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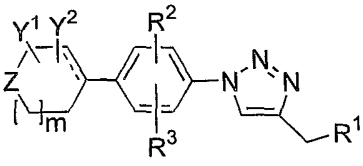
(54) Title: NOVEL ANTIINFECTIVE COMPOUNDS AND THEIR PHARMACEUTICAL COMPOSITIONS

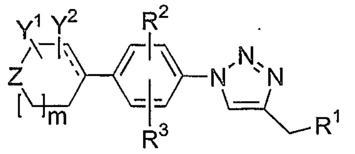


(I)

(57) Abstract: The present invention provides novel triazole compounds of formula (I), their pharmaceutically acceptable salts and their pharmaceutical compositions, where all symbols are as defined in the specification

Field of the Invention

The present invention provides novel triazole compounds of formula (I)



(I)

where R^1 represents halogen, azido, thioalcohol, isothiocyanate, hydroxy, isoindole-1,3-dione, optionally substituted alkylsulfonyloxy, arylsulfonyloxy, acyloxy group, NHR^4 where R^4 represents optionally substituted groups selected from alkyl, acyl, thioacyl, alkoxycarbonyl, cycloalkoxycarbonyl, cycloalkoxythiocarbonyl, alkenyloxycarbonyl, alkenylcarbonyl, heteroaryl, aryloxycarbonyl, heteroarylcarbonyl, heteroarylthiocarbonyl, alkoxythiocarbonyl, alkenyloxythiocarbonyl, aryloxythiocarbonyl, -C(=O)-C(=O)-alkyl, -C(=O)-C(=O)-aryl, -C(=O)-C(=O)-alkoxy, -C(=O)-C(=O)-aryloxy, -C(=O)-C(=S)-alkyl, -C(=O)-C(=S)-aryl, -C(=S)-S-alkyl, -C(=S)-NH_2, -C(=S)-NH-alkyl, -C(=S)-N-$(alkyl)_2$, -C(=S)-NH-alkenyl, -C(=S)-C(=O)-alkoxy, -C(=S)-C(=O)-aryloxy, -C(=S)-O-C(=O)- alkyl, -C(=S)-C(=S)-alkyl, -C(=S)-C(=S)-aryl, -C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl, -C(=NH)-NH_2, -C(=NH)-alkyl, -C(=NH)-aryl, -S $(O)_2$alkyl, -S$(O)_2$aryl, thiomorpholinylthiocarbonyl, pyrrolidinylthiocarbonyl or –C(=S)-N(R'R"), where R' and R" together form a optionally substituted 5 or 6 member heterocycle ring containing nitrogen and optionally having one or two additional hetero atoms selected from O, S or N; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '…' represents a bond or no bond; 'm' represents 0-3; their pharmaceutically acceptable salts and their pharmaceutical compositions containing them.

Background of the Invention

Since the discovery of penicillin, pharmaceutical companies have produced more than one hundred antibacterial agents to combat a wide variety of bacterial infections. In the past several years, there has been rapid emergence of bacterial resistance to several of these antibiotics. The multidrug resistance among these bacterial pathogens may also be due to mutation leading to more virulent clinical isolation; the most disturbing milestone has been the acquisition of resistance to vancomycin, an antibiotic generally regarded as the agent of last resort for serious Gram-positive infections. This growing multidrug resistance has recently rekindled interest in the search for new structural class of antibiotic that inhibit or kill these bacteria possibly by novel mechanisms.

A problem of larger dimension is the increasing incidence of the more virulent, methicillin-resistant *Staphylococcus aureas* (MRSA) among clinical isolates found worldwide. As with vancomycin resistant organisms, many MRSA strains are resistant to most of the known antibiotics, but MRSA strains have remained sensitive to vancomycin. However, in view of the increasing reports of vancomycin resistant clinical isolates and growing problem of bacterial resistance, there is an urgent need for new molecular entities effective against the emerging and currently problematic Gram-positive organisms.

Recently, several oxazolidinones have been discovered, which inhibit protein synthesis by binding to the 50S-ribosomal subunit which is close to the site to which chloramphenicol and lincomycin bind but their mode of action is mechanistically distinct from these two antibiotics.

Various 1, 2, 3-triazoles, 1, 2, 4-triazoles and benzotriazoles have been reported to show various biological activities and have therefore found applications in medicinal chemistry.

Some of the literature refences are:

(a) Chem. Pharm. Bull. 48(12), 1935-1946 (2000) discloses the triazoles of formula (ia) and (ib), which are reported as antifungal agents,

(b) US 6054471 discloses fluorinated triazoles of the formula (ii), which are reported for the treatment of neuropathic pain and associated hyperalgesia, including trigeminal and herpectic neuralgia, diabetic neuropathic pain, migraine, causalgia and deafferentation syndromes such as brachial plexus avulsion,

(c) J. Med. Chem., 2843, 1991 discloses compound of formula (iii), which is an anticoccidiostat and also been found to have antiproliferative activity in several disease models and to posses antimetastatic activity in a model of ovarian cancer progression,

(d) J. Heterocycl. Chem., 609, 1989 discloses compound of formula (iv), which is reported for anti-inflammatory effects,

(e) EPO publication no 0304221 A2 discloses compounds of formula (v), which are reported as antiproliferative reagents.

(f) PCT publication no. WO03/059894 (by Dr. Reddy's Laboratories Ltd.) discloses 1,2,3-triazoles as antibacterial agents.

The novel triazole compound of the present invention is useful for the treatment of various infections

Summary of the Invention

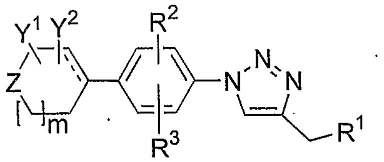
According to one aspect of the present invention, there is provided novel triazole compounds of the general formula (I) as defined above, their pharmaceutically acceptable salts and their pharmaceutical compositions containing them.

Another aspect fo the present invention provides process for the preparation of novel triazole compounds of the formula (I).

Yet another aspect of the pesent invention provides the use of novel compounds of formula (I) or its pharmaceutical compositions in the treatment of bacterial infections.

Detailed description of the Invention

The present invention provides compounds of general formula (I)



(I)

where R^1 represents halogen, azido, thioalcohol, isothiocyanate, hydroxy, isoindole-1,3-dione, optionally substituted alkylsulfonyloxy, arylsulfonyloxy, acyloxy group, NHR^4 where R^4 represents optionally substituted groups selected from alkyl, acyl, thioacyl, alkoxycarbonyl, cycloalkoxycarbonyl, cycloalkoxythiocarbonyl, alkenyloxycarbonyl, alkenylcarbonyl, heteroaryl, aryloxycarbonyl, heteroarylcarbonyl, heteroarylthiocarbonyl, alkoxythiocarbonyl, alkenyloxythiocarbonyl, aryloxythiocarbonyl, -C(=O)-C(=O)-alkyl, -C(=O)-C(=O)-aryl, -C(=O)-C(=O)-alkoxy, -C(=O)-C(=O)-aryloxy, -C(=O)-C(=S)-alkyl, -C(=O)-C(=S)-aryl, -C(=S)-S-alkyl, $-C(=S)-NH_2$, -C(=S)-NH-alkyl, $-C(=S)-N-(alkyl)_2$, -C(=S)-NH-alkenyl,

-C(=S)-C(=O)-alkoxy, -C(=S)-C(=O)-aryloxy, -C(=S)-O-C(=O)- alkyl, -C(=S)-C(=S)-alkyl, -C(=S)-C(=S)-aryl, -C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl, -C(=NH)-NH_2, -C(=NH)-alkyl, -C(=NH)-aryl, -S $(O)_2$alkyl, -S$(O)_2$aryl, thiomorpholinylthiocarbonyl, pyrrolidinylthiocarbonyl or –C(=S)-N(R'R"), where R' and R" together form a optionally substituted 5 or 6 member heterocycle ring containing nitrogen and optionally having one or two additional hetero atoms selected from O, S or N; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; their pharmaceutically acceptable salts and their pharmaceutical compositions containing them.

A 5 or 6 member heterocycle ring formed by R' & R" containing nitrogen, optionally having one or two additional heteroatoms selected from oxygen, nitrogen or sulfur, is selected from unsubstituted or substituted pyrrolidinyl, pyrrolyl, morpholinyl, thiomorpholinyl, benzothiazole, benzoimidazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl and the like.

When the groups represented by R^4, R, R^7 and heterocycles formed by R'and R" are substituted, the substituents may be selected from halogen, hydroxy, amino, cyano, nitro, alkyl, hydroxyalkyl, alkoxy, =O, =S, aryl, hydroxyaryl, pyridyl, monoalkylamino, dialkylamino, acyl, thioacyl, alkoxycarbonyl, alkoxyaryl, or carboxylic acid or its derivatives

Suitable groups represented by R^2 and R^3 may be selected from hydrogen, halogen atom, cyano, nitro, optionally substituted alkyl, haloalkyl, aryl, heteroaryl or aralkyl group.

OR^a where R^a represents optionally substituted alkyl group.

Suitable substitutents on R^2, R^3 and R^a are selected from hydroxy, halogen, nitro, amino,alkyl, alkoxy, =O, =S, cyano group, or carboxylic acid or its derivatives. These groups are as defined above.

When the groups represented by Y^1 and Y^2 are substituted, the substituents may be selected from hydroxy, nitro, cyano, amino, *tert*-butyldimethylsilyloxy (TBSO), halogen, alkyl, alkoxy, cycloalkyl, aryl, benzyloxy, acyl or acyloxy group.

When the groups represented by R^c and R^d as defined below are substituted, the substituents are selected from halogen, hydroxy, nitro, amino, cyano, alkyl or alkoxy.

When the suitable cites of the above defined groups are substituted, mono, di or tri substitutions are possible.

One aspect of the present invention provides compounds of the formula (I),
R^1 represents NHR^4 where R^4 represents optionally substituted acyl or alkoxycarbonyl;
R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;
Z represents S, SO ro SO_2;
Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

Another aspect of the present invention provides compounds of the formula (I),
R^1 represents NHR^4 where R^4 represents optionally substituted acyl or alkoxycarbonyl;
R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;
Z represents O;
Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S,

optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

Another aspect of the present invention provides compounds of the formula (I),
R^1 represents NHR^4 where R^4 represents optionally substituted thioacyl or alkoxythiocarbonyl;
R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;
Z represents S, SO ro SO_2;
Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

Another aspect of the present invention provides compounds of the formula (I),
R^1 represents NHR^4 where R^4 represents optionally substituted thioacyl or alkoxythiocarbonyl;
R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;
Z represents O;
Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

In another aspect of the compound of the formula (I), wherein:
R^4 is acyl, alkoxycarbonyl,
R^2 and R^3 independently represent hydrogen or halogen,
'm' represents 1,
'Z' represents S, SO or SO_2,
'.....' represents a bond,
R^2 and R^3 independently represent hydrogen or halogen,
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is acyl, alkoxycarbonyl,
R^2 and R^3 independently represent hydrogen or halogen,
'm' represents 1,
'Z' represents O,
'.....' represents a bond,
R^2 and R^3 independently represent hydrogen or halogen,
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is thioacyl, alkoxythiocarbonyl,
R^2 and R^3 independently represent hydrogen or halogen,
'm' represents 1,
'Z' represents S, SO or SO_2,
'.....' represents a bond,
R^2 and R^3 independently represent hydrogen or halogen,
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is thioacyl, alkoxythiocarbonyl,
R^2 and R^3 independently represent hydrogen or halogen,
'm' represents 1,

'Z' represents O,
'.....' represents a bond,
R^2 and R^3 independently represent hydrogen or halogen,
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is –C(=O)-CH_3, -C(=O)-OCH_3,
m represents 1;
'....' represents a bond;
'Z' represents S, SO or SO_2,
R^2 and R^3 independently represent hydrogen or fluorine;
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is –C(=O)-CH_3, -C(=O)-OCH_3,
m represents 1;
'....' represents a bond;
'Z' represents O,
R^2 and R^3 independently represent hydrogen or fluorine;
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is –C(=S)-CH_3, -C(=S)-OCH_3,
m represents 1;
'....' represents a bond;
'Z' represents S, SO or SO_2,
R^2 and R^3 independently represent hydrogen or fluorine;
Y^1 and Y^2 independently represent hydrogen atom.

In another aspect of the compound of the formula (I), wherein:
R^4 is –C(=S)-CH_3, -C(=S)-OCH_3,
m represents 1;

'....' represents a bond;

'Z' represents O,

R^2 and R^3 independently represent hydrogen or fluorine;

Y^1 and Y^2 independently represent hydrogen atom.

The definitions of the various groups defined above in the general formula (I) are as follows:

Halogen is fluorine, chlorine, bromine, or iodine;

Alkyl group is $(C_1\text{-}C_{10})$alkyl group. Exemplary alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl and the like, which may be substituted;

Cycloalkyl group is $(C_3\text{-}C_8)$cycloalkyl group. Exemplary cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like, which may be substituted;

Alkoxy group is $(C_1\text{-}C_{10})$alkoxy group. Exemplary alkoxy groups include methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, *tert*-butoxy and the like, which may be substituted;

Alkoxyalkyl, where alkoxy and alkyl groups are as defined above. Exemplary alkoxyalkyl groups include methoxymethyl, methoxyethyl, methoxypropyl, ethoxymethyl, ethoxyethyl, ethoxypropyl, *iso*-propoxymethyl, iso-propoxyethyl, iso-propoxypropyl and the like, which may be substituted.

Hydroxyalkyl, where alkyl group is as defined above. Exemplary hydroxyalkyl groups include hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, hydroxypentyl, hydroxyhexyl, hydroxyheptyl, hydroxyoctyl and the like, which may be substituted;

Haloalkyl, where alkyl group is as defined above. Exemplary haloalkyl groups include halomethyl, haloethyl, halopropyl, halobutyl, halopentyl, halohexyl, haloheptyl, halooctyl, haloiso-propyl, haloiso-butyl and the like, which may be substituted;

Carboxyalkyl, where alkyl group is as defined above. Exemplary carboxyalkyl groups include carboxymethyl, carboxyethyl, carboxypropyl and the like.

Monoalkylamino, where alkyl group is as defined above. Exemplary monoalkylamino groups include methylamino, ethylamino, propylamino, isopropylamino and the like, , which may be substituted;

Dialkylamino, where alkyl group is as defined above. Exemplary dialkylamino groups include dimethylamino, diethylamino and the like, which may be substituted;

Acyl group is (C_1-C_{10})acyl group. Exemplary acyl groups include $-C(=O)H$, $-C(=O)CH_3$, $-C(=O)CH_2CH_3$, $-C(=O)(CH_2)_2CH_3$, $-C(=O)(CH_2)_3CH_3$, $-C(=O)(CH_2)_4CH_3$, $-C(=O)(CH_2)_5CH_3$, $-C(=O)Ph$ and the like, which may be substituted;

Acyloxy is acyl-O-, where acyl group is defined above. Exemplary acyloxy group includes H-CO-O, acyloxy groups include acetyloxy, propionyloxy, and the like, which may be substituted;

Thioacyl group is thio(C_1-C_{10})acyl group, where acyl group is as defined above. Exemplary thioacyl groups include $-C(=S)H$, $-C(=S)CH_3$, $-C(=S)CH_2CH_3$, $-C(=S)Ph$ and the like, which may be substituted;

Alkoxycarbonyl, where alkoxy group is as defined above. Exemplary alkoxycarbonyl groups include which may be linear or branched such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl and the like, which may be substituted;

Alkylsulfonyl, where alkyl group is as defined above. Exemplary alkylsulfonyl groups include methylsulfonyl, ethylsulfonyl, propylsulfonyl and the like, which may be substituted.

Alkylsulfonyloxy, where alkyl group is as defined above. Exemplary alkylsulfonyloxy groups include methylsulfonyloxy, ethylsulfonyloxy and the like, which may be substituted.

Arylsulfonyloxy, where aryl group is as defined above. Exemplary arylsulfonyloxy groups include phenylsulfonyloxy, naphthylsulfonyloxy and the like, which may be substituted.

Cycloalkoxycarbonyl is (C_3-C_{10})cycloalkoxycarbonyl. Exemplary cycloalkoxycarbonyl group includes cyclopropoxycarbonyl, cyclobutoxycarbonyl and the like, which may be substituted;

Cycloalkoxythiocarbonyl is (C_3-C_{10})cycloalkoxythiocarbonyl. Exemplary cycloalkoxythiocarbonyl groups include cyclopropoxythiocarbonyl, cyclobutoxythiocarbonyl and the like, which may be substituted;

Alkylcarbonylaminoalkyl, where alkyl group is as defined above. Exemplary alkylcarbonylaminoalkyl groups include methylcarbonylaminomethyl, ethylcarbonylaminomethyl, methylcarbonylaminoethyl and the like, which may be substituted;

Arylcarbonylaminoalkyl, where alkyl and aryl are as defined above. Exemplary arylcarbonylaminoalkyl groups include phenylcarbonylaminomethyl, phenylcarbonylaminoethyl and the like, which may be substituted;

Alkylcarbonyloxyalkyl, where alkyl group is as defined above. Exemplary alkylcarbonyloxyalkyl group includes methylcarbonyloxymethyl, ethylcarbonylxoymethyl, methylcarbonyloxyethyl, propylcarbonyloxymethyl, propylcarbonyloxyethyl, propylcarbonyloxypropyl and the like, which may be substituted;

Alkenylcarbonyl is (C_2-C_{10})alkenylcarbonyl group. Exemplary alkenylcarbonyl groups include ethenylcarbonyl, propenylcarbonyl, butenylcarbonyl and the like, which may be substituted;

Aryl is optionally substituted monocylic or multicyclic ring system of about 6 to 14 carbon atoms. Exemplary groups include phenyl, naphthyl and the like.

Arylamino, where aryl group is as defined above. Exemplary arylamino groups include phenylamino, naphthylamino and the like.

Aryloxy group includes phenoxy, naphthyloxy and the like, which may be substituted;

Aralkyl group includes benzyl, phenethyl, $C_6H_5CH_2CH_2CH_2$, naphthylmethyl and the like, which may be substituted;

Alkoxyaryl, where alkoxy and aryl groups are as defind above. Exemplary alkoxyaryl groups incude methoxyphenyl, methoxynaphthyl, ethoxyphenyl, ethoxynaphthyl, propoxyphenyl, propoxynaphthyl and the like, which may be substituted.

Heteroaryl group includes pyridyl, furyl, thiophenyl, benzothiazoyl, purinyl, benzimidazoyl, pyrimidinyl, tetrazolyl and the like, which may be substituted;

Heteroaralkyl is heteroaryl-alkyl, where heteroayl and alkyl groups are as defined above. Exemplary heteroaryalkyl groups include imidazolemethyl, imidazoleethyl, pyridylmethyl, furyl methyl, oxazolemethyl, imidazolyl and the like, which may be substituted;

Heterocyclyl groups include pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl and the like, which may be substituted;

Heterocycloalkyl is heterocycle-alkyl, where heterocycle and alkyl groups are as defined above. Exemplary heterocylcloalkyl groups include pyrrolidinemethyl, piperidinemethyl, morpholinemethyl, piperazinemethyl and the like, which may be substituted;

Heteroarylcarbonyl, where heteroaryl group is as defined above. Exemplary heteroarylcarbonyl groups include pyridylcarbonyl, furylcarbonyl, thiophenylcarbonyl, benzothiazoylcarbonyl, benzimidazoylcarbonyl, pyrimidinylcarbonyl, pyridazinecarbonyl, pyrimidinecarbonyl, pyrazinecarbonyl, tetrazolylcarbonyl and the like, which may be substituted,

Heteroarylthiocarbonyl group includes pyridylthiocarbonyl, furylthiocarbonyl, thiophenylthiocarbonyl, benzothiazoylthiocarbonyl, benzimidazoylthiocarbonyl, pyrimidinylthiocarbonyl, pyridazinethiocarbonyl, pyrimidinethiocarbonyl, pyrazinethiocarbonyl, tetrazolylthiocarbonyl and the like, which may be substituted,

Alkenyloxycarbonyl is (C_2-C_{10})alkenyloxycarbonyl group. Exemplary alkenyloxycarbonyl groups include ethenyloxycarbonyl, propenyloxycarbonyl, butenyloxycarbonyl and the like, which may be substituted;

Aryloxycarbonyl group includes phenoxycarbonyl, benzyloxycarbonyl group and the like, which may be substituted;

Alkoxythiocarbonyl is (C_1-C_{10})alkoxythiocarbonyl group. Exemplary alkoxythiocarbonyl groups include CH_3O-C(=S)-, C_2H_5O-C(=S)- C_3H_7O-C(=S)- and the like, which may be substituted;

Alkenyloxythiocarbonyl is (C_2-C_{10})alkenyloxythiocarbonyl group. Exemplary alkenyloxythiocarbonyl group includes ethenyloxythiocarbonyl, propenyloxythiocarbonyl, butenyloxythiocarbonyl and the like, which may be substituted;

Aryloxythiocarbonyl group is (phenyl)O-C(=S)-, (benzyl)O-C(=S)- and the like, which may be substituted;

-C(=O)-C(=O)-alkyl, where alkyl group is as defined above. Exemplary -C(=O)-C(=O)-alkyl group includes -C(=O)-C(=O)methyl , -C(=O)-C(=O)ethyl, -C(=O)-C(=O)propyl and the like, which may be substituted;

-C(=O)-C(=O)-aryl group includes -C(=O)-C(=O)phenyl, -C(=O)-C(=O)naphthyl and the like, which may be substituted;

-C(=O)-C(=O)-alkoxy, where alkoxy group is as defined above. Exemplary -C(=O)-C(=O)-alkoxy groups include -C(=O)-C(=O)methoxy, -C(=O)-C(=O)ethoxy, -C(=O)-C(=O)propyloxy and the like, which may be substituted;

-C(=O)-C(=O)-aryloxy group includes -C(=O)-C(=O)phenyloxy, -C(=O)-C(=O)benzyloxy, which may be substituted;

-C(=O)-C(=S)-alkyl, where alkyl group is as defined above. Exemplary -C(=O)-C(=S)-alkyl group includes -C(=O)-C(=S)-methyl, -C(=O)-C(=S)-ethyl, -C(=O)-C(=S)-propyl, -C(=O)-C(=S)-butyl and the like, which may be substituted;

-C(=O)-C(=S)-aryl group includes -C(=O)-C(=S)-phenyl, -C(=O)-C(=S)-naphthyl and the like, which may be substituted;

-(C=S)-S-alkyl, where alkyl group is as defined above. Exemplary -(C=S)-S-alkyl groups include -(C=S)-S-methyl, -(C=S)-S-ethyl, -(C=S)-S-propyl and the like, which may be substituted;

-(C=S)-NH_2, which may be substituted;

-(C=S)-NH-alkyl, where alkyl group is as defined above. Exemplary -(C=S)-NH-alkyl groups include -(C=S)-NH-methyl, -(C=S)-NH-ethyl, -(C=S)-NH-propyl and the like, which may be substituted;

-C(=S)-N-$(alkyl)_2$, where alkyl group is as defined above. Exeplary -C(=S)-N-$(alkyl)_2$ groups includes -C(=S)-N-$(methyl)_2$, -C(=S)-N-$(ethyl)_2$, -C(=S)-N-$(propyl)_2$ and the like, which may be substituted;

-C(=S)-NH-alkenyl is -C(=S)-NH-(C_2-C_{10})alkenyl group. Exemplary -C(=S)-NH-alkenyl such as -C(=S)-NH-ethenyl, -C(=S)-NH-propenyl, -C (=S)-NH-butenyl and the like, which may be substituted;

-(C=S)-(C=O)-alkoxy, where alkoxy group is as defined above. Exemplary -(C=S)-(C=O)-alkoxy group includes -(C=S)-(C=O)-methoxy, -(C=S)-(C=O)-ethoxy, -(C=S)-(C=O)-propoxy and the like, which may be substituted;

-(C=S)-(C=O)-aryloxy includes -(C=S)-(C=O)-phenyloxy, -(C=S)-(C=O)-naphthyloxy and the like, which may be substituted;

-C(=S)-O-(C=O)-alkyl, where alkyl group is as defined as above. Exemplary -C(=S)-O-(C=O)-alkyl groups include -C(=S)-O-(C=O)-methyl, -C(=S)-O-(C=O)-ethyl, -C(=S)-O-(C=O)-propyl and the like, which may be substituted;

-C(=S)-C(=S)-alkyl, where alkyl group is as defined above. Exemplary -C(=S)-C(=S)-alkyl groups include -C(=S)-C(=S)methyl, -C(=S)-C(=S)ethyl, -C(=S)-C(=S)propyl and the like, which may be substituted;

-C(=S)-C(=S)-aryl group includes -C(=S)-C(=S)phenyl, -C(=S)-C(=S)naphthyl and the like, which may be substituted;

-C(=S)-NH-C(=O)-aryl group includes -C(=S)-NH-C(=O)-phenyl, -C(=S)-NH-C(=O)-naphthyl and the like, which may be substituted;

-C(=S)-NH-aralkyl group includes -C(=S)-NH-benzyl, -C(=S)-NH-phenethyl, -C(=S)-NH-$C_6H_5CH_2CH_2CH_2$, -C(=S)-NH-naphthylmethyl and the like, which may be substituted;

-C(=S)-NH-heteroaralkyl group includes -C(=S)-NH-pyridinemethyl, -C(=S)-NH-furanmethyl, -C(=S)-NH-thiophenylenemethyl, -C(=S)-NH-benzothiazolemethyl, -C(=S)-NH-benzimidazolemethyl, -C(=S)-NH-pyrimidinemethyl, -C(=S)-NH-pyrimidinemethyl, -C(=S)-NH-pyrazinemethyl, -C(=S)-NH-tetrazolemethyl and the like, which may be substituted;

-C(=NH)-NH$_2$, which may be substituted;

-C(=NH)-alkyl, where alkyl group is as defined above. Exemplary -C(=NH)-alkyl groups include -C(=NH)-methyl, -C(=NH)-ethyl, -C(=NH)-propyl and the like, which may be substituted;

-C(=NH)-aryl group includes -C(=NH)-phenyl, -C(=NH)-naphthyl and the like, which may be substituted;

S(O)$_2$-alkyl, where alkyl group is as defined above. Exemplary S(O)$_2$-alkyl groups include S(O)$_2$-methyl, S(O)$_2$-ethyl, S(O)$_2$-propyl, S(O)$_2$-isopropyl, S(O)$_2$-butyl, S(O)$_2$-isobutyl and the like, which may be substituted;

S(O)$_2$-aryl group includes S(O)$_2$-phenyl, S(O)$_2$-naphthyl and the like, which may be substituted;

Carboxylic acid or its derivatives may be carboxylicamides or carboxylicesters. Exemplary carboxylic acid groups include CONH$_2$, CONHCH$_3$, CONHCH$_2$CH$_3$, CONHCH$_2$CH$_2$CH$_3$, CONHCH$_2$CH$_3$, CON(CH$_2$CH$_3$)$_2$, CONHC$_6$H$_5$, CONHCH$_2$C$_6$H$_5$, COOH, COOCH$_3$, COOC$_2$H$_5$, COOC$_3$H$_7$, COO*iso*-C$_3$H$_7$, COOC$_6$H$_5$, , COOCH$_2$C$_6$H$_5$ and the like.

Thiomorpholinylthiocarbonyl, which may be substituted;

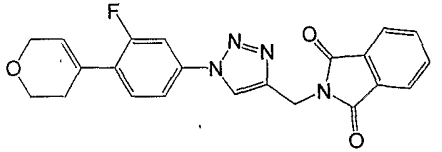
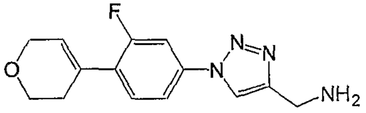
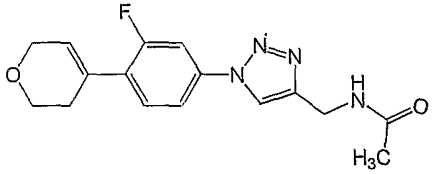
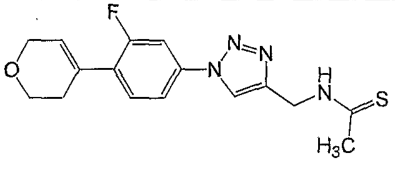
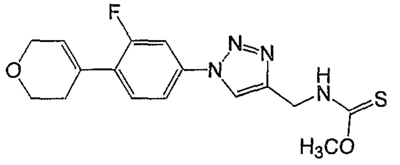
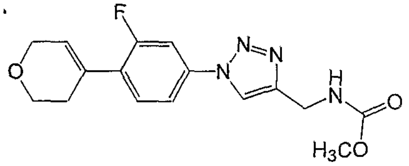
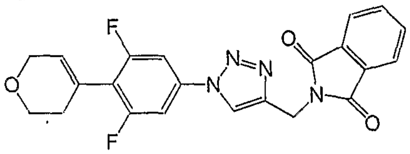
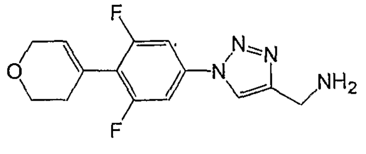
Pyrrolidinylthiocarbonyl, which may be substituted;

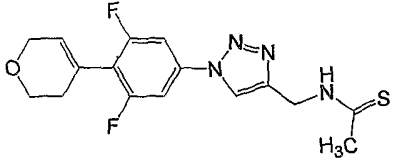
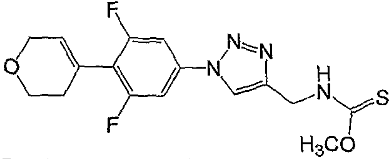
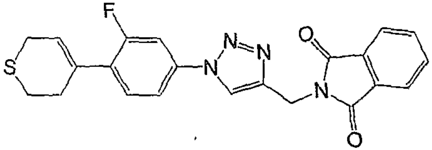
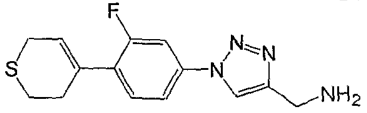
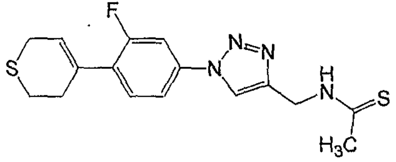
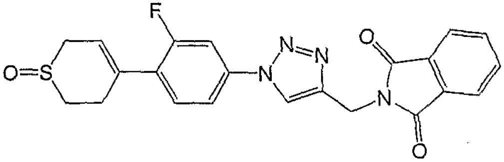
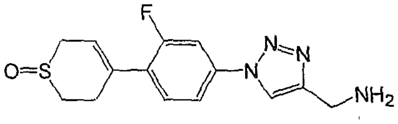
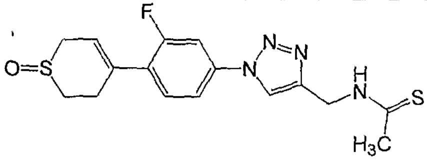
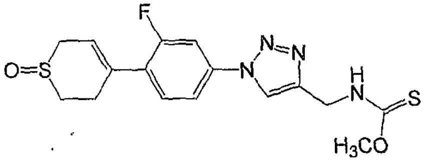
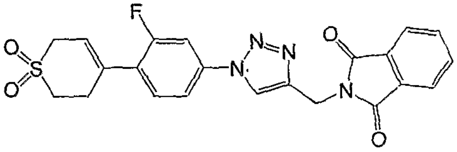
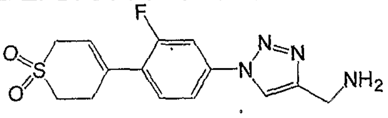
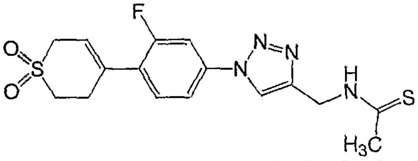
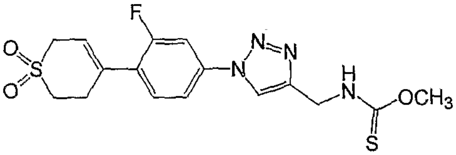
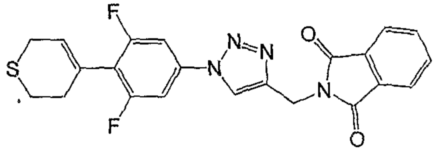
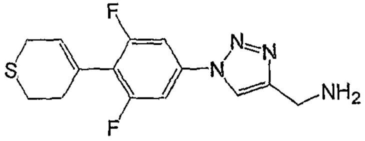
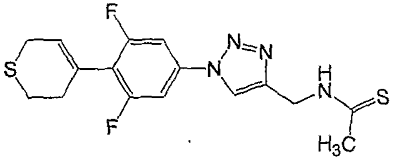
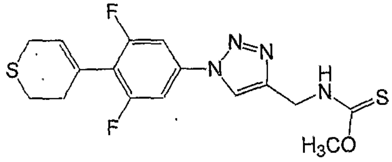
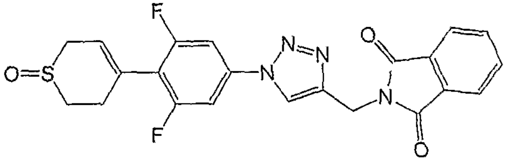
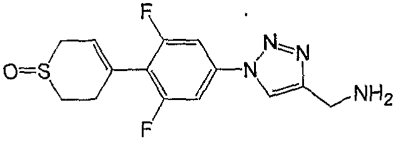
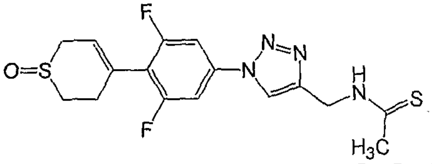
–C(=S)-N(R'R") where R'R" are as defined above.

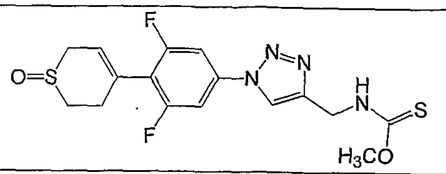
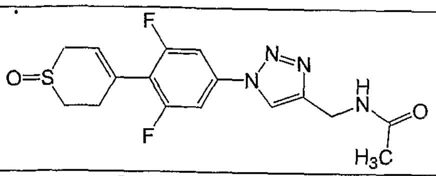
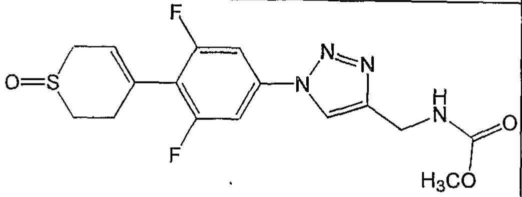
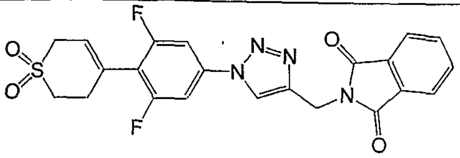
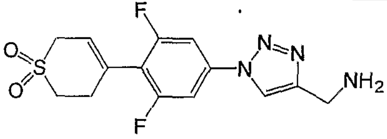
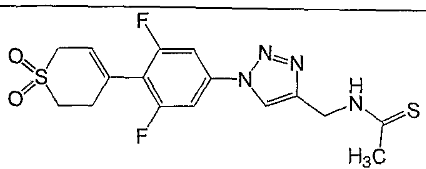
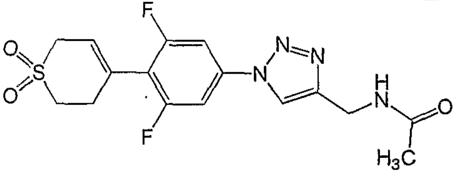
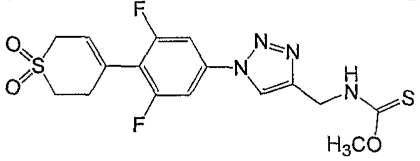
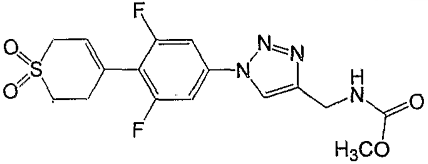
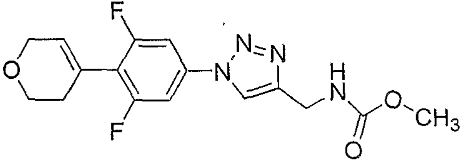
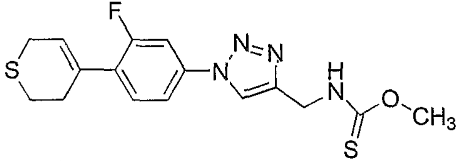
Pharmaceutically acceptable salts forming part of this invention include salts derived from inorganic bases such as Li, Na, K, Ca, Mg, Fe, Cu, Zn, Mn; salts of organic bases such as N,N'-diacetylethylenediamine, betaine, caffeine, 2-diethylaminoethanol, 2-dimethylaminoethanol, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, hydrabamine, isopropylamine, methylglucamine, morpholine, piperazine, piperidine, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, diethanolamine, meglumine, ethylenediamine, N,N'-diphenylethylenediamine, N,N'-dibenzylethylenediamine, N-benzyl phenylethylamine, choline, choline hydroxide, dicyclohexylamine, metformin, benzylamine, phenylethylamine, dialkylamine, trialkylamine, thiamine, aminopyrimidine, aminopyridine, purine, spermidine, and the like; chiral bases like alkylphenylamine, glycinol, phenyl glycinol and the like, salts of natural amino acids such as glycine, alanine, valine, leucine, isoleucine, norleucine, tyrosine, cystine, cysteine, methionine, proline, hydroxy proline, histidine, ornithine, lysine, arginine, serine, threonine, phenylalanine; unnatural amino acids such as D-isomers or substituted amino acids; guanidine, substituted guanidine wherein the substituents are selected from nitro, amino, alkyl such as methyl, ethyl, propyl and the like; alkenyl such as ethenyl, propenyl, butenyl and the like; alkynyl such as ethynyl, propynyl and the like; ammonium or substituted ammonium salts and aluminum salts. Salts may include acid addition salts where appropriate which are, sulphates, nitrates, phosphates, perchlorates, borates, halides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates and the like.

Representative compounds in accordance with the present invention are presented in Table 1. This table is not intended to be exclusive of the compounds of the present invention, but rather exemplary of the compounds that are encompassed by this invention

Table-1:

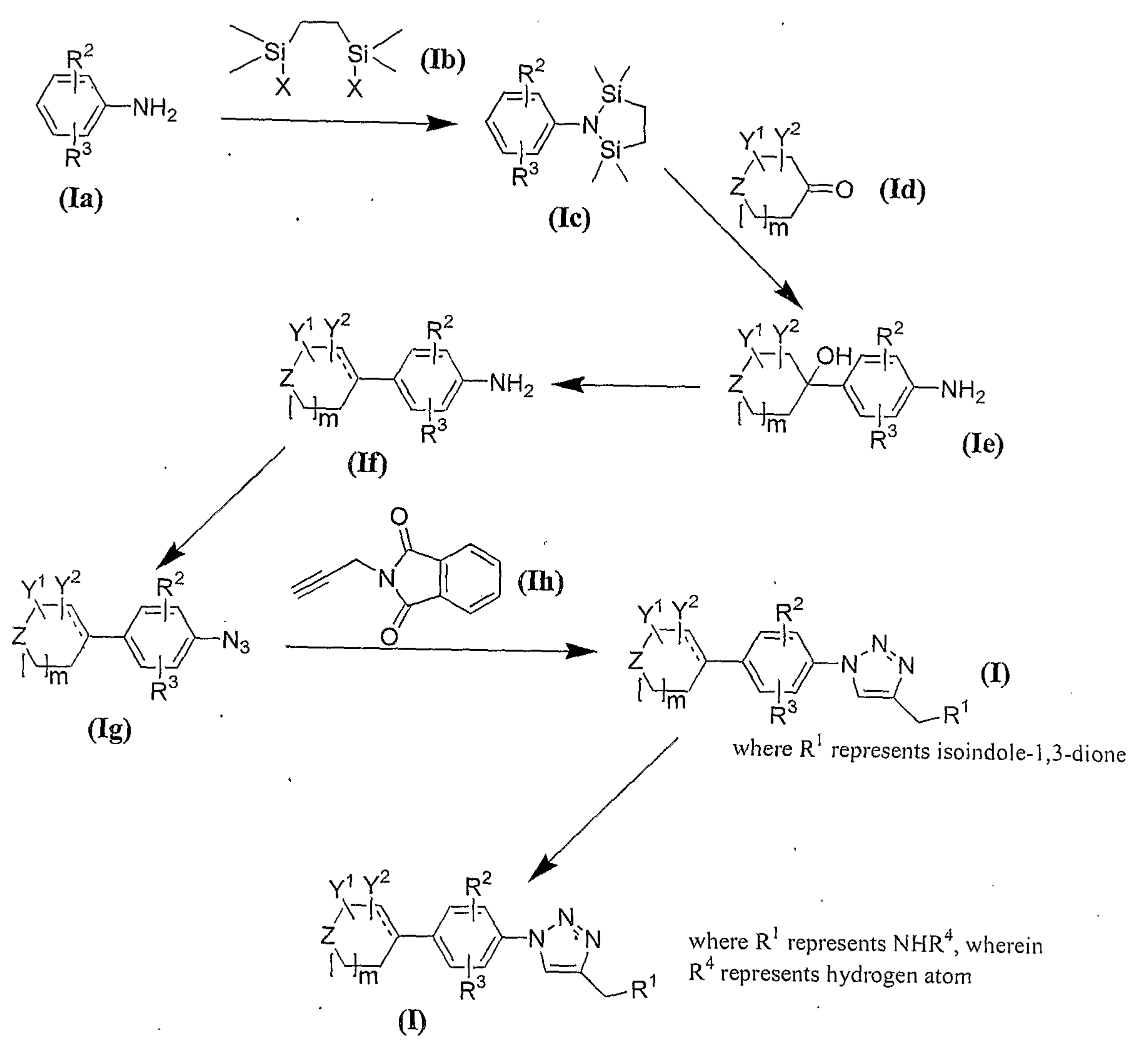
	
	
	
	

or their pharmaceutically acceptable salts thereof.

In another aspect of the present invention, there is provided a process for the preparation of the compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom, Z represents O or S, and all other symbols are as defined earlier, which is shown in the following Scheme-I, comprising the following steps::



where R^1 represents isoindole-1,3-dione

where R^1 represents NHR^4, wherein R^4 represents hydrogen atom

where X represents halogen atom; R^2, R^3, Y^1, Y^2, Z and m are defined as earlier.

Scheme-I

The compound of formula (Ia) is reacted with a compound of formula (Ib), to obtain a compound of formula (Ic), when X represents halogen atom, by using alkyllithium such as methyllithium (MeLi), n-butyllithium (n-BuLi), secondary butyllithium (sec.BuLi), tertiary butyllithium (ter.BuLi) and the like. The compound of formula (Ic), where X represents hydrogen atom is obtained by treating with cesium fluoride (CsF). The solvent used in the reaction may be selected from tetrahydrofuran (THF), hexamethylphosphoramide (HMPA), diethylether and the like. The temperature and duration of the reaction can be maintained in the range of about -78 to about 100 °C and about 30 min to about 1.5 hours respectively.

The compound of formula (Ic) is reacted with a compound of formula (Id), to obtain a compound of formula (Ie), by using a reagent alkyllithium such as methyllithium (MeLi), n-butyllithium (n-BuLi), secondary butyllithium (sec.BuLi), tertiary butyllithium (ter.BuLi) and the like. The solvent used in the reaction may be selected from THF, HMPA, diethyl ether, 1,4-dioxane and the like. The temperature and duration of the reaction can be maintained in the range of about -78 to about 50 °C and about 4 to about 10 hours respectively.

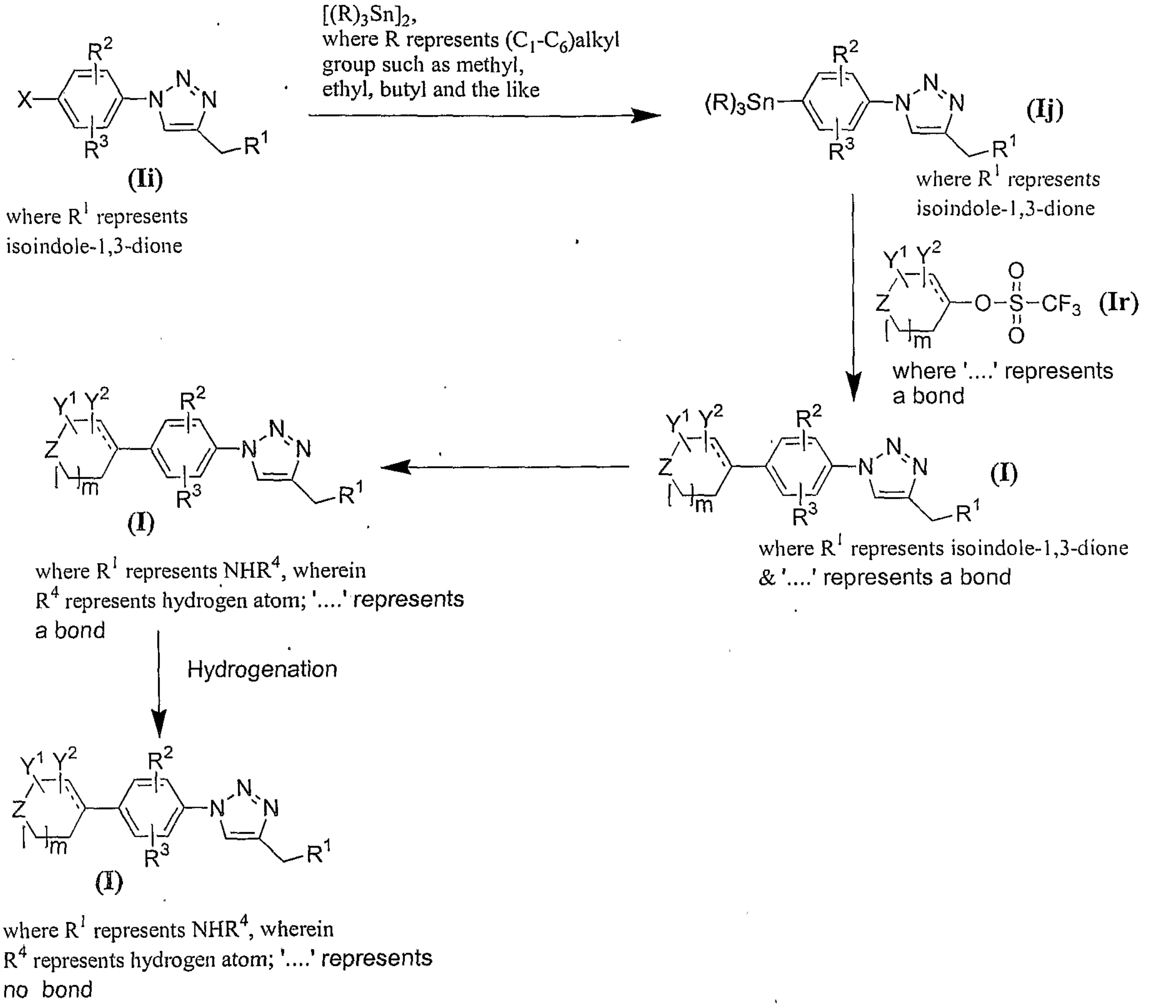
The compound of formula (Ie) is treated with any of the reagents selected from conc HCl, p-toluene sulfonic acid (p-TSA), mesyl chloride & triethylamine, 1,2-diazabicyclo[5,4,0]undec-7-ene (DBU), phosphorous oxychloride ($POCl_3$), The solvent used in the reaction is selected from pyridine, dichloromethane, acetonitrile, toluene and the like, to obtain a compound of formula (If), where '....' represents a bond, The temperature and duration of the reaction can be maintained in the range of about 0 to about 150 °C and about 30 min to about 24 hours respectively. The above obtained compound of formula (Ie) is converted to compound of formula (Ie), where '....' represents no bond, by treating with triethylsilane (Et_3SiH) & borantrifluoride diethyl etherate ($BF_3.OEt_2$), triethylsilane (Et_3SiH) & trifluoroaceticacid (CF_3COOH), trimethylsilylchloride (TMSCl), sodium iodide (NaI), diiodo dimethylsilane (Me_2SiI_2), tributyltinhydride (Bu_3SnH) and the like, under the above reaction conditions.

The compound of formula (If) is reacted with sodium nitrite ($NaNO_2$), sodium azide (NaN_3), t-Butyl nitrile and the like, to obtain a compound of formula (Ig), The temperature and duration of the reaction can be maintained in the range of about 0 to about 150 °C and about 30 minutes to about 24 hours respectively.

The compound of formula (Ig) is reacted with a compound of formula (Ih), to obtain a compound of formula (I), by using a reagent such as cuprous iodide (CuI), cuprous chloride (CuCl) and the like. The solvent used in the reaction may be selected from acetonitrile, toluene, diemthyl formamide (DMF) and the like. The reaction may be carried out in the presence of such as diisoporpylethylamine, triethylamine and the like. The temperature and duration of the reaction can be maintained in the range of about 0 to about 100 °C and about 30 minutes to about 12 hours respectively.

The compound of formula (I), where R^1 represents isoindole-1,3-dione to a compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom, is carried out by using hydrazine hydride. The solvent used in the reaction is selected from (C_1-C_6)alcohol such as methanol, ethanol, propanol, isopropanol and the like or mixtures thereof. The temperature of the reaction is maintained at the reflux temperature of the solvent used. The duration of the reaction is maintained in the range of about 2-4 hours.

Another aspect of the present invention provides, an alternate process for the preparation of compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents hydrogen atom and all other symbols are as defined earlier, which is shown in the following Scheme-II:



where X represents halogen atom; R^2, R^3, Y^1, Y^2, Z and m are defined as earlier.

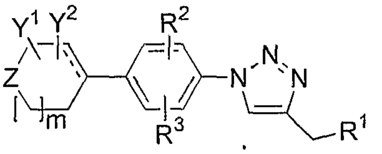
Scheme-II

The conversion of compound of formula (Ii) to a compound of formula (Ij) and compound of formula (Ij) to a compound of formula (I), is carried out by using a palladium reagent such as triphenyl phosphine palladium (II) chloride ($PdCl_2(PPh_3)$), tris(dibenzylidineacetone)dipalldium ($Pd_2(dba)_3$) and the like. The solvent used in the reaction is selected from DMF, acetonitrile, 1,4-dioxane and the like. The temperature and duration of the reaction are maintained in the range of about 20 to about 100 °C and about 2 to about 12 hours respectively.

The compound of formula (I), where R^1 represents isoindole-1,3-dione, '....' represents a bond, to a compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom, is carried out by using hydrazine hydride. The solvent used in the reaction is selected from $(C_1$-$C_6)$alcohol such as methanol, ethanol, propanol, isopropanol and the like or mixtures thereof. The temperature of the reaction is maintained at the reflux temperature of the solvent used. The duration of the reaction is maintained in the range of 2-4 hours. The above obtained compound of formula (I) is converted to a compound of formula (I), where '.....' represents no bond, by conventional hydrogenation methods, by using reagent such as platinum dioxide (PtO_2), palladium/carbon (Pd/C), Raney nickel, and the like, along with H_2 gas. The solvent used in the reaction is selected from methanol, ethanol, sodium acetate, acetic acid and other related reagents.

Another aspect of the present invention provides the alternate process for the preparation of the compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents hydrogen atom, Z represents SO or SO_2, and all other symbols are as defined earlier, which comprises:

(i) converting the compound of formula (I)



(I)

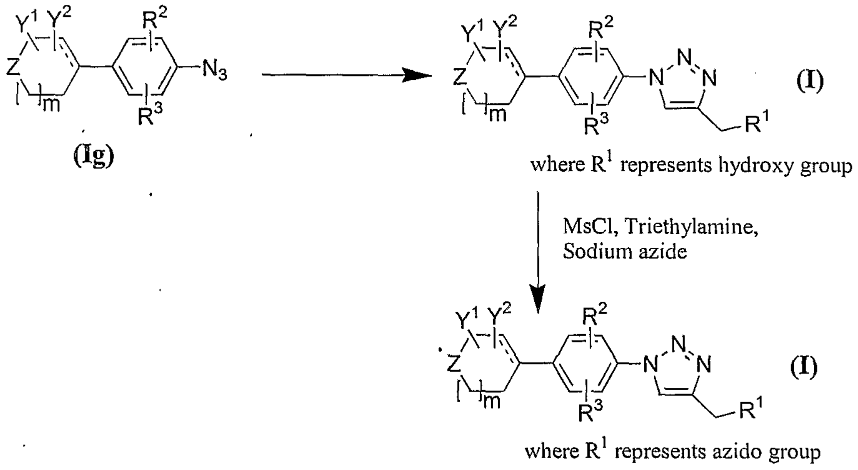
where R^1 represents isoindole-1,3-dione, Z represents S, all other symbols are as defined earlier, to a compound of formula (I), where Z represents SO or SO_2 and

(ii) converting the above obtained compound of formula (I), to a compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom and all other symbols are as defined earlier.

The compound of formula (I), where Z represent S, to a compound of formula (I), where Z represents SO or SO_2, can be carried out by using reagents like Siodiumperiodate ($NaIO_4$), aluminium oxide (Al_2O_3), m-chloroperbenzoicacid, potassium permanganate ($KMnO_4$), ruthenium chloride ($RuCl_3$), periodic acid (H_5IO_6), oxone™ in presence of solvents like dichlromethane, acetonitrile, water and the like The temperature and duration of the reaction can be maintained in the range of about 0 to about 60 °C and about 30 minutes to about 36 hours respectively.

The compound of formula (I), where R^1 represents isoindole-1,3-dione, to a compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom, in the presence of reagents such as hydrazine hydrate, sodiumborohydrate, N-methyl amine, phenyl hydrazine, Dianion WA-20 in presence of solvents like methnol, isopropanol, ethanol.and like. The temperature and duration of the reaction can be maintained in the range of about 0 to about 100 °C and about 30 minutes to about 36 hours respectively.

Another aspect of the present invention provides an alternative process for the preparation of the compound of formula (I) where R^1 represents azido and all other symbols are as defined earlier, which is shown in Scheme-III:



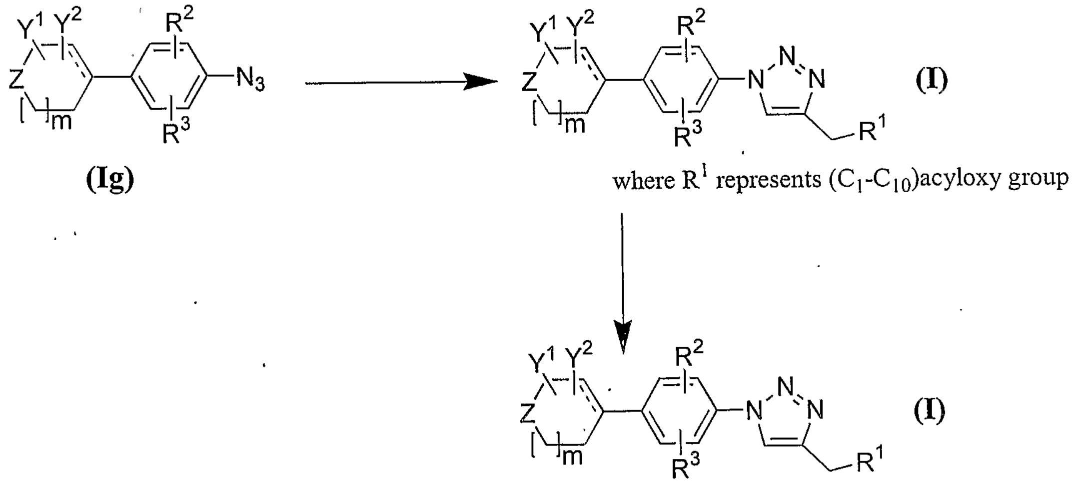
where R^2, R^3, Y^1, Y^2, Z and m are defined as earlier.

Scheme-III

The compound of formula (Ig) may be converted to a compound of formula (I), where R^1 represents hydroxy group, by treating with propargyl alcohol. The solvent used in the reaction may be selected from benzene, toluene, xylene, acetonitrile, THF, DMF and the like. The temperature of the reaction may be maintained in the range of about 10 to about 200 °C, preferably about 20 to about 70 °C. The duration of the reaction may be in the range of about 1 to about 25 hours, preferably in the range of about 5 to about 20 hours.

The compound of formula (I) where R^1 represents hydroxy group may be converted to a compound of formula (I) where R^1 represents azido group was carried out in two steps. In step (1) the compound of formula (I) where R^1 represents OH is converted to compound of formula (I) where R^1 represents leaving group such as halogen atom, by treating with tetrabromomethane/triphenylphosphine (CBr_4/PPh_3), tribromiophosphine (PBr_3), sulfonyl chloride ($SOCl_2$) and the like. The reaction may be carried out in the presence of chloroform, dichloromethane, THF, dioxane and the like or mixtures thereof. The reaction may be carried out in the presence or absence of a base such as triethylamine (Et_3N), diisopropyl ethylamine, sodium carbonate (Na_2CO_3), potassium carbonate (K_2CO_3) and the like. The temperature of the reaction may be maintained in the range of 0 to 80°C, preferably in the range of 0 to 50°C. The duration of the reaction may be in the range of about 1 to 12 hours, preferably in the range of about 1 to 4 hours. In step (2), the compound of formula (I) where R^1 represents halogen atom may be converted to compound of formula (I) where R^1 represents azido group by treating with sodium azide (NaN_3), lithium azide (LiN_3), trialkylsilylazide and the like. The solvent used in the reaction may be selected from acetone, THF, DMF, dimethyl sulfoxide (DMSO), methylcyanide and the like. The temperature of the reaction may be maintained in the range of about 20 to about 120°C, preferably about 20 to about 80 °C. The duration of the reaction may be in the range of about 1 to about 12 hours, preferably about 1 to about 4 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I) where R^1 represents hydroxy group, which is shown in the following Scheme-IV:



(Ig)

(I) where R^1 represents (C_1-C_{10})acyloxy group

(I) where R^1 representshydroxy group group

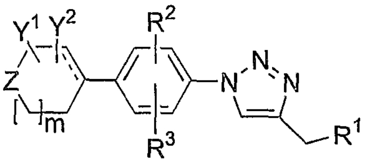
where R^2, R^3, Y^1, Y^2, Z and m are defined as earlier.

Scheme-IV

The conversion of compound of formula (Ig) to a compound of formula (I) where R^1 represents acyloxy group, may be carried out in the presence of alkyl or aryl esters of propargyl alcohol. The solvent used in the reaction may be selected from benzene, toluene, xylene, acetonitrile, THF and the like. The temperature of the reaction may be maintained in the range of about 10 to about 200 °C, preferably room temperature to the boiling temperature of the solvent. The duration of the reaction may be in the range of about 1 to about 25 hours, preferably in the range of about 5 to about 20 hours.

The hydrolysis of compound of formula (I) where R^1 represents acyloxy group, to a compound of formula (I), where R^1 represents hydroxy group, may be carried out by using conventional ester hydrolysis procedures.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted acetyl group and all other symbols are as defined earlier, from a compound of formula (I) where R^1 represents azido group,

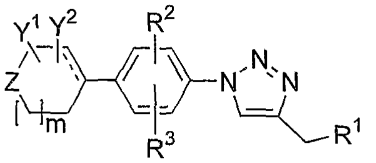


(I)

where Z, Y^1, Y^2, R^2, R^3 and m are as defined earlier,

The compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted acetyl group may be prepared from compound of formula (I), where R^1 represents azido group may be carried out by using thiolacetic acid with or without using solvent such as THF, DMF, toluene and the like. The reaction may be carried out at a temperature in the range of about 25 to about 40 °C, preferably at room temperature. The duration of the reaction may be in the range from about 3 to about 24 hours, preferably from about 4 to about 12 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-R^{4a}$, wherein R^{4a} represents optionally substituted alkyl, haloalkyl, aryl, heteroaryl, -C(=O)-alkoxy, -C(=O)-alkoxy, -C(=O)-aryloxy, -C(=S)-alkyl or -C(=S)-aryl; from compound of formula (I), where R^1 represents NHR^4, where R^4 represents$-C(=O)-R^{4a}$, wherein R^{4a} represents optionally substituted alkyl, haloalkyl, aryl, heteroaryl, -C(=O)-alkoxy, -C(=O)-aryloxy, -C(=S)-alkyl or -C(=S)-aryl



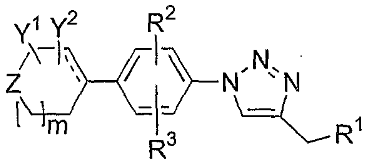
(I)

where all symbols are as defined earlier.

The compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents–C(=S)-R^{4a}, from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents–C(=O)-R^{4a}, wherein R^{4a} is as defined above, may be carried out by taking a solution of the amide and Lawesson's reagent (2,4-bis(methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide) in dry dioxane, toluene, THF, DMF and the like. The reaction may be carried out at a temperature in the range of about 20 to about 130°C, preferably in the range of about 55 to about 90 °C. The duration of the reaction may be in the range from about 3 to about 24 hours, preferably from about 3 to about 10 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents–C(=S)-OR^{4b}, wherein R^{4b} represents optionally substituted alkyl, cycloalkyl, aryl, alkenyl or -C(=O)-alkyl group, which comprises:

(i) reacting compound of formula (I)



(I)

where R^1 represents azido group; and all other symbols are as defined earlier, with triphenylphosphine/water or H_2-Pd/C, to produce a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom and all other symbols are as defined earlier,

(ii) reacting compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom, with thiophosgene or carbon disulfide and chloromethylformate, in the presence of a base to produce a compound of formula (I), where R^1 represents isothiocyanate group; and all symbols are as defined earlier,

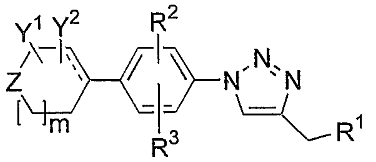
(iii) converting compound of formula (I) where R^1 represents isothiocynate group, to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-OR^{4b}$, wherein R^{4b} is as defined above and all other symbols are as defined earlier.

The conversion of compound of formula (I), where R^1 represents azido to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom may be carried out in the presence of gaseous hydrogen and a catalyst such as Ru, Pd, Rh, Pt, Ni on solid beads such as charcoal, alumina, asbestos and the like. The reduction may be conducted in the presence of a solvent such as dioxane, acetic acid, ethyl acetate, THF, alcohol such as methanol, ethanol, propanol, isopropanol and the like or mixtures thereof. A pressure between atmospheric pressure to 60 psi may be used. The reaction may be carried out at a temperature in the range of 25 to 60 °C, preferably in the range of room temperature to 80°C. The duration of the reaction may be in the range of about 2 to about 48 hours, preferably in the range of about 5 to about 15 hours. The reduction may also be carried out by employing PPh_3 and water.

The compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom may be converted to a compound of formula (I) where R^1 represents isothiocyanate group, by using thiophosgene or carbon disulfide and chloromethylformate in the presence of a base such as Et_3N, K_2CO_3, sodium hydroxide (NaOH) and the like. The reaction may be carried out in the presence of a solvent such as dichloromethane (CH_2Cl_2), acetonitrile, chloroform ($CHCl_3$), DMF, THF and the like. The reaction may be carried at a temperature in the range of 0 to 60°C, preferably at 0 °C. The reaction may be carried out in an inert atmosphere using argon or any other inert gas. The duration of the reaction may be in the range of about 1 to about 24 hours, preferably about 2 to about 10 hours.

The conversion of compound of formula (I) where R^1 represents isothiocyanate group, to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-OR^{4b}$, wherein R^{4b} is as defined above, may be carried out by using respective alcohol such as methanol, ethanol, propanol, cyclohexanol and the like, in the absence or presence of a base such as sodiumhydride (NaH), potassiumhydride (KH) and the like. The reaction may be carried out in the presence of a solvent such as THF, toluene, DMF and the like. The reaction may be carried out at a temperature in the range of about 20 to about 130°C, preferably at reflux temperature of the solvent used. The duration of the reaction may be in the range of about 6 to about 24 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted groups selected from -C(=S)-NH_2, -C(=S)-NH-alkyl, -C(=S)-N-$(alkyl)_2$, -C(=S)-NH-alkenyl, C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl or -C(=S)-N(R'R"), wherein R' and R" groups together form a optionally substituted 5 or 6 membered cyclic structures containing nitrogen and optionally one or two additional hetero atoms selected from oxygen, nitrogen or sulfur; from a compound of formula (I) where R^1 represents isothiocyanate group,



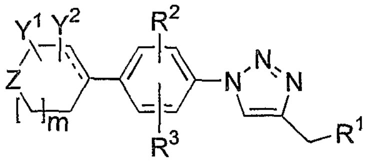
(I)

where all symbols are as defined earlier.

The compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted -C(=S)-NH_2, may be prepared by passing ammonia gas into a solution of compound of formula (I) where R^1 represents isothiocyanate group, in the presence of a solvent such as THF, toluene, and the like. The reaction may be carried out at a temperature in the range of about -10 to about 40 °C, preferably at about -10 °C. The duration of the reaction may be in the range from about 20 minutes to about 4 hours, preferably about 30 minutes.

The compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted groups selected from –C(=S)-NH-alkyl, -C(=S)-N-$(alkyl)_2$, -C(=S)-NH-alkenyl, C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl or -C(=S)-N(R'R"), wherein R' and R" groups together form a optionally substituted 5 or 6 membered cyclic structures containing nitrogen and optionally one or two additional hetero atoms selected from oxygen, nitrogen or sulfur, may be carried out by treating a compound of formula (I) where R^1 represents isothiocyanate group with appropriate amine such as methylamine, ethylamine, diemthylamine, diethylamine, benzylamine, aniline, proline, morpholine, thiomorpholine, pyridiylmethylamine and the like, in the presence of a solvent such as THF, DMF, toluene, and the like. The reaction may be carried out at a temperature in the range of 20 about to about 140 °C, preferably at about 20 to about 100°C. The duration of the reaction may be in the range of about 0.5 to about 24 hours, preferably about 0.5 to about 12 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-SR^{4c}$, wherein R^{4c} represents optionally substituted alkyl group, from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom,

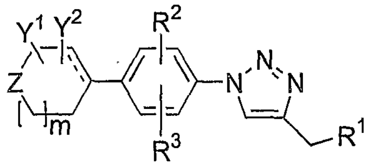


(I)

where all other symbols are as defined earlier.

The compound of fomula (I), where R^1 represents NHR^4, wherein R^4 represents$-C(=S)-SR^{4c}$, wherein R^{4c} is as defined above, may be prepared from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom, by using CS_2 in the presence of a base such as Et_3N, diisopropyl ethylamine, K_2CO_3, NaH, tertiary butylalcohol (t-BuOK) and the like. The reaction may be carried out in the presence of alkyl halide such as methyliodide, ethylbromide, propylbromide and the like. The solvent used in the reaction may be selected from ethanol, methanol, isopropanol, THF, diethylether, acetonitrile and the like, or mixtures thereof. The reaction may be carried out at a temperature in the range of about 20 to about 60 °C, preferably at about 20 to about 40 °C. The duration of the reaction may be in the range of about 6 to about 24 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH-R^{4d}$, wherein R^{4d} represents optionally substituted -C(=O)-aryl group, from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom,

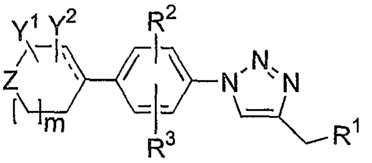


(I)

where all other symbols are as defined earlier.

The compound of fomula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH-R^{4d}$ wherein R^{4d} is as defined above, may be prepared from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom by using benzoylisothiocyanate. The solvent used in the reaction may be selected from acetone, ethanol, methanol, isopropanol, THF, diethylether, acetonitrile and the like. The temperature of the reaction may be maintained in the range of about 0 to about 80°C, preferably in the range of about 20 to about 60 °C. The duration of the reaction may be in the range of about 1 to about 20 hours, preferably in the range of about 1 to about 10 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted –C(=O)-heteroaryl, from a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom,

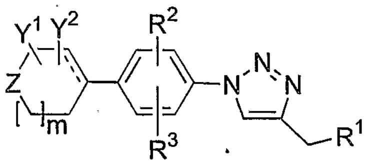


(I)

where all other symbols are as defined earlier.

The compound of fomula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted –C(=O)-heteroaryl, may be prepared from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom by treating with corresponding heteroaroyl acid chloride and base such such as pyridine, triethylamine or diisopropylamine. The reaction may also be carried out by using corresponding heteroaryl acid and dicyclohexylcarbodiimide (DCC) in the presence of dimethylaminopyridine (DMAP). The solvent used in the reaction may be selected from acetonitrile, THF, methylcyanide, Et_2O and the like. The temperature of the reaction may be maintained in the range of about –5 to about 100 °C, preferably in the range of about 0 to about 80°C. The duration of the reaction may be in the range of about 1 to about 15 hours, preferably in the range of about 2 to about 12 hours.

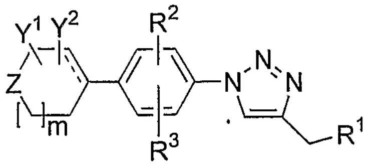
Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents $-C(=O)-R^{4e}$ wherein R^{4e} represents optionally substituted alkyl, alkoxy, alkenyl, haloalkyl, aryl, aryloxy, heteroaryl, alkenyloxy, alkylcarbonyl, arylcarbonyl, aryloxycarbonyl, alkoxycarbonyl, alkylthiocarbonyl or arylthiocarbonyl; from a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom,


(I)

where all other symbols are as defined earlier.

The compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=O)-R^{4e}$, wherein R^{4e} is as defined above, may be prepared from compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom, by treating with appropriate acid halide such as acetyl chloride, propionyl chloride and the like; alkylchloroformate like methylchloroformate, ethylchloroformate and the like; aralkylchloroformate like benzylchloroformate and the like; or anhydride of the corresponding acid such as acetic anhydride. The reaction may be carried out in the presence of a solvent such as CH_2Cl_2, $CHCl_3$, toluene, THF and the like or mixtures thereof. The reaction may also be carried out in the presence of a base like Et_3N, diisopropyl ethylamine, pyridine, K_2CO_3, NaH, t-BuOK and the like. The temperature of the reaction may be maintained in the range of about -20 to about 60 °C, preferably in the range of about 0 to about 40 °C. The duration of the reaction may be in the range of about 1 to about 12 hours, preferably from about 1 to about 4 hours.

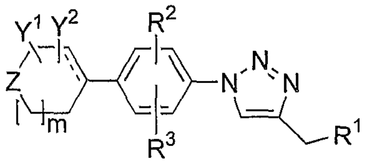
Another aspect of the present invention provides a process for the preparation of compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents optionally substituted $-C(=NH)-NH_2$, by reacting a compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents hydrogen atom, with di-*tert*-butoxy carbonyl thiourea,


(I)

where all other symbols are as defined earlier.

The compound of formula (I) where R^1 represents NHR^4 where R^4 represents optionally substituted group selected from $-C(=NH)-NH_2$, may be prepared by reacting the compound of formula (I), where R^1 represents NHR^4 where R^4 represents hydrogen atom, with di-*tert*-butoxy carbonyl thiourea in two steps. In the first step, the reaction may be carried out in the presence of solvents such as DMF, acetone, THF, dichloromethane and the like. The base used in the reaction may be selected from triethylamine, diisopropylethylamine, pyridine and the like. The temperature of the reaction may be in the range of 0 to 120°C, preferably in the range of 0 to 90°C. The duration of the reaction may be in the range of 0.2 to 15 hours, preferably in the range of 0.5 to 10 hours. In the second step, the compound obtained in the first step may be reacted with trifluoroacetic acid in the presence of a solvent such as dichloromethane, chloroform, THF and the like. The temperature of the reaction may be in the range of about 0 to about 110 °C, preferably in the range of about 0 to about 90 °C. The duration of the reaction may be in the range of about 0.5 to about 60 hours, preferably in the range of about 0.5 to about 54 hours.

Another aspect of the present invention provides an alternative process for the preparation of compound of formula (I) where R^1 represents NHR^4 where R^4 represents optionally substituted group selected from $-C(=NH)-NH_2$, by reacting a compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents optionally substituted group selected from $-S(O)_2$-alkyl or $-S(O)_2$-aryl group, with guanidine hydrochloride,



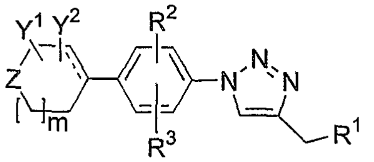
(I)

where all other symbols are as defined earlier.

The compound of formula (I) where R^1 represents NHR^4 where R^4 represents optionally substituted group selected from $-C(=NH)-NH_2$, may be prepared by reacting the compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents optionally substituted group selected from $-S(O)_2$-alkyl or $-S(O)_2$-aryl group, with guanidine hydrochloride. The solvent used in the reaction may be seleceted form t-butyl alcohol. The base used in the reaction may be selected from NaH, KH, sodium hexamethyldisilazide (Na-HMDS) and the like. The temperature of the reaction may be in the range of about 0 °C to boiling temperature of the solvent used. The duration of the reaction may be in the range of about 1 to about 30 hours, preferably in the range of about 1 to about 24 hours.

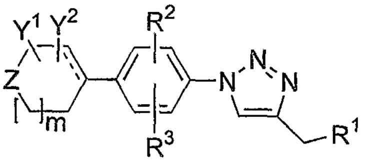
Another aspect of the present invention provides a process for the preparation of compound of formula (I) where R^1 represents NHR^4 where R^4 represents optionally substituted group selected from -C(=NH)-alkyl or –C(=NH)-aryl, which comprises:

(i) reacting the compound of formula (I)



(I)

where R^1 repersents NHR^4, wherein R^4 represents $-C(=S)-NH_2$ and all other symbols are as defined earlier, with di *tert*-butoxy carbonyl ether ($(BOC)_2O$), to produce a compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH_2$ group substituted with *tert*-butoxy carbonyl group and all symbols are as defined earlier and

(ii) reacting the above compound of formula (I), with a compound of formula (Ik)

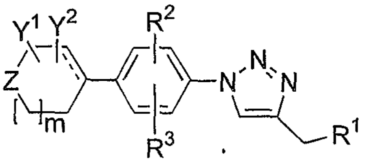
$$R^7\text{-}NH_2 \qquad \text{(Ik)}$$

where R^7 represents optionally substituted alkyl or aryl group, to produce a compound of formula (I) where R^1 represents NHR^4 where R^4 represents optionally substituted group selected from -C(=NH)-alkyl or -C(=NH)-aryl group and all other symbols are as defined earlier.

The conversion of the compound of formula (I) where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH_2$, to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH_2$ group substituted with *tert*-butoxy carbonyl group may be carried out by reacting with $(BOC)_2O$, in the presence of solvent such as THF, diethylether and the like. The base used in the reaction may be selected from NaH, KH, sodium hexamethyldisilazane (Na-HMDS) and the like. The temperature of the reaction may be in the range of about 0 to boiling temperature of the solvent. The duration of the reaction may be in the range of about 0.5 to about 14 hours, preferably in the range of about 0.5 to about 10 hours.

The conversion of the compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH_2$ group substituted with *tert*-butoxy carbonyl group, to a compound of formula (I) may be carried out by reacting with the compound of formula (Ik) in two steps. In the first step, the reaction may be carried out in the presence of a solvent such as DMF, THF, chloroform, dichloromethane and the like. The base used in the reaction may be selected from triethylamine, diisopropylethylamine, pyridine and the like. The temperature of the reaction may be in the range of about 0 to about 120°C, preferably in the range of about 0 to about 90°C. The duration of the reaction may be in the range of about 0.5 to about 24 h, preferably in the range of about 0.5 to about 20 hours. In the second step, the compound obtained in the first step may be reacted with trifluoroacetic acid in the presence of a solvent such as dichloromethane, chloroform, THF and the like. The temperature of the reaction may be in the range of about 0 to about 110°C, preferably in the range of about 0 to about 90°C. The duration of the reaction may be in the range of about 0.5 to about 60 hours, preferably in the range of about 0.5 to about 54 hours.

Another aspect of the present invention provides a process for the preparation of a compound of formula (I) where R^1 represents halogen, from compound of formula (I) where R^1 represents hydroxy group,

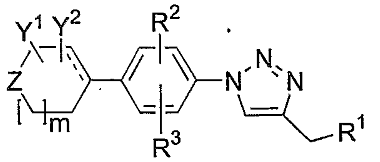


(I)

where all other symbols are as defined above.

The compound of formula (I) where R^1 represents halogen is prepared from compound of formula (I) where R^1 represents hydroxy group may be carried out by treating with $SOCl_2$, PCl_5, PBr_3, tetrahalomethane group such as carbontetrabromide (CBr_4), carbontetrachloride (CCl_4) and the like, in the presence of triphenylphonsphine (PPh_3), trialkylphosphine ($P(alkyl)_3$) and the like. The reaction may be carried out in the presence of a solvent such as dry dichloromethane, chloroform, tetrachloromethane, benzene, DMF, DMSO, THF and the like. The temperature of the reaction may be maintained in the range of about 0 to about 60 °C, preferably about 20 to about 40 °C. The duration of the reaction may be in the range of about 0.5 to about 24 hours, preferably about 1 to about 13 hours.

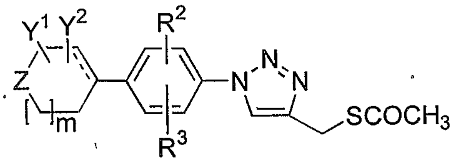
Another aspect of the present invention provides a process for the preparation of a compound of formula (I) where R^1 represents 'SH',



(I)

where all other symbols are as defined above, which comprises:

(i) reacting the compound of formula (I) where R^1 represents halogen atom, to produce a compound of formula (Im),



(Im)

where all other symbols are as defined earlier, with a base and thiolacetic acid,

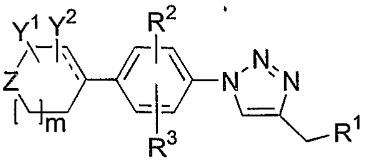
(ii) reacting the compound of formula (Im), to produce a compound of formula (I) where R^1 represents 'SH' group and all other symbols are as defined earlier, with base.

The compound of formula (Im) is prepared from compound of formula (I) where R^1 represents halogen atom may be prepared by using thiolacetic acid in the presence of a base such as triethylamine, di-isopropylamine, di-isopropylethylamine, pyridine, piperidine, DMAP, DBU, lithium diisopropylamide (LDA), potassium bis-(trimethyl silyl)amide, BuLi, Na_2CO_3, K_2CO_3, NaOH, KOH, sodiummethoxide (NaOMe), sodiumethoxide (NaOEt), sodium *iso* propoxide (NaO-iPr), t-BuOK, NaH, KH and the like. The solvent used in the reaction may be seleceted from THF, benzene, dioxane and the like. The temperature of the reaction may be maintained in the range of about 20 °C to reflux temperature, preferably at reflux temperature. The duration of the reaction may be in the range of about 2 to about 24 hours, preferably about 6 hours.

The compound of formula (I), where R^1 represents 'SH' group may be prepared from a compound of formula (Im) by reacting with a base such as K_2CO_3, NaOH, KOH, BuLi and the like. The reaction may be carried out at a temperature in the range of about 20 °C to reflux temprature. The duration of the reaction may be in the range of about 1 to about 24 hours.

Another aspect of the present invention provides a process for the preparation of compound of formula (I), where R^1 represent NHR^4 wherein R^4 represents optionally substituted $-S(O)_2$-alkyl or $-S(O)_2$aryl group, from a compound of formula (I) where R^1 represents NHR^4 where R^4 represents hydrogen atom,

(i) reacting the compound of formula (I),

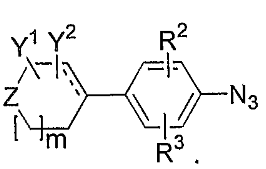


(I)

where R^1 represents NHR^4 where R^4 represents hydrogen atom and all other symbols are as defined in the description, to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted group selected from $-S(O)_2$-alkyl or $-S(O)_2$-aryl group and all other symbols are as defined in the description, to a compound of formula (I).

The conversion of compound of formula (I), where R^1 represents NHR^4 where R^4 represents hydrogen atom, to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted group selected from $-S(O)_2$-alkyl or $-S(O)_2$-aryl group, may be carried out by treating with alkylsulfonylchloride or arylsulfonylchloride such as methanesulfonyl chloride, p-toluenesulfonyl chloride and the like. The solvent used may be selected from dichloromethane, tetrahydrofuran, acetonitrile, dimethylformamide, dimethylsulfoxide and the like. The temperature of the reaction may be in the range of about 0 to about 50 °C, for duration of about 1 to about 6 hours.

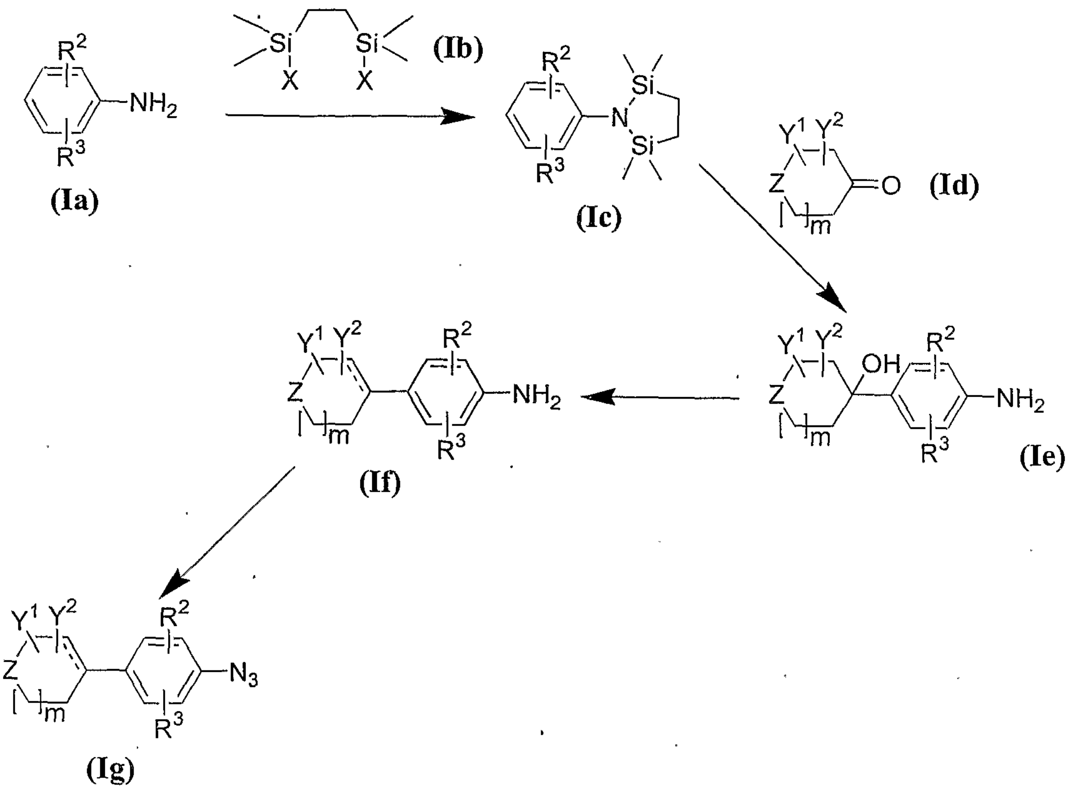
Another aspect of the present invention provides a novel intermediate of the formula (Ig),



(Ig)

where Z, Y^1, Y^2, R^2, R^3 and m are as defined earlier.

Yet another aspect of the present invention provides a process for the preparation of novel intermediate of formula (Ig), which comprises:



where Z, Y^1, Y^2, R^2, R^3 and m are as defined earlier.

The compound of formula (Ia) is reacted with a compound of formula (Ib), to obtain a compound of formula (Ic), when X represents halogen atom, by using a reagent such as BuLi and the like. The compound of formula (Ic), where X represents hydrogen atom is obtained by treating with CsF. The solvent used in the reaction may be selected from tetrahydrofuran (THF), hexamethylphosphoramide (HMPA), diethylether and the like. The temperature and duration of the reaction can be maintained in the range of about -78 to about 100 °C and about 30 minutes to about 1.5 hours respectively.

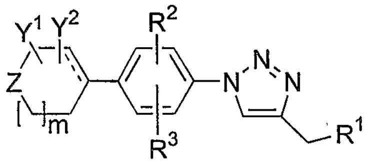
The compound of formula (Ic) is reacted with a compound of formula (Id), to obtain a compound of formula (Ie), by using a reagent such as methyllithium (MeLi), n-butyllithium (n-BuLi), secondary butyllithium (sec.BuLi), tertiary butyllithium (ter.BuLi) and the like. The solvent used in the reaction may be selected from THF, HMPA, diethyl ether, 1,4-dioxane and the like. The temperature and duration of the reaction can be maintained in the range of about -78 to about 50 °C and about 4 to about 10 hours respectively.

The compound of formula (Ie) is treated with any of the reagents selected from conc HCl, p-toluene sulfonic acid (p-TSA), mesyl chloride & triethylamine, 1,2-

diazabicyclo[5,4,0]undec-7-ene (DBU), phosphorous oxychloride ($POCl_3$), The solvent used in the reaction is selected from pyridine, dichloromethane, acetonitrile, toluene and the like, to obtain a compound of formula (If), where '....' represents a bond, The temperature and duration of the reaction can be maintained in the range of about 0 to about 150 °C and about 30 minutes to about 24 hours respectively. The above obtained compound of formula (Ie) is converted to compound of formula (Ie), where '....' represents no bond, by treating with Et_3SiH & $BF_3.OEt_2$, Et_3SiH & CF_3COOH, TMSCl, NaI, Me_2SiI_2, Bu_3SnH and the like, under the above reaction conditions.

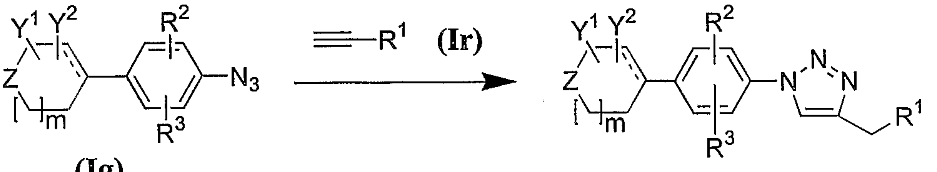
The compound of formula (If) is reacted with $NaNO_2$, NaN_3, t-Butyl nitrile and the like, to obtain a compound of formula (Ig), The temperature and duration of the reaction can be maintained in the range of about 0 to about 150 °C and about 30 minutes to about 24 hours respectively.

Another aspect of the present invention provides an alternate process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4 wherein R^4 and all other symbols are as defined earlier.



(Ig)

(I)

where R^d, Z, Y^1, Y^2, R^2, R^3 and m are as defined earlier.

Scheme-V

The above compound of formula (I) may be prepared by reacting the compound of formula (Ig) with a compound of formula (Ir), in the presence of Cu(1)I, and a base such as triethylamine, ethyldiisopropylamine, 1,4-diazabicyclo[2,2,2]octane (DABCO) and the like. The reaction may be carried out in the presence of a solvent such as dichloromethane, chloroform, THF, DMF, DMSO, acetonitrile and the like.

When the groups represented by R^{4a}, R^{4b}, 4^{4c}, 4^{4d}, R^{4e} may be be substituted by groups selected from halogen, hydroxy, amino, cyano, nitro, alkyl, hydroxyalkyl, alkoxy, =O, =S, aryl, hydroxyaryl, pyridyl, monoalkylamino, dialkylamino, acyl, thioacyl, alkoxycarbonyl, alkoxyaryl, or carboxylic acid or its derivatives. The groups given above are defined as described earlier.

It is appreciated that in any of the above-mentioned reactions, any reactive group in the substrate molecule may be protected according to conventional chemical practice. Suitable protecting groups in any of the above mentioned reactions are tertiarybutyldimethylsilyl, methoxymethyl, triphenyl methyl, benzyloxycarbonyl, tetrahydropyran(THP) etc, to protect hydroxyl or phenolic hydroxy group; N-tert-butoxycarbonyl (N-Boc), N-benzyloxycarbonyl (N-Cbz), N-9-fluorenyl methoxy carbonyl (-N-FMOC), benzophenoneimine, propargyloxy carbonyl (POC) etc, for protection of amino or anilino group, acetal protection for aldehyde, ketal protection for ketone and the like. The methods of formation and removal of such protecting groups are those conventional methods appropriate to the molecule being protected.

A method of treating or preventing an bacterial infections in a subject is provided by administering an therapeutically effective amount of compound of formula (I).

The term "therapeutically effective amount" shall mean that amount of a drug or pharmaceutical agent that will elicit the biological or medical response of a tissue, system or patient that is being sought.

The pharmaceutically acceptable salts are prepared by reacting the compounds of formula (I) wherever applicable with 1 to 4 equivalents of a base such as sodium hydroxide, sodium methoxide, sodium hydride, potassium t-butoxide, calcium hydroxide, magnesium hydroxide and the like, in the presence of a solvent like ether, THF, methanol, t-butanol, dioxane, isopropanol, ethanol etc. Mixture of solvents may be used. Organic bases like lysine, arginine, diethanolamine, choline, tromethamine, guanidine and their derivatives etc. may also be used. Alternatively, acid addition salts wherever applicable are prepared by treatment with acids such as hydrochloric acid, hydrobromic acid, nitric acid, sulfuric acid, phosphoric acid, p-toluenesulphonic acid, methanesulfonic acid, acetic acid, citric acid, maleic acid salicylic acid, hydroxynaphthoic acid, ascorbic acid, palmitic acid, succinic acid, benzoic acid, benzenesulfonic acid, tartaric acid and the like in the presence of a solvent like ethyl acetate, ether, alcohols, acetone, THF, dioxane etc. Mixture of solvent may also be used. The salts of amino acid groups and other groups may be prepared by reacting the compounds of formula (I) with the respective groups in the presence of a solvent like alcohols, ketones, ether etc. Mixture of solvents may be used.

The present invention also provides pharmaceutical compositions, containing compounds of the general formula (I), their pharmaceutically acceptable salts The pharmaceutical compositions according to this invention can be used for the treatment of bacterial infections. They can also be used for the treatment of bacterial infections associated with multidrug resistance. The pharmaceutical compositions according to this invention can also be administered prophylatically for the prevention of bacterial infections in a patient at risk of developing a bacterial infection.

The pharmaceutical compositions may be in the forms normally employed, such as tablets, capsules, powders, dispersible granules, cachets, suppositories, syrups, solutions, suspensions and the like, may contain flavorants, sweeteners etc. in suitable solid or liquid carriers or diluents, or in suitable sterile media to form injectable solutions or suspensions. Such compositions typically contain from 0.5 to 90 % by weight of active compound, the remainder of the composition being pharmaceutically acceptable carriers, diluents or solvents.

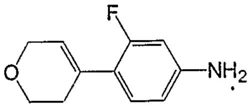
Suitable pharmaceutically acceptable carriers include solid fillers or diluents and sterile aqueous or organic solutions. The active compounds will be present in such pharmaceutical compositions in the amounts sufficient to provide the desired dosage in the range as described above. Thus, for oral administration, the compounds can be combined with a suitable solid, liquid carrier or diluent to form capsules, tablets, powders, syrups, solutions, suspensions and the like. The pharmaceutical compositions, may, if desired, contain additional components such as flavorants, sweeteners, excipients and the like. For parenteral administration, the compounds can be combined with sterile aqueous or organic media to form injectable solutions or suspensions. For example, solutions in sesame or peanut oil, aqueous propylene glycol and the like can be used, as well as aqueous solutions of water-soluble pharmaceutically-acceptable acid addition salts or salts with base of the compounds. The injectable solutions prepared in this manner can then be administered intravenously, intraperitoneally, subcutaneously, or intramuscularly, with intramuscular administration being preferred in humans.

The compounds of the formula (I) or pharmaceutical compositions thereof as defined above are clinically administered to mammals, including human beings, via oral, parenteral and/or topical routes. Administration by the oral route is preferred, being more convenient and avoiding the possible pain and irritation of injection. However, in circumstances where the patient cannot swallow the medication, or absorption following oral administration is impaired, as by disease or other abnormality, it is essential that the drug be administered parenterally. By either route, the dosage is in the range of about 0.1 mg/kg to about 100 mg / kg, morepreferably about 3.0 mg/kg to about 50 mg/kg of body weight of the subject per day administered singly or as a divided dose. However, the optimum dosage whether for prevention or treatment for the individual subject being treated will be determined by the person responsible for treatment, Initial dosage may be smaller than the optimum and the daily dosage may be progressively increased during the course of treatment depending on the particular situation. If desired, the daily dose may also be divided into multiple doses for administering, e.g. 2-4 times per day. It is to be understood that the dosages may vary depending upon the requirements of the patient, the severity of the bacterial infection being treated, and the particular compound being used. In a topical treatment an effective amount of compound of formula (I) is admixed in a pharmaceutically acceptable gel or cream vehicle that can be applied to the patient's skin at the area of treatment. Such creams and gels can be prepared by the procedures available in the literature and can include penetration enhancers.

The manner in which the compounds of this invention can be prepared is illustrated in the following examples, which demonstrate the preparation of typical species of the invention. In these examples, the identities of compounds, intermediates and final, were confirmed by infrared, nuclear magnetic spectral analyses as necessary. The examples are for the purpose of illustration only and should not be regarded as limiting the invention in any way.

Preparation-1

4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluorophenylamine



n-Butyllithium (124 mL, 1.6 M in hexane, 198.4 mmol) was added drop wise to a solution of 3-fluoroaniline (10 grams, 90.1 mmol) in THF (200 mL) at –78 °C under nitrogen atmosphere and stirred for 20 minutes. A solution of 1,2-bis(chlorodimethylsilyl)ethane (21.3 grams, 99.1 mmol) in dry THF (200 mL) was added and stirred at the same temperature for 45 minutes.. The reaction mixture was brought to room temperature and then quenched with water (120 mL). The mixture was extracted with diethyl ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed under vacuum to obtain 1-(3-fluorophenyl)-2,2,5,5-tetramethyl-[1,2,5]azadisilolidine (21.2 grams) and this crude product was used in the next step without purification. To a solution of 1-(3-fluorophenyl)-2,2,5,5-tetramethyl-[1,2,5]azadisilolidine (15 grams, 59.3 mmol) in THF (130 mL) was slowly added 55 mL (71.1 mmol) of *sec*-BuLi (1.3 M in cyclohexane/hexane) at –78 °C under nitrogen and stirred the reaction at the same temperature for 4 h. A solution of tetrahydro-4-pyranone (7.11 grams, 71.1 mmol) in dry THF (10 mL) was added to the reaction mixture and allowed to rise to room temperature. The reaction mixture was quenched slowly by the addition of water (150 mL) at 0 °C and was concentrated under vacuum. The resulting residue was acidified with conc. HCl and the acidic solution was extracted with diethyl ether (3 x 500 mL). The aqueous layer was basified with aqueous NaOH solution and extracted with diethyl ether (500 mL). The organic layer was washed with brine, dried over sodium sulfate and evaporated under vacuum. The resulting residue was refluxed with conc. HCl (40 mL) for 3 h and then allowed to cool to room temperature. The reaction mixture was basified with aqueous NH_3 (30%) and was extracted with dichloromethane. The solvent was evaporated and the required product (3 grams, 26%) was separated as a light brown solid by silica gel column chromatography (ethyl acetate / hexane; 3:17).

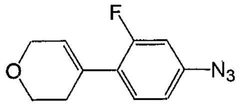
^1H NMR ($CDCl_3$): δ 7.05 (t, *J* = 8.8 Hz, 1H), 6.52-6.28 (m, 2H), 6.00-5.88 (m, 1H), 4.40-4.23 (m, 2H), 3.91 (t, *J* = 5.3 Hz, 2H), 3.87-3.60 (m, 2H), 2.60-2.34 (m, 2H);

MS (m/e): 194 (M^++1), 161;

IR (neat): 3358, 2927, 2856, 1829, 1512, 1446, 1321, 1166, 1043 cm^{-1}.

Preparation-2

4-(4-Azido-2-fluoro-phenyl)-3,6-dihydro-2*H*-pyran:



A saturated solution of sodium nitrite (2.86 grams, 41.4 mmol) in water (5 mL) was slowly added to an ice cooled solution of 4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluorophenylamine (4 grams, 20.7 mmol) obtained in preparation 1, in 6N HCl (18 mL) and stirred for 0.5 h. Then a saturated solution of sodium azide (2.69 grams, 41.4 mmol) and sodium acetate (33.98 grams, 414 mmol) in water (100 mL) was added slowly. The reaction mixture was stirred for another 0.5 h, diluted with water and extracted with ethyl acetate (2 x 100 mL). The organic layer was washed with water followed by brine and dried over sodium sulfate. Evaporation of volatiles and purification of the residue by flash chromatography (ethyl acetate/ hexane; 1:9) yielded the title compound as a yellow solid (3.1 grams, 68%).

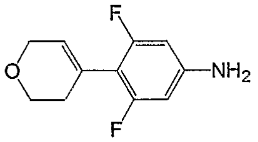
^{1}H NMR ($CDCl_3$): δ 7.23 (t, J = 8.4 Hz, 1H), 6.81-6.68 (m, 2H), 6.09-5.98 (m, 1H), 4.50-4.17 (m, 2H), 3.90 (t, J = 5.4 Hz, 2H), 2.64-2.32 (m, 2H);

MS (m/e): 220 (M^++1), 192, 174;

IR (KBr): 3357, 2938, 2116, 1614, 1425, 1308, 1049 cm^{-1}.

Preparation-3

4-(3,6-Dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenylamine:



n-Butyllithium (55 mL, 1.6 M in hexane, 7.18 mmol) was added drop wise to a solution of 3,5-difluoroaniline (5 grams, 38.76 mmol) in THF (78 mL) at -78°C under nitrogen atmosphere and stirred for 20 minutes. A solution of 1,2-bis(chlorodimethylsilyl)ethane (8.33 grams, 38.76 mmol) in THF (78 mL) was added to the reaction mixture and stirred for 45 minutes and then it was brought to room temperature. The reaction mixture was quenched with water (115 mL) and extracted with diethyl ether. The combined organic layers were washed with water and brine and dried over Na_2SO_4. The solvent was removed under vacuum to obtain 1-(3,5-difluorophenyl)-2,2,5,5-tetramethyl-[1,2,5]azadisilolidine (10.12 grams) and this crude product was used in the next step without purification. To a solution of 1-(3,5-difluorophenyl)-2,2,5,5-tetramethyl-[1,2,5]azadisilolidine (10.12 grams, 37.3 mmol) in THF (60 mL) was slowly added 27 mL (42.96 mmol) of *n*-BuLi (1.6 M in hexane) at –78 °C under nitrogen and stirred for 4 h. A solution of tetrahydro-4-pyranone (7.11 grams, 71.1 mmol) in dry THF (10 mL) was added to the above mixture and warmed to room temperature. The reaction mixture was stirred for 18 h, then quenched with 100 mL of water and concentrated under vacuum. The resulting residue was acidified with conc. HCl and the acidic solution was extracted with diethyl ether (150 mL). The aqueous layer was basified with 40% aqueous NaOH solution at 0 °C and extracted with diethyl ether. The organic layer was washed with brine, dried over sodium sulfate and evaporated on rotavapor. The resulting residue was refluxed with conc. HCl (40 mL) for 3 h and then allowed to cool to room temperature. The reaction mixture was basified with aqueous NH_3

(30%) and was extracted with dichloromethane. The solvent was evaporated on rotavapor and the residue was purified through silica gel column (ethyl acetate / hexane; 3:17) to furnish the required product (2.2 grams, 27%) as a pale brown solid.

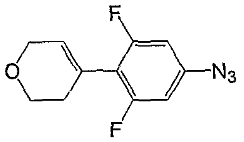
^{1}H NMR ($CDCl_3$): δ 6.21-6.10 (d, *J* = 11.6 Hz, 2H), 5.83-5.78 (m, 1H), 4.18-4.12 (m, 2H), 3.93-3.87 (m, 4H), 2.42-2.26 (m, 2H);

MS (m/e): 212 (M^++1);

IR (KBr): 3464, 3346, 3229, 1761, 1649, 1571, 1364, 1015 cm^{-1}.

Preparation-4

4-(4-Azido-2,6-difluoro-phenyl)-3,6-dihydro-2*H*-pyran:



A saturated solution of sodium nitrite (590 mg, 8.55 mmol) in water (5 mL) was slowly added to a solution of 4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluorophenylamine (900 mg, 4.26 mmol) in HCl (6N, 16 mL), obtained in preparation-3, cooled to 0 °C, and stirred for 0.5 h. Then a saturated solution of sodium azide (550 mg, 8.54 mmol) and sodium acetate (7 grams, 85.4 mmol) in water (100 mL) was added slowly at the same temperature. The reaction mixture was stirred for another 0.5 h and then diluted with ethyl acetate (250 mL). The organic layer was washed with water followed by brine and dried over Na_2SO_4. The solvent was evaporated and the residue was purified by flash chromatography (ethyl acetate/ hexane; 1:9) to get the title compound as a pale yellow solid (560 mg, 58%).

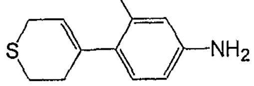
^{1}H NMR ($CDCl_3$): δ 6.63-6.53 (d, *J* = 12.5 Hz, 2H), 5.86-5.82 (m, 1H), 4.37-4.23 (m, 2H), 3.92 (t, *J* = 5.4 Hz, 2H), 2.46-2.37 (m, 2H);

MS (m/e): 238 (M^++1), 212, 194, 135;

IR (KBr): 2935, 2818, 2133, 1633, 1570, 1494, 1238 cm^{-1}.

Preparation-5

4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenylamine:



n-Butyllithium (62 mL, 1.6 M in hexane, 99.2 mmol) was added drop wise to a solution of 3-fluoroaniline (5 grams, 45 mmol) in THF (100 mL) at –78 °C under nitrogen atmosphere Then a solution of 1,2-bis(chlorodimethylsilyl)ethane (10.65 grams, 49.53 mmol) in THF (100 mL) was added drop wise. The reaction mixture was stirred at the same temperature for 0.5 h and then it was brought to room temperature. The reaction mixture was quenched with water (135 mL), extracted with diethyl ether and washed with brine. The solvent was removed under vacuum to obtain 1-(3-fluorophenyl)-2,2,5,5-tetramethyl-[1,2,5]azadisilolidine (11.8 grams) and this crude product was used in the next step without purification. To a solution of 1-(3-fluorophenyl)-2,2,5,5-tetramethyl-[1,2,5]azadisilolidine (11.8 grams, 46.6 mmol) in THF (350 mL) was slowly added 43 mL of *sec*-BuLi (55.9 mmol, 1.6 M in hexane) at –78 °C and stirred for 4 h. A solution of tetrahydro-4-thiopyranone (6 grams, 51.75 mmol) in THF (50 mL) was added to the reaction mixture at -78 °C. The reaction mixture was slowly brought to room temperature and was stirred for further 18 h. It was then quenched with water (60 mL), concentrated under vacuum to remove most of the THF and the residue was acidified with conc. HCl. The acidic solution was extracted with diethyl ether. The aqueous layer was basified with 40% aqueous NaOH solution and extracted with diethyl ether (300 mL). The organic layer was washed with brine, dried over sodium sulfate and evaporated under vacuum. The resulting residue was refluxed with conc. HCl (70 mL) for 3.5 h and then allowed to cool to room temperature. The reaction mixture was basified with aqueous NH_3 (30%) and was extracted with dichloromethane. The solvent was evaporated on rotavapor and the required product (5.1 grams, 54%) was separated as a pale brown solid by silica gel column chromatography (ethyl acetate / petroleum ether; 3:17).

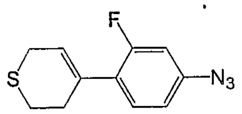
^{1}H NMR ($CDCl_3$ + CD_3OD): δ 6.99 (t, J = 8.8 Hz, 1H), 6.42-6.39 (m, 2H), 5.95-5.87 (m, 1H), 3.36-3.28 (m, 2H), 3.18-3.08 (m, 2H), 2.85 (t, J = 5.6 Hz, 2H), 2.68-2.56 (m, 2H);

CI-MS (m/e): 210 (M^++1);

IR (neat): 3360, 2916, 1630, 1510, 1444, 1164, 965 cm^{-1}.

Preparation-6

4-(4-Azido-2-fluoro-phenyl)-3,6-dihydro-2*H*-thiopyran:



A saturated aqueous solution of sodium nitrite (1g, 14.6 mmol) was slowly added to an ice cooled solution of 4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluorophenylamine (1.52 grams, 7.3 mmol), obtained in preparation-5, in 6 N HCl (16 mL), and stirred for 0.5 h. Then a solution of sodium azide (945 mg, 14.6 mmol) and sodium acetate (12 grams, 146 mmol) in water (50 mL) was added at the same temperature and stirred for another 0.5 h. Then diluted with ethyl acetate (250 mL). The organic layer was washed with water followed by brine and dried over sodium sulfate. Evaporation of solvent and purification of the resulting residue by flash chromatography (ethyl acetate/ hexane; 3:17) yielded the desired compound (752 mg, 43%) as a brown oily material.

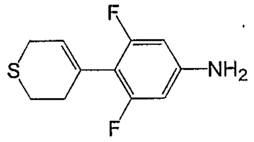
^{1}H NMR ($CDCl_3$): δ 7.19 (t, J = 8.2 Hz, 1H), 6.81-6.68 (m, 2H), 6.08-5.98 (m, 1H), 3.41-3.28 (m, 2H), 2.86 (t, J = 5.6 Hz, 2H), 2.68-2.62 (m, 2H);

CI-MS (m/e): 236 (M^++1), 210;

IR (neat): 2916, 2114, 1618, 1569, 1498, 1209, 1099 cm^{-1}.

Preparation-7

4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenylamine:



n-Butyllithium (55 mL, 1.6 M in hexane, 87.18 mmol) was added drop wise to a solution of 3,5-difluoroaniline (5 grams, 38.75 mmol) in THF (78 mL) at –78 °C under nitrogen atmosphere and stirred for 20 minutes., a solution of 1,2-bis(chlorodimethylsilyl)ethane (8.5 grams, 39.53 mmol) in THF (78 mL) was added drop wise. The reaction mixture was stirred at the same temperature for 0.5 h and then allowed to warm to room temperature. The reaction mixture was quenched with water (100 mL), extracted with diethyl ether and then the organic layer was washed with brine. The solvent was removed under vacuum to obtain 1-(3,5-difluorophenyl)-2,2,5,5-tetramethyl-[1,2,5] azadisilolidine (10.7 grams) and this crude product was used in the next step without purification. To a solution of 1-(3,5-difluorophenyl)-2,2,5,5-tetramethyl-[1,2,5] azadisilolidine (10.7 grams, 39.4 mmol)) in THF (80 mL) was slowly added 28.4 mL of n-BuLi (45.3 mmol,1.6 M in hexane) at –78 °C. under nitrogen and stirred the same for 4 h. Then a solution of tetrahydro-4-thiopyranone (5.26 grams, 45.3 mmol) in THF (30 mL) was added to the reaction mixture and slowly brought to room temperature and stirred for further 18 h. The reaction mixture was quenched with water (50 mL), concentrated under vacuum and the resulting residue was acidified with conc. HCl. The acidic solution was extracted with diethyl ether. The aqueous layer was basified with 40% aqueous NaOH solution and extracted with diethyl ether (3 x 150 mL). The organic layer was washed with brine, dried over sodium sulfate and evaporated under vacuum. The resulting residue was refluxed with conc. HCl (60 mL) for 3.5 h and then allowed to cool to room temperature. The reaction mixture was basified with aqueous NH_3 (30%) and was extracted with dichloromethane. The solvent was evaporated on a rotavapor and the crude product was column chromatographed over silica gel (ethyl acetate / petroleum ether; 3:17) to get the desired compound (3.8 grams, 43%) as a pale brown solid.

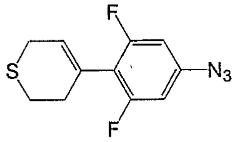
^{1}H NMR ($CDCl_3$): δ 6.20-6.16 (m, 2H), 5.96-5.82 (m, 1H), 3.95-3.81 (m, 2H), 3.36-3.27 (m, 2H), 2.85 (t, *J* = 5.9 Hz, 2H), 2.56-2.43 (m, 2H);

MS (m/e): 228 (M^++1), 142;

IR (KBr):3496, 3386, 2925, 1648, 1578, 1459, 1159, 1007, 822 cm^{-1}.

Preparation-8

4-(4-Azido-2,6-difluoro-phenyl)-3,6-dihydro-2*H*-thiopyran:



A saturated solution of sodium nitrite (79 mg, 1.14 mmol) in water (3 mL) was slowly added to an ice cooled solution of 4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluorophenylamine (130 mg, 0.57 mmol), obtained in preparation-7, in 6N HCl (8 mL), and stirred for 0.5 h. Then a solution of sodium azide (75 mg, 1.15 mmol) and sodium acetate (950 mg, 11.58 mmol) in water (15 mL) were added respectively at the same temperature. The reaction mixture was stirred for additional 0.5 h and then diluted with ethyl acetate (100 mL). The organic layer was washed with water followed by brine and dried over sodium sulfate. Evaporation of volatiles and purification of the resulting residue by flash chromatography (ethyl acetate/ hexane; 3:17) yielded the title compound as a pale orange solid (80 mg, 56%).

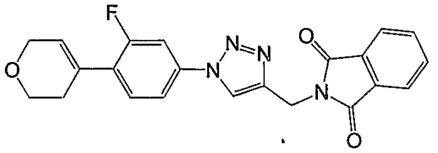
^{1}H NMR ($CDCl_3$): δ 6.62-6.58 (m, 2H), 5.98-5.90 (m, 1H), 3.40-3.27 (m, 2H), 2.88 (t, *J* = 5.6 Hz, 2H), 2.61-2.47 (m, 2H).

MS (m/e): 254 (M^++1), 228.

IR (KBr): 2925, 2116, 1633, 1570, 1494, 1237 cm^{-1}.

Example-1

2-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}--isoindole-1,3-dione:

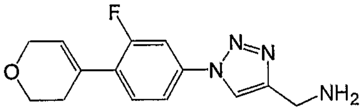


To a solution of 4-(4-azido-2-fluoro-phenyl)-3,6-dihydro-2*H*-pyran (3 grams, 13.7 mmol), obtained in preparation-2, and *N, N* -diisopropylethylamine base (4.78 mL, 27.4 mmol) in acetonitrile (100 mL) was added 2-prop-2-ynyl-isoindole-1,3-dione (3 grams, 16.4 mmol) followed by the addition of cuprous iodide (2.86 grams, 15.1 mmol) and stirred at room temperature for 1 h. The reaction mixture was filtered through a celite and washed thoroughly with MeOH/$CHCl_3$. The filtrate was concentrated under vacuum and the residue was purified by flash chromatography (ethyl acetate/ hexane; 6:4) to obtain the required compound as a light yellow solid (3 grams, 54%).

^{1}H NMR (DMSO-d_6): δ 8.85 (s, 1H), 8.00-7.66 (m, 6H), 7.62 (t, *J* = 8.3 Hz, 1H), 6.28-6.12 (m, 1H), 4.93 (s, 2H), 4.33-4.16 (m, 2H), 3.82 (t, *J* = 5.3 Hz, 2H), 2.68-2.30 (m, 2H).
MS (m/e): 405 (M^++1), 377, 236, 183.
IR (KBr): 3394, 3370, 1790, 1742, 1633, 1533, 1449, 1372, 1269 cm^{-1}

Example-2

***C*-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:**



Hydrazine hydrate (3.1 mL) was added to a solution of 2-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-isoindole-1,3-dione (2.9 grams, 7.18 mmol), obtained in example-1, in methanol (15 mL) and refluxed for 2 h followed by stirring at room temperature for 10 h. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The residue was purified by flash chromatography (ethyl acetate/ hexane; 1:9) to afford the title compound as a white solid (800 mg, 41%).

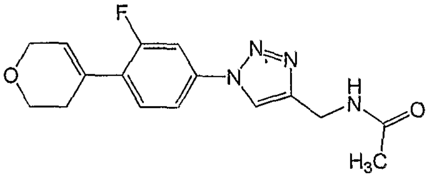
^{1}H NMR (DMSO-d_6): δ 9.28-8.78 (m, 2H), 8.67 (s, 1H), 7.93-7.63 (m, 2H), 7.58 (t, *J* = 8.1 Hz, 1H), 6.30-6.12 (m, 1H), 4.52-3.20 (m, 6H), 2.60-2.39 (m, 2H).

MS (m/e): 275 (M^++1), 230, 217.

IR (KBr): 3297, 1665, 1517, 1436, 1375, 1233, 1044 cm^{-1}.

Example-3

N-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-acetamide:



Triethylamine (0.08 mL, 0.73 mmol) was added to a solution of C-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}methylamine (100 mg, 0.365 mmol), obtained in example-2, in dichloromethane (5 mL), cooled to 0 °C, followed by the addition of acetyl chloride (0.028 mL, 0.4 mmol) and stirred at room temperature for 3 h. The reaction mixture was concentrated on rotavapor and the residue was purified by column chromatography over silica gel (2% methanol in chloroform) to get the required compound (62 mg, 54%) as a white powder, mp 186-188 °C.

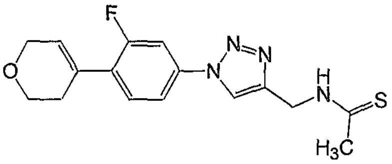
^{1}H NMR (DMSO-d_6): δ 8.70 (s, 1H), 8.52-8.38 (m, 1H), 7.92-7.65 (m, 2H), 7.59 (t, *J* = 8.4 Hz, 1H), 6.29-6.18 (m, 1H), 4.36 (d, *J* = 5.7 Hz, 2H), 4.25-4.18 (m, 2H), 3.83 (t, *J* = 5.3 Hz, 2H), 2.61-2.32 (m, 2H), 2.10 (s, 3H).

MS (m/e): 317 (M^++1), 288, 230.

IR (KBr): 3281, 3149, 2926, 1644, 1558, 1460, 1291, 1047 cm^{-1}.

Example-4

N-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thioacetamide:



To a solution of *C*-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}methylamine (100 mg, 0.365 mmol), obtained in example-2, in THF (5 mL) was added triethylamine (0.103 mL, 0.73 mmol) followed by the addition of ethyl dithioacetate (0.05 ml, 0.44 mmol) and stirred at room temperature for 16 h. The reaction mixture was concentrated and the resulting residue was purified by column chromatography using 2% methanol in chloroform as eluent. The desired product was obtained as a creamy white solid (62 mg, 51%), mp 159-161°C.

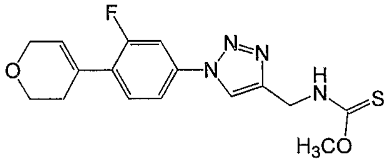
^{1}H NMR (DMSO-d$_6$): δ 10.60-10.40 (m, 1H), 8.82 (s, 1H), 7.92-7.50 (m, 2H), 7.60 (t, *J* = 8.3 Hz, 1H), 6.27-6.12 (m, 1H), 4.84 (d, *J* = 4.8 Hz, 2H), 4.32-4.18 (m, 2H), 3.83 (t, *J* = 5.4 Hz, 2H), 2.60-2.30 (m, 5H).

MS (m/e): 333 (M$^+$+1), 304, 230.

IR (KBr): 3243, 3055, 2926, 1579, 1460, 1406, 1362, 1231 cm^{-1}.

Example-5

{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid *O*-methyl ester:



To a solution of *C*-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}methylamine (100 mg, 0.365 mmol), obtained in example-2, in dichloromethane (10 mL) was added a solution of sodium bicarbonate (77 mg, 0.92 mmol) in water (3 mL) followed by cooling in ice bath. Thiophosgene (0.034 mL, 0.44 mmol) was added to the mixture at 0 °C and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed with water, brine and dried over sodium sulfate. The solvent was evaporated and the residue was refluxed with methanol (15 mL) for 16 h. Removal of methanol and purification of the residue by column chromatography (ethyl acetate/hexane; 3:10) yielded the required compound (65 mg, 51%) as a white powder, mp 116-120 °C.

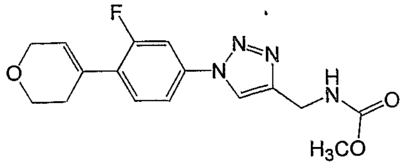
^{1}H NMR (DMSO-d$_6$): δ 9.79-9.60 (m, 1H), 8.76 and 8.70 (two s, 1H, rotamers in a ratio of 4:1), 8.01-7.63 (m, 2H), 7.59 (t, *J* = 8.6 Hz, 1H), 6.30-6.13 (m, 1H), 4.73 and 4.45 (two d, *J* = 5.4 Hz, 2H, rotamers in a ratio of 4:1), 4.37-4.14 (m, 2H), 4.00-3.68 (m, 5H), 2.69-2.30 (m, 2H).

MS (m/e): 349 (M$^+$+1), 317, 230.

IR (KBr, film): 3438, 3214, 2925, 1619, 1512, 1458, 1365, 1218 cm^{-1}.

Example-6

{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-carbamic acid methyl ester:



To a solution of *C*-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (90 mg, 0.33 mmol), obtained in example-2, in dichloromethane (5 mL), cooled to 0 °C, was added *N, N*-diisopropylethylamine (0.126 mL, 0.72 mmol) followed by the addition of methyl chloroformate (0.031 mL, 0.39 mmol) and stirred at the same temperature for 2 h. And the organic layer was washed with water followed by brine and dried over sodium sulfate. The solvent was evaporated and the residue was purified by column chromatography over silica gel (methanol/ chloroform; 1:24) to afford the required product (50 mg, 46%) as a creamy white solid, mp 140-144 °C.

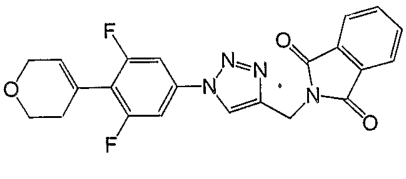
^{1}H NMR (DMSO-d$_6$): δ 8.70 (s, 1H), 7.97-7.66 (m, 2H), 7.58 (t, *J* = 8.3 Hz, 1H), 6.30-6.16 (m, 1H), 4.31 (d, *J* = 5.9 Hz, 2H), 4.25-4.18 (m, 2H), 3.83 (t, *J* = 5.1 Hz, 2H), 3.56 (s, 3H), 2.60-2.32 (m, 2H).

MS (m/e): 333 (M$^+$+1).

IR (KBr): 3297, 2924, 1688, 1535, 1463, 1262, 1045 cm^{-1}.

Example-7

2-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-1,3-isoindole-1,3-dione:



To a solution of 4-(4-azido-2,6-difluoro-phenyl)-3,6-dihydro-2*H*-pyran (545 mg, 2.30 mmol), obtained in preparation 4, and *N,N*-diisipropylethylamine (0.80 mL, 4.59 mmol) in acetonitrile (20 mL) was added 2-prop-2-ynyl-isoindole-1,3-dione (642 mg, 3.47 mmol) followed by the addition of cuprous iodide (655 mg, 3.45 mmol) and stirred at room temperature for 2 h. The reaction mixture was filtered through a celite pad. The filtrate was concentrated under vacuum and the residue was purified by chromatography over silica gel

(3% methanol in chloroform) to obtain the required compound (350 mg, 39%) as a pale yellow solid

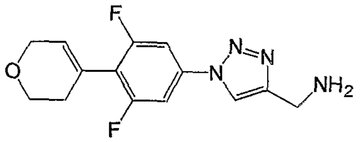
^{1}H NMR (CDCl$_3$): δ 8.94 (s, 1H), 8.08-7.73 (m, 6H), 6.12-6.04 (m, 1H), 4.99 (s, 2H), 4.35-4.22 (m, 2H), 3.88 (t, J = 5.4 Hz, 2H), 3.55-3.20 (m, 2H).

MS (m/e): 423 (M$^+$+1), 173, 131.

IR (KBr): 3442, 2925, 1716, 1634, 1395, 1280, 1094 cm^{-1}.

Example-8

C-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:



To a solution of 2-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-1,3-isoindole-1,3-dione (325 mg, 0.768 mmol), obtained in example-7, in methanol (10 mL) was added hydrazine hydrate (0.41 mL) and refluxed for 2 h followed by stirring at room temperature for 10 h. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The product was purified by flash chromatography on silica (5% methanol in chloroform) to afford the desired product (100 mg, 47%).

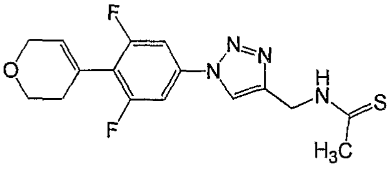
^{1}H NMR (DMSO-d$_6$): δ 8.67 (s, 1H), 7.75 (d, J = 8.3 Hz, 2H), 6.05-5.93 (m, 1H), 4.30-4.12 (m, 2H), 3.92-3.72 (m, 4H), 2.63-2.38 (m, 2H).

MS (m/e): 293 (M$^+$+1), 236, 163.

IR (KBr): 3368, 3127, 2924, 2850, 1631, 1592, 1513, 1448, 1227, 1126, 1025 cm^{-1}.

Example-9

N-{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thioacetamide:



Triethylamine (0.053 mL, 0.38 mmol) was added to a solution of C-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (50 mg, 0.17 mmol), obtained in example-8, in THF (5 mL) followed by the addition of ethyl dithioacetate (0.03 ml, 0.26 mmol) and stirred at room temperature for 16 h. The reaction mixture was diluted with ethyl acetate (50 mL), washed with water followed by brine and dried over sodium sulfate. Solvent was evaporated and the residue was purified by column chromatography using 4% methanol in chloroform as eluent. Relevant fractions were combined and evaporated to obtain the desired product as a white powder (28 mg, 47%), mp 138 °C.

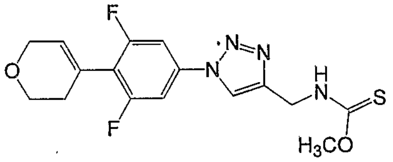
^{1}H NMR ($CDCl_3$): δ 8.28-8.21 (m, 1H), 8.14 (s, 1H), 7.35 (d, *J* = 7.8 Hz, 2H), 5.98-5.92 (m, 1H), 5.02 (d, *J* = 5.7 Hz, 2H), 4.38-4.31 (m, 2H), 3.95 (t, *J* = 5.4 Hz, 2H), 2.61 (s, 3H), 2.48-2.40 (m, 2H).

MS (m/e): 351 (M^++1), 335, 323, 252.

IR (KBr): 3221, 3041, 2929, 1631, 1510, 1452, 1386, 1028 cm^{-1}.

Example-10

{1-[4-(3,6-Dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid O-methyl ester:



To a solution of *C*-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}methylamine (50 mg, 0.17 mmol), obtained in example-8, in dichloromethane (4 mL) was added a saturated solution of sodium bicarbonate (35 mg, 0.42 mmol) in water (3 mL) followed by cooling in ice bath. Thiophosgene (0.016 mL, 0.21 mmol) was added to the above mixture at 0 °C and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), and the organic layer with water followed by brine and dried over sodium sulfate. Evaporation of volatiles left a residue, which was refluxed with methanol (5 mL) for 16 h. Methanol was removed under vacuum and the residue was purified by column chromatography over silica gel (methanol/ chloroform; 1:25) to get the title compound as a pale pink solid (41 mg, 72%), mp 132 °C.

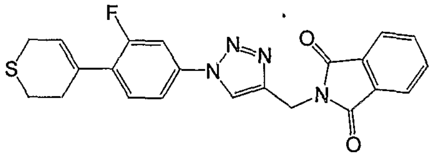
^{1}H NMR ($CDCl_3$): δ 8.12 and 7.89 (two s, 1H, rotamers in a ratio of 4:1), 7.35 (d, *J* = 7.3 Hz, 2H), 6.98-6.91 (m, 1H), 5.98-5.93 (m, 1H), 4.92 and 4.65 (d, *J* = 6.3 Hz, 2H, rotamers in ratio of 4:1), 4.39-4.32 (m, 2H), 4.10 and 4.00 (two s, 3H, rotamers in a ratio of 1:4), 3.95 (t, *J* = 5.4 Hz, 2H), 2.48-2.41 (m, 2H).

MS (m/e): 367 (M^++1), 335, 319, 278.

IR (KBr): 3237, 3126, 1632, 1586, 1448, 1199 cm^{-1}.

Example-11

2-{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-isoindole-1,3-dione:



To a solution of 4-(4-azido-2-fluoro-phenyl)-3,6-dihydro-2*H*-thiopyran (630 mg, 2.68 mmol), obtained in preaparation-6, and *N*, *N*-diisopropylethylamine (0.936 mL, 5.36 mmol) in acetonitrile (10 mL) was added 2-prop-2-ynyl-isoindole-1,3-dione (691 mg, 3.74 mmol) followed by the addition of cuprous iodide (561 mg, 2.95 mmol) and stirred at room temperature for 1 h. The reaction mixture was filtered through a celite pad and washed thoroughly with MeOH. Concentration of the filtrate under vacuum and purification of the resulting residue by flash chromatography (ethyl acetate/ hexane; 4:6) afforded the title compound as a white solid (550 mg, 49%).

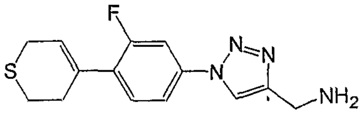
^{1}H NMR ($CDCl_3$): δ 8.02 (s, 1H), 7.89-7.86 (m, 2H), 7.75-7.71 (m, 2H), 7.49-7.26 (m, 3H), 6.08-6.02 (m, 1H), 5.08 (s, 2H), 3.40-3.25 (m, 2H), 2.87 (t, *J* = 5.6 Hz, 2H), 2.69-2.60 (m, 2H).

MS (m/e): 421 (M^++1), 389, 276, 248.

IR (KBr): 3458, 2921, 1767, 1617, 1512, 1395, 1236, 1045 cm^{-1}

Example-12

***C*-{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine**:



To a solution of 2-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-isoindole-1,3-dione (520 mg, 1.24 mmol), obtained in example-11, in methanol (10 mL), was added hydrazine hydrate (0.53 mL) and refluxed for 2 h followed by stirring at room temperature for 10 h. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The residue was purified by flash chromatography (methanol/ chloroform; 1:9) to obtain the desired compound as a creamy white solid (205 mg, 57%).

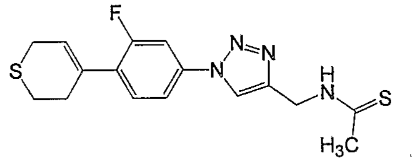
^{1}H NMR (DMSO-d$_6$): δ 8.67 (s, 1H), 7.95-7.62 (m, 2H), 7.62-7.29 (m, 1H), 6.20-6.03 (m, 1H), 4.10-3.78 (m, 2H), 3.78-3.09 (m, 2H), 2.84 (t, *J* = 5.5 Hz, 2H), 2.70-2.38 (m, 2H).

MS (m/e): 291 (M$^+$+1), 246, 233.

IR (KBr): 3442, 2929, 1740, 1661, 1575, 1494, 1360, 1231, 1015 cm^{-1}.

Example-13

***N*-{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thioacetamide:**



Triethylamine (0.077 mL, 0.55 mmol) was added to a solution of C-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (80 mg, 0.276 mmol), obtained in example-12, in THF (5 mL) followed by the addition of ethyl dithioacetate (0.049 mL, 0.43 mmol) and stirred at ambient temperature for 16 h. The reaction mixture was concentrated under vacuum and the residue was purified by a silica gel column (1% methanol in chloroform) to give the desired product as a white solid (55 mg, 57%), Mp 107-110 °C.

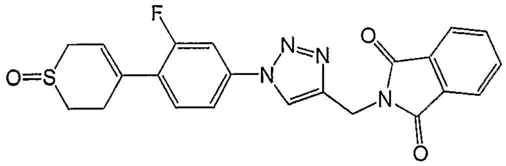
^{1}H NMR (CDCl$_3$): δ 8.19-8.02 (m, 2H), 7.56-7.18 (m, 3H), 6.17-6.05 (m, 1H), 5.02 (d, *J* = 5.3 Hz, 2H), 3.40-3.30 (m, 2H), 2.88 (t, *J* = 5.6 Hz, 2H), 2.80-2.50 (m, 2H), 260 (s, 3H).

MS (m/e): 349 (M$^+$+1), 206, 149, 126.

IR (KBr): 3496, 3194, 2925, 1621, 1566, 1458, 1366, 1234, 1055 cm^{-1}.

Example-14

2-{1-[3-Fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione:

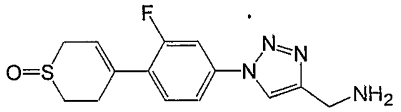


Sodium periodate (915 mg, 4.28 mmol) in water (10 mL) was added to an ice cooled solution of 2-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-isoindole-1,3-dione (400 mg, 0.95 mmol), obtained in example-1, in methanol (12 mL) and ethyl acetate (12 mL) and stirred for 1 h. The reaction mixture was brought to room temperature and stirred for 16 h. The reaction mixture was diluted with MeOH/$CHCl_3$ (1:19), filtered and the filtrate was concentrated under vacuum. The residue obtained was dissolved in chloroform, washed with saturated solution of Na_2SO_3 and $NaHCO_3$ respectively and dried over sodium sulfate. The solvent was evaporated and the residue was purified by column chromatography over silica gel to afford the desired product (55 mg, 33%) as a white solid.

^{1}H NMR ($CDCl_3$): δ 8.04 (s, 1H), 7.87-7.78 (m, 2H), 7.78-7.68 (m, 2H), 7.68-7.35 (m, 3H), 5.86-5.82 (m, 1H), 5.08 (s, 2H), 3.69-3.43 (m, 2H), 3.26-3.10 (m, 2H), 3.05-2.69 (m, 2H).
MS (m/e): 437 (M^++1), 421, 405, 148.
IR (KBr): 3434, 2923, 2361, 1718, 1513, 1395, 1232, 1032 cm^{-1}.

Example-15

C-{1-[3-Fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:

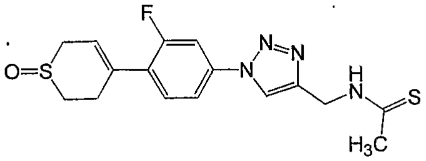


To a solution of 2-{1-[3-fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione (250 mg, 0.57 mmol), obtained in example-14, in methanol (5 mL) was added hydrazine hydrate (0.24 mL) and refluxed for 3 h followed by stirring at room temperature for 10 h. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The residue was purified by flash chromatography over silica gel (6% methanol in chloroform) to furnish the title compound (105 mg, 60%) as a pale yellow solid.

^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 8.09 (s, 1H), 7.75-7.62 (m, 2H), 7.46-7.39 (m, 1H), 5.95-5.85 (m, 1H), 4.07 (s, 2H), 3.63-3.51 (m, 2H), 3.19-2.98 (m, 4H).
MS (m/e): 307 (M^++1), 291, 273, 259.
IR (KBr): 3427, 2924, 1618, 1515, 1228, 1029 cm^{-1}.

Example-16

N-{1-[3-Fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thioacetamide:



To a solution of C-{1-[3-fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (45 mg, 0.15 mmol), obtained in example-15, in THF (5 mL) was added triethylamine (0.045 mL, 0.23 mmol) followed by the addition of ethyl dithioacetate (0.025 mL, 0.23 mmol) and stirred at room temperature for 16 h. The solvent was evaporated and the crude residue was purified by column chromatography over silica gel (3% methanol in chloroform) to obtain the desired product as a white solid (28 mg, 52%), mp 204 °C.

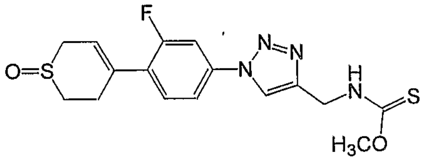
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 8.40 (s, 2H), 7.66-7.50 (m, 3H), 6.07-5.92 (m, 1H), 4.97 (s, 2H), 4.17 (s, 2H), 3.81-3.47 (m, 2H), 3.34-3.08 (m, 2H), 2.55 (s, 3H).

ES-MS (m/e): 387 (M^++23), 365 (M^++1).

IR (KBr): 3428, 3012, 2924, 1620, 1543, 1391, 1231, 1030 cm^{-1}.

Example-17

{1-[3-Fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid O-methyl ester:



A saturated aqueous solution of sodium bicarbonate (41 mg, 0.48 mmol) was added to a solution of C-{1-[3-fluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (50 mg, 0.16 mmol), obtained in example-15, in dichloromethane (5 mL) and then cooled to 0 °C. Thiophosgene (0.018 mL, 0.23 mmol) was added to the above mixture and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed with water followed by brine and dried over Na_2SO_4. The solvent was evaporated and the residue was refluxed with methanol (10 mL) for 16 h. After evaporation of solvent, the residue was purified by column chromatography over silica gel (methanol/chloroform; 1:49) to get the title compound as a white solid (35 mg, 56%), mp 153 °C.

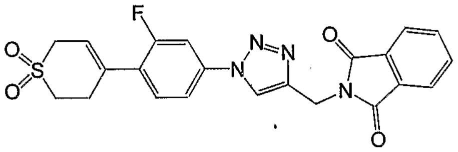
^{1}H NMR ($CDCl_3$ + Methanol-d_4): δ 8.27 and 8.08 (two s, 1H, rotamers in ratio of 4:1), 7.60-7.52 (m, 2H), 7.47-7.43 (m, 1H), 5.96-5.82 (m, 1H), 4.86 and 4.61 (s, 2H, rotamers in ratio of 4:1), 3.99 and 4.10 (two s, 3H, rotamers in ratio of 1:4), 3.72-3.67 (m, 1H), 3.54- 3.44 (m, 1H), 3.37-3.24 (m, 1H), 3.15-2.96 (m, 2H), 2.80-2.75 (m, 1H).

MS (m/e): 349 (M^+-OCH_3), 317, 292, 280.

IR (KBr): 3189, 3026, 2927, 1619, 1541, 1408, 1200, 1012 cm^{-1}.

Example-18

2-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione:



To a solution of 2-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-isoindole-1,3-dione (620 mg, 1.48 mmol), obtained in example-1, in dichloromethane (25 mL), cooled to 0 °C, was added m-chloroperbenzoic acid (1.1 grams, 70% w/w, 4.44 mmol) in portion and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL) and washed with saturated aqueous solutions of sodium bisulfite and sodium bicarbonate respectively. The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography over silica gel to afford the desired sulfone derivative (400 mg, 60%) as a white solid along with some sulfoxide(28 mg, 28%)

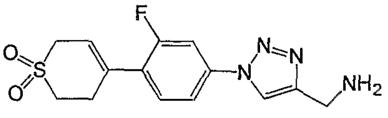
^{1}H NMR ($CDCl_3$): δ 8.42 (s, 1H), 7.97-7.76 (m, 4H), 7.71-7.55 (m, 2H), 7.42-7.38 (m, 1H), 5.98-5.85 (m, 1H), 5.05 (s, 2H), 3.88-3.82 (m, 2H), 3.30-3.27 (m, 2H), 2.86-2.59 (m, 2H).

CI-MS (m/e): 453 (M^++1)

IR (KBr): 3427, 2920, 1713, 1620, 1515, 1396, 1286, 1167, 937 cm^{-1}.

Example-19

C-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:



Hydrazine hydrate (0.37 mL) was added to a solution of 2-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-iso indole-1,3-dione (400 mg, 0.88 mmol), obtained in example-18, in methanol (10 mL) and refluxed for 2 h followed by stirring at room temperature for 0.5 h. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The residue was purified by flash chromatography over silica gel (6% methanol in chloroform) to produce the title compound as a white solid (220 mg, 77%).

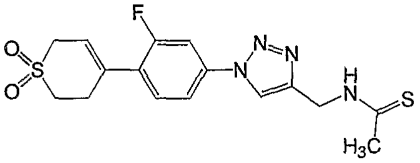
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 8.14 (s, 1H), 7.69-7.52 (m, 2H), 7.47-7.38 (m, 1H), 5.96-5.82 (m, 1H), 4.08 (s, 2H), 3.96-3.81 (m, 2H), 3.38-3.18 (m, 2H), 3.18-3.05 (m, 2H).

MS (m/e): 323 (M^++1), 285, 259, 187.

IR (KBr): 3346, 2923, 1619, 1515, 1315, 1285, 1123, 1045 cm^{-1}.

Example-20

N-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thioacetamide:



To a solution of *C*-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (100 mg, 0.31 mmol), obtained in example-19, in THF (5 mL) was added triethylamine (0.095 mL, 0.68 mmol) followed by the addition of ethyl dithioacetate (0.052 mL, 0.45 mmol) and stirred at room temperature for 18 h. The solvent was evaporated and the crude residue was purified by column chromatography over silica gel (3% methanol in chloroform) to obtain the desired product (83 mg, 70%) as a pale yellow solid, mp 188 °C.

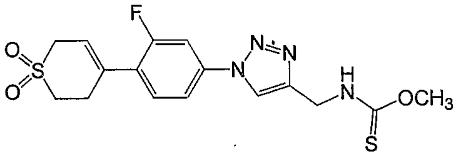
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 10.21-10.15 (m, 1H), 8.59 (s, 1H), 7.82-7.70 (m, 2H), 7.49 (t, *J* = 8.6 Hz, 1H), 5.96-5.84 (m, 1H), 4.92 (d, *J* = 4.9 Hz, 2H), 3.99-3.92 (m, 2H), 3.38-3.25 (m, 2H), 3.18-3.10 (m, 2H), 2.51 (s, 3H).

CI-MS (m/e): 381 (M^++1), 349, 317, 308.

IR (KBr): 3292, 2924, 1621, 1515, 1315, 1287, 1167, 1045 cm^{-1}

Example-21

{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid *O*-methyl ester:



To a solution of *C*-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (100 mg, 0.31 mmol), obtained in example-19, in dichloromethane (8 mL) was added a saturated aqueous solution of sodium bicarbonate (65 mg, 0.77 mmol) followed by cooling in ice bath. Thiophosgene (0.029 mL, 0.37 mmol) was added to the reacion mixture at 0 °C and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed the organic layer with water, brine and dried over sodium sulfate. The solvent was evaporated and the residue was refluxed with methanol (10 mL) for 16 h. Methanol was evaporated on rotavapor and the residue was purified by column chromatography over silica gel (4% methanol in chloroform) to yield the title compound as a white solid (86 mg, 70%), mp 178 °C.

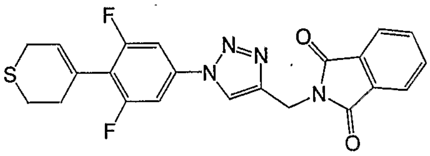
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 9.02-8.87 and 8.87-8.80 (two m, 1H, rotamers in ratio of 1:4), 8.30 and 8.18 (two s, 1H, rotamers in ratio of 4:1), 7.65-7.56 (m, 2H), 7.46-7.39 (m, 1H), 5.97-5.88 (m, 1H), 4.87 and 4.60 (two d, *J* = 5.6 Hz, 2H, rotamers in ratio of 4:1), 4.10 and 3.98 (two s, 3H, rotamers in ratio of 1:4), 3.89-3.81 (m, 2H), 3.38-3.20 (m, 2H), 3.19-3.01 (m, 2H).

MS (m/e): 365 (M^+-OCH_3), 333, 308, 280.

IR (KBr): 3428, 3291, 2924, 2854, 1620, 1515, 1315, 1277, 1041 cm^{-1}.

Example-22

2-{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-isoindole-1,3-dione:



To a solution of 4-(4-azido-2,6-difluoro-phenyl)-3,6-dihydro-2*H*-thiopyran (2.13 grams, 8.40 mmol), obtained in preparation-8, and *N*, *N*-diisopropylethylamine (2.9 mL, 16.8

mmol) in acetonitrile (25 mL) was added 2-prop-ynyl-isoindole-1,3-dione (2.35 grams, 12.6 mmol) followed by the addition of cuprous iodide (2.40 grams, 12.60 mmol) and stirred at room temperature for 1 h. The reaction mixture was filtered through a celite pad and washed thoroughly with MeOH/$CHCl_3$ (1:10).Concentration of the filtrate under vacuum and purification of the resulting residue by flash chromatography (ethyl acetate/hexane; 4:6) yielded the title compound as a light yellow solid (1.60 grams, 44%).

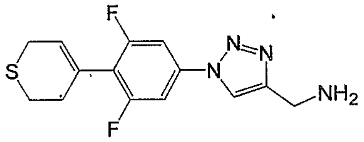
^{1}H NMR ($CDCl_3$): δ 8.02 (s, 1H), 7.97-7.82 (m, 2H), 7.81-7.65 (m, 2H), 7.32 (d, J = 7.5 Hz, 2H), 6.05-5.97 (m, 1H), 5.08 (s, 2H), 3.39-3.35 (m, 2H), 2.88 (t, J = 5.6 Hz, 2H), 2.61-2.47 (m, 2H).

MS (m/e): 439 (M^++1), 266, 148.

IR (KBr): 3149, 3067, 2922, 1712, 1633, 1512, 1394, 1094 cm^{-1}.

Example-23

***C*-{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:**



To a solution of 2-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3] triazol-4-ylmethyl}-isoindole-1,3-dione (400 mg, 0.91 mmol), obtained in example-22, in methanol (12 mL) was added hydrazine hydrate (0.41 mL) and refluxed for 2 h followed by stirring at room temperature for 10 h. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The resultant residue was dissolved in chloroform (100 mL), washed the organic layer with water followed by brine and dried (sodium sulfate). Evaporation of the solvent on a rotavapor and purification of the resulting residue by flash chromatography (ethyl acetate/ hexane; 1:10) afforded the title compound as a pale yellow solid (260 mg, 93%).

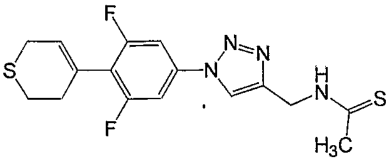
^{1}H NMR ($CDCl_3$): δ 7.87 (s, 1H), 7.33 (d, J = 7.8 Hz, 2H), 6.15-5.98 (m, 1H), 4.08 (s, 2H), 3.41-3.32 (m, 2H), 2.89 (t, J = 5.6 Hz, 2H), 2.61-2.45 (m, 2H).

MS (m/e): 309 (M^++1), 280.

IR (KBr): 3357, 3128, 2920, 1631, 1595, 1449, 1220, 1028 cm^{-1}.

Example-24

N-{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thioacetamide:



To a solution of *C*-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (100 mg, 0.32 mmol), obtained in example-23, in THF (5 mL) was added triethylamine (0.1 mL, 0.72 mmol) followed by the addition of ethyl dithioacetate (0.06 ml, 0.49 mmol) and stirred at room temperature for 16 h. The reaction mixture was diluted with ethyl acetate (75 mL), washed the organic layer with water followed by brine and dried over sodium sulfate. Solvent was evaporated and the residue was purified by column chromatography (silica gel), using 15% methanol in chloroform as eluent, to give the desired product as a white powder (58 mg, 50%), mp 178-179 °C.

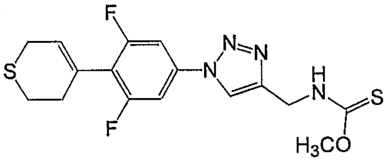
^{1}H NMR ($CDCl_3$): δ 8.18-8.09 (m, 2H), 7.34 (d, *J* = 7.3 Hz, 2H), 6.08-6.01 (m, 1H), 5.02 (d, J = 5.4 Hz, 2H), 3.40-3.31 (m, 2H), 2.89 (t, *J* = 5.4 Hz, 2H), 2.68-2.48 (m, 5H).

MS (m/e): 367 (M^++1), 339, 189.

IR (KBr): 3204, 2999, 1632, 1510, 1344, 1050 cm^{-1}.

Example-25

{1-[4-(3,6-Dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid *O*-methyl ester:



To a solution of *C*-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (90 mg, 0.29 mmol), obtained in example-23, in dichloromethane (10 mL) was added a solution of sodium bicarbonate (62 mg, 0.73 mmol) in water (3 mL) followed by cooling in ice bath. Thiophosgene (0.03 mL, 0.35 mmol) was added to the above mixture at 0 °C and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed the organic layer with water followed by brine and dried over sodium sulfate. Evaporation of volatiles left a residue, which was refluxed with methanol (15 mL) for 16 h. Removal of solvent on rotavapor and purification of the residue by column chromatography (ethyl acetate/ hexane; 3:10) yielded the title compound as a white powder (72 mg, 65%), mp 156-158 °C.

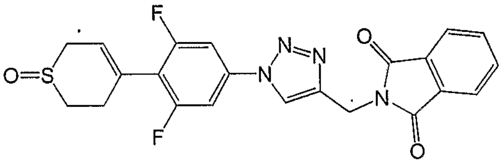
^{1}H NMR ($CDCl_3$): δ 8.10 (s, 1H), 7.34 (d, J = 7.8 Hz, 2H), 6.15-5.97 (m, 1H), 4.91 and 4.68 (two d, J = 5.9 Hz, 2H, rotamers in ratio of 4:1); 4.12 and 3.99 (two s, 3H, rotamers in ratio of 1:4), 3.40-3.31 (m, 2H), 2.89 (t, J = 5.6 Hz, 2H), 2.61-2.50 (m, 2H).

MS (m/e): 383 (M^++1), 351, 335, 294.

IR (KBr): 3193, 3123, 2924, 1633, 1593, 1454, 1125 cm^{-1}.

Example-26

2-{1-[3,5-Difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione:



Sodium periodate (410 mg, 1.92 mmol) in water (5 mL) was added to an ice cooled solution of 2-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-1,3-isoindole-1,3-dione (350 mg, 0.79 mmol), obtained in example-22, in methanol (12 mL) and ethyl acetate (12 mL) and stirred at the same temperature for 1 h. The reaction mixture was warmed to room temperature and stirred for 16 h. The reaction mixture was diluted with methanol (1 mL) and chloroform (19 mL), and filtered. The filtrate was concentrated under vacuum. The residue obtained was dissolved in chloroform, washed with saturated solutions of Na_2SO_3 and $NaHCO_3$ and dried over sodium sulfate. Evaporation of solvent and purification of the residue by column chromatography over silica gel (ethyl acetate) afforded the desired product (295 mg, 81%) as a pale yellow solid.

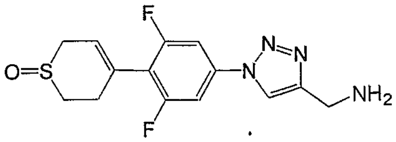
^{1}H NMR (DMSO-d_6): δ 8.86 (s, 1H), 8.00-7.68 (m, 6H), 5.86-5.76 (m, 1H), 4.94 (s, 2H), 4.01-3.92 (m, 2H), 3.45-3.18 (m, 2H), 2.96-2.82 (m, 2H),

MS (m/e): 455 (M^++1), 439, 421

IR (KBr): 3459, 1714, 1428, 1395, 1208, 1034 cm^{-1}.

Example-27

***C*-{1-[3,5-Difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:**



To a solution of 2-{1-[3,5-difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione (290 mg, 0.64 mmol), obtained in example-26, in methanol (10 mL) was added hydrazine hydrate (0.27 mL) and refluxed for 2 h followed by stirring at room temperature for 10 h. The reaction mixture was filtered and washed with chloroform (5% methanol). The filtrate was concentrated under vacuum and the residue was purified by flash chromatography. (3% methanol in chloroform) to afford the title compound (126 mg, 62%) as a white solid.

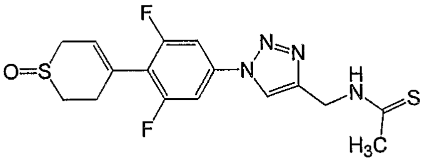
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 8.58 (s, 1H), 7.66 (d, J = 8.3 Hz, 2H), 5.84-5.80 (m, 1H), 3.94 (s, 2H), 3.75-2.96 (m, 6H).

MS (m/e): 325 (M^++1), 309, 181.

IR (KBr): 3441, 2924, 1632, 1583, 1452, 1366, 1207, 1034 cm^{-1}.

Example-28

***N*-{1-[3,5-Difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}thioacetamide:**



To a solution of C-{1-[3,5-difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (60 mg, 0.185 mmol), obtained in example-27, in THF (5 mL) was added triethylamine (0.058 mL, 0.41 mmol) followed by the addition of ethyl dithioacetate (0.033 mL, 0.28 mmol) and stirred at room temperature for 16 h. The solvent was evaporated from the reaction mixture and the residue was purified by column chromatography (2% methanol in chloroform) to obtain the desired product as a pale yellow solid (40 mg, 57%), mp 182-184 °C.

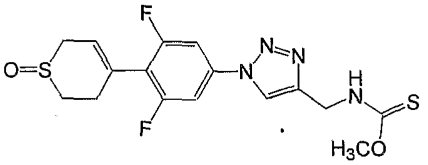
^1H NMR ($CDCl_3$ + DMSO-d_6): δ 10.15-10.10 (m, 1H), 8.38 (s, 1H), 7.50-7.38 (m, 2H), 5.84-5.81 (m, 1H), 4.95 (d, *J* = 5.4 Hz, 2H), 3.71-3.66 (m, 2H), 3.48-3.43 (m, 2H), 3.24-3.18 (m, 2H), 2.58 (s, 3H).

MS (m/e): 383 (M^++1), 367, 365, 339, 310.

IR (KBr): 3184, 3003, 1632, 1562, 1450, 1280, 1023 cm^{-1}.

Example-29

{1-[3,5-Difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid *O*-methyl ester:



A solution of sodium bicarbonate (41 mg, 0.48 mmol) in water (5 mL) was added to an ice cooled solution of *C*-{1-[3,5-difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (63 mg, 0.194 mmol), obtained in example-27, in dichloromethane (5 mL). Thiophosgene (0.020 mL, 0.26 mmol) was added to the reaction mixture and stirred for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed the organic layer with water followed by brine and dried over sodium sulfate. The solvent was evaporated and the residue was refluxed with methanol (15 mL) for 16 h. After evaporation of methanol, the residue was purified by column chromatography over silica gel (methanol/chloroform; 1:25) to furnish the title compound as a white powder (50 mg, 65%), mp 206-208 °C.

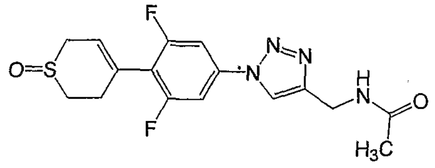
^1H NMR ($CDCl_3$ + DMSO-d_6): δ 8.58-8.54 and 8.46-8.39 (two m, 1H, rotamers in ratio of 1:4), 8.14 and 8.00 (two s, 1H, rotamers in ratio of 4:1), 7.33 (d, *J* = 7.8 Hz, 2H), 5.75-5.71 (m, 1H), 4.74 and 4.45 (two d, *J* = 5.9 Hz, 2H, rotamers in ratio of 4:1), 3.90 and 3.86 (two s, 3H, rotamers in ratio of 1:4), 3.60-3.55 (m, 2H), 3.37-3.32 (m, 2H), 3.11-3.07 (m, 2H).

MS (m/e): 367 (M^+-OCH_3), 351, 335, 325, 294.

IR (KBr): 3442, 2924, 1715, 1634, 1518, 1452, 1233, 1030 cm^{-1}.

Example-30

***N*-{1-[3,5-Difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-acetamide:**



To a solution of C-{1-[3,5-difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (80 mg, 0.25 mmol), obtained in example-27, in dichloromethane (5 mL), cooled to 0 °C was added triethylamine (0.069 mL, 0.49 mmol) followed by the addition of acetyl chloride (0.02 mL, 0.29 mmol) and stirred at room temperature for 3 h. The solvent was evaporated from the reaction mixture and the residue was purified by column chromatography on silica (4% methanol in chloroform) to afford the required compound as a creamy white solid (45 mg, 50%), mp 177-180 °C.

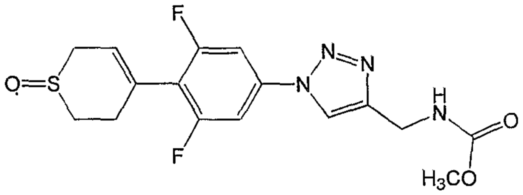
^{1}H NMR (DMSO-d$_6$): δ 8.74 (s, 1H), 8.54-8.39 (m, 1H), 7..84 (d, *J* = 8.3 Hz, 2H), 5.92-5.78 (m, 1H), 4.37 (d, *J* = 5.6 Hz, 2H), 3.80-3.10 (m, 6H), 1.86 (s, 3H).

MS (m/e): 367 (M$^+$+1), 318, 290, 231.

IR (KBr): 3323, 3128, 2926, 1648, 1532, 1455, 1206, 1026 cm^{-1}.

Example-31

{1-[3,5-Difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-carbamic acid methyl ester:



N,N-Diisopropylethylamine (0.11 mL, 0.63 mmol) was added to an ice cooled solution of C-{1-[3,5-difluoro-4-(1-oxo-1,2,3,6-tetrahydro-1lambda*4*-thiopyran-4-yl)-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine obtained in example-27 (80 mg, 0.25 mmol) in dichloromethane (5 mL), followed by the addition of methyl chloroformate (0.023 mL, 0.29 mmol) and stirred for 2 h. The reaction mixture was concentrated on rotavapor and the resulting residue was purified by column chromatography (3% methanol in chloroform) to yield the desired product (50 mg, 53%) as a creamy white solid, mp 172-174 °C.

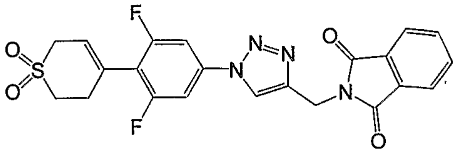
^{1}H NMR (DMSO-d$_6$): δ 8.75 (s, 1H), 7.98-7.72 (m, 3H), 5.91-5.80 (m, 1H), 4.32 (d, *J* = 5.8 Hz, 2H), 3.80-3.10 (m, 6H), 3.57 (s, 3H).

MS (m/e): 383 (M$^+$+1), 351.

IR (KBr): 3333, 2924, 2854, 1696, 1543, 1454, 1264, 1032 cm^{-1}.

Example-32

2-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione:



To a solution of 2-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-1,3-isoindole-1,3-dione (710 mg, 1.6 mmol), obtained in example-7, in dichloromethane (25 mL), was added m-chloroperbenzoic acid (1.3 grams, 5.26 mmol, 70% w/w) in portion at 0 °C and the mixture was stirred for 0.5 h. The reaction mixture was diluted with dichloromethane (75 mL) and washed with water followed by brine. The organic layer was dried over sodium sulfate and evaporated. The residue was purified by column chromatography over silica gel (4% methanol in chloroform) to afford the desired product (375 mg, 49%) as a white solid.

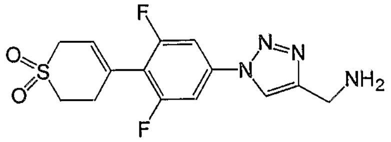
^{1}H NMR (DMSO-d$_6$): δ 8.85 (s, 1H), 7.88-7.78 (m, 4H), 7.75 (d, J = 8.6 Hz, 2H), 5.92-5.79 (m, 1H), 4.97 (s, 2H), 3.96-3.89 (m, 2H), 3.32-3.18 (m, 2H), 3.02-2.86 (m, 2H).

MS (m/e): 471 (M$^+$+1), 391, 298, 185.

IR (KBr): 3459, 3146, 1713, 1634, 1396, 1286, 1031 cm^{-1}.

Example-33

C-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine:



Hydrazine hydrate (0.312 mL) was added to a solution of 2-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4ylmethyl}-isoindole-1,3-dione (350 mg, 0.74 mmol), obtained in example-32, in methanol (15 mL) and refluxed for 2 h followed by stirring at room temperature for 16 h. The reaction mixture was filtered and washed with a mixture of chloroform/methanol. The filtrate was concentrated under vacuum and the residue was purified by flash chromatography over silica gel (4% methanol in chloroform) to get the title compound as a white solid (195 mg, 77%).

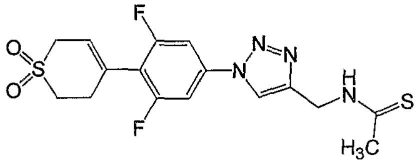
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 8.38 (s, 1H),. 7.58 (d, *J* = 7.8 Hz, 2H), 5.92-5.83 (m, 1H), 4.03 (s, 2H), 3.93-3.87 (m, 2H), 3.18-2.96 (m, 2H), 2.60-2.58 (m, 2H).

MS (m/e): 341 (M^++1), 277, 181.

IR (KBr): 3449, 2923, 1634, 1599, 1515, 1324, 1288, 1029 cm^{-1}.

Example-34

***N*-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}thioacetamide:**



To a solution of *C*-{1-[4-(1,1dioxo-1;2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (100 mg, 0.294 mmol), obtained in example-33, in THF (5 mL) was added triethylamine (0.082 mL, 0.58 mmol) followed by the addition of ethyl dithioacetate (0.051 mL, 0.44 mmol). The reaction mixture was stirred at ambient temperature for 16 h and then concentrated on rotavapor The residue was purified by column chromatography (2% methanol in chloroform) to obtain the desired product (58 mg, 50%) as a pale yellow solid, mp 210 °C.

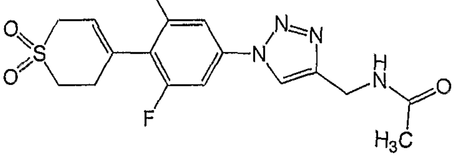
^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 9.96-9.82 (m, 1H), 8.33 (s, 1H), 7.46 (d, *J* = 7.8 Hz, 2H), 5.96-5.82 (m, 1H), 4.98 (d, *J* = 5.4 Hz, 2H), 3.95-3.82 (m, 2H), 3.29-3.26 (m, 2H), 3.18-3.06 (m, 2H), 2.56 (s, 3H).

MS (m/e): 399 (M^++1), 371, 271.

IR (KBr): 3482, 3291, 2921, 1632, 1551, 1454, 1282, 1168 cm^{-1}.

Example-35

***N*-{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-acetamide:**



To a solution of *C*-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (100 mg, 0.29 mmol), obtained in example-33, in dichloromethane (5 mL), cooled to 0 °C, was added triethylamine (0.91 mL, 0.65 mmol) followed by the addition of acetyl chloride (0.023 mL, 0.320 mmol). The reaction mixture was brought to room temperature and stirred for 3 h. Evaporation of solvent from the reaction mixture and purification of the residue by column chromatography (methanol/ chloroform; 1:24) yielded the title compound (60 mg, 53%) as a white solid, mp 242-246 °C.

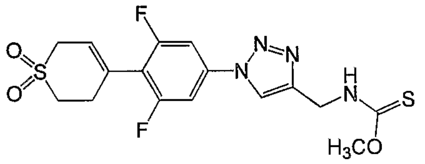
^1H NMR (DMSO-d_6): δ 8.74 (s, 1H), 8.52-8.40 (m, 1H), 7.84 (d, *J* = 8.6 Hz, 2H), 5.90-5.84 (m, 1H), 4.36 (d, *J* = 5.6 Hz, 2H), 4.04-3.91 (m, 2H), 3.44-3.13 (m, 2H), 2.98-2.87 (m, 2H), 1.86 (s, 3H).

MS (m/e): 383 (M^++1), 239..

IR (KBr): 3287, 3094, 2926, 1630, 1543, 1286, 1058 cm^{-1}.

Example-36

{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-thiocarbamic acid O-methyl ester:



To a solution of *C*-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (90 mg, 0.26 mmol), obtained in example-33, in dichloromethane (5 mL) was added a saturated solution of sodium bicarbonate (64 mg, 0.76 mmol) in water (5 mL) followed by cooling in ice bath. Thiophosgene (0.027 mL, 0.35 mmol) was added to the above mixture at 0 °C and stirred for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed the organic layer with water, brine and dried over sodium sulfate. The solvent was evaporated and the residue was refluxed with methanol (5 mL) for 16 h. Methanol was evaporated on a rotavapor and the residue was purified by column chromatography over silica gel (4% methanol in chloroform) to yield the title compound as a white powder (54 mg, 50%), mp 196 °C.

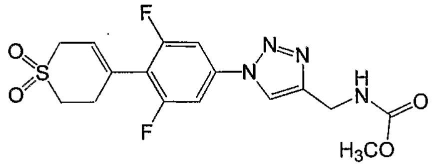
^1H NMR ($CDCl_3$): δ 8.14 and 7.90 (two s, 1H, rotamers in ratio of 4:1), 7.40 (d, *J* = 7.8 Hz, 2H), 6.96-6.85 (m, 1H), 5.90-5.82 (m, 1H), 4.92 and 4.65 (two d, *J* = 5.9 Hz, 2H, rotamers in ratio of 4:1), 4.10 and 4.00 (two s, 3H, rotamers in ratio of 1:4), 3.92-3.83 (m, 2H), 3.38-3.21 (m, 2H), 3.18-3.08 (m, 2H).

MS (m/e): 415 (M^++1), 383, 326, 298.

IR (KBr): 3269, 1634, 1530, 1451, 1322, 1282, 1201, 1027 cm $^{-1}$

Example-37

{1-[4-(1,1-Dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-ylmethyl}-carbamic acid methyl ester:



To an ice cooled solution of *C*-{1-[4-(1,1-dioxo-1,2,3,6-tetrahydro-1lambda*6*-thiopyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (60 mg, 0.8 mmol), obtained in example-33, in dichloromethane (5 mL), was added *N, N*-diisopropylethylamine (0.067 mL, 0.38 mmol) followed by the addition of methyl chloroformate (0.016 mL, 0.21 mmol). The reaction mixture was stirred at the same temperature for 2 h. The solvent was evaporated from the reaction mixture and the residue was purified by column chromatography over silica gel (methanol/ chloroform; 1:9) to afford the required product (42 mg, 60%) as a creamy white solid, mp 190-194 °C.

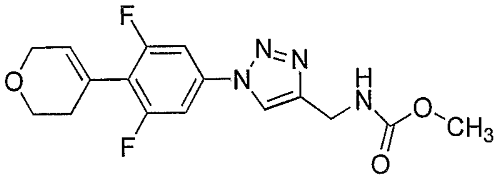
^{1}H NMR (DMSO-d_6): δ 8.77 (s, 1H), 7.84-7.75 (m, 1H), 7.84 (d, J = 7.3 Hz, 2H), 5.92-5.82 (m, 1H), 4.33 (d, J = 5.8 Hz, 2H), 4.08-3.90 (m, 2H), 3.57 (s, 3H), 3.50-3.19 (m, 2H), 2.99-2.82 (m, 2H).

MS (m/e): 399 (M^++1), 367.

IR (KBr): 3334, 2925, 1691, 1541, 1456, 1263, 1031 cm^{-1}.

Example-38

{1-[4-(3,6-Dihydro-2H-pyran-4-yl)-3,5-difluorophenyl]-1H-[1,2,3]triazol-4-ylmethyl}-carbamicacid methyl ester:



N-Diisopropylethylamine (0.127 mL, 0.729 mmol) was added to an ice cooled solution of C-{1-[4-(3,6-dihydro-2*H*-pyran-4-yl)-3,5-difluoro-phenyl]-1*H*-[1,2,3]triazol-4-

yl}-methylamine (100mg, 0.365 mmol), obtained in example-8, in dichloromethane (5 mL), followed by the addition of methyl chloroformate (0.034 mL, 0.438 mmol) and stirred at the same temperature for 3 h. The reaction mixture was concentrated on rotavapor and the resulting residue was purified by column chromatography over silica gel (3% methanol in chloroform) yielded the desired product (60 mg, 47%) as a white solid, mp 165-170 °C.

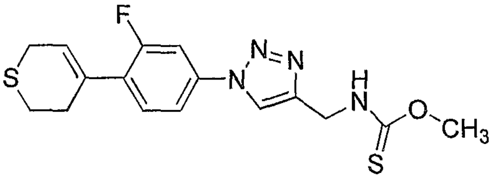
^{1}H NMR (CDCl$_3$): δ 7.99 (s, 1H), 7.34(d, J=7.8 Hz, 2H), 6.00-5.96 (m, 1H), 4.51 (d, J = 5.6 Hz, 2H), 4.38-4.31 (m, 2H), 3.94 (t, J=5.3 Hz, 2H), 3.69(s, 3H), 2.45-2.38(m, 2H).

CI-MS (m/e): 351 (M^++1).

IR (KBr): 3341, 2928, 1698, 1635, 1549, 1454, 1267, 1028, 860, 773 cm^{-1}.

Example-39

{1-[4-(3,6-Dihydro-2H-thiopyran-4-yl)-3-fluoro-phenyl]-1H-[1,2,3]triazol-4-ylmethyl} thiocarbamic acid O-methyl ester:



A saturated solution of sodium bicarbonate (133mg, 1.58mmol) in water (5ml) was added to an ice cooled solution of C-{1-[4-(3,6-dihydro-2*H*-thiopyran-4-yl)-3-fluoro-phenyl]-1*H*-[1,2,3]triazol-4-yl}-methylamine (200 mg, 0.689 mmol), obtained in example-12, in dichloromethane (5 mL). Thiophosgene (0.068 mL, 0.895 mmol) was added to the reaction mixture and stirred at the same temperature for 0.5 h. The reaction mixture was diluted with dichloromethane (50 mL), washed the organic layer with water followed by brine and dried over sodium sulfate. The solvent was evaporated and the residue was refluxed with methanol (15 mL) for 16 h. After evaporation of methanol, the residue was purified by column chromatography over silica gel (methanol/chloroform; 1:25) to furnish the title compound as a creamy white solid (150 mg, 60%), mp 110-113 °C.

^{1}H NMR (CDCl$_3$): δ 7.99 (s, 1H), 7.56-7.32 (m, 3H), 6.16-6.05 (m, 1H), 4.52(d, J=6.3 Hz, 2H), 3.70 (s, 3H), 3.42-3.31(m, 2H), 2.88 (t, J=5.8 Hz, 2H), 2.75-2.63 (m, 2H).

CI-MS (m/e): 365(M^++1).

IR (KBr): 3329, 3149, 2923, 1619, 1540, 1514, 1458, 1357, 1266, 1229, 1145, 1046, 1011, 872, 619 cm^{-1}.

In vitro Data

Minimum Inhibiton Concentrations (MICs) were determined by broth microdilution technique as per the guidelines prescribed in the fifth edition of Approved Standards, NCCLS document *M7-A5 Vol 20 - No 2, 2000* Villinova, PA.

Initial stock solution of the test compound was prepared in DMSO. Subsequent two fold dilutions were carried out in sterile Mueller Hinton Broth (Difco) (MHB).

Frozen cultures stocks were inoculated into 50 ml sterile MHB in 250 ml Erlyn Meyer flasks.

Composition of MHB is as follows:
Beef Extract Powder - 2.0 grams/litre
Acid Digest of Casein - 17.5 grams/ litre
Soluble Starch - 1.5 grams/litre
Final pH 7.3 ± 0.1

Flasks were incubated for 4 to 5 h at 35 °C on a rotary shaker at 150 rpm. Inoculum was prepared by diluting the culture in sterile MHB to obtain a turbidity of 0.5 McFarland standard. This corresponds to 1-2 x 10^8 CFU/ml. The stock was further diluted in sterile broth to obtain 1-2 X 10^6 CFU/ml. 50 µl of the above diluted inoculum was added from 1-10 wells. The plates were incubated overnight at 37 °C.

MIC is read as the lowest concentration of the compound that completely inhibits growth of the organism in the microdilution wells as detected by the unaided eye.

Organism	Culture No.	DRCC No.
Staphylococcus aureus	ATCC 33591	019
Staphylococcus aureus	ATCC 49951	213
Staphylococcus aureus	ATCC 29213	035
Enterococcus faecalis	ATCC 29212	034
Enterococcus faecalis	NCTC 12201	153
Enterococcus faecium	NCTC 12202	154
Escherichia coli	ATCC 25922	018
Haemophilus influenzae	ATCC 49247	432
Haemophilus influenzae	ATCC 49766	433
Haemophilus influenzae	ATCC 9006	529
Moraxella catarrhalis	ATCC 25238	300
Streptococcus pneumoniae	ATCC 6303	236
Streptococcus pneumoniae	ATCC 49619	237
Streptococcus pneumoniae	ATCC 700673	238
S.aureus - MRSA	-	446
S.aureus - MRSA	-	448

S.aureus - MRSA	-	449
Corynebacterium jeikeium		
Viridans Streptococci		

ATCC: American Type Culture Collection, USA

NCTC: National Collections of Type Cultures, Colindale, UK

DRCC: Dr. Reddy's Culture Collection, Hyderabad, India.

The *in vitro* antibacterial activity data is shown in TABLE 2.

TABLE 2

In vitro Activity of Compounds against Gram positive and Gram negative bacteria

Example No.	Antimicrobial Screening (MIC) µg/mL							
	Staphylococcus aureus			*Enterococcus sp*			Mycobacterium	Salmonella
	019 MRSA	*213 Smith S*	*035 S*	*034 S*	*153 R*	*154 R*	*MTCC006*	*TA97*
4	0.25	0.25	0.5	0.25	0.25	0.25	4	>4
13	0.125	0.25	0.25	0.25	0.25	0.125	32	32
20	0.25	0.25	0.25	0.25	0.25	0.25	16	>32
37	8	8	8	16	16	16	32	32
39	1	1	2	1	2	1	32	32

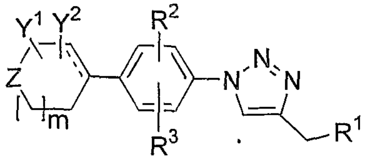
In vivo efficacy studies: Mice Systemic Infection

- *S.aureus* ATCC 29213 and other tested strains were grown overnight on Columbia Blood agar (DIFCO).
- The inoculum was prepared by suspending the culture in 0.9% saline and adjusted to 100 x LD_{50} dose in 10% Hog Gastric Mucin (DIFCO). 0.5ml was injected intraperitonially to Swiss albino mice weighing 18-22g (n=6)
- Test compounds were solubilised in suitable formulation and 0.25ml was administered intra venously or orally or sub-cutaneously at 1 hr and 5 hr post infection by BID or TID or single dose protocol
- The animals were observed for 5-7 days and the survival was noted.
- ED_{50} was calculated by probit analysis.

Example No.	**MIC (µg/ml)**	**ED_{50} (mg/kg)**
21	1	3.55
36	0.5	3.2

We claim:

1. A compound of formula (I)



(I)

where R^1 represents halogen, azido, thioalcohol, isothiocyanate, hydroxy, isoindole-1,3-dione, optionally substituted alkylsulfonyloxy, arylsulfonyloxy, acyloxy group, NHR^4 where R^4 represents optionally substituted groups selected from alkyl, acyl, thioacyl, alkoxycarbonyl, cycloalkoxycarbonyl, cycloalkoxythiocarbonyl, alkenyloxycarbonyl, alkenylcarbonyl, heteroaryl, aryloxycarbonyl, heteroarylcarbonyl, heteroarylthiocarbonyl, alkoxythiocarbonyl, alkenyloxythiocarbonyl, aryloxythiocarbonyl, -C(=O)-C(=O)-alkyl, -C(=O)-C(=O)-aryl, -C(=O)-C(=O)-alkoxy, -C(=O)-C(=O)-aryloxy, -C(=O)-C(=S)-alkyl, -C(=O)-C(=S)-aryl, -C(=S)-S-alkyl, -C(=S)-NH_2, -C(=S)-NH-alkyl, -C(=S)-N-$(alkyl)_2$, -C(=S)-NH-alkenyl, -C(=S)-C(=O)-alkoxy, -C(=S)-C(=O)-aryloxy, -C(=S)-O-C(=O)- alkyl, -C(=S)-C(=S)-alkyl, -C(=S)-C(=S)-aryl, -C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl, -C(=NH)-NH_2, -C(=NH)-alkyl, -C(=NH)-aryl, -S $(O)_2$alkyl, -S$(O)_2$aryl, thiomorpholinylthiocarbonyl, pyrrolidinylthiocarbonyl or –C(=S)-N(R'R"), where R' and R" together form a optionally substituted 5 or 6 member heterocycle ring containing nitrogen and optionally having one or two additional hetero atoms selected from O, S or N; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl group, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; their pharmaceutically acceptable salts.

2. The compound of formula (I), as claimed in claim 1, wherein a 5 or 6 member heterocycle ring formed by R' & R" containing nitrogen, optionally having one or two

additional heteroatoms selected from oxygen, nitrogen or sulfur, is selected from unsubstituted or substituted pyrrolidinyl, pyrrolyl, morpholinyl, thiomorpholinyl, benzothiazole, benzoimidazolyl, pyridinyl, pyridazinyl, pyrimidinyl or pyrazinyl.

3. The compound of formula (I), as claimed in claim 1, where in the substituents on the groups represented by R^4, R, R^7 and heterocycles formed by R'and R" are selected from halogen, hydroxy, amino, cyano, nitro, alkyl, hydroxyalkyl, alkoxy, =O, =S, aryl, hydroxyaryl, pyridyl, monoalkylamino, dialkylamino, acyl, thioacyl, alkoxycarbonyl, alkoxyaryl, or carboxylic acid or its derivatives

4. The compound as claimed in claim 1, wherein the substituents on R^2, R^3 and R^a are selected from hydroxy, halogen, nitro, amino, alkyl, alkoxy, =O, =S, cyano group, or carboxylic acid or its derivatives.

5. The compound as claimed in claim 1, wherein the substituents on Y^1 and Y^2 are selected from hydroxy, nitro, cyano, amino, *tert*-butyldimethylsilyloxy (TBSO), halogen, alkyl, alkoxy, cycloalkyl, aryl, benzyloxy, acyl or acyloxy group.

6. The compound of formula (I) as claimed in claim 1, wherein R^1 represents NHR^4 where R^4 represents optionally substituted acyl or alkoxycarbonyl;

R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;

Z represents S, SO ro SO_2;

Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

7. The compound of formula (I) as claimed in claim 1 wherein, R^1 represents NHR^4 where R^4 represents optionally substituted acyl or alkoxycarbonyl;

R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;

Z represents O;

Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

8. The compound of formula (I) as claimed in claim 1, wherein R^1 represents NHR^4 where R^4 represents optionally substituted thioacyl or alkoxythiocarbonyl;

R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;

Z represents S, SO ro SO_2;

Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

9. The compound of formula (I) as claimed in claim 1, wherein R^1 represents NHR^4 where R^4 represents optionally substituted thioacyl or alkoxythiocarbonyl;

R^2 and R^3 may be same or different and independently represent hydrogen, halogen, optionally substituted alkyl or haloalkyl;

Z represents O;

Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; their pharmaceutically acceptable salts.

10. The compound of formula (I) as claimed in claim 1, wherein R^4 represents acyl, alkoxycarbonyl,

R^2 and R^3 independently represent hydrogen or halogen,

'm' represents 1,

'Z' represents S, SO or SO_2,

'.....' represents a bond,

R^2 and R^3 independently represent hydrogen or halogen,

Y^1 and Y^2 independently represent hydrogen atom.

11. The compound of formula (I) as claimed in claim 1, wherein R^4 represents acyl, alkoxycarbonyl,

R^2 and R^3 independently represent hydrogen or halogen,

'm' represents 1,

'Z' represents O,

'.....' represents a bond,

R^2 and R^3 independently represent hydrogen or halogen,

Y^1 and Y^2 independently represent hydrogen atom.

12. The compound of formula (I) as claimed in claim 1, wherein R^4 represents thioacyl, alkoxythiocarbonyl,

R^2 and R^3 independently represent hydrogen or halogen,

'm' represents 1,

'Z' represents S, SO or SO_2,

'.....' represents a bond,

R^2 and R^3 independently represent hydrogen or halogen,

Y^1 and Y^2 independently represent hydrogen atom.

13. The compound of formula (I) as claimed in claim 1, wherein R^4 represents thioacyl, alkoxythiocarbonyl,

R^2 and R^3 independently represent hydrogen or halogen,

'm' represents 1,

'Z' represents O,

'.....' represents a bond,

R^2 and R^3 independently represent hydrogen or halogen,

Y^1 and Y^2 independently represent hydrogen atom.

14. The compound of formula (I) as claimed in claim 1, wherein R^4 represents –C(=O)-CH_3, -C(=O)-OCH_3,

m represents 1;

'....' represents a bond;

'Z' represents S, SO or SO_2,

R^2 and R^3 independently represent hydrogen or fluorine;

Y^1 and Y^2 independently represent hydrogen atom.

15. The compound of formula (I) as claimed in claim 1, wherein R^4 represents –C(=O)-CH_3, -C(=O)-OCH_3,

m represents 1;

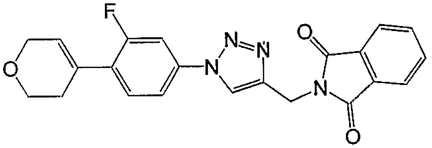
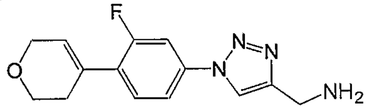
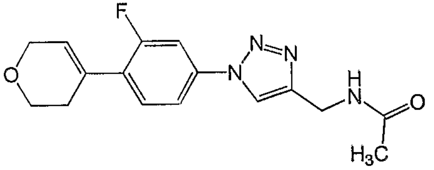
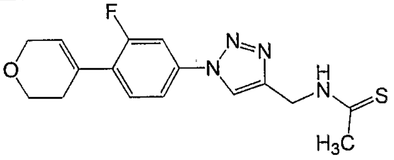
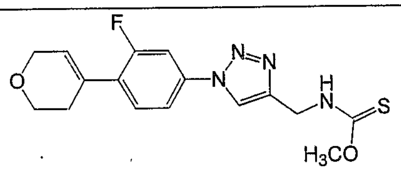
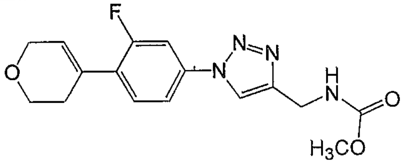
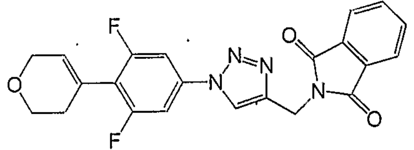
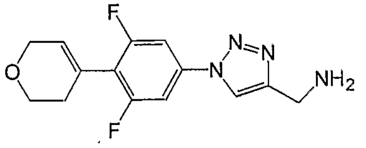
'....' represents a bond;

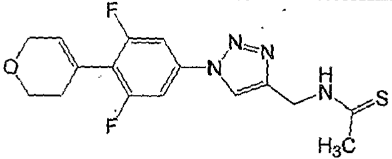
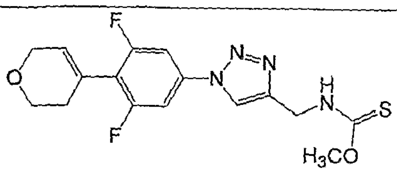
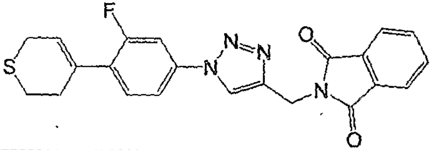
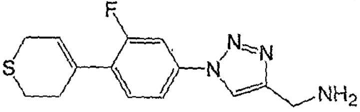
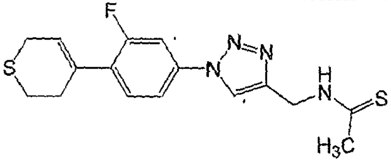
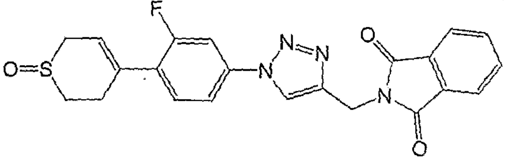
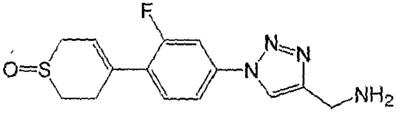
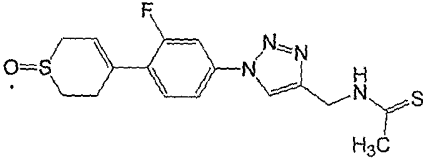
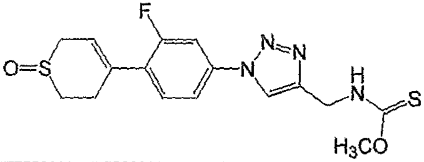
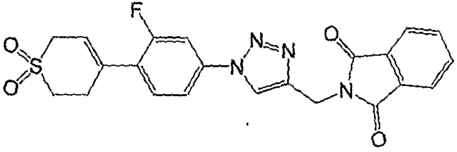
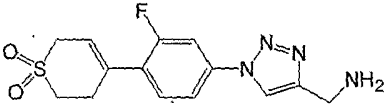
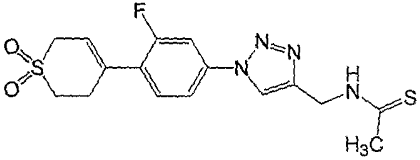
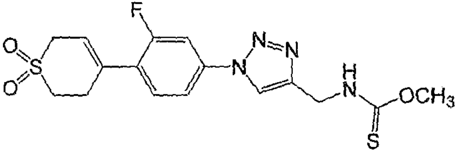
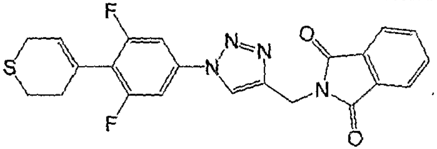
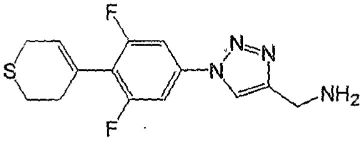
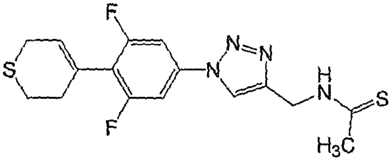
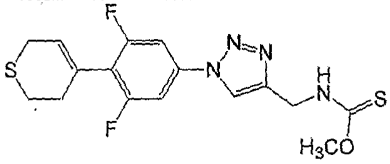
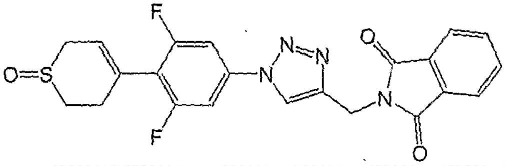
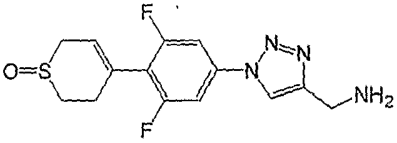
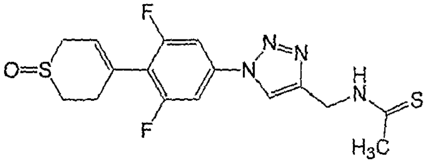
'Z' represents O,

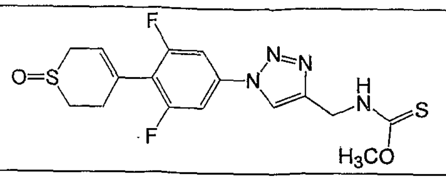
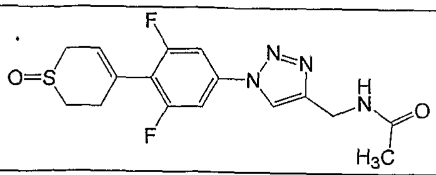
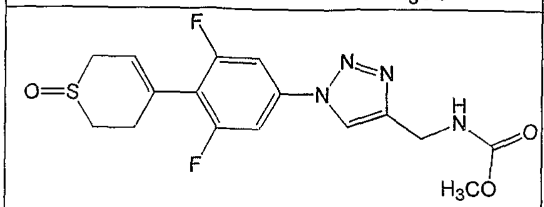
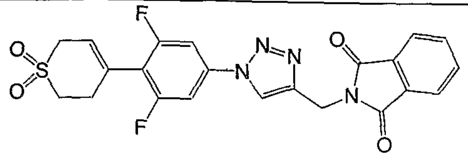
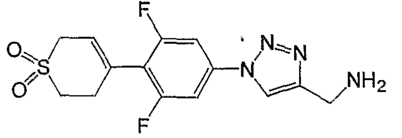
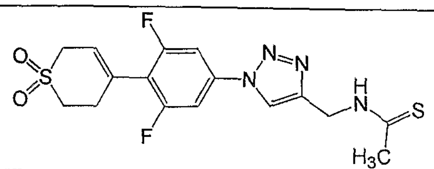
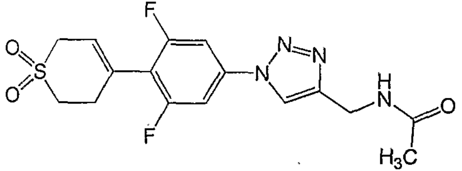
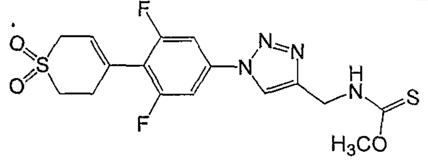
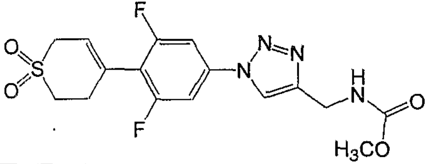
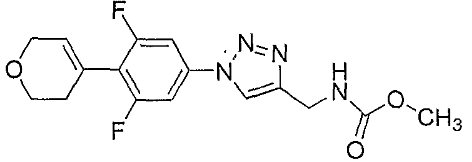
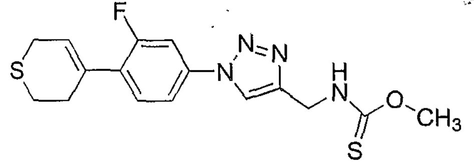
R^2 and R^3 independently represent hydrogen or fluorine;

Y^1 and Y^2 independently represent hydrogen atom.

16. The compound of the formula (I) as claimed in claim 1 is

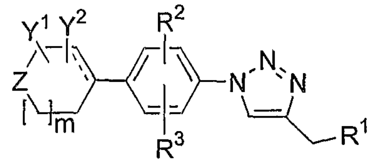
	
	
	
	

or a pharmaceutically aceeptable salts thereof

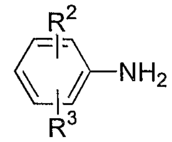
17. A process for the preparation of compound of formula (I),



(I)

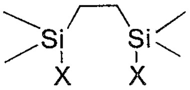
where R^1 represents NHR^4 wherein R^4 represents hydrogen atom; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(a) (i) reacting the compound of formula (Ia)



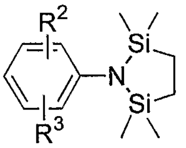
(Ia)

R^2 and R^3 are as defined above, with a compound of formula (Ib)



(Ib)

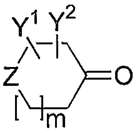
where X represents hydrogen or halogen atom, to produce a compound of formula (Ic)



(Ic)

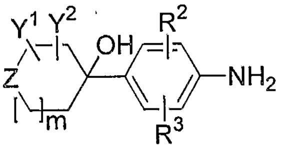
where R^2 and R^3 are as defined above,

(ii) reacting the compund of formula (Ic) with a compound of formula (Id)



(Id)

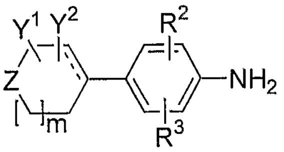
where Z represents O or S, Y^1, Y^2 and m are as defined above, to obtain a compound of formula (Ie)



(Ie)

where Z represents O or S; all other symbols are as defined above,

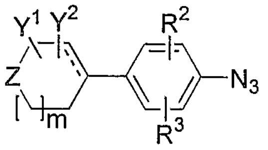
(iii) converting the compound of formula (Ie) to a compound of formula (If)



(If)

where '...' represents a bond or no bond; Z represents O or S, Y^1, Y^2, R^2, R^3 and m are as defined above,

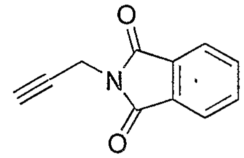
(iv) converting the compound of formula (If), to a compound of formula (Ig)



(Ig)

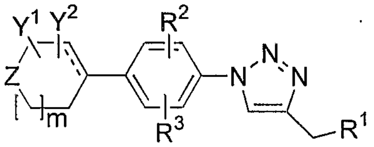
where all symbols are as defined above,

(v) reacting the compound of formula (Ig) with a compound of formula (Ih)



(Ih)

to obatain a compound of formula (I)

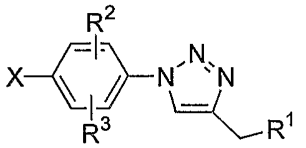


(I)

where R^1 represents isoindole-1,3-dione, Z represents O or S, all other symbols are as defined above and

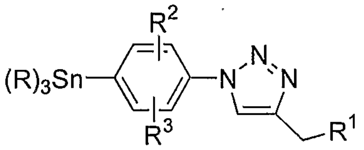
(vi) converting the above compound of formula (I), to a compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom. ***OR***

(b) (i) reacing the compound of formula (Ii)



(Ii)

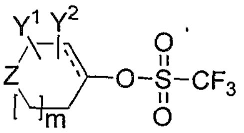
where X represents halogen atom, R^1 represents isoindole-1,3-dione, R^2 and R^3 are as defined above, with $[(R)_3Sn]_2$, wherein R represents $(C_1\text{-}C_6)$alkyl group, to obtain a compound of formula (Ij)



(Ij)

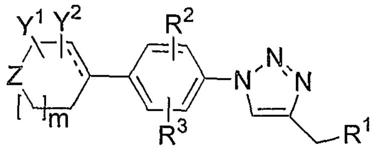
where R, R^1, R^2 and R^3 are as defined above and

(ii) reacting the above compound of formula (Ij), with a compound of formula (Ir),



(Ir)

where Z, m, Y^1 and Y^2 are as defined above; '....' represents a bond, to obtain a compound of formula (I)



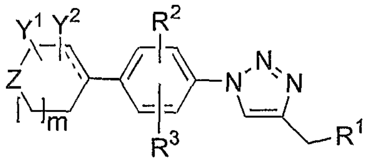
(I)

where R^1 represents isoindole-1,3-dione; '....' represents a bond and all other symbols are as defined above and

(iii) converting the above compound of formula (I), to a compound of formula (I), where R^1 represents NHR^4 wherein R^4 represents hydrogen atom and

(iv) converting the above obtained compound of formula (I), to a compound of formula (I), where '....' represents no bond, by conventional hydrogenation methods, by using a reagent selected from PtO_2, Pd/C, Raney nickel or other related reagent, along with H_2 gas.

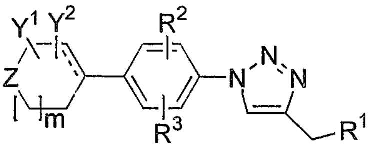
18. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4 wherein R^4 represents hydrogen atom; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(i) converting the compound of formula (I).

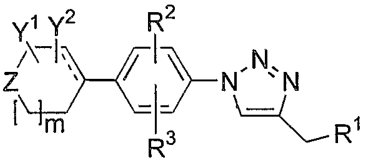


(I)

where R^1 represents isoindole-1,3-dione, Z represents S, and all other symbols are as defined above, to a compound of formula (I), where R^1 represents isoindole-1,3-dione, Z represents SO or SO_2 and

(ii) converting the compound of formula (I), where R^1 represents isoindole-1,3-dione, Z represents SO or SO_2, to a compound of formula (I) where R^1 represents NHR^4 wherein R^4 represents hydrogen atom and all other symbols are as defined above.

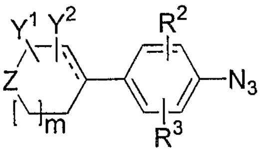
19. A process for the preparation of compound of formula (I)



(I)

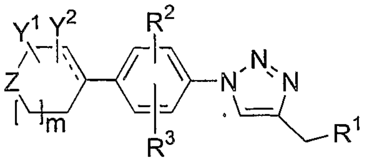
where R^1 represents azido group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(i) converting the compound of formula (Ig)



(Ig)

where Z, Y^1, Y^2, R^2, R^3 and m are as defined above, to a compound of formula (I)

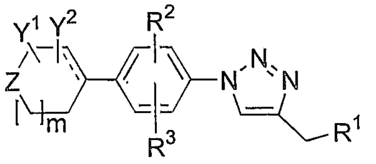


(I)

where R^1 represents hydroxy; Z, Y^1, Y^2, R^2, R^3 and m are as defined above and

(ii) reacting the compound of formula (I) where R^1 represents hydroxy group, with MsCl, triethylamine and sodium azide to give a compound of formula (I) where R^1 represents azido group and all other symbols are as defined above.

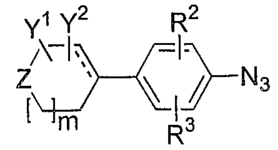
20. A process for the preparation of compound of formula (I)



(I)

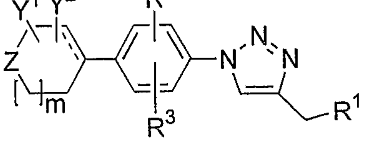
where R^1 represents hydroxy group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(i) converting the compound of formula (Ig),



(Ig)

where Z; Y^1, Y^2, R^2, R^3 and m are as defined above, to a compound of formula (I),

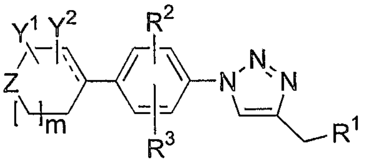


(I)

where R^1 represents optionally substituted $(C_1\text{-}C_{10})$acyloxy group, and all other symbols are as defined above and

(ii) hydrolysis of the compound of formula (I) where R^1 represents $(C_1\text{-}C_{10})$acyloxy group, to a compound of formula (I), where R^1 represents hydroxy group and all other symbols are as defined above.

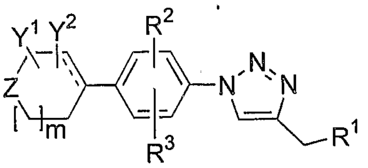
21. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents optionally substituted acetyl group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents azido group and all other symbols are as defined above.

22. A process for the preparation of compound of formula (I)

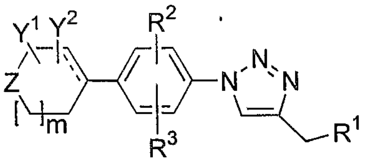


(I)

where R^1 represents NHR^4, wherein R^4 represents–C(=S)-R^{4a}, wherein R^{4a} represents optionally substituted alkyl, haloalkyl, aryl, heteroaryl, -C(=O)-alkoxy, -C(=O)-alkoxy, -C(=O)-aryloxy, -C(=S)-alkyl or -C(=S)-aryl; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group;

Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents NHR^4, where R^4 represents–$C(=O)-R^{4a}$, wherein R^{4a} represents optionally substituted alkyl, haloalkyl, aryl, heteroaryl, -C(=O)-alkoxy, -C(=O)-aryloxy, -C(=S)-alkyl or -C(=S)-aryl.

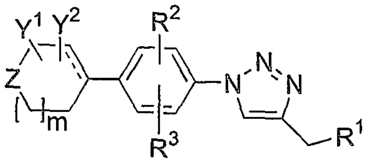
23. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents–$C(=S)-OR^{4b}$, wherein R^{4b} represents optionally substituted alkyl, cycloalkyl, aryl, alkenyl or -C(=O)-alkyl group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(i) reacting compound of formula (I)

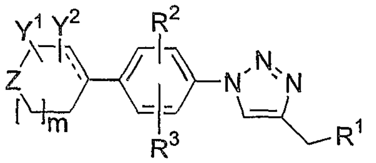

(I)

where R^1 represents azido group; and all other symbols are as defined above, with triphenylphosphine/water or H_2-Pd/C, to produce a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom and all other symbols are as defined above,

(ii) reacting compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom, with thiophosgene or carbon disulfide and chloromethylformate, in the presence of a base to produce a compound of formula (I), where R^1 represents isothiocyanate group; and all symbols are as defined earlier,

(iii) converting compound of formula (I) where R^1 represents isothiocynate group, to a compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-OR^{4b}$, wherein R^{4b} is as defined above and all other symbols are as defined above.

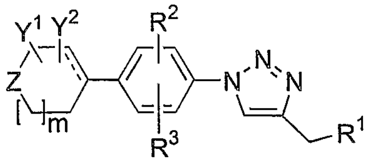
24. A process for the preparation of compound of formula (I)


(I)

where R^1 represents NHR^4, wherein R^4 represents optionally substituted groups selected from -C(=S)-NH$_2$, -C(=S)-NH-alkyl, -C(=S)-N-(alkyl)$_2$, -C(=S)-NH-alkenyl, C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl or -C(=S)-N(R'R"), wherein R' and R" groups together form a optionally substituted 5 or 6 membered cyclic structures containing nitrogen and optionally one or two additional hetero atoms selected from oxygen, nitrogen or sulfur; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1,

Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I) where R^1 represents isothiocyanate group.

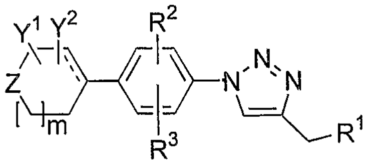
25. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents–C(=S)-SR^{4c}, wherein R^{4c} represents optionally substituted alkyl group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom.

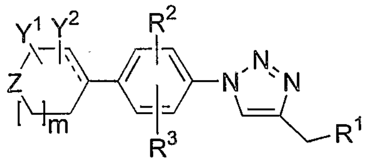
26. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents–C(=S)-NH-R^{4d}, wherein R^{4d} represents optionally substituted -C(=O)-aryl group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom.

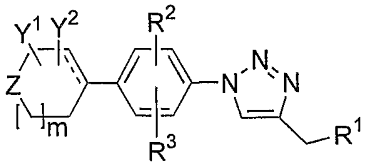
27. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents optionally substituted –C(=O)-heteroaryl; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom.

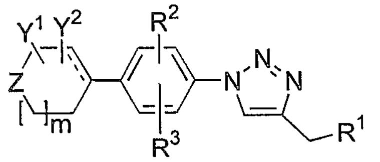
28. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4, wherein R^4 represents–C(=O)-R^{4e} wherein R^{4e} represents optionally substituted alkyl, alkoxy, alkenyl, haloalkyl, aryl, aryloxy, heteroaryl, alkenyloxy, alkylcarbonyl, arylcarbonyl, aryloxycarbonyl, alkoxycarbonyl, alkylthiocarbonyl or arylthiocarbonyl; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom.

29. A process for the preparation of compound of formula (I)



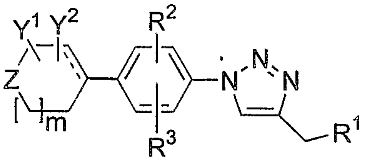
(I)

where R^1 represents NHR^4, wherein R^4 represents optionally substituted -C(=NH)-NH_2; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(a) converting the compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents hydrogen atom. *OR*

(b) converting the compound of formula (I), where R^1 represents NHR^4, wherein R^4 represents optionally substituted group selected from $-S(O)_2$alkyl or $-S(O)_2$aryl group.

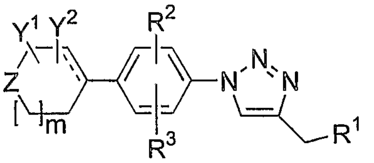
30. A process for the preparation of compound of formula (I)



(I)

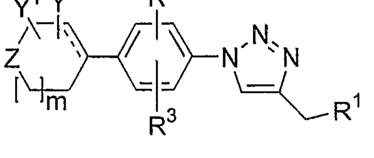
where R^1 represents NHR^4, wherein R^4 represents optionally substituted group selected from -C(=NH)-alkyl or –C(=NH)-aryl; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

(i) reacting the compound of formula (I)



(I)

where R^1 repersents NHR^4, wherein R^4 represents $-C(=S)-NH_2$ and all other symbols are as defined above, with di *tert*-butoxy carbonyl ether ($(BOC)_2O$), to produce a compound of formula (I)



(I)

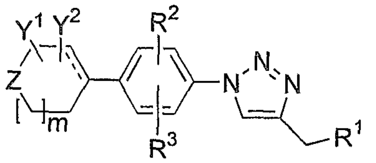
where R^1 represents NHR^4, wherein R^4 represents $-C(=S)-NH_2$ group substituted with *tert*-butoxy carbonyl group and all symbols are as defined above and

(ii) reacting the above compound of formula (I), with a compound of formula (Ik)

R^7-NH_2 **(Ik)**

where R^7 represents optionally substituted alkyl or aryl group, to produce a compound of formula (I) where R^1 represents NHR^4 where R^4 represents optionally substituted group selected from -C(=NH)-alkyl or -C(=NH)-aryl group and all other symbols are as defined above.

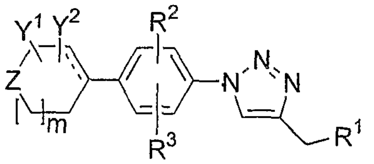
31. A process for the preparation of compound of formula (I)



(I)

where R^1 represents halogen atom; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents hydroxy group.

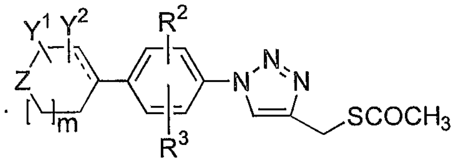
32. A process for the preparation of compound of formula (I)



(I)

where R^1 represents thioalcohol; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one. or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises:

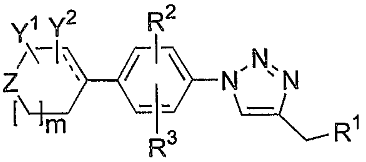
(i) reacting the compound of formula (I) where R^1 represents halogen atom, to produce a compound of formula (Im),


(Im)

where all other symbols are as defined above, with a base and thiolacetic acid and

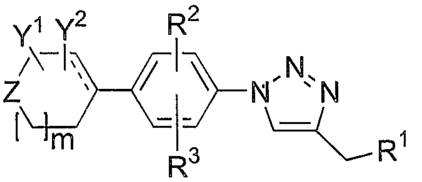
(ii) reacting the compound of formula (Im),, to produce a compound of formula (I) where R^1 represents 'SH' group and all other symbols are as defined above.

33. A process for the preparation of compound of formula (I)


(I)

where R^1 represents NHR^4 wherein R^4 represents optionally substituted $-S(O)_2$alkyl or $-S(O)_2$aryl group; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3; which comprises: converting the compound of formula (I), where R^1 represents NHR^4 where R^4 represents hydrogen atom.

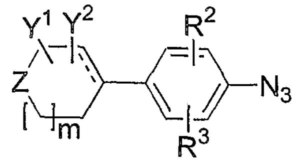
34. A process for the preparation of compound of formula (I)



(I)

where R^1 represents NHR^4 wherein R^4 represents optionally substituted groups selected from alkyl, acyl, thioacyl, alkoxycarbonyl, cycloalkoxycarbonyl, cycloalkoxythiocarbonyl, alkenyloxycarbonyl, alkenylcarbonyl, heteroaryl, aryloxycarbonyl, heteroarylcarbonyl, heteroarylthiocarbonyl, alkoxythiocarbonyl, alkenyloxythiocarbonyl, aryloxythiocarbonyl, -C(=O)-C(=O)-alkyl, -C(=O)-C(=O)-aryl, -C(=O)-C(=O)-alkoxy, -C(=O)-C(=O)-aryloxy, -C(=O)-C(=S)-alkyl, -C(=O)-C(=S)-aryl, -C(=S)-S-alkyl, -C(=S)-NH_2, -C(=S)-NH-alkyl, -C(=S)-N-$(alkyl)_2$, -C(=S)-NH-alkenyl, -C(=S)-C(=O)-alkoxy, -C(=S)-C(=O)-aryloxy, -C(=S)-O-C(=O)- alkyl, -C(=S)-C(=S)-alkyl, -C(=S)-C(=S)-aryl, -C(=S)-NH-C(=O)-aryl, -C(=S)-NH-aralkyl, -C(=S)-NH-heteroaralkyl, -C(=NH)-NH_2, -C(=NH)-alkyl, -C(=NH)-aryl, -S $(O)_2$alkyl, -S$(O)_2$aryl, thiomorpholinylthiocarbonyl, pyrrolidinylthiocarbonyl or –C(=S)-N(R'R"), where R' and R" together form a optionally substituted 5 or 6 member heterocycle ring containing nitrogen and optionally having one or two additional hetero atoms selected from O, S or N; R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '…' represents a bond or no bond; 'm' represents 0-3; which comprises:

(i) converting the compound of formula (Ig),

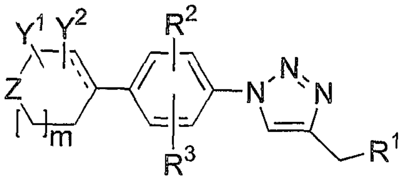


(Ig)

where A, B, D, Y^1, Y^2, R^2 and R^3 are as defined above, with a compound of formula (Ir)

(Ir)

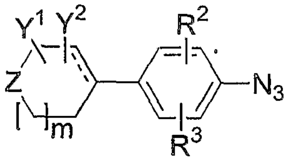
where R^1 is as defined above, to a compound of formula (I)



(I)

where Z, Y^1, Y^2, Y^3, R^d, R^2 and R^3 are as defined above.

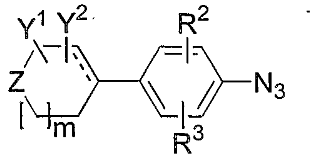
35. A compound of formula (Ig)



(Ig)

where R^2 and R^3 may be same or different and independently represent hydrogen, halogen atom, optionally substituted alkyl, haloalkyl, aryl, heteroaryl, aralkyl, cyano, nitro, OR^a where R^a represents optionally substituted alkyl group; Y^1 and Y^2 may be same or different and independently represent hydrogen, halogen, cyano, nitro, formyl, hydroxy, amino, carboxyl or optionally substituted groups selected from alkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, carboxyalkyl, alkylsulfonyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, monoalkylamino, di alkylamino, arylamino, alkoxy, aryl, aryloxy, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocycloalkyl; or any one or two of Y^1, Y^2 may represent =O, =S, optionally substituted =NOR''' group, where R''' represents hydrogen, alkyl, alkoxy, aryl, heteroaryl or aralkyl group; Z represents O, S, SO or SO_2; '...' represents a bond or no bond; 'm' represents 0-3.

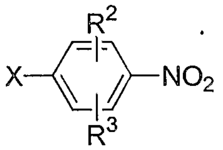
36. A process for the preparation of compound of formula (Ig), as claimed in claim 43,



(Ig)

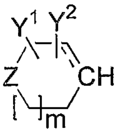
where Z, Y^1, Y^2, R^2, R^3 and m are as defined in claim 43, which comprises:

(i) reacting the compound of formula (In)



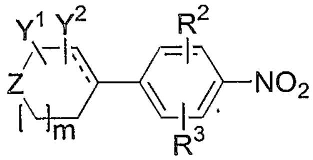
(In)

where X represents halogen atom; R^2 and R^3 are as defined in claim 43, with a compound of formula (Io)



(Io)

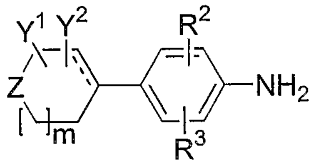
where D, Y^1, Y^2 and m are as defined in claim 43, to produce a compound of formula (Ip)



(Ip)

where Z, Y^1, Y^2, R^2, R^3 and m are as defined in claim 43,

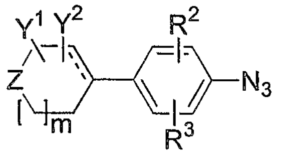
(ii) reducing the compound of formula (Ip) by using reducing agent to a compound of formula (If)



(If)

where Z, Y^1, Y^2, R^2, R^3 and m are as defined in claim 43,

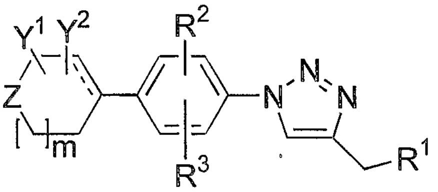
(iii) converting the compound of formula (If) to a compound of formula (Ig)



(Ig).

where Z, Y^1, Y^2, R^2, R^3 and m are as defined in claim 43.

37. A pharmaceutical composition comprising a compound of formula (I)



(I)

as claimed in claim 1 and a pharmaceutically acceptable carrier, diluent, excipient or solvate.

38. The pharmaceutical composition as claimed in claim 37, in the form of a tablet, capsule, powder, syrup, solution or suspension.

39. A method of treating or preventing a bacterial infection comprising administering a therapeutically effective amount of a compound of formula (I) as claimed in claim 1, to a patient in need thereof. .

40. A method of treating or preventing a bacterial infection comprising administering a therapeutically effective amount of a pharmaceutical composition as claimed in claim 37 or 38, to a patient in need thereof.

41. A pharmaceutical composition comprising a compound as claimed in claim 16 and a pharmaceutically acceptable carrier, diluent, excipient or solvate.

42. The pharmaceutical composition as claimed in claim 41, in the form of a tablet, capsule, powder, syrup, solution or suspension.

43. A method of treating or preventing a bacterial infection comprising administering a therapeutically effective amount of a compound as claimed in claim 16 to a patient in need thereof.

44. A method of treating or preventing a bacterial infection comprising administering a therapeutically effective amount of a composition as claimed in claim 41 or 42 to a patient in need thereof.