[3-(trifluoromethyl)phenyl]-2*H*-chromene-3,4-dione



Step-1:- Preparation of 2,2-dimethyl-7-[3-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



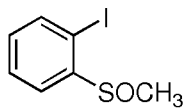
A mixture of 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4) (0.600 g, 1.99 mmol), potassium carbonate (0.825 g, 5.98 mmol), [3-(trifluoromethyl)phenyl]boronic acid (0.571 g, 2.99 mmol), tetrakis(triphenylphosphine)palladium(0) (0.461 g, 0.398 mmol) in DMSO (5 mL) was stirred at 80-90°C for 5-6 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.43 (s, 6H), 2.84 (s, 2H), 7.35-7.43 (m, 2H), 7.69-7.83 (m, 3H), 8.03 (s, 2H); MS $[M+H]^+$:321.18.

Step-2:- Preparation of 2,2-dimethyl-7-[3-(trifluoromethyl)phenyl]-2*H*-chromene-3,4-dione:-

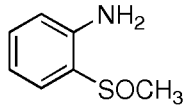
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[3-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.500 g), isoamyl nitrite (2.5 mL) and HCl (2.5 mL) to afford 0.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.44 (s, 6 H), 7.42-7.45 (m, 1 H), 7.71-7.86 (m, 4 H), 8.04 (s, 2H).

Intermediate –45

2-Iodophenyl methyl sulfoxide



Step-1:- Preperation of 2-(methylsulfinyl)aniline:-



To a solution of 2-(methylsulfanyl)aniline (1.0 g, 7.194 mmol) in DCM (15 mL) was added m-CPBA (1.859 g, 10.791 mmol). The reaction mass was stirred at RT for 12-15 hours. The organic layer was washed with water and concentrated to afford 0.500 g of

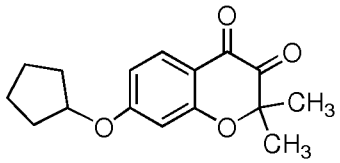
desired product. ^{1}HNMR (DMSO-d_6): δ 2.92 (s, 3H), 5.10-5.20 (br s, 2H), 6.68-6.77 (m, 2H), 7.21-7.26 (m, 2H).

Ste-2:- Preperation of 2-iodophenyl methyl sulfoxide

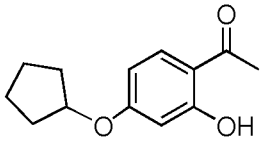
The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2-(methylsulfinyl)aniline (0.500 g, 3.22 mmol), conc. HCl (0.807 g), sodium nitrite (0.330 g, 3.66 mmol) and potassium iodide (0.580 g, 4.20 mmol) to afford 0.350 g of desired product.

Intermediate –46

7-(Cyclopentyloxy)-2,2-dimethyl-2*H*-chromene-3,4-dione

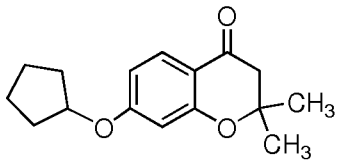


Step-1:- Preperation of 1-[4-(cyclopentyloxy)-2-hydroxyphenyl]ethanone:-



The title compound was prepared according the same procedure as described in Intermediate-36 by using 2,4-dihydroxy acetophenone (4.0 g, 26.31 mmol), potassium carbonate (9.10 g, 9.08 mmol) and cyclopentyl bromide (7.82 g, 52.48 mmol) in DMF (10 mL) to afford 5.0 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.58-1.95 (m, 8H), 2.54 (s, 3H), 4.90 (m, 1H), 6.40 (s, 1H), 6.48 (d, J = 8.7 Hz, 1H), 7.81 (d, J = 8.7 Hz, 1H), 13.61 (s, 1H).

Step-2:- Preperation of 7-(cyclopentyloxy)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one



The title compound was prepared according the same procedure as described in step-1 of Intermediate-1 by using 1-[4-(cyclopentyloxy)-2-hydroxyphenyl]ethanone (10.0 g, 45.4 mmol) and pyrrolidine (6.93 g, 0.099 mmol) in ethanol (50 mL) to afford 3.0 g of desired

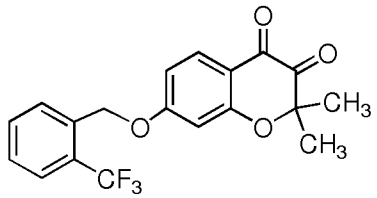
product. ^{1}HNMR (DMSO-d_6): δ 1.37 (s, 6H), 1.57-1.93 (m, 8H), 2.69 (s, 2H), 4.88 (m, 1H), 6.42 (s, 1H), 6.53 (dd, J = 1.8 Hz, 1H), 7.62 (d, J = 8.7 Hz, 1H).

Step-3:- Preperation of 7-(cyclopentyloxy)-2,2-dimethyl-2*H*-chromene-3,4-dione

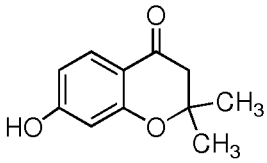
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 7-(cyclopentyloxy)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (2.5 g), isoamyl nitrite (8 mL) and HCl (5 mL) to afford 1.4 g of desired product.

Intermediate –47

2,2-Dimethyl-7-{[2-(trifluoromethyl)benzyl]oxy}-2*H*-chromene-3,4-dione

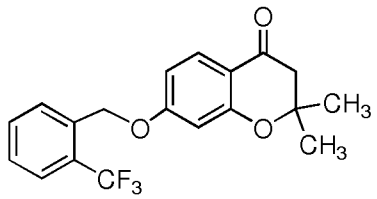


Step-1:- Preparation of 7-hydroxy-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-



A mixture of 7-(cyclopentyloxy)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step-2 of Intermediate-46, 2.0 g, 7.69 mmol) in a mixture of acetic acid and 48% HBr (10 mL) in a ratio of 2:3, was stirred for 4-5 hours at 100°C. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 1.5 g of desired product.

Step-2:- Preparation of 2,2-dimethyl-7-{[2-(trifluoromethyl)benzyl]oxy}-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according the same procedure as described in Intermediate-36 by using 7-hydroxy-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (1.0 g, 5.208 mmol), DMF, potassium carbonate (1.078 g, 7.81 mmol) and 1-(bromomethyl)-2-(trifluoromethyl)benzene (1.867 g, 7.811 mmol) to afford 0.500 g of desired product.

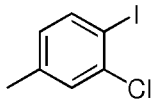
^{1}HNMR ($CDCl_3$): δ 1.46 (s, 6H), 2.67 (s, 2H), 5.27 (s, 2H), 6.45 (s, 1H), 6.44-6.60 (dd, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 8.7 Hz, 1H).

Step-3:- Preparation of 2,2-dimethyl-7-{[2-(trifluoromethyl)benzyl]oxy}-2*H*-chromene-3,4-dione:-

The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-{[2-(trifluoromethyl)benzyl]oxy}-2,3-dihydro-4*H*-chromen-4-one (0.500 g), isoamyl nitrite (2.5 mL) and HCl (2.5 mL) to afford 0.300 g of desired product.

Intermediate –48

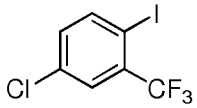
2-Chloro-1-iodo-4-methylbenzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2-chloro-4-methylaniline (1.0 g, 7.06 mmol), sodium nitrite (0.730 g, 10.5 mmol), potassium iodide (1.75 g, 10.5 mmol) and 50% HCl to afford 0.700 g of desired product. ^{1}HNMR (DMSO-d_6): δ 2.23 (s, 3H), 6.89 (d, *J* = 7.8 Hz, 1H), 7.10 (s, 1H), 7.76 (d, *J* = 7.8 Hz, 1H).

Intermediate –49

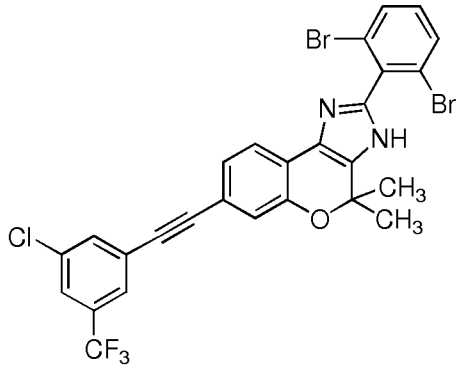
4-Chloro-1-iodo-2-(trifluoromethyl)benzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 2-trifluoromethyl-4-chloro aniline (2.0 g, 0.010 mmol), sodium nitrite (1.050 g, 0.015 mmol), potassium iodide (2.54 g, 0.015 mmol) and 50% HCl to afford 1.5 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.43-7.47 (dd, *J* = 2.1 Hz, 1.8 Hz, 1H), 7.77 (s, 1H), 8.01 (d, *J* = 5.7 Hz, 1H); MS $[M+H]^+$: 242.42.

Intermediate –50

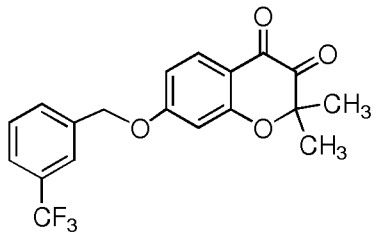
7-{[3-Chloro-5-(trifluoromethyl)phenyl]ethynyl}-2-(2,6-dibromophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



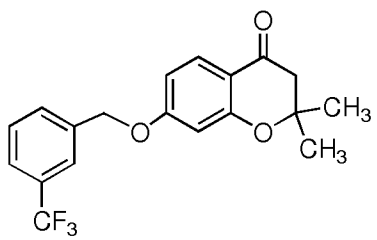
The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2,6-dibromo-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole (Step-4 of Inermediate-7, 0.500 g, 1.09 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic ampunt), 4-chloro-1-iodo-2-(trifluoromethyl)benzene (0.501 g, 1.63 mmol) and tetra butyl ammonium fluoride (1.03 g, 3.27 mmol) to afford 0.170 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.23 (s, 3H), 1.62 (s, 3H), 7.01 (s, 1H), 7.16 (d, J = 7.8 Hz, 1H), 7.38-7.46 (m, 2H), 7.46-7.84 (m, 4H), 7.92 (s, 1H), 13.40 (br s, 1H); MS $[M+H]^+$: 637.26.

Intermediate –51

2,2-Dimethyl-7-{[3-(trifluoromethyl)benzyl]oxy}-2*H*-chromene-3,4-dione



Step-1:- Preparation of 2,2-dimethyl-7-{[3-(trifluoromethyl)benzyl]oxy}-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according the same procedure as described in Intermediate-36 by using 7-hydroxy-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step-

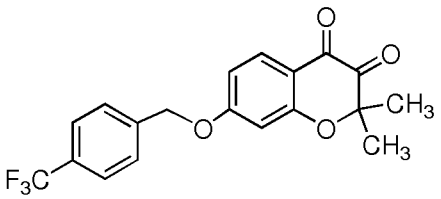
1 of Intermediate-47, 1.0 g, 5.208 mmol), DMF, potassium carbonate (1.078 g, 7.81 mmol) and 1-(bromomethyl)-3-(trifluoromethyl)benzene (1.867 g, 7.811 mmol) to afford 0.600 g of desired product.

Step-2:- Preparation of 2,2-dimethyl-7-{[3-(trifluoromethyl)benzyl]oxy}-2*H*-chromene-3,4-dione:-

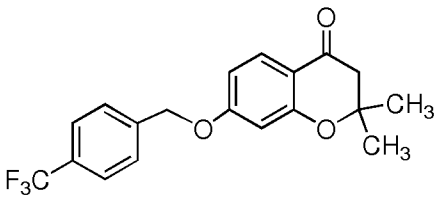
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-{[3-(trifluoromethyl)benzyl]oxy}-2,3-dihydro-4*H*-chromen-4-one (0.500 g), isoamyl nitrite (2.5 mL) and HCl (2.5 mL) to afford 0.250 g of desired product.

Intermediate –52

2,2-Dimethyl-7-{[4-(trifluoromethyl)benzyl]oxy}-2*H*-chromene-3,4-dione



Step-1:- Preparation of 2,2-dimethyl-7-{[4-(trifluoromethyl)benzyl]oxy}-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 7-hydroxy-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step- 1 of Intermediate-47, 1.0 g, 5.208 mmol), DMF (10 mL), potassium carbonate (1.078 g, 7.81 mmol) and 1-(bromomethyl)-4-(trifluoromethyl)benzene (1.867 g, 7.811 mmol) to afford 0.600 g of desired product.

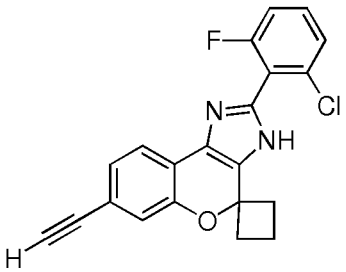
Step-2:- Preparation of 2,2-dimethyl-7-{[4-(trifluoromethyl)benzyl]oxy}-2*H*-chromene-3,4-dione

The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-{[4-(trifluoromethyl)benzyl]oxy}-2,3-dihydro-

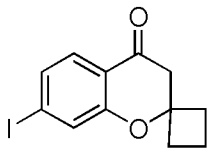
4*H*-chromen-4-one (0.500 g), isoamyl nitrite (2.5 mL) and HCl (2.5 mL) to afford 0.200 g of desired product.

Intermediate –53

2-(2-Chloro-6-fluorophenyl)-7-ethynyl-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane]

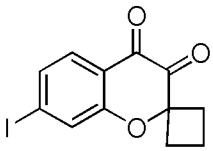


Step-1:- Preparation of 7-iodospiro[chromene-2,1'-cyclobutan]-4(3*H*)-one:-



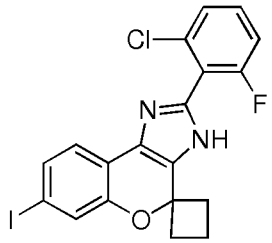
The title compound was prepared according the same procedure as described in step-1 of Intermediate-1 by using 1-(2-hydroxy-4-iodophenyl)ethanone (step-2 of Intermediate-4, 5.0 g, 19.08 mmol), pyrrolidine (5 mL), methanol (50 mL) and cyclobutanone (5 mL) to afford 3.2 g of desired product. MS $[M+H]^+$: 315.19.

Step-2:- Preparation of 7-iodospiro[chromene-2,1'-cyclobutane]-3,4-dione:-



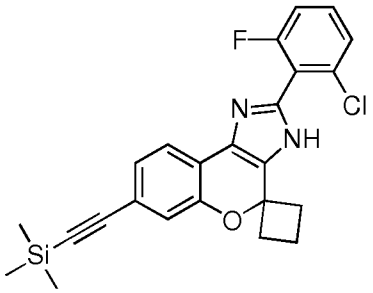
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 7-iodo spiro[chromene-2,1'-cyclobutan]-4(3*H*)-one (1.0 g, 3.18 mmol), isoamyl nitrite (2 mL) and HCl (2 mL) to afford 1.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.67-1.90 (m, 1H), 1.91-1.99 (m, 1H), 2.19-2.60 (m, 4H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.41 (s, 1H), 7.51 (d, *J* = 8.1 Hz, 1H); MS $[M+H]^+$: 328.99.

Step-3:- Preparation of 2-(2-chloro-6-fluorophenyl)-7-iodo-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane]:-



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-iodospiro[chromene-2,1'-cyclobutane]-3,4-dione (1.00 g, 3.05 mmol), 2-chloro-6-fluoro benzaldehyde (0.726 g, 4.58 mmol) and ammonium acetate (1.17 g, 15.29 mmol) in acetic acid (10 mL) to afford 1.0 g of desired product. ^{1}HNMR (DMSO): δ 1.90-1.98 (m, 2H), 2.50 (m, 4H), 7.18 (d, J = 7.8 Hz, 1H), 7.29-7.34 (m, 2H), 7.40-7.53 (m, 2H), 7.56-7.61 (m, 1H), 13.14 (s, 1H); MS $[M+H]^+$:467.24.

Step-4:- Preparation of 2-(2-chloro-6-fluorophenyl)-7-[(trimethylsilyl)ethynyl]-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane]:-



The title compound was prepared by following the same procedure as described for step-1 of Intermediate-6 by using 2-(2-chloro-6-fluorophenyl)-7-iodo-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane] (1.000 g, 2.14 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), triethyl amine (5.0 mL) and trimethylsilylacetylene (0.315 g, 3.21 mmol) in DMSO (3 mL) to afford 1.000 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.18 (s, 9H), 1.86 (m, 2H), 2.69 (m, 4H), 7.00-7.19 (m, 3H), 7.26-7.33 (m, 3H), 11.00 (br s, 1H); MS $[M+H]^+$: 437.36.

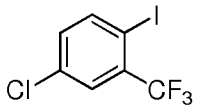
Step-5:- Preparation of 2-(2-chloro-6-fluorophenyl)-7-ethynyl-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane]:-

The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2-chloro-6-fluorophenyl)-7-[(trimethylsilyl)ethynyl]-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane] (1.000 g, 2.29 mmol), tetra butyl

ammonium fluoride (1.08 g, 3.34 mmol) in DCM (20 mL) to afford 0.050 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.90-1.98 (m, 2H), 2.49 (m, 4H), 4.19 (s, 1H), 7.00 (s, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 7.35-7.47 (m, 2H), 7.51-7.64 (m, 2H), 13.18 (s, 1H).

Intermediate –54

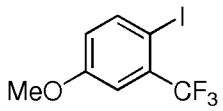
4-Chloro-1-iodo-2-(trifluoromethyl)benzene



The title compound was prepared by following the same procedure as described for Intermediate-11 by using 4-chloro-2-trifluoromethylaniline (2.0 g, 10.23 mmol), sodium nitrite (1.050 g, 15.21 mmol), potassium iodide (2.54 g, 15.30 mmol) and 50% HCl to afford 1.500 g of desired product. ^{1}HNMR (DMSO-d_6): δ 7.43-7.47 (dd, *J* = 2.1 Hz,1.8 Hz, 1H), 7.77 (s, 1H), 8.01 (d, *J* = 5.7 Hz, 1H).

Intermediate –55

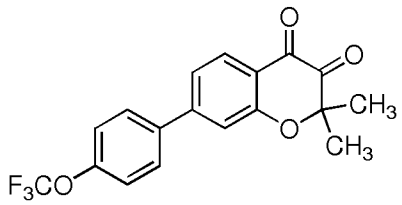
1-Iodo-4-methoxy-2-(trifluoromethyl)benzene



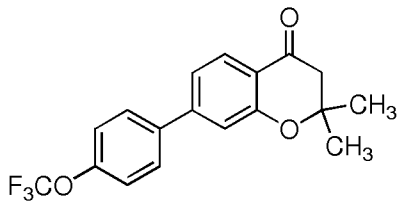
The title compound was prepared by following the same procedure as described for Intermediate-11 by using 4-methoxy-2-(trifluoromethyl)aniline (1.00 g, 5.23 mmol), sodium nitrite (0.541 g, 7.83 mmol), potassium iodide (1.30 g, 7.83 mmol) and 50% HCl to afford 0.500 g of desired product.

Intermediate – 56

2,2-Dimethyl-7-[4-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione



Step-1:- Preparation of 2,2-dimethyl-7-[4-(trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



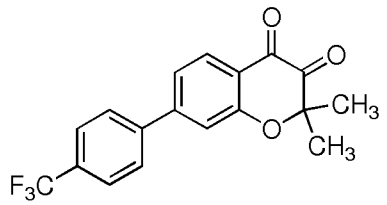
The title compound was prepared according the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4, 0.600 g, 1.99 mmol), potassium carbonate (0.825 g, 5.69 mmol), [3-(trifluoromethoxy)phenyl]boronic acid (0.618 g, 2.99 mmol), tetrakis(triphenylphosphine)palladium(0) (0.461 g, 0.398 mmol) and DMSO (5 mL) to afford 0.500 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.76 (s, 2H), 7.12 (s, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 1H); MS $[M+H]^+$:337.20.

Step-2:- Preparation of 2,2-dimethyl-7-[4-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione:-

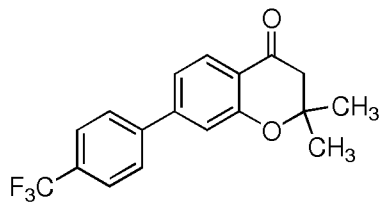
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[4-(trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.400 g, 1.19 mmol), isoamyl nitrite (2.8 mL), ethanol (10 mL) and hydrochloric acid (2 mL) to afford 0.300 g of desired product.

Intermediate – 57

2,2-Dimethyl-7-[4-(trifluoromethyl)phenyl]-2*H*-chromene-3,4-dione



Step-1:- Preparation of 2,2-dimethyl-7-[4-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



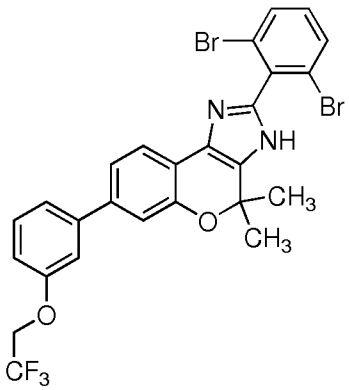
The title compound was prepared according the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4, 0.600 g, 1.99 mmol), potassium carbonate (0.825 g, 5.69 mmol), [4-(trifluoromethyl)phenyl]boronic acid (0.571 g, 2.99 mmol), tetrakis(triphenylphosphine)palladium(0) (0.461 g, 0.398 mmol) and DMSO (5 mL) to afford 0.500 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.50 (s, 6H), 2.77 (s, 2H), 7.17-7.38 (m, 2H), 7.71 (s, 4H), 7.96 (d, J = 8.1 Hz, 1H); MS $[M+H]^+$:321.24.

Step-2:- Preparation of 2,2-dimethyl-7-[4-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione:-

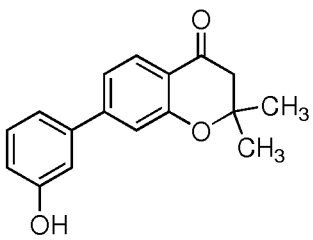
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[4-(trifluoromethoyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.400 g, 1.19 mmol), isoamyl nitrite (2.0 mL), ethanol (10 mL) and hydrochloric acid (2 mL) to afford 0.300 g of desired product.

Intermediate – 58

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole

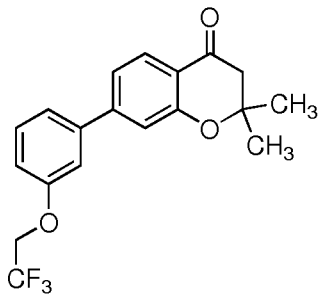


Step-1:- Preparation of 7-(3-hydroxyphenyl)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-



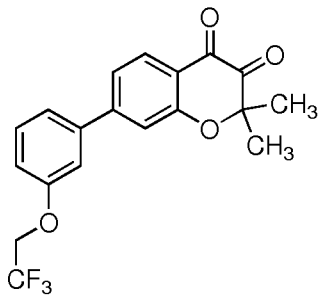
The title compound was prepared according the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4, 0.500 g, 1.66 mmol), potassium carbonate (0.687 g, 4.98 mmol), 3-hydroxy phenyl boronic acid (0.459 g, 3.33 mmol), tetrakis(triphenylphosphine)palladium(0) (0.095 g, 0.083 mmol) and DMSO (5 mL) to afford 0.300 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.41 (s, 6H), 2.81 (s, 2H), 6.82 (d, J = 8.1 Hz, 1H), 7.04 (s, 1H), 7.10-7.15 (m, 2H), 7.24-7.29 (m, 2H), 7.78 (d, J = 8.4 Hz, 1H), 9.63 (s, 1H); MS $[M+H]^+$:269.25.

Step-2:- Preparation of 2,2-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



To a solution of 7-(3-hydroxyphenyl)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (0.300 g, 1.119 mmol) in DMF (3 mL) was added potassium carbonate (0.463 g, 3.350 mmol). The reaction mass was stirred at 80°C for 12-15 hours. The reaction mass was quenched with water and adjusted pH ~ 6 by dil HCl and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.200 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.42 (s, 6H), 2.82 (s, 2H), 4.88 (q, J = 8.7 Hz, 2H), 7.10 (br s, 1H), 7.36-7.41 (br s, 5H), 7.79 (d, J = 7.8 Hz, 1H); MS $[M+H]^+$: 351.30.

Step-3:- Preparation of 2,2-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-2*H*-chromene-3,4-dione:-



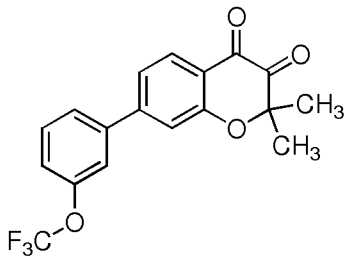
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.200 g, 0.569 mmol), isoamyl nitrite (1.0 mL), ethanol (2 mL) and hydrochloric acid (1 mL) to afford 0.200 g of desired product.

Step-4:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

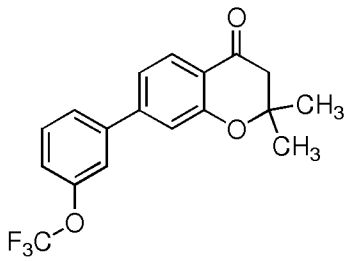
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-2*H*-chromene-3,4-dione (0.200 g, 0.549 mmol) and 2,6-di bromo benzaldehyde (0.217 g, 0.824 mmol) and ammonium acetate (0.212 g, 2.74 mmol) in acetic acid (5 mL) to afford 0.200 g of desired product. ^{1}HNMR DMSO-d_6): ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 4.88 (q, J = 9.0 Hz, 2H), 7.02 (br s, 1H), 7.27-7.41 (m, 7H), 7.83 (d, J = 7.8 Hz, 2H), 12.97 (br s, 1H); MS $[M+H]^+$: 609.14.

Intermediate – 59

2,2-Dimethyl-7-[3-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione



Step-1:- Preparation of 2,2-dimethyl-7-[4-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



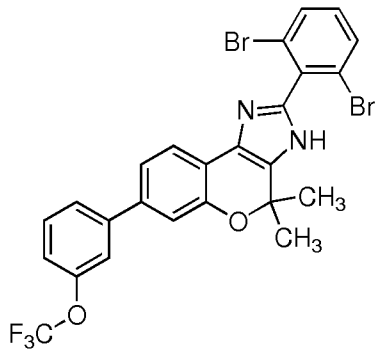
The title compound was prepared according the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4, 0.500 g, 1.66 mmol), potassium carbonate (0.687 g, 4.989 mmol), [3-(trifluoromethoxy)phenyl]boronic acid (0.712 g, 2.49 mmol), tetrakis(triphenylphosphine)palladium(0) (0.383 g, 0.330 mmol) and DMSO (5 mL) to afford 0.300 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.76 (s, 2H), 6.73-6.79 (m, 1H), 7.14 (s, 1H), 7.20 (t, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 2H),7.52 (t, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H); MS $[M+H]^+$:337.26.

Step-2:- Preparation of 2,2-dimethyl-7-[3-(trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-

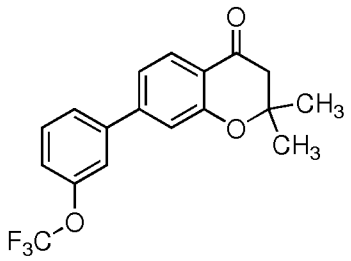
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[4-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.300 g, 0.892 mmol), isoamyl nitrite (3.0 mL), ethanol (10 mL) and hydrochloric acid (3 mL) to afford 0.200 g of desired product ^{1}HNMR ($CDCl_3$): δ 1.48 (s, 6H), 6.71-6.75 (m, 1H), 7.15-7.27 (m, 2H), 7.45-7.53 (m, 3H), 7.92 (t, *J* = 8.4 Hz, 1H); MS $[M+H]^+$:350.99.

Intermediate – 60

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[3-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole

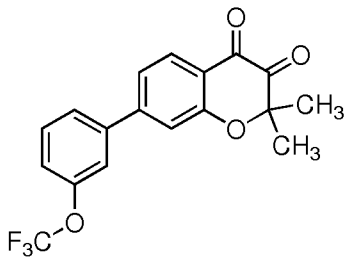


Step-1:- Preparation of 2,2-dimethyl-7-[3-(trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4, 0.600 g, 1.66 mmol), potassium carbonate (0.819 g, 5.94 mmol), 3-trifluoromethoxy phenyl boronic acid (0.614 g, 2.98 mmol), tetrakis(triphenylphosphine)palladium(0) (0.114 g, 0.099 mmol) and DMSO (5 mL) to afford 0.450 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.50 (s, 6H), 2.76 (s, 2H), 7.14 (s, 1H), 7.19 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 8.1 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.93 (d, J = 7.8Hz, 1H); MS $[M+H]^+$:337.19.

Step-2:- Preparation of 2,2-dimethyl-7-[3-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione:-



The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[3-(2,2,2-trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.450 g, 1.335 mmol), isoamyl nitrite (2.0 mL), ethanol (2 mL) and hydrochloric acid (1 mL) to afford 0.450 g of desired product.

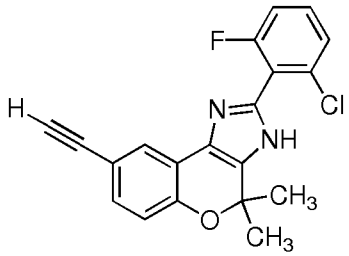
Step-3:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[3-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[3-(2,2,2-trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione (0.450 g, 1.280 mmol), 2,6-di bromo benzaldehyde (0.509 g, 1.92

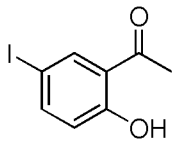
mmol) and ammonium acetate (0.492 g, 6.40 mmol) in acetic acid (8 mL) to afford 0.300 g of desired product. ^{1}HNMR DMSO-d_6): ^{1}HNMR (DMSO-d_6): δ 1.60 (s, 6H), 7.23 (d, J = 7.5 Hz, 2H), 7.30-7.44 (m, 3H), 7.35-7.61 (m, 2H), 7.71 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 7.8 Hz, 2H); MS $[M+H]^+$: 595.10.

Intermediate – 61

2-(2-Chloro-6-fluorophenyl)-8-ethynyl-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole

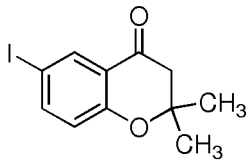


Step-1:- Preparation of 1-(2-hydroxy-5-iodo-phenyl)-ethanone:-



To a solution of 2-hydroxy acetophenone (0.500 g, 3.67 mmol) in acetonitrile (10 mL) was added N-iodo succinamide (0.908 g, 4.037 mmol) and p-toluene sulphonic acid (0.698 g, 3.67 mmol) under nitrogen atmosphere. The reaction mixture was stirred at RT for 3-4 hours. The reaction mass was quenched in water and extracted with water. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.400 g of desired product. ^{1}HNMR (DMSO): δ 2.62 (s, 3H), 6.80 (d, J = 8.1 Hz, 1H), 7.75–7.79 (m, 1H), 8.08 (s, 1H), 11.75 (s,1H).

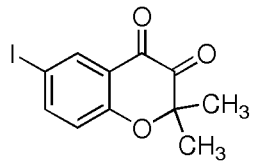
Step-2:- Preparation of 6-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according the same procedure as described in step-1 of Intermediate-1 by using 1-(2-hydroxy-5-iodo-phenyl)-ethanone (0.100 g, 0.403 mmol) and pyrrolidine (3 mL) in ethanol (5 mL) to afford 0.060 g of desired product. ^{1}HNMR

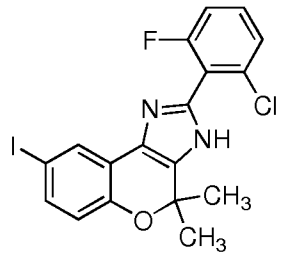
(DMSO): δ 1.38 (s, 6H), 2.81 (s, 2H), 6.85 (d, *J* = 9.0 Hz, 1H), 7.81–7.84 (m, 1H), 7.92-7.94 (s,1H); MS $[M-H]^-$:301.40.

Step-3:- Preparation of 6-bromo-2,2-dimethyl-2*H*-chromene-3,4-dione:-



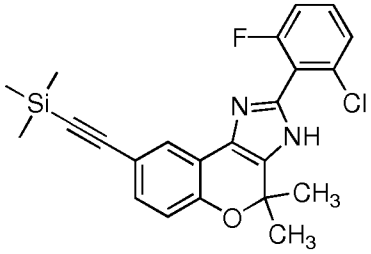
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 6-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (2.5 g, 8.278 mmol), ethanol (8 mL), hydrochloric acid (10 mL) and isoamyl nitrite (10 mL) to afford 2.0 g of desired product.

Step-4:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-8-iodo-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole:-



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 6-bromo-2,2-dimethyl-2*H*-chromene-3,4-dione (2.500 g, 9.29 mmol), acetic acid (10 mL), ammonium acetate (5.0 g, 64.93 mmol) and 2-chloro-6-fluoro benzaldehyde (2.200 g,13.92 mmol) to afford 0.100 g of desired product. ^{1}HNMR (DMSO): δ 1.37 (s, 6H), 7.36-7.77 (m, 6H), 13.05 (s, 1H).

Step-5:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-8-trimethylsilanylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole:-



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2-chloro-6-fluoro-phenyl)-8-iodo-4,4-dimethyl-1,4-

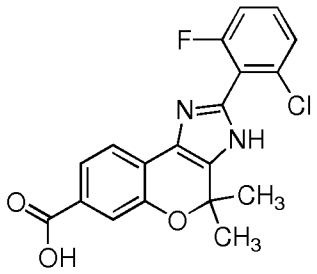
dihydro-chromeno[3,4-d]imidazole (2.200 g, 4.858 mmol), DMSO (10 mL), copper iodide (catalytic amount), dichloro-bis(triphenylphosphine)palladium (II) (catalytic amount), triethyl amine (10.0 mL) and trimethylsilylacetylene (0.713 g,7.259 mmol) to afford 1.500 g of desire product.

Step-6:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole:-

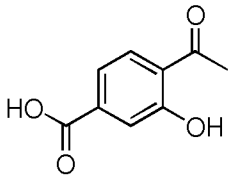
To a solution of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-8-trimethylsilanylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole (2.2 g, 5.188 mmol) in DCM was added tetra butyl ammonium fluoride (1.80 g, 5.71 mmol). The reaction mass was stirred at room temperature for 2-3 hours. The reaction mass was quenched in water and filtered through celite bed and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford 0.550 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.60 (s, 6H), 3.99-4.08 (m, 1H), 6.86-6.91 (m, 1H), 7.18-7.23 (m, 1H), 7.42 (d, *J* = 8.70 Hz, 1H), 7.50-7.60 (m, 3H), 13.06 (s, 1H); MS $[M+H]^+$: 353.26.

Intermediate – 62

2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid



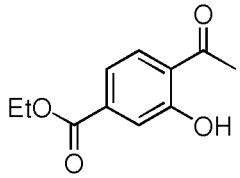
Step-1:- Preparation of 4-acetyl-3-hydroxybenzoic acid:-



To 3-acetoxy benzoic acid (5.0 g, 0.027 mol) was added aluminum trichloride (14.7 g, 0.111 mol) and the reaction mass was heated at 160°C for 5 hours. The reaction mixture was acidified with 1N HCl and extracted with ethyl acetate. The organic layer was dried

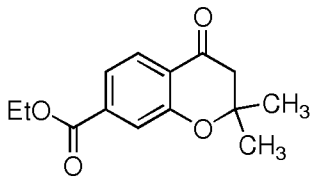
over anhydrous sodium sulphate and concentrated to afford 3.0 g of desired product. ^{1}HNMR (DMSO d_6): δ 2.63 (s, 6H), 6.97 (d, J = 8.7 Hz, 1H), 7.52–7.55 (dd, J = 2.4 Hz, J = 2.4 Hz, 1H), 7.96 (s,1H); MS $[M+H]^+$:181.19.

Step-2:- Preparation of ethyl 4-acetyl-3-hydroxybenzoate:-



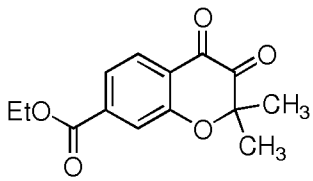
To the solution of 4-acetyl-3-hydroxybenzoic acid (5.0 g, 27.75 mol) in ethanol was added few drops of conc.sulphuric acid and the reaction mass was refluxed for 12 hours. Ethanol was removed under vacuum and basified the reaction mass with sodium bicarbonate and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.650 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.32 (t, J = 6.9 Hz, 3H), 2.65 (s, 3H), 4.32 (q, J = 6.9 Hz, 6.9 Hz, 2H), 7.44-7.49 (m, 2H), 7.90 (d, J = 8.4 Hz, 1H), 11.60 (s,1H).

Step-3:- Preparation of ethyl 2,2-dimethyl-4-oxochromane-7-carboxylate:-



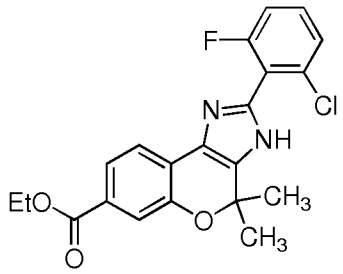
To the solution of ethyl 4-acetyl-3-hydroxybenzoate (0.100 g, 0.403 mmol) in ethanol was added pyrrolidine (3.0 mL) and acetone (5.0 mL). The reaction mass was stirred at 70°C for 6 hours. The reaction mass was quenched in water and acidified with dil HCl and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.060 g of desired product.^{1}HNMR (DMSO d_6): δ 1.31 (t, J = 6.6 Hz, 3H), 1.40 (s, 6H), 2.86 (s, 2H), 4.31 (q, J = 6.9 Hz, 7.5 Hz, 2H), 7.46 (s, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H).

Step-4:- Preparation of ethyl 2,2-dimethyl-3,4-dioxochromane-7-carboxylate:-



The title compound was prepared by following the same procedure as described for step-2 of Intermediate-1 by using 2,2-dimethyl-4-oxochromane-7-carboxylate (0.200 g, 0.805 mmol), ethanol (2.0 mL), isopentyl nitrite (5.0 mL) and conc.HCl (5.0 mL) to afford 0.150 g of desired product.

Step-5:- Preparation of ethyl 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylate



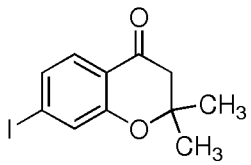
The title compound was prepared by following the same procedure as described for Intermediate-5 by using ethyl 2,2-dimethyl-3,4-dioxochromane-7-carboxylate (1.1 g, 4.198 mmol), acetic acid (5 mL), 2-chloro-6-fluoro benzaldehyde (0.072 g, 0.455 mmol) and ammonium acetate (2.37 g, 30.77 mmol) to aford 0.500 g of desired product.[1]HNMR (DMSO d_6): δ 1.31 (t, J = 7.2 Hz, 3H), 1.61 (s, 6H), 4.28 (q, J = 6.9 Hz, 6.9 Hz, 2H), 7.39-7.61 (m, 6H), 13.27 (s, 1H); MS $[M-H]^-$:399.40.

Step-6:- Preparation of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid

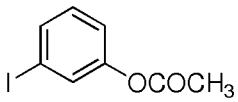
To the solution of ethyl 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylate (0.600 g, 1.497 mmol) in ethanol was added aq. solution of sodium hydroxide (0.161 g, 4.03 mmol) at 10-15°C. The reaction mass was stirred for 24 hours. Ethanol was removed under vacuum and water was added. The reaction mass was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to get 0.500 g of desired product. [1]HNMR (DMSO d_6): δ 1.61 (s, 6H), 7.36-7.61 (m, 6H), 13.23 (br s, 1H); MS $[M+H]^+$:373.45.

Intermediate – 63

7-Iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one

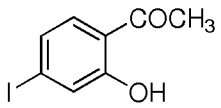


Step-1:- Preparation of 3-iodophenyl acetate:-



A mixture of 3-ido phenol (10.0 g, 0.045 mol), pyridine (40 mL) and acetic anhydride (6.9 mL, 0.068 mol) was stirred at 50°C for 30 mins. The reaction mixture was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 10 g of desired product. ^{1}HNMR (DMSO): δ 2.50 (s, 3H), 7.15-7.24 (m, 2H), 7.56 (s, 1H), 7.62-7.64 (d, 1H, *J* = 7.2 Hz) .

Step-2: Preparation of 1-(2-hydroxy-4-iodophenyl)ethanone:-



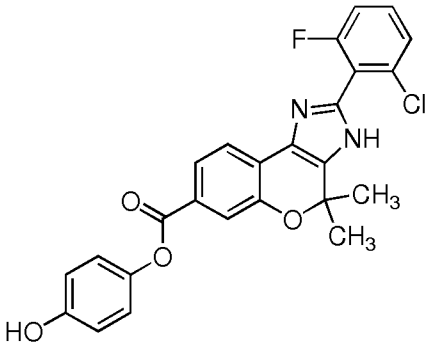
To 3-iodophenyl acetate (10 g, 0.03 mol) was added anhydrous aluminium chloride (15.17 g, 0.114 mol). The reaction mixture was stirred at 100°C. After the completion of reaction, the reaction mixture was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 3 g of desired product. ^{1}HNMR ($CdCl_3$): δ 2.60 (s, 3H), 7.24-7.27 (m, 1H), 7.39-7.48 (m, 2H), 12.25 (s, 1H).

Step-3:- Preparation of 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-

The title compound was prepared according the same procedure as described in step-1 of Intermediate-1 by using 1-(2-hydroxy-4-iodophenyl)ethanone (3 g, 0.114 mol), pyrrolidine (10 mL) and methanol (10 mL) to afford 2.0 g of desire product. ^{1}HNMR ($CdCl_3$): δ 1.44 (s, 6H), 2.70 (s, 2H), 7.31 (s, 1H), 7.36 (d, 1H, *J* = 8.7 Hz), 7.53 (d, 1H, *J* = 8.4 Hz).

Intermediate – 64

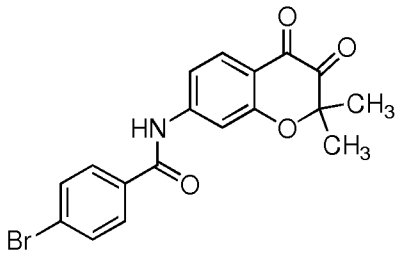
4-Hydroxyphenyl-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylate



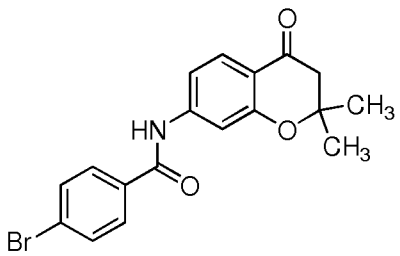
To a solution of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.150 g, 0.403 mmol) in THF was added p-nitro phenol (0.062 g, 0.443 mmol), EDC HCl (0.115 g, 0.604 mmol) and TEA (0.082 g, 0.806 mmol). The reaction mass was stirred at RT for 15 hours. THF was removed under vacuum and the reaction mass was quenched in water and acidified with HCl and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated under vacuum to afford 0.100 g of desired product.

Intermediate – 65

4-Bromo-*N*-(2,2-dimethyl-3,4-dioxo-3,4-dihydro-2*H*-chromen-7-yl)benzamide



Step-1:- Preparation of 4-bromo-*N*-(2,2-dimethyl-4-oxo-3,4-dihydro-2*H*-chromen-7-yl)benzamide:-



The mixture of 4-bromo benzamide (0. 066 g, 0.332 mmol), 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step-3 of Intermediate-4, 0.100 g 0.332 mmol), xanthophos (0.019 g, 0.0033 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.016 g, 0.016 mmol)

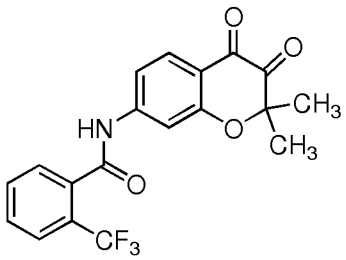
and sodium tert. butoxide (0.048 g, 0.493 mmol) was refluxed for 3- 4 hours. The reaction mass was filtered through celite and the filtrate was quenched in water. The reaction mass was extracted with ethyl acetate and organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.030 g of desired product.

Step-2:- Preparation of 4-bromo-*N*-(2,2-dimethyl-3,4-dioxo-3,4-dihydro-2*H*-chromen-7-yl)benzamide:-

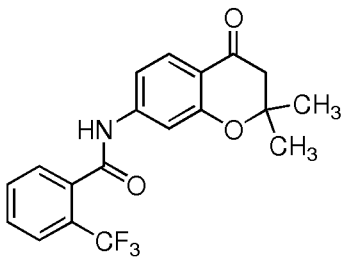
The title compound was prepared following the procedure described for step-2 of Intermediate-1 but starting from 4-bromo-*N*-(2,2-dimethyl-4-oxo-3,4-dihydro-2*H*-chromen-7-yl)benzamide (0.140 g), isopentyl nitrite (3.0 mL), HCl (3 mL) and ethanol (5 mL) to afford 0.140 g of desired product.

Intermediate – 66

N-(2,2-Dimethyl-3,4-dioxo-3,4-dihydro-2*H*-chromen-7-yl)-2-(trifluoromethyl)benzamide



Step-1:- Preparation of *N*-(2,2-dimethyl-4-oxo-3,4-dihydro-2*H*-chromen-7-yl)-2-(trifluoromethyl)benzamide:-



The title compound was prepared following the procedure described for step-1 of Intermediate-65 by using 2-(trifluoromethyl)benzamide (0. 0.156 g g, 0.830 mmol), 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step-3 of Intermediate-4, 0.250 g 0.830 mmol), xanthophos (0.048 g, 0.083 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.038 g, 0.041 mmol) and sodium tert. butoxide (0.119 g, 1.245 mmol) to afford 0.180 g of desired product. ^{1}HNMR (DMSO

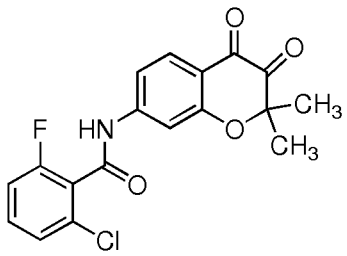
d_6): δ 1.40 (s, 6H), 2.75 (s, 2H), 7.22 (d, *J* = 8.7Hz, 1H), 7.46 (s, 1H), 7.69-7.76 (m, 3H), 7.81 (d, *J* = 7.8Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 10.89 (s, 1H).

Step-2:- Preparation of *N*-(2,2-dimethyl-3,4-dioxo-3,4-dihydro-2*H*-chromen-7-yl)-2-(trifluoromethyl)benzamide:-

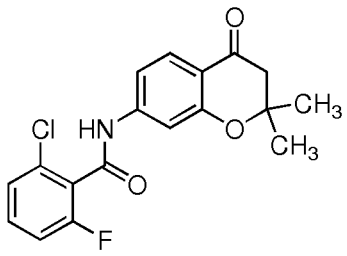
The title compound was prepared following the procedure described for step-2 of intermediate-1 by using *N*-(2,2-dimethyl-4-oxo-3,4-dihydro-2*H*-chromen-7-yl)-2-(trifluoromethyl)benzamide (0.180 g), isopentyl nitrite (3.0 mL), HCl (3 mL) and ethanol (5 mL) to afford 0.140 g of desired product.

Intermediate – 67

2-Chloro-N-(2,2-dimethyl-3,4-dioxo-3,4-dihydro-2H-chromen-7-yl)-6-fluorobenzamide



Step-1:- Preparation of 2-chloro-N-(2,2-dimethyl-4-oxo-3,4-dihydro-2H-chromen-7-yl)-6-fluorobenzamide:-



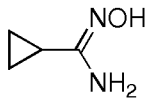
The title compound was prepared following the procedure described for step-1 of Intermediate-65 but starting from 2-chloro-6-fluorobenzamide (0.143 g, 0.830 mmol), 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step-3 of Intermediate-4, 0.250 g 0.830 mmol), xanthophos (0.048 g, 0.083 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.038 g, 0.041 mmol) and sodium tert. butoxide (0.119 g, 1.245 mmol) to afford 0.180 g of desired product. . ^{1}HNMR (DMSO d_6): δ 1.40 (s, 6H), 2.75 (s, 2H), 7.21 (d, *J* = 8.7 Hz, 1H), 7.41 (t, *J* = 9.0 Hz, 1H), 7.46-7.48 (m, 2H), 7.54-7.59 (m, 1H), 7.72 (d, *J* = 8.7Hz, 1H), 11.12 (s, 1H).

Step-2:- Preparation of 2-chloro-N-(2,2-dimethyl-3,4-dioxo-3,4-dihydro-2H-chromen-7-yl)-6-fluorobenzamide:-

The title compound was prepared following the procedure described for step-2 of Intermediate-1 by using from 2-chloro-N-(2,2-dimethyl-4-oxo-3,4-dihydro-2H-chromen-7-yl)-6-fluorobenzamide (0.180 g), isopentyl nitrite (3.0 mL), HCl (3 mL) and ethanol (5 mL) to afford 0.120 g of desired product.

Intermediate – 68

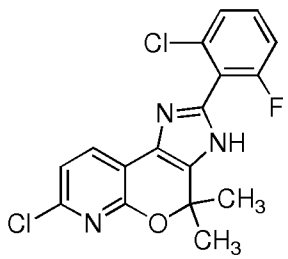
N'-Hydroxycyclopropanecarboximidamide



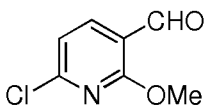
To the stirred solution of hydroxyl amine hydrochloride (1.2 g, 17.39 mmol) and potassium carbonate (3.7 g, 26.81 mmol) in THF was added cyclopropyl cyanide (0.600 g, 8.9 mmol). The reaction mixture was refluxed for 24 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.300 g of desired product. MS $[M+H]^+$: 101.10

Intermediate –69

7-Chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydroimidazo[4',5':4,5] pyrano[2,3-*b*]pyridine



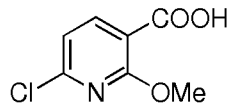
Step-1:- Preparation of 6-chloro-2-methoxypyridine-3-carbaldehyde:-



To a cold solution of 2-chloro-6-methoxypyridine (50.0 g, 0.348 mol) in THF was added tert. butyl lithium (26.74 g, 0.417 mol) at -78°C. The reaction mass was stirred at -78°C for 1 hour follwed by addition of DMF at same tempreture. The reaction mass was stirred for 3-4 hours at -78°C. Acetic acid was added to the reaction mass to maintain pH~6 at -

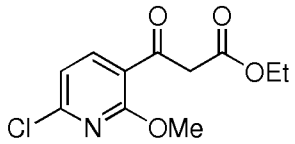
78°C and again continued stirring for 1 hour. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 50.0 g of desired product. ^{1}HNMR (DMSO-d_6): δ 4.04 (s, 3H), 7.03 (d, J = 7.2 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H,), 10.30 (s, 1H).

Step-2: Preparation of 6-chloro-2-methoxypyridine-3-carboxylic acid:-



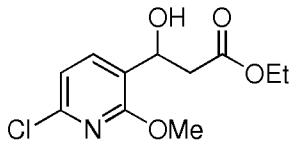
To a cold solution of 6-chloro-2-methoxypyridine-3-carbaldehyde (15.0 g, 0.087 mol) in acetone was added sulphamic acid (10.1 g, 0.105 mol) and sodium chlorite (9.4 g, 0.105 mol) at 0°C. The reaction mass was stirred at room tempreture for 2 hours. Acetone was removed under vaccume and water was added to the reaction mass. The reaction mass fwas stirred for 1 hour and filtered to afford 15.0 g of desired product.^{1}HNMR (DMSO-d_6): δ 3.91 (s, 3H), 7.18 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H,), 13.15 (br s, 1H); MS $[M+H]^+$:190.18.

Step-3:- Preparation of ethyl 3-(6-chloro-2-methoxypyridin-3-yl)-3-oxopropanoate:-



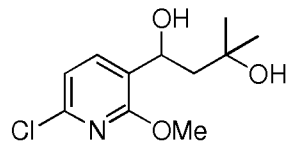
To a solution of 6-chloro-2-methoxypyridine-3-carboxylic acid (45.0 g, 0.240 mol) in (1:1) THF: acetonitrile (300 mL) was added 1,1-carbonyl imimdazole (42.93 g, 0.264 mol). The reaction mass was stirred at room tempreture. The solution of potassium 3-ethoxy-3-oxopropanoate (47.78 g, 0.264 mol), $MgCl_2$ (34.2 g, 0.36 mol) and TEA (145 ml, 1.44 mol) in acetonitrile (100 mL) was prepared. The reaction mass was stirred at 0°C for 1 hour followed by stirring at room tempreture for 5-6 hours. The above prepared solution was added to it and again continued stiring for12-15 hours. The reaction mass was quenched in water and adjusted pH ~5-6 by acetic acid and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 45.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.25 (t, J = 8.4 Hz, 3H), 4.05 (s, 2H), 4.18 (s, 3H), 4.23-4.28 (m, 2H), 7.03 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.7 Hz, 1H); MS $[M+H]^+$:258.03.

Step-4:- Preparation of ethyl 3-(6-chloro-2-methoxypyridin-3-yl)-3-hydroxypropanoate:-



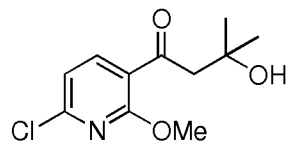
To a solution of ethyl 3-(6-chloro-2-methoxypyridin-3-yl)-3-oxopropanoate (45.0 g, 0.174 mol) in THF was added sodium borohydride (4.51 g, 0.122 mol) at 0°C. The reaction mass was stirred at 0°C for 4-5 hours. The reaction mass was quenched in water and adjudted pH ~ 6-7 by acetic acid and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 35.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.27 (t, *J* = 7.2 Hz, 3H), 2.57 (dd, *J* = 9.3 Hz, 9.0 Hz, 1H), 2.85 (dd, *J* = 3.6 Hz, 3.3 Hz, 1H), 3.97 (s, 3H), 4.18 (q, *J* = 7.5 Hz, 6.9 Hz, 2H), 5.20 (dd, *J* = 2.4 Hz, 3.0 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$:260.19.

Step-5:- Preparation of 1-(6-chloro-2-methoxypyridin-3-yl)-3-methylbutane-1,3-diol:-



To a solution of ethyl 3-(6-chloro-2-methoxypyridin-3-yl)-3-hydroxypropanoate (35.0 g, 0.134 mol) in THF (300 mL) was added methyl magnesium bromide (48.15 g, 0.403 mol) at 0°C. The reaction mass was stirred at 0°C for 3-4 hours. The reaction mass was quenched in water and adjusted pH ~6 by acetic acid and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 20.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.28 (s, 3H), 1.44 (s, 3H), 1.76 (s, 2H), 3.96 (s, 3H), 5.22 (dd, *J* = 3.6 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$:246.21.

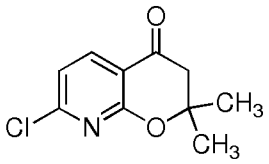
Step-6:- Preparation of 1-(6-chloro-2-methoxypyridin-3-yl)-3-hydroxy-3-methylbutan-1-one:-



To a solution of 1-(6-chloro-2-methoxypyridin-3-yl)-3-methylbutane-1,3-diol (20.0 g, 0.0814 mol) in DCM was added pyridinium chlorochromate (52.54 g, 0.244 mol) at room

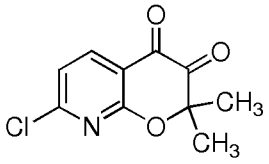
tempreture. The reaction mass was stirred for 3 hours. The reaction mass was filtered through celite and the filtrate was concentrated to afford 12.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.32 (s, 6H), 3.18 (s, 2H), 4.08 (s, 3H), 7.02 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H).

Step-7:- Preparation of 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



A solution of 1-(6-chloro-2-methoxypyridin-3-yl)-3-hydroxy-3-methylbutan-1-one (2.5 g, 10.28 mol) in 48% HBr in acetic acid was stirred at 80°C for 30 mins. The reaction mass was cooled and quenched in cold water. The reaction mass was filtered to afford 1.8 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.53 (s, 6H), 2.77 (s, 2H), 7.21 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H).

Step-8:- Preparation of 7-chloro-2,2-dimethyl-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione:-



The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (0.150 g, 0.710 mmol), isoamyl nitrite (1.0 mL), ethanol (2 mL) and hydrochloric acid (1 mL) to afford 0.100 g of desired product .

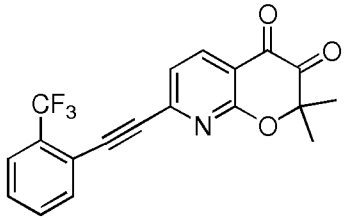
Step-9:- Preparation of 7-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydroimidazo[4',5':4,5]pyrano[2,3-*b*]pyridine:-

The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-chloro-2,2-dimethyl-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione (0.100 g, 0.439 mmol), 2-chloro-6-fluoro benzaldehyde (0.104 g, 0.659 mmol) and ammonium acetate (0.170 g, 2.19 mmol) in acetic acid (3 mL) to afford 0.006 g of desired product. ^{1}HNMR (DMSO): δ 1.70 (s, 6H), 7.07-7.15 (m, 1H), 7.43 (t, *J* = 9.0 Hz,

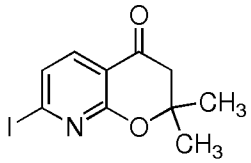
1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.57-7.61 (m, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 13.25 (br s, 1H); MS $[M+H]^+$:364.22.

Intermediate – 70

2,2-Dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione

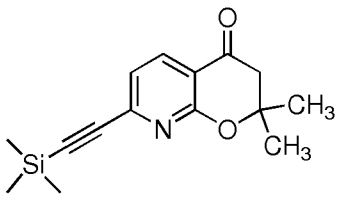


Step-1:- Preparation of 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



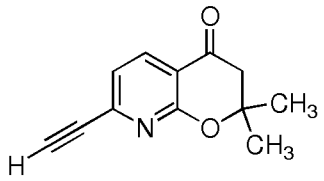
To a solution of 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (step-7 of Intermediate-69, 6.0 g, 28.43 mmol) in THF was added 4M HCl in dioxane (20 mL). The reaction mass was stirred at RT for 5 h. The reaction mass was concentrated to get a solid. Sodium iodide (10 g, 66.66 mmol) was heated at 150°C and added to concentrated reaction mass. The reaction mass was diluted with acetonitrile and refluxed for 24 h. The reaction mass was neutralized with sodium bicarbonate and diluted with water. The reaction mass was extracted with ethyl acetate and concentrated to afford 5.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.53 (s, 6H), 2.77 (s, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H); $[M+H]^+$: 353.26.

Step-2:- Preparation of 2,2-dimethyl-7-[(trimethylsilyl)ethynyl]-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



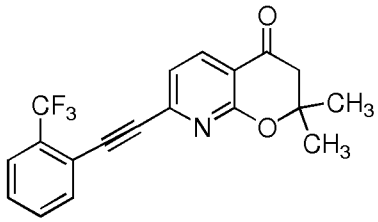
The title compound was prepared according the same procedure as described in step-5 of Intermediate-7 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (5.000 g, 16.501 mmol), trimethylsilylacetylene (2.4 g, 24.48 mmol), copper iodide (0.062 g, 0.326 mmol), dichloro-bis(triphenylphosphine)palladium (II) (0.346 g, 0.493 mmol) and triethyl amine (10.0 mL) in DMSO (20 mL) to afford 5.0 g of desired product.

Step-3:- Preparation of 7-ethynyl-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



The title compound was prepared according the same procedure as described in step-6 of Intermediate-61 by using 2,2-dimethyl-7-[(trimethylsilyl)ethynyl]-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (5.0 g, 18.24 mmol), tert. butyl ammonium fluoride (4.76 g, 18.2 mmol) and DCM (20 ml) to afford 1.3 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.53 (s, 6H), 2.78 (s, 2H), 3.30 (s, 1H), 7.20 (d, *J* = 7.80 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$: 202.21.

Step-4:- Preparation of 2,2-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



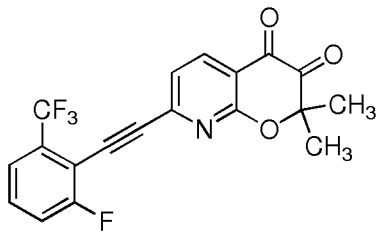
The title compound was prepared according the same procedure as described in step-5 of Intermediate-7 by using 7-ethynyl-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (0.250 g, 1.23 mmol), 1-iodo-2-(trifluoromethyl)benzene (0.505 g, 1.85 mmol), copper iodide (0.005 g, 0.026 mmol), dichloro-bis(triphenylphosphine)palladium (II) (0.034 g, 0.0.37 mmol) and triethyl amine (1.0 mL) in DMSO (3.0 mL) to afford 0.200 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.54 (s, 6H), 2.80 (s, 2H), 7.27 (s, 1H), 7.48 (d, *J* = 7.80 Hz, 1H), 7.58 (d, *J* = 6.9 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 2H), 8.20 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$: 346.14.

Step-5:- Preparation of 2,2-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione:-

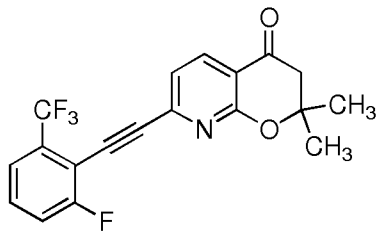
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (0.200 g, 0.579 mmol), ethanol (4 mL), hydrochloric acid (1.0 mL) and isoamyl nitrite (1.0 mL) to afford 0.200 g of desired product.

Intermediate – 71

7-{[2-Fluoro-6-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione



Step-1:- Preparation of 7-{[2-fluoro-6-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



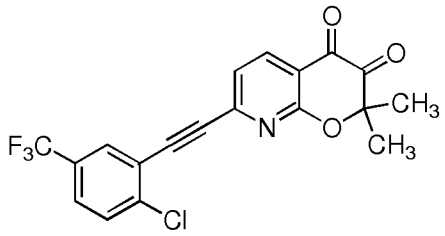
The title compound was prepared according the same procedure as described in step-5 of Intermediate-7 by using 7-ethynyl-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (step-3 of Intermediate-70, 0.250 g, 1.23 mmol), 1-fluoro-2-iodo-3-(trifluoromethyl)benzene (0.535 g, 1.84 mmol), copper iodide (0.005 g, 0.026 mmol), dichloro-bis(triphenylphosphine)palladium (II) (0.034 g, 0.0.37 mmol) and triethyl amine (1.0 mL) in DMSO (3.0 mL) to afford 0.100 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.55 (s, 6H), 2.80 (s, 2H), 7.29-7.34 (m, 2H), 7.52 (m, 2H), 8.21 (d, J = 7.8 Hz, 1H); MS $[M+H]^+$: 364.17.

Step-2:- Preparation of 7-{[2-fluoro-6-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione:-

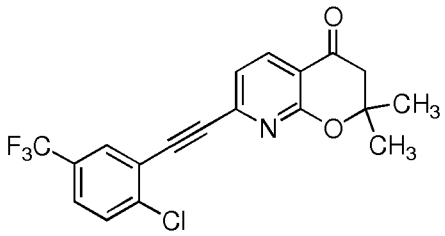
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 7-{[2-fluoro-6-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (0.100 g, 0.275 mmol), ethanol (2 mL), hydrochloric acid (1.0 mL) and isoamyl nitrite (1.0 mL) to afford 0.100 g of desired product.

Intermediate – 72

7-{[2-Chloro-5-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione



Step-1:- Preparation of 7-{[2-chloro-5-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one:-



The title compound was prepared according the same procedure as described in step-5 of Intermediate-7 by using 7-ethynyl-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (step-3 of intermediate-63, 0.250 g, 1.23 mmol), 1-chloro-2-iodo-4-(trifluoromethyl)benzene (0.564 g, 1.84 mmol), copper iodide (0.005 g, 0.026 mmol), dichloro-bis(triphenylphosphine)palladium (II) (0.034 g, 0.0.37 mmol) and triethyl amine (1.0 mL) in DMSO (3.0 mL) to afford 0.200 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.55 (s, 6H), 2.80 (s, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.58 (s, 2H), 7.88 (s, 1H), 7.23 (d, *J* = 7.8 Hz, 1H); MS $[M+H]^+$: 380.13.

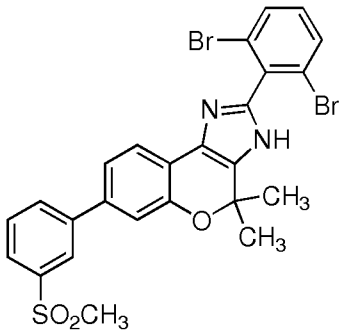
Step-2:- Preparation of 7-{[2-chloro-5-(trifluoromethyl)phenyl]ethynyl}-2,2-dimethyl-2*H*-pyrano[2,3-*b*]pyridine-3,4-dione:-

The title compound was prepared according to the same procedure as described in step-2 of Intermediate-1 by using 7-{[2-chloro-5-(trifluoromethyl)phenyl]ethynyl}-2,2-

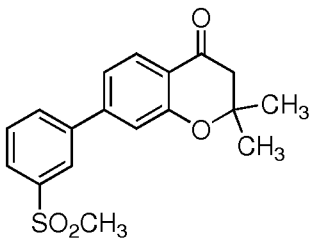
dimethyl-2,3-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one (0.200 g, 0.526 mmol), ethanol (2 mL), hydrochloric acid (1.0 mL) and isoamyl nitrite (1.0 mL) to afford 0.200 g of desired product.

Intermediate – 73

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[3-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole

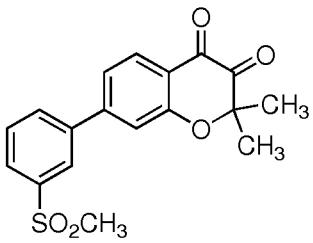


Step-1:- Preparation of 2,2-dimethyl-7-[3-(methylsulfonyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (Step-3 of Intermediate-4, 0.500 g, 1.66 mmol), K_2CO_3 (0.687 g, 4.98 mmol), [3-(methylsulfonyl)phenyl]boronic acid (0.666 g, 3.33 mmol), tetrakis(triphenylphosphine)palladium(0) (0.096 g, 0.083 mmol) and DMSO (5 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 10 % EA:DCM to afford 0.300 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.50 (s, 6H), 2.77 (s, 2H), 3.11 (s, 3H), 7.22 (d, J = 6.3 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.97 (d, J = 6.6 Hz, 2H), 8.18 (s, 1H); MS $[M+H]^+$:331.25.

Step-2:- Preparation of 2,2-dimethyl-7-[3-(methylsulfonyl)phenyl]-2*H*-chromene-3,4-dione:-



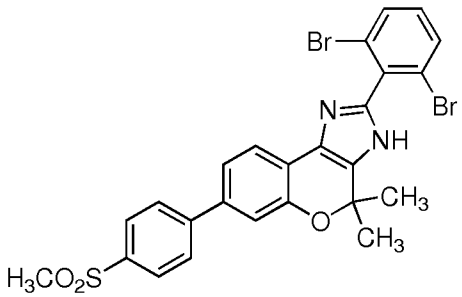
The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[3-(methylsulfonyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.330 g, 0.909 mmol), isoamyl nitrite (1.0 mL), ethanol (4 mL) and hydrochloric acid (1 mL) to afford 0.300 g of desired product.

Step-3:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[3-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

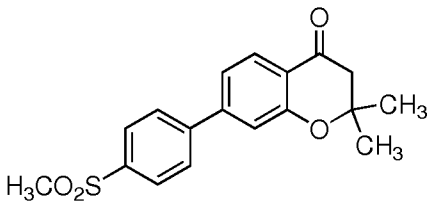
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[3-(methylsulfonyl)phenyl]-2*H*-chromene-3,4-dione (0.300 g, 0.872 mmol), 2,6-dibromo benzaldehyde (0.345 g, 1.30 mmol), ammonium acetate (0.335 g, 4.36 mmol) and acetic acid (4 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 7% EA:DCM to afford 0.150 g of desired product. ^{1}HNMR DMSO-d_6): δ 1.63 (s, 6H), 3.31 (s, 3H), 7.12-7.49 (m, 4H), 7.72 (t, J = 7.8 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 7.2 Hz, 1H), 8.17 (s, 1H), 13.03 (s, 1H); MS $[M-H]^-$: 587.07.

Intermediate – 74

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[4-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole

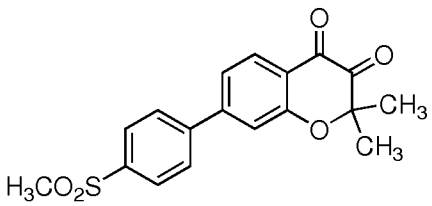


Step-1:- Preparation of 2,2-dimethyl-7-[4-(methylsulfonyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according to the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (Step-3 of Intermediate-4, 0.500 g, 1.66 mmol), K_2CO_3 (0.687 g, 4.98 mmol), [4-(methylsulfonyl)phenyl]boronic acid (0.666 g, 3.33 mmol), tetrakis(triphenylphosphine)palladium(0) (0.096 g, 0.083 mmol) and DMSO (5 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 7 % EA:DCM to afford 0.400 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.50 (s, 6H), 2.77 (s, 2H), 3.11 (s, 3H), 7.18-7.22 (m, 2H), 7.78 (d, *J* = 7.8Hz, 2H), 7.97 (d, *J* = 8.4Hz, 1H), 8.03 (d, *J* = 8.1Hz, 2H).

Step-2:- Preparation of 2,2-dimethyl-7-[4-(methylsulfonyl)phenyl]-2*H*-chromene-3,4-dione:-



The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[4-(methylsulfonyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.400 g, 1.21 mmol), isoamyl nitrite (1.0 mL), ethanol (3 mL) and hydrochloric acid (1 mL) to afford 0.300 g of desired product.

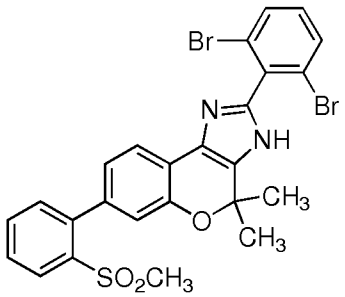
Step-3:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[4-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[4-(methylsulfonyl)phenyl]-2*H*-chromene-3,4-dione (0.300 g, 0.872 mmol), 2,6-di bromo benzaldehyde (0.345 g, 1.30 mmol), ammonium acetate (0.335 g, 4.36 mmol) and acetic acid (4 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 8% EA:DCM to afford 0.250 g of desired product. ^{1}HNMR DMSO-d_6): δ 1.63 (s, 6H), 3.25

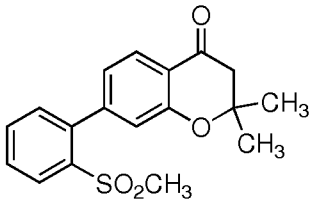
(s, 3H), 7.33-7.46 (m, 4H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.96 (s, 4H), 13.04 (br s, 1H); MS $[M+H]^+$: 589.38.

Intermediate – 75

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[2-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole

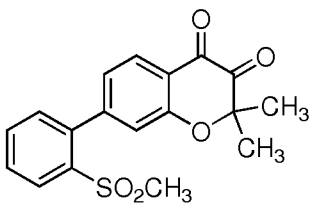


Step-1:- Preparation of 2,2-dimethyl-7-[2-(methylsulfonyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according to the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (Step-3 of Intermediate-4, 0.500 g, 1.66 mmol), K_2CO_3 (0.687 g, 4.98 mmol), [2-(methylsulfonyl)phenyl]boronic acid (0.666 g, 3.33 mmol), tetrakis(triphenylphosphine)palladium(0) (0.096 g, 0.083 mmol) and DMSO (5 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 6% EA:DCM to afford 0.400 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.78 (s, 3H), 3.06 (s, 2H), 7.04 (br s, 1H), 7.59-7.67 (m, 4H), 7.90-7.97 (m, 2H).

Step-2:- Preparation of 2,2-dimethyl-7-[2-(methylsulfonyl)phenyl]-2*H*-chromene-3,4-dione:-



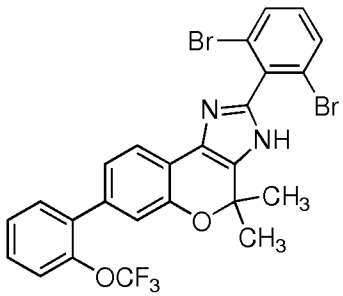
The title compound was prepared according to the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[2-(methylsulfonyl)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.400 g, 1.21 mmol), isoamyl nitrite (1.0 mL), ethanol (3 mL) and hydrochloric acid (1 mL) to afford 0.300 g of desired product.

Step-3:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[2-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

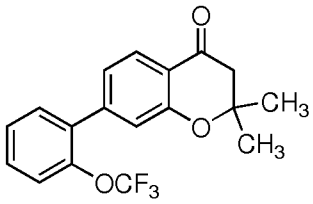
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[2-(methylsulfonyl)phenyl]-2*H*-chromene-3,4-dione (0.300 g, 0.872 mmol), 2,6-di bromo benzaldehyde (0.345 g, 1.30 mmol), ammonium acetate (0.335 g, 4.36 mmol) and acetic acid (4 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 10% EA:DCM to afford 0.300 g of desired product. ^{1}HNMR DMSO-d_6): δ 1.61 (s, 6H), 2.87 (s, 3H), 6.93 (s, 1H), 6.98 (d, J = 7.8 Hz, 1H), 7.41-7.48 (m, 2H), 7.05-7.85 (m, 4H), 8.03-8.14 (m, 2H), 13.03 (s, 1H); MS $[M-H]^-$: 587.16.

Intermediate – 76

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[2-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole



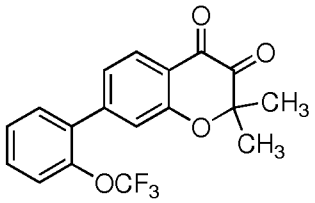
Step-1:- Preparation of 2,2-dimethyl-7-[2-(trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according to the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3

of Intermediate-4, 0.600 g, 1.98 mmol), K_2CO_3 (0.819 g, 5.948 mmol), [2-(trifluoromethoxy)phenyl]boronic acid (0.613 g, 2.98 mmol), tetrakis(triphenylphosphine)palladium(0) (0.114 g, 0.099 mmol) and DMSO (6 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 7% EA:DCM to afford 0.450 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.76 (s, 2H), 7.04 (br s, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 7.34-7.44 (m, 4H), 7.90 (d, *J* = 7.8 Hz, 1H); MS $[M-H]^-$: 337.37.

Step-2:- Preparation of 2,2-dimethyl-7-[2-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione:-



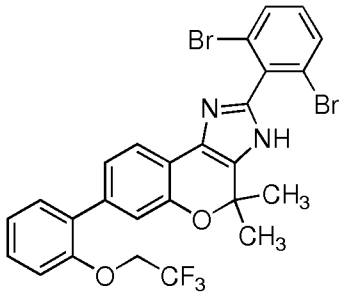
The title compound was prepared according to the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[2-(trifluoromethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.400 g, 1.21 mmol), isoamyl nitrite (1.0 mL), ethanol (3 mL) and hydrochloric acid (1 mL) to afford 0.350 g of desired product.

Step-3:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[2-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

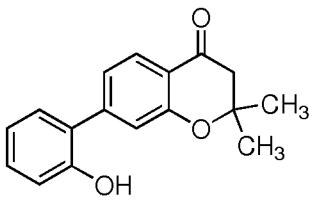
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[2-(trifluoromethoxy)phenyl]-2*H*-chromene-3,4-dione (0.350 g, 1.14 mmol), 2,6-di bromo benzaldehyde (0.452 g, 1.71 mmol), ammonium acetate (0.438 g, 5.7 mmol) and acetic acid (4 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 10% EA:DCM to afford 0.200 g of desired product. ^{1}HNMR DMSO-d_6): δ 1.61 (s, 6H), 6.98 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 7.38-7.67 (m, 6H), 7.84 (d, *J* = 7.8 Hz, 2H), 13.03 (s, 1H); MS $[M+H]^+$: 595.24.

Intermediate – 77

2-(2,6-Dibromophenyl)-4,4-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole

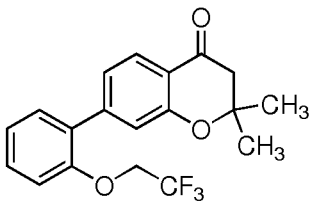


Step-1:- Preparation of 7-(2-hydroxyphenyl)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared according to the same procedure as described in step-1 of Intermediate-44 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (step-3 of Intermediate-4, 0.700 g, 2.31 mmol), K_2CO_3 (0.956 g, 6.93 mmol), 2-hydroxyphenyl boronic acid (0.479 g, 3.47 mmol), tetrakis(triphenylphosphine)palladium(0) (0.133 g, 0.115 mmol) and DMSO (6 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 10% EA:DCM to afford 0.450 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.75 (s, 2H), 5.59 (br s, 1H), 6.78-6.90 (m, 1H), 6.96-7.03 (m, 2H), 7.09 (s, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.28-7.30 (m, 1H), 7.94 (d, *J* = 8.1 Hz, 1H) ; MS $[M+H]^+$: 269.37.

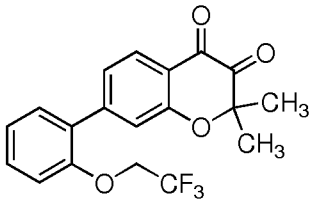
Step-2:- Preparation of 2,2-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one:-



The title compound was prepared by following the same procedure as described for Intermediate-36 by using 7-(2-hydroxyphenyl)-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (0.450 g, 1.67 mmol), DMF (4.0 mL), K_2CO_3 (0.695 g, 5.03 mmol) and 1,1,1-trifluoro-2-iodoethane (0.528 g, 2.51 mmol). The obtained crude product was further

purified by colum chromatography on silica gel eluting with 20 % EA:DCM to afford 0.300 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.75 (s, 2H), 4.30 (d, *J* = 7.2Hz, 2H), 6.98 (d, *J* = 7.2Hz, 1H), 7.10 (s, 1H), 7.16 (d, *J* = 6.9 Hz, 2H), 7.37 (m, 2H), 7.88 (d, *J* = 7.2 Hz, 1H) ; MS $[M+H]^+$: 351.23.

Step-3:- Preparation of 2,2-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-2*H*-chromene-3,4-dione:-



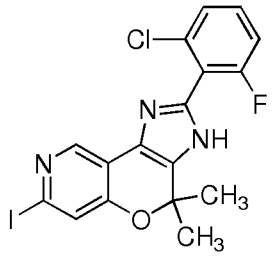
The title compound was prepared according to the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-2,3-dihydro-4*H*-chromen-4-one (0.300 g, 0.954 mmol), isoamyl nitrite (1.0 mL), ethanol (3 mL) and hydrochloric acid (1 mL) to afford 0.200 g of desired product.

Step-4:- Preparation of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole:-

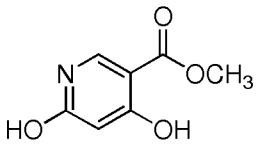
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-2*H*-chromene-3,4-dione (0.200 g, 0.549 mmol), 2,6-di bromo benzaldehyde (0.217 g, 0.824 mmol), ammonium acetate (0.213 g, 2.74 mmol) and acetic acid (4 mL). The obtained crude product was further purified by colum chromatography on silica gel eluting with 20% EA:DCM to afford 0.122 g of desired product. ^{1}HNMR DMSO-d_6): δ 1.61 (s, 6H), 4.74 (q, *J* = 8.7Hz, 2H), 7.02-7.17 (m, 4H), 7.20-7.47 (m, 4H), 7.81 (d, *J* = 8.4 Hz, 2H), 12.92 (s, 1H); MS $[M+H]^+$: 609.17.

Intermediate –78

2-(2-Chloro-6-fluorophenyl)-7-iodo-4,4-dimethyl-1,4-dihydroimidazo[4',5':4,5] pyrano[3,2-*c*]pyridine

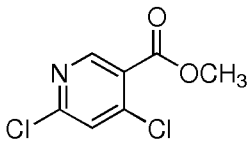


Step-1:- Preparation of methyl 4,6-dihydroxypyridine-3-carboxylate:-



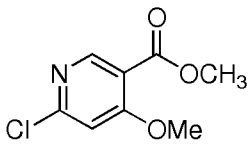
A mixture of dimethyl 3-oxopentanedioate (5.0 g, 28.735 mmol), triethyl ortho formate (4.25 g, 28.71 mmol) and acetic anhydride was stirred at 130°C for 2 h. The reaction mass was allowed to cool at RT. Excess of solvent was removed under vaccum at 85°C. The obtained compound was cooled at 0°C and liquid ammonia (10 mL) was added. The reaction mass was stirred at 0°C for 1 h. The reaction mass was acidified with 6 N HCl and again stirred at RT for 20 mins. The obtained crude product was stirred in benzene at 60°C. The reaction mass was filtered to afford 2.5 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.78 (s, 3H), 5.20 (s, 1H), 5.85 (br hump, 2H), 7.81 (s, 1H); $[M+H]^+$: 170.14.

Step-2: Preparation of methyl 4,6-dichloropyridine-3-carboxylate:-



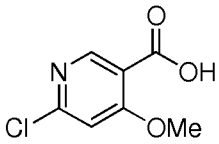
To a solution of methyl 4,6-dihydroxypyridine-3-carboxylate (25.0 g, 0.147 mol) in N,N-diethyl aniline (37.23 g, 0.248 mol) was added phosphorous oxychloride (200.0 mL). The reaction mass was refluxed for 3 h followed by stirring at RT for 18 h. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated. The obtained crude product was further purified by column chromatography on silica gel eluting with 4.0 % EA: pet ether to afford 23.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 3.97 (s, 3H), 7.48 (s, 1H), 8.64 (s, 1H); MS $[M+H]^+$:206.27.

Step-3:- Preparation of methyl 6-chloro-4-methoxypyridine-3-carboxylate:-



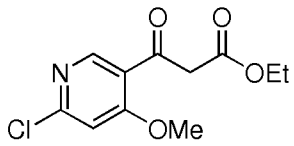
To a solution of methyl 4, 6-dichloropyridine-3-carboxylate (23.0 g, 0.111 mol) in dry methanol (180 mL) was added sodium methoxide (5.9 g, 0.111 mol) at 0°C. The reaction mass was stirred at RT for 3 h. Excess of solvent was removed under vacuum and water was added to reaction mixture. The organic layer was dried over anhydrous sodium sulphate and concentrated. The obtained crude product was further purified by column chromatography on silica gel eluting with 5.0 % EA: DCM to afford 13.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 3.91 (s, 3H), 3.98 (s, 3H), 6.93 (s, 1H), 8.71(s, 1H); MS $[M+H]^+$: 202.20.

Step-4:- Preparation of methyl 6-chloro-4-methoxypyridine-3-carboxylic acid:-



To a solution of methyl 6-chloro-4-methoxypyridine-3-carboxylate (13.0 g, 0.064 mol) in THF (50.0 mL) was added $LiOH.H_2O$ (3.23 g, 0.077 mol). The reaction mass was stirred at RT for 3 h. Excess of solvent was removed under vacuum and cold water was added to the reaction mass. The obtained solid was filtered and dried to afford 8.5 g of desired product. ^{1}HNMR (DMSO-d_6): δ 3.92 (s, 3H), 7.30 (s, 1H), 8.51 (s, 1H),13-14 (br s, 1H); MS $[M+H]^+$: 188.23.

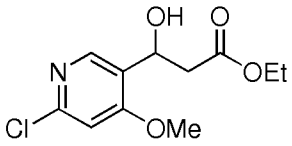
Step-5:- Preparation of ethyl 3-(6-chloro-4-methoxypyridin-3-yl)-3-oxopropanoate:-



The title compound was prepared by following the same procedure as described for step-3 of Intermediate-69 by using methyl 6-chloro-4-methoxypyridine-3-carboxylic acid (8.5 g, 0.045 mol), THF: acetonitrile (1:1) (40 mL), CDI (14.6 g, 0.090 mmol), potassium 3-ethoxy-3-oxopropanoate (9.0 g, 0.049 mol), acetonitrile (90 mL), magnesium chloride (11.42 g, 0.120 mol) and TEA (48.5 g, 0.48 mol). The obtained product was further purified by column chromatography on silica gel eluting with 5.0 % EA: pet ether to

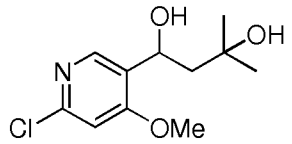
afford 6.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.24 (t, *J* = 7.24 Hz, 3H), 3.92 (s, 2H), 3.98 (s, 3H), 4.18 (q, *J* = 6.6 Hz, 6.9 Hz, 2H), 6.94 (s, 1H), 8.73 (s, 1H); MS $[M+H]^+$:258.11.

Step-6:- Preparation of ethyl 3-(6-chloro-4-methoxypyridin-3-yl)-3-hydroxypropanoate:-



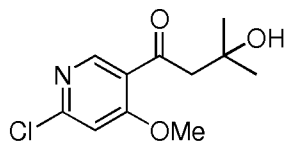
The title compound was prepared by following the same procedure as described for step-4 of Intermediate-69 by using ethyl 3-(6-chloro-4-methoxypyridin-3-yl)-3-oxopropanoate (8.5 g, 0.032 mol), $NaBH_4$ (0.875 g, 0.023 mol) and methanol (25 mL) to afford 6.0 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.30 (t, *J* =9.3 Hz, 3H), 2.61-2.70 (m, 1H), 2.77-2.84 (m, 1H), 3.58 (br s, 1H), 3.90 (s, 3H), 4.17 (q, *J* = 7.2Hz, 6.9Hz, 2H), 5.31 (d, *J* = 6.3 Hz, 1H), 6.81 (br s, 1H), 8.35(br s, 1H); MS $[M+H]^+$:260.25.

Step-7:- Preparation of 1-(6-chloro-4-methoxypyridin-3-yl)-3-methylbutane-1,3-diol:-



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-69 by using ethyl 3-(6-chloro-4-methoxypyridin-3-yl)-3-hydroxypropanoate (6.0 g, 0.023 mol) and methyl magnesium bromide (3.0 M in DEE) (22.29 ml, 0.069 mol) in THF (40 mL) at 0°C to afford 3.0 g of desired product ^{1}HNMR (DMSO-d_6): δ 1.14 (s, 3H), 1.20 (s, 3H), 1.59 (s, 2H), 3.87 (s, 3H), 4.66 (s, 1H), 5.03-5.05 (br s, 1H), 5.34 (s, 1H), 7.09 (s, 1H), 8.21 (s, 1H); MS $[M+H]^+$:246.35.

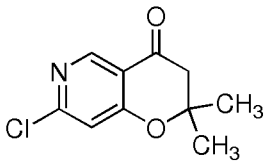
Step-8:- Preparation of 1-(6-chloro-4-methoxypyridin-3-yl)-3-hydroxy-3-methylbutan-1-one:-



To a solution of 1-(6-chloro-4-methoxypyridin-3-yl)-3-methylbutane-1,3-diol (3.0 g, 0.012 mol) in DCM was added PCC (8.0 g, 0.036 mol) at RT. The reaction mass was stirred for 3 h. The reaction mass was filtered through celite and concentrated to afford

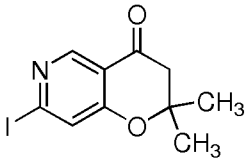
1.5 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.32 (s, 6H), 3.12 (s, 2H), 4.00 (s, 3H), 6.93 (s, 1H), 8.56 (s, 1H); MS $[M+H]^+$: 244.31.

Step-9:- Preparation of 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[3,2-*c*]pyridin-4-one:-



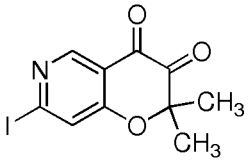
To a solution of 1-(6-chloro-4-methoxypyridin-3-yl)-3-hydroxy-3-methylbutan-1-one (1.5 g, 0.006 mol) in DCM (10 mL) was added BBr_3 (1M in DCM) (3.85 g, 0.015 mol) at 0°C. The reaction mass was stirred at same tempreture for 30 mins. The reaction mass was quenched in cold water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 1.2 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.58 (s, 6H), 2.89 (s, 2H), 7.15 (s, 1H), 8.93 (s, 1H).

Step-10:- Preparation of 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[3,2-*c*]pyridin-4-one:-



The title compound was prepared by following the same procedure as described for step-1 of intermediate-70 by using 7-chloro-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[3,2-*c*]pyridin-4-one (1.2 g, 0.003 mol), 4M HCl in dioxane (10 mL), sodium iodide (1.78 g, 0.011 mol), THF (10 mL) and acetonitrile (10 mL) to afford 0.600 g of desired product. ^{1}HNMR ($CDCl_3$): δ 1.49 (s, 6H), 2.76 (s, 2H), 6.92 (s, 1H), 8.77 (s, 1H).

Step-11:- Preparation of 7-iodo-2,2-dimethyl-2*H*-pyrano[3,2-*c*]pyridine-3,4-dione:-



The title compound was prepared according to the same procedure as described in step-2 of Intermediate-1 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-pyrano[3,2-*c*]pyridin-4-

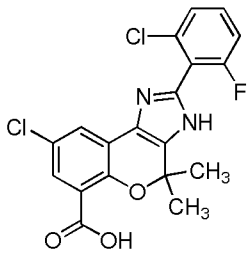
one (0.600 g, 1.98 mmol), isoamyl nitrite (2.0 mL), ethanol (4 mL) and hydrochloric acid (2 mL) to afford 0.600 g of desired product.

Step-12:- Preparation of 2-(2-chloro-6-fluorophenyl)-7-iodo-4,4-dimethyl-1,4-dihydroimidazo [4',5':4,5]pyrano[3,2-*c*]pyridine:-

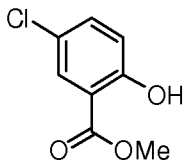
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-iodo-2,2-dimethyl-2*H*-pyrano[3,2-*c*]pyridine-3,4-dione (0.600 g, 1.89 mmol), 2-chloro-6-fluoro benzaldehyde (0.447 g, 2.83 mmol), ammonium acetate (0.735 g, 9.49 mmol) and acetic acid (5 mL). The obtained product was further purified by column chromatography on silica gel eluting with 8.0% EA: DCM to afford 0.300 g of desired product.^{1}HNMR (DMSO): δ 1.64 (s, 6H), 7.04 (d, *J* = 8.1Hz, 1H), 7.35-7.62 (m, 3H), 8.34 (d, *J* = 8.1 Hz, 1H), 13.32 (s, 1H); MS $[M+H]^+$:455.38.

Intermediate –79

8-Chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxylic acid

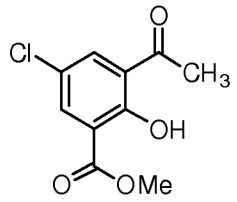


Step-1:- Preparation of methyl 5-chloro-2-hydroxybenzoate



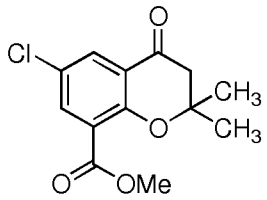
To a solution of 5-chloro salicylic acid (13..0 g, 0.07 mol) in methanol was added few drops of conc.sulphuric acid and the reaction mass was refluxed for 12 hours. Methanol was removed under vaccum, quenched in water and extracted with DCM. The organic layer was washed with $NaHCO_3$ solution, dried over anhydrous sodium sulphate and concentrated to afford 7.50 g of desired product. ^{1}HNMR ($CDCl_3$): δ 3.96 ((s, 3H), 6.88 (d, *J* = 9.0 Hz, 1H), 7.53 (dd, *J* = 2.4 Hz, 2.7 Hz, 1H), 7.96 (s, 1H).

Step-2:- Preparation of methyl 3-acetyl-5-chloro-2-hydroxybenzoate:-



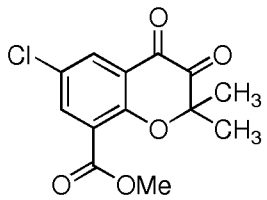
To a mixture of methyl 5-chloro-2-hydroxybenzoate (7.2 g, 0.038 mmol) and acetyl chloride (7.54 g, 0.096 mol) was added aluminium trichloride (15.4 g, 0.11 mol) lot wise at 10-15°C. The reaction mass was stirred at RT for 1 h followerd by stirring at 80°C for 7 h. The reaction mass was quenched in water and extacted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 1.50 g of desired product. ^{1}HNMR ($CDCl_3$): δ 2.69 (s, 3H), 3.98 (s, 3H), 7.95 (d, *J* = 2.4 Hz, 1H),8.01 (d, *J* = 2.7 Hz, 1H), 12.12 (s, 1H); MS $[M+H]^+$: 228.98.

Step-3:- Preparation of methyl 6-chloro-2,2-dimethyl-4-oxochroman-8-carboxylate:-



To a solution of methyl 3-acetyl-5-chloro-2-hydroxybenzoate (1.5 g, 6.57 mmol) in methanol (10.0 mL) was added pyridine (7.0 mL) and acetone (15.0 mL). The reaction mass was stirred at 70°C for 6 hours. The reaction mass was quenched in water and acidified with dil HCl and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 1.5 g of desired product. ^{1}HNMR ($CdCl_3$): δ 1.40 (s, 6H), 2.90 (s, 2H), 3.82 (s, 3H), 7.85 (d, *J* = 2.4 Hz, 1H), 7.93 (d,*J* = 2.4 Hz, 1H).

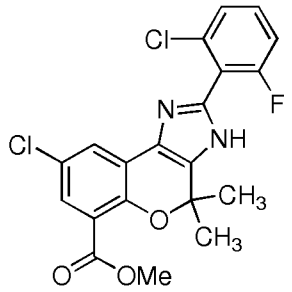
Step 4:- Preparation of methyl 6-chloro-2,2-dimethyl-3,4-dioxochroman-8-carboxylate:-



The title compound was prepared according the procedure described in step-2 of intermediate-1 using methyl 6-chloro-2,2-dimethyl-4-oxochroman-8-carboxylate (1.0 g,

3.73 mmol), isoamyl nitrite (5 mL) and conc. HCl (3mL). The crude product obtained from this reaction was taken forward for next step.

Step-5:- Preparation of methyl 8-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxylate:-



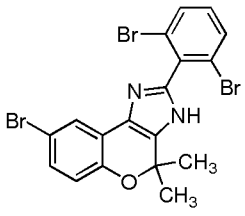
The title compound was prepared according the procedure described in Intermediate-5 by using methyl 6-chloro-2,2-dimethyl-3,4-dioxochroman-8-carboxylate (1.3 g, 0.0069 mmol), 2-chloro-6-fluoro benzaldehyde (1.46 g, 0.009 mol), ammonium acetate (3.3 g, 0.0437 mmol) and acetic acid (5.0 mL) to afford 1.0 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.26 (s, 6H), 3.37 (s, 3H), 7.05 (t, J = 7.8 Hz, 2H), 7.11-7.19 (m, 3H), 12.73 (s, 1H); MS $[M+H]^+$:421.09.

Step-5:- Preparation of 8-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxylic acid :-

The title compound was prepared according to the procedure described in Step-6 of Intermedaite-62 by using methyl 8-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxylate (1.0 g, 2.37 mmol), sodium hydroxide (2.0 g, 50.0 mmol), methanol (3.0 mL) and water (25.0 ml) to afford 0.600 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.16 (s, 6H), 7.22-7.61 (m, 5H), 13.17 (br s, 1H); MS $[M+H]^+$:407.09.

Example-1

8-Bromo-2-(2,6-dibromophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 6-bromo-2,2-dimethyl-2*H*-chromene-3,4-dione (Intermediate-1) (0.050 g, 0.185 mmol), acetic acid (2 mL), ammonium acetate (0.071 g, 0.929 mmol) and 2,6-dibromobenzaldehyde (0.054 g, 0.204 mmol) to afford 0.051 g of desired product. ^{1}HNMR (DMSO): δ 1.59-1.62 (d, 9H, two singlets merged), 6.84-6.87 (m, 1.5 H), 7.22-7.24 (m, 1.5H), 7.38-7.43 (t, 2H, two triplets merged), 7.53 (s, 1H), 7.81-7.84 (d, 3H, J = 8.7 Hz), 12.79 (br s, ½ H, d-exchangable), 12.90 (br s, 1H, d-exchangable); MS $[M+H]^+$:515.08.

The following compounds were prepared following the procedure as described for Intermediate-5.

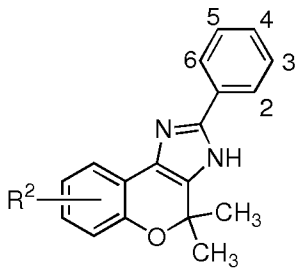
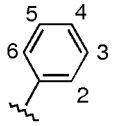
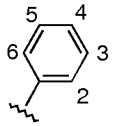
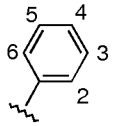


Table-1:

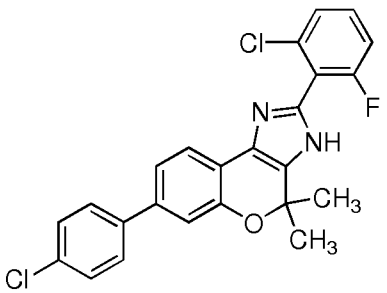
Ex. No.	R^2		Starting material	Analytical details
2	8-Br	2-Cl, 6-F	Intermediate-1 (0.050 g, 0.185 mmol) and 2-chloro-6-fluoro benzaldehyde (0.038 g, 0.241 mmol)	^{1}HNMR (DMSO): δ 1.59-1.63 (d, 9H, two singlets merged), 6.85-6.88 (m, 3H, two doublets merged), 7.23-7.25 (m, 1H), 7.40-7.45 (m, 2H, two triplets merged), 7.50-7.61 (m, 3H, two doublets merged), 10.24-12.89 (br s, ½ H, d-exchangable), 13.07 (br s, 1H, d-exchangable); MS $[M+H]^+$: 409.30.
3	7-Cl	2-Br, 6-Br	Intermediate-2 (0.050 g, 0.220 mmol) and 2,6-dibromobenzaldehyde (0.075 g,	Yield: 0.050 g ^{1}HNMR (DMSO): δ 1.59-1.63 (d, 9H), 6.97-7.04 (m, 3H), 7.32-7.46 (m,

Ex. No.	R^2		Starting material	Analytical details
			0.286 mmol)	3H), 7.83 (d, 3H, *J* = 8.1 Hz), 12.74 (br s, ½ H, d-exchangable), 13.00 (br s, 1H, d-exchangable); MS $[M+H]^+$: 469.21.
4	7-Cl	2-Cl, 6-F	Intermediate-2 (0.200 g, 0.882 mmol) and 2-chloro-6-fluoro benzaldehyde (0.181 g, 1.14 mmol)	Yield: 0.100 g ^{1}HNMR (DMSO): δ 1.60-1.64 (d, 9H,), 6.95-7.05 (m, 3H), 7.38-7.48 (m, 3H), 7.50-7.60 (m, 3H), 12.84 (br s, ½ H, d-exchangable), 13.01 (br s, 1H, d-exchangable); MS $[M+H]^+$: 365.25
5	7-Br	2-Br, 6-Br	Intermediate-3 (0.200 g, 0.743 mmol) and 2,6-dibromobenzaldehyde (0.255 g, 0.966 mmol)	Yield: 0.100 g ^{1}HNMR (DMSO): δ 1.59-1.62 (d, 9H), 7.07-7.14 (m, 3H), 7.20-7.29 (d, *J* = 9.0 Hz, 1 H), 7.40-7.42 (t, 2H, two triplets merged), 7.81-7.83 (d, 3H), 12.84 (br s, ½ H, d-exchangable), 13.01 (br s, 1H, d-exchangable); MS $[M+H]^+$:515.0
6	7-Br	2-Cl, 6-F	Intermediate-3 (0.200 g, 0.743 mmol) and 2-chloro-6-fluoro benzaldehyde (0.353 g, 2.236 mmol)	Yield: (0.102 g) ^{1}HNMR (DMSO): δ 1.59-1.63 (d, 9H), 7.09-7.16 (m, 3H), 7.32-7.35 (d, *J* = 7.8 Hz, 1H), 7.39-7.45 (m, 2H, two triplets merged), 7.50-7.60 (m, 3H), 12.86 (br s, ½ H, d-exchangable), 13.11 (br s, 1H, d-exchangable); MS $[M+H]^+$: 409.19
7	7-Br	4-F, 6-CF_3	Intermediate-3 (0.200 g, 0.743	Yield: 0.030 g

Ex. No.	R^2		Starting material	Analytical details
			mmol) and 4-fluoro-2-(trifluoromethyl) benzaldehyde (0.171 g, 0.892 mmol)	^{1}HNMR (DMSO): δ 1.57-1.63 (d, 9H, two singlets merged), 7.09-7.18 (m, 3H), 7.35-7.38 (d, 1.5 H, *J* = 7.8 Hz), 7.71 (m, 1.5 H), 7.81-7.83 (d, 3H, *J* = 6.3 Hz), 12.70 (br s, ½ H, d-exchangable), 12.99 (br s, 1H, d-exchangable); MS [M-H]- : 439.19
8	7-Br	2-Cl, 3-CF_3	Intermediate-3 (0.100 g, 0.371 mmol) and 2-chloro-3-(trifluoromethyl) benzaldehyde (0.093 g, 0.446 mmol)	Yield: 0.086 g ^{1}HNMR (DMSO): δ 1.61 (br s, 9H), 7.11-7.17 (m, 3H), 7.44 (m, 1.5 H), 7.66-7.70 (t, 1.5 H, *J* = 7.5 Hz), 7.97-8.03 (m, 3H), 12.85 (br s, ½ H, d-exchangable), 12.99 (br s, 1H, d-exchangable); MS [M-H]- : 457.26

Example-9

2-(2-Chloro-6-fluorophenyl)-7-(4-chlorophenyl)-4,4-dimethyl-1,4-dihydrochromeno [3,4-*d*]imidazole

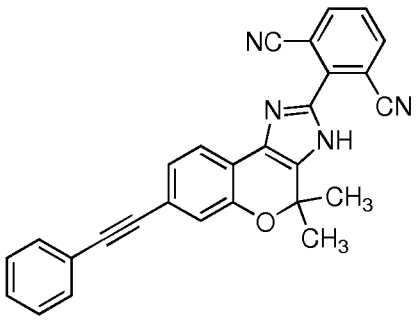


The title compound was prepared by following the same procedure as described for step-1 of Intermediate-44 by using 7-bromo-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole (0.400 g, 1.486 mmol), DME (15 mL), tetrakis triphenyl phosphine Pd(0) (catalytic amount), 4-chloro phenyl boronic acid (0.231 g,

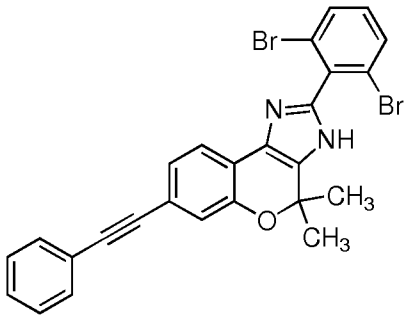
1.477 mmol) and sodium carbonate (0.209 g, 0.1.970 mmol) to afford desired product. ^{1}HNMR (DMSO): δ 1.45-1.49 (d, 4.5H, two singlets merged), 1.62-1..66 (d, 4.5H, two singlets merged), 7.13-7.74 (m, 15H), 12.85 (br s, 1H, d-exchangable), 13.09 (br s, ½ H, d-exchangable); MS $[M-H]^-$: 438.27.

Example-10

2-[4,4-Dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl]isophthalonitrile



Step 1 :- 2-(2,6-Dibromophenyl)-4,4-dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno[3,4-*d*]imidazole:



The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-(phenylethynyl)-2*H*-chromene-3,4-dione (1.0 g, 3.460 mmol), 2,6-dibromo benzaldehyde (1.180 g, 4.49 mmol), ammonium acetate (1.30 g, 17.0 mmol) and acetic acid (10 mL) to afford 0.600 g of desired product. ^{1}HNMR (DMSO): δ 1.62 (s, 6H), 7.00-7.02 (m, 1H), 7.12-7.15 (m, 1H), 7.33-7.48 (m, 5H), 7.51-7.53 (m, 2H), 7.80-7.82 (d, *J* = 8.4 Hz, 2H), 13.02 (s, 1H d-exchangable); MS $[M+H]^+$:535.16

Step 2 :- 2-[4,4-Dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl]isophthalonitrile:

To the solution of 2-(2,6-dibromophenyl)-4,4-dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno[3,4-*d*]imidazole (0.250 g, 0.469 mmol) in N-methyl-2-pyrrolidinone (5 mL) was added copper cyanide (0.115 g, 1.279 mmol) and the reaction mixture was stirred at 100-110°C for 12-14 hours. The reaction mixture was quenched in water and extracted with ethyl acetate. The organic layer was concentrated to afford 0.020 g of desired product. ^{1}HNMR (DMSO): δ 2.80 (s, 6H), 6.67 (d, *J* = 7.8 Hz, 1H), 7.02 (s, 2H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.45-7.47 (m, 3H), 7.59-7.61 (m, 2H), 7.765-7.83 (m, 2H), 11.96 (br s, 1H d-exchangable); MS $[M+H]^+$:427.32.

The compounds of Table-2 were prepared following the process described for preparation of compound designated as Intermediate-5 (process 'A') or the process for the preparation of step-2 intermediate of Example-10 (process 'B')

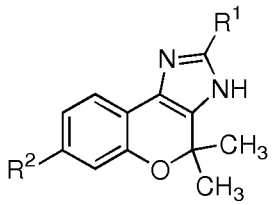
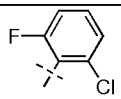
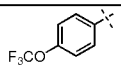
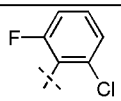
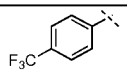
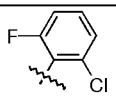
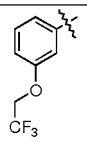
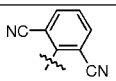
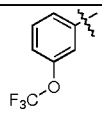
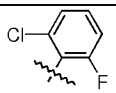
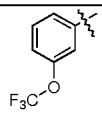
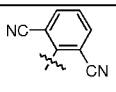
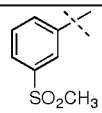
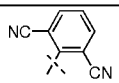
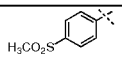
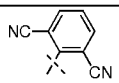
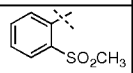
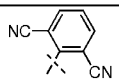
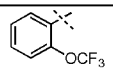
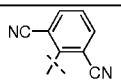
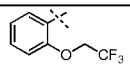
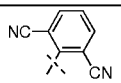


Table-2:

Ex. No.	R^2	R^1	Process	Starting Materials	Analytical details
11			A	Intermediate-44 (0.500 g, 1.49 mmol) and 2-chloro-6-fluoro benzaldehyde (0.356 g, 2.24 mmol), ammonium acetate (0.576 g, 7.48 mmol), acetic acid (10 mL)	Yield: 0.050 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.29-7.46 (m, 3H), 7.52-7.56 (m, 5H), 7.58-7.69 (m, 3H), 7.99 (m, 2H), 13.11 (s, 1H); MS $[M+H]^+$: 473.41
12			A	Intermediate-56 (0.300 g, 0.857 mmol), 2-chloro-6-fluoro benzaldehyde (0.203 g, 1.28 mmol), Ammonium acetate (0.330 g, 4.28 mmol) and acetic acid (10 mL)	Yield: 0.100 g ^{1}HNMR (DMSO): δ 1.62 (s, 6H), 7.25 (s, 1H), 7.32 (d, *J* = 6.3 Hz, 1H), 7.40-7.61 (m, 6H), 7.82 (d, *J* = 8.7 Hz, 2H), 13.10 (s, 1H)

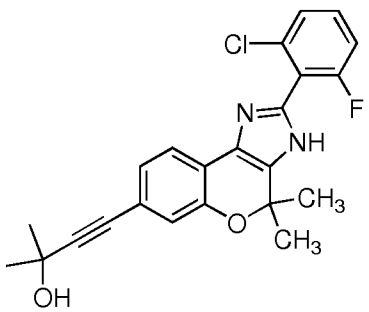
Ex. No.	R^2	R^1	Process	Starting Materials	Analytical details
13			A	Intermediate-57 (0.300 g, 0.898 mmol), 2-chloro-6-fluoro benzaldehyde (0.212 g, 1.34 mmol), Ammonium acetate (0.345 g, 4.46 mmol) and acetic acid (10 mL)	Yield: 0.050 g ^{1}HNMR (DMSO): δ 1.63 (s, 6H), 7.28-7.51 (m, 3H), 7.54-7.62 (m, 3H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.92 (d, *J* = 7.8 Hz, 2H), 13.13 (s, 1H)
14			B	Intermediate-58 (0.150 g, 0.246 mmol), copper cyanide (0.066 g, 0.740 mmol), DMF (3 mL)	Yield: 0.040 g ^{1}HNMR (DMSO-d_6): δ 1.79 (s, 6H), 4.42 (q, *J* = 7.8 Hz, 2H), 7.93 (d, *J* = 7.2 Hz, 1H), 7.18-7.39 (m, 6H), 7.55 (t, 1H), 8.99 (d, *J* = 8.1 Hz, 2H), 10.28-10.26 (br s, 1H); MS $[M+H]^+$: 501.30
15			A	Intermediate-59 (0.200 g, 0.570 mmol), 2-chloro-6-fluoro benzaldehyde (0.135 g, 0.850 mmol), Ammonium acetate (0.220 g, 2.85 mmol) and acetic acid (5 mL)	Yield: 0.120 g ^{1}HNMR (DMSO): δ 1.63 (s, 6H), 7.25-7.50 (m, 4H), 7.51-7.59 (m, 4H), 7.66 (s, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 13.13 (s, 1H); MS $[M+H]^+$: 489.36
16			B	Intermediate-60 (0.300 g, 0.505 mmol), copper cyanide (0.090 g, 1.01 mmol), DMF (4 mL)	Yield: 0.073 g ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 7.32-7.58 (m, 3H), 7.61 (m, 2H), 7.69 (m, 1H), 7.76 (m, 1H), 7.85 (m, 1H), 8.35 (d, *J* = 7.2 Hz, 2H), 13.66 (br s, 1H); MS $[M+H]^+$: 487.30

Ex. No.	R^2	R^1	Process	Starting Materials	Analytical details
17			B	Intermediate-73 (0.150 g, 0.255 mmol), copper cyanide (0.068 g, 0.765 mmol), DMF (4 mL)	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 3.15 (s, 3H), 7.40 (s, 1H), 7.46 (d, J = 7.5 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.86 (t, J = 6.9 Hz, 2H), 8.06 (d, J = 7.8 Hz, 1H), 8.17 (s, 1H), 8.34 (d, J = 8.1 Hz, 2H), 13.65 (br s, 1H); MS $[M-H]^-$: 479.46
18			B	Intermediate-74 (0.250 g, 0.425 mmol), copper cyanide (0.114 g, 1.27 mmol), DMF (4 mL)	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.67 (s, 6H), 3.27 (s, 3H), 7.38 (s, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.86 (t, J = 8.1 Hz, 1H), 7.99 (s, 4H), 7.37 (d, J = 8.4 Hz, 2H), 13.68 (s, 1H); MS $[M-H]^-$: 479.29
19			B	Intermediate-75 (0.300 g, 0.510 mmol), copper cyanide (0.137 g, 1.53 mmol), DMF (5 mL)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 2.78 (s, 3H), 6.96 (s, 2H), 7.44 (d, J = 7.2 Hz, 2H), 7.52 (d, J = 7.8 Hz, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.74 (t, J = 7.2 Hz, 1H), 8.48 (t, J = 7.8 Hz, 1H), 8.08 (d, J = 7.5 Hz, 1H), 8.34 (d, J = 7.8 Hz, 1H), 13.63 (s, 1H); MS $[M-H]^-$: 479.28

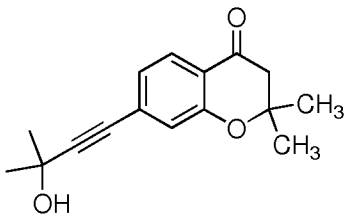
Ex. No.	R^2	R^1	Process	Starting Materials	Analytical details
20			B	Intermediate-76 (0.200 g, 0.360 mmol), copper cyanide (0.090 g, 1.01 mmol), DMF (4 mL)	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 7.03 (s, 1H), 7.12 (d, J = 7.8 Hz, 1H), 7.49-7.57 (m, 5H), 7.86 (t, J = 7.8 Hz, 1H), 8.35 (d, J = 8.4 Hz, 2H), 13.64 (s, 1H); MS $[M-H]^-$: 485.42
21			B	Intermediate-77 (0.120 g, 0.197 mmol), copper cyanide (0.052 g, 059 mmol), DMF (4 mL)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 4.76 (q, J = 9.3 Hz, 1H), 7.06-7.038 (m, 5H), 7.53 (d, J = 7.8 Hz, 2H), 7.84 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 7.8 Hz, 2H), 13.60 (br s, 1H); MS $[M-H]^-$: 499.33

Example-22

4-[2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]-2-methylbut-3-yn-2-ol

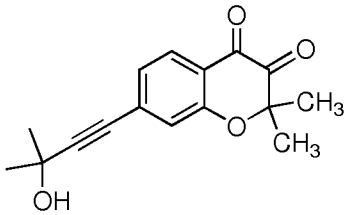


Step 1:- Preparation of 7-(3-hydroxy-3-methyl-but-1-ynyl)-2,2-dimethyl-chroman-4-one:-



The title compound was prepared by following the same procedure as described for step-1 of Intermediate-6 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4H-chromen-4-one (Step-3 of Intermediate-4) (1.00 g, 0.003 mol), N,N-dimethyl formamide (10 mL), copper iodide (catalytic amount), dichloro-bis(triphenylphosphine)palladium (II) (catalytic amount), triethyl amine (2.0 mL) and 2-methylbut-3-yn-2-ol (0.307 g, 0.0036 mol) to afford 0.500 g of desired product. ^{1}HNMR ($CdCl_3$): δ 1.26 (s, 6H), 1.38 (s, 6H), 2.81 (s, 2H), 5.56 (s, 1H), 6.94 (s, 1H), 6.99-7.01 (d, J = 7.8 Hz, 1H), 7.68-7.71 (d, J = 8.1 Hz, 1H).

Step 2:- Preparation of 7-(3-hydroxy-3-methylbut-1-yn-1-yl)-2,2-dimethyl-2*H*-chromene-3,4-dione:-



The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 7-(3-hydroxy-3-methyl-but-1-ynyl)-2,2-dimethyl-chroman-4-one (0.500 g, 1.937 mmol), isoamyl nitrite (0.454 g, 3.875 mmol), conc. HCl (2 mL) and ethyl alcohol (5 mL) to afford 0.200 g of desired product. ^{1}HNMR (DMSO): δ 1.19 (s, 6H), 1.45 (s, 6H), 5.56 (br s, 1H), 6.64 (s, 1H), 7.00-7.03 (d, 1H, J = 7.8 Hz), 7.70-7.72 (d, 1H, J = 7.8 Hz); MS $[M+H]^+$:272.93.

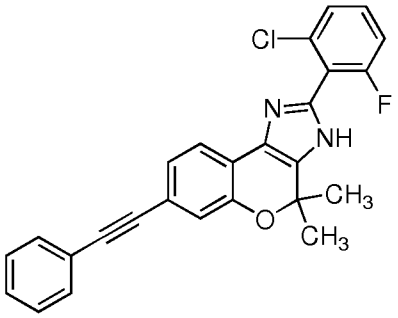
Step 3:- Preparation of 4-[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]-2-methylbut-3-yn-2-ol:-

The title compound was prepared by following the same procedure as described for Intermediate-5 by using 7-(3-hydroxy-3-methylbut-1-yn-1-yl)-2,2-dimethyl-2*H*-chromene-3,4-dione (0.125 g, 0.459 mmol), 2-chloro-6-fluoro benzaldehyde (0.087 g, 0.551mmol), ammonium acetate (0177 g, 2.29 mmol) and acetic acid (3 mL) to afford 0.100 g of desired product. ^{1}HNMR (DMSO): δ 1.45 (d, 9H, two singlets merged), 1.58

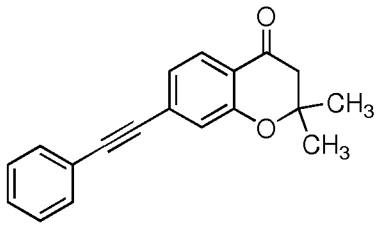
(d, 9H, two singlets merged), 5.46 (s, 1.5 H, d-exchangable), 6.82-7.63 (m, 9H), 12.85 (br s, ½ H , d-exchangable), 13.09 (br s, 1H , d-exchangable); MS $[M+H]^+$:411.22.

Example-23

2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno [3,4-*d*]imidazole

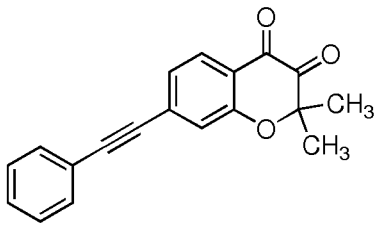


Step 1:- Preparation of 2,2-dimethyl-7-phenylethynyl-chroman-4-one:-



The title compound was prepared by following the same procedure as described for step-1 of Intermediate-6 by using 7-iodo-2,2-dimethyl-2,3-dihydro-4*H*-chromen-4-one (step 3 of Intermediate-4, 0.500 g, 1.661 mmol), copper iodide (catalytic amount), dichloro-bis(triphenylphosphine)palladium (II) (catalytic amount), triethyl amine (1 mL), phenyl acetylene (0.187 g, 1.82 mmol), N,N-dimethyl formamide (5 mL) to afford 0.300 g of desired product. ^{1}HNMR ($CdCl_3$): δ 1.46 (s, 6H), 2.73 (s, 2H), 7.09-7.13 (d, 2H, J = 9.9 Hz), 7.37 (br s, 3H), 7.53 (br s, 2H), 7.81-7.84 (d, 1H, J = 8.1 Hz).

Step 2:- Preparation of 2,2-dimethyl-7-(phenylethynyl)-2*H*-chromene-3,4-dione:-



The title compound was prepared according the same procedure as described in step-2 of Intermediate-1 by using 2,2-dimethyl-7-(phenylethynyl)-2,3-dihydro-4*H*-chromen-4-one

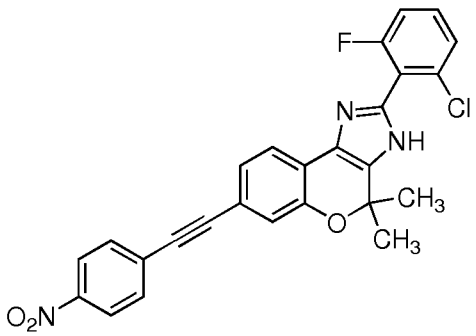
(0.300 g, 1.090 mmol), isoamyl nitrite (0.255 g, 2.181 mmol), conc. HCl (1 mL) and ethyl alcohol (5 mL) to afford 0.100 g of desired product. ^{1}HNMR ($CdCl_3$): δ 1.47 (s, 3H), 1.65 (s, 3H), 7.12-726 (m, 2H), 7.54-7.55 (br s, 3H), 7.84-7.87 (d, 2H, *J* = 8.1 Hz), 7.92-7.94 (d, 1H, *J* = 7.8 Hz); MS $[M+H]^+$:291.01.

Step 3:- Preparation of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-(phenylethynyl)-1,4-dihydro chromeno[3,4-*d*]imidazole:-

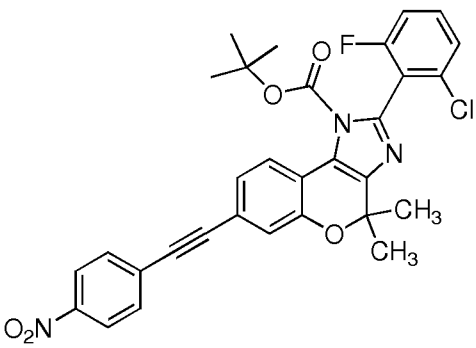
The title compound was prepared by following the same procedure as described for Intermediate-5 by using 2,2-dimethyl-7-(phenylethynyl)-2*H*-chromene-3,4-dione (0.125 g, 0.459 mmol), 2-chloro-6-fluoro benzaldehyde (0.100 g, 0.346 mmol), ammonium acetate (0.133 g, 1.73 mmol) and acetic acid (4 mL) to afford 0.080 g of desired product.

Example24

2-(2-Chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-nitro-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole



Step 1:-Preparation of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-nitro-phenylethynyl)-4H-chromeno[3,4-d]imidazole-1-carboxylic acid tert-butyl ester:-



The title compound was prepared by following the same procedure as described for step-1 of Intermediate-6 by using 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-4H-chromeno[3,4-d]imidazole-1-carboxylic acid tert-butyl ester (Intermediate-6, 0.030 g,

0.066 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), triethyl amine (0.3 mL), 1-iodo-4-nitro-benzene (0.017 g, 0.0.69 mmol), DMSO (3 mL) to afford desired product (0.030 g). ^{1}HNMR (DMSO-d_6): δ 1.23 (s, 9H), 1.62 (s, 6H), 7.19-7.24 (m, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.46 (t, *J* = 8.7 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 2H), 8.29 (d, *J* = 8.4 Hz, 2H).

Step 2:- Preparation of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-nitro-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole:-

To a solution of 2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-nitro-phenylethynyl)-4H-chromeno[3,4-d]imidazole-1-carboxylic acid tert-butyl ester (0.030 g, 0.052 mmol) in DCM was added trifluoro acetic acid (0.5 mL) at 0-5°C. The reaction mass was stirred at room temperature for 1-2 hours. Solvent was removed under reduced pressure, neutralized with sodium carbonate and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford desired product (0.012 g). ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.13 (s, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.41-7.65 (m, 5H), 7.81 (d, *J* = 8.1 Hz, 2H), 8.28 (d, *J* = 8.7 Hz, 2H); MS $[M+H]^+$:474.25.

The compounds of Table-3 were prepared following the process described for the preparation of step-1 of intermediate 6 (process "C")

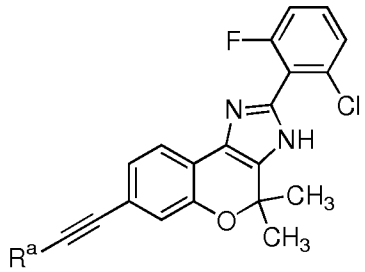
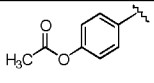
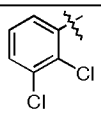
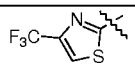
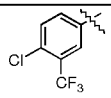
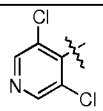
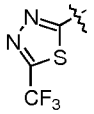


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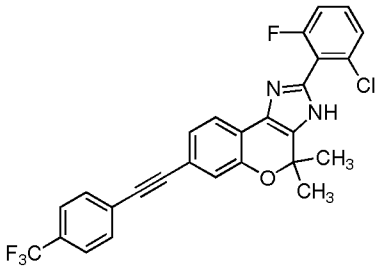
Ex. No.	R^a	Starting material	Analytical details
25		Intermediate-5 (0.100 g, 0.219 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 2.29 (s, 3H), 7.03-7.05 (m,

Ex. No.	R[a]	Starting material	Analytical details
		amount), triethyl amine (1 mL), acetic acid, 4-ethynyl-phenyl ester (0.070 g, 0.439 mmol), N,N-dimethyl formamide (3 mL)	1H), 7.14-7.22 (m, 3H), 7.41-7.46 (m, 2H), 7.51-7.64 (m, 4H), 13.17 (s, 1H); MS $[M+H]^+$: 487.22
26		Step-2 of Intermediate-6 (0.060 g,0.170 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1,2-dichloro-3-iodobenzene (Intermediate-12, 0.050 g, 0.185 mmol), TEA (1m L), DMSO (3 mL)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.06-7.08 (m, 1H), 7.19-7.24 (m, 1H), 7.42-7.47 (m, 2H), 7.51-7.71 (m, 5H), 13.20 (s, 1H); MS $[M+H]^+$: 497.36
27		Step-2 of Intermediate-6 (0.050 g,0.142 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-Iodo-4-trifluoromethyl-thiazole (Intermediate-14, 0.039 g, 0.140 mmol), TEA (1 mL), DMSO (3 mL)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 1H), 6.86 (s, 1H), 7.16 (s, 1H), 7.31 (s, 1H), 7.41-7.53 (m, 3H), 8.64 (s, 1H); MS $[M-H]^-$: 502.46
28		Step-2 of Intermediate-6, 0.050 g,0.142 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-chloro-4-iodo-2-trifluoromethyl-benzene (0.043 g, 0.140 mmol), TEA (1 mL), DMSO (3 mL)	Yield: 0.018 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.10-7.12 (m, 1H), 7.21-7.23 (s, 1H), 7.43-7.62 (m, 4H), 7.78-7.87 (m, 2H), 8.02 (s, 1H), 13.19 (s, 1H); MS $[M+H]^+$: 530.44
29		Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 3,5-dichloro-4-iodo-pyridine (0.116 g, 0.426 mmol), TEA (2 mL),	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 6.97-7.24 (m, 3H), 7.43-7.61 (m, 3H), 9.05 (s, 2H), 13.20 (br s, 1H); MS [M-]:

Ex. No.	R^a	Starting material	Analytical details
		DMSO (3 mL)	498.87
30		Step-2 of Intermediate-6 (0.050 g,0.142 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-Iodo-5-trifluoromethyl-[1,3,4]thiadiazole (Intermediate-11, 0.038 g, 0.136 mmol) and TEA (1 mL)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.09 (s, 1H), 7.22-7.25 (m, 1H), 7.41-7.61 (m, 4H), 13.20 (s, 1H)

Example-31

2-(2-Chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2-chloro-6-fluoro-phenyl)-7-ethynyl-4,4-dimethyl-4H-chromeno[3,4-d]imidazole-1-carboxylic acid tert-butyl ester (Intermediate-6, 0.100 g, 0.221mmol), dichloro bis (triphenyl phosphine)palladium (II) (4.64 g, 0.006 mmol), tetra butyl ammonium fluoride (0.173 g, 0.663 mmol), 1-iodo-4-(trifluoromethyl) benzene (0.060 g, 0.221 mmol) to afford desired product (0.015 g). ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.10 (d, J = 6.3 Hz, 1H), 7.21-7.24 (m, 1H), 7.43-7.46 (m, 2H), 7.52-7.62 (m, 2H), 7.74-7.79 (m, 4H), 13.18 (s, 1H); MS $[M+H]^+$: 497.16.

The compounds of Table-4 were prepared following the process described for preparation step-5 of Intermediate-7

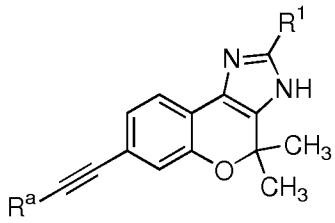
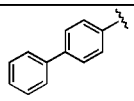
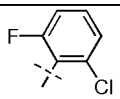
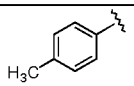
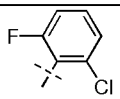
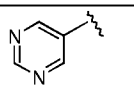
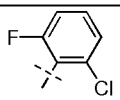
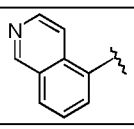
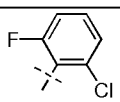
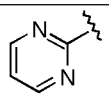
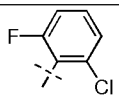
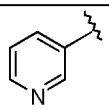
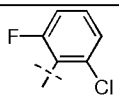
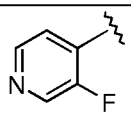
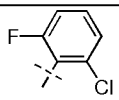
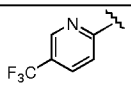
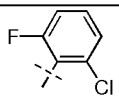
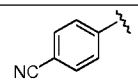
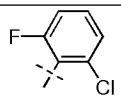
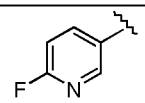
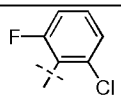
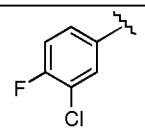
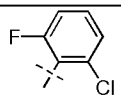
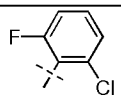
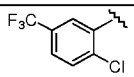
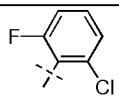
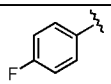
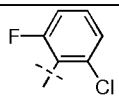
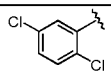
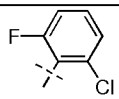
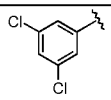
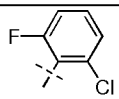


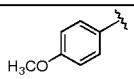
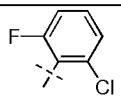
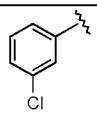
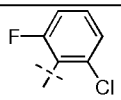
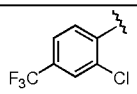
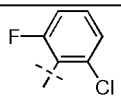
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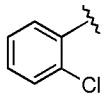
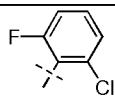
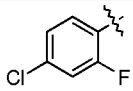
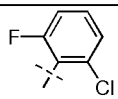
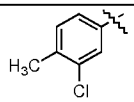
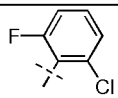
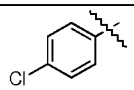
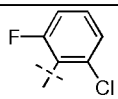
Ex. No.	R^a	R^1	Starting material	Analytical details
32			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 4-iodobiphenyl (0.080 g, 0.284 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.06 (d, *J* = 6.3 Hz, 1H), 7.19 -7.21 (m, 1H), 7.40-7.76 (m, 13H), 13.16 (s, 1H); MS $[M+H]^+$: 505.26
33			Intermediate-6 (0.200 g, 0.44 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), tetra butyl ammonium fluoride (0.346 g, 1.32 mmol), 4-iodotolunene (0.096 g, 0.44 mmol)	Yield: 0.013 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 2.34 (s, 3H), 6.69 (s, 1H), 6.91 (s, 1H), 7.23-7.25 (m, 2H), 7.42-7.51 (m, 3H), 7.53-7.61 (m, 3H), 12.91(br s, 1H); MS $[M+H]^+$: 443.25
34			Step-2 of Intermediate-6, 0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 5-bromopyrimidine (0.045 g, 0.283 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.76 (s, 6H), 7.10 (s, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.40-7.61 (m, 4H), 9.01 (s, 2H), 9.19 (s, 1H), 13.12 (br s, 1H); MS $[M+H]^+$: 431.26
35			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s,

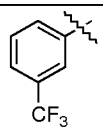
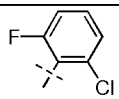
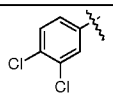
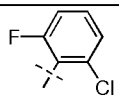
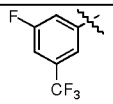
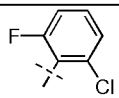
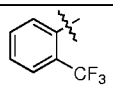
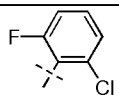
Ex. No.	R^a	R^1	Starting material	Analytical details
			fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 5-iodo isoquinoline (0.072 g, 0.282 mmol)	6H), 7.24-7.26 (m, 1H), 7.33-7.35 (m, 1H), 7.41-7.62 (m, 4H), 7.74 (d, *J* = 7.8 Hz, 1H), 8.05 (d, *J* = 6.9 Hz, 1H), 8.22 (m, 2H), 8.66 (br s, 1H), 9.41 (br s, 1H), 13.19 (br s, 1H); MS $[M+H]^+$: 480.44
36			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 2-bromopyrimidine (0.045 g, 0.283 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.09-7.11 (m, 1H), 7.25-7.30 (m, 2H), 7.41-7.65 (m, 4H), 8.85 (s, 2H), 13.22 (br s, 1H); MS $[M+H]^+$: 431.26
37			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 3-iodo-pyridine (0.045 g, 0.283 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.07-7.09 (br s, 1H), 7.18-7.22 (m, 1H), 7.40-7.64 (m, 5H), 7.97 (d, *J* = 7.8 Hz, 1H), 8.58 (s, 1H), 8.75 (s, 1H), 13.18 (br s, 1H); MS $[M+H]^+$: 430.43
38			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 3-fluoro-4-iodopyridine (0.063 g, 0.283 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.09-7.12 (br s, 1H), 7.24-7.27 (m, 1H), 7.40-7.67 (m, 5H), 8.49 (d, *J* = 4.5 Hz, 1H), 8.71 (s, 1H), 13.21 (s, 1H); MS $[M+H]^+$: 448.43
39			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetrabutyl ammonium	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s,

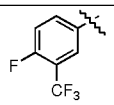
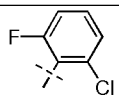
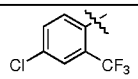
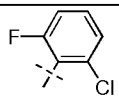
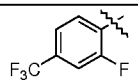
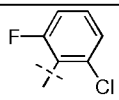
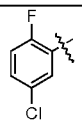
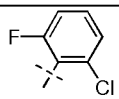
Ex. No.	R^a	R^1	Starting material	Analytical details
			fluoride (0.334 g, 1.200 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.009 mmol), 2-iodo-5-trifluoromethyl-pyridine (0.077 g, 0.426 mmol)	6H), 7.13-7.15 (m, 1H), 7.25-7.28 (m, 1H), 7.30-7.65 (m, 4H), 7.87 (d, *J* = 8.1 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 9.00 (s, 1H), 13.21 (s, 1H); MS $[M+H]^+$: 498.34
40			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetrabutyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 4-iodo benzonitrile (0.098 g, 0.426 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.10 (s, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.43-7.61 (m, 4H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 13.21 (s, 1H); MS $[M+H]^+$: 454.38
41			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 2-fluoro-5-iodo-pyridine (0.095 g, 0.426 mmol)	Yield: 0.018 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.06-08 (m, 1H), 7.19-7.22 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.40-7.61 (m, 4H), 8.17 (t, *J* = 6.3 Hz, 1H), 8.46 (s, 1H), 13.16 (s, 1H); MS $[M+H]^+$: 448.39
42			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.223 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.006 g, 0.008 mmol), 2-chloro-1-fluoro-4-iodo-benzene (0.163 g, 0.639 mmol)	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.05-7.07 (m, 1H), 7.17-7.19 (m, 1H), 7.42-7.59 (m, 5H), 7.81-7.83 (m, 1H), 7.95 (m, 1H), 13.15 (s, 1H); MS $[M+H]^+$: 481.26
43			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium	Yield: 0.022 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s,

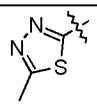
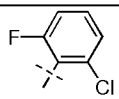
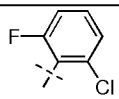
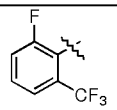
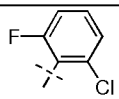
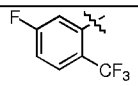
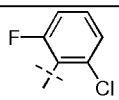
Ex. No.	R^a	R^1	Starting material	Analytical details
			fluoride (0.334 g, 1.278 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.008 g, 0.008 mmol), 1-chloro-2-fluoro-3-iodo-benzene (0.164 g, 0.639 mmol)	6H), 7.06 (s, 1H), 7.20 (d, J = 6.9 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 7.40-7.68 (m, 5H), 13.15 (s, 1H); MS $[M+H]^+$: 481.41
44			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.278 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.008 g, 0.008 mmol), 1-chloro-2-iodo-4-(trifluoromethyl) benzene (0.164 g, 0.639 mmol)	Yield: 0.022 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.10-7.12 (m, 1H), 7.21-7.25 (m, 1H), 7.40-7.61 (m, 4H), 7.77-7.87 (m, 2H), 8.07 (s, 1H), 13.18 (s, 1H); MS $[M+H]^+$: 531.30
45			Step-2 of Intermediate-6 (0.200 g, 0.568 mmol), tetra butyl ammonium fluoride (0.445 g, 1.70 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.012 g, 0.017 mmol), 1-fluoro-4-iodo-benzene (0.189 g, 0.852 mmol)	Yield: 0.030 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.04 (s, 1H), 7.16 (d, J = 7.2 Hz, 1H), 7.28 (t, J = 9.0 Hz, 2H), 7.42-7.63 (m, 6H), 13.13 (s, 1H); MS $[M+H]^+$ 447.41
46			Step-2 of Intermediate-6 (0.150 g, 0.568 mmol), tetra butyl ammonium fluoride (0.334 g, 1.28 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1,4-dichloro-2-iodo-benzene (0.174 g, 0.639 mmol)	Yield: 0.025 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.06-7.08 (m, 1H), 7.20-7.22 (m, 1H), 7.40-7.65 (m, 6H), 7.78 (s, 1H), 13.20 (br s, 1H); MS $[M+H]^+$ 498.81
47			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium	Yield: 0.022 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s,

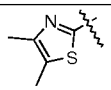
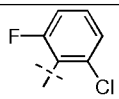
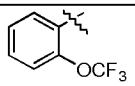
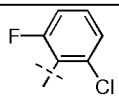
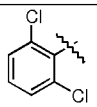
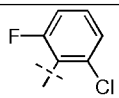
Ex. No.	R^a	R^1	Starting material	Analytical details
			fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 3,5-dichoro-iodo-benzene (0.174 g, 0.639 mmol)	6H), 7.07-7.09 (m, 1H), 7.21 (m, 1H), 7.40-7.64 (m, 6H), 7.69 (s,1H), 13.18 (s, 1H); MS $[M+H]^+$ 497.23
48			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 4-methoxy iodo benzene (0.149 g, 0.639 mmol)	Yield: 0.022 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 3.79 (s, 3H), 6.97-7.00 (m, 3H), 7.10-7.14 (m, 1H), 7.39-7.60 (m, 6H), 13.12 (s, 1H); MS $[M-H]^-$: 457.31
49			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 3-chloro iodo benzene (0.152 g, 0.639 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.05-7.07 (m, 1H), 7.18-7.20 (m, 1H), 7.42-7.62 (m, 7H), 13.17 (s, 1H)
50			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1-chloro-2-iodo-4-trifluoromethyl-benzene (0.195 g, 0.639 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.09-7.11 (m, 1H), 7.21-7.26 (m, 1H), 7.40-7.61 (m, 4H), 7.78 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 8.04 (s, 1H), 13.21 (s, 1H); MS $[M+H]^+$: 533.23

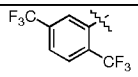
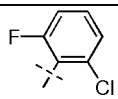
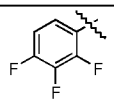
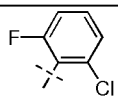
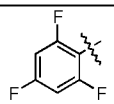
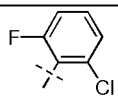
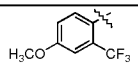
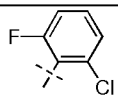
Ex. No.	R^a	R^1	Starting material	Analytical details
51			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1-chloro-2-iodobenzene (0.152 g, 0.639 mmol)	Yield: 0.021 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.04-7.05 (m, 1H), 7.16-7.21 (m, 1H), 7.40-7.46 (m, 3H), 7.51-7.68 (m, 5H), 13.17 (s, 1H); MS $[M+H]^+$: 465.30
52			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 4-chloro-2-fluoro-1-iodo-benzene (0.163 g, 0.639 mmol)	Yield: 0.018 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.03 (m, 1H), 7.05-7.20 (m, 1H), 7.36-7.53 (m, 3H), 7.65-7.68 (m, 4H), 13.17 (s, 1H); MS $[M+H]^+$: 483.25
53			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 4-bromo-2-chloro-1-methyl benzene (0.131 g, 0.639 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 2.36 (s, 3H), 7.05 (m, 1H), 7.16 (m, 1H), 7.41 (m, 3H), 7.50-7.60 (m, 4H), 13.15 (s, 1H); MS $[M+H]^+$: 479.28
54			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 4-chloro iodo benzene (0.152 g, 0.639 mmol)	Yield: 0.014 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.05 (m, 1H), 7.18 (m, 1H), 7.51-7.58 (m, 8H), 13.18 (s, 1H); MS $[M+H]^+$: 465.31

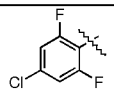
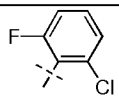
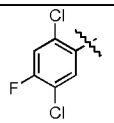
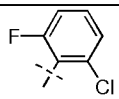
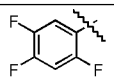
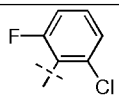
Ex. No.	R^a	R^1	Starting material	Analytical details
55			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 3-(trifluoromethyl) iodo benzene (0.152 g, 0.639 mmol)	Yield: 0.014 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.09-7.11 (m, 1H), 7.43-7.46 (m, 1H), 7.51-7.91 (m, 8H), 13.17 (s, 1H); MS $[M-H]^-$: 499.36
56			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 3,4-dichloro iodo benzene (0.174 g, 0.639 mmol)	Yield: 0.014 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.06-7.08 (m, 1H), 7.18-7.20 (m, 1H), 7.42-7.61 (m, 5H), 7.69 (d, J = 8.4 Hz, 1H), 7.85 (s, 1H), 13.16 (s, 1H)
57			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1-fluoro-3-iodo-5-trifluoromethyl benzene (0.155 g, 0.639 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.10-7.12 (m, 1H), 7.22 (d, J = 6.9 Hz, 1H),7.43-7.62 (m, 4H), 7.80 (m, 3H), 13.18 (s, 1H); MS $[M+H]^+$: 515.30
58			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1-iodo-2-trifluoromethyl-benzene (0.174 g,	Yield: 0.017 g ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 7.02 (m, 1H), 7.16 (m, 1H), 7.46-7.61 (m, 5H), 7.73-7.82 (m, 3H), 13.19 (s, 1H); MS $[M+H]^+$: 497.36

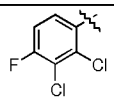
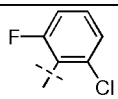
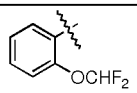
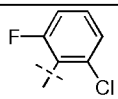
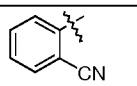
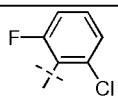
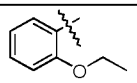
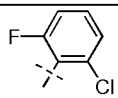
Ex. No.	R^a	R^1	Starting material	Analytical details
			0.639 mmol)	
59			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1-fluoro-4-iodo-2-trifluoromethyl-benzene (0.155 g, 0.639 mmol)	Yield: 0.014 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.08 (m, 1H), 7.18 (d, J = 6.6 Hz, 1H), 7.40-7.77 (m, 6H), 7.94-7.96 (m, 1H), 13.14 (s, 1H); MS $[M+H]^+$: 515.34
60			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 1-bromo-4-chloro-2-(trifluoromethyl)benzene (0.165 g, 0.639 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.02 (m, 1H), 7.17 (m, 1H), 7.45-7.53 (m, 4H), 7.82 (s, 2H), 7.93 (s, 1H), 13.21 (s, 1H); MS $[M+H]^+$: 533.33
61			Step-2 of Intermediate-6, 0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 2-bromo-1-fluoro-4-trifluoromethyl-benzene (0.155 g, 0.639 mmol)	Yield: 0.016 g ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 7.09-7.11 (m, 1H), 7.22-7.25 (m, 1H), 7.41-7.63 (m, 5H), 7.87 (m, 1H), 7.08 (d, J = 4.4 Hz, 1H), 13.20 (s, 1H); MS $[M-H]^-$: 514.40
62			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl	Yield: 0.014 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.05-7.07 (m, 1H), 7.17-7.22 (m, 1H), 7.38-7.46 (m, 3H), 7.52-

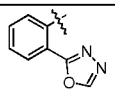
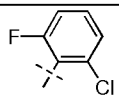
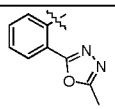
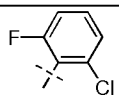
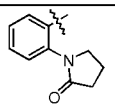
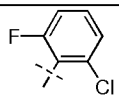
Ex. No.	R^a	R^1	Starting material	Analytical details
			phosphine)palladium (II) (0.009 g, 0.012 mmol), 2-bromo-4-chloro-1-fluoro-benzene (0.156g, 0.639 mmol)	7.62 (m, 3H), 7.75 (d, *J* = 3.9 Hz, 1H), 13.19 (s, 1H); MS $[M+H]^+$: 483.23
63			Step-2 of Intermediate-6 (0.150 g, 0.426 mmol), tetra butyl ammonium fluoride (0.334 g, 1.27 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), 2-iodo-5-methyl-[1,3,4]thiadiazole (0.144 g, 0.639 mmol)	Yield: 0.010 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.33 (s, 3H), 7.07 (s, 1H), 7.20-7.23 (m, 1H), 7.39-7.59 (m, 4H), 13.19 (s, 1H); MS $[M-H]^-$: 449.42
64			Step-2 of Intermediate-6 (0.200 g, 0.568 mmol), tetra butyl ammonium fluoride (0.445 g, 1.70 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.012 g, 0.017 mmol), 2-iodo-5-methyl-thiazole (0.192 g, 0.852 mmol)	Yield: 0.014 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 3.33 (s, 3H), 7.07-7.11 (m, 1H), 7.21-7.26 (m, 1H), 7.40-7.65 (m, 5H), 13.20 (s, 1H); MS $[M+H]^+$: 452.37
65			Step-2 of Intermediate-6 (0.200 g, 0.568 mmol), tetra butyl ammonium fluoride (0.445 g, 1.70 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.012 g, 0.017 mmol), 2-bromo-1-fluoro-3-trifluoromethyl-benzene (0.155 g, 0.639 mmol)	Yield: 0.013 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.06-7.08 (m, 1H), 7.20-7.22 (m, 1H), 7.38-7.58 (m, 5H), 7.84 (s, 1H), 8.05 (d, *J* = 5.1 Hz, 1H), 13.17 (s, 1H)
66			Step-2 of Intermediate-6 (0.200 g, 0.568 mmol), tetra butyl ammonium	Yield: 0.013 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s,

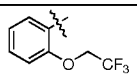
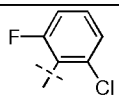
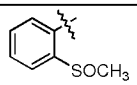
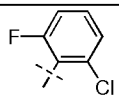
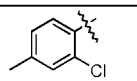
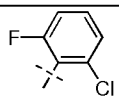
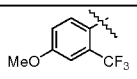
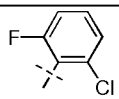
Ex. No.	R^a	R^1	Starting material	Analytical details
			fluoride (0.445 g, 1.70 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.012 g, 0.017 mmol), 2-bromo-4-fluoro-1-trifluoromethyl-benzene (0.155 g, 0.639 mmol).	6H), 7.01-7.15 (m, 1H), 7.17-7.19 (m, 1H), 7.40-7.59 (m, 5H), 7.43-7.62 (s, 1H), 7.88-7.93 (m, 1H), 13.22 (s, 1H); MS $[M+H]^+$: 515.34
67			Step-2 of Intermediate-6 (0.150 g,0.142 mmol), tetra butyl ammonium fluoride (0.234 g, 1.2 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-iodo-4,5-dimethyl-thiazole (step-1 of Intermediate-15, 0.152 g, 0.639 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 3H), 1.65 (s, 3H), 2.30 (s, 3H), 2.39 (s, 3H), 7.06 (m, 1H), 7.21-7.24 (m, 1H), 7.40-7.61 (m, 4H), 13.20 (s, 1H); MS $[M+H]^+$: 464.38
68			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.255 g, 0.810 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-trifluoromethoxy-benzene (0.122 g, 0.426 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.00 (m, 1H), 7.20 (m, 1H), 7.44-7.53 (m, 7H), 7.80 (m, 1H), 13.20 (s, 1H); MS $[M+H]^+$: 513.39
69			Step-2 of Intermediate-6 (0.064 g, 0.183 mmol), tetra butyl ammonium fluoride (0.143 g, 0.549 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1,3-dichloro-2-iodo-benzene (0.050 g, 0.183 mmol)	Yield: 0.010 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.06 (m, 1H), 7.21 (m, 2H), 7.43-7.62 (m, 6H), 13.21 (s, 1H); MS [M+] : 497.27

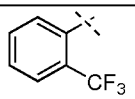
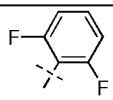
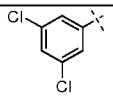
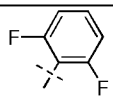
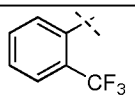
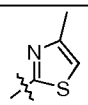
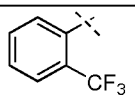
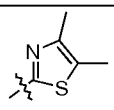
Ex. No.	R^a	R^1	Starting material	Analytical details
70			Step-2 of Intermediate-6 (0.050 g, 0.136 mmol), tetra butyl ammonium fluoride (0.143 g, 0.549 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-iodo-1,4-bis-trifluoromethyl-benzene (Intermediate-18, 0.055 g, 0.163 mmol) to afford	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.09 (s, 1H), 7.21 (d, J = 8.7 Hz, 1H), 7.45 (t, J = 8.7 Hz, 1H), 7.55 (m, 2H), 7.61-7.63 (m, 1H), 8.00 (m, 1H), 8.09 (d, J = 8.7 Hz, 1H), 8.23 (s, 1H); MS $[M+H]^+$: 565.68
71			Step-2 of Intermediate-6 (0.050 g, 0.136 mmol), tetra butyl ammonium fluoride (0.143 g, 0.549 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount) 2,3,4-trifluoro-1-iodo-benzene (Intermediate-20, 0.042 g, 0.162 mmol)	Yield: 0.015 g. ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.06 (s, 1H), 7.18-7.21 (m, 1H), 7.40-7.61 (m, 6H); MS $[M+H]^+$: 483.45
72			Step-2 of Intermediate-6 (0.075 g,0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2,4,6-trifluoro-1-iodo-benzene (Intermediate-22, 0.066 g, 0.255 mmol)	Yield: 0.015 g. ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.03 (s, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.38-7.61 (m, 6H), 13.25 (br s, 1H); MS $[M+H]^+$: 483.45
73			Step-2 of Intermediate-6 (0.075 g, 0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 3.88 (s, 3H), 6.97 (s, 2H), 7.13 (d, J = 6.9 Hz, 2H), 7.26-

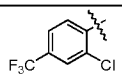
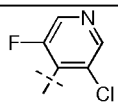
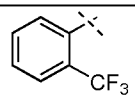
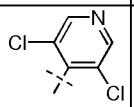
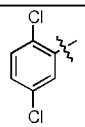
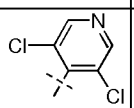
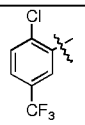
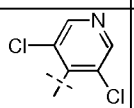
Ex. No.	R^a	R^1	Starting material	Analytical details
			phosphine)palladium (II) (catalytic amount), 1-iodo-4-methoxy-2-trifluoromethyl-benzene (Intermediate-23, 0.077 g, 0.254 mmol)	7.43 (m, 2H), 7.45-7.53 (m, 2H), 7.72 (d, *J* = 8.1Hz, 1H), 13.17 (br s, 1H); MS $[M+H]^+$: 526.38
74			Step-2 of Intermediate-6 (0.075 g, 0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 5-chloro-1,3-difluoro-2-iodo-benzene (Intermediate-24, 0.070 g, 0.254 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.04 (s, 1H), 7.19-7.22 (m, 1H), 7.40-7.47 (m, 1H), 7.50-7.61 (m, 5H), 13.19 (br s, 1H); MS $[M+H]^+$: 499.33
75			Step-2 of Intermediate-6 (0.075 g, 0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1,4-dichloro-2-fluoro-5-iodo-benzene (Intermediate-25, 0.074 g, 0.254 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.07 (s, 1H), 7.19-7.21 (m, 1H), 7.40-7.46 (m, 2H), 7.51-7.61 (m, 2H), 7.89 (d, *J* = 9.3 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H),13.20 (br s, 1H); MS $[M+H]^+$: 517.20
76			Step-2 of Intermediate-6 (0.075 g, 0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2,4,5-trifluoro-1-iodo-benzene (Intermediate-27, 0.066 g, 0.254 mmol)	Yield: 0.012 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.03-7.05 (m, 1H), 7.18-7.20 (m, 1H), 7.40-7.46 (m, 2H), 7.51-7.56 (m, 1H), 7.59-7.70 (m, 2H), 7.76-7.86 (m, 1H), 13.19 (br s, 1H); MS $[M+H]^+$: 483.43

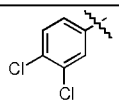
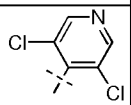
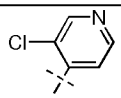
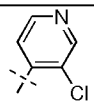
Ex. No.	R^a	R^1	Starting material	Analytical details
77			Step-2 of Intermediate-6, 0.075 g, 0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2,3-dichloro-1-fluoro-4-iodo-benzene (Intermediate-28, 0.074 g, 0.254 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.07 (d, J = 5.7 Hz, 1H), 7.19 (t, J = 6.3 Hz, 1H), 7.40-7.64 (m, 2H), 7.53-7.64 (m, 3H), 7.71-7.76 (m, 1H),13.19 (br s, 1H); MS $[M+H]^+$: 517.25
78			Step-2 of Intermediate-6 (0.075 g, 0.213 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-difluoromethoxy-2-iodo-benzene (Intermediate-29, 0.069 g, 0.254 mmol).	Yield: 0.018 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.01-7.17 (m, 3H), 7.29-7.31 (m, 2H), 7.43-7.64 (m, 6H), 12.16 (s, 1H); MS $[M+H]^+$: 495.35
79			step-2 of Intermediate-06 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.850 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-iodobenzonitrile (0.097 g, 0.423 mmol)	Yield: 0.015 g ^{1}HNMR DMSO-d_6): δ 1.62 (s, 6H), 7.06-7.08 (m, 1H), 7.21-7.23 (m, 1H), 7.40-7.62 (m, 6H), 7.96 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 8.7 Hz, 1H), 13.21 (br s, 1H)
80			Step-2 of Intermediate-6 (0.050 g, 0.140 mmol), tetra butyl ammonium fluoride (0.167 g, 0.639 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-ethoxy-2-iodobenzene	Yield: 0.011 g ^{1}HNMR DMSO-d_6): δ 1.39 (t, J = 6.9 Hz, 3H), 1.61 (s, 6H), 4.12 (q, J = 6.9 Hz, 2H), 6.96 (m, 2H), 7.08 (m, 2H), 7.40-7.53 (m, 6H), 13.25 (br s, 1H); MS $[M+H]^+$:

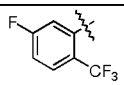
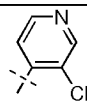
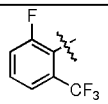
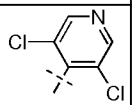
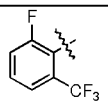
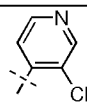
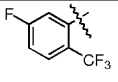
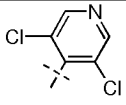
Ex. No.	R^a	R^1	Starting material	Analytical details
			(Intermediate-36, 0.084 g, 0.338 mmol)	473.33
81			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-(2-iodophenyl)-1,3,4-oxadiazole (Intermediate-37, 0.093 g, 0.340 mmol)	Yield: 0.020 g ^{1}HNMR DMSO-d_6): δ 1.62 (s, 6H), 7.19-7.77 (m, 10H), 9.52 (s, 1H), 13.18 (br s, 1H); MS $[M-H]^-$: 495.37
82			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-(2-iodophenyl)-5-methyl-1,3,4-oxadiazole (Intermediate-38, 0.097 g, 0.340 mmol)	Yield: 0.020 g ^{1}HNMR DMSO-d_6): δ 1.63 (s, 6H), 2.63 (s, 3H), 6.65 (d, J = 8.1 Hz, 1H), 6.98 (t, J = 10.2 Hz, 1H), 7.66 (s, 1H), 7.12 (s, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.40-7.65 (m, 2H), 7.74 (d, J = 6.9 Hz, 1H), 8.01 (d, J = 7.5 Hz, 1H), 9.04 (s, 1H), 13.25 (br s, 1H); MS $[M+H]^+$: 511.34
83			Step-2 of Intermediate-6, 0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-(2-iodophenyl) pyrrolidin-2-one (Intermediate-42, 0.098 g, 0.340 mmol)	Yield: 0.030 g ^{1}HNMR DMSO-d_6): δ 1.60 (s, 6H), 2.09-2.15 (m, 2H), 3.14 (m, 2H), 3.83 (m, 2H), 6.97 (m, 1H), 7.12 (m, 1H), 7.37-7.60 (m, 8H), 13.20 (br s, 1H); MS $[M+H]^+$: 512.42

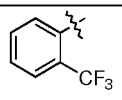
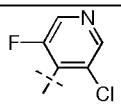
Ex. No.	R^a	R^1	Starting material	Analytical details
84			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-(2,2,2-trifluoro ethoxy)benzene (Intermediate-43, 0.102 g, 0.340 mmol)	Yield: 0.030 g ^{1}HNMR DMSO-d_6): δ 1.62 (s, 6H), 4.88 (q, J = 8.7 Hz, 2H), 6.95 (s, 1H), 7.06-7.11 (m, 2H), 7.21 (d, J = 8.4 Hz, 1H), 7.39-7.63 (m, 6H), 13.25 (br s, 1H); MS $[M+H]^+$: 527.32
85			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-iodophenyl methyl sulfoxide (Intermediate-45, 0.090 g, 0.338 mmol)	Yield: 0.020 g ^{1}HNMR DMSO-d_6): δ 1.60 (s, 6H), 2.85 (s, 3H), 7.05-7.09 (m, 1H), 7.19-7.21 (m, 1H), 7.39-7.71 (m, 7H), 7.85 (d, J = 7.2 Hz, 1H), 13.18 (s, 1H); MS $[M+H]^+$: 491.24
86			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-chloro-1-iodo-4-methylbenzene (Intermediate-48, 0.107 g, 0.426 mmol)	Yield: 0.025 g ^{1}HNMR DMSO-d_6): δ 1.62 (s, 6H), 2.29 (s, 3H), 7.02-7.22 (m, 3H), 7.43-7.61 (m, 6H), 13.20 (s, 1H); MS $[M+H]^+$: 477.50
87			Step-2 of Intermediate-6 (0.100 g, 0.284 mmol), tetra butyl ammonium fluoride (0.268 g, 0.852 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic	Yield: 0.040 g ^{1}HNMR DMSO-d_6): δ 1.62 (s, 6H), 3.88 (s, 3H), 6.97 (s, 1H), 7.12 (d, J = 7.8 Hz, 1H), 7.28-7.50 (m, 2H), 7.53-7.64 (m, 4H),

Ex. No.	R^a	R^1	Starting material	Analytical details
			amount), 1-iodo-4-methoxy-2-(trifluoromethyl)benzene (Intermediate-55, 0.130 g, 0.420 mmol)	7.72 (d, *J* = 8.4 Hz, 1H), 13.16 (br s, 1H); MS $[M+H]^+$: 527.39
88			Intermediate-32, 0.100 g, 0.297 mmol), tetra butyl ammonium fluoride (0.097 g, 0.357 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-(trifluoromethyl) benzene (0.097 g, 0.357 mmol)	Yield:0.020 g. ^{1}HNMR DMSO-d_6): δ 1.61 (s, 6H), 7.01 (s, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.55-7.63 (m, 3H), 7.70-8.31 (m, 3H), 13.15 (br s, 1H) ; MS $[M+H]^+$: 481.34
89			Intermediate-32 (0.100 g, 0.297 mmol), tetra butyl ammonium fluoride (0.097 g, 0.357 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1,3-dichloro-5-iodobenzene (0.097 g, 0.357 mmol)	Yield: 0.040 g. ^{1}HNMR DMSO-d_6): δ 1.63 (s, 6H), 7.08 (s, 1H), 7.21-7.30 (m, 3H), 7.56-7.68 (m, 5H), 13.20 (br s, 1H); MS $[M+H]^+$: 481.36
90			Intermediate-10, (0.050 g, 0.249 mmol), tetra butyl ammonium fluoride (0.235 g, 0.747 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-trifluoromethyl-benzene (0.101 g, 0.373 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 7.00 (s, 1H), 7.15 (d, *J* = 7.2 Hz, 1H), 7.38 (s, 1H), 7.59-7.64 (m, 1H), 7.73-7.85 (m, 4H), 13.82 (s, 1H); MS $[M-H]^-$: 464.37
91			Intermediate-16, (0.100 g, 0.298 mmol), tetrabutyl ammonium fluoride (0.282 g, 0.895 mmol), dichloro bis (triphenyl	Yield: 0.025 g ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 2.35 (s, 3H), 2.39 (s, 3H), 6.98 (s, 1H), 7.14 (d, *J* = 7.8 Hz,

Ex. No.	R^a	R^1	Starting material	Analytical details
			phosphine)palladium (II) (catalytic amount), 1-iodo-2-trifluoromethyl-benzene (0.122 g, 0.447 mmol)	1H), 7.61-7.84 (m, 5H), 13.69 (m, 1H); MS $[M+H]^+$: 480.52
92			Intermediate-33 (0.060 g, 0.169 mmol), tetra butyl ammonium fluoride (0.160 g, 0.508 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-chloro-1-iodo-4-(trifluoromethyl)benzene (0.062 g, 0.203 mmol)	Yield: 0.020 g ^{1}HNMR DMSO-d_6): δ 1.63 (s, 6H), 7.13 (m, 1H), 7.26-7.29 (m, 1H), 7.57 (m, 1H), 7.79 (m, 1H), 7.88-7.90 (m, 1H), 8.04-8.11 (m, 1H), 8.75-8.80 (m, 2H), 13.46 (br s, 1H); MS $[M-H]^-$: 530.50
93			Intermediate-17 (0.100 g, 0.270 mmol), tetra butyl ammonium fluoride (0.255 g, 0.810 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-trifluoromethyl-benzene (0.110 g, 0.405 mmol)	Yield: 0.025 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.01 (s, 1H), 7.16 (d, J = 7.5 Hz, 1H), 7.47-7.83 (m, 5H), 8.37 (s, 2H), 13.40 (s, 1H); MS $[M+H]^+$: 514.39
94			Intermediate-17 (0.100 g, 0.270 mmol), tetra butyl ammonium fluoride (0.255 g, 0.810 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1,4-dichloro-2-iodo-benzene (0.110 g, 0.405 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.09-7.23 (m, 2H), 7.50-7.79 (m, 4H), 8.85 (s, 2H), 13.40 (s, 1H)
95			Intermediate-17 (0.100 g, 0.270 mmol), tetrabutyl ammonium fluoride (0.255 g, 0.810 mmol), dichloro bis (triphenyl	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 3H), 1.66 (s, 3H), 7.11-7.13 (m, 1H), 7.21-7.27 (m,1H), 7.47 (d, J

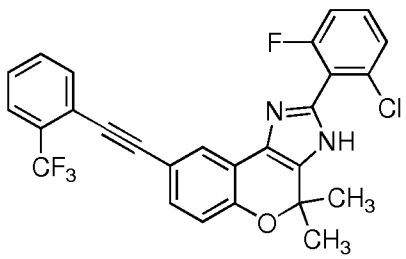
Ex. No.	R^a	R^1	Starting material	Analytical details
			phosphine)palladium (II) (catalytic amount), 1-chloro-2-iodo-4-trifluoromethyl-benzene (0.125 g, 0.405 mmol)	= 8.1 Hz, 1H), 7.78-7.87 (m, 2H), 8.08 (s, 1H), 8.85 (s, 2H), 13.12 (s, 1H); MS $[M+H]^+$: 550.43
96			Intermediate-17 (0.050 g, 0.135 mmol), tetrabutyl ammonium fluoride (0.127 g, 0.403 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1,2-dichloro-4-iodo-benzene (Intermediate-19, 0.044 g, 0.161 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.09 (m, 1H), 7.19-7.21 (m, 1H), 7.48-7.55 (m, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.85 (s, 1H), 8.85 (s, 2H), 13.39 (s, 1H); MS $[M+H]^+$: 516.39
97			Intermediate-21 (0.050 g, 0.149 mmol), tetrabutyl ammonium fluoride (0.140 g, 0.444 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-trifluoromethyl-benzene (0.140 g, 0.444 mmol)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.02 (m, 1H), 7.19-7.21 (m, 1H), 7.59-7.84 (m, 6H), 8.63 (d, J = 5.1 Hz, 1H), 8.78 (s, 1H), 13.24 (s, 1H); MS [M+] : 480.41
98			Intermediate-21 (0.100 g, 0.298 mmol), tetra butyl ammonium fluoride (0.282 g, 0.895 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2,5-dichloro-1-iodobenzene (0.098 g, 0.358 mmol)	Yield: 0.040 g ^{1}HNMR (DMSO-d_6): δ 1.63 (s, 6H), 7.07 (s, 1H), 7.22 (d, J = 7.5 Hz, 1H), 7.48-7.60 (m, 3H), 7.77 (s, 1H), 7.81 (d, J = 5.1 Hz, 1H), 8.61 (d, J = 4.8 Hz, 1H), 8.76 (s, 1H), 13.21 (br s, 1H); MS [M+2] : 482.37

Ex. No.	R^a	R^1	Starting material	Analytical details
99			Intermediate-21 (0.100 g, 0.298 mmol), tetra butyl ammonium fluoride (0.282 g, 0.895 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-bromo-4-fluoro-1-trifluoromethyl-benzene (0.087 g, 0.358 mmol)	Yield: 0.035 g ^{1}HNMR (DMSO-d_6): δ 1.33 (s, 6H), 7.09 (m, 1H), 7.53-7.65 (m, 4H), 7.79-7.84 (m, 2H), 8.64 (br s, 1H), 8.78 (s, 1H), 13.21 (br s, 1H); MS $[M-H]^-$: 496.38
100			Intermediate-26 (0.100 g, 0.270 mmol), tetrabutyl ammonium fluoride (0.255 g, 0.810 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-bromo-1-fluoro-3-trifluoromethyl-benzene (0.079 g, 0.324 mmol)	Yield: 0.025 g ^{1}HNMR DMSO-d_6): δ 1.66 (s, 6H), 7.09 (m, 1H), 7.20 (m, 1H), 7.52 (m, 2H), 7.64 (d, 1H), 7.78 (s, 1H), 8.85 (s, 2H), 13.40 (br s, 1H)
101			Intermediate-21 (0.100 g, 0.298 mmol), tetrabutyl ammonium fluoride (0.282 g, 0.895 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 2-bromo-1-fluoro-3-trifluoromethyl-benzene (0.109 g, 0.447 mmol)	Yield: 0.030 g ^{1}HNMR DMSO-d_6): δ 1.66 (s, 6H), 6.91 (d, J = 8.1 Hz, 2H), 6.96-6.99 (t, 1H), 7.11-7.14 (m, 2H), 7.83 (s, 2H), 8.62 (s, 1H), 8.76 (s, 1H), 13.09 (br s, 1H); MS $[M-H]^-$: 496.34
102			Intermediate-26 (0.100 g, 0.270 mmol), tetrabutyl ammonium fluoride (0.255 g, 0.810 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic	Yield: 0.025 g ^{1}HNMR DMSO-d_6): δ 1.66 (s, 6H), 7.09 (m, 1H), 7.20 (m, 1H), 7.52 (m, 2H), 7.64 (d, 1H), 7.78 (s, 1H), 8.85 (s, 2H), 13.40 (br s,

Ex. No.	R^a	R^1	Starting material	Analytical details
			amount), 2-bromo-4-fluoro-1-trifluoromethyl-benzene (0.079 g, 0.324 mmol)	1H)
103			Intermediate-33 (0.060 g, 0.169 mmol), tetra butyl ammonium fluoride (0.160 g, 0.508 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-(trifluoromethyl)benzene (0.055 g, 0.203 mmol)	Yield: 0.020 g ^{1}HNMR DMSO-d_6): δ 1.62 (s, 6H), 7.02-7.04 (m, 1H), 7.15-7.21 (m, 1H), 7.55-7.61 (m, 2H), 7.71-7.85 (m, 3H), 8.75-8.80 (m, 2H), 13.44 (br s, 1H); MS $[M+H]^+$: 498.27

Example-104

2-(2-Chloro-6-fluoro-phenyl)-4,4-dimethyl-8-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole



The title compound was prepared by following the same procedure as described for step-5 of Intermediate-7 by using 2-(2-chloro-6-fluoro-phenyl)-8-ethynyl-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole (Intermediate-61, 0.050 g, 0.141 mmol), DMSO (2 mL), tetra butyl ammonium fluoride (0.110 g, 0.421 mmol), 2-trifluoromethyl-iodo benzene (0.057 g, 0.210 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.003 g, 0.004 mmol) to afford 0.015 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 6.99 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 9.3 Hz, 1H), 7.51-7.64 (m, 4H), 7.69-7.83 (m, 3H), 13.16 (br s,1H).

Following compounds were also prepared following the procedure described for the preparation of step-5 of Intermediate-7

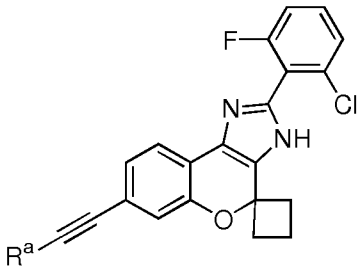
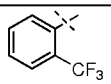
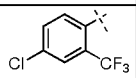
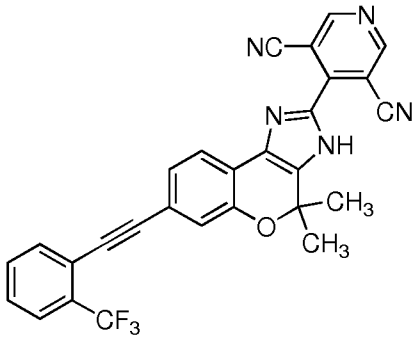


Table-5

Ex No.	R^a	Starting material	Analytical details
105		Intermediate-53 (0.100 g, 0.270 mmol), tetra butyl ammonium fluoride (0.260 g, 0.820 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 1-iodo-2-(trifluoromethyl)benzene (0.112 g, 0.410 mmol)	Yield: 0.045 g. ^{1}HNMR DMSO-d_6): δ 1.92 (m, 2H), 2.48 (m, 4H), 7.03 (s, 1H), 7.13 (d, J = 7.2 Hz, 1H), 7.34-7.57 (m, 5H), 7.68 (t, J = 7.5 Hz, 1H), 7.78 (t, J = 8.4 Hz, 2H), 13.20 (br s, 1H); MS $[M+H]^+$: 509.23
106		Intermediate-53 (0.100 g, 0.270 mmol), tetra butyl ammonium fluoride (0.260 g, 0.820 mmol), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), 4-chloro-1-iodo-2-(trifluoromethyl)benzene (Intermediate-54, 0.126 g, 0.410 mmol)	0.050 g. ^{1}HNMR DMSO-d_6): δ 1.96 (m, 2H), 2.50 (m, 4H), 7.07 (s, 1H),7.16 (d, J = 7.2 Hz, 1H), 7.42-7.63 (m, 4H), 7.82 (s, 2H),7.92 (s, 1H), 13.26 (s, 1H); MS $[M+H]^+$: 543.34

Example-107

4-[4,4-Dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazol-2-yl]-pyridine-3,5-dicarbonitrile



The title compound was prepared by following the same procedure as described for step-2 of Example-10 by using 2-(3,5-dibromo-pyridin-4-yl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydrochromeno[3,4-d]imidazole (Intermediate-30, 0.120 g, 0.199 mmol), copper cyanide (0.053 g, 0.597 mmol) and DMF (3 mL) to afford 0.015 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.02 (m, 1H), 7.22 (m, 1H), 7.61 (m, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.82 (t, J = 8.4 Hz, 2H),7.95 (s,1H), 7.95 (m, 2H), 9.24 (m, 2H), 13.80-14.00 (s, 1H); MS $[M-H]^-$: 494.44.

Following compounds were prepared following the procedure described for the preparation of step-2 intermediate of Example-10

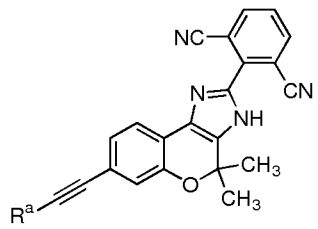
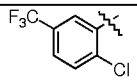
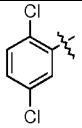
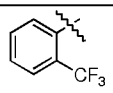
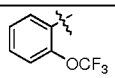
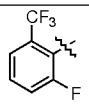
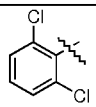
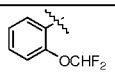
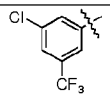


Table-6

Ex No.	R^a	Starting material	Analytical details
108		Intermediate-7 (0.200 g, 0.314 mol), copper cyanide (0.085 g, 0.942 mol), DMF (5 mL)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.15 (s, 1H), 7.29 (m, 1H), 7.57 (m, 1H), 7.81-7.86 (m, 3H), 8.09 (s, 1H), 8.36 (d, J = 7.8 Hz, 2H), 13.71 (s, 1H); MS $[M-H]^-$: 527.36
109		Intermediate-8 (0.150 g, 0.248 mol), copper cyanide (0.067 g, 0.745 mol), DMF (3 mL)	Yield: 0.015 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.07 (m, 1H), 7.23 (m, 1H), 7.52 (t, J = 8.4 Hz, 2H),

Ex No.	R[a]	Starting material	Analytical details
			7.63 (d, *J* = 8.7 Hz, 1H), 7.79 (m, 2H), 8.28 (m, 2H), 13.18 (s, 1H); MS $[M-H]^-$: 493.35
110		Intermediate-13 (0.150 g, 0.248 mol), copper cyanide (0.067 g, 0.745 mol), DMF (3 mL)	Yield: 0.013 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.05 (m, 1H), 7.22-7.24 (m, 1H), 7.55-7.64 (m, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.80-7.89 (m,3H), 8.31-8.38 (m, 2H), 13.71 (s, 1H); MS $[M-H]^-$: 493.43
111		Intermediate-31 (0.250 g, 0.403 mmol), copper cyanide (0.108 g, 1.211 mmol), DMF (3 mL)	Yield: 0.050 g ^{1}HNMR (DMSO-d_6): δ 1.62 (s, 6H), 7.03 (m, 1H), 7.19-7.22 (m, 1H), 7.44-7.57 (m, 4H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.85 (t, *J* = 7.2 Hz, 1H), 8.35 (d, *J* = 8.1 Hz, 2H), 13.16 (s, 1H); MS $[M+H]^+$: 511.60
112		Intermediate-35 (0.130 g, 0.209 mmol), copper cyanide (0.056 g, 0.628 mmol), DMF (3 mL)	Yield: 0.050 g ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.03 (m, 1H), 7.26 (m, 1H), 7.59-7.71 (m, 4H), 7.87 (m, 1H), 7.36 (d, *J* = 7.5 Hz, 2H), 13.74 (s, 1H); MS $[M+H]^+$: 513.29
113		Intermediate-40 (0.160 g, 0.265 mmol), copper cyanide (0.120 g, 1.32 mmol), DMF (3 mL)	Yield: 0.025 g ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 7.06 (s, 1H), 7.26 (m, 1H), 7.44 (t, *J* = 8.1 Hz, 1H), 7.60-7.62 (m, 3H), 7.87 (t, *J* = 7.8 Hz, 1H), 8.37 (d, *J* = 7.8 Hz, 2H), 13.73 (br s, 1H); MS $[M]^+$: 495.30
114		Intermediate-41 (0.130 g, 0.216 mmol), copper cyanide (0.098 g, 1.08 mmol), DMF (3 mL)	Yield: 0.025 g ^{1}HNMR (DMSO-d_6): δ 1.66 (s, 6H), 7.05-7.13 (m, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.29 (m, 1H), 7.46-7.57 (m, 2H), 7.65 (d, *J* = 6.9

Ex No.	R^a	Starting material	Analytical details
			Hz, 1H), 7.87 (t, *J* = 7.8 Hz, 1H), 8.31-8.37 (m, 4H), 13.69 (br s, 1H); MS $[M-H]^-$: 491.42
115		Intermediate-50 (0.170 g, 0.267 mmol), copper cyanide (0.121 g, 1.33 mmol), DMF (3 mL)	Yield: 0.020 g ^{1}HNMR (DMSO-d_6): δ 1.64 (s, 6H), 7.06 (br s, 1H), 7.22-7.24 (m, 1H), 7.57 (br s, 1H), 7.83-7.93 (m, 4H), 8.36 (d, *J* = 8.1 Hz, 2H), 13.72 (s, 1H); MS $[M-H]^-$: 527.42

The compounds of Table-7 were prepared following the process described for preparation of compound designated as Intermediate-5 (process 'A') or the process for the preparation of step-1 intermediate of Intermediate-6 (process 'C')

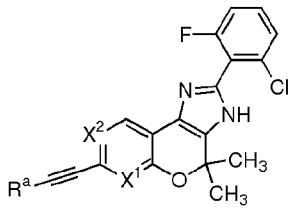
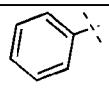
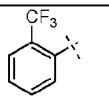
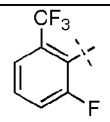
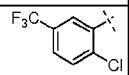
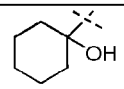
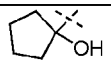
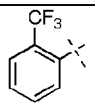


Table-7

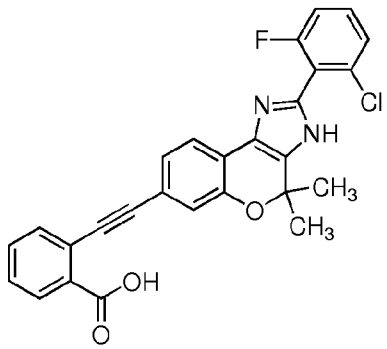
Ex No.	R^a	X^1	X^2	Process	Starting material	Analytical details
116		N	C	C	Intermediate-69 (0.150 g, 0.549 mmol), phenylacetylene (0.084 g, 0.824 mmol), copper iodide (catalytic amount), dichloro bis (triphenyl phosphine)palladium (II) (catalytic amount), triethyl amine (0.5 mL), DMSO (3 mL)	Yield: 0.050 g ^{1}HNMR (DMSO-d6): δ 1.67 (s, 6H), 7.14-7.31 (m, 2H), 7.41-7.46 (m, 4H), 7.51-.7.57 (m, 4H), 13.28 (br s, 1H); MS $[M+H]^+$: 430.30
117		N	C	A	Intermediate-70 (0.200 g, 0.555 mmol), 2-chloro-6-fluoro	Yield: 0.020 g ^{1}HNMR (DMSO): δ 1.68 (s,

					benzaldehyde (0.131 g, 0.832 mmol), ammonium acetate (0.214 g, 2.77 mmol) and acetic acid (4.0 mL)	6H), 7.25-7.31 (m, 1H), 7.44 (t, J = 9.3 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.52-7.55 (m, 2H), 7.60-7.65 (m, 2H), 7.84-7.87 (m, 2H), 13.34 (brs, 1H); $[M+H]^+$: 498.27
118		N	C	A	Intermediate-71 (0.100 g, 0.264 mmol), 2-chloro-6-fluoro benzaldehyde (0.063 g, 0.396 mmol), ammonium acetate (0.102 g, 1.32 mmol) and acetic acid (3.0 mL)	Yield: 0.025 g ^{1}HNMR (DMSO): δ 1.68 (s, 6H), 7.31 (m, 1H), 7.44 (t, J = 9.0 Hz, 1H), 7.52-7.61(m, 2H), 7.73 (m, 4H), 11.36 (brs, 1H); $[M-H]^-$: 514.30
119		N	C	A	Intermediate-72 (0.200 g, 0.507 mmol), 2-chloro-6-fluoro benzaldehyde (0.120 g, 0.750 mmol), ammonium acetate (0.195 g, 2.53 mmol) and acetic acid (5.0 mL)	Yield: 0.050 g ^{1}HNMR (DMSO): δ 1.51 (s, 6H), 7.35-7.52 (m, 2H), 7.55-7.63 (m, 3H), 7.65-7.86 (m, 2H), 8.10 (s, 1H), 13.34 (s, 1H); $[M+H]^+$: 532.27
120		C	C	C	Intermediate-5 (0.100 g, 0.219 mmol), copper iodide (0.001 g, 0.0052 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.005 g, 0.007 mmol), triethyl amine (0.5 mL), 1-ethynylcyclohexanol (0.041 g, 0.330 mmol), DMSO (3 mL)	Yield: 0.040 g ^{1}HNMR (DMSO-d_6): δ 1.53 (m, 6H), 1.82 (m, 8H), 1.98 (s, 2H), 5.42 (s, 1H), 6.85 (s, 1H), 7.00 (d, *J* = 7.2 Hz, 1H), 7.35-7.45 (m, 2H), 7.50-7.60 (m, 2H), 13.10 (s, 1H); MS $[M+H]^+$: 451.36

121		C	C	C	Intermediate-5 (0.250 g, 0.550 mmol), copper iodide (0.002 g, 0.011 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.012 g, 0.017 mmol), triethyl amine (0.5 mL), 1-ethynylcyclopentanol (0.121 g, 1.10 mmol), DMSO (3 mL)	Yield: 0.050 g ^{1}HNMR (DMSO-d_6): δ 1.33-1.71 (m, 14H), 5.31 (s, 1H), 6.84 (s, 1H), 6.99 (d, *J* = 6.9 Hz, 1H), 7.34-7.45 (m, 2H), 7.50-7.60 (m, 2H), 13.10 (s, 1H); MS $[M+H]^+$: 437.31
122		C	N	C	Intermediate-78 (0.150 g, 0.329 mmol), copper iodide (0.001 g, 0.005 mmol), dichloro bis (triphenyl phosphine)palladium (II) (0.009 g, 0.012 mmol), triethyl amine (0.5 mL), 1-iodo-2-(trifluoromethyl)benzene (0.084 g, 0.493 mmol), DMSO (3 mL)	Yield: 0.006 g ^{1}HNMR (DMSO-d_6): δ 1.68 (s, 6H), 7.09 (s, 1H), 7.44 (t, 1H), 7.52-7.69 (br m, 3H), 7.76 (t, 1H), 7.86 (d, *J* = 7.8Hz, 2H), 8.59 (s, 1H), 13-14 (br s, 1H); MS $[M+H]^+$: 498.34

Example-123

2-{[2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}benzoic acid



To the solution of methyl 2-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}benzoate (Intermediate-34, 0.040 g, 0.082 mmol) in methanol (5 mL) was added aq. solution of sodium hydroxide (6.56 g, 0.16 mmol). The reaction mass was stirred at RT for 15 h. Water was added and the reaction

mass was washed with diethyl ether. The aqueous layer was cooled at 0°C and acidified with dil acetic acid and filtered off the obtained solid to afford 0.020 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.61 (s, 6H), 6.99 (s, 1H), 7.10 (d, J = 7.8 Hz, 1H), 7.36-7.67 (m, 8H), 13.30 (br s, 1H); MS $[M+H]^+$: 473.33.

The compounds of Table-8 were prepared following the procedure described for the preparation of Intermediate-5 (process 'A')

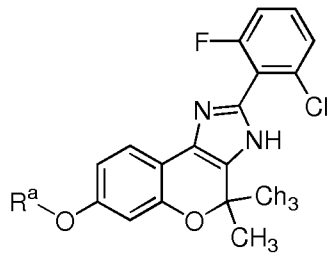
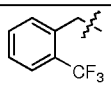
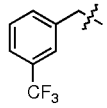
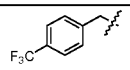


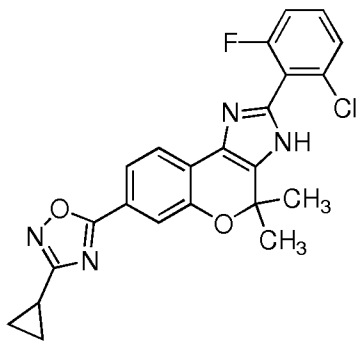
Table-8

Ex No.	R^a	Starting material	Analytical details
124		Intermediate-47 (0.500 g, 1.37 mmol 1.49 mmol) and 2-chloro-6-fluoro benzaldehyde (0.325 g, 2.05 mmol), ammonium acetate (0.527 g, 6.84 mmol), acetic acid (10 mL)	Yield: 0.045 g ^{1}HNMR DMSO-d_6): ^{1}HNMR ($CDCl_3$): δ 1.60 (s, 6H), 5.19 (s, 2H), 6.55-6.63 (m, 2H), 7.30-7.59 (m, 5H), 7.68-7.80 (m, 3H), 12.88 (s, 1H); MS $[M+H]^+$: 503.27
125		Intermediate-46 (1.000 g, 3.64 mmol) and 2-chloro-6-fluoro benzaldehyde (0.868 g, 5.49 mmol), ammonium acetate (1.120 g, 14.54 mmol), acetic acid (10 mL)	Yield: 0. 500 g ^{1}HNMR DMSO-d_6): ^{1}HNMR ($CDCl_3$): δ 1.60 (s, 6H), 1.69 (m, 5H), 1.90 (m, 3H), 4.79 (m, 1H), 6.45-6.52 (m, 2H), 7.27-7.57 (m, 4H), 12.84 (s, 1H)

Ex No.	R[a]	Starting material	Analytical details
126		Intermediate-51 (0.500 g, 1.37 mmol 1.49 mmol) and 2-chloro-6-fluoro benzaldehyde (0.325 g, 2.05 mmol), ammonium acetate (0.527 g, 6.84 mmol), acetic acid (10 mL)	Yield: 0.041 g ^{1}HNMR ($CDCl_3$): δ 1.61 (s, 6H), 5.21 (s, 2H), 6.59-6.66 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 6.3 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.77 (d, *J* = 7.8 Hz, 2H), 12.88 (s, 1H); MS $[M+H]^+$: 503.36
127		Intermediate-52 (0.500 g, 1.37 mmol) and 2-chloro-6-fluoro benzaldehyde (0.325 g, 2.05 mmol), ammonium acetate (0.527 g, 6.84 mmol), acetic acid (10 mL)	Yield: 0.030 g ^{1}HNMR DMSO-d_6): ^{1}HNMR ($CDCl_3$): δ 1.57 (s, 6H), 5.20 (s, 2H), 6.60-6.76 (m, 2H), 7.32 (d, *J* = 8.1Hz, 1H), 7.40 (d, *J* = 9.0Hz, 1H), 7.48-7.81 (m, 6H), 12.88 (s, 1H)

Example-128

2-(2-Chloro-6-fluorophenyl)-7-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole

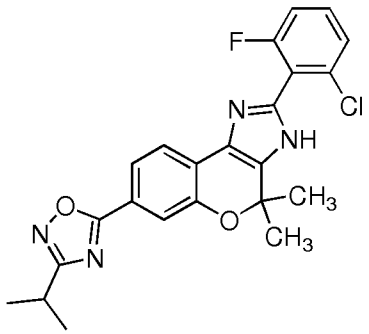


To a solution of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.200 g, 0.537 mmol) and *N*'-hydroxycyclopropanecarboximidamide (Intermediate-68, 0.054 g, 0.537 mmol) in dioxane was added N,N'-dicyclohexyl carbodimide (0.122 g, 0.591 mmol) was added.

The reaction mass was refluxed for 24 hours. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.016 g of desired product.[1]HNMR (DMSO d_6): δ 0.98 (m, 2H), 1.10 (m, 2H), 1.62 (s, 6H), 2.17 (m, 1H), 7.43-7.45 (m, 2H), 7.52 (d, J = 7.8Hz, 2H), 7.59 (t, J = 6.6Hz, 1H), 7.66 (s, 1H), 13.33 (s, 1H); MS $[M+H]^+$: 437.27.

Example-129

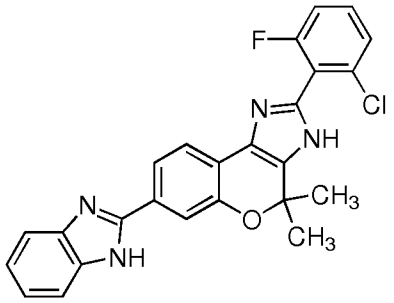
2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-7-[3-(propan-2-yl)-1,2,4-oxadiazol-5-yl]-1,4-dihydrochromeno[3,4-*d*]imidazole



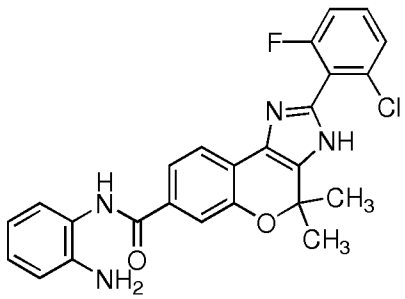
To a solution of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.100 g, 0.268 mmol) in DMF was added (1*Z*)-*N*'-hydroxy-2-methylpropanimidamide (0.030 g, 0.295 mmol), TEA (0.082 g, 0.806 mmol), EDC HCl (0.250 g, 1.344 mmol) and T_3P (0.214 g, 0.672 mmol).The reaction mass was heated at 80°C for 12-14 h. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated. The obtained crude product was further purified by column chromatography on silica gel eluting with 10 % EA: DCM to afford 0.005 g of desired product. [1]HNMR (DMSO d_6): δ 1.40 (s, 6H), 1.80 (d, J = 8.1Hz, 6H), 3.10-3.17 (m, 1H), 7.41-7.62 (m, 5H), 7.69-7.74 (m, 1H), 13.23 (s, 1H); MS $[M-H]^-$: 437.29.

Example-130

7-(1*H*-Benzimidazol-2-yl)- 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole



Step-1:- Preparation of *N*-(2-aminophenyl)-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide:-



To a solution of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.100 g, 0.268 mmol) in DMF was added benzene-1,2-diamine (0.032 g, 0.295 mmol), TEA (0.082 g, 0.806 mmol) and T_3P (0.214 g, 0.672 mmol). The reaction mass was heated at 80°C for 12-14 h. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated. The obtained crude product was further purified by column chromatography on silica gel eluting with 20% EA: DCM to afford 0.060 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.67 (s, 6H), 4.39 (m, 2H), 6.34-6.37 (m, 1H), 6.46-6.49 (m, 1H), 6.59 (t, *J* = 7.8Hz, 1H), 6.77 (d, *J* = 8.4Hz, 1H), 6.96 (t, *J* = 7.8Hz, 1H), 7.15 (d, *J* = 7.8Hz, 1H), 7.43 (d, *J* = 8.7Hz, 1H), 7.48-7.59 (m, 3H), 9.60 (s, 1H), 10.20 (s, 1H).

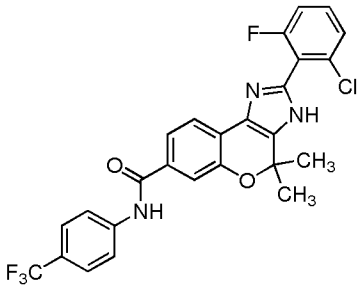
Step-2:- Preparation of 7-(1*H*-benzimidazol-2-yl)-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole:-

To a solution of *N*-(2-aminophenyl)-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide (0.060 g, 0.129 mmol) in DMF (5.0 mL) was added $POCl_3$ (catalytic amount). The reaction mass was refluxed at 80°C for 12 h. The reaction mass was quenched in water and extracted with EA. The organic layer

was dried over anhydrous sodium sulphate and concentrated. The obtained crude product was further purified by column chromatography on silica gel eluting with 10 % E A : DCM to afford 0.009 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.43 (s, 6H), 6.98 (m, 1H), 7.18 (m, 2H), 7.44-7.70 (m, 6H), 7.80 (m, 1H), 12.82 (br s, 1H), 13.17 (br s, 1H); MS $[M+H]^+$: 443.35.

Example-131

2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-*N*-[4-(trifluoromethyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide



To a solution of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.050 g, 0.134 mmol) in THF was added TEA (0.015 g, 0.141 mmol), 4-trifluoro methyl aniline (0.024 g, 0.147 mmol). The reaction mass was stirred for 2-3 h. Then ethyl chloro formate (0.016 g, 0.147 mmol) was added and the reaction mass was stirred at RT for 24 h. THF was removed under reduced pressure and the reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 9.5 g of desired product.^{1}HNMR (DMSO d_6): δ 1.65 (s, 6H), 7.43-7.73 (m, 8H), 8.02 (d, J = 7.8 Hz, 2H), 10.47 (s, 1H), 13.25 (br s, 1H); MS $[M+H]^+$:516.34

The compounds of Table-9 were prepared following the procedure described for the preparation of Example 132.

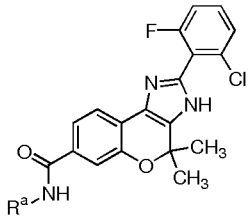
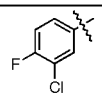
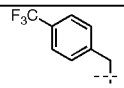
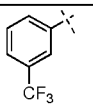
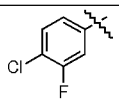
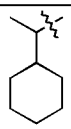
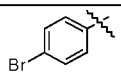


Table-9

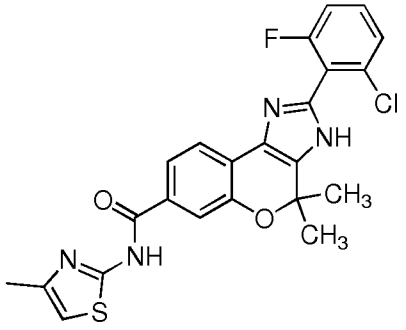
Ex No.	R[a]	Starting material	Analytical details
132		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 3-chloro-4-fluoro aniline (0.030 g, 0.206 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.017 g ^{1}HNMR (DMSO d_6): δ 1.63 (s, 6H), 7.41-7.72 (m, 8H), 8.09 (s, 1H), 10.33 (s, 1H), 13.24 (s, 1H); MS $[M+H]^+$:500.30
133		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 1-[4-(trifluoromethyl)phenyl]methanamine (0.036 g, 0.206 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.018 g ^{1}HNMR (DMSO d_6): δ 1.61 (s, 6H), 4.54 (s, 2H), 7.4-7.61 (m, 8H), 7.70 (d, J = 7.8 Hz, 2H), 9.02 (s, 1H), 13.10 (br s, 1H); MS $[M+H]^+$:530.43
134		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), cis-myrtanylamine (0.032 g, 0.206 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO d_6): δ 1.64 (s, 6H), 1.81-1.92 (m, 6H), 2.27-2.31 (m, 3H), 2.72 (s, 6H), 2.82 (m, 2H), 7.36-7.61 (m, 6H), 8.38 (br s, 1H), 13.16 (br s, 1H); MS $[M+H]^+$:508.43
135		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), cyclo hexanamine (0.032 g, 0.323 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO d_6): δ 1.64 (s, 6H), 2.44 (m, 10H), 3.73 (m, 1H), 7.39-7.61 (m, 4H), 8.13 (d, J = 8.1 Hz, 1H), 13.15 (br s, 1H); MS $[M+H]^+$454.49
136		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 3-(tri fluoro methyl) aniline (0.033 g, 0.206 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.010 g ^{1}HNMR (DMSO d_6): δ 1.61 (s, 6H), 7.41-7.63 (m, 8H), 8.07 (d, J = 7.8 Hz, 1H), 8.27 (s, 1H), 10.44 (s, 1H), 13.24 (s, 1H); MS $[M-H]^-$: 514.42
137		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 2-fluoro	Yield: 0.015 g ^{1}HNMR (DMSO d_6): δ 1.63 (s, 6H),

Ex No.	R[a]	Starting material	Analytical details
		aniline (0.023 g, 0.212 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	7.21-7.29 (m, 3H), 7.26-7.61 (m, 7H), 10.04 (s, 1H), 13.23 (s, 1H); MS $[M+H]^+$: 466.40
138		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 3,4-dichloro aniline (0.033 g, 0.206 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO d_6): δ 1.63 (s, 6H), 7.43-7.79 (m, 8H), 8.18 (s, 1H), 10.39 (s, 1H), 13.24 (s, 1H); MS $[M+H]^+$: 516.39
139		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), cyclopentyl amine (0.018 g, 0.211 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.015 g ^{1}HNMR (DMSO d_6): δ 0.83 (m, 2H), 1.04-1.09 (m, 2H), 1.62 (s, 6H), 1.83 (m, 4H), 4.17-4.20 (m, 1H), 7.38-7.59 (m, 6H), 8.18 (d, J = 7.2 Hz, 1H), 13.13 (s, 1H); MS $[M+H]^+$: 440.33
140		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 4-chloro-3-fluoro aniline (0.136 g, 0.940 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.006 g ^{1}HNMR (DMSO d_6): δ 1.63 (m, 6H), 7.41-7.60 (m, 8H), 7.93-7.97 (m, 1H), 10.44 (s, 1H), 13.23 (s, 1H); MS $[M+H]^+$: 500.0
141		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), R-(-)-cyclo hexyl ethyl amine (0.026 g, 0.204 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.014 g ^{1}HNMR (DMSO d_6): δ 0.83-0.95 (m, 5H), 1.38 (m, 3H), 1.64 (s, 6H), 1.71 (m, 6H), 3.82 (m, 1H), 7.39-7.60 (m, 6H), 8.05 (d, J = 8.4Hz, 1H), 13.15 (s, 1H); MS $[M+H]^+$: 482.52
142		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), i*sopino campheyl amine* (0.032 g, 0.208 mmol), ethyl chloro formate (0.023g, 0.206	Yield: 0.012 g ^{1}HNMR (DMSO d_6): δ 1.06 (s, 6H), 1.65 (s, 6H), 1.79 (m, 1H), 1.92 (m, 1H), 2.07 (m, 2H), 2.27-2.44 (m, 6H), 4.37 (m,

Ex No.	R[a]	Starting material	Analytical details
		mmol)	1H), 7.39-7.60 (m, 6H), 8.25 (d, *J* = 8.7Hz, 1H), 13.15 (br s, 1H); MS $[M+H]^+$: 508.50
143		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 4-bromo aniline (0.036 g, 0.206 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.007 g ^{1}HNMR (DMSO d_6): δ 1.63 (m, 6H), 7.41-7.60 (m, 8H), 7.93-7.97 (m, 1H), 10.44 (s, 1H), 13.23 (s, 1H); MS $[M+H]^+$: 526.38
144		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), 1-adamantanamine (0.031 g, 0.205 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.010 g ^{1}HNMR (DMSO d_6): δ 0.87 (m, 2H), 1.23 (m, 2H), 1.61 (m, 6H), 2.06 (m, 5H), 2.72 (m, 6H), 7.35-7.61 (m, 6H), 13.20 (br s, 1H); MS $[M+H]^+$: 506.55
145		Intermediate-62 (0.070 g, 0.188 mmol), TEA (0.020 g, 0.206 mmol), R-(-)-3,3-dimethyl-2-butyl amine (0.021 g, 0.208 mmol), ethyl chloro formate (0.023g, 0.206 mmol)	Yield: 0.010 g ^{1}HNMR (DMSO d_6): δ 0.89 (s, 9H), 1.33 (s, 3H), 1.62 (s, 6H), 3.93-3.99 (m, 1H), 7.40-7.61 (m, 6H), 7.90 (d, *J* = 9.3Hz, 1H), 13.20 (br s, 1H); MS $[M+H]^+$: 456.38

Example-146

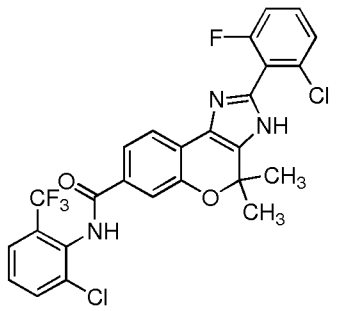
2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-*N*-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide



To the solution of 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.030 g, 0.080 mmol) in DCM:THF was added N-methyl morpholine (0.017 g, 0.169 mmol), 4-methyl-1,3-thiazol-2-amine (0.009 g, 0.080 mmol). The reaction mass was stirred at RT for 30 mins. Then EDC HCl (0.016 g, 0.080 mmol), HOBT (0.013g, 0.080 mmol) and DMAP (0.002 g, 0.001 mmol) was added and the reaction mass was stirred at 60°C for 12 hours. THF was removed under reduced pressure and acidified with dil HCl and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.010 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.66 (s, 6H), 2.11 (s, 3H), 7.21 (s, 1H), 7.43-7.57 (m, 5H), 7.59 (m, 1H), 12.20 (s, 1H), 13.23 (s, 1H); MS $[M+H]^+$: 469.20.

Example-147

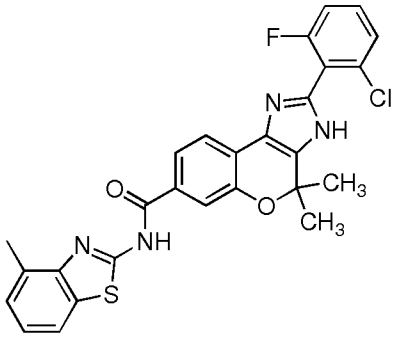
2-(2-Chloro-6-fluorophenyl)-*N*-[2-chloro-6-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide



To a solution of 2-chloro-6-(trifluoromethyl)aniline (0.119 g, 0.607 mmol) in THF was added sodium hydride (0.022 g, 0.607 mmol) at 10-15°C. The reaction mass was stirred for 30 mins. Then added 4-hydroxyphenyl 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylate (Intermediate-64, 0.100 g, 0.202 mmol). The reaction mass was stirred at RT for 5-6 h. The reaction mass was quenched in water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated under vacuum to afford 0.005 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.58 (s,6H), 7.37-7.57 (m, 7H), 8.36 (br s, 2H), 9.02 (s, 1H), 13.13 (brs, 1H); MS $[M+H]^+$: 549.33.

Example-148

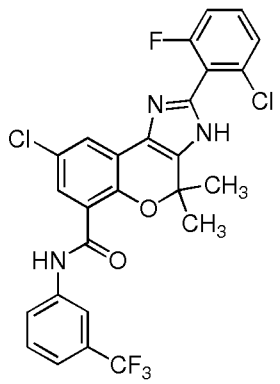
2-(2-Chloro-6-fluorophenyl)-4,4-dimethyl-*N*-(4-methyl-1,3-benzothiazol-2-yl)-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide



The title compound was prepared following the procedure described for Example-131 but starting from 2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxylic acid (Intermediate-62, 0.060 g, 0.161 mmol), 4-methyl-1,3-benzothiazol-2-amine (0.029 g, 0.177 mmol), N-methyl morpholine (0.040 g, 0.403 mmol), EDC HCl (0.031 g, 0.161 mmol), HOBT (0.025g, 0.161 mmol), DMAP (0.004 g, 0.032 mmol) and THF (3 mL) to afford 0.008 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.64 (s,6H), 2.72 (s, 3H), 7.22-7.27 (m, 2H), 7.45 (m, 1H), 7.53 (d, J = 8.4Hz, 2H), 7.60-7.66 (m, 2H), 7.81(d, J = 6.3Hz, 2H), 12.75 (br s, 1H), 13.30 (br s, 1H); MS $[M+H]^+$: 519.31.

Example-149

8-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-N-(3-(trifluoromethyl)phenyl)-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxamide



To 8-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxylic acid (Intermediate-79, 0.080 g, 0.195 mmol) was added thionyl chloride (5.0 mL).The reaction mass was refluxed for 2-3 h. The reaction mass was cooled at RT and diluted with THF.

Meanwhile, to a solution of 3-(trifluoromethyl)aniline (0.095 g, 0.586 mmol) in THF was added DIPEA (1.0 mL).The reaction mass was stirred at RT for 1 h. To this reaction mass above prepared acid chloride solution was added at 5-10°C. The whole reaction mass was stirred at RT for 2-3 h. Excess of solvent was removed under vacum and the reaction mass was quenched in water, extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated to afford 0.015 g of desired product. ^{1}HNMR (DMSO-d_6): δ 1.65 (s, 6H), 7.41-7.63 (m, 7H), 7.86 (d, J = 7.8 Hz, 1H), 8.26 (s, 1H), 10.53 (s, 1H), 13.22 (s, 1H); MS $[M+H]^+$:548.24.

The compounds of Table-10 were prepared following the procedure described for the preparation of Example 149

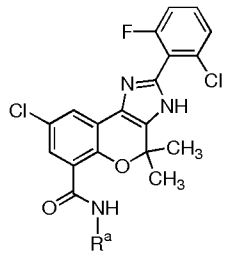
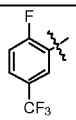
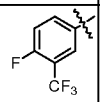
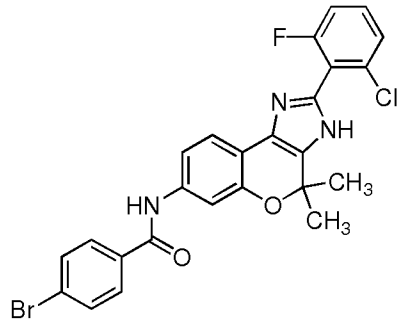


Table-10

Ex No.	R^a	Starting material	Analytical details
150		Intermediate-79 (0.080 g, 0.195 mmol), DIPEA (1.0 mL), 2-fluoro-5-trifluoromethyl aniline (0.105 g, 0.586 mmol), thionyl chloride (5.0 mL), THF (10.0 mL)	Yield: 0.010 g ^{1}HNMR (DMSO d_6): δ 1.78 (s, 6H), 7.45-7.79 (m, 7H), 8.82 (s, 1H), 10.64 (s, 1H), 13.31 (s, 1H); MS $[M+H]^+$: 568.07
151		Intermediate-79 (0.080 g, 0.195 mmol), DIPEA (1.0 mL), 4-fluoro-3-trifluoromethyl aniline (0.105 g, 0.586 mmol), thionyl chloride (5.0 mL), THF (10.0 mL)	Yield: 0.025 g ^{1}HNMR (DMSO d_6): δ 1.64 (s, 6H), 7.41-7.62 (m, 5H), 7.92 (m, 1H), 8.25 (m, 1H), 10.54 (s, 1H), 13.21 (s, 1H); MS $[M+H]^+$: 568.07

Example-152

4-Bromo-*N*-[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]benzamide



The title compound was prepared following the procedure described for step-2 of Intermediate-1 but starting from 4-bromo-*N*-(2,2-dimethyl-3,4-dioxo-3,4-dihydro-2*H*-chromen-7-yl)benzamide (Intermediate-65, 0.140 g, 0.374 mmol), 2-chloro-6-fluoro benzaldehyde (0.080 g, 0.449 mmol), ammonium acetate (0.202 g, 2.62 mmol) and acetic acid (4 mL) to afford 0.030 g of desired product. ^{1}HNMR (DMSO d_6): δ 1.59 (s,6H), 7.36 (s, 2H), 7.43 (d, J = 6.9Hz, 2H), 7.49-7.59 (m, 2H), 7.75 (d, J = 8.1Hz, 2H), 7.88 (d, J = 8.1Hz, 2H),10.29 (s, 1H), 12.96 (s, 1H); MS $[M+H]^+$: 526.41.

The compounds of Table-11 were prepared following the procedure described for the preparation of Example 152.

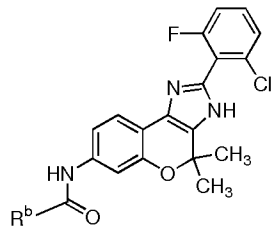
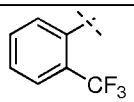
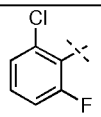


Table-11

Ex No.	R^b	Starting material	Analytical details
153		Intermediate-66 (0.180 g, 0.472 mmol), 2-chloro-6-fluoro benzaldehyde (0.112 g, 0.708 mmol), ammonium acetate (0.256 g, 3.32 mmol) and acetic acid (4 mL)	Yield: 0.015 g ^{1}HNMR (DMSO d_6): δ 1.59 (s, 6H), 7.29-7.44 (m, 5H), 7.49-7.59 (m, 2H), 7.69-7.72 (m, 1H), 7.80 (d, J = 7.2Hz, 1H), 7.85 (d, J = 7.2Hz, 1H), 10.55 (br s, 1H), 12.98 (br s, 1H); MS $[M+H]^+$: 516.39
154		Intermediate-67 (0.180 g, 0.498	Yield: 0.010 g

		mmol), 2-chloro-6-fluoro benzaldehyde (0.095 g, 0.598 mmol), ammonium acetate (0.268 g, 3.49 mmol) and acetic acid (3 mL)	^{1}HNMR (DMSO d_6): δ 1.59 (s, 6H), 7.28-7.57 (m, 9H), 10.78 (s, 1H), 13.00 (br s, 1H); MS $[M+H]^+$: 500.28

Pharmacological activity

In-vitro Protocol for screening of mPGES-1 inhibitors:

mPGES-1 (microsomal prostaglandin E synthase-1) is a microsomal enzyme that converts endoperoxide substrate PGH_2 (prostaglandin H_2) to product PGE_2 (prostaglandin E_2) by isomerization in the presence of reduced glutathione (GSH). mPGES-1 inhibitors were screened by assessing their ability to inhibit formation of PGE_2 from PGH_2 in presence of mPGES-1 using anti-PGE_2 antibody based detection method. Recombinant human mPGES-1 was generated in-house by expressing in CHO cells (Ouellet M *et al.* (2002), Protein Expression and Purification 26: 489 – 495). Assay was set up using crude microsomal fractions at protein concentration of 40-60 g/mL. Test compounds were prepared in 100 % dimethyl sulfoxide (DMSO) to obtain 20 mM stock solution and then diluted using assay buffer comprising 0.1 M Potassium phosphate buffer with 2 mM EDTA. Final concentration of DMSO in reaction was 0.5 % (v/v). Negative controls comprised of all assay reagents except the enzyme. Positive controls comprised of enzyme reaction in the absence of any inhibitor. Test compounds were incubated for 10 minutes in assay buffer containing 2.5 mM GSH and mPGES-1 enzyme followed by addition of PGH_2 at a concentration of 15 M for 1 minute. Reaction was stopped by addition of Stannous chloride (11mg/ml) and PGE_2 levels were measured (Masse F *et al.* (2005), Journal of Biomolecular Screening 10(6) 599 – 605., Goedken RE *et al.* (2008), Journal of Biomolecular Screening 13(7): 619 – 625) by HTRF kit (CisBio).

Inhibition of mPGES-1 enzyme activity was measured using percent of reaction occurring in the positive control. Concentration response curves were plotted using percent inhibition of maximum enzyme reaction. IC_{50} value was calculated from concentration response curve by nonlinear regression analysis using GraphPad PRISM software.

The compounds prepared were tested using the above assay procedure and the results obtained are given in Table 12. Percentage inhibition at concentrations of 1.0 μM and 10.0 μM are given in the table along with IC_{50} (nM) details for selected examples. The IC_{50} (nM) values of the compounds are set forth in Table 12 wherein "A" refers to an IC_{50} value of less than 250 nM, "B" refers to IC_{50} value in range of 250.01 to 500.0 nM and "C" refers to IC_{50} values more than 500 nM.

Table-12: In-vitro screening results of compounds of the invention:

Examples	**% inhibition at**		**IC_{50} (nM)**
	1 uM	**10 uM**	
Example-1	53.56	77.6	-
Example-2	50.99	87.08	C
Example-3	73.96	88.7	B
Example-4	58.65	95.98	C
Example-5	68.56	91.97	C
Example-6	46.8	94.09	C
Example-7	33.79	89.03	-
Example-8	9.89	32.09	-
Example-9	76.04	94.3	B
Example-10	82.51	89.05	A
Example-11	91.41	94.62	A
Example-12	70.08	86.89	-
Example-13	81.37	83.31	A
Example-14	99.51	98.98	A
Example-15	97.93	91.77	A
Example-16	92.94	98.52	A
Example-17	25.41	72.22	
Example-18	25.73	76.84	
Example-19	4.13	62.14	
Example-20	85.9	96.3	A
Example-21	46.1	96.4	

Examples	% inhibition at		IC_{50} (nM)
	1 uM	10 uM	
Example-22	13.19	62.1	-
Example-23	67.71	96.36	A
Example-24	84.37	84.31	A
Example-25	82.64	89.51	A
Example-26	87.14	87.05	A
Example-27	50.34	83.04	-
Example-28	NT		-
Example-29	14.77	23.76	-
Example-30	15.64	39.66	-
Example-31	87.53	92.22	A
Example-32	69.39	71.34	
Example-33	91.92	99.5	A
Example-34	66.25	93.29	C
Example-35	76.65	76.36	A
Example-36	22.13	51.99	-
Example-37	39.63	74.04	-
Example-38	59.76	82.86	C
Example-39	80.07	92.52	B
Example-40	75.94	83.51	C
Example-41	50.32	92.9	C
Example-42	91.28	90.7	A
Example-43	89.15	90..28	A
Example-44	87.31	89.49	A
Example-45	91.93	93.76	A
Example-46	97.78	94.23	A
Example-47	87.96	88.7	A
Example-48	67.7	87.4	A
Example-49	85	91.9	A
Example-50	95.94	85.5	A
Example-51	91.93	92.71	A
Example-52	65.05	87.31	A
Example-53	84.04	80.09	A
Example-54	92.24	90.15	A
Example-55	85	90.21	A
Example-56	84.3	85.28	A
Example-57	90.62	93.85	A

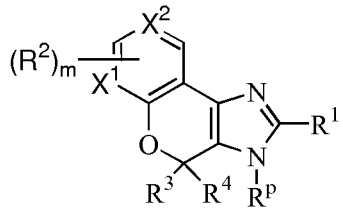
Examples	% inhibition at		IC_{50} (nM)
	1 uM	10 uM	
Example-58	93.58	93.69	A
Example-59	92.1	90.52	A
Example-60	92.35	93.31	A
Example-61	92.25	92.9	A
Example-62	89.41	93.13	A
Example-63	21.02	40.46	-
Example-64	61.4	82.32	B
Example-65	86.17	91.85	A
Example-66	86.67	92.13	A
Example-67	65.48	72.20	-
Example-68	85.58	92.82	A
Example-69	86.41	93.07	A
Example-70	79.88	82.16	A
Example-71	89.53	97.05	A
Example-72	89.30	91.90	A
Example-73	81.71	78.98	A
Example-74	86.50	89.78	A
Example-75	86.15	86.01	A
Example-76	88.86	86.56	A
Example-77	84.79	87.39	A
Example-78	93.19	95.78	A
Example-79	74.35	83.64	-
Example-80	72.37	78.16	-
Example-81	54.47	64.18	-
Example-82	58.60	71.70	-
Example-83	15.51	39.79	-
Example-84	64.16	75.11	-
Example-85	37.26	59.09	-
Example-86	64.75	72.03	-
Example-87	89.97	86.61	A
Example-88	53.36	66.82	-
Example-89	46.33	54.72	-
Example-90	33.08	36.57	-
Example-91	13.40	9.21	-
Example-92	85.98	96.11	A
Example-93	93.46	95.40	A

Examples	% inhibition at		IC_{50} (nM)
	1 uM	10 uM	
Example-94	98.55	99.78	A
Example-95	94.15	99.50	A
Example-96	93.36	98.21	A
Example-97	68.16	77.39	-
Example-98	50.88	77.90	-
Example-99	72.93	92.29	-
Example-100	48.32	94.47	-
Example-101	69.65	96.61	-
Example-102	89.57	97.66	A
Example-103	91.22	93.17	A
Example-104	31.23	24.05	-
Example-105	90.31	90.47	A
Example-106	67.62	75.76	-
Example-107	76.42	94.85	B
Example-108	98.7	100	A
Example-109	99.39	97.37	A
Example-110	94.25	99.12	A
Example-111	98.89	96.14	A
Example-112	98.74	93.23	A
Example-113	97.99	99.39	A
Example-114	90.37	97.69	A
Example-115	91.26	97.57	A
Example-116	20.61	65.63	
Example-117	83.37	83.14	B
Example-118	75.16	76.39	-
Example-119	65.80	63.96	-
Example-120	55.71	90.26	
Example-121	44.81	88.75	
Example-122	85.62	87.45	B
Example-123	62.19	76.61	-
Example-124	57.88	88.69	-
Example-125	46.80	67.92	-
Example-126	65.71	87.15	-
Example-127	83.85	91.47	B
Example-128	89.00	98.58	A
Example-129	58.7	95.1	

Examples	% inhibition at		IC_{50} (nM)
	1 uM	10 uM	
Example-130	12.2	75.5	
Example-131	86.69	92.80	B
Example-132	79.70	84.83	B
Example-133	36.36	54.22	-
Example-134	37.75	47.06	-
Example-135	56.03	67.99	-
Example-136	70.36	83.60	-
Example-137	28.81	75.84	-
Example-138	81.69	82.57	A
Example-139	40.52	52.91	-
Example-140	83.54	84.52	A
Example-141	53.54	49.85	-
Example-142	53.91	59.55	-
Example-143	78.95	87.38	-
Example-144	61.91	65.94	-
Example-145	14.94	46.57	-
Example-146	52.78	67.15	-
Example-147	13.26	28.66	-
Example-148	58.62	79.64	-
Example-149	33.47	55.51	-
Example-150	35.54	44.89	-
Example-151	43.0	51.67	-
Example-152	78.92	80.57	-
Example-153	6.16	60.85	-
Example-154	27.93	70.27	-

Claims:

1. A compound of formula (I):



(I)

wherein,

X^1 and X^2 are independently selected from –CH- and –N-;

R^1 is selected from substituted or unsubstituted aryl and heteroaryl;

R^2, at each occurrence, is independently selected from halogen, $-C\equiv CR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)R^b$, $-OR^a$, substituted or unsubstituted aryl, heteroaryl and heterocyclic ring;

R^3 and R^4 may be same or different, are independently selected from substituted or unsubstituted alkyl or R^3 and R^4 taken together with the carbon atom to which they are attached may form an optionally substituted 3 to 7 membered saturated or unsaturated cyclic ring, which may optionally include heteroatoms selected from O, N or S;

R^a and R^b, at each occurrence, are independently selected from hydrogen, hydroxyl, halogen, substituted or unsubstituted alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclic ring, and heterocyclylalkyl;

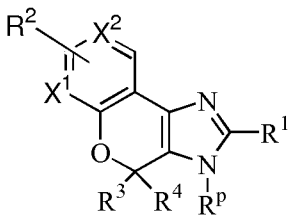
R^p is hydrogen, substituted or unsubstituted alkyl or arylalkyl;

'm' is integer selected from 0 to 3, both inclusive;

and at each occurrence, 'n' is integer selected from 0 to 3, both inclusive;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 having the formula (Ia),



(Ia)

wherein,

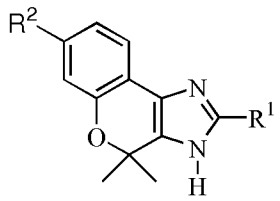
X^1, X^2, R^1, R^3, R^4, and R^p are as defined in claim 1;

R^2 is selected from halogen, substituted or unsubstituted aryl, herteroaryl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1 or 2 having the formula (Ia')



(Ia')

wherein,

R^1 is substituted or unsubstituted aryl, wherein the substitution(s) on the substituted group are one or more selected from halogen and cyano;

R^2 is selected from halogen, substituted or unsubstituted aryl, herteroaryl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, cyano, $-OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl and cycloalkyl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 3, wherein R^2 is substituted phenyl and the substituents are halogen, trifluoromethyl, trifluoromethoxy, trifluoroethoxy and methylsulfonyl.

5. The compound according to claim 3, wherein R^2 is benzimidazole.

6. The compound according to claim 3, wherein R^2 is substituted oxadiazole and the substituents are propyl or cyclopropyl.

7. The compound according to claim 3 selected from

7-chloro-2-(2,6-dibromophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,

7-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
7-bromo-2-(2,6-dibromophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
7-bromo-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
7-bromo-2-[4-fluoro-6-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
7-bromo-2-[2-chloro-3-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-7-(4-chlorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-[3-(trifluoromethyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-[4-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-[4-(trifluoromethyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-{4,4-dimethyl-7-[3-(2,2,2-trifluoroethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}-3-isocyanobenzonitrile,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-[3-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-{4,4-dimethyl-7-[3-(trifluoromethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile,
2-{4,4-dimethyl-7-[3-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile
2-{4,4-dimethyl-7-[4-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile,
2-{4,4-dimethyl-7-[2-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile,
2-{4,4-dimethyl-7-[2-(methylsulfonyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile,

2-{4,4-dimethyl-7-[2-(2,2,2-trifluoroethoxy)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile,

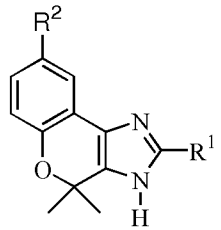
2-(2-chloro-6-fluorophenyl)-7-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-[3-(propan-2-yl)-1,2,4-oxadiazol-5-yl]-1,4-dihydrochromeno[3,4-*d*]imidazole and

7-(1*H*-benzimidazol-2-yl)-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole

or a pharmaceutically acceptable salt thereof.

8. A compound according to claim 1 or 2 having the formula (Ia'')



(Ia'')

wherein,

R^1 is substituted or unsubstituted aryl, wherein the substitution(s) on the substituted group are one or more selected halogen and cyano; and

R^2 is halogen.

or a pharmaceutically acceptable salt thereof.

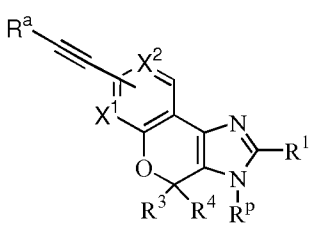
9. The compound according to claim 8 selected from

8-bromo-2-(2,6-dibromophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole and

8-bromo-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole

or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 1 having the formula (Ib):



(Ib)

wherein,

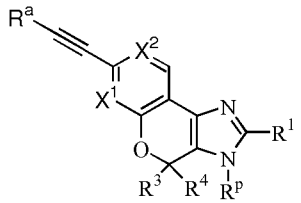
X^1, X^2, R^1, R^3, R^4, and R^p are as defined in claim 1;

R^a is selected from hydrogen, substituted or unsubstituted alkyl, cycloalkyl, aryl, heteroaryl, heteroarylalkyl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

11. A compound according to claim 1 or 10 having the formula (Ia'):



(Ib')

wherein,

X^1, X^2, R^1, R^3, R^4, and R^p are as defined in claim 1;

R^a is selected from hydrogen, substituted or unsubstituted alkyl, cycloalkyl, aryl, heteroaryl and heterocyclic ring; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

12. The compound according to claim 11, wherein R^1 is substituted aryl or heteroaryl.

13. The compound according to claim 12, wherein substituents are halogen, cyano, alkyl, haloalkyl or haloalkoxy.

14. The compound according to claim 11, wherein X^1 and X^2 is CH.

15. The compound according to claim 11, wherein either of X^1 and X^2 is N.

16. The compound according to claim 11, wherein R^P is hydrogen.

17. The compound according to claim 11, wherein both R^3 and R^4 are methyl.

18. The compound according to claim 11, wherein R^3 and R^4 combine together to form a cyclobutyl ring.

19. The compound of claim 11, wherein R^a is 2-hydroxy-prop-2-yl.

20. The compound of claim 11, wherein R^a is substituted or unsubstituted aryl, heteroaryl or cycloalkyl.

21. The compound of claim 20, wherein R^a is phenyl, thiazole, thiadiazole, pyridine pyrimidine or isoquinoline.

22. The compound of claim 20, wherein substituents are halogen, cyano, alkyl, nitro, COOH, alkyl-C(O)O-, alkoxy, haloalkyl, haloalkoxy, alkylsulfinyl, aryl, heteroaryl and heterocyclic ring.

23. The compound according to claim 11 selected from:

2-[4,4-dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl]isophthalonitrile,

4-[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]-2-methylbut-3-yn-2-ol,

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-(phenylethynyl)-1,4-dihydrochromeno[3,4-*d*]imidazole,

2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-nitro-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,

acetic acid 4-[2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazol-7-ylethynyl]-phenyl ester,

2-(2-chloro-6-fluoro-phenyl)-7-(2,3-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-trifluoromethyl-thiazol-2-ylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-7-(4-chloro-3-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-7-(3,5-dichloro-pyridin-4-ylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(5-trifluoromethyl-[1,3,4]thiadiazol-2-ylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(4-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
7-biphenyl-4-ylethynyl-2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-p-tolylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-pyrimidin-5-ylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-isoquinolin-5-ylethynyl-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-pyrimidin-2-ylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-pyridin-3-ylethynyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3-fluoro-pyridin-4-ylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(5-trifluoromethyl-pyridin-2-ylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
4-[2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazol-7-ylethynyl]-benzonitrile,
2-(2-chloro-6-fluoro-phenyl)-7-(6-fluoro-pyridin-3-ylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3-chloro-4-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3-chloro-2-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2-chloro-5-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-7-(2,5-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3,5-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-methoxy-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3-chloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2-chloro-4-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2-chloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-chloro-2-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3-chloro-4-methyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-chloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(3-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3,4-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(3-fluoro-5-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-fluoro-3-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-chloro-2-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(2-chloro-6-fluoro-phenyl)-7-(2-fluoro-4-trifluoromethyl-penylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(5-chloro-2-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(5-methyl-[1,3,4]thiadiazol-2-ylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(5-methyl-thiazol-2-ylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2-fluoro-6-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(5-fluoro-2-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4,5-dimethyl-thiazol-2-ylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(2-trifluoromethoxy-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2,6-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
7-(2,5-bis-trifluoromethyl-phenylethynyl)-2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(2,3,4-trifluoro-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(2,4,6-trifluoro-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(4-methoxy-2-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
7-(4-chloro-2,6-difluoro-phenylethynyl)-2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2,5-dichloro-4-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,

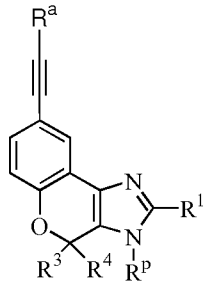
2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-7-(2,4,5-trifluoro-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2,3-dichloro-4-fluoro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(2-chloro-6-fluoro-phenyl)-7-(2-difluoromethoxy-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}benzonitrile,
2-(2-chloro-6-fluorophenyl)-7-[(2-ethoxyphenyl)ethynyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(1,3,4-oxadiazol-2-yl)phenyl]ethynyl}-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl]ethynyl}-1,4-dihydrochromeno[3,4-*d*]imidazole,
1-(2-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}phenyl)pyrrolidin-2-one,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(2,2,2-trifluoroethoxy)phenyl]ethynyl}-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(methylsulfinyl)phenyl]ethynyl}-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-7-[(2-chloro-4-methylphenyl)ethynyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-7-{[4-methoxy-2-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2,6-difluorophenyl)-4,4-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-1,4-dihydrochromeno[3,4-*d*]imidazole,
7-[(3,5-dichlorophenyl)ethynyl]-2-(2,6-difluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
4,4-dimethyl-2-(4-methyl-thiazol-2-yl)-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,

2-(4,5-dimethyl-thiazol-2-yl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3-chloro-5-fluoropyridin-4-yl)-7-{[2-chloro-4-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(3,5-dichloro-pyridin-4-yl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
7-(2,5-dichloro-phenylethynyl)-2-(3,5-dichloro-pyridin-4-yl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
7-(2-chloro-5-trifluoromethyl-phenylethynyl)-2-(3,5-dichloro-pyridin-4-yl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
7-(3,4-dichloro-phenylethynyl)-2-(3,5-dichloro-pyridin-4-yl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3-chloro-pyridin-4-yl)-4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3-chloro-pyridin-4-yl)-7-(2,5-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3-chloro-pyridin-4-yl)-7-(5-fluoro-2-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3,5-dichloro-pyridin-4-yl)-7-(2-fluoro-6-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3-chloro-pyridin-4-yl)-7-(2-fluoro-6-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3,5-dichloro-pyridin-4-yl)-7-(5-fluoro-2-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazole,
2-(3-chloro-5-fluoropyridin-4-yl)-4,4-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-7-{[2-(trifluoromethyl)phenyl]ethynyl}-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane],
2-(2-chloro-6-fluorophenyl)-7-{[4-chloro-2-(trifluoromethyl)phenyl]ethynyl}-1*H*-spiro[chromeno[3,4-*d*]imidazole-4,1'-cyclobutane,

4-[4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazol-2-yl]-pyridine-3,5-dicarbonitrile,
2-[7-(2-chloro-5-trifluoromethyl-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazol-2-yl]-isophthalonitrile,
2-[7-(2,5-dichloro-phenylethynyl)-4,4-dimethyl-1,4-dihydro-chromeno[3,4-d]imidazol-2-yl]-isophthalonitrile,
2-[4,4-dimethyl-7-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazol-2-yl]-isophthalonitrile,
2-[4,4-dimethyl-7-(2-trifluoromethoxy-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazol-2-yl]-isophthalonitrile,
2-(7-{[2-fluoro-6-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl)benzene-1,3-dicarbonitrile,
2-{7-[(2,6-dichlorophenyl)ethynyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl}benzene-1,3-dicarbonitrile,
2-(7-{[2-(difluoromethoxy)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl)benzene-1,3-dicarbonitrile,
2-(7-{[3-chloro-5-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-2-yl)benzene-1,3-dicarbonitrile,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-(phenylethynyl)-1,4-dihydroimidazo[4',5':4,5]pyrano[2,3-*b*]pyridine,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-1,4-dihydroimidazo[4',5':4,5]pyrano[2,3-*b*]pyridine,
2-(2-chloro-6-fluorophenyl)-7-{[2-fluoro-6-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydroimidazo[4',5':4,5]pyrano[2,3-*b*]pyridine,
2-(2-chloro-6-fluorophenyl)-7-{[2-chloro-5-(trifluoromethyl)phenyl]ethynyl}-4,4-dimethyl-1,4-dihydroimidazo[4',5':4,5]pyrano[2,3-*b*]pyridine,
1-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}cyclohexanol,
1-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}cyclopentanol,

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(trifluoromethyl)phenyl]ethynyl}-1,4-dihydroimidazo[4',5':4,5]pyrano[3,2-*c*]pyridine and
2-{[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]ethynyl}benzoic acid
or a pharmaceutically acceptable salt thereof.

24. A compound according to claim 1 or 10 having the formula (Ib''),



(Ib'')

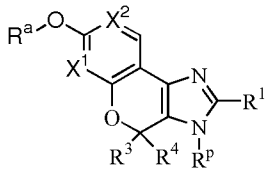
wherein,

R^1, R^3, R^4 and R^p are as defined in claim 1;

R^a is selected from hydrogen and substituted or unsubstituted aryl; whererin the substitution on the substituted groups are one or more selected from halogen, substituted or unsubstituted alkyl and haloalkyl;
or a pharmaceutically acceptable salt thereof.

25. The compound according to claim 24 wherein the compound is
2-(2-Chloro-6-fluoro-phenyl)-4,4-dimethyl-8-(2-trifluoromethyl-phenylethynyl)-1,4-dihydro-chromeno[3,4-d]imidazole
or a pharmaceutically acceptable salt thereof.

26. A compound according to claim 1 having the formula (Ic),



(Ic)

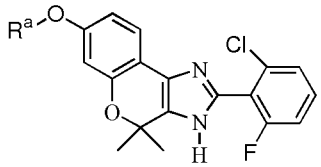
wherein,

X^1, X^2, R^1, R^3, R^4, and R^p are as defined in claim 1;

R^a is selected from hydrogen, substituted or unsubstituted cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl and heteroarylalkyl, whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, -OR_x, -$OC(O)R_x$, -$C(O)OR_x$, -SO_2R_x, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;
or a pharmaceutically acceptable salt thereof.

27. A compound according to claim 1 or 26 having the formula (Ic'),



(Ic')

wherein,

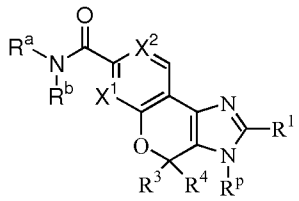
R^a is selected from substituted or unsubstituted cycloalkyl and arylalkyl, whererin the substitution on the substituted group is haloalkyl;
or a pharmaceutically acceptable salt thereof.

28. The compound according to claim 27, wherein R^a is substituted phenylalkyl and the substituent is trifluoromethyl.

29. The compound according to claim 27, wherein R^a is cyclopentyl.

30. The compound according to claim 27 selected from
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[2-(trifluoromethyl)benzyl]oxy}-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-7-(cyclopentyloxy)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[3-(trifluoromethyl)benzyl]oxy}-1,4-dihydrochromeno[3,4-*d*]imidazole and
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-7-{[4-(trifluoromethyl)benzyl]oxy}-1,4-dihydrochromeno[3,4-*d*]imidazole
or a pharmaceutically acceptable salt thereof.

31. A compound according to claim 1 having the formula (Id),



(Id)

wherein,

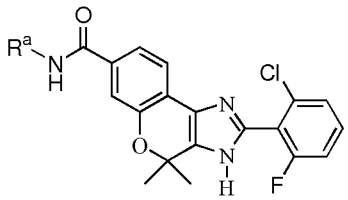
X^1, X^2, R^1, R^3, R^4 and R^p are as defined in claim 1;

R^a and R^b are independently selected from hydrogen, substituted or unsubstituted alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, heterocyclic ring and heterocyclylalkyl; whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R_x is selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

32. A compound according to claim 1 or 31 having the formula (Id'),



(Id')

wherein,

R^a is selected from substituted or unsubstituted alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl and heteroaryl, whererin the substitution on the substituted groups are one or more selected from halogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

33. The compound according to claim 32, wherein R^a is substituted or unsubstituted aryl or heteroaryl.

34. The compound according to claim 32, wherein R^a is substituted phenyl, thiazole or benzthiazole.

35. The compound according to claim 33 or 34, wherein the substitution is halogen, methyl or trifluoromethyl.

36. The compound according to claim 32, wherein R^a is 6,6-dimethylbicyclo[3.1.1]hept-3-yl, 2,6,6-trimethylbicyclo[3.1.1]hept-3-yl, cyclohexyl, cyclohexylethyl, cyclopentyl, adamantan-1-yl or 3,3-dimethyl-2-butyl.

37. The compound according to claim 32 selected from

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-*N*-[4-(trifluoromethyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-(3-chloro-4-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-*N*-[4-(trifluoromethyl)benzyl]-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-[(6,6-dimethylbicyclo[3.1.1]hept-3-yl)methyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-cyclohexyl-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-*N*-[3-(trifluoromethyl)phenyl]-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-(2-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-(3,4-dichlorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-cyclopentyl-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-*N*-(4-chloro-3-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

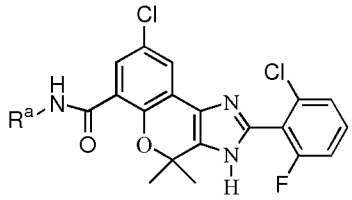
2-(2-chloro-6-fluorophenyl)-*N*-(1-cyclohexylethyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-*N*-(2,6,6-trimethylbicyclo[3.1.1]hept-3-yl)-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

N-(4-bromophenyl)-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,

2-(2-chloro-6-fluoro-phenyl)-4,4-dimethyl-3,4-dihydro-chromeno[3,4-d]imidazole-7-carboxylic acid adamantan-1-ylamide,
2-(2-chloro-6-fluorophenyl)-*N*-(3,3-dimethylbutan-2-yl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-*N*-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide,
2-(2-chloro-6-fluorophenyl)-*N*-[2-chloro-6-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide and
2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-*N*-(4-methyl-1,3-benzothiazol-2-yl)-1,4-dihydrochromeno[3,4-*d*]imidazole-7-carboxamide
or a pharmaceutically acceptable salt thereof.

38. A compound according to claim 1 having the formula (Ie),



(Ie)

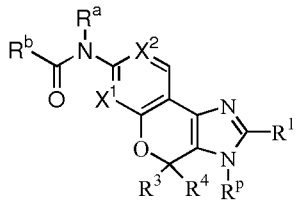
wherein,

R^a is substituted or unsubstituted aryl, whererin the substitution on the substituted group are one or more selected from halogen and substituted or unsubstituted haloalkyl or a pharmaceutically acceptable salt thereof.

39. The compound according to claim 38, whererin R^a is substituted phenyl and the substituents are halogen and trifluoromethyl.

40. The compound according to claim 38 selected from
8-chloro-2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-N-(3-(trifluoromethyl)phenyl)-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxamide,
8-chloro-2-(2-chloro-6-fluorophenyl)-N-(2-fluoro-5-(trifluoromethyl)phenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxamide and
8-chloro-2-(2-chloro-6-fluorophenyl)-N-(4-fluoro-3-(trifluoromethyl)phenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazole-6-carboxamide
or a pharmaceutically acceptable salt thereof.

41. A compound according to claim 1 having the formula (If),



(If)

wherein,

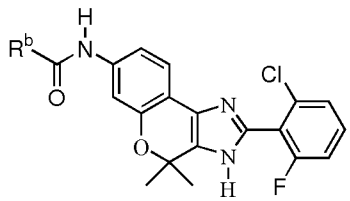
X^1, X^2, R^1, R^3, R^4, and R^p are as defined in claim 1;

R^b is selected from substituted or unsubstituted aryl and heteroaryl, whererin the substitution on the substituted groups are one or more selected from halogen, nitro, cyano, hydroxyl, $-OR_x$, $-OC(O)R_x$, $-C(O)OR_x$, $-SO_2R_x$, substituted or unsubstituted alkyl, haloalkyl, cycloalkyl, aryl and heteroaryl; and

R^a and R_x are independently selected from hydrogen, substituted or unsubstituted alkyl and haloalkyl;

or a pharmaceutically acceptable salt thereof.

42. A compound according to claim 1 or 41 having the formula (If'),



(If')

wherein,

R^b is selected from substituted or unsubstituted aryl, whererin the substitution on the substituted group are one or more selected from halogen and substituted or unsubstituted haloalkyl;

or a pharmaceutically acceptable salt thereof.

43. The compound according to claim 42, whererin R^b is substituted phenyl and the substituents are halogen or trifluoromethyl.

44. The compound according to claim 42 selected from

4-bromo-*N*-[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]benzamide,

N-[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-*d*]imidazol-7-yl]-2-(trifluoromethyl)benzamide and

2-chloro-N-[2-(2-chloro-6-fluorophenyl)-4,4-dimethyl-1,4-dihydrochromeno[3,4-d]imidazol-7-yl]-6-fluorobenzamide

or a pharmaceutically acceptable salt thereof.

45. A pharmaceutical composition comprising a compound according to any one of claims 1 to 44, either as a free base or pharmaceutically acceptable salt form and a pharmaceutically acceptable excipient.

46. The pharmaceutical composition according to claim 45, wherein the pharmaceutically acceptable excipient is a carrier or diluent.

47. The compound according to any one of claims 1 to 44 for use in prevention or treatment of a mPGES-1 mediated disease, disorder or syndrome in a subject.

48. A method of treatement of disease, disorder, syndrome or condition selected from the group consisting of asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, inflammatory bowel disease, irritable bowel syndrome, pain, inflammatory pain, chronic pain, acute pain, fever, migraine, headache, low back pain, fibromyalgia, myofascial disorders, viral infections, influenza, common cold, herpes zoster, hepatitis C, AIDS, bacterial infections, fungal infections, dysmenorrhea, burns, surgical or dental procedures, malignancies hyperprostaglandin E syndrome, classic Bartter syndrome, synovitis, atherosclerosis, gout, arthritis, osteoarthritis, juvenile arthritis, rheumatoid arthritis, juvenile onset rheumatoid arthritis, rheumatic fever, ankylosing spondylitis, Hodgkin's disease, systemic lupus erythematosus, vasculitis, pancreatitis, nephritis, bursitis, conjunctivitis, iritis, scleritis, uveitis, wound healing, dermatitis, eczema, psoriasis, stroke, diabetes mellitus, cancer, neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis and multiple sclerosis, autoimmune diseases, allergic disorders, rhinitis, ulcers, mild to moderately active ulcerative colitis, familial adenomatous polyposis, coronary heart disease, and sarcoidosis by administration of a compound according to any one of claims 1-44.

49. The method according to claim 48, wherein the symptoms of a disease or condition is associated with pain.

50. The method according to claim 48, wherein the symptoms of a disease or condition is associated with chronic or acute pain.

51. The method according to claim 48, wherein the symptoms of a disease or condition is associated with rheumatoid arthritic pain or osteoarthritic pain.

52. The method according to claim 48, wherein the symptoms of a disease or condition is associated with neurodegenerative diseases selected from Parkinson's disease, Alzheimer's disease and amyotrophic lateral sclerosis.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2011/054031

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: C07D491/-; A61K31/-; A61P29/-

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)

WPI; EPODOC; CNPAT; CNKI; REGISTRY; CAPLUS: chromeno, imidazole, benzopyrano, mpges, inflammatory, pain

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP0057932A1 (E. I. DU PONT DE NEMOURS & CO.) 18 Aug. 1982 (18. 08.1982) see examples	1-52
A	US4305954A (E. I. DU PONT DE NEMOURS & CO.) 15 Dec. 1981 (15.12.1981) see examples	1-52
A	WO9625411A1 (NEUROGEN CORP.) 22 Aug. 1996 (22.08.1996) see examples	1-52

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

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim (S) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 May 2012 (30.05.2012)	**12 Jul. 2012 (12.07.2012)**
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 CHEN, Ning Telephone No. (86-10)82246779

Form PCT/ISA /210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2011/054031

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
EP0057932A1	18.08.1982	NO820392A	06.09.1982
		FI820449A	30.09.1982
		JP57163384A	07.10.1982
		US4371541A	01.02.1983
		DK8200571A	24.01.1983
		PT74413A	31.05.1983
		ES8305364A	01.07.1983
		HUT27608A	28.10.1983
US4305954A	15.12.1981	ZA8200847A	10.08.1983
WO9625411A1	22.08.1996	AU4867496A	04.09.1996
		EP0809641A1	03.12.1997
		US5773616A	30.06.1998
		US5789410A	04.08.1998
		JPH10508871A	02.09.1998
		US5948912A	07.09.1999
		MX9706245A1	01.08.1998
		US6211366B1	03.04.2001
		CA2213197C	07.08.2001
		US2001034444A1	25.10.2001
		US6436941B1	20.08.2002
		JP3332929B2	07.10.2002

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2011/054031

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.: 48-52
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 48-52 relate to methods of surgical or therapeutic treatment of the human or animal body. The opinion is based on the following subject matter: the use of the said compounds for the manufacture of medicaments.

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

International application No.
PCT/IB2011/054031

Continuation of : A. CLASSIFICATION OF SUBJECT MATTER

C07D491/052 (2006.01)i

C07D491/147 (2006.01)i

A61K31/4164 (2006.01)i

A61P29/00 (2006.01)i