BICYCLIC IMIDAZOL DERIVATIVES AGAINST FLAVIVIRIDAE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application Serial No. 60/492,108 which application is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

[0002] The invention relates to the field of pharmaceutical chemistry, in particular to compounds, compositions and methods for treating viral infections in mammals mediated, at least in part, by a virus in the *Flaviviridae* family of viruses.

REFERENCES

[0003] The following publications are cited in this application as superscript numbers:

1. Giangaspero, *et al.*, Arch. Virol. Suppl., 7: 53-62 (1993);

2. Giangaspero, *et al.*, Int. J. STD. AIDS, 4(5): 300-302 (1993);

3. Yolken, *et al.*, Lancet, 1(8637): 517-20 (1989);

4. Wilks, *et al.*, Lancet, 1(8629): 107 (1989);

5. Giangaspero, *et al.*, Lancet, 2: 110 (1988);

6. Potts, *et al.*, Lancet, 1(8539): 972-973 (1987);

7. Cornberg, *et al.*, "Hepatitis C: therapeutic perspectives." Forum (Genova), 11(2):154-62 (2001);

8. Dymock, *et al.*, Antivir. Chem. Chemother. 11(2):79-96 (2000);

9. Devos, *et al.*, International Patent Application Publication No. WO 02/18404 A2, published 7 March, 2002;

10. Sommadossi, *et al.*, International Patent Application Publication No. WO 01/90121, published 23 May, 2001;

11. Carroll, S.S., *et al.*, International Patent Application Publication No. WO 02057287, published 25 July, 2002;

12. Carroll, S.S., *et al.*, International Patent Application Publication No. WO 02057425, published 25 July, 2002;

13. Herr, J. R., Bioorg. Med. Chem., 10: 3379-3393 (2002);

14. Andersen, K.E. *et al.*, Eur. J. Med. Chem, 31: 417-425 (1996);

15. Thornber, C.W. Chem. Soc. Rev. 8: 563-580 (1979);

16. Lipinski, C.A. Annual Reports in Med. Chem. 21: 283-297 (1986);

17. Wissner, A. *et al.*, J. Med. Chem. 23: 715-717 (1980);

18. Patani,, G.A. *et al.*, Chem. Rev. 96: 3147-3176 (1996).

[0004] All of the above publications applications are herein incorporated by reference in their entirety to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference in its entirety.

STATE OF THE ART

[0005] The *Flaviviridae* family of viruses is composed of three genera: pestivirus, flavivirus and hepacivirus (hepatitis C virus). Of these genera, flaviviruses and hepaciviruses represent important pathogens of man and are prevalent throughout the world. There are 38 flaviviruses associated with human disease, including the dengue fever viruses, yellow fever virus and Japanese encephalitis virus. Flaviviruses cause a

range of acute febrile illnesses and encephalitic and hemorrhagic diseases. Hepaciviruses currently infect approximately 2 to 3% of the world population and cause persistent infections leading to chronic liver disease, cirrhosis, hepatocellular carcinoma and liver failure. Human pestiviruses have not been as extensively characterized as the animal pestiviruses. However, serological surveys indicate considerable pestivirus exposure in humans. Pestivirus infections in man have been implicated in several diseases including, but not likely limited to, congenital brain injury, infantile gastroenteritis and chronic diarrhea in human immunodeficiency virus (HIV) positive patients.[1-6]

[0006] Currently, there are no antiviral pharmaceutical drugs to prevent or treat pestivirus or flavivirus infections. For hepacivirus, i.e., hepatitis C virus (HCV) infections, interferon alpha (IFN) is currently the only approved drug in the United States. HCV is a major causative agent for post-transfusion and for sporadic non-A, non-B hepatitis. Infection by HCV is insidious in a high proportion of chronically infected (and infectious) carriers who may not experience clinical symptoms for many years.

[0007] At present, the only acceptable treatment for chronic HCV is interferon (IFN-alpha) and this requires at least six (6) months of treatment and/or ribavirin, which can inhibit viral replication in infected cells and also improve liver function in some people.

[0008] IFN-alpha belongs to a family of naturally occurring small proteins with characteristic biological effects such as antiviral, immunoregulatory and antitumoral activities that are produced and secreted by most animal nucleated cells in response to several diseases, in particular viral infections. IFN-alpha is an important regulator of growth and differentiation affecting cellular communication and immunological control. Treatment of HCV with interferon, however, has limited long term efficacy with a response rate about 25%. In addition, treatment of HCV with interferon has frequently been associated with adverse side effects such as fatigue, fever, chills, headache, myalgias, arthralgias, mild alopecia, psychiatric effects and associated disorders, autoimmune phenomena and associated disorders and thyroid dysfunction.

[0009] Ribavirin (1-β-D-ribofuranosyl-1 H-1,2,-4-triazole-3-carboxamide), an inhibitor of inosine 5'-monophosphate dehydrogenase (IMPDH), enhances the efficacy of IFN-alpha in the treatment of HCV. Despite the introduction of ribavirin, more than 50% of the patients do not eliminate the virus with the current standard therapy of interferon-alpha (IFN) and ribavirin. By now, standard therapy of chronic hepatitis C has been changed to the combination of PEG-IFN plus ribavirin. However, a number of patients still have significant side effects, primarily related to ribaviran. Ribavirin causes significant hemolysis in 10-20% of patients treated at currently recommended doses, and the drug is both teratogenic and embryotoxic.

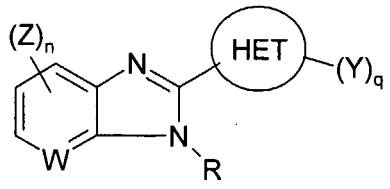
[0010] Other approaches are being taken to combat the virus. They include, for example, application of antisense oligonucleotides or ribozymes for inhibiting HCV replication. Furthermore, low-molecular weight compounds that directly inhibit HCV proteins and interfere with viral replication are considered as attractive strategies to control HCV infection. NS3/4A serine protease, ribonucleic acid (RNA) helicase, RNA-dependent RNA polymerase are considered as potential targets for new drugs.[7,8]

[0011] Devos, *et al.*[9] describes purine and pyrimidine nucleoside derivatives and their use as inhibitors of HCV RNA replication. Sommadossi, *et al.*[10] describes 1', 2' or 3'-modified nucleosides and their use for treating a host infected with HCV. Carroll, *et al.*[11,12], describes nucleosides as inhibitors of RNA-dependent RNA viral polymerase.

Given the fact of the worldwide epidemic level of HCV and other members of the *Flaviviridae* family of viruses, there is a strong need for new effective drugs for treatment of *Flaviviridae* family viruses. The present invention provides compounds for treating such infections.

SUMMARY OF THE INVENTION

[0012] This invention is directed to novel compounds that are useful in the treatment of viral infections in mammals mediated at least in part by a member of the *Flaviviridae* family viruses such as HCV. Specifically, the compounds of this invention are represented by formula I:



I

wherein:

W is CH or N;

R is selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -$NR^{12}R^{13}$,

where each of R^{12} and R^{13} is independently selected from the group consisting of (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{12} and R^{13} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

Z is selected from the group consisting of

a) -C(=O)OR^7, wherein R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; b) -C(=O)NR^8R^9, wherein R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

c) tetrazolyl or –C(O)$NHS(O)_2R^4$, wherein R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

d) $-C(X)-N(R^3)CR^2R^{2'}C(=O)R^1$, wherein X is selected from the group consisting of =O, =S, and $=NR^{11}$, where R^{11} is hydrogen or alkyl, R^1 is selected from the group consisting of $-OR^7$ and $-NR^8R^9$;

wherein R^7, R^8 and R^9 are as defined above;

each R^2 and $R^{2'}$ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic,

or, alternatively, R^2 and $R^{2'}$ as defined are taken together with the carbon atom pendent thereto to form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic group,

or, still further alternatively, one or R^2 or $R^{2'}$ is hydrogen, alkyl or substituted alkyl, and the other is joined, together with the carbon atom pendent thereto, with either the R^7 and the oxygen atom pendent thereto or R^8 and the nitrogen atom pendent thereto to form a heterocyclic or substituted heterocyclic group;

R^3 is selected from the group consisting of hydrogen and alkyl or, when R^2 and $R^{2'}$ are not taken together to form a ring and when $R^2/R^{2'}$ and R^7 or R^8 are not joined to form a heterocyclic or substituted heterocyclic group, then R^3, together with the nitrogen atom pendent thereto, may be taken together with one of R^2 or $R^{2'}$ to form a heterocyclic or substituted heterocyclic ring group;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

each Y is independently selected from the group consisting of halo, cyano, nitro, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cyclo-alkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

n is an integer equal to 0, 1 or 2;

q is an integer equal to 1, 2 or 3;

and pharmaceutically acceptable salts or tautomers thereof.

[0013] In one preferred embodiment, *n* is zero (i.e., Z = hydrogen).

[0014] In another preferred embodiment, *n* is one or two; more preferably, *n* is one.

[0015] When *n* is not zero, preferred Z groups fall into several embodiments. For example, in one preferred embodiment, Z is 1*H*-tetrazol-5-yl or –$COOR^7$ where R^7 is as defined above. In a particularly preferred aspect of this embodiment, Z is selected from the group consisting of 1*H*-tetrazol-5-yl, -C(=O)OH, and –C(=O)OR" where R" is (C_1-C_6)alkyl and especially (C_1-C_2)alkyl. Further with regard to this embodiment, Z is most preferably –C(=O)OH.

[0016] In another preferred embodiment, Z is $-C(=O)NR^8R^9$ where R^8 and R^9 are as defined above. In one particularly preferred aspect of this embodiment, R^8 is hydrogen and R^9 is as defined above. Even more preferably, in this aspect, R^9 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic.

[0017] Preferred R^9 substituted alkyl groups comprise 1 to 2 substituents selected from the group consisting of sulfonic acid, carboxy and carboxy ester.

Particularly preferred R^9 substituted alkyl groups include, by way of example, $-CH_2CH_2SO_3H$ and $-CH_2CH_2COOH$.

[0018] Preferred R^9 aryl and substituted aryl groups include, for example, 7-hydroxynaphth-1-yl, 6-hydroxynaphth-1-yl, 5-hydroxynaphth-1-yl, 4-methyl-2-oxo-2*H*-chromen-7yl, 6-carboxynaphth-2-yl, (4-$HOOCCH_2$-)phenyl, (3,4-dicarboxy)phenyl, 3-carboxyphenyl, 3-carboxy-4-hydroxyphenyl, 2-carboxy-naphthen-6-yl, (4-carboxymethyl)phenyl, (3,4-dicarboxy)phenyl, 4-hydroxy-3-carboxyphenyl and 3-carboxyphenyl.

[0019] Preferred R^9 heteroaryl and substituted heteroaryl groups include, for example, 1-phenyl-4-carboxy-1H-pyrazol-5-yl, 5-carboxypyrid-2-yl, 2-carboxypyrazin-3-yl, and 3-carboxythien-2-yl.

[0020] In Another preferred embodiement, R^9 is heterocyclic, more preferably, N-morpholino.

[0021] In another particularly preferred aspect of this embodiment, R^8 and R^9, together with the nitrogen atom pendent thereto, form a heterocyclic or substituted heterocyclic ring. Preferred heterocyclic and substituted heterocyclic rings include 4 to 8 membered rings containing 1 to 3 heteroatoms and particularly 1 to 2 nitrogen atoms including, for example, piperidine, substituted piperidine, piperazine, substituted piperazine, morpholino, substituted morpholino, thiomorpholino and substituted thiomorpholino wherein the sulfur atom of the thiomorpholino or substituted thiomorpholino ring is optionally oxidized to provide for sulfoxide and sulfones. Particularly preferred heterocyclic and substituted heterocyclic groups include, by way of example, 4-hydroxypiperidin-1-yl, 1,2,3,4-tetrahydro-3-carboxy-isoquinolin-2-yl, 4-methylpiperizin-1-yl, morpholin-4-yl, and thiomorpholin-4-yl.

[0022] In still another preferred embodiment, Z is $-C(X)-N(R^3)-CR^2R^{2'}-C(=O)R^1$.

[0023] In one aspect of this embodiment, Z is $-C(O)NHCHR^2C(=O)R^1$. In this aspect, preferred R^2 groups include hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl. Particularly preferred R^2 groups include hydrogen, alkyl, substituted alkyl, and cycloalkyl including,for example, hydrogen, methyl, 1-methylprop-1-yl, *sec*-butyl, hydroxymethyl, 1-hydroxyeth-1-yl, 4-amino-*n*-butyl, 2-carboxyeth-1-yl, carboxymethyl, benzyl, (1*H*-imidazol-4-yl)methyl, (4-phenyl)benzyl, (4-phenylcarbonyl)benzyl, cyclohexylmethyl, cyclohexyl, 5-hydroxy-1*H*-indol-3-yl, 2-methylthioeth-1-yl, *iso*-propyl, carbamoylmethyl, 2-carbamoyleth-1-yl, (4-hydroxy)benzyl and 3-guanidino-*n*-propyl.

[0024] In this aspect, preferred R1 groups include, for example, hydroxy, amino, and amino(N-morpholino).

[0025] In another aspect of the above embodiment, Z is $-C(O)N(R^3)CHR^2C(=O)R^1$ where R^2 and R^3, together with the carbon atom and nitrogen atom bound thereto respectively, are joined to form a heterocyclic or substituted heterocyclic group. In this aspect, preferred heterocyclic and substituted heterocyclic groups include, by way of example, pyrrolidinyl, 2-carboxypyrrolidinyl, 2-carboxy-4-hydroxypyrrolidinyl, and 3-carboxy-1,2,3,4-tetrahydroisoquinolin-3-yl.

[0026] In still another preferred embodiment, Z is $-C(O)NHS(O)_2R^4$. In this preferred aspect, R^4 is preferably alkyl, substituted alkyl, aryl and substituted aryl. More preferably, R^4 is exemplified bymethyl, trifluoromethyl, phenyl, 4-bromophenyl, 4-nitrophenyl or 4-methylphenyl.

[0027] In another preferred embodiment, Z is a carboxylic acid isostere such as those recited in references 13 to 18 as listed: Herr, J. R., Bioorg. Med. Chem., 10: 3379-3393 (2002)[13]; Andersen, K.E. et al., Eur. J. Med. Chem, 31: 417-425 (1996)[14]; Thornber, C.W. Chem. Soc. Rev. 8: 563-580 (1979)[15]; Lipinski, C.A. Annual Reports in Med. Chem. 21: 283-297 (1986)[16]; Wissner, A. et al., J. Med. Chem. 23: 715-717 (1980)[17]; and, Patani,, G.A. et al., Chem. Rev. 96: 3147-3176 (1996)[18].

[0028] In another preferred embodiment, R is selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, -substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

[0029] Particularly preferred R groups include hydrogen, alkyl, substituted alkyl, cycloalkyl and substituted cycloalkyl which are exemplified by, for example, hydrogen, ethyl, *iso*-propyl, *sec*-butyl, 3-methyl-*n*-butyl, cyclopropyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, 2-(N,N-dimethylamino)eth-1-yl. Most preferably, R is cyclohexyl.

[0030] In one embodiment, W is N. Preferably, however, W is CH.

[0031] In one preferred embodiment, the HET group is a fused bicyclic nitrogen-containing heterocyclic or heteroaryl ring. More preferably, the HET group contains a total of 1 to 4 nitrogen ring atoms in one or both ring groups and optionally 1 to 2 hetero ring atoms selected from the group consisting of -O-, -S-, -S(O)- and -$S(O)_2$- again, in one or both ring groups. Preferably, there are no more than 3 nitrogen ring atoms in any one of the fused rings and, even more preferably, there are no more than 2 nitrogen ring atoms in any one of the fused rings.

[0032] In a particularly preferred aspect of this embodiment, the HET group is selected from the group consisting of quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, pteridinyl, cinnolinyl, [1,8]naphthyridinyl, [1,5]naphthyridinyl, 1,2,3,4-tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,4-dioxo-1,4-dihydrophthalazinyl, 4-oxo-1,4-dihydroquinolinyl, 4-oxo-1,4-dihydroquinazolinyl, 1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazinyl, and 1,4-dihydroisoquinolinyl which groups are exemplified by, for example, quinolin-6-yl, isoquinolin-6-yl, quinolin-7-yl, quinoxalin-6-yl, quinazolin-7-yl, pteridin-6-yl, cinnolin-3-yl, [1,8]naphthyridin-3-yl, [1,5]naphthyridin-2-yl, 1,2,3,4-tetrahydroquinolin-6-yl, 1,4-dioxo-1,4-dihydrophthalazin-6-yl, 4-oxo-1,4-

dihydroquinolin-6-yl, 4-oxo-1,4-dihydroquinazolin-6-yl, 1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazin-7-yl, and 1,4-dihydroisoquinolin-6-yl.

[0033] In another preferred embodiment, the heterocyclic or heteroaryl ring of the HET group is an oxygen-containing heterocyclic or heteroaryl ring. Preferably, the HET group contains 1 to 2 oxygen ring atoms and optionally 1 to 2 hetero ring atoms selected from the group consisting of -S-, -S(O)- and -$S(O)_2$-.

[0034] In a particularly preferred aspect of this embodiment, the HET group is selected from the group consisting of 2-oxo-2*H*-chromenyl, 4-oxo-2*H*-chromenyl, and 4-oxo-4*H*-chromen-6-yl which groups are exemplified, for example, by 2-oxo-2*H*-chromen-7-yl, 4-oxo-2*H*-chromen-6-yl, 4-oxo-2*H*-chromen-7-yl, and 4-oxo-4*H*-chromen-6-yl.

[0035] In another particularly preferred embodiment, the HET group is naphthyl.

[0036] Preferably, Y is selected from the group consisting of (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, amino, substituted amino, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, halo, heteroaryl, substituted heteroaryl, substituted heterocyclic, -$C(O)NR^{14}R^{15}$, -OR^{14}, and -SR^{14}.

[0037] One set of preferred Y groups, for example, amino substituted amino (hydrazine) and mono- and disubstituted amino groups. Mono-substituted amino groups include alkylamino, substituted alkylamino, arylamino, substituted arylamino. Disubstituted amino groups include substituents independently selected from alkyl, substituted alkyl, aryl and substituted aryl groups. Examples of preferred amino Y groups include, for instance, amino, phenylamino, [2-(*t*-butoxycarbonylaminoethyl]amino, N-(4-chlorophenyl)amino, N,N-dimethylamino, 4-hydroxybutylamino, 3-imidazol-1-yl-propylamino, and hydrazino.

[0038] Another set of preferred Y groups include (C_1-C_{10}) alkyl, substituted (C_1-C_{10}) alkyl, cycloalkyl, and substituted cycloalkyl. Preferred substituents for substituted (C_1-C_{10}) alkyl Y groups include, for example, hydroxy, amino, substituted amino, aryl, substituted aryl, heteroaryl and substituted heteroaryl. Preferred substituents for substituted cycloalkyl include, for example, carboxymethyl and methyl. Examples of preferred alkyl, substituted alkyl and substituted cycloalkyl Y groups include, for instance, methyl, 3-hydroxypropyl, (N,N-di-*n*-propyl)aminomethyl, diphenylmethyl (benzhydryl), and 2-(pyrazol-1-yl)eth-1-yl and 3-carboxymethyl-2,2-dimethylcyclobutyl.

[0039] Another set of preferred Y groups include carboxy, carboxy esters, halo (particularly fluoro), cyano, and nitro..

[0040] Another set of preferred Y groups include -C(O)$NR^{14}R^{15}$ where each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl and substituted aryl or where R^{14} and R^{15}, together with the nitrogen atom pendent thereto, form a heterocyclic and substituted heterocyclic group. Preferred substituents on the substituted alkyl and substituted aryl include, for example, halo, hydroxy, carbamoyl, and the like. These preferred Y groups are exemplified by, for instance, 1-carbamoylethyl-carbamoyl, 1-carbamoyl-2-(1H-imidazol-2-yl)ethylcarbamoyl, 1-carbamoyl-2-hydroxyethylcarbamoyl, 1-carbamoyl-2-methylpropylcarbamoyl, 4-chlorophenylcarbamoyl, and pyrrolidin-1-ylcarbonyl.

[0041] Another set of preferred Y groups include aryl groups which are exemplified by, for instance, phenyl, naphthalen-1-yl, and 5,6,7,8-tetrahydronaphthalen-2-yl.

[0042] Another set of preferred Y groups include substituted aryl. In one embodiment, the substituted aryls are substituted with non-aryl groups. In another embodiment, the substituted aryl is substituted with an aryl or substituted aryl to form, e.g., a biphenyl group.

[0043] Preferred substituents for substituted aryl Y groups include, for example, acylamino, amino, substituted amino, alkyl, substituted alkyl, alkoxy, substituted alkoxy, aryl, substituted aryl, aryloxy, substituted aryloxy, cycloalkyl, substituted cycloalkyl, halo, heterocyclic, substituted heterocyclic, heteroaryl, substituted heteroaryl, hydroxy, nitro and $-C(O)NR^{14}R^{15}$ where each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl and substituted aryl or where R^{14} and R^{15}, together with the nitrogen atom pendent thereto, form a heterocyclic and substituted heterocyclic group.

[0044] Substituted aryl Y groups which are not substituted by an aryl or substituted aryl group are, for example, 4-acetylaminophenyl, 4-aminophenyl, 4-amino-3-bromophenyl, 4-amino-3,5-dichlorophenyl, 4-benzyloxy-2-hydroxy-3-methylphenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 5-bromo-2-hydroxyphenyl, 3-carbamoyl-4-hydroxyphenyl, 3-carboxymethoxyphenyl, 2-cyclohexyl-5-methoxyphenyl, 3,4-dichlorophenyl, 2,4-dihydroxyphenyl, 3,5-dihydroxyphenyl, 4-(N,N-dimethylamino)phenyl, 4-fluorophenyl, 2-furan-2-yl-5-methoxyphenyl, 3-hydroxyphenyl, 2-hydroxy-4-,6-dimethoxyphenyl, 2-hydroxynaphthalen-1-yl, 2-hydroxy-6-methoxyphenyl, 2-hydroxy-5-methyl-3-nitrophenyl, 4-(imidazol-1-yl)phenyl, 3-(2-methoxyethoxy)phenyl, 2-methoxy-5-nitrophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 5-methoxy-2-thiophen-2-ylphenyl, 4-methylphenyl, 4-morpholinophenyl, 6-methylnaphthalen-2-yl, 2-nitrophenyl, 3-(2-oxo-2-pyrrolidin-1-ylethoxy)phenyl, 4-phenoxyphenyl, (4-piperazin-1-yl)phenyl, 3-[pyrrolidin-1-ylcarbonyl]-phenyl, 3-[3-(pyrrolidin-1-ylpropoxy)]phenyl. 2-(2,4-dimethoxypyrimidin-5-yl)-4-methoxyphenyl, and 2-(pyrid-4-yl)phenyl.

[0045] Substituted aryl Y groups which are substituted by an aryl or substituted aryl group are exemplified, for example, by biphen-2-yl, biphen-4-yl, 4-amino-4'-chlorobiphen-2-yl, 4'-aminomethyl-4-methoxybiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carbamoyl-4'-fluorobiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carbamoyl-4'-nitrobiphen-2-yl, 4-(carbamoylmethylcarbamoyl)biphen-2-yl, 4-(carbamoylmethylcarbamoyl)-4'-chlorobiphen-2-yl, 4-carboxy-4'-chlorobiphen-2-yl, 3-carboxy-4'-methoxybiphen-2-yl, 4-carboxy-4'-methoxybiphen-2-yl, 4'-carboxy-4-

(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-carboxymethoxybiphen-2-yl, 4-carboxymethoxy-4'-chlorobiphen-2-yl, 4'-chlorobiphen-2-yl, 4'-chloro-4-chlorobiphen-2-yl, 4'-chloro-4-(dimethylaminoethylcarbamoylbiphen-2-yl, 4'-chloro-4-(2-ethoxyethoxy)biphen-2-yl, 3'-chloro-4'-fluoro-4-methoxybiphen-2-yl, 4'-chloro-4-fluorobiphen-2-yl, 4'-chloro-4-hydroxybiphen-2-yl, 3'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-methylcarbamoylbiphen-2-yl, 4'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-(2-methoxyethoxy)biphen-2-yl, 4'-chloro-4-nitrobiphen-2-yl, 4'-chloro-4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4'-chloro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-chloro-4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, 4'-cyano-4-methoxybiphen-2-yl, 3',4'-dichloro-4-methoxybiphen-2-yl, 4,4'-dimethoxybiphen-2-yl, 3',4'-dimethoxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-dimethylamino-4-methoxybiphen-2-yl, 4-(2-dimethylaminoethylcarbamoyl)biphen-2-yl, 4'-ethoxy-4-methoxybiphen-2-yl, 4'-fluoro-4-methoxybiphen-2-yl, 4-hydroxybiphenyl, 4-methoxybiphenyl, 4-methoxy-4'-hydroxybiphen-2-yl, 4-(2-methoxyethoxy)biphen-2-yl, 4-methoxy-4'-methylbiphen-2-yl, 4-methoxy-3'-nitrobiphen-2-yl, 4-methoxy-4'-nitrobiphen-2-yl, 4-methylcarbamoylbiphen-2-yl, 3'-methyl-4-methoxybiphen-2-yl, 4'-nitro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, and 4'-trifluoromethyl-4-methoxybiphen-2-yl.

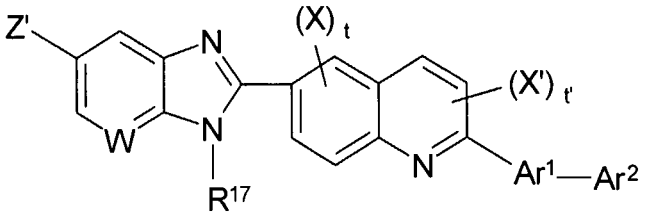
[0046] Another set of preferred Y groups include heteroaryl groups which are exemplified by, for instance, benzo[1,3]dioxol-5-yl, benzofuran-2-yl, 2,3-dihydrobenzofuran-5-yl, pyrazin-2-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1*H*-pyrrol-2-yl, 1*H*-pyrrol-3-yl, quinolin-4-yl, 3-oxo-3,4-dihydro-2*H*-benzo[1,4]oxazin-6-yl, and thien-2-yl.

[0047] Another set of preferred Y groups include substituted heteroaryl. Preferred substituents on the substituted heteroaryl Y groups include amino, substituted amino, alkyl, substituted alkyl, aryl, substituted aryl, alkoxy, substituted alkoxy, halo, heteroaryl, substituted heteroaryl, hydroxy, nitro and cyano. Such groups are exemplified by, for example, 2-amino-4-methylthiazol-5-yl, 3-amino-5-phenylthiophen-2-yl, 5-benzyloxy-2-methylbenzofuran-3-yl, 7-bromo-5-methoxybenzofuran-2-yl, 6-chloro-9-methyl-9*H*-carbazol-3-yl, 5-(4-chlorophenyl)-2-methylfuran-2-yl, 3-(4-chlorophenyl)-5-

methylisoxazol-4-yl, 2-(4-chlorophenyl)-4-methylthiazol-5-yl, 1-(2-chloropyrid-3-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl, 3-(3,4-dichlorophenyl)isoxazol-5-yl, 7-hydroxybenzofuran-2-yl,
5-methoxybenzofuran-3-yl, 3,5-dimethyl-1-phenyl-1*H*-pyrazol-4-yl, 2,4-dimethylthiazol-5-yl, 5-methyl-2-phenyl-thiophen-3-yl, and 1-phenyl-1*H*-pyrazol-4-yl.

[0048] Another set of preferred Y groups include alkoxy, thioalkyl, substituted alkoxy, substituted thioalkyl, aryloxy and substituted aryloxy group. Such groups are exemplified by, for example, 2-chloro-4-(4-chlorophenyl)phenoxy, ethoxy, 7-hydroxynaphthalen-2-oxy, phenoxy, and phenylsulfanyl.

[0049] A particularly preferred class of compounds of this invention are set forth in formula II below:



II

wherein:

W is CH or N;

Z' is selected from the group consisting of carboxy, carboxy ester, and tetrazolyl,

R^{17} is selected from the group consisting of cycloalkyl, cycloalkyl substituted with 1 to 3 alkyl groups, heterocyclic and heterocyclic substituted with 1 to 3 alkyl groups;

X and X' are independently selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, halo, hydroxy, and nitro;

Ar^1 and Ar^2 are independently selected from the group consisting of aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

t is an integer equal to 0, 1 or 2;

t' is an integer equal to 0 or 1;

and pharmaceutically acceptable salts thereof.

[0050] Preferably, W is CH.

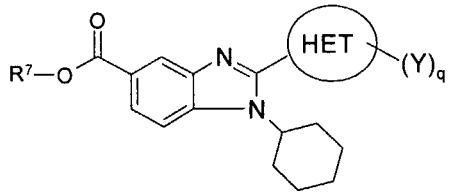
[0051] Preferably, R^{17} is cycloalkyl and, more preferably, is cyclohexyl.

[0052] In one preferred embodiment, -Ar^1-Ar^2- are selected from the group consisting of –aryl-aryl, -aryl-substituted aryl, -substituted aryl-aryl, and -substituted aryl-substituted aryl. Examples of such preferred embodiments include, for instance, biphen-2-yl, biphen-4-yl, 4-amino-4'-chlorobiphen-2-yl, 4'-aminomethyl-4-methoxybiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carbamoyl-4'-fluorobiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carbamoyl-4'-nitrobiphen-2-yl, 4-(carbamoylmethylcarbamoyl)-biphen-2-yl, 4-(carbamoylmethylcarbamoyl)-4'-chlorobiphen-2-yl, 4-carboxy-4'-chlorobiphen-2-yl, 3-carboxy-4'-methoxybiphen-2-yl, 4-carboxy-4'-methoxybiphen-2-yl, 4'-carboxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-carboxymethoxybiphen-2-yl, 4-carboxymethoxy-4'-chlorobiphen-2-yl, 4'-chlorobiphen-2-yl, 4'-chloro-4-chlorobiphen-2-yl, 4'-chloro-4-(dimethylaminoethylcarbamoylbiphen-2-yl, 4'-chloro-4-(2-ethoxyethoxy)biphen-2-yl, 3'-chloro-4'-fluoro-4-methoxybiphen-2-yl, 4'-chloro-4-fluorobiphen-2-yl, 4'-chloro-4-hydroxybiphen-2-yl, 3'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-methylcarbamoylbiphen-2-yl, 4'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-(2-methoxyethoxy)biphen-2-yl, 4'-chloro-4-nitrobiphen-2-yl, 4'-chloro-4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4'-chloro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-chloro-4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, 4'-cyano-4-methoxybiphen-2-yl, 3',4'-dichloro-4-methoxybiphen-2-yl, 4,4'-dimethoxybiphen-2-yl, 3',4'-dimethoxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-dimethylamino-4-methoxybiphen-2-yl, 4-(2-dimethylaminoethylcarbamoyl)biphen-2-yl, 4'-ethoxy-4-methoxybiphen-2-yl, 4'-fluoro-4-methoxybiphen-2-yl, 4-hydroxybiphenyl, 4-methoxybiphenyl, 4-methoxy-4'-hydroxybiphen-2-yl, 4-(2-methoxyethoxy)biphen-2-yl, 4-methoxy-4'-methylbiphen-2-yl, 4-methoxy-3'-nitrobiphen-2-yl, 4-methoxy-4'-nitrobiphen-2-yl, 4-methylcarbamoylbiphen-2-yl, 3'-methyl-4-methoxybiphen-2-yl, 4'-nitro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, and 4'-trifluoromethyl-4-methoxybiphen-2-yl.

[0053] In another preferred embodiment, -Ar^1-Ar^2- are selected from the group consisting of -aryl-heteroaryl, -aryl-substituted heteroaryl, -substituted aryl-heteroaryl, -substituted aryl-substituted heteroaryl, heteroaryl-aryl, heteroaryl-substituted aryl, substituted heteroaryl-aryl, and substituted heteroaryl-substituted aryl. Examples of such preferred embodiments include, for instance, 2-furan-2-yl-5-methoxyphenyl, 4-(imidazol-1-yl)phenyl, 5-methoxy-2-thiophen-2-ylphenyl, 2-(2,4-dimethoxypyrimidin-5-yl)-4-methoxyphenyl, 2-(pyrid-4-yl)phenyl, 3-amino-5-phenylthiophen-2-yl, 5-(4-chlorophenyl)-2-methylfuran-2-yl, 3-(4-chlorophenyl)-5-methylisoxazol-4-yl, 2-(4-chlorophenyl)-4-methylthiazol-5-yl, 3-(3,4-dichloro-phenyl)isoxazol-5-yl, 3,5-dimethyl-1-phenyl-1*H*-pyrazol-4-yl, 5-methyl-2-phenylthiophen-3-yl, and 1-phenyl-1*H*-pyrazol-4-yl.

[0054] In another preferred embodiment, -Ar^1-Ar^2- are selected from the group consisting of -aryl-cycloalkyl, -aryl-substituted cycloalkyl, -substituted aryl-cycloalkyl, -substituted aryl-substituted cycloalkyl, -aryl-heterocyclic, aryl-substituted heterocyclic, substituted aryl-heterocyclic, and substituted aryl-substituted heterocyclic. Examples of such preferred embodiments include, (4-piperazin-1-yl)phenyl, 2-cyclohexyl-5-methoxyphenyl, and 4-morpholinophenyl.

[0055] In another embodiment of the invention, the compounds are represented by formula III:



III

wherein:

q is an integer equal to 1, 2 or 3;

R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

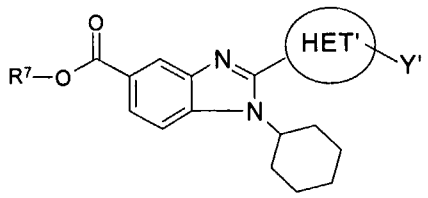
each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, $-SR^{14}$, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cyclo-alkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

and pharmaceutically acceptable salts and/or tautomers thereof.

[0056] Preferred R^7, HET and Y groups are as defined above.

[0057] In another embodiment of the invention, the compounds are represented by formula IV:



IV

wherein:

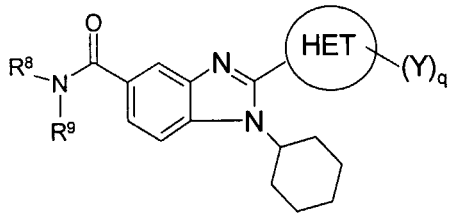
R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

[0058] In another embodiment of the invention, the compounds are represented by formula V:



V

wherein:

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

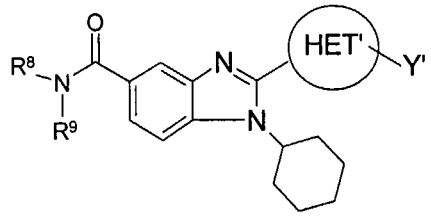
each Y is independently selected from the group consisting of halo, cyano, nitro, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, acyl, acyloxy, guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

[0059] In yet another embodiment, the compounds are represented by the formula VI:



VI

wherein:

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto,

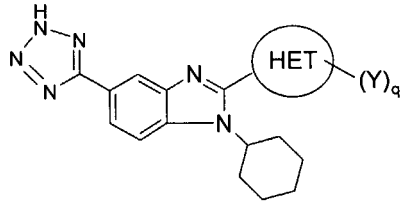
form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

[0060] In yet another embodiment, the compounds are represented by the formula VII:



VII

wherein:

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

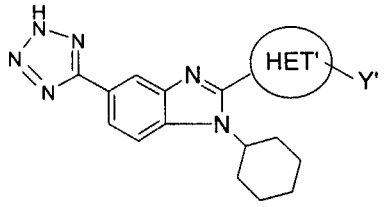
each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

[0061] In yet another embodiment, the compounds are represented by the formula VIII:



VIII

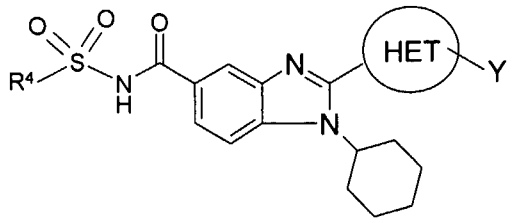
wherein:

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

[0062] In yet another embodiment, the compounds are represented by the formula IX:



IX

wherein:

R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

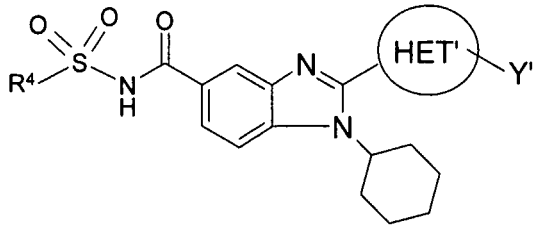
each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

[0063] In yet another embodiment, the compounds are represented by the formula X:



X

wherein:

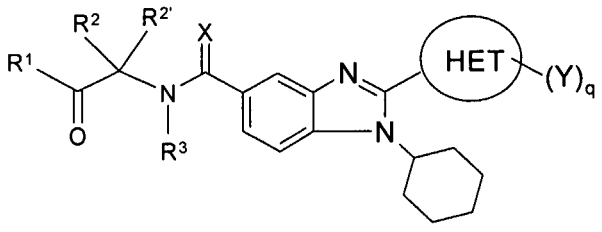
R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

[0064] In yet another embodiment, the compounds are represented by the formula XI:



XI

wherein X is selected from the group consisting of =O, =S, and $=NR^{11}$, where R^{11} is hydrogen or alkyl, R^1 is selected from the group consisting of $-OR^7$ and $-NR^8R^9$ where

R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

each R^2 and $R^{2'}$ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic,

or, alternatively, R^2 and $R^{2'}$ as defined are taken together with the carbon atom pendent thereto to form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic group,

or, still further alternatively, one or R^2 or $R^{2'}$ is hydrogen, alkyl or substituted alkyl, and the other is joined, together with the carbon atom pendent thereto, with either the R^7 and the oxygen atom pendent thereto or R^8 and the nitrogen atom pendent thereto to form a heterocyclic or substituted heterocyclic group;

R^3 is selected from the group consisting of hydrogen and alkyl or, when R^2 and $R^{2'}$ are not taken together to form a ring and when $R^2/R^{2'}$ and R^7 or R^8 are not joined to form a heterocyclic or substituted heterocyclic group, then R^3, together with the nitrogen atom pendent thereto, may be taken together with one of R^2 and $R^{2'}$ to form a heterocyclic or substituted heterocyclic ring group;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}$

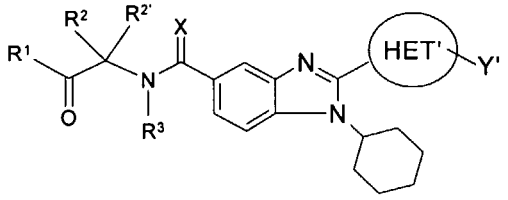
C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, -CO_2R^7, -$NR^{14}R^{15}$, -$NHNR^{14}R^{15}$, -$C(X)NR^{14}R^{15}$, -OR^{14}, SR^{14}, -$S(O)R^{14}$, -$S(O)_2R^{14}$, and -$S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; s as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

[0065] In yet another embodiment, the compounds are represented by the formula XII:



XII

wherein X is selected from the group consisting of =O, =S, and $=NR^{11}$, where R^{11} is hydrogen or alkyl, R^1 is selected from the group consisting of –OR^7 and –NR^8R^9 where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl,

substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

each R^2 and $R^{2'}$ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic,

or, alternatively, R^2 and $R^{2'}$ as defined are taken together with the carbon atom pendent thereto to form a ring group,

R^3 is selected from the group consisting of hydrogen and alkyl or, when R^2 and $R^{2'}$ are not taken together to form a ring then R^3 may be taken together with one of R^2 and $R^{2'}$ to form a heterocyclic or substituted heterocyclic ring group;

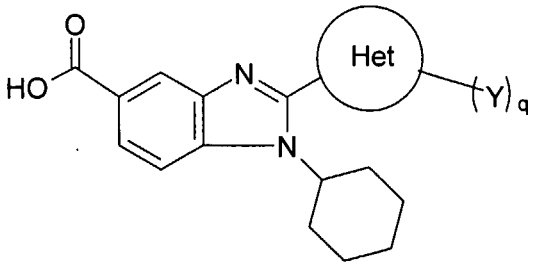
HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

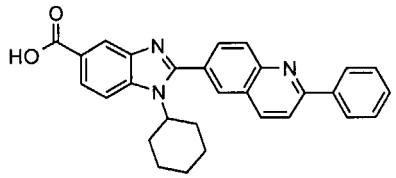
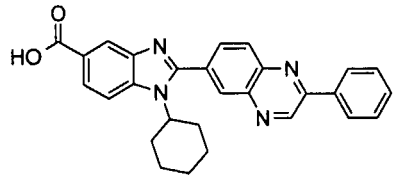
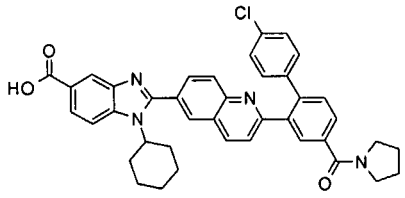
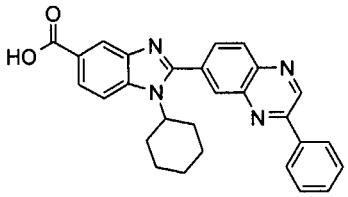
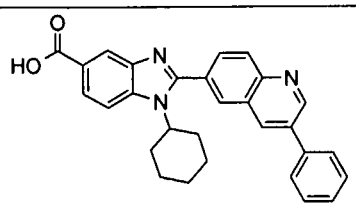
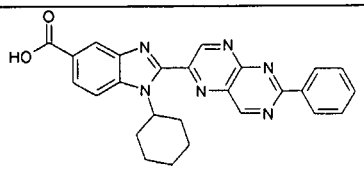
Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

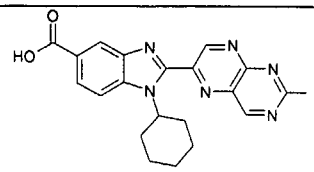
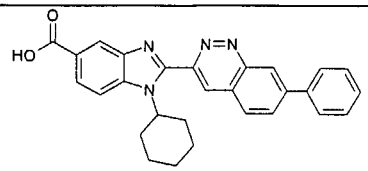
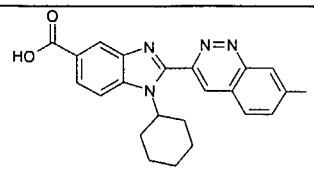
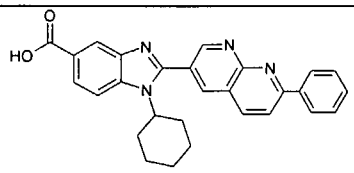
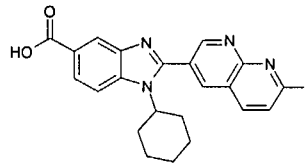
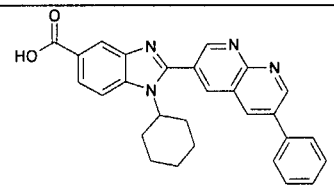
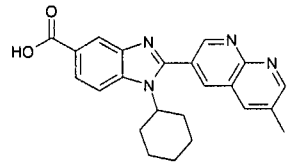
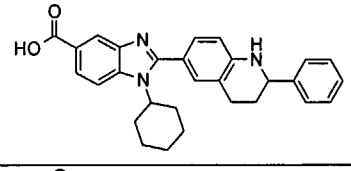
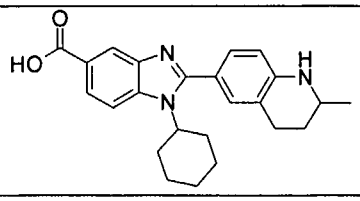
pharmaceutically acceptable salts and/or tautomers thereof.

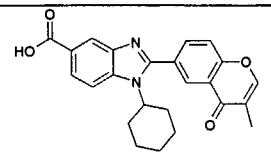
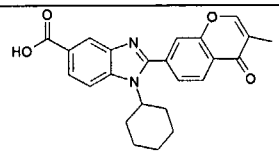
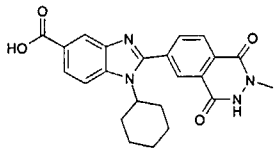
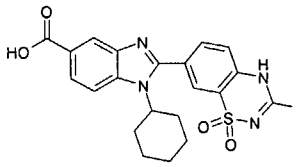
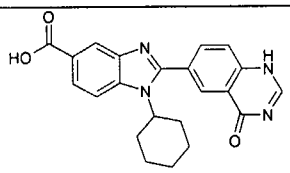
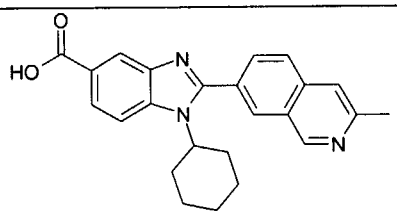
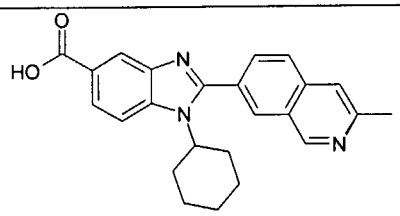
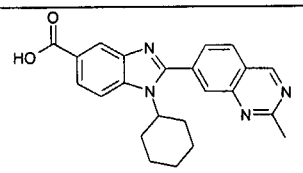
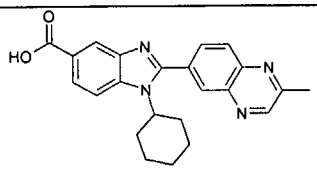
[0066] Compounds within the scope of this invention include those of Formula I as set forth in Tables I-VIII as follows:

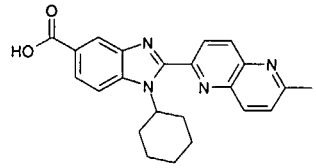
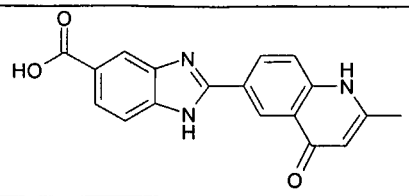
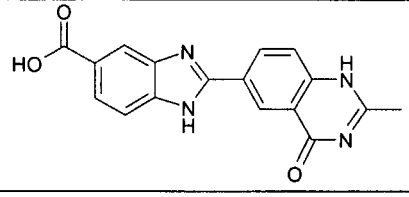
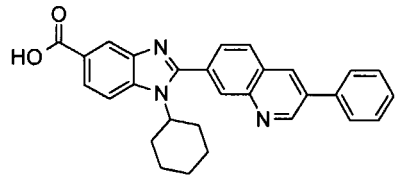
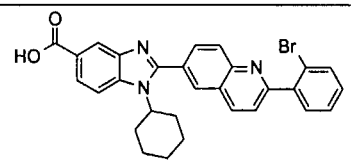
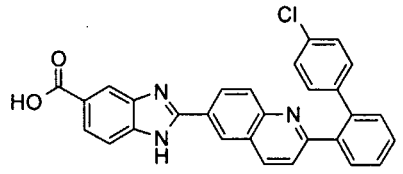
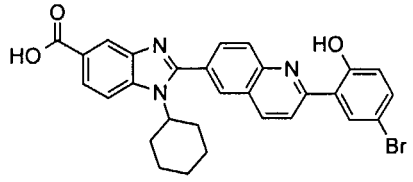
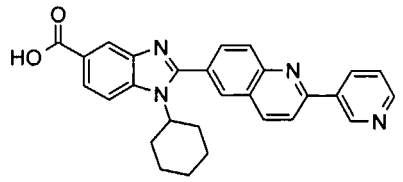
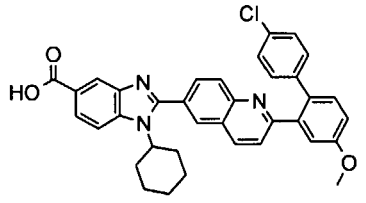
Table I

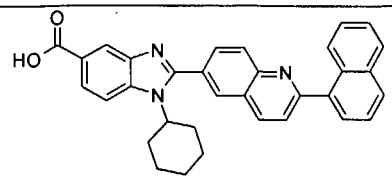
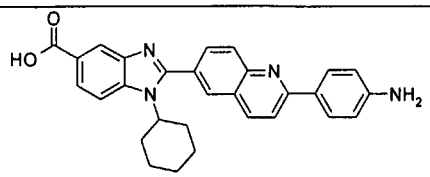
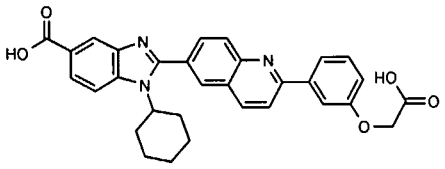
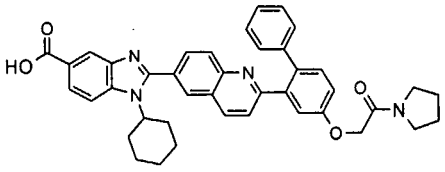
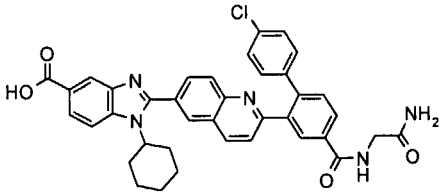
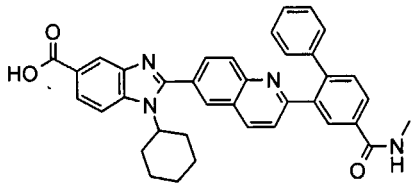
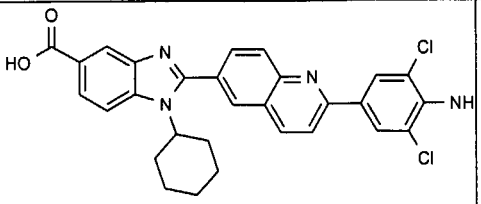
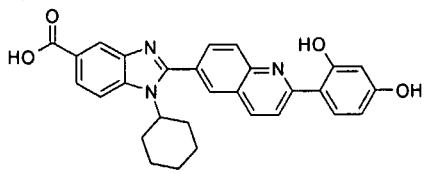


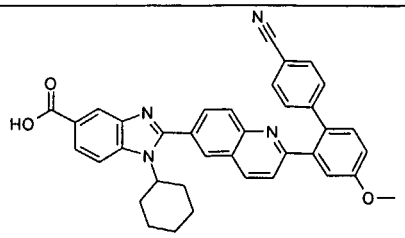
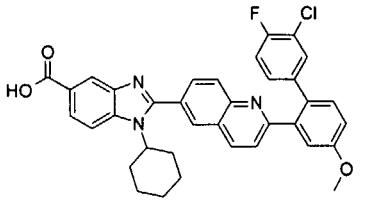
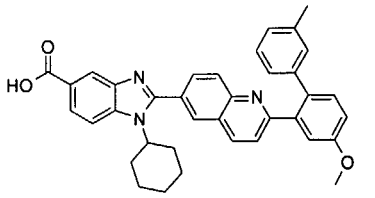
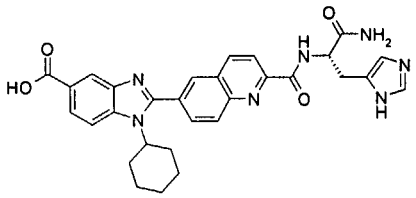
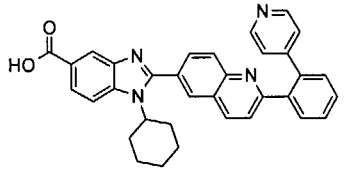
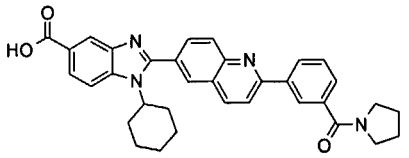
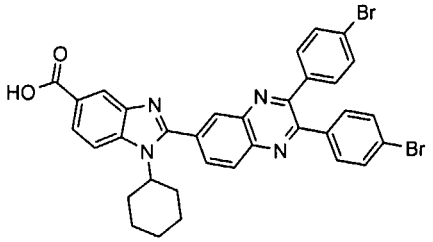
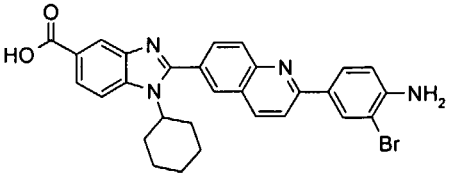
Cmpd#	Structure	*q*	Y	Het	Name
201		1	phenyl	quinolin-6-yl	1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic-acid
203		1	phenyl	quinoxalin-6-yl	1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid
204		1	4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(pyrrolidinyl-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
205		1	phenyl	quinoxalin-6-yl	1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid
206		1	phenyl	quinolin-6-yl	1-cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
207		1	phenyl	pteridin-6-yl	1-cyclohexyl-2-(2-phenyl-pteridin-6-yl)-1H-benzoimidazole-5-carboxylic acid

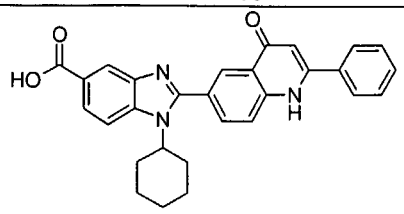
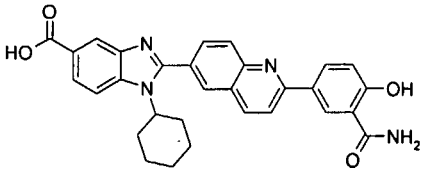
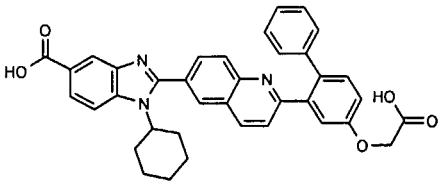
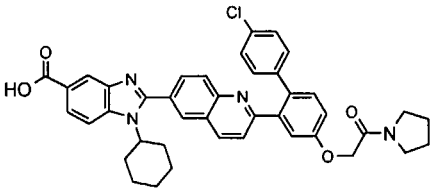
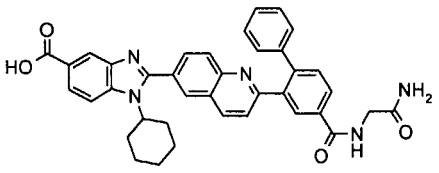
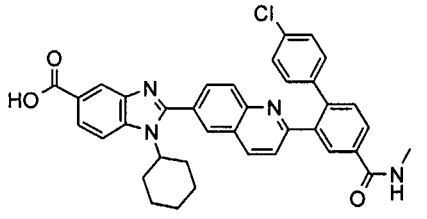
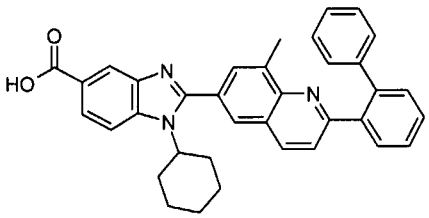
Cmpd#	Structure	*q*	Y	Het	Name
208		1	methyl	pteridin-6-yl	1-cyclohexyl-2-(2-methyl-pteridin-6-yl)-1H-benzoimidazole-5-carboxylic acid
209		1	Phenyl	cinnolin-3-yl	1-cyclohexyl-2-(7-phenyl-cinnolin-3-yl)-1H-benzoimidazole-5-carboxylic acid
210		1	Methyl	cinnolin-3-yl	1-cyclohexyl-2-(7-methyl-cinnolin-3-yl)-1H-benzoimidazole-5-carboxylic acid
211		1	Phenyl	[1,8]naph-thyridin-3-yl	1-cyclohexyl-2-(7-phenyl[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid
212		1	Methyl	[1,8]naph-thyridin-3-yl	1-cyclohexyl-2-(7-methyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid
213		1	Phenyl	[1,8]naph-thyridin-3-yl	1-cyclohexyl-2-(6-phenyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid
214		1	Methyl	[1,8]naph-thyridin-3-yl	1-cyclohexyl-2-(6-methyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid
215		1	Phenyl	1,2,3,4-tetrahydro-quinolin-6-yl	1-cyclohexyl-2-(2-phenyl-1,2,3,4-tetrahydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
216		1	Methyl	1,2,3,4-tetrahydro-quinolin-6-yl	1-cyclohexyl-2-(2-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid

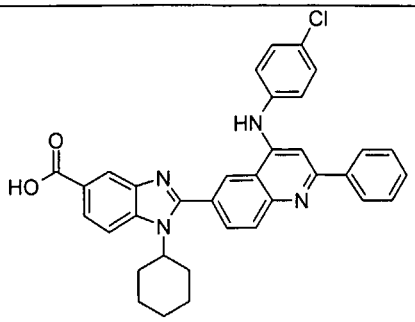
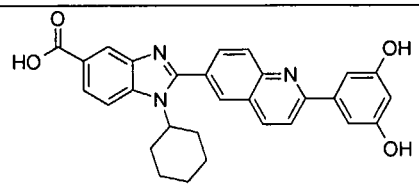
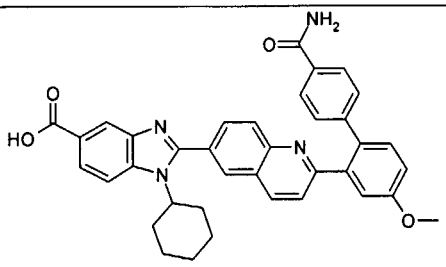
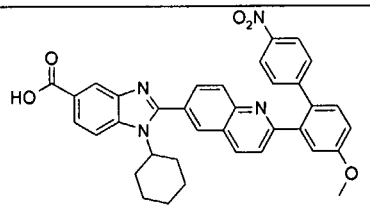
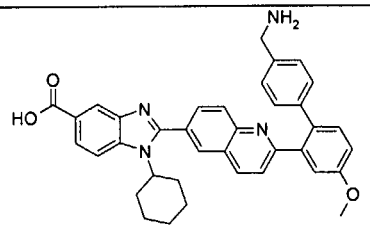
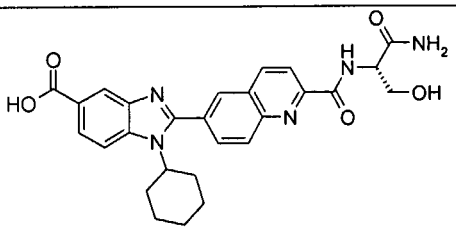
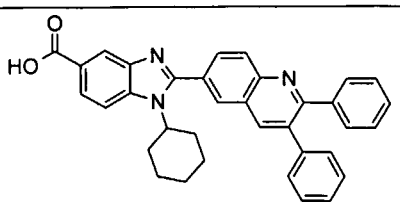
Cmpd#	Structure	*q*	Y	Het	Name
217		1	Methyl	4-oxo-2H-chromen-6-yl	1-cyclohexyl-2-(3-methyl-4-oxo-chromen-6-yl)-1H-benzoimidazole-5-carboxylic acid
218		1	Methyl	4-oxo-2H-chromen-7-yl	1-cyclohexyl-2-(3-methyl-4-oxo-chromen-7-yl)-1H-benzoimidazole-5-carboxylic acid
219		1	Methyl	1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl	1-cyclohexyl-2-(2-methyl-1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl)-1H-benzoimidazole-5-carboxylic acid
220		1	Methyl	1,1-dioxo-1,4-dihydro-1λ6-benzo-[1,2,4] thiadiazin-7-yl	1-cyclohexyl-2-(3-methyl-1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4] thiadiazin-7-yl)-1H-benzoimidazole-5-carboxylic acid
221		0		4-oxo-1,4-dihydro-quinazolin-6-yl	1-cyclohexyl-2-(4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
222		1	Methyl	Isoquinolin-6-yl	1-cyclohexyl-2-(3-methyl-isoquinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
223		1	Methyl	1,4-dihydro-isoquinolin-6-yl	1-cyclohexyl-2-(3-methyl-1,4-dihydro-isoquinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
224		1	Methyl	quinazolin-7-yl	1-cyclohexyl-2-(2-methyl-quinazolin-7-yl)-1H-benzoimidazole-5-carboxylic acid
225		1	Methyl	quinoxalin-6-yl	1-cyclohexyl-2-(2-methyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid

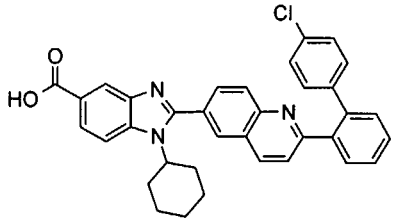
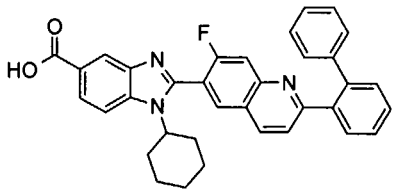
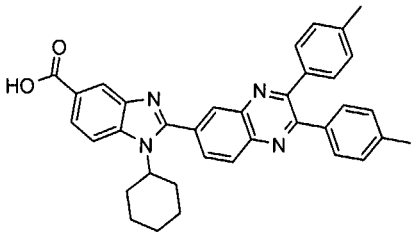
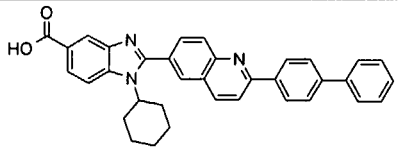
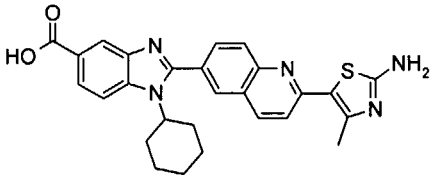
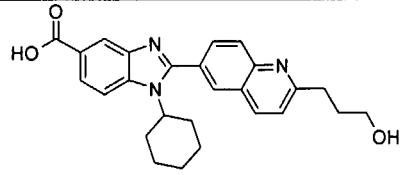
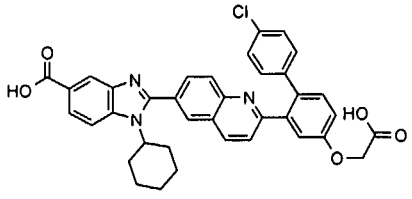
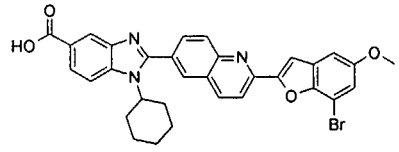
Cmpd#	Structure	q	Y	Het	Name
226		1	Methyl	[1,5]naph-thyridin-2-yl	1-cyclohexyl-2-(6-methyl-[1,5]naphthyridin-2-yl)-1H-benzoimidazole-5-carboxylic acid
227		1	Methyl	4-oxo-1,4-dihydro-quinolin-6-yl	1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
228		1	Methyl	4-oxo-1,4-dihydro-quinazolin-6-yl	1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
351		1	Phenyl	quinolin-7-yl	1-cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid
352		1	2-bromo-phenyl	quinolin-6-yl	2-[2-(2-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
353		1	4'-chloro-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
354		1	5-bromo-2-hydroxy-phenyl	quinolin-6-yl	2-[2-(5-bromo-2-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
355		1	pyridin-3-yl	quinolin-6-yl	1-cyclohexyl-2-(2-pyridin-3-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
356		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

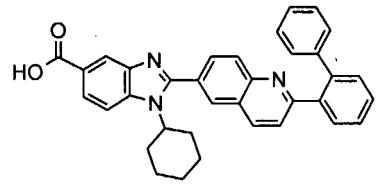
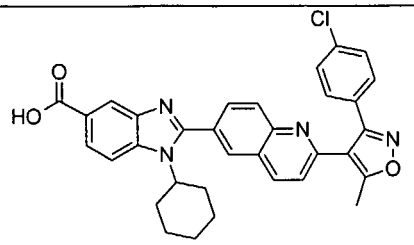
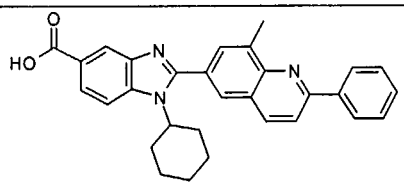
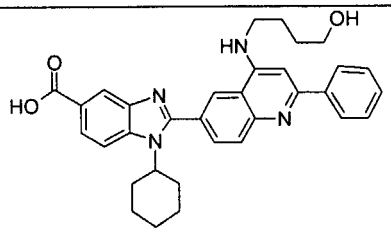
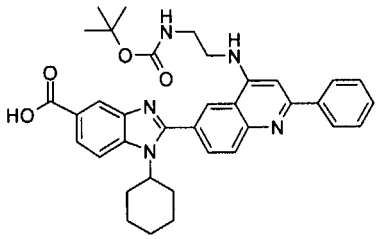
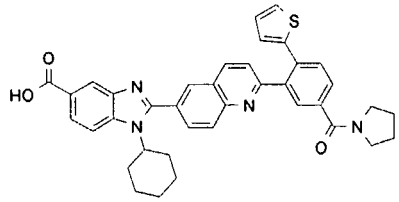
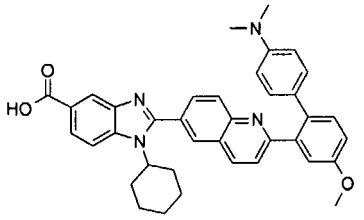
Cmpd#	Structure	q	Y	Het	Name
357		1	naphthalen-1-yl-	quinolin-6-yl	1-cyclohexyl-2-(2-naphthalen-1-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
358		1	4-amino-phenyl	quinolin-6-yl	2-[2-(4-amino-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
359		1	3-carboxy-methoxy-phenyl	quinolin-6-yl	2-[2-(3-carboxymethoxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
360		1	4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
361		1	4-(carbamoyl methyl-carbamoyl)-4'-chloro-biphen-2-yl	quinolin-6-yl	2-{2-[4-(carbamoylmethyl-carbamoyl)-4'-chloro-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
362		1	4-methyl-carbamoyl-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methylcarbamoyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
363		1	4-amino-3,5-dichloro-phenyl	quinolin-6-yl	2-[2-(4-amino-3,5-dichloro-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
364		1	2,4-dihydroxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2,4-dihydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid

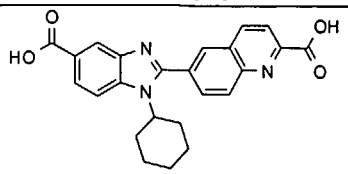
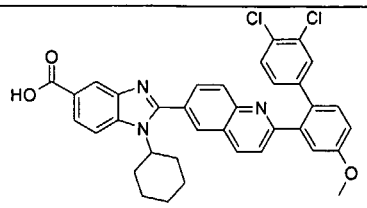
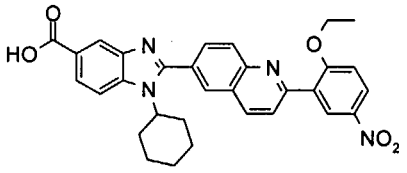
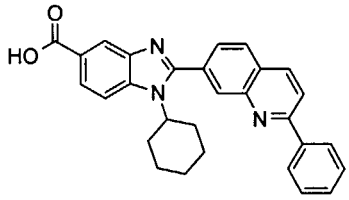
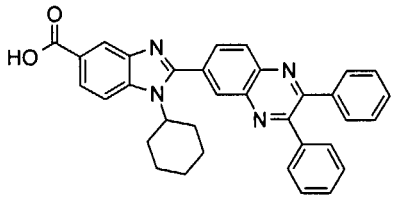
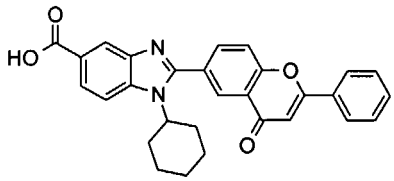
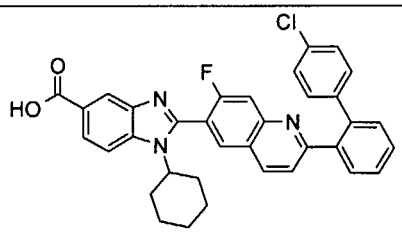
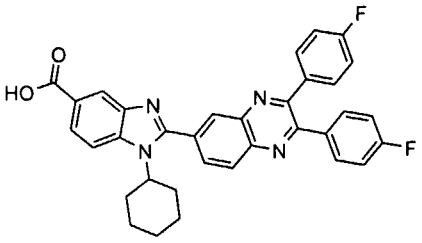
Cmpd#	Structure	*q*	Y	Het	Name
365		1	4'-cyano-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-cyano-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
366		1	3'-chloro-4'-fluoro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(3'-chloro-4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
367		1	4-methoxy-3'-methyl-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methoxy-3'-methyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
368		1	1-carbamoyl-2-(1H-imidazol-2-yl)ethyl-carbamoyl	quinolin-6-yl	2-{2-[1-carbamoyl-2-(1H-imidazol-2-yl)ethylcarbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
369		1	2-pyridin-4-yl-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-pyridin-4-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
370		1	3-(pyrrolidinyl-1-carbonyl)-phenyl	quinolin-6-yl	1-cyclohexyl-2-{2-[3-(pyrrolidinyl-1-carbonyl)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
371		2	4-bromo-phenyl AND 4-bromo-phenyl	quinoxalin-6-yl	2-[2,3-bis-(4-bromophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
372		1	4-amino-3-bromo-phenyl	quinolin-6-yl	2-[2-(4-amino-3-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

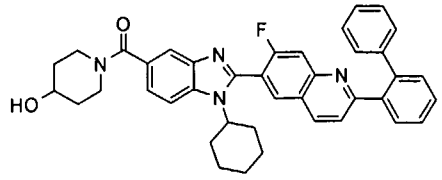
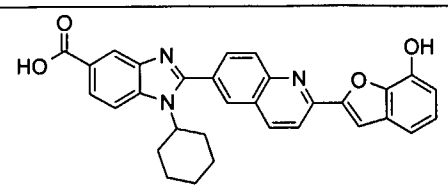
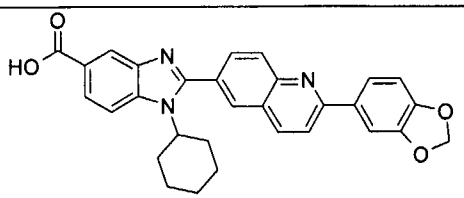
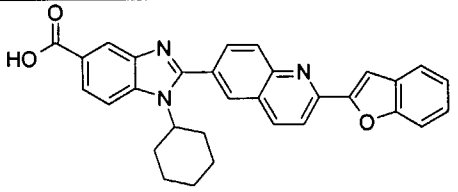
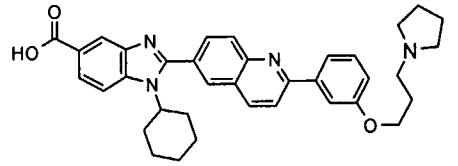
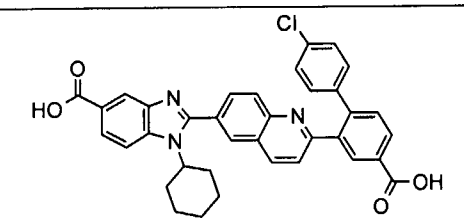
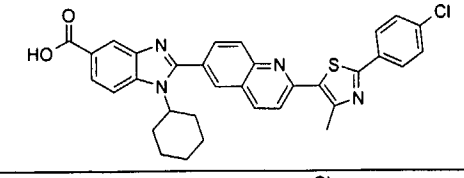
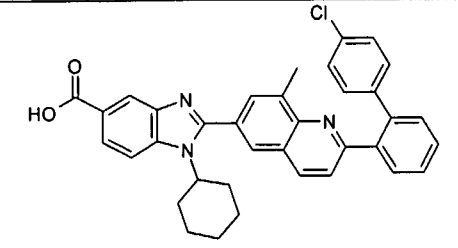
Cmpd#	Structure	q	Y	Het	Name
373		1	Phenyl	4-oxo-1,4-dihydro-quinolin-6-yl	1-cyclohexyl-2-(4-oxo-2-phenyl-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
374		1	3-carbamoyl-4-hydroxy-phenyl	quinolin-6-yl	2-[2-(3-carbamoyl-4-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
375		1	4-carboxy-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4-carboxymethoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
376		1	4'-chloro-4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
377		1	4-(carbamoyl methyl-carbamoyl)-biphen-2-yl	2-[4-(carbamoyl-methyl-carbamoyl)-biphen-2-yl]-quinolin-6-yl	2-{2-[4-(carbamoylmethyl-carbamoyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
378		1	4'-chloro-4-methyl-carbamoyl-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methylcarbamoyl-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
379		2	biphen-2-yl AND methyl	quinolin-6-yl	2-(2-biphen-2-yl-8-methyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

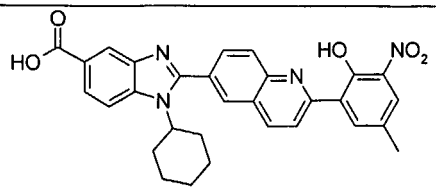
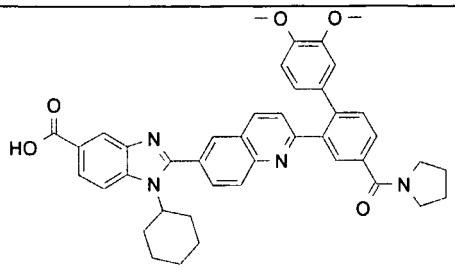
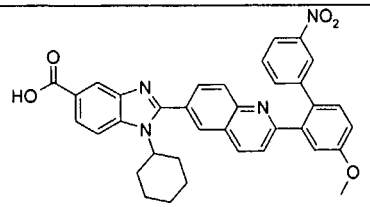
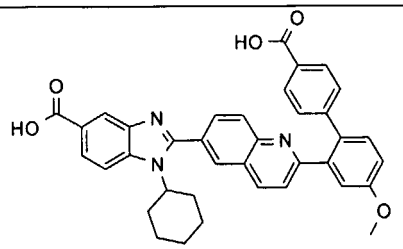
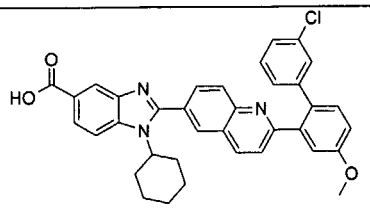
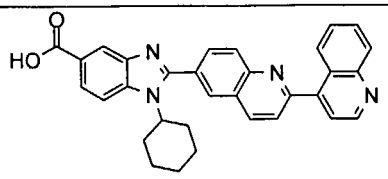
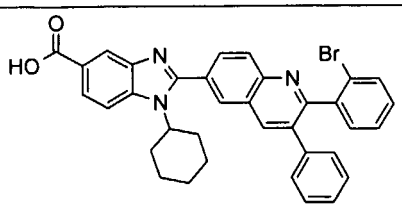
Cmpd#	Structure	*q*	Y	Het	Name
380		2	(4-chloro-phenyl)-amino AND phenyl	quinolin-6-yl	2-[4-(4-chloro-phenylamino)-2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
381		1	3,5-dihydroxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(3,5-dihydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
382		1	4'-carbamoyl-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-carbamoyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
383		1	4-methoxy-4'-nitro-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methoxy-4'-nitro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
384		1	4'-amino-methyl-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-aminomethyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
385		1	1-carbamoyl-2-hydroxy-ethyl-carbamoyl	quinolin-6-yl	2-[2-(1-carbamoyl-2-hydroxyethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
386		2	Phenyl AND phenyl	quinolin-6-yl	1-cyclohexyl-2-(2,3-diphenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid

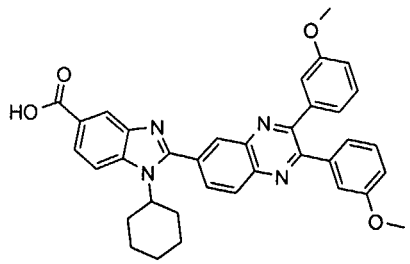
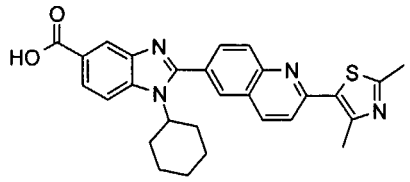
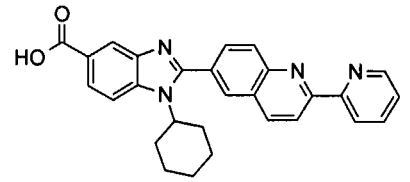
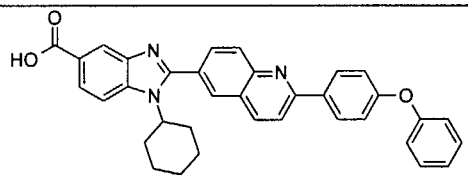
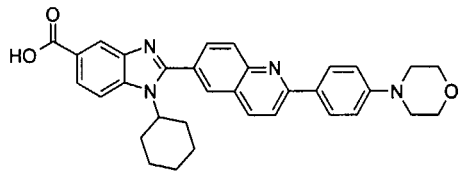
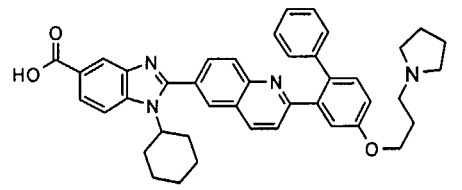
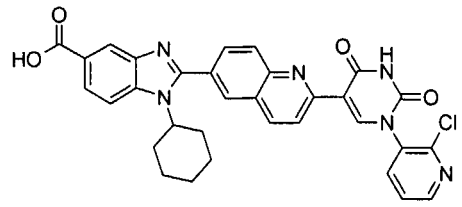
Cmpd#	Structure	*q*	Y	Het	Name
387		1	4'-chloro-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
388		2	biphen-2-yl AND fluoro	quinolin-6-yl	2-(2-biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
389		2	*p*-tolyl AND *p*-tolyl	quinoxalin-6-yl	1-cyclohexyl-2-(2,3-di-p-tolylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid
390		1	biphen-4-yl-	quinolin-6-yl	2-(2-biphen-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
391		1	2-amino-4-methyl-thiazol-5-yl	quinolin-6-yl	2-[2-(2-amino-4-methyl-thiazol-5-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
392		1	3-hydroxy-propyl	quinolin-6-yl	1-cyclohexyl-2-[2-(3-hydroxy-propyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
393		1	4-carboxy-methoxy-4'-chloro-biphen-2-yl	quinolin-6-yl	2-[2-(4-carboxymethoxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
394		1	7-bromo-5-methoxy-benzofuran-2-yl	quinolin-6-yl	2-[2-(7-bromo-5-methoxy-benzofuran-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

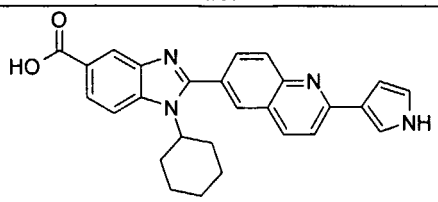
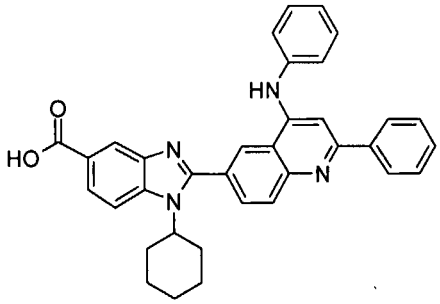
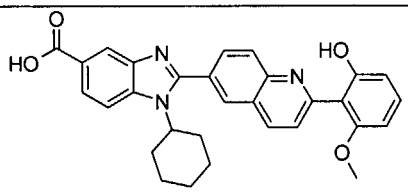
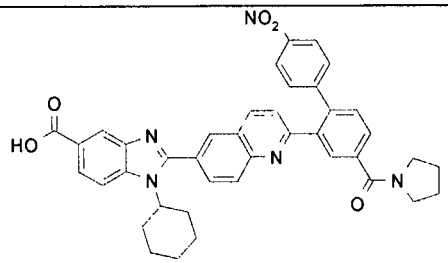
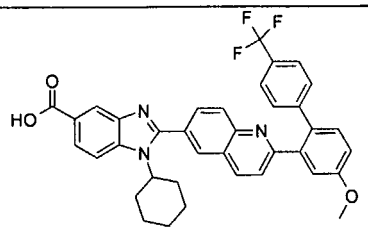
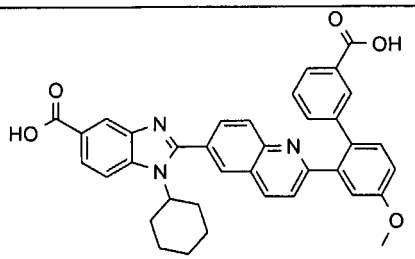
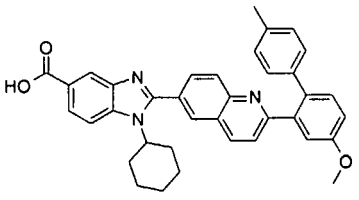
Cmpd#	Structure	*q*	Y	Het	Name
395		1	biphen-2-yl	quinolin-6-yl	2-(2-biphen-2-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
396		1	3-(4-chloro-phenyl)-5-methyl-isoxazol-4-yl	quinolin-6-yl	2-{2-[3-(4-chloro-phenyl)-5-methyl-isoxazol-4-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
397		2	Methyl AND phenyl	quinolin-6-yl)-	1-cyclohexyl-2-(8-methyl-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
398		2	4-hydroxy-butylamino AND phenyl	quinolin-6-yl	1-cyclohexyl-2-[4-(4-hydroxy-butylamino)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
399		2	2-*tert*-butoxy-carbonyl-aminoethyl-amino AND phenyl	quinolin-6-yl	2-[4-(2-*tert*-butoxycarbonylamino-ethylamino)-2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
400		1	5-(pyrrolidinyl-1-carbonyl)-2-thiophen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[5-(pyrrolidinyl-1-carbonyl)-2-thiophen-2-yl]quinoline-6-yl}-1H-benzimidazole-5-carboxylic acid
401		1	4'-dimethyl-amino-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4'-dimethylamino-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid

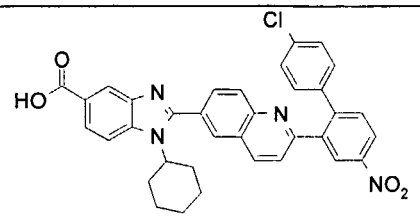
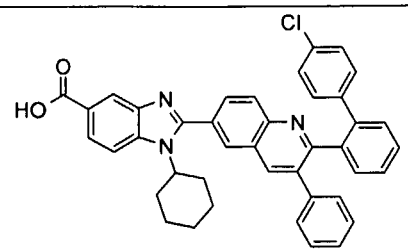
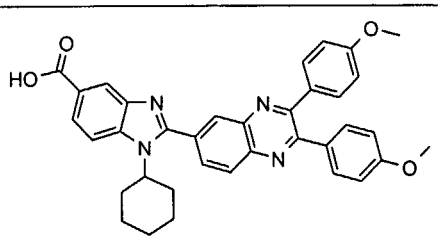
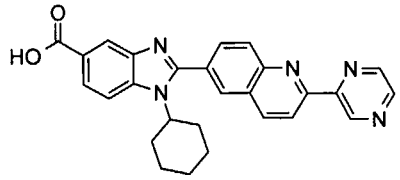
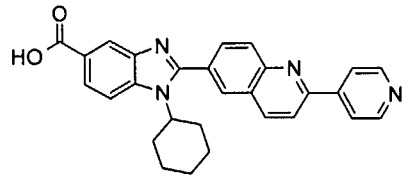
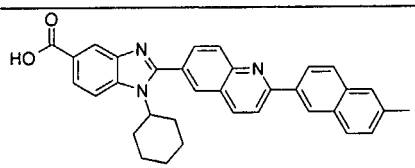
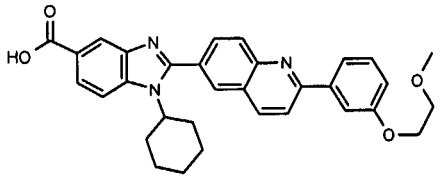
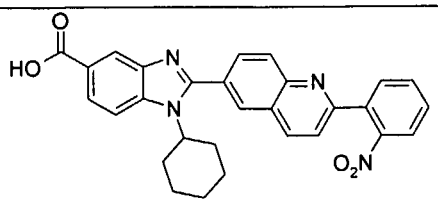
Cmpd#	Structure	q	Y	Het	Name
402		1	carboxyl	quinolin-6-yl	6-(5-carboxy-1-cyclohexyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid
403		1	3',4'-dichloro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(3',4'-dichloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
404		1	2-ethoxy-5-nitrophenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-ethoxy-5-nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
405		1	Phenyl	quinolin-7-yl	1-cyclohexyl-2-(2-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid
406		2	Phenyl AND phenyl	quinoxalin-6-yl	cyclohexyl-2-(2,3-diphenylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid
407		1	Phenyl	4-oxo-4H-chromen-6-yl	cyclohexyl-2-(4-oxo-2-phenyl-4H-chromen-6-yl)-1H-benzoimidazole-5-carboxylic acid
408		2	4'-chloro-biphen-2-yl AND fluoro	quinolin-6-yl	2-[2-(4'-chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
409		2	4-fluoro-phenyl AND 4-fluoro-phenyl	quinoxalin-6-yl	2-[2,3-bis-(4-fluorophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid

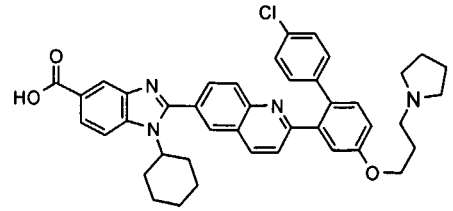
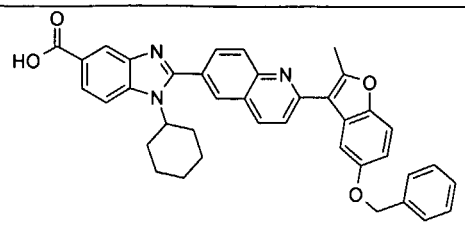
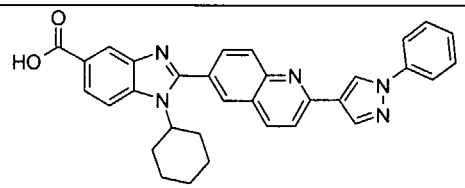
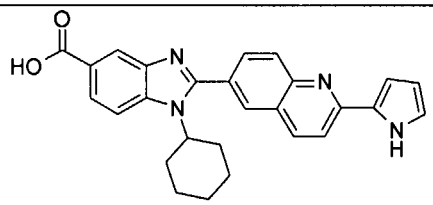
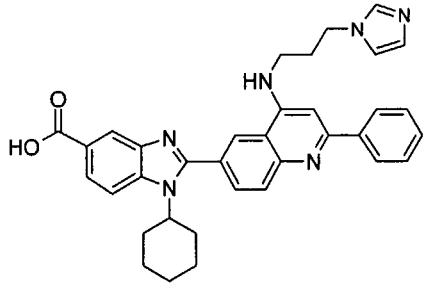
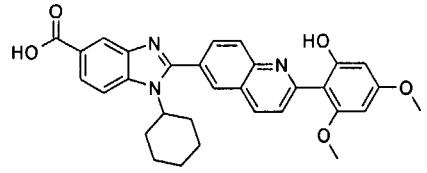
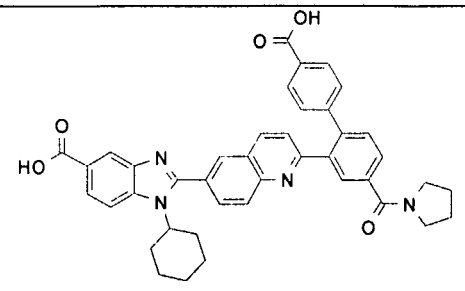
Cmpd#	Structure	*q*	Y	Het	Name
410		2	biphen-2-yl AND fluoro	quinolin-6-yl	2-(2-biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazol-5-yl]-(4-hydroxy-piperidin-1-yl)-methanone
411		1	7-hydroxy-benzofuran-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(7-hydroxy-benzofuran-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
412		1	benzo[1,3]dioxol-5-yl	quinolin-6-yl	2-(2-benzo[1,3]dioxol-5-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
413		1	benzofuran-2-yl	quinolin-6-yl	2-(2-benzofuran-2-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
414		1	3-(3-pyrrolidin-1-yl-propoxy)phenyl	quinolin-6-yl	1-cyclohexyl-2-{2-[3-(3-pyrrolidin-1-yl-propoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
415		1	4-carboxy-4'-chloro-biphen-2-yl	quinolin-6-yl	2-[2-(4-carboxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
416		1	2-(4-chloro-phenyl)-4-methyl-thiazol-5-yl	quinolin-6-yl	2-{2-[2-(4-chloro-phenyl)-4-methyl-thiazol-5-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
417		2	4'-chloro-biphen-2-yl AND methyl	quinolin-6-yl	2-[2-(4'-chloro-biphen-2-yl)-8-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

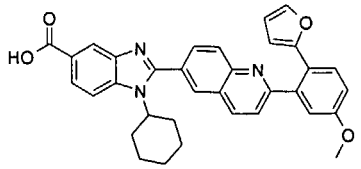
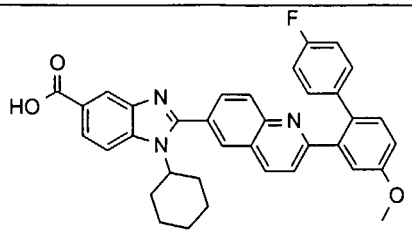
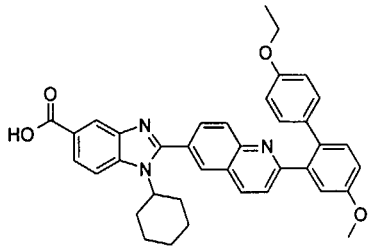
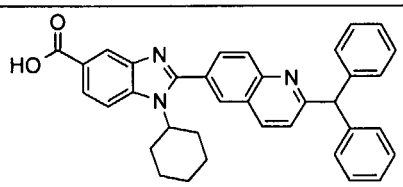
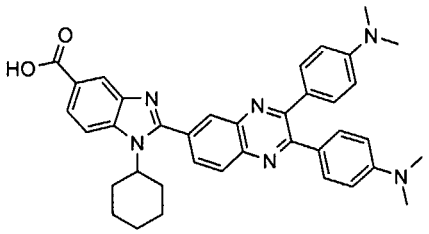
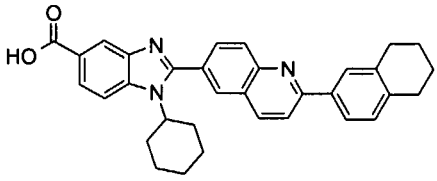
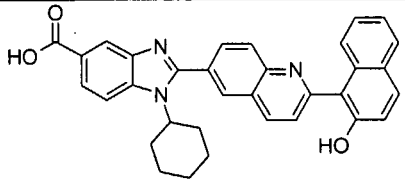
Cmpd#	Structure	*q*	Y	Het	Name
418		1	2-hydroxy-5-methyl-3-nitrophenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-hydroxy-5-methyl-3-nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
419		1	3',4'-dimethoxy-4-(pyrrolidinyl-1-carbonyl)-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[3',4'-dimethoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid
420		1	4-methoxy-3'-nitro-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methoxy-3'-nitro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
421		1	4'-carboxy-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-carboxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
422		1	3'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(3'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
423		1	quinolin-4-yl	quinolin-6-yl	2-[2,4']biquinolinyl-6-yl-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
424		2	2-bromo-phenyl AND phenyl	quinolin-6-yl	2-[2-(2-bromo-phenyl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

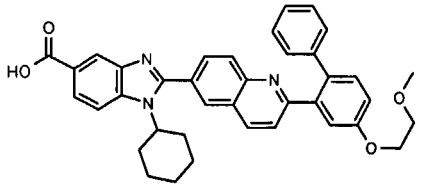
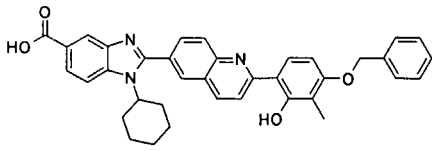
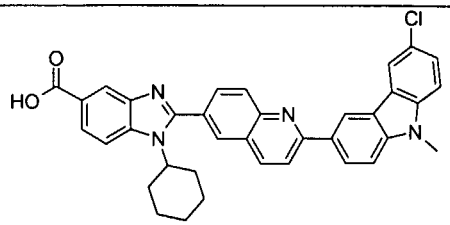
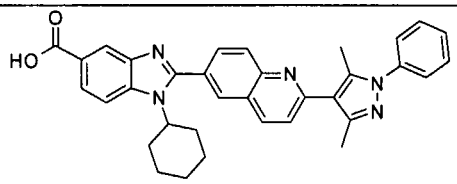
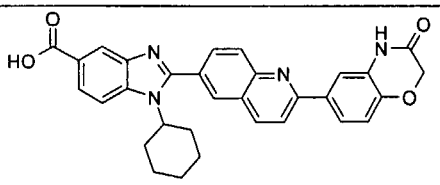
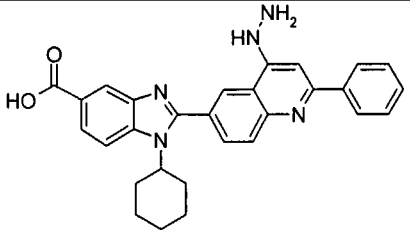
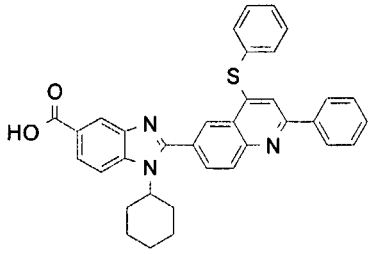
Cmpd#	Structure	q	Y	Het	Name
425		2	3-methoxy-phenyl AND 3-methoxy-phenyl	quinoxalin-6-yl	2-[2,3-bis-(3-methoxyphenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
426		1	2,4-dimethyl-thiazol-5-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(2,4-dimethyl-thiazol-5-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
427		1	pyridin-2-yl	quinolin-6-yl	1-cyclohexyl-2-(2-pyridin-2-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
428		1	4-phenoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-phenoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
429		1	4-morpholin-4-yl-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-morpholin-4-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
430		1	4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
431		1	1-(2-chloro-pyridin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl	quinolin-6-yl	2-{2-[1-(2-chloro-pyridin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

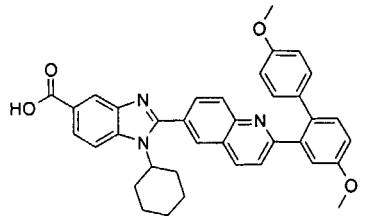
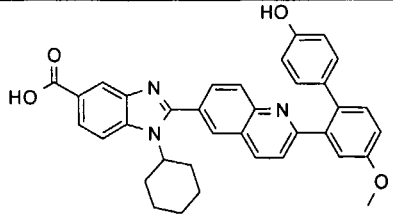
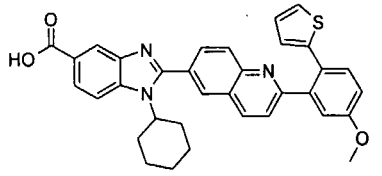
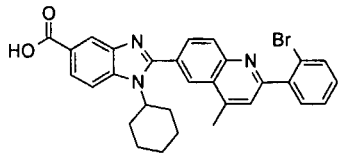
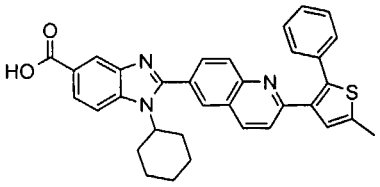
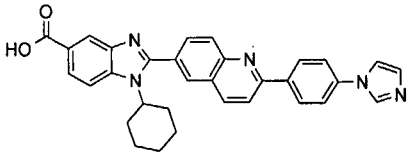
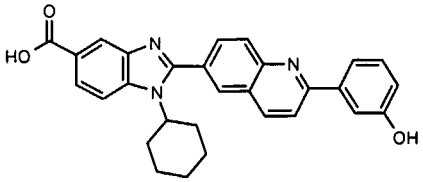
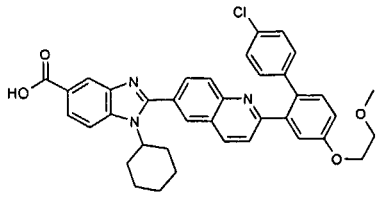
Cmpd#	Structure	*q*	Y	Het	Name
432		1	1H-pyrrol-3-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(1H-pyrrol-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
433		2	Phenyl AND Phenyl-amino	quinolin-6-yl	1-cyclohexyl-2-(2-phenyl-4-phenylamino-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
434		1	2-hydroxy-6-methoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-hydroxy-6-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
435		1	2-[4'-nitro-4-(pyrrolidinyl-1-carbonyl)-biphen-2-yl]	quinolin-6-yl	1-cyclohexyl-2-{2-[4'-nitro-4-(pyrrolidinyl-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid
436		1	4-methoxy-4'-trifluoro-methyl-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methoxy-4'-trifluoromethyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
437		1	3'-carboxy-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(3'-carboxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
438		1	4-methoxy-4'-methyl-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methoxy-4'-methyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid

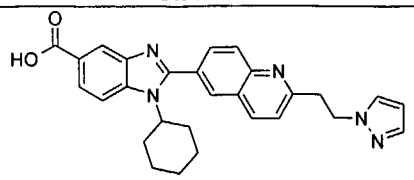
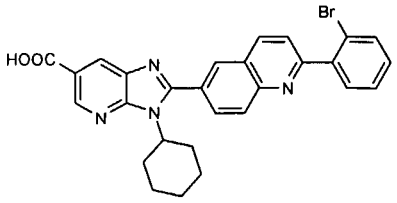
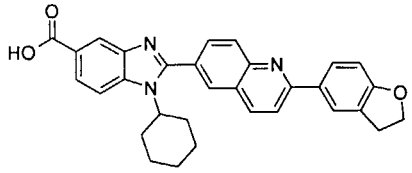
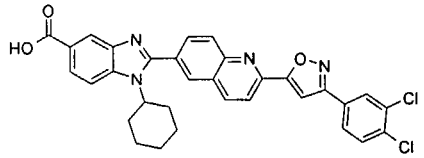
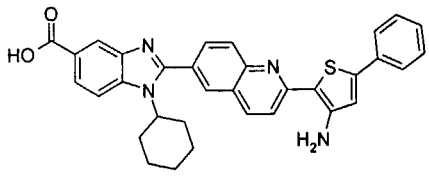
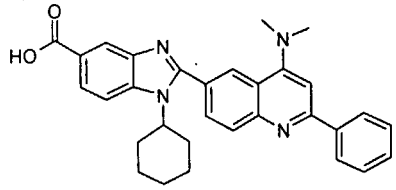
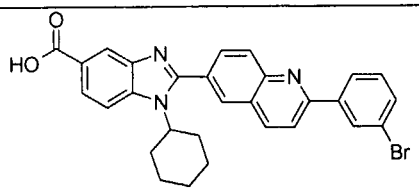
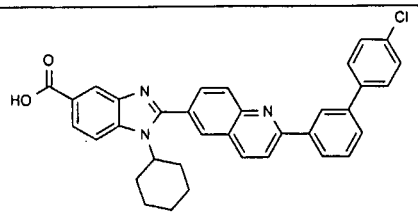
Cmpd#	Structure	*q*	Y	Het	Name
439		1	4'-chloro-4-nitrobiphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-nitro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
440		2	4'-chloro-biphen-2-yl AND phenyl	quinolin-6-yl	2-[2-(4'-chloro-biphen-2-yl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
441		2	4-methoxy-phenyl AND 4-methoxy-phenyl	quinoxalin-6-yl	2-[2,3-bis-(4-methoxyphenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
442		1	pyrazin-2-yl	quinolin-6-yl	1-cyclohexyl-2-(2-pyrazin-2-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
443		1	pyridin-4-yl	quinolin-6-yl	1-cyclohexyl-2-(2-pyridin-4-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
444		1	6-methyl-naphthalen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(6-methyl-naphthalen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
445		1	3-(2-methoxy-ethoxy)-phenyl	quinolin-6-yl	1-cyclohexyl-2-{2-[3-(2-methoxy-ethoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
446		1	2-nitro-phenyl	quinolin-6-yl	2-[6-(2-nitrophenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid

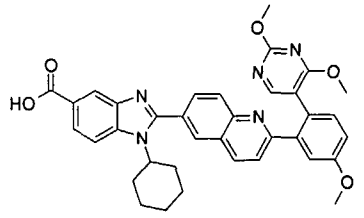
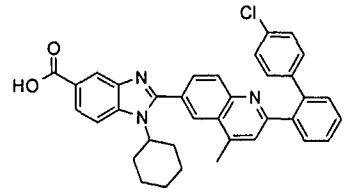
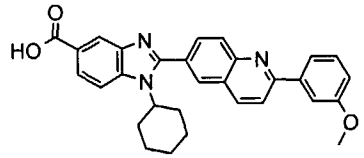
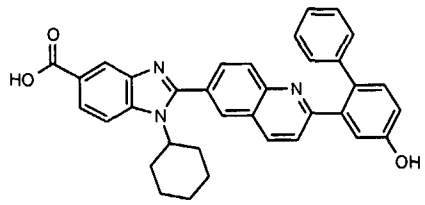
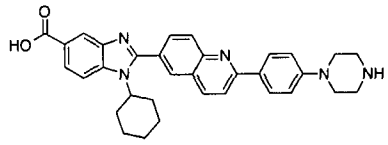
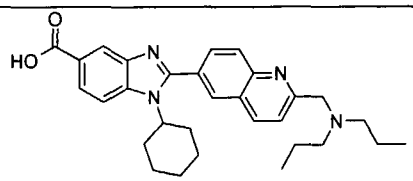
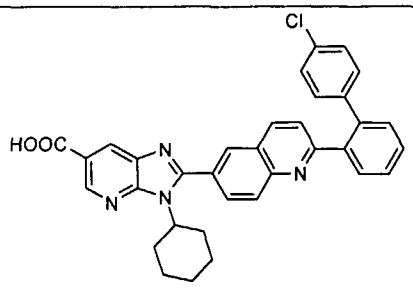
Cmpd#	Structure	*q*	Y	Het	Name
447		1	4'-chloro-4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
448		1	5-benzyl-oxy-2-methyl-benzofuran-3-yl	quinolin-6-yl	2-[2-(5-benzyloxy-2-methyl-benzofuran-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
449		1	1-phenyl-1H-pyrazol-4-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(1-phenyl-1H-pyrazol-4-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
450		1	1H-pyrrol-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(1H-pyrrol-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
451		1	(3-imidazol-1-yl-propyl-amino)-2-phenyl	quinolin-6-yl	1-cyclohexyl-2-[4-(3-imidazol-1-yl-propylamino)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
452		1	2-hydroxy-4,6-dimethoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-hydroxy-4,6-dimethoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
453		1	4'-carboxy-4-(pyrrolidine-1-carbonyl)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-carboxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid

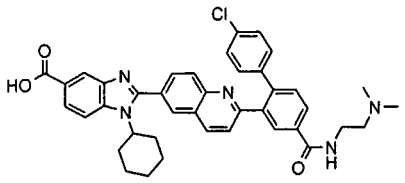
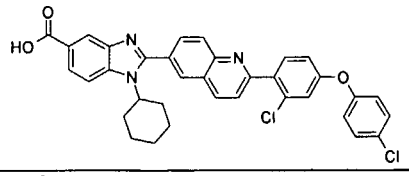
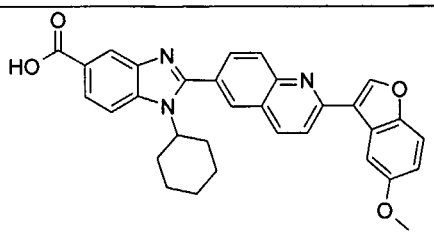
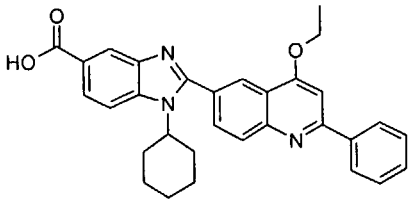
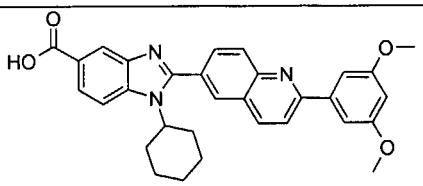
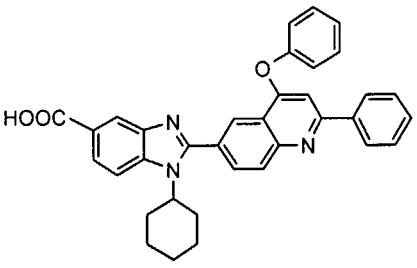
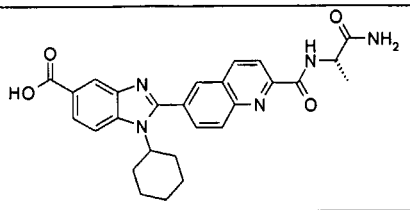
Cmpd#	Structure	q	Y	Het	Name
454		1	2-furan-2-yl-5-methoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-furan-2-yl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
455		1	4'-fluoro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
456		1	4'-ethoxy-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[4'-ethoxy-4-methoxybiphen-2yl]-1H-benzoimidazole-5-carboxylic acid
457		1	Diphenyl-methyl	quinolin-6-yl	2-(2-dimethylphenylquinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
458		2	4-dimethyl-amino-phenyl AND 4-dimethyl-amino-phenyl	quinoxalin-6-yl	2-[2,3-bis-(4-dimethyl-aminophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
459		1	5,6,7,8-tetrahydro-naphthalen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[5,6,7,8-tetrahydronaphthalen-2-yl]-1H-benzoimidazole-5-carboxylic acid
460		1	2-hydroxy-naphthalen-1-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-hydroxy-naphthalen-1-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid

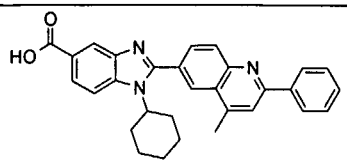
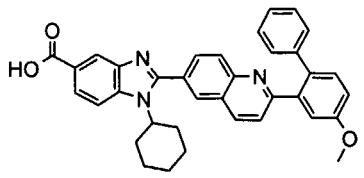
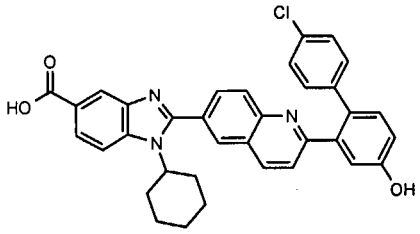
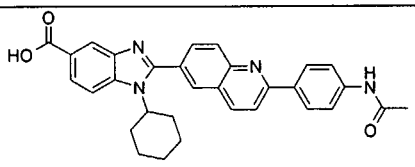
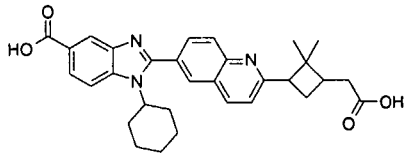
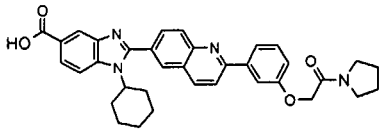
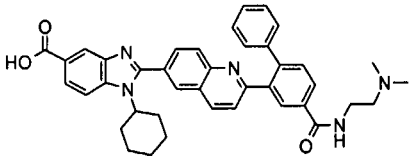
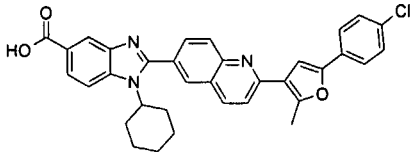
Cmpd#	Structure	q	Y	Het	Name
461		1	4-(2-methoxy-ethoxy)-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
462		1	2-(4-benzyloxy-2-hydroxy-3-methyl-phenyl)-	quinolin-6-yl	2-[2-(4-benzyloxy-2-hydroxy-3-methyl-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
463		1	6-chloro-9-methyl-9H-carbazol-3-yl	quinolin-6-yl	2-[2-(6-chloro-9-methyl-9H-carbazol-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
464		1	3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
465		1	3-oxo-3,4-dihydro-2H-benzo[1,4]-oxazin-6-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
466		2	hydrazino AND phenyl	quinolin-6-yl	1-cyclohexyl-2-(4-hydrazino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
467		2	phenyl AND Phenyl-sulfanyl	quinolin-6-yl	1-cyclohexyl-2-(2-phenyl-4-phenylsulfanyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid

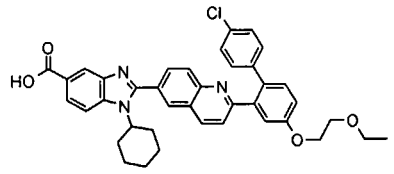
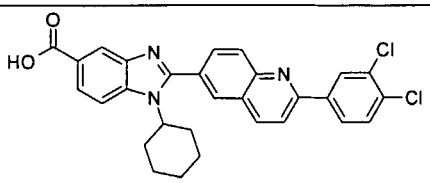
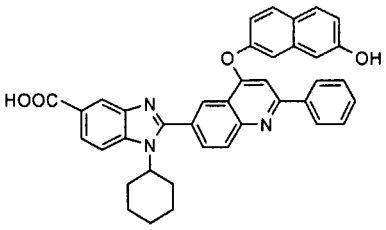
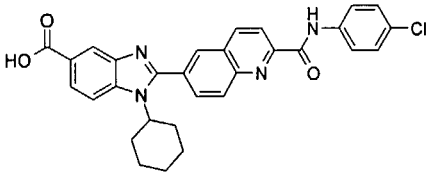
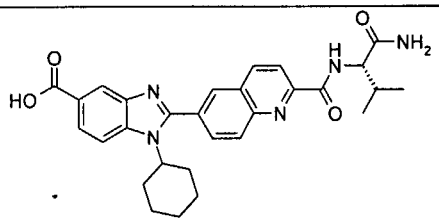
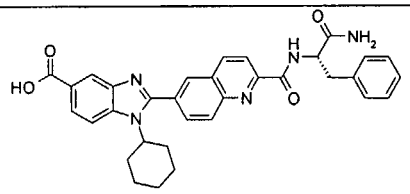
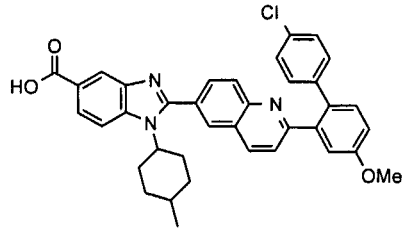
Cmpd#	Structure	q	Y	Het	Name
468		1	4,4'-dimethoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4,4'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
469		1	4'-hydroxy-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4'-hydroxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
470		1	5-methoxy-2-thiophen-2-yl-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(5-methoxy-2-thiophen-2-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
471		2	2-bromo-phenyl AND methyl	quinolin-6-yl	2-[2-(2-bromo-phenyl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
472		1	5-methyl-2-phenyl-thiophen-3-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(5-methyl-2-phenyl-thiophen-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
473		1	4-imidazol-1-yl-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-imidazol-1-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
474		1	3-hydroxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(3-hydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
475		1	4'-chloro-4-(2-methoxy-ethoxy)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

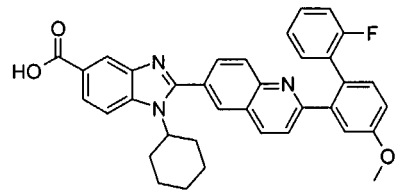
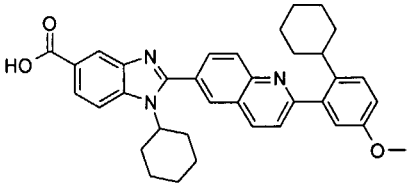
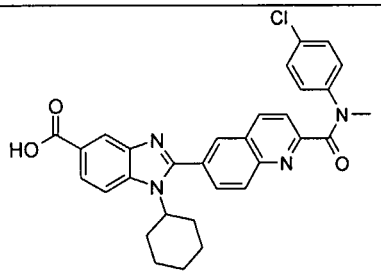
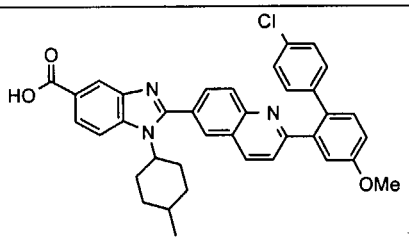
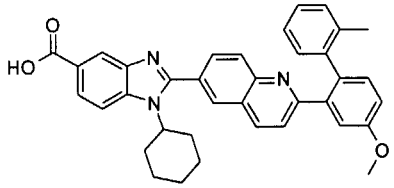
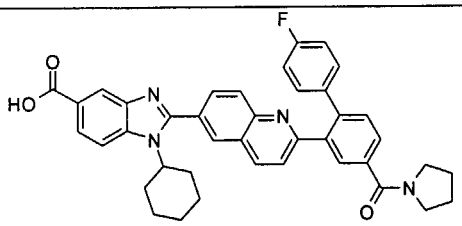
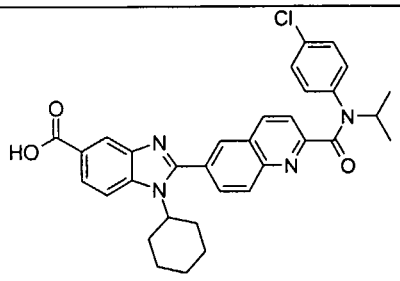
Cmpd#	Structure	*q*	Y	Het	Name
476		1	2-pyrazol-1-yl-eth-1-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-pyrazol-1-yl-eth-1-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
477		1	2-bromo-phenyl	quinolin-6-yl	2-[2-(2-bromo-phenyl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic
478		1	2,3-dihydro-benzofuran-5-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(2,3-dihydro-benzofuran-5-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
479		1	3-(3,4-dichloro-phenyl)-isoxazol-5-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[3-(3,4-dichloro-phenyl)-isoxazol-5-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
480		1	3-amino-5-phenyl-thiophen-2-yl	quinolin-6-yl	2-[2-(3-amino-5-phenyl-thiophen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
481		2	Dimethyl-amino AND phenyl	quinolin-6-yl	1-cyclohexyl-2-(4-dimethylamino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
482		1	3-bromo-phenyl	quinolin-6-yl	2-[2-(3-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
483		1	4'-chloro-biphenyl-3-yl	quinolin-6-yl	2-[2-(4'-chloro-biphen-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

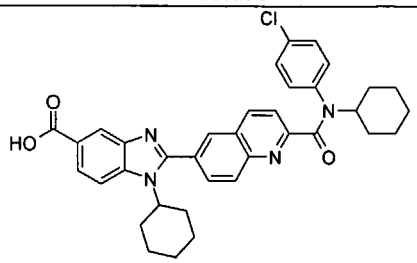
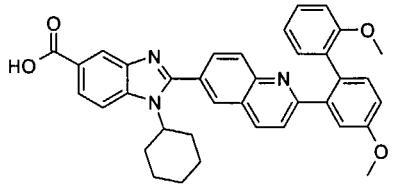
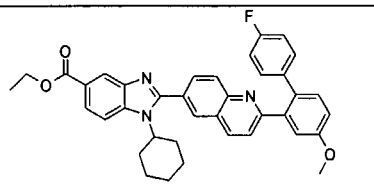
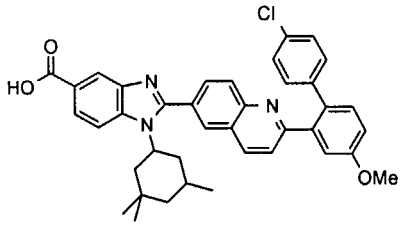
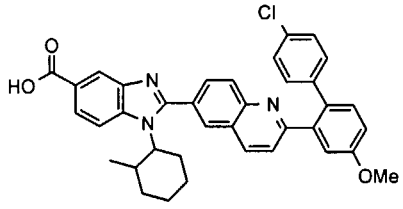
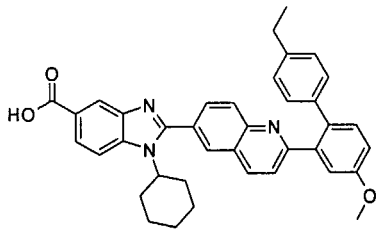
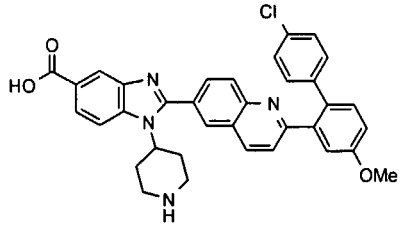
Cmpd#	Structure	*q*	Y	Het	Name
484		1	2-(2,4-dimethoxy-pyrimidin-5-yl)-5-methoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-{2-[2-(2,4-dimethoxy-pyrimidin-5-yl)-5-methoxy-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
485		2	2-(4'-chloro-biphen-2-yl) AND methyl	quinolin-6-yl	2-[2-(4'-chloro-biphen-2-yl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
486		1	3-methoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(3-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
487		1	4-hydroxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
488		1	4-piperazin-1-yl-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-piperazin-1-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
489		1	Dipropyl-amino-methyl	quinolin-6-yl	1-cyclohexyl-2-(2-dipropylaminomethyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
490		1	4'-chloro-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chlorobiphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid

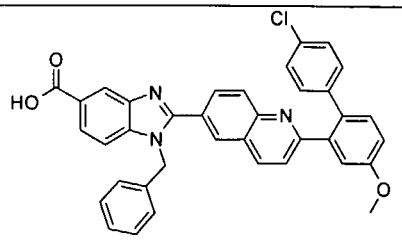
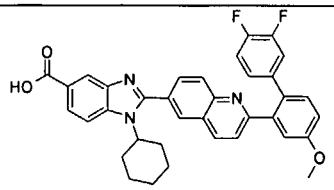
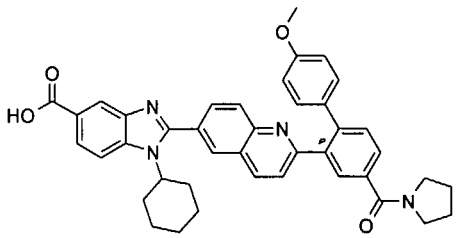
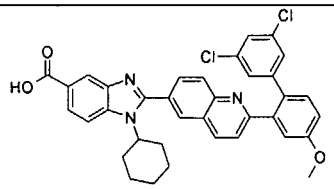
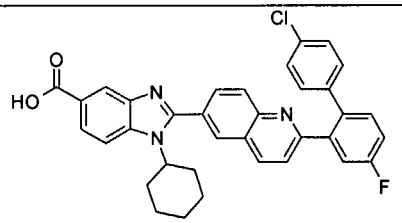
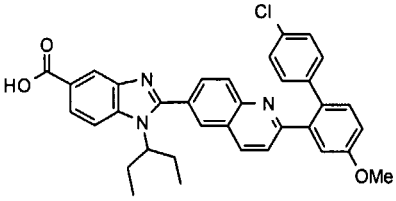
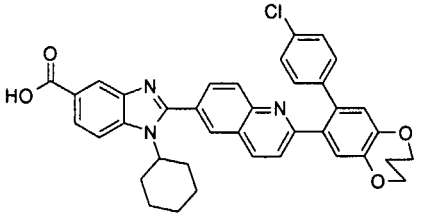
Cmpd#	Structure	q	Y	Het	Name
491		1	4'-chloro-4-(2-dimethyl-aminoethyl-carbamoyl)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(2-dimethylamino-ethylcarbamoyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
492		1	2-chloro-4-(4-chloro-phenoxy)-phenyl	quinolin-6-yl	2-{2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
493		1	5-methoxy-benzofuran-3-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(5-methoxy-benzofuran-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
494		2	ethoxy AND phenyl	quinolin-6-yl	1-cyclohexyl-2-(4-ethoxy-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
495		1	3,5-dimethoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(3,5-dimethoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
496		2	phenoxy AND phenyl	quinolin-6-yl	1-cyclohexyl-2-(4-phenoxy-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
497		1	1-carbamoyl-ethyl-carbamoyl	quinolin-6-yl	2-[2-(1-carbamoylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid

Cmpd#	Structure	*q*	Y	Het	Name
498		2	methyl AND phenyl	quinolin-6-yl	1-cyclohexyl-2-(4-methyl-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid
499		1	4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
500		1	4'-chloro-4-hydroxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
501		1	4-acetylamino phenyl	quinolin-6-yl	2-[2-(4-acetylamino-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
502		1	3-carboxy-methyl-2,2-dimethyl-cyclobutyl	quinolin-6-yl	2-[2-(3-carboxymethyl-2,2-dimethyl-cyclobutyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
503		1	3-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-phenyl	quinolin-6-yl	1-cyclohexyl-2-{2-[3-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
504		1	4-(2-dimethyl-aminoethyl-carbamoyl)-biphen-2-yl]-	quinolin-6-yl	1-cyclohexyl-2-{2-[4-(2-dimethylamino-ethylcarbamoyl)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid
505		1	5-(4-chloro-phenyl)-2-methyl-furan-3-yl	quinolin-6-yl	2-{2-[5-(4-chloro-phenyl)-2-methyl-furan-3-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

Cmpd#	Structure	*q*	Y	Het	Name
507		1	4'-chloro-4-(2-ethoxy-ethoxy)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(2-ethoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
508		1	3,4-dichloro-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(3,4-dichloro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
509		2	7-hydroxy-naphthalen-2-oxy AND phenyl	quinolin-6-yl	1-cyclohexyl-2-[4-(7-hydroxy-naphthalen-2-yloxy)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
510		1	4-chloro-phenyl-carbamoyl	quinolin-6-yl	2-[2-(4-chlorophenylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
511		1	1-carbamoyl-2-methyl-propyl-carbamoyl	quinolin-6-yl	2-[2-(1-carbamoyl-2-methylpropylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
542		1	1-carbamoyl-2-phenyl-ethyl-carbamoyl	quinolin-6-yl	2-[2-(1-carbamoyl-2-phenylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
543	 Isomer A	1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(4-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid

Cmpd#	Structure	*q*	Y	Het	Name
544		1	2'-fluoro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(2'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
545		1	2-cyclohexyl-5-methoxy-phenyl	quinolin-6-yl	1-cyclohexyl-2-[2-(2-cyclohexyl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
546		1	(4-chloro-phenyl) methyl carbamoyl	quinolin-6-yl	2-{2-[(4-chlorophenyl) methyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
547	 Isomer B	1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(4-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid
548		1	biphen-4-yl-	quinolin-6-yl	2-(2-biphen-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
549		1	4'-fluoro-4-(pyrrolidin-1-ylcarbonyl)-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[4'-fluoro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid
550		1	(4-chloro-phenyl) isopropyl carbamoyl	quinolin-6-yl	2-{2-[(4-chlorophenyl) isopropyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid

Cmpd#	Structure	q	Y	Het	Name
551		1	(4-chloro-phenyl) cyclohexyl carbamoyl	quinolin-6-yl	2-{2-[(4-chlorophenyl) cyclohexyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid
552		1	4,2'-dimethoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4,2'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
554		1	4'-fluoro-4-methoxy-biphen-2-yl	quinolin-6-yl	Ethyl 1-cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
555		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxybiphen-2-yl)-quinolin-6-yl]-1-(3,3,5-trimethyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid
556		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(2-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid
557		1	4'-ethyl-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4'-ethyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
558		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-piperidin-4-yl-1H-benzoimidazole-5-carboxylic acid

Cmpd#	Structure	*q*	Y	Het	Name
559		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-benzyl-2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
560		1	3',4'-difluoro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(3',4'-difluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
561		1	4'-methoxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-{2-[4'-methoxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid
562		1	3',5'-dichloro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(3',5'-dichloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
563		1	4'-chloro-4-fluoro-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-fluoro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
564		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(1-ethyl-propyl)-1H-benzoimidazole-5-carboxylic acid
565		1	8-(4-chloro-phenyl)-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl	quinolin-6-yl	2-{2-[8-(4-chloro-phenyl)-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid

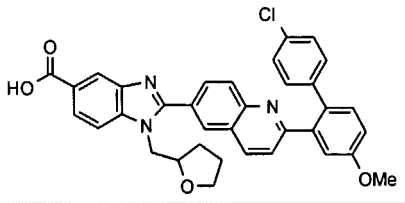
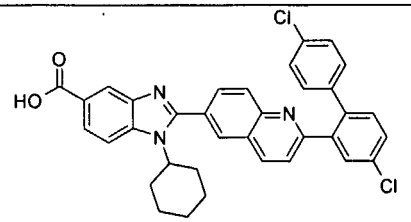
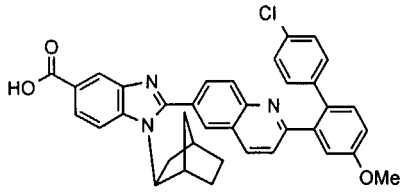
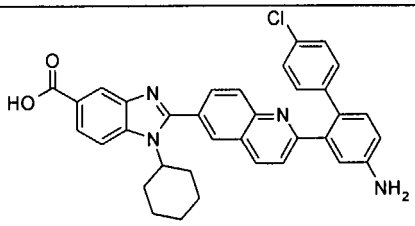
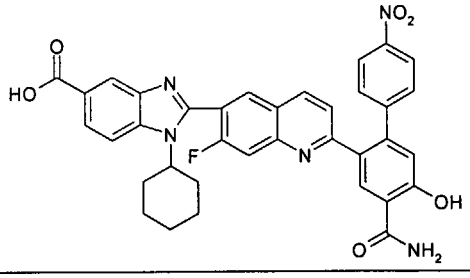
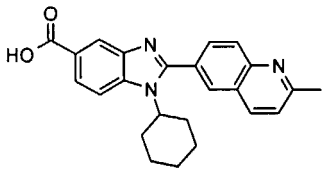
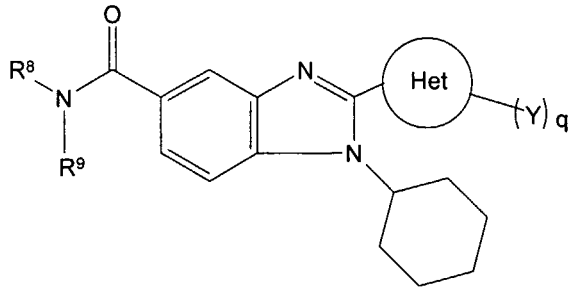
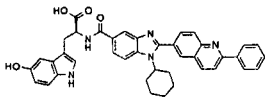
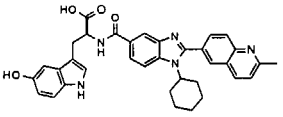
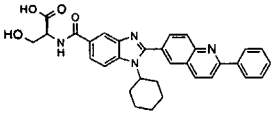
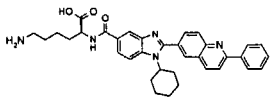
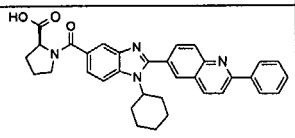
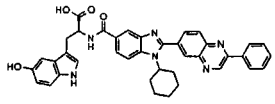
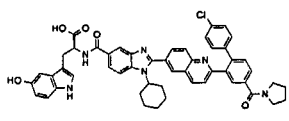
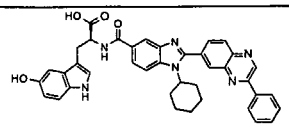
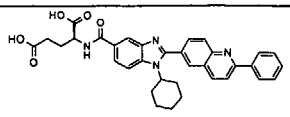
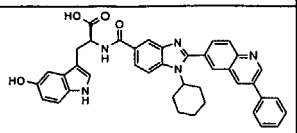
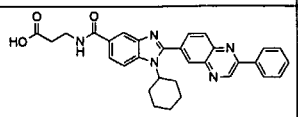
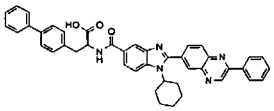
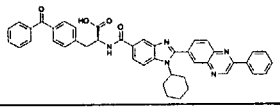
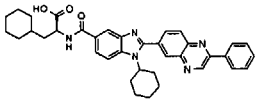
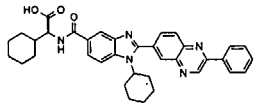
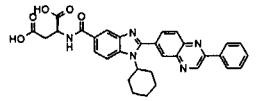
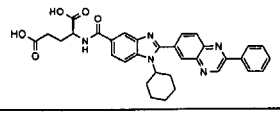
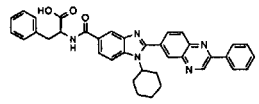
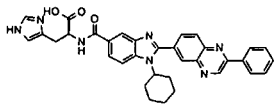
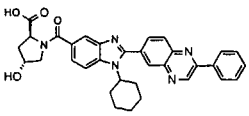
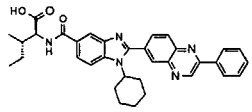
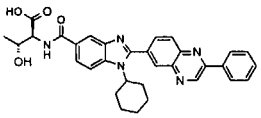
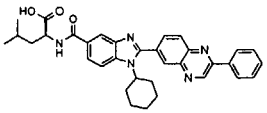
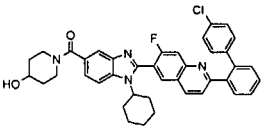
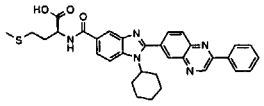
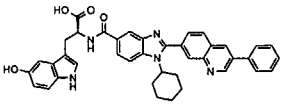
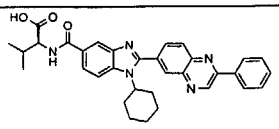
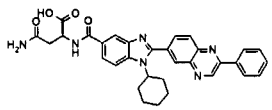
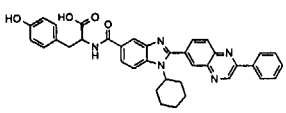
Cmpd#	Structure	*q*	Y	Het	Name
566		1	4'-chloro-4-methoxy-biphen-2-yl)	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(tetrahydrofuran-2-yl-methyl)-1H-benzoimidazole-5-carboxylic acid
567		1	4,4'-dichloro-biphen-2-yl	quinolin-6-yl	1-cyclohexyl-2-[2-(4,4'-dichloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid
568		1	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	1-bicyclo[2.2.1]hept-2-yl-2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]1H-benzoimidazole-5-carboxylic acid
569		1	4-amino-4'-chloro-biphen-2-yl	quinolin-6-yl	2-[2-(4-amino-4'-chlorobiphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
		2	fluoro AND 4-carbamoyl-5-hydroxy-4'-nitrobiphen-2-yl	quinolin-6-yl	2-[2-(4-carbamoyl-5-hydroxy-4'-nitro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid
573		1	methyl	quinolin-6-yl	1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid

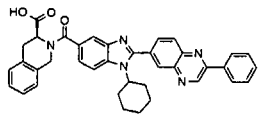
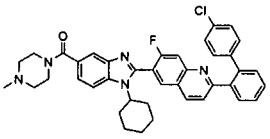
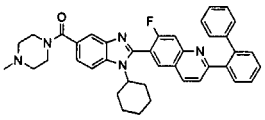
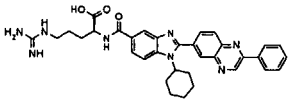
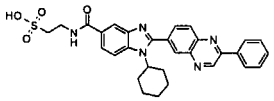
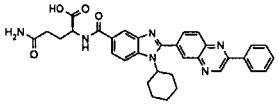
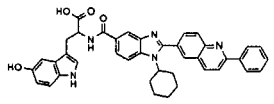
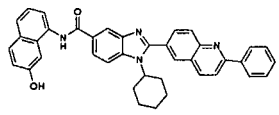
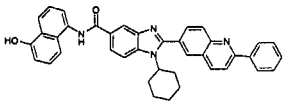
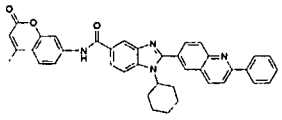
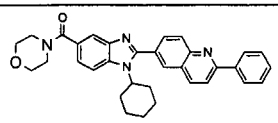
Table II



Cmpd#	Structure	R^8	R^9	Y	Het	Name
229		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	phenyl	Quinolin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
230		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	methyl	Quinolin-6-yl)-	2-{[1-cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
231		H	3-hydroxy-propionic acid	phenyl	Quinolin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-hydroxy-propionic acid
232		H	6-amino-hexanoic acid	phenyl	Quinolin-6-yl	6-amino-2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-hexanoic acid
233		pyrrolidine-2-carboxylic acid		phenyl	Quinolin-6-yl	1-[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-pyrrolidine-2-carboxylic acid
234		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	phenyl	Quinoxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
235		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl	Quinolin-6-yl	2-[(2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
236		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	phenyl	Quinoxalin-6-yl	2-{[1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid

Cmpd#	Structure	R^8	R^9	Y	Het	Name
237		H	pentanedioic acid	phenyl	Quin-olin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-pentanedioic acid
238		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	phenyl	Quin-olin-6-yl	2-{[1-cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
239		H	propionic acid	phenyl	Quin-oxalin-6-yl	3-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid
240		H	3-biphenyl-4-yl propionic acid	phenyl	Quin-oxalin-6-yl	3-biphenyl-4-yl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid
241		H	3-(4-benzoyl-phenyl)-propionic acid	phenyl	Quin-oxalin-6-yl	3-(4-benzoyl-phenyl)-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid
242		H	3-cyclohexyl-propionic acid	phenyl	Quin-oxalin-6-yl	3-cyclohexyl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid
243		H	cyclohexyl-acetic acid	phenyl	Quin-oxalin-6-yl	cyclohexyl-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid
244		H	succinic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-succinic acid
245		H	pentanedioic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-pentanedioic acid
246		H	3-phenyl-propionic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-phenyl-propionic acid
247		H	3-(1H-imidazol-4-yl)-propionic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(1H-imidazol-4-yl)-propionic acid

Cmpd#	Structure	R^8	R^9	Y	Het	Name
248		-pyrrolidine-2-carboxylic acid		phenyl	Quin-oxalin-6-yl	1-[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-4-hydroxy-pyrrolidine-2-carboxylic acid
249		H	3-methyl-pentanoic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-methyl-pentanoic acid
512		H	3-hydroxy-butyric acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-hydroxy-butyric acid
513		H	4-methyl-pentanoic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methyl-pentanoic acid
514		4-hydroxy-piperidin-1-y		2-(4'-chloro-biphen-2-yl)-7-fluoro-	Quin-olin-6-yl	{2-[2-(4'-chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(4-hydroxy-piperidin-1-yl)-methanone
515		H	4-methylsulfanyl-butyric acid	2-phenyl-	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methylsulfanyl-butyric acid
516		H	3-(5-hydroxy-1H-indol-3-yl)-propionic acid	3-phenyl	Quin-olin-7-yl	2-{[1-cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
517		H	3-methyl-butyric acid	2-phenyl-	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-methyl-butyric acid
518		H	succinamic acid	2-phenyl-	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-succinamic acid
519		H	3-(4-hydroxy-phenyl)-propionic acid	2-phenyl-	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(4-hydroxy-phenyl)-propionic acid

Cmpd#	Structure	R^8	R^9	Y	Het	Name
520		1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid		2-phenyl-	Quin-oxalin-6-yl	2-[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid
521		4-methyl-piperazin-1-yl		4'-chloro-biphen-2-yl)-fluoro	Quin-olin-6-yl	{2-[2-(4'-chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(4-methyl-piperazin-1-yl)-methanone
522		4-methyl-piperazin-1-yl		biphen-2-yl-fluoro	Quin-olin-6-yl	[2-(2-biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazol-5-yl]-(4-methyl-piperazin-1-yl)-methanone
523		H	5-guanidino-pentanoic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-5-guanidino-pentanoic acid
524		H	ethanesulfonic acid	phenyl	Quin-oxalin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-ethanesulfonic acid
541		H	butyric acid	phenyl	Quin-oxalin-6-yl	4-carbamoyl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-butyric acid
250		H	3-(5-Hydroxy-1H-indol-3-yl)-2-propionic acid	phenyl	Quin-olin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid
251		H	7-hydroxy-naphthalen-1-yl	phenyl	Quin-olin-6-yl	1-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-7-hydroxy-naphthalene
252		H	5-hydroxy-naphthalen-1-yl	phenyl	Quin-olin-6-yl	1-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-5-hydroxy-naphthalene
253		H	4-methyl-2-oxo-chromen-7-yl	phenyl	Quin-olin-6-yl	7-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methyl-2-oxo-chromene
254		H	morpholin-4-yl	phenyl	Quin-olin-6-yl	{2-[2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(morpholin-4-yl)-methanone

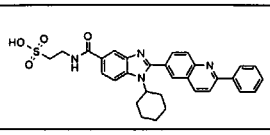
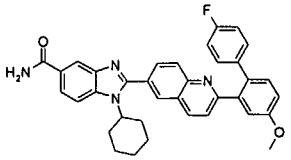
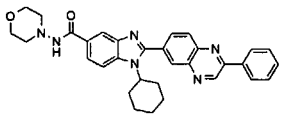
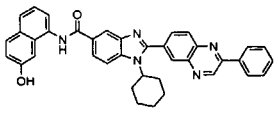
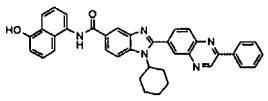
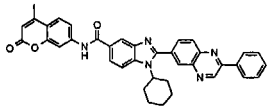
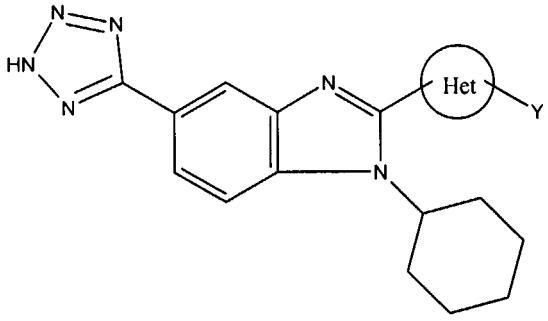
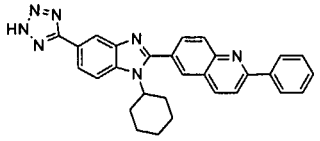
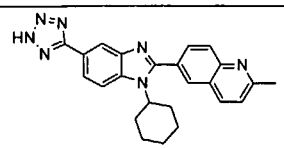
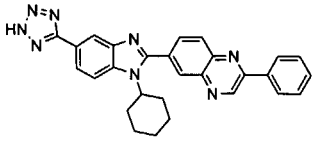
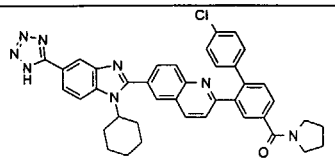
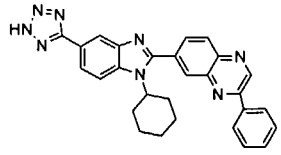
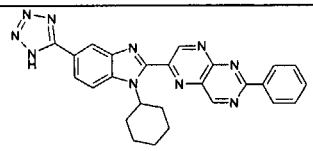
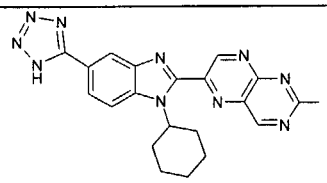
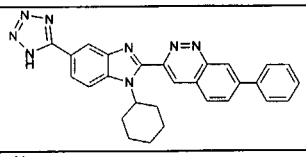
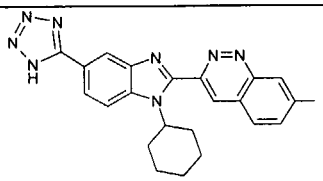
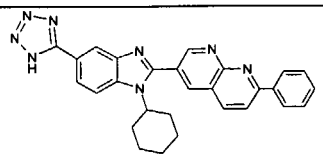
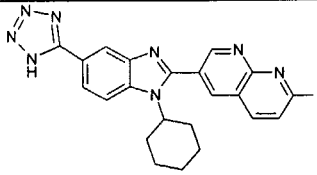
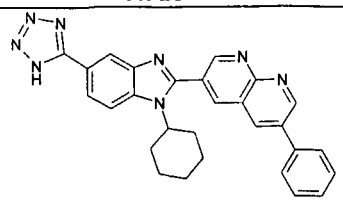
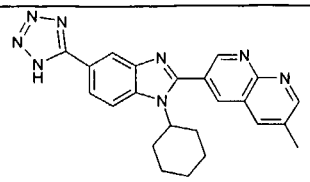
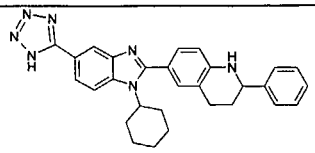
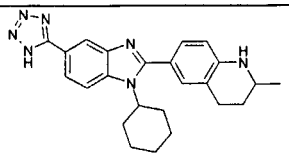
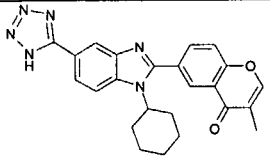
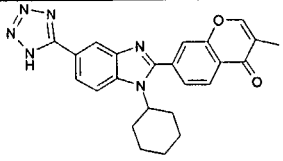
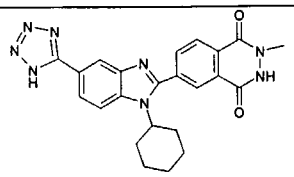
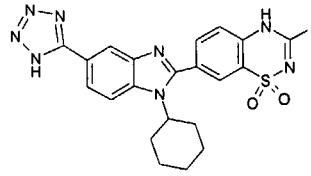
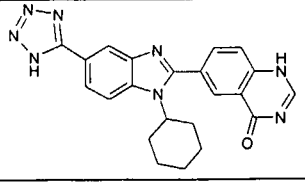
Cmpd#	Structure	R^8	R^9	Y	Het	Name
255		H	Ethanesulfonic acid-1-yl	phenyl	Quinolin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-ethanesulfonic acid
570		H	H	4'-fluoro-4-methoxy-biphen-2-yl	Quinolin-6-yl	1-cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid amide
574		H	morpholin-4-yl	phenyl	Quinoxalin-6-yl	1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid morpholin-4-ylamide
575		H	7-hydroxy-naphthalen-1-yl	phenyl	Quinoxalin-6-yl	1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (7-hydroxy-naphthalen-1-yl)-amide
576		H	5-hydroxy-naphthalen-1-yl	phenyl	Quinoxalin-6-yl	1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (5-hydroxy-naphthalen-1-yl)-amide
577		H	4-methyl-2-oxo-2H-chromen-7-yl	phenyl	Quinoxalin-6-yl	1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (4-methyl-2-oxo-2H-chromen-7-yl)-amide

Table III



Cmpd#	Structure	Y	Het	Name
256		phenyl	quinolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylquinoline

Cmpd#	Structure	Y	Het	Name
257		methyl	quinolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methylquinoline
258		phenyl	quinoxalin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylquinoxaline
259		4'-chloro-4-(pyrrolidin-1-ylcarbonyl)-biphen-2-yl	quinoxalin-6-yl	(4'-chloro-2-{6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzimidazol-2-yl]-quinolin-2-yl}-biphen-4-yl)-pyrrolidin-1-yl-methanone
260		phenyl	quinoxalin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-phenylquinoxaline
261		phenyl	pteridin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylpteridine
262		methyl	pteridin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methylpteridine
263		phenyl	cinnolin-3-yl	3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-phenylcinnoline
264		methyl	cinnolin-3-yl	3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-methylcinnoline
265		phenyl	[1,8]naph-thyridin-3-yl	3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-phenyl[1,8]naphthyridine
266		methyl	[1,8]naph-thyridin-3-yl	3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-methyl[1,8]naphthyridine

Cmpd#	Structure	Y	Het	Name
267		phenyl	[1,8]naph-thyridin-3-yl	3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-6-phenyl[1,8]naphthyridine
268		methyl	[1,8]naph-thyridin-3-yl	3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-6-methyl[1,8]naphthyridine
269		phenyl	1,2,3,4-tetrahydro-quinolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenyl-1,2,3,4-tetrahydroquinoline
270		methyl	1,2,3,4-tetrahydro-quinolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-1,2,3,4-tetrahydroquinoline
271		methyl	4-oxo-2H-chromen-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-4-oxo-2H-chromene
272		methyl	2-oxo-2H-chromen-7-yl	7-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-2-oxo-2H-chromene
273		methyl	1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-1,4-dioxo-1,2,3,4-tetrahydro-phthalazine
274		methyl	1,1-dioxo-1,4-dihydro-1λ6-benzo-[1,2,4]thia-diazin-7-yl	7-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazine
275			4-oxo-1,4-dihydro-quinazolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-4-oxo-1,4-dihydro-quinazoline

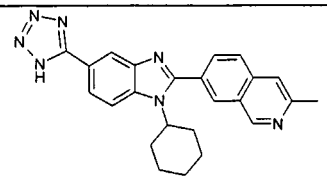
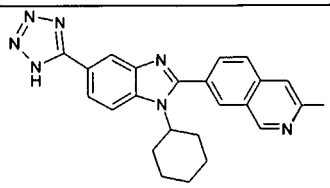
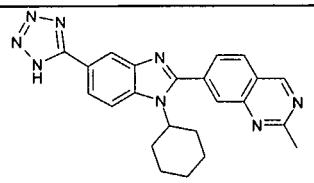
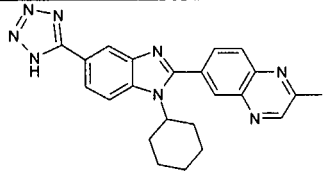
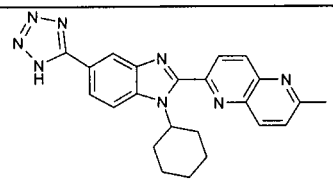
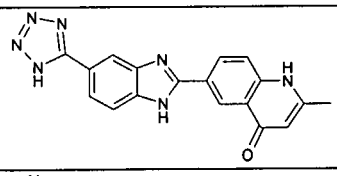
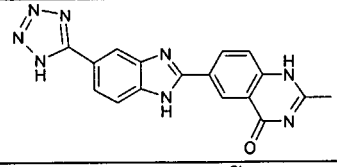
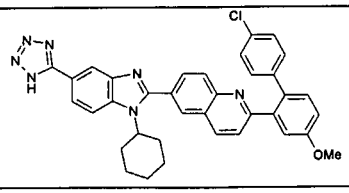
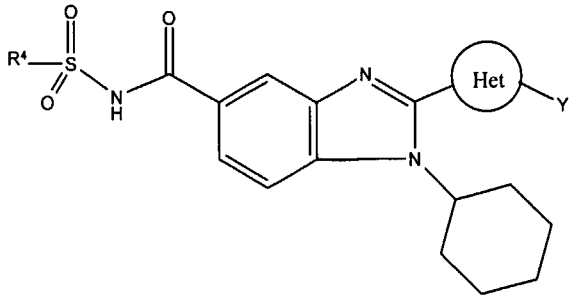
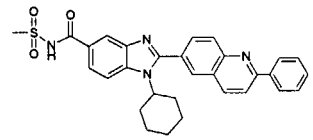
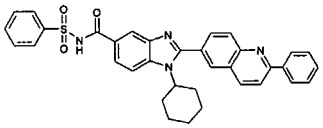
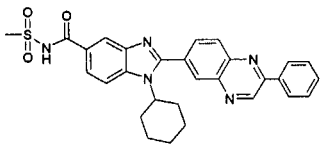
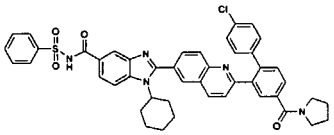
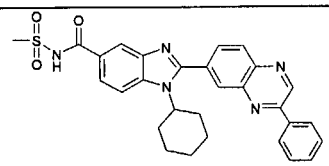
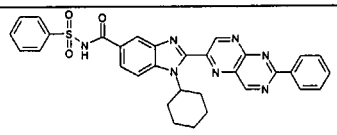
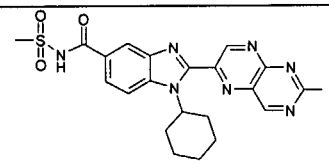
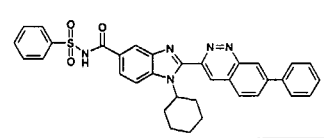
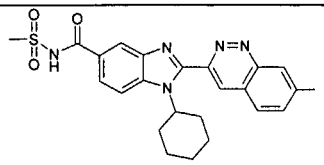
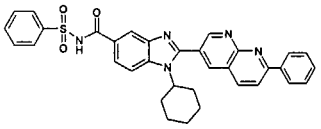
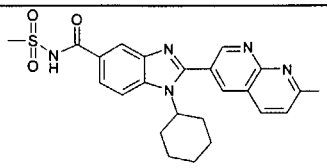
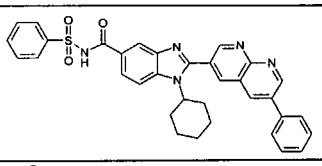
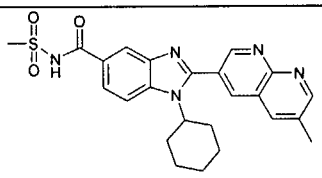
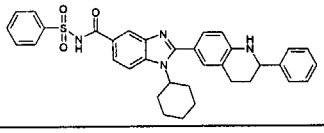
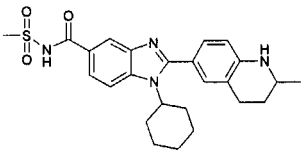
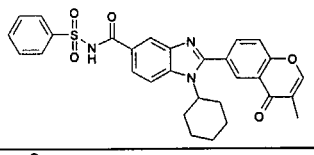
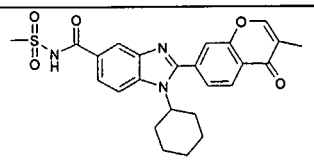
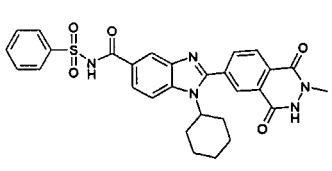
Cmpd#	Structure	Y	Het	Name
276		methyl	Isoquinolin -6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-isoquinoline
277		methyl	1,4-dihydro-isoquinolin -6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-1,4-dihydro- isoquinoline
278		methyl	quinazolin-7-yl	7-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-quinazoline
279		methyl	quinoxalin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-quinoxaline
280		methyl	[1,5]naph-thyridin-2-yl	2-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-6-methyl-[1,5]naphthyridine
281		methyl	4-oxo-1,4-dihydro-quinolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-4-oxo-1,4-dihydro-quinoline
282		methyl	4-oxo-1,4-dihydro-quinazolin-6-yl	6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-4-oxo-1,4-dihydro-quinazoline
525		4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-(4'-chloro-4-methoxy-biphen-2-yl)-6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzoimidazol-2-yl]-quinoline

Table IV



Cmpd#	Structure	R^4	Y	Het	Name
283		methyl	Phenyl	quinolin-6-yl	N-[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
284		phenyl	Methyl	quinolin-6-yl	N-[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)- 1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
285		methyl	Phenyl	Quin-oxalin-6-yl	N-[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
286		phenyl	4'-chloro-4-(pyrrol-idine-1-carbonyl)-biphen-2-yl-	quinolin-6-yl	N-[1-cyclohexyl-2-(2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
287		methyl	phenyl	Quin-oxalin-6-yl	N-[1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
288		phenyl	phenyl	pteridin-6-yl	N-[1-cyclohexyl-2-(2-phenyl- pteridin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
289		methyl	methyl	pteridin-6-yl	N-[1-cyclohexyl-2-(2-methyl- pteridin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
290		phenyl	phenyl	cinnolin-3-yl	N-[1-cyclohexyl-2-(7-phenyl-cinnolin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine

Cmpd#	Structure	R^4	Y	Het	Name
291		methyl	methyl	cinnolin-3-yl	N-[1-cyclohexyl-2-(7-methyl-cinnolin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
292		phenyl	phenyl	[1,8]naphthyridin-3-yl	N-[1-cyclohexyl-2-(7-phenyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
293		methyl	methyl	[1,8]naphthyridin-3-yl	N-[1-cyclohexyl-2-(7-methyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
294		phenyl	phenyl	[1,8]naphthyridin-3-yl	N-[1-cyclohexyl-2-(6-phenyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
295		methyl	methyl	[1,8]naphthyridin-3-yl	N-[1-cyclohexyl-2-(6-methyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
296		phenyl	phenyl	1,2,3,4-tetrahydroquinolin-6-yl	N-[1-cyclohexyl-2-(2-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
297		methyl	methyl	1,2,3,4-tetrahydroquinolin-6-yl	N-[1-cyclohexyl-2-(2-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
298		phenyl	methyl	4-oxo-2H-chromen-6-yl	N-[1-cyclohexyl-2-(3-methyl-4-oxo-2H-chromen-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
299		methyl	methyl	2-oxo-2H-chromen-7-yl	N-[1-cyclohexyl-2-(3-methyl-2-oxo-2H-chromen-7-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
300		phenyl	methyl	1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl	N-[1-cyclohexyl-2-(2-methyl-1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine

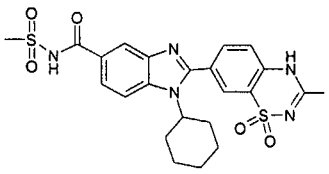
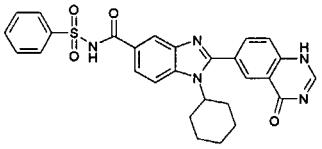
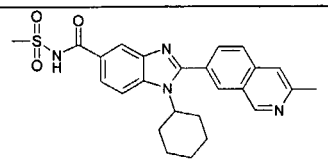
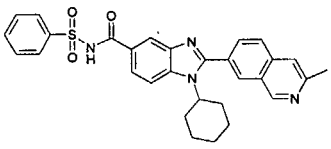
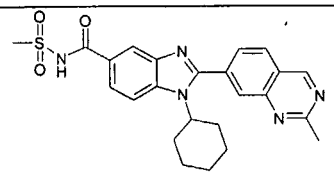
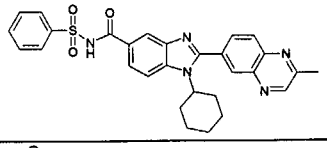
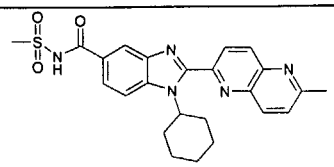
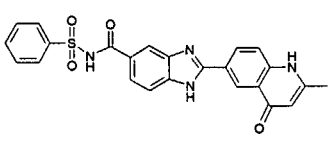
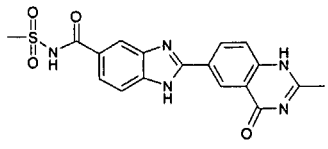
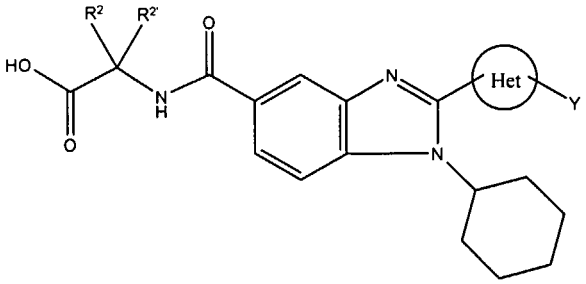
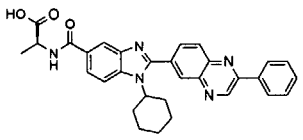
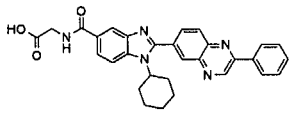
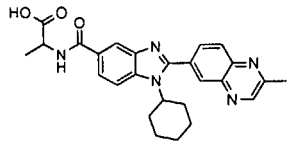
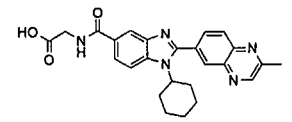
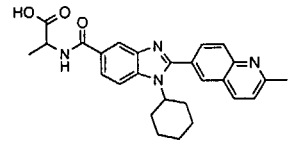
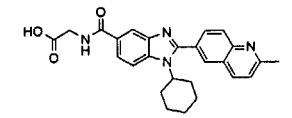
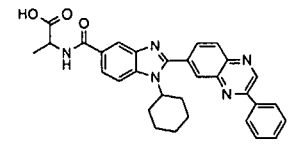
Cmpd#	Structure	R^4	Y	Het	Name
301		methyl	methyl	1,1-dioxo-1,4-dihydro-1λ6-benzo-[1,2,4]-thiadi-azin-7-yl	N-[1-cyclohexyl-2-(3-methyl-1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazin-7-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
302		phenyl		4-oxo-1,4-dihydro-quinazolin-6-yl	N-[1-cyclohexyl-2-(4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
303		methyl	methyl	isoquinolin-6-yl	N-[1-cyclohexyl-2-(3-methyl-isoquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
304		phenyl	methyl	1,4-dihydro-isoquin-olin-6-yl	N-[1-cyclohexyl-2-(3-methyl-1,4-dihydro-isoquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
305		methyl	methyl	Quin-azolin-7-yl	N-[1-cyclohexyl-2-(2-methyl-quinazolin7-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
306		phenyl	methyl	Quin-oxalin-6-yl	N-[1-cyclohexyl-2-(2-methyl-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
307		methyl	methyl	[1,5]naph thyridin-2-yl	N-[1-cyclohexyl-2-(6-methyl-[1,5]naphthyridin-2-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine
308		phenyl	methyl	4-oxo-1,4-dihydro-quinolin-6-yl	N-[1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine
309		methyl	methyl	4-oxo-1,4-dihydro-quinazoli n-6-yl	N-[1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine

Table V



Cmpd#	Structure	R^2	$R^{2'}$	Y	Het-Y	Name
310		methyl	H	phenyl	quinoxalin-6-yl	2-[(2-(2-phenyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid
311		H	H	phenyl	quinoxalin-6-yl	{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid
312		methyl	H	methyl	quinoxalin-6-yl	2-[(2-(2-methyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid
313		H	H	methyl	quinoxalin-6-yl	{[1-cyclohexyl-2-(2-methyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid
314		methyl	H	methyl	quinolin-6-yl	2-[(2-(2-methyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid
315		H	H	methyl	quinolin-6-yl	{[1-cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid
316		methyl	H	phenyl	quinoxalin-6-yl	2-[(2-(3-phenyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid

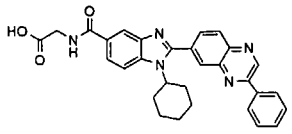
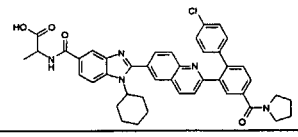
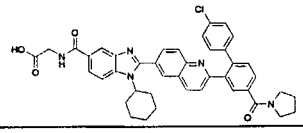
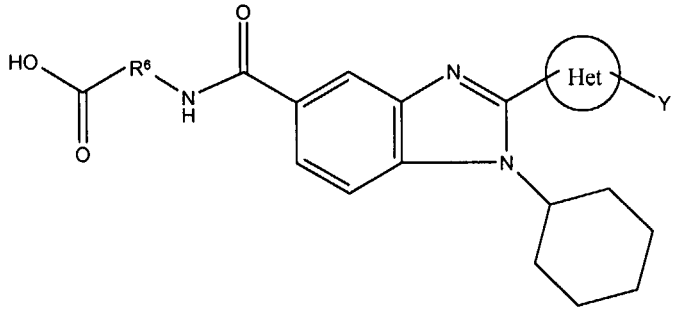
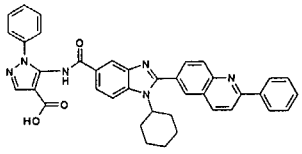
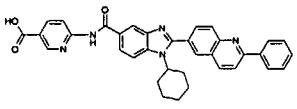
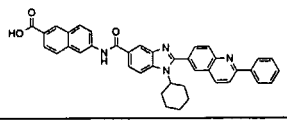
Cmpd#	Structure	R^2	$R^{2'}$	Y	Het-Y	Name
317		H	H	phenyl	quinoxalin-6-yl	{[1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid
318		methyl	H	4'-chloro-4-(pyrrolidin-1-ylcarbonyl)-biphen-2-yl	quinolin-6-yl	2-[(2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid
319		H	H	4'-chloro-4-(pyrrolidin-1-ylcarbonyl)-biphen-2-yl	quinolin-6-yl	2-[(2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]- acetic acid

Table VI



Cmpd#		R^6-COOH	Y	Het	Name
320		1-phenyl-1H-pyrazole-4-carboxylic acid-5-yl	phenyl	quinolin-6-yl	5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-1-phenyl-1H-pyrazole-4-carboxylic acid
321		nicotinic acid-6-yl	phenyl	quinolin-6-yl	5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}- nicotinic acid
322		naphthalene-2-carboxylic acid -6-yl	phenyl	quinolin-6-yl	6-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-naphthalene-2-carboxylic acid

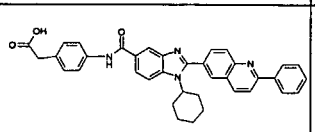
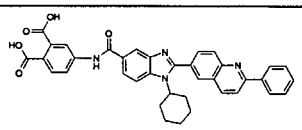
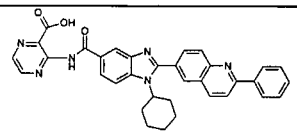
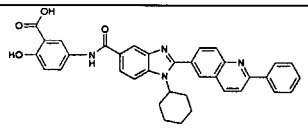
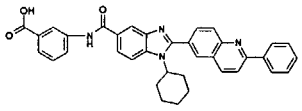
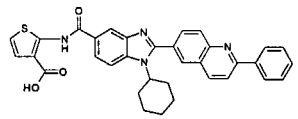
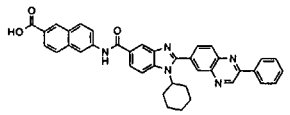
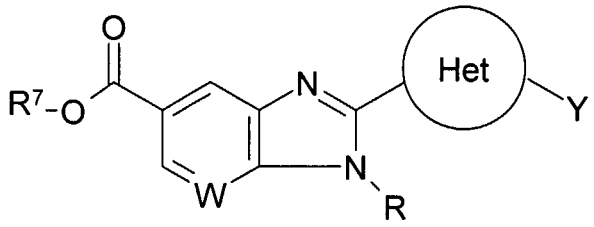
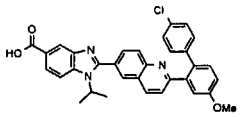
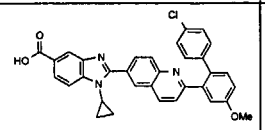
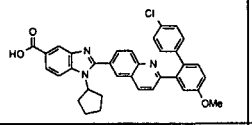
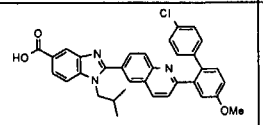
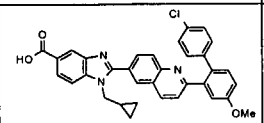
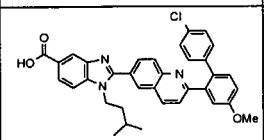
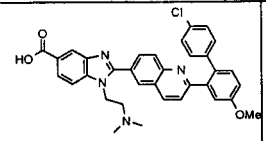
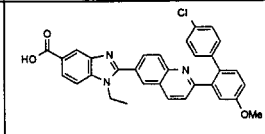
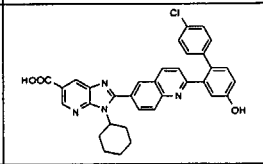
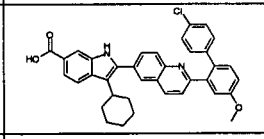
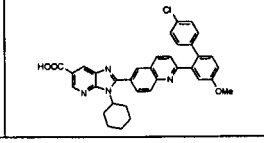
Cmpd#		R^6-COOH	Y	Het	Name
323		phenylacetic acid-4-yl	phenyl	quinolin-6-yl	4-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-phenylacetic acid
324		phthalic acid-4-yl	phenyl	quinolin-6-yl	4-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-phthalic acid
325		pyrazine-2-carboxylic acid-3-yl	phenyl	quinolin-6-yl	3-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}- pyrazine-2-carboxylic acid
326		2-hydroxy-benzoic acid-5-yl	phenyl	quinolin-6-yl	5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-2-hydroxy-benzoic acid
327		benzoic acid- 5-yl	phenyl	quinolin-6-yl	5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-benzoic acid
328		thiophene-3-carboxylic acid-2-yl	phenyl	quinolin-6-yl	2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-thiophene-3-carboxylic acid
526		naphthalene-2-carboxylic acid	phenyl	Quin-oxalin-6-yl	6-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-naphthalene-2-carboxylic acid

Table VII



Cmpd#	Structure	W	R^7	R	Y	Het	Name
527		CH	H	isopropyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-isopropyl-1H-benzoimidazole-5-carboxylic acid

Cmpd#	Structure	W	R^7	R	Y	Het	Name
528		CH	H	Cyclo-propyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopropyl-1H-benzoimidazole-5-carboxylic acid
529		CH	H	Cyclo-pentyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopentyl-1H-benzoimidazole-5-carboxylic acid
530		CH	H	isobutyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-isobutyl-1H-benzoimidazole-5-carboxylic acid
531		CH	H	Cyclo-propyl-methyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopropylmethyl-1H-benzoimidazole-5-carboxylic acid
532		CH	H	2-methyl-butyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(3-methyl-butyl)-1H-benzoimidazole-5-carboxylic acid
533		CH	H	2-(N,N-di-methyl)-ethyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(2-dimethylamino-ethyl)-1H-benzoimidazole-5-carboxylic acid
534		CH	H	ethyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxybiphen-2-yl)-quinolin-6-yl]-1-ethyl-1H-benzoimidazole-5-carboxylic acid
535		N	H	Cyclo-hexyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid
536		CH	H	Cyclo-hexyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-1H-indole-6-carboxylic acid
537		N	H	Cyclo-hexyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid

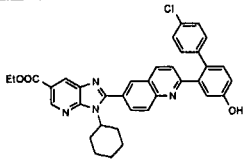
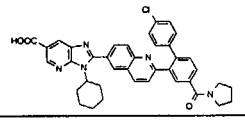
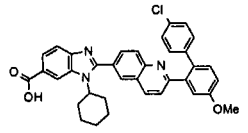
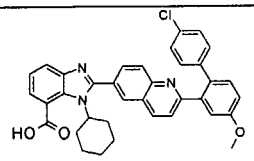
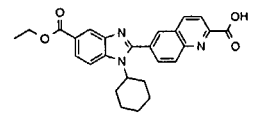
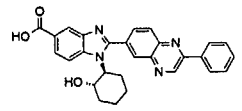
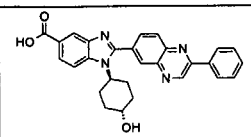
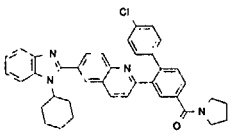
Cmpd#	Structure	W	R^7	R	Y	Het	Name
538		N	ethyl	Cyclo-hexyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid ethyl ester
539		N	H	Cyclo-hexyl	4'-chloro-4-(pyrrolidin-1-ylcarbonyl)-biphen-2-yl	quinolin-6-yl	2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid
571		CH	H	Cyclo-hexyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-[2-(4'-chloro-4-methoxybiphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-5-carboxylic acid
572		CH	H	Cyclo-hexyl	4'-chloro-4-methoxy-biphen-2-yl	quinolin-6-yl	2-(4'-chloro-4-methoxybiphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-4-carboxylic acid
402a		CH	Et	Cyclo-hexyl	carboxylic acid	quinolin-6-yl	6-(1-cyclohexyl-5-ethoxycarbonyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid
578		CH	H	trans-2-hydroxy-cyclohexyl	phenyl	Quin-oxalin-6-yl	1-(trans-2-hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid
579		CH	H	trans-4-hydroxy-cyclo-hexyl	phenyl	Quin-oxalin-6-yl	1-(trans-4-hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid

Table VIII

Cmpd#	Structure	W	R^7	R	Y	Het	Name
540		CH	H	cyclohexyl	4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl	quinolin-6-yl	{4'-chloro-2-[6-(1-cyclohexyl-1H-benzoimidazol-2-yl)-quinolin-2-yl]-biphen-4-yl}-pyrrolidin-1-yl-methanone

[0067] In still another embodiment the present invention is contemplated to include the following compounds

N-[1-cyclohexyl-2-(4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-4-oxo-1,4-dihydro-quinazoline;

1-cyclohexyl-2-(4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazole-5-carboxylic acid; and

pharmaceutically acceptable tautomers and salts thereof.

[0068] This invention is also directed to pharmaceutical compositions comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of one of the compounds described herein or mixtures of one or more of such compounds.

[0069] This invention is still further directed to methods for treating a viral infection mediated at least in part by a virus in the *flaviviridae* family of viruses, such as HCV, in mammals which methods comprise administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of one of the compounds described herein or mixtures of one or more of such compounds.

[0070] In yet another embodiment of the invention, methods of treating or preventing viral infections in mammals are provided where in the compounds of this invention are administered in combination with the administration of a therapeutically effective amount of one or more agents active against HCV. Active agents against HCV include ribavirin, levovirin, thymosin alpha-1, an inhibitor of NS3 serine protease, and inhibitor of inosine monophosphate dehydrogenase, interferon-alpha, pegylated interferon-alpha, alone or in combination with ribavirin or levovirin. Prefereably the additional agent active against HCV is interferon-alpha or pegylated interferon-alpha alone or in combination with ribavirin or levovirin.

DETAILED DESCRIPTION OF THE INVENTION

[0071] The invention is directed to compounds, compositions and methods for treating *Flaviviridae* family viral infections. However, prior to describing this invention in detail, the following terms will first be defined.

DEFINITIONS

[0072] Before the present invention is described in detail, it is to be understood that, unless otherwise indicated, this invention is not limited to any particular composition or pharmaceutical carrier, as such may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the present invention.

[0073] It must be noted that as used herein and in the claims, the singular forms "a," "and" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "pharmaceutically acceptable diluent" in a composition includes two or more pharmaceutically acceptable diluents, and so forth.

[0074] In this specification and in the claims that follow, reference will be made to a number of terms that shall be defined to have the following meanings:

[0075] As used herein, "alkyl" refers to monovalent alkyl groups having from 1 to 10 carbon atoms, preferably from 1 to 5 carbon atoms and more preferably 1 to 3 carbon atoms. This term is exemplified by groups such as methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *t*-butyl, *n*-pentyl and the like.

[0076] "Substituted alkyl" refers to an alkyl group having from 1 to 3, and preferably 1 to 2, substituents selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy ester, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.

[0077] As used herein, "alkylene" refers to straight chain and branched divalent alkyl groups having from 1 to 10 carbon atoms, preferably from 1 to 5 carbon atoms and more preferably 1 to 3 carbon atoms. This term is exemplified by groups such as methylene, ethylene, propylene, butylene, and the like.

[0078] "Substituted alkylene" refers to an alkylene group having from 1 to 3, and preferably 1 to 2, substituents selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy ester, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.

[0079] "Alkoxy" refers to the group "alkyl-O-" which includes, by way of example, methoxy, ethoxy, *n*-propoxy, *iso*-propoxy, *n*-butoxy, *t*-butoxy, *sec*-butoxy, *n*-pentoxy and the like.

[0080] "Substituted alkoxy" refers to the group "substituted alkyl-O-".

[0081] "Acyl" refers to the groups H-C(O)-, alkyl-C(O)-, substituted alkyl-C(O)-, alkenyl-C(O)-, substituted alkenyl-C(O)-, alkynyl-C(O)-, substituted alkynyl-C(O)- cycloalkyl-C(O)-, substituted cycloalkyl-C(O)-, aryl-C(O)-, substituted aryl-C(O)-, heteroaryl-C(O)-, substituted heteroaryl-C(O), heterocyclic-C(O)-, and substituted heterocyclic-C(O)-.

[0082] "Acylamino" refers to the group -C(O)NR^{20}R^{21} where R^{20} and R^{21} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and where R^{20} and R^{21} are joined to form together with the nitrogen atom a heterocyclic or substituted heterocyclic ring.

[0083] "Acyloxy" refers to the groups alkyl-C(O)O-, substituted alkyl-C(O)O-, alkenyl-C(O)O-, substituted alkenyl-C(O)O-, alkynyl-C(O)O-, substituted alkynyl-C(O)O-, aryl-C(O)O-, substituted aryl-C(O)O-, cycloalkyl-C(O)O-, substituted cycloalkyl-C(O)O-, heteroaryl-C(O)O-, substituted heteroaryl-C(O)O-, heterocyclic-C(O)O-, and substituted heterocyclic-C(O)O-.

[0084] "Alkenyl" refers to alkenyl group having from 2 to 10 carbon atoms, preferably having from 2 to 6 carbon atoms, and more preferably 2 to 4 carbon atoms and having at least 1 and preferably from 1-2 sites of alkenyl unsaturation.

[0085] "Substituted alkenyl" refers to alkenyl groups having from 1 to 3 substituents, and preferably 1 to 2 substituents, selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy ester, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.

[0086] "Alkynyl" refers to alkynyl group having from 2 to 10 carbon atoms, preferably having from 2 to 6 carbon atoms, and more preferably 2 to 3 carbon atoms and having at least 1 and preferably from 1-2 sites of alkynyl unsaturation.

[0087] "Substituted alkynyl" refers to alkynyl groups having from 1 to 3 substituents, and preferably 1 to 2 substituents, selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy ester, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.

[0088] "Amino" refers to the group $-NH_2$.

[0089] "Substituted amino" refers to the group $-NR^{22}R^{23}$ where R^{22} and R^{23} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl,

alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and where R^{22} and R^{23} are joined, together with the nitrogen bound thereto to form a heterocyclic or substituted heterocyclic group provided that R^{22} and R^{23} are both not hydrogen. When R^{22} is hydrogen and R^{23} is alkyl, the substituted amino group is sometimes referred to herein as alkylamino. When R^{22} and R^{23} are alkyl, the substituted amino group is sometimes referred to herein as dialkylamino.

[0090] "Aminoacyl" refers to the groups $-NR^{24}C(O)$alkyl, $-NR^{24}C(O)$substituted alkyl, $-NR^{24}C(O)$-cycloalkyl, $-NR^{24}C(O)$substituted cycloalkyl, $-NR^{24}C(O)$alkenyl, $-NR^{24}C(O)$substituted alkenyl, $-NR^{24}C(O)$alkynyl, $-NR^{24}C(O)$substituted alkynyl, $-NR^{24}C(O)$aryl, $-NR^{24}C(O)$substituted aryl, $-NR^{24}C(O)$heteroaryl, $-NR^{24}C(O)$substituted heteroaryl, $-NR^{24}C(O)$heterocyclic, and $-NR^{24}C(O)$substituted heterocyclic where R^{24} is hydrogen or alkyl.

[0091] The term "aminocarbonylamino" refers to the group $-NR^{25}C(O)NR^{26}R^{27}$ where R^{25} is hydrogen or alkyl and R^{26} and R^{27} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and where R^{26} and R^{27} are joined, together with the nitrogen bound thereto to form a heterocyclic or substituted heterocyclic group.

[0092] The term "aminocarbonyloxy" refers to the group $-NR^{28}C(O)OR^{29}$ where R^{28} is hydrogen or alkyl and R^{29} is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic.

[0093] "Aryl" or "Ar" refers to a monovalent aromatic carbocyclic group of from 6 to 14 carbon atoms having a single ring (e.g., phenyl) or multiple condensed rings (e.g., naphthyl or anthryl) which condensed rings may or may not be aromatic (e.g., 2-

benzoxazolinone, 2H-1,4-benzoxazin-3(4H)-one-7-yl, and the like) provided that the point of attachment is to an aromatic ring atom. Preferred aryls include phenyl and naphthyl.

[0094] "Substituted aryl" refers to aryl groups which are substituted with from 1 to 3 substituents, and preferably 1 to 2 substituents, selected from the group consisting of hydroxy, acyl, acylamino, acyloxy, alkyl, substituted alkyl, alkoxy, substituted alkoxy, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cycloalkoxy, substituted cycloalkoxy, carboxy, carboxy esters, cyano, thiol, cycloalkyl, substituted cycloalkyl, halo, nitro, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, and substituted heterocyclyloxy.

[0095] "Aryloxy" refers to the group aryl-O- that includes, by way of example, phenoxy, naphthoxy, and the like.

[0096] "Substituted aryloxy" refers to substituted aryl-O- groups.

[0097] "Carboxy" refers to –COOH or salts thereof.

[0098] "Carboxy esters" refers to the groups -C(O)O-alkyl, -C(O)O-substituted alkyl, -C(O)O-alkenyl, -C(O)O-substituted alkenyl, -C(O)O-alkynyl, -C(O)O-substituted alkynyl, -C(O)O-aryl, -C(O)O-substituted aryl, -C(O)O-heteroaryl, -C(O)O-substituted heteroaryl, -C(O)O-heterocyclic, and -C(O)O-substituted heterocyclic. Preferred carboxy esters are -C(O)O-alkyl, -C(O)O-substituted alkyl, -C(O)O-aryl, and -C(O)O-substituted aryl.

[0099] "Cycloalkyl" refers to cyclic alkyl groups of from 3 to 10 carbon atoms having single or multiple cyclic rings optionally comprising 1 to 3 exo carbonyl or thiocarbonyl groups. Suitable cycloalkyl groups include, by way of example, adamantyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclooctyl, 3-oxocyclohexyl, and the

like. In multiple condensed rings, one or more of the rings may be other than cycloalkyl (e.g., aryl, heteroaryl or heterocyclic) provided that the point of attachment is to a carbon ring atom of the cycloalkyl group. In one embodiment, the cycloalkyl group does not comprise 1 to 3 exo carbonyl or thiocarbonyl groups. In another embodiment, the cycloalkyl group does comprise 1 to 3 exo carbonyl or thiocarbonyl groups. It is understood, that the term "exo" refers to the attachment of a carbonyl or thiocarbonyl to a carbon ring atom of the cycloalkyl group.

[0100] In a preferred embodiment, cycloalkyl includes alkyl groups of from 3 to 10 carbon atoms having single or multiple cyclic rings including, by way of example, adamantyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclooctyl, and the like.

[0101] "Cycloalkenyl" refers to cyclic alkenyl groups of from 4 to 10 carbon atoms having single or multiple cyclic rings and further having at least 1 and preferably from 1 to 2 internal sites of ethylenic (>C=C<) unsaturation optionally comprising 1 to 3 exo carbonyl or thiocarbonyl groups. Suitable cycloalkenyl groups include, by way of example, cyclopentenyl, cyclohexenyl, cyclooctenyl, 3-oxocyclohex-1,2-enyl, and the like. In one embodiment, the cycloalkenyl group does not comprise 1 to 3 exo carbonyl or thiocarbonyl groups. In a preferred embodiment, the cycloalkenyl group does comprise 1 to 3 exo carbonyl or thiocarbonyl groups. It is understood, that the term "exo" refers to the attachment of a carbonyl or thiocarbonyl to a carbon ring atom of the cycloalkenyl group.

[0102] "Substituted cycloalkyl" and "substituted cycloalkenyl" refers to an cycloalkyl or cycloalkenyl group, having from 1 to 5 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy esters, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic. Preferred substituted cycloalkyl and substituted cycloalkenyl include cycloalkyl or cycloalkenyl group, having from 1 to 5 substituents selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino,

aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy esters, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.

[0103] "Cycloalkoxy" refers to -O-cycloalkyl groups.

[0104] "Substituted cycloalkoxy" refers to -O-substituted cycloalkyl groups.

[0105] The term "guanidino" refers to the group $-NHC(=NH)NH_2$ and the term substituted "guanidino" refers to $-NR^{30}C(=NR^{30})N(R^{30})_2$ where each R^{30} is independently hydrogen or alkyl.

[0106] "Halo" or "halogen" refers to fluoro, chloro, bromo and iodo and preferably is fluoro or chloro.

[0107] "Haloalkyl" refers to an alkyl group substituted with at least one halogen such that a monohaloalkyl, a polyhaloalkyl or a perhaloalkyl are encompassed by the term haloalkyl.

[0108] "Heteroaryl" refers to an aromatic group of from 1 to 15 carbon atoms, preferably from 1 to 10 carbon atoms, and 1 to 4 heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur, -S(O)-, and $-S(O)_2-$ within the ring. Preferably, such heteroaryl groups are aromatic groups of from 1 to 15 carbon atoms, preferably from 1 to 10 carbon atoms, and 1 to 4 heteroatoms selected from the group consisting of oxygen, nitrogen, and sulfurwithin the ring. Such heteroaryl groups can have a single ring (e.g., pyridyl or furyl) or multiple condensed rings (e.g., indolizinyl or benzothienyl).

[0109] "Substituted heteroaryl" refers to heteroaryl groups that are substituted with from 1 to 3 substituents selected from the same group of substituents defined for substituted aryl.

[0110] "Heteroaryloxy" refers to the group -O-heteroaryl and "substituted heteroaryloxy" refers to the group -O-substituted heteroaryl.

[0111] "Heterocycle" or "heterocyclic" refers to a saturated or unsaturated group having a single ring or multiple condensed rings, from 1 to 10 carbon atoms and from 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur, -S(O)-, -$S(O)_2$- or oxygen within the ring which ring may optionally comprise 1 to 3 exo carbonyl or thiocarbonyl groups. Preferably, such heterocyclic groups are saturated or unsaturated group having a single ring or multiple condensed rings, from 1 to 10 carbon atoms and from 1 to 4 hetero atoms selected from the group consisting of nitrogen, sulfur, or oxygen within the ring.

[0112] In multiple condensed rings, one or more of the rings may be other than heterocyclic (e.g., aryl, heteroaryl or cycloalkyl) provided that the point of attachment is to a heterocyclic ring atom. In one embodiment, the heterocyclic group does not comprise 1 to 3 exo carbonyl or thiocarbonyl groups. In a preferred embodiment, the heterocyclic group does comprise 1 to 3 exo carbonyl or thiocarbonyl groups. It is understood, that the term "exo" refers to the attachment of a carbonyl or thiocarbonyl to a carbon ring atom of the heterocyclic group.

[0113] "Substituted heterocyclic" refers to heterocycle groups that are substituted with from 1 to 3 of the same substituents as defined for substituted cycloalkyl. Preferred substituents for substituted heterocyclic groups include heterocyclic groups having from 1 to 5 having substituents selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxy, nitro, carboxy, carboxy esters, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.

[0114] Examples of heterocycles and heteroaryls include, but are not limited to, azetidine, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine,

pyridazine, indolizine, isoindole, indole, dihydroindole, indazole, purine, quinolizine, isoquinoline, quinoline, phthalazine, naphthylpyridine, quinoxaline, quinazoline, cinnoline, carbazole, carboline, phenanthridine, acridine, phenanthroline, isothiazole, phenazine, isoxazole, phenoxazine, phenothiazine, imidazolidine, imidazoline, piperidine, piperazine, indoline, phthalimide, 1,2,3,4-tetrahydro-isoquinoline, 4,5,6,7-tetrahydrobenzo[b]thiophene, thiazole, thiazolidine, thiophene, benzo[b]thiophene, morpholinyl, thiomorpholinyl (also referred to as thiamorpholinyl), piperidinyl, pyrrolidine, tetrahydrofuranyl, and the like.

[0115] "Heterocyclyloxy" refers to the group -O-heterocyclic and "substituted heterocyclyloxy" refers to the group -O-substituted heterocyclic.

[0116] The term "oxycarbonylamino" refers to the group –O(CO)NR31R32 where R31 and R32 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and where R^{31} and R^{32} are joined, together with the nitrogen bound thereto to form a heterocyclic or substituted heterocyclic group.

[0117] The term "oxycarbonyloxy" refers to the group $-OC(O)OR^{33}$ where R^{33} is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic.

[0118] The term "thiol" refers to the group –SH.

[0119] The term "thioalkyl" refers to the group –S-alkyl and the term "substituted thioalkyl" refers to the group –S-substituted alkyl.

[0120] The term "amino acid" refers to β-amino acids or to α-amino acids of the formula $HR^{34}NCH(R^2)COOH$ where R^2 is as defined above and R^{34} is hydrogen, alkyl, substituted alkyl or aryl,. Preferably, the α-amino acid is one of the twenty naturally occurring L amino acids.

[0121] "Pharmaceutically acceptable salt" refers to pharmaceutically acceptable salts of a compound, which salts are derived from a variety of organic and inorganic counter ions well known in the art and include, by way of example only, sodium, potassium, calcium, magnesium, ammonium, tetraalkylammonium, and the like; and when the molecule contains a basic functionality, salts of organic or inorganic acids, such as hydrochloride, hydrobromide, tartrate, mesylate, acetate, maleate, oxalate and the like.

[0122] It is understood that in all substituted groups defined above, polymers arrived at by defining substituents with further substituents to themselves (e.g., substituted aryl having a substituted aryl group as a substituent which is itself substituted with a substituted aryl group, etc.) are not intended for inclusion herein. In such cases, the maximum number of such substituents is three. That is to say that each of the above definitions is constrained by a limitation that, for example, substituted aryl groups are limited to –substituted aryl-(substituted aryl)-substituted aryl.

[0123] Similarly, it is understood that the above definitions are not intended to include impermissible substitution patterns (e.g., methyl substituted with 5 fluoro groups or a hydroxy group alpha to ethenylic or acetylenic unsaturation). Such impermissible substitution patterns are well known to the skilled artisan.

GENERAL SYNTHETIC METHODS

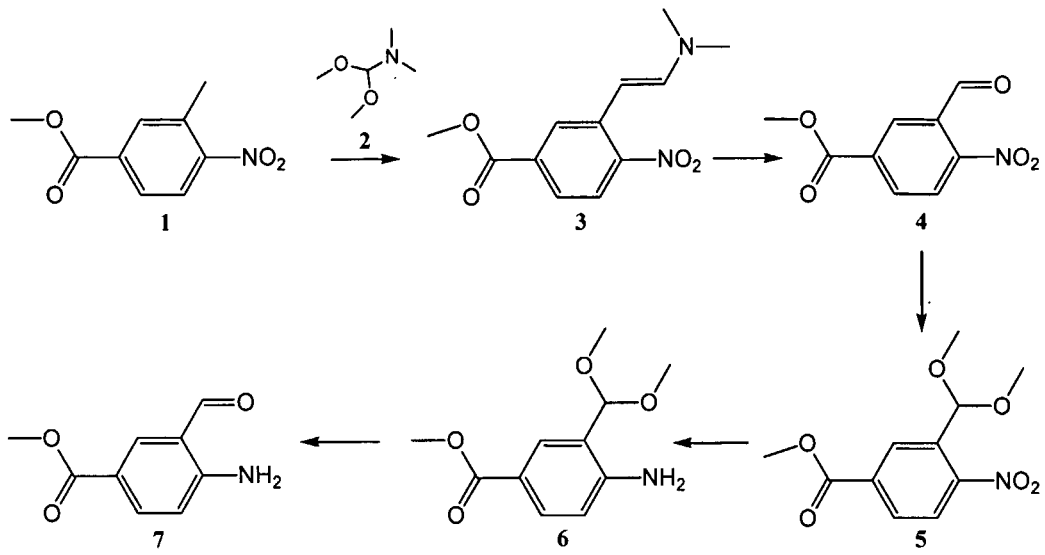
[0124] The compounds of this invention can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given, other

process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

[0125] Additionally, as will be apparent to those skilled in the art, conventional protecting groups may be necessary to prevent certain functional groups from undergoing undesired reactions. Suitable protecting groups for various functional groups as well as suitable conditions for protecting and deprotecting particular functional groups are well known in the art. For example, numerous protecting groups are described in T. W. Greene and P. G. M. Wuts, *Protecting Groups in Organic Synthesis*, Third Edition, Wiley, New York, 1999, and references cited therein.

[0126] If the compounds of this invention contain one or more chiral centers, such compounds can be prepared or isolated as pure stereoisomers, i.e., as individual enantiomers or diastereomers, or as stereoisomer-enriched mixtures. All such stereoisomers (and enriched mixtures) are included within the scope of this invention, unless otherwise indicated. Pure stereoisomers (or enriched mixtures) may be prepared using, for example, optically active starting materials or stereoselective reagents well-known in the art. Alternatively, racemic mixtures of such compounds can be separated using, for example, chiral column chromatography, chiral resolving agents and the like.

[0127] The following synthetic protocols illustrate the general manner for preparing the compounds described herein.



Scheme I. General Synthesis of 4-amino-3-formyl-benzoic acid methyl ester **7**.

[0128] Scheme I illustrates the conventional preparation of 4-amino-3-formyl-benzoic acid methyl ester, compound **7**, which is a starting material in the preparation of quinoline or substituted quinoline groups, i.e., Het-Y. Specifically, in Scheme I, commercially available 3-methyl-4-nitrobenzoic acid methyl ester, compound **1**, is contacted with at least a stoichiometric equivalent of commercially available dimethoxymethyl-dimethyl-amine, also known as *N,N*-dimethylformamide dimethylacetal, compound **2**, under conditions to form 3-(2-dimethylamino-vinyl)-4-nitro-benzoic acid methyl ester, compound **3**. The reaction is preferably conducted in an inert diluent such as *N,N*-dimethylformamide at an elevated temperature of from about 100 to 160 °C for a period of time to effect substantial completion of the reaction which typically occurs within 12 to 48 hours. After reaction completion, the resulting product, compound **3**, can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0129] 3-(2-dimethylamino-vinyl)-4-nitro-benzoic acid methyl ester, **3**, is subsequently converted to the formaldehyde by contact with at least a stoichiometric amount of oxidant, under conditions appropriate, to form 3-formyl-4-nitro-benzoic acid methyl ester **4**. The reaction is conducted in a suitable solvent, such as THF, in the

presence of water. Preferably, the reaction is conducted at a temperature of from room temperature to 50 °C. The reaction is continued until it is substantially complete which typically occurs within about 0.5 to 2 hours. Suitable oxidants are well known in the art and include, for example, sodium periodate, $NaIO_4$. While Compound **4** may be prepared in this manner, the compound is also commercially available.

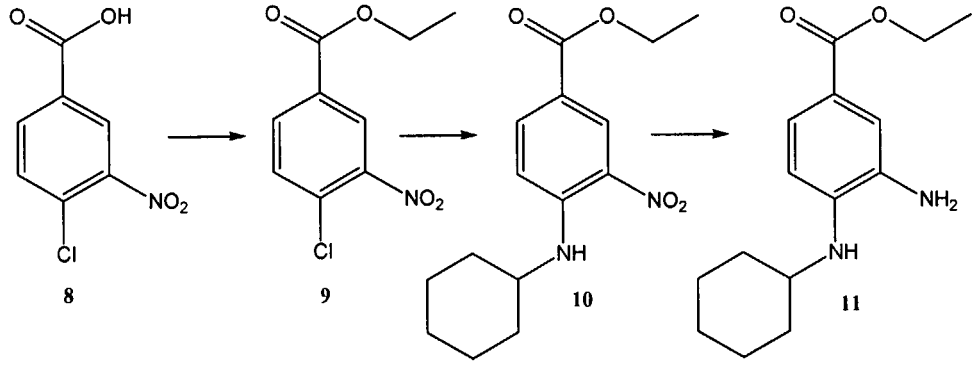
[0130] The formyl group of 3-formyl-4-nitro-benzoic acid methyl ester **4** is protected with a suitable protecting group, for example, as the acetal to form 3-dimethoxymethyl-4-nitro-benzoic acid methyl ester **5**. Other protecting groups are well known in the art and may also be used. In the acetal reaction, compound **4** is contacted with an acidic solution in methanol, under conditions appropriate to form compound **5**. The reaction is preferably conducted at an elevated temperature of from 80 to 100 °C. The reaction is continued until it is substantially complete which typically occurs within about 10 to 30 minutes. Upon reaction completion, the 3-dimethoxymethyl-4-nitro-benzoic acid methyl ester, compound **5**, can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like; or, alternatively, used in the next step without purification and/or isolation.

[0131] The nitro group of 3-dimethoxymethyl-4-nitro-benzoic acid methyl ester, compound **5** is then converted to the primary amine by conventional reducing procedures to provide 4-amino-3-dimethoxymethyl-benzoic acid methyl ester, compound **6**. Conventional reducing procedures include, but are not limited to, hydrogenation utilizing Pd/C. The reaction is preferably conducted in a suitable vessel such as a Parr apparatus, at room temperature for a time sufficient to provide substantial reaction completion, which typically occurs in from 15 minutes to 1.5 hours. Compound **6** can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like; or, alternatively, used in the next step without purification and/or isolation.

[0132] 4-Amino-3-formyl-benzoic acid methyl ester, compound **7**, is obtained by conventional deprotection of the protecting group. Preferably, the acetal of compound **6** is hydrolyzed under standard reaction conditions. Acetal hydrolysis

conditions are well known in the art and may be achieved by treating compound **6** with, for example, an acidic aqueous solution. The reaction is preferably conducted at room temperature and continued until it is substantially complete which typically occurs within about 15 to 30 minutes. Upon reaction completion, the product 4-amino-3-formyl-benzoic acid methyl ester, compound **7**, can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like.

[0133] Alternatively, Compound 7 may be prepared directly from Compound 4 by reduction with iron sulfate and ammonium hydroxide.



Scheme II. General synthesis of 3-amino-4-cyclohexylamino-benzoic acid ethyl ester **11**.

[0134] Scheme II illustrates the general synthesis of 3-amino-4-cyclohexylamino-benzoic acid ethyl ester, compound **11,** which is used as a starting material in the preparation of 2-Het-Y substituted 1-cyclohexyl-1H-benzoimidazole-5-carboxylic acids. It is understood that the cyclohexyl group in Scheme II is only for illustrative purposes and that other R groups can be prepared using the protocols described herein merely by replacing the cyclohexylamine with other suitable amines.

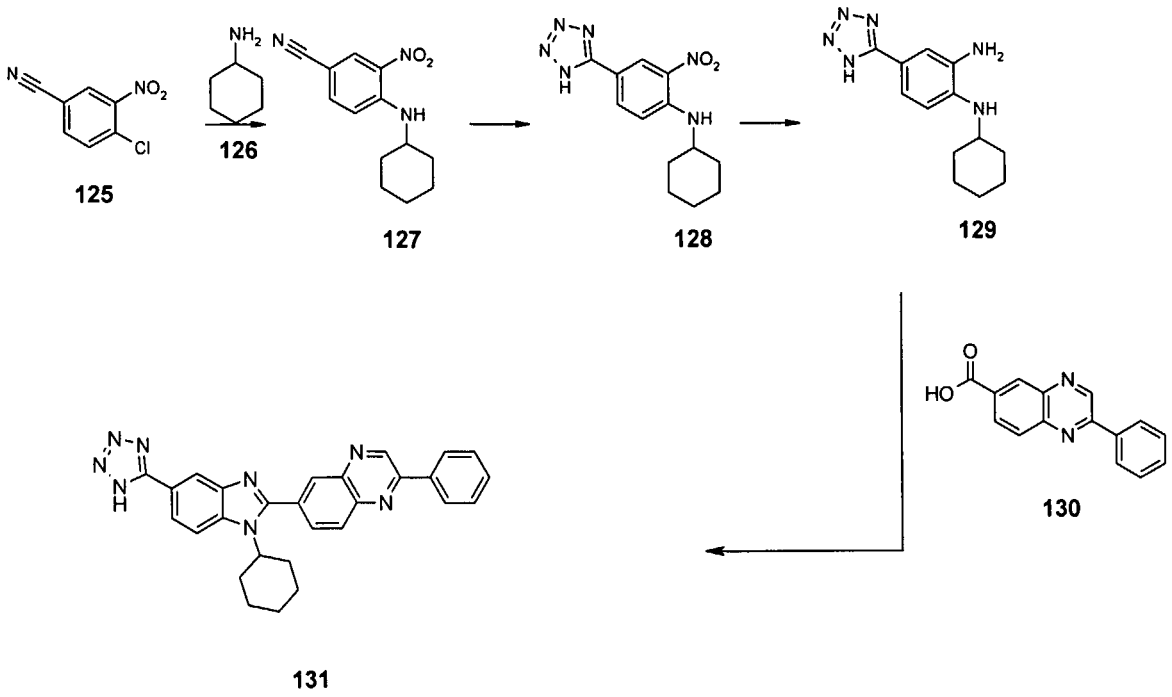
[0135] Specifically, in Scheme II, commercially available 4-chloro-3-nitro-benzoic acid, compound **8**, is converted to the corresponding ethyl ester using conventional alkylation protocols. In one preferred method, compound **8** is contacted with a molar excess of the appropriate alcohol (ethanol) in the presence of an acid at an elevated temperature. The reaction is maintained at an elevated temperature, preferably at the reflux temperature of the alcohol solvent/reactant, until reaction completion, which is

typically achieved in about 10 to 24 hours. Upon reaction completion, the resulting 4-chloro-3-nitro-benzoic acid ethyl ester, compound **9**, can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like; or, alternatively, used in the next step without purification and/or isolation.

[0136] 4-chloro-3-nitro-benzoic acid ethyl ester, compound **9** is then aminated to provide 4-cyclohexylamino-3-nitro-benzoic acid ethyl ester, compound **10**. In this reaction, compound **9** is treated with cyclohexylamine in the presence of TEA. The reaction is preferably conducted in an inert diluent such as acetonitrile, at an elevated temperature, preferably at the reflux temperature of the solvent, for a period of time to effect substantial completion of the reaction which typically occurs within 10 to 48 hours. After reaction completion, the resulting product, compound **10**, can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0137] 3-Amino-4-cyclohexylamino-benzoic acid ethyl ester, compound **11**, is provided by reducing the nitro functionality of compound **10**. Reduction protocols are well known in the art and include, for example, hydrogenation with Pd/C. The reaction is preferably conducted at room temperature in a suitable inert solvent such as ethyl acetate and is continued until a substantial amount of product is obtained, which typically occurs in about 2 to 8 hours. The resulting 3-amino-4-cyclohexylamino-benzoic acid ethyl ester, compound **11**, can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like.

[0138] Tetrazolyl-substituted compounds are similarly obtained using 4-chloro-3-nitro-benzonitrile, as shown in Scheme IIa below.



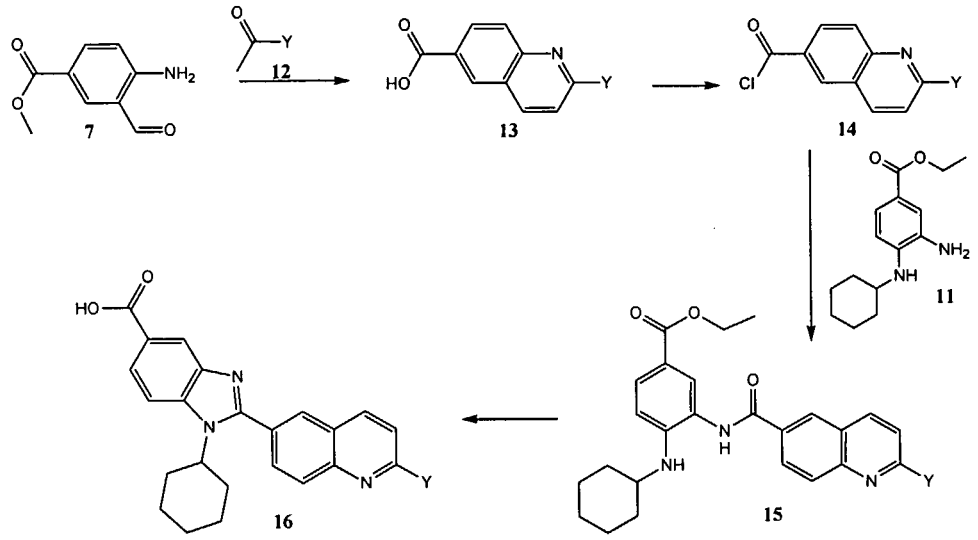
Scheme IIa. General synthesis of 1-cyclohexyl-5-(tetrazol-2-yl)-2-(3-phenylquinoxalin-6-yl)benzoimidazole **131**.

[0139] Initially, commercially available 2-chloro-5-cyano-nitrobenzene, compound **125**, is aminated as described above with cyclohexylamine, compound 126 to provide for compound **127**. As before, cyclohexylamine is representative of suitable amines which can be used in this protocol. Conversion of the cyano group of the 2-cyclohexylamino-5-cyano-nitrobenzene, compound **127**, to the corresponding tetrazolyl derivative, compound **128**, proceeds via conventional conditions such as contacting compound **127** with trimethyltin azide in the presence of refluxing toluene. An aqueous acid is then added and acidic hydrolysis proceeds for several hours at room temperature to provide for compound **128** which can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like; or, alternatively, used in the next step without purification and/or isolation.

[0140] The nitro group of compound **128** is then converted to the primary amine by conventional reducing procedures to provide for compound **129**. Conventional reducing procedures include, but are not limited to, hydrogenation utilizing Pd/C. The reaction is preferably conducted in a suitable vessel such as a Parr apparatus, at room

temperature for a time sufficient to provide substantial reaction completion, which typically occurs in from 15 minutes to 1.5 hours. Compound **129** can be recovered by conventional techniques such as extraction, precipitation, chromatography, filtration and the like; or, alternatively, used in the next step without purification and/or isolation.

[0141] Subsequent conventional coupling of compound **129** with 2-phenyl-6-carboxyquinoxaline, compound **130**, provides for compound **131**.



Scheme III. General synthesis of 1-cyclohexyl-2-(2-"Y"-quinolin-6-yl)-1H-Benzoimidazole-5-carboxylic acid. .

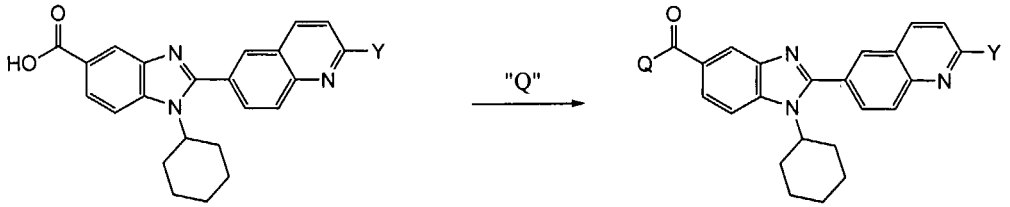
[0142] Compound **7** as prepared above is combined with a suitable ketone, such as acetophenone (where Y = phenyl or substituted phenyl), in a basic alcohol solvent system such as KOH/EtOH to provide the aromatized product, 2-Y-quinoline-6-carboxylic acid, compound **13**. Y may be an aryl group such as phenyl, substituted phenyl or an alkyl group such as methyl or other suitable functionality such as those particularly disclosed herein. Preferably, the reaction is allowed to proceed at an elevated temperature, preferably at the solvent reflux temperature, for a time sufficient to effect substantial completion of the reaction which typically occurs within 10 to 48 hours. After reaction completion, the resulting 2-Y-quinoline-6-carboxylic acid, compound **13**, can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0143] The carboxylic acid moiety of compound **13** is then converted to an acyl chloride by treating **13** with a suitable chlorinating agent. Chlorinating agents are well known in the art, and preferable chlorinating agents include thionyl chloride, oxalyl chloride, phosphorus trichloride, and the like. The reaction is subjected to conventional reaction conditions. Preferably, compound **13** is treated with thionyl chloride and the reaction is run neat, in the absence of other solvents, until substantial reaction completion. Typically, the reaction requires elevated temperatures such as the reflux temperature of thionyl chloride, for a time sufficient to produce substantial product, usually about 1 to 2 hours. After reaction completion, the resulting acyl chloride, compound **14**, can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0144] 2-Y-quinoline-6-carbonyl chloride, compound **14** undergoes aminolysis with compound **11**, as provided above, to produce the intermediate 4-cyclohexylamino-3-[(2-Y-quinoline-6-carbonyl)-amino]-benzoic acid ethyl ester, compound **15**. The aminolysis reaction is preferably conducted in the presence of an inert solvent such as DMF and requires at least a stoichiometric amount of compound **11**. The reaction is preferably conducted for a time sufficient for substantial reaction completion. Compound **15** can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like and is used in the subsequent step without further purification.

[0145] Compound **15** is then treated with acetic acid to affect cyclization and provide 1-cyclohexyl-2-(2-Y-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester (not shown). Cyclization is preferably performed at elevated temperatures, typically reflux temperatures of the solvent which usually occurs between 130 to 145 °C, for a time sufficient to provide substantial reaction completion, which typically occurs in 2 to 5 hours. Upon reaction completion, the resulting compound can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternatively, may be used in the next step without purification and/or isolation. An alternate cyclization protocol involves treating **15** with 10%TFA in

1,2-dichloroethane at the reflux temperature of the solution for a time sufficient to affect substantial reaction completion, which typically occurs between 3 to 10 hours. Upon reaction completion, the resulting compound can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternatively, may be used in the next step without purification and/or isolation. The ethyl ester is subsequently deprotected under basic reaction conditions in an appropriate aqueous alcoholic solvent such as ethanol. Preferably, the ethyl ester is treated with a base such as aqueous NaOH at an elevated temperature, such as the reflux temperature of the solvent. The reaction is allowed to continue for a time sufficient to effect substantial reaction completion, typically from 1 to 3 hours to provide compound **16**. Upon reaction completion, the resulting compound can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or additionally, purified **16** may be converted to the acid salt by treatment with HCl or other acid salt in an appropriate solvent, such as dioxane and ether, for a time sufficient to provide substantial salt formation, followed by conventional recovery techniques.

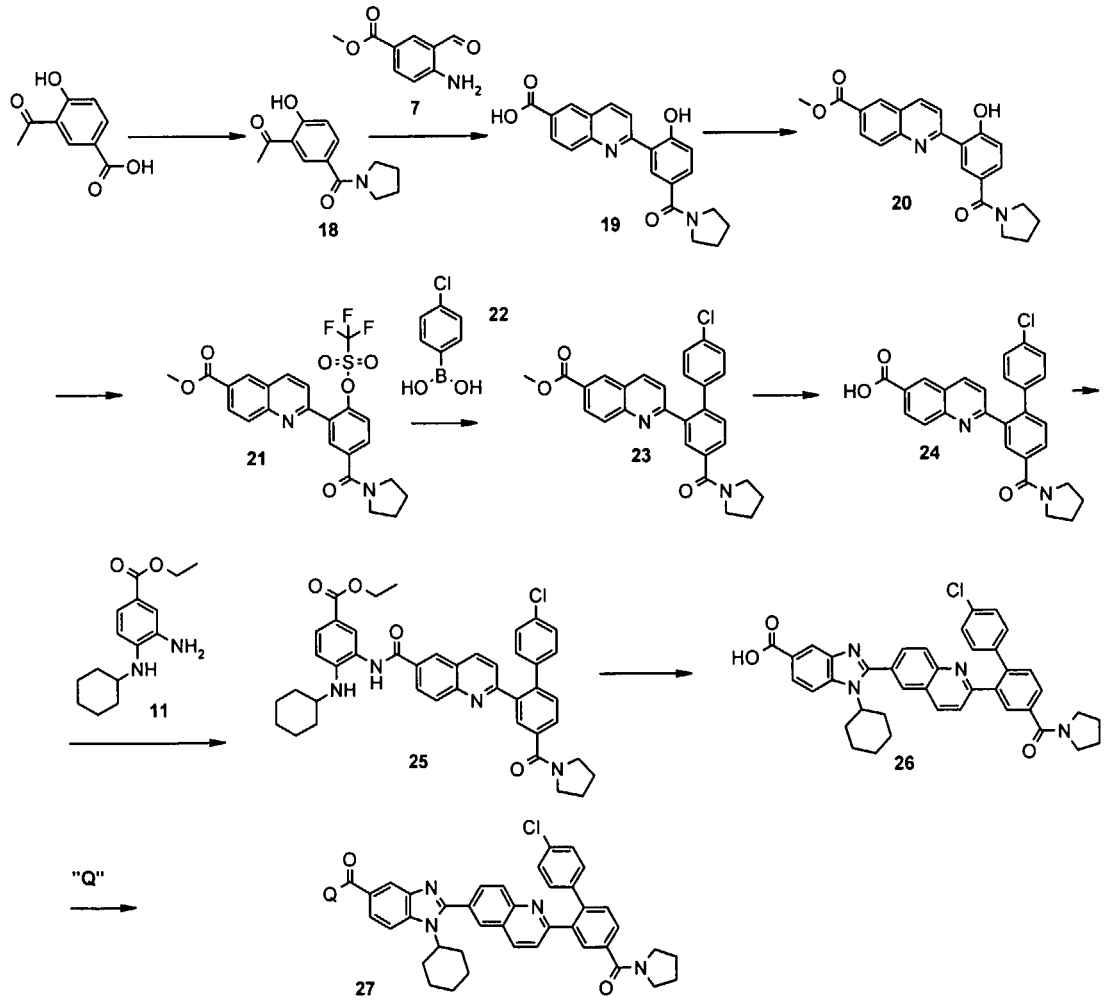


16 17

Scheme IV. General synthesis of 5-"Q"- 1-cyclohexyl-2-(2-"Y"-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid, compound **17**.

[0146] Compound **16** is further derivatized with a suitable moiety, Q. Preferred Q groups include those which give rise to Z groups as recited for the compounds of Formula I when Z is as defined in Formula I subset (b), (c – $C(O)NHSO_2R^4$)or (d). Preferably, compound **16** is coupled with Q wherein Q is a heteroatom containing group, preferably an amino or substituted amino group including, for example, substituted amino acids such as L-5-hydroxytryptophane. Suitable amino groups are well known in the art and include a variety of commercially available primary or secondary amines, and preferably, an amino acid or substituted amino acid derived

from an L isomer of an amino acid. Compound **16** is activated by conventional means, such as treatment with HBTU and DIEA at room temperature for a time sufficient to promote activation, typically from 5 to 20 minutes. Activated **16** is then treated with Q, for example, a nitrogen containing group, in an inert diluent such as *N,N*-dimethylformamide at room temperature for a period of time to effect substantial completion of the reaction which typically occurs within 30 minutes to 1 hour. After reaction completion, the resulting product, compound **17**, can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like. The purified product may also be converted to the acid salt by treatment of **17** with an appropriate acid salt, such as TFA, for a time sufficient for substantial reaction completion.



Scheme V. General synthetic scheme for the synthesis of 2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl derivatives.

[0147] Scheme V illustrates the general synthetic scheme for the synthesis of 2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl derivatives of the title compounds. Specifically, the carboxylic acid moiety of commercially available 3-acetyl-4-hydroxy-benzoic acid is converted to an amide by coupling with pyrrolidine. Other basic nitrogen containing compounds may be used in this reaction if other primary or secondary amide moieties are desired. The reaction is preferably conducted in the presence of an inert solvent such as DMF, and is performed at room temperature for a time sufficient to provide substantial conversion to the product, 1-[2-hydroxy-5-(pyrrolidine-1-carbonyl)-phenyl]ethanone **18** which typically occurs in from 30 minutes to 2 hours. After reaction completion, the resulting product can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, may be used in subsequent reaction without further purification.

[0148] Compound **18** is treated with compound **7**, which is produced as shown above, in an alcohol solvent. Treatment of the mixture with a base under inert atmosphere provides conditions appropriate for cyclization and affords compound **19**. Cyclization is preferably performed at elevated temperatures for a time sufficient to provide substantial reaction completion, which typically occurs in 10 to 48 hours. A suitable base/solvent can be, for example, KOH/ethanol, although other bases and solvents may also be used. Upon reaction completion, the resulting compound **19** can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternative, may be used in subsequent synthetic steps without purification and/or isolation.

[0149] The carboxylic acid of compound **19** is protected as a methyl ester by treatment of **19** with acidic methanol under conventional reaction conditions. Preferably, the reaction is performed at elevated temperature, from 50 to 80 °C for a time such that substantial conversion of starting material to the methyl ester has occurred, which typically is 12 to 24 hours. The corresponding methyl ester, **20**, once obtained, can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternatively, may be used in subsequent synthetic steps without purification and/or isolation.

[0150] The phenol of **20** is subsequently converted to the corresponding triflate or other good leaving group by treatment of **20** with, for example, triflic anhydride. The reaction is preferably conducted in an inert solvent, such as DCM in the presence of base, such as DMAP or pyridine. The reaction is typically conducted at room temperature for a time sufficient to provide substantial reaction completion, which typically occurs in about 10 to 48 hours. Compound **21** can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternative, may be used in subsequent synthetic steps without purification and/or isolation.

[0151] Compound **21** is coupled with a suitable boronic acid, such as para-chlorophenylboronic acid **22** to provide the biphenyl derivative, **23**. Other boronic acids may be used if other substituents or substitution patterns are desired. The reaction is conducted under conventional coupling reaction conditions, such as in the presence of a lithium salt and palladium catalyst in dioxane under an inert atmosphere. The reaction is preferably conducted at elevated temperatures, such as the reflux temperature of the solvent, for a time sufficient to allow substantial completion of the reaction, which typically occurs in 10 to 48 hours. Compound **23** can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternatively, may be used in subsequent synthetic steps without purification and/or isolation.

[0152] The methyl ester of compound **23** is then removed under basic conditions to provide compound **24**, which may be used in a subsequent synthetic step without purification and/or isolation. Deprotection protocols are well known in the art and preferably, the reaction involves treating **23** with a suitable base, such as aqueous sodium hydroxide, in an alcohol solvent at reflux temperature for about 1 to 3 hours to provide the quinolin carboxylic acid **24**.

[0153] The carboxylic acid of **24** is subsequently treated with compound **11**, which is prepared above, under conditions suitable to effect an amide linkage.

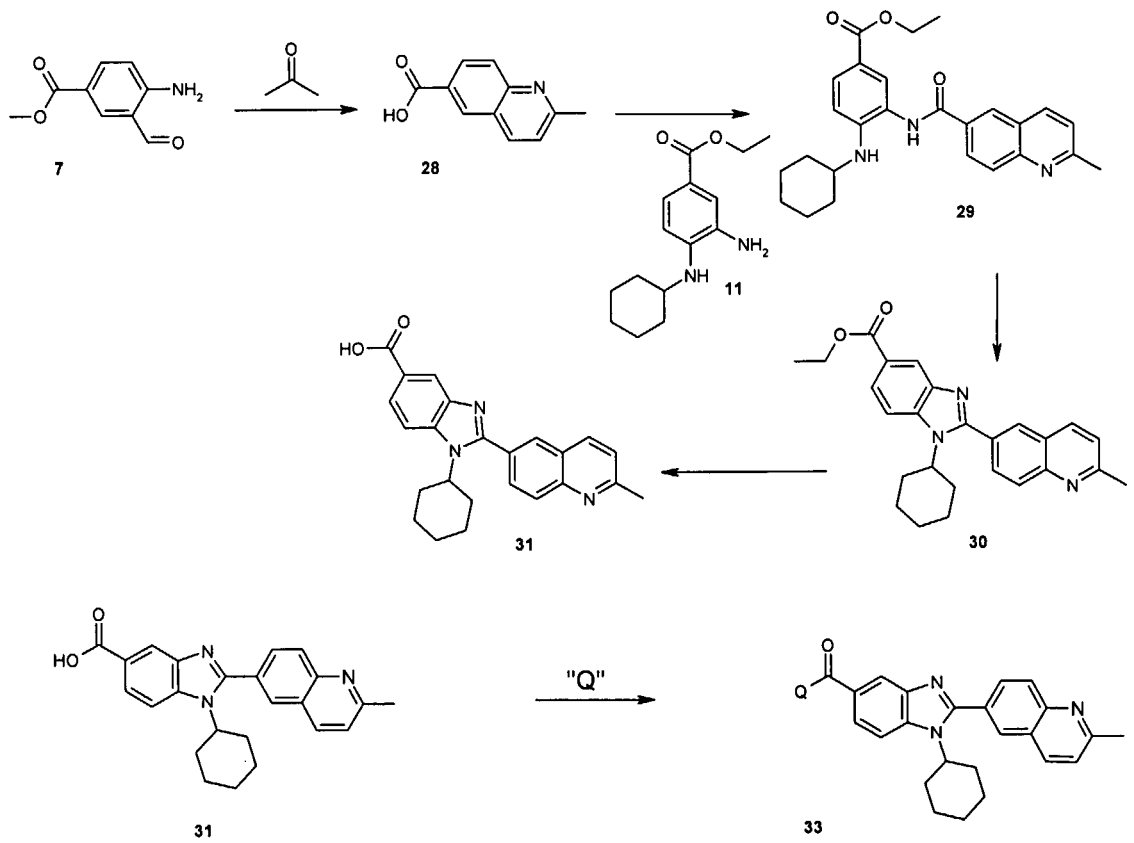
Preferably, compound **24** is activated with, for example, HATU and DIEA at room temperature for a time of from 10 to 30 minutes and is then treated with compound **11** at room temperature for a time sufficient to effect substantial reaction completion, typically between 10 to 48 hours. The resulting amide **25** may be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternatively, may be used in subsequent synthetic steps without purification and/or isolation.

[0154] Compound **25** is then treated with acetic acid to affect cyclization and provide the benzoimidazole-5-carboxylic acid ethyl ester (not shown). Cyclization is preferably performed at elevated temperatures, typically reflux temperature of the solution which usually occurs between 130 to 145 °C, for a time sufficient to provide substantial reaction completion, which typically occurs in 2 to 5 hours. Upon reaction completion, the resulting compound can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or, alternatively, may be used in the next step without purification and/or isolation. The ethyl ester is subsequently deprotected under basic reaction conditions in an appropriate alcoholic solvent such as ethanol. Preferably, the ethyl ester is treated with a base such as aqueous NaOH at an elevated temperature, such as the reflux temperature of the solvent. The reaction is allowed to continue for a time sufficient to effect substantial reaction completion, typically from 1 to 3 hours to provide compound **26**. Upon reaction completion, the resulting compound can be recovered by conventional techniques such as neutralization, extraction, precipitation, chromatography, filtration and the like; or additionally, purified compound **26** may be converted to the acid salt by treatment with HCl or other acid salt in an appropriate solvent, such as dioxane and ether, for a time sufficient to provide substantial salt formation, followed by conventional recovery techniques.

[0155] Compound **26** is further derivatized with any suitable Q moiety as recited above. Preferably, compound **26** is coupled with a substituted amino group, preferably a substituted amino acid such as L-5-hydroxytryptophane. Suitable amino groups are well known in the art and include a variety of commercially available primary

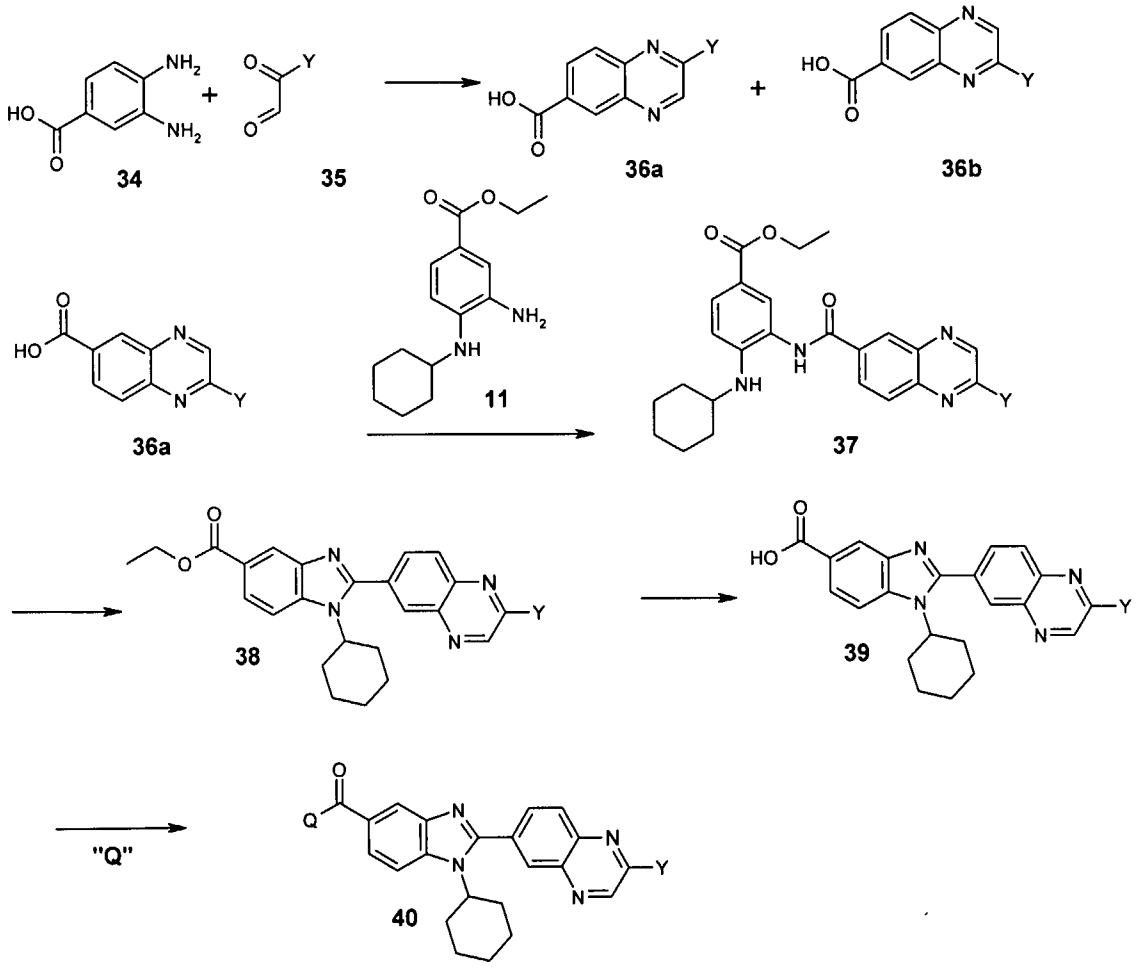
or secondary amines, and preferably, an amino acid or substituted amino acid derived from an L isomer of an amino acid. Compound **26** is activated by conventional means, such as treatment with HBTU and DIEA at room temperature for a time sufficient to promote activation, typically from 5 to 20 minutes. Activated compound **26** is then coupled with Q, such as, for example, an amino group, in an inert diluent such as *N,N*-dimethylformamide at room temperature for a period of time to effect substantial completion of the reaction which typically occurs within 30 minutes to 1 hour. After reaction completion, the resulting product, compound **27**, can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like. The purified product may also be converted to the acid salt by treatment of compound **27** with an appropriate acid salt, such as HCl, for a time sufficient for substantial reaction completion.

[0156] Compound **26** is shown in the tables as Compound **204**.



Scheme VI. General synthetic scheme for methyl substituted quinoline derivatives.

[0157] Scheme VI illustrates a synthetic scheme for producing methyl substituted quinoline derivatives of the title compounds utilizing the protocols provided in Schemes III and IV above.



Scheme VII. General synthesis of 2-"Y"-substituted quinoxaline derivates.

[0158] Scheme VII illustrates the conventional preparation of substituted quinoxaline derivates of the title compounds. Specifically, in Scheme VII, commercially available 3,4-diaminobenzoic acid is treated with a readily available dione, such as phenyl glyoxal (where Y = phenyl) under reaction conditions appropriate to effect cyclization to the quinoxaline. Preferably, the reaction is conducted under inert atmosphere under acidic reaction conditions, such as in acetic acid. The reaction is allowed to proceed at an elevated temperature, typically the reflux temperature of the solution, for a time sufficient to effect substantial cyclization, which typically occurs in about 1 to 4 hours. The

resulting quinoxaline isomers, **36a** and **36b** can be separated by conventional techniques such as by chromatography. Alternatively, the major isomer, compound **36a**, may be prepared using an alcoholic solvent such as ethanol at reduced temperatures such as 0°C for a time sufficient to effect substantial cyclization, typically 10 to 48 hours. The major isomer is then obtained by conventional separation techniques, such as, for example, filtration.

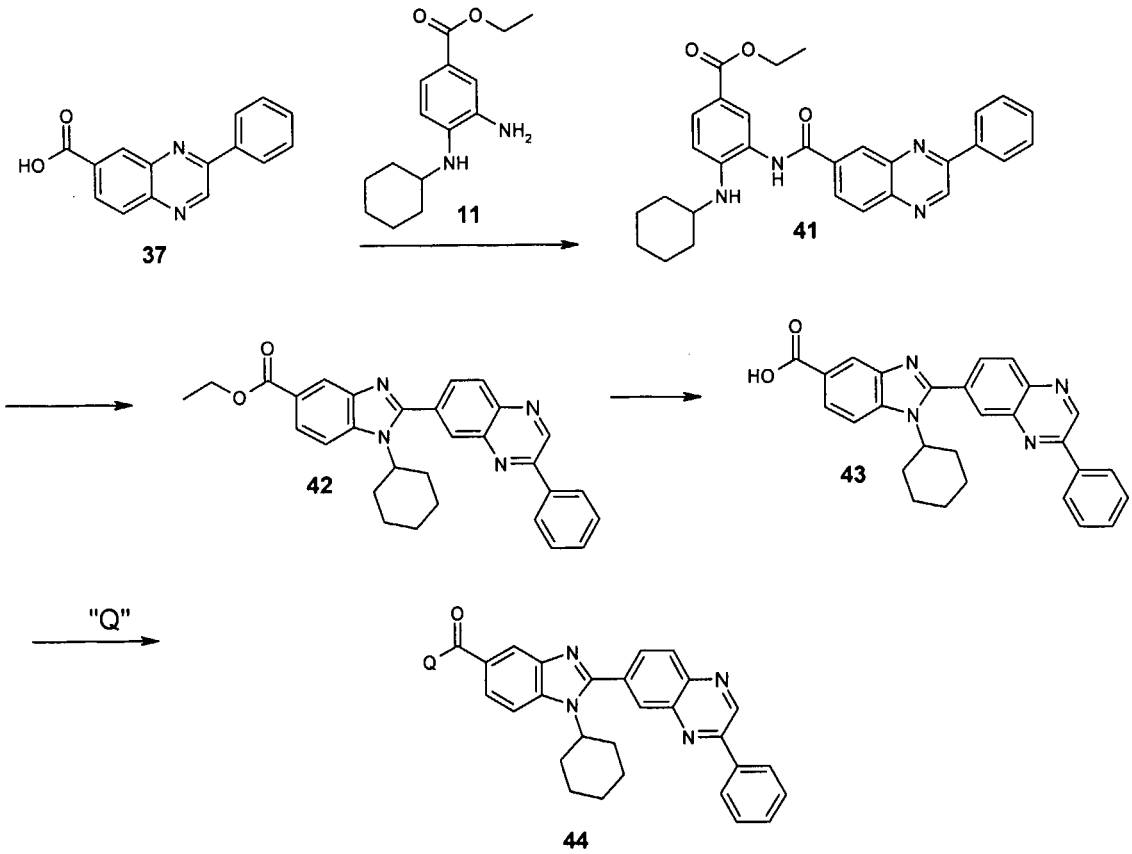
[0159] Compound **36a** is subsequently coupled with compound **11** as formed above to provide the intermediate amide product, compound **37**. Preferably, the reaction is conducted in an inert solvent, such as DMF, and compound **36a** is activated, for example, by treatment with HATU and DIEA for a time such that activation occurs, typically 5 to 30 minutes. Preferably, compound **11** is added to the reaction mixture under conditions appropriate to afford the amide product. Preferably, the reaction is conducted at around room temperature for a time sufficient to establish substantial product, compound **37**, which typically occurs in about 10 to 24 hours. Upon reaction completion, the resulting amide can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0160] The amide, compound **37,** is subsequently cyclized by treatment with acid at elevated reaction temperatures. Preferably, the reaction is conducted at, for example, reflux temperature of the solution, for a time sufficient to promote substantial cyclization, which typically occurs in from 2 to 6 hours. Preferably, the reaction is run neat in glacial acetic acid. The resulting product, compound **38**, may be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0161] The ethyl ester of compound **38** is subsequently removed by treatment with an aqueous base in an appropriate alcoholic solvent. Preferably, the reaction is conducted at elevated temperatures in the presence of a base such as NaOH for a time sufficient to afford substantial deprotection and production of the corresponding carboxylic acid, compound **39**. The resulting product, compound **39**, may

be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.

[0162] Compound **39** is optionally derivatized with any suitable amino or substituted amino moiety shown as "Q". Amino groups are well known in the art and it is apparent that readily available amines may be used in this reaction. Preferably, compound **39** is treated with a substituted amino acid such as L-5-hydroxytryptophane. The reaction is preferably conducted in an inert diluent such as DMF at room temperature for a portion of time to effect substantial completion of the reaction which typically occurs within 30 minutes to 1 hour. After reaction completion, the resulting product, **40** can be isolated by conventional techniques such as extraction, filtration, chromatography, and the like; or, alternatively, used in the next step without purification and/or isolation.



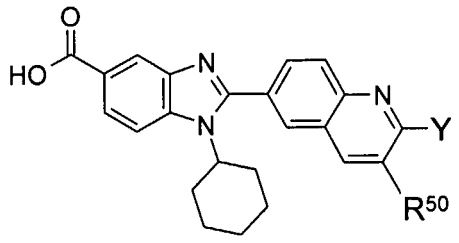
Scheme VIIa. General synthesis of 3-phenyl-substituted quinoxaline derivates.

[0163] Scheme VIIa illustrates the conventional preparation of 3-substituted quinoxaline derivates of the title compounds. More specifically, the phenyl-

substituted derivative is exemplified above, although this group is readily substituted with, for example, a methyl group as has been shown with the previous examples. Compound **37** as obtained above, is aminated with compound **11** under conventional protocols, such as those described above, to afford the quinoxaline derivative **41**. Similarly to the above synthetic schemes, compound **41** may undergo cyclization under acidic reaction conditions to afford the cyclized product **42**. Hydrolysis of the ethyl ester protecting group, as in the above Schemes, provides compound **43**. Optional derivatization with an amino group, represented by "Q" affords product **44**. The synthetic protocols in this Scheme may be inferred from the examples depicted in the Schemes above.

[0164] In addition to the foregoing Schemes, the following examples illustrate Het-Y groups that are within the scope of the present invention. Specifically, illustrative compounds **I-A** to **I-W** below optionally may be further derivatized with functional groups, for example, with amino, substituted alkyl, heteroaryl, sulfonamido, or other suitable functional groups. It is recognized throughout that further derivatization may require the use of protecting groups and protecting group strategies such that selective reactions may be pursued. Accompanying the illustrative examples below are preferred synthetic protocols which are useful in obtaining the the compounds of formula **I-A** to **I-W**. In the illustrations below, R^{50}, which is selected from hydrogen, Y or X', denotes an optional substituent on HET (when R^{50} is not hydrogen) where X' and Y are as defined above.

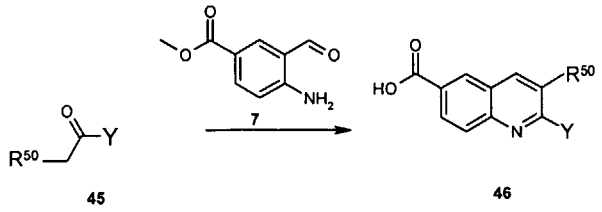
3-Substituted Quinoline Het-Y:



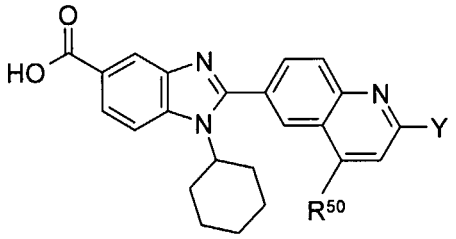
I-A

[0165] **I-A** may be obtained by the protocols above using the intermediate **46** the synthesis is as described below. The preferred intermediate **46** is to be synthesized

as described for **19** except **18** is replaced with the analogues alkyl-aryl-ketone, **45,** whose synthesis is described in R.P.Thummel, S.Chirayl, C.Hery, J-L. Lim, T-L Wang, J.Org.Chem., 1993, **58**, 1666-1671.

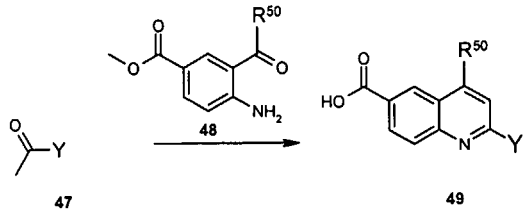


4-Substituted Quinoline Het-Y:

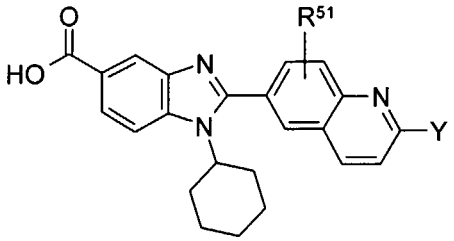


I-B

[0166] I-B may be optionally further modified as per the above Schemes to afford title compounds with a 4-substituted quinolin Het-Y moiety. I-B may be obtained as shown above, using compound **49** as an intermediate the synthesis of which is described below. The preferred compound **49** is to be synthesized as described for compound **19** except compound **7** is replaced with alkyl-aryl-ketone, compound **47**, whose synthesis is described in R.P.Thummel, S.Chirayl, C.Hery, J-L. Lim, T-L Wang, J.Org.Chem., 1993, **58**, 1666-1671.

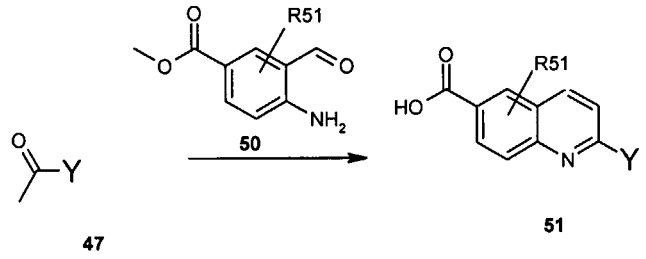


5 or 7 or 8-Substituted Quinoline Het-Y:



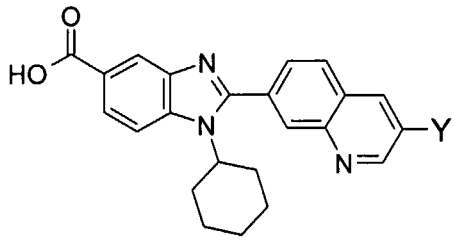
I-C

[0167] In formula I-C, R^{51} is selected from hydrogen, X and Y where X and Y are as defined above. I-C may be optionally further modified as per the above Schemes to afford the title compounds with a 5 or 7 or 8-substituted quinoline Het-Y moiety. I-C may be obtained from the intermediate **51** the synthesis of which is described below. The preferred intermediate is to be synthesized as described for **19** except **7** is replaced with the analogues alkyl-substituted amino-aldehyde, **50**, synthesized as described in R.P.Thummel, S.Chirayl, C.Hery, J-L. Lim, T-L Wang, J.Org.Chem., 1993, **58**, 1666-1671.



47 **50** **51**

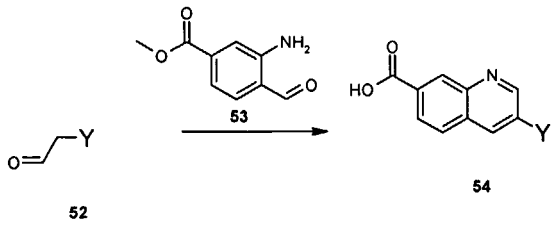
3,7-Quinoline Het-Y:



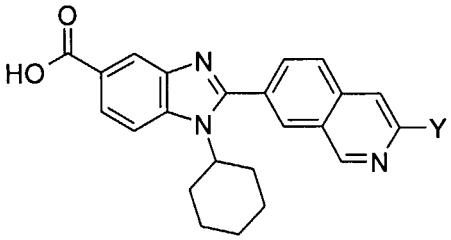
I-D

[0168] I-D may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-quinoline Het-Y moiety. I-D may be obtained from the intermediate **54** the synthesis of which is described below. The preferred intermediate

is to be synthesized as described for **19** except **7** and **18** are replaced with **53** and **52**, respectively, synthesized as described in R.P.Thummel, S.Chirayl, C.Hery, J-L. Lim, T-L Wang, J.Org.Chem., 1993, **58**, 1666-1671.

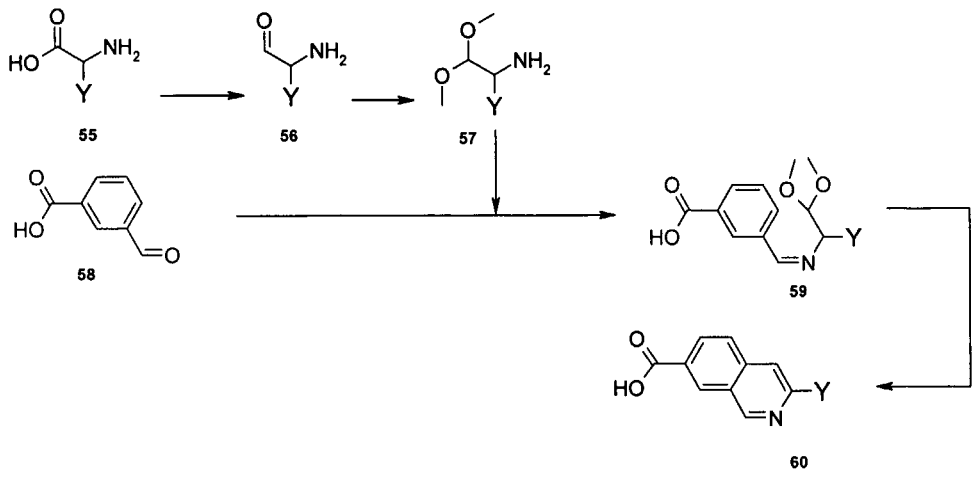


3,7-Isoquinoline Het-Y:

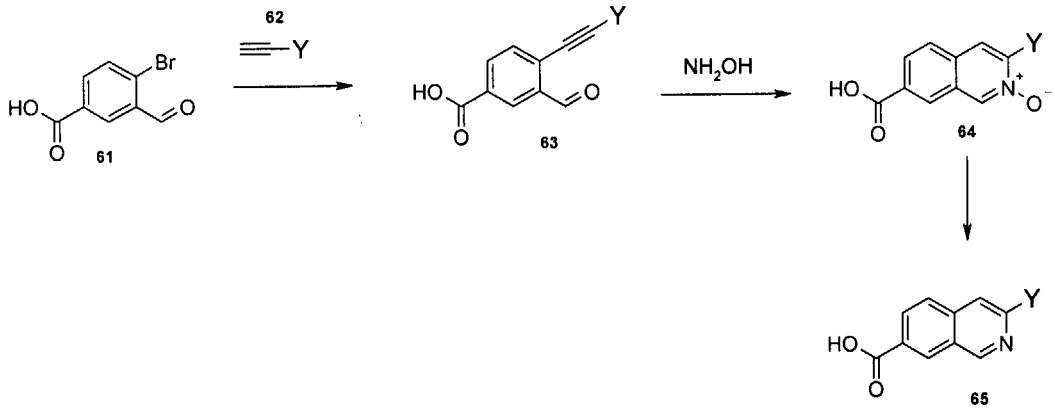


I-E

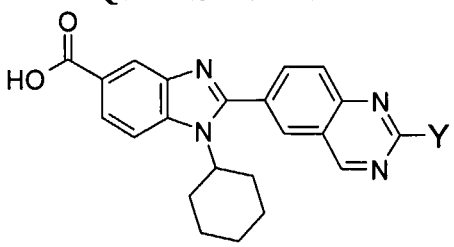
[0169] I-E may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-isoquinoline Het-Y moiety. I-E may be obtained from the intermediate **60** the synthesis of which is described below. The preferred 3,7-isoquinoline intermediate **60** is synthesized by a modification of the Pomeranz-Fritsch reaction described in Gensler, W.J., Organic Reactions, 1951, 6, 191 and Kucznierz, R. et al., Synth. Commun., 1999, 29, 1617 and shown directly below with numerical indicators **55** to **60**.



[0170] Alternatively, another preferred protocol is utilized to synthesize the key 3,7-isoquinoline intermediate by modification of the procedure described in Numata, A., et al., Synthesis, 1999, 306, followed by reduction of the isoquinoline N-oxide with triphenylphospine as described in Katrizky, A.R., Lam, J.N., Heterocycles, 1992, 33, 1011, as shown directly below with the compounds numbered **61** to **65**. Note that the alternative procedure provides the same preferred intermediate above, with the numerical indicator **65** illustrating the second reaction protocol. Thus, **60** is the same intermediate as **65**.

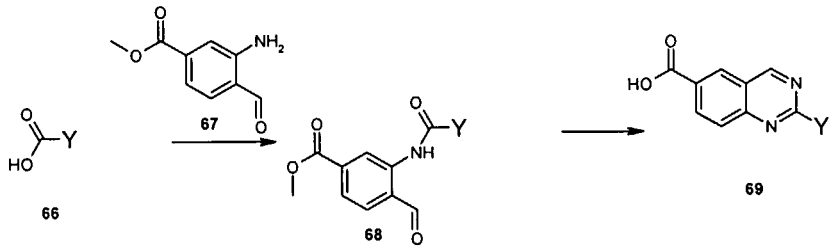


Quinazoline Het-Y:



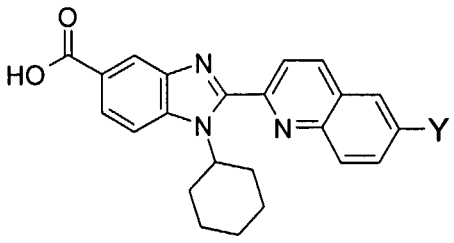
I-F

[0171] I-F may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-isoquinoline Het-Y moiety. I-F may be obtained from the intermediate **69** the synthesis of which is provided as shown below.



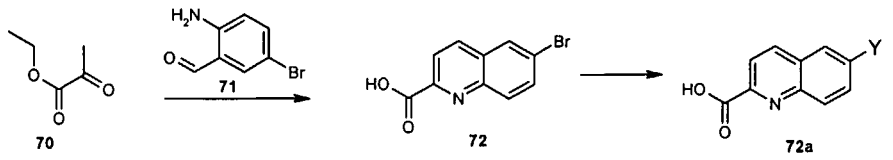
[0172] To form the preferred intermediate, **67** is first acylated with **66** using a standard coupling reagent (e.g. HATU). The resulting amide, **68** is to be heated with alcoholic ammonia as described by A. Biscler et al., Berichte, 1895, 28 to afford the intermediate **69**.

Reverse 2,6-Quinoline linker Het-Y:



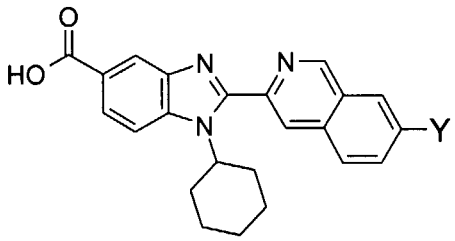
I-G

[0173] I-G may be optionally further modified as per the above Schemes to afford the title compounds with a 2,6-quinoline Het-Y moiety. I-G may be obtained from the intermediate **72** which is provided as shown below.



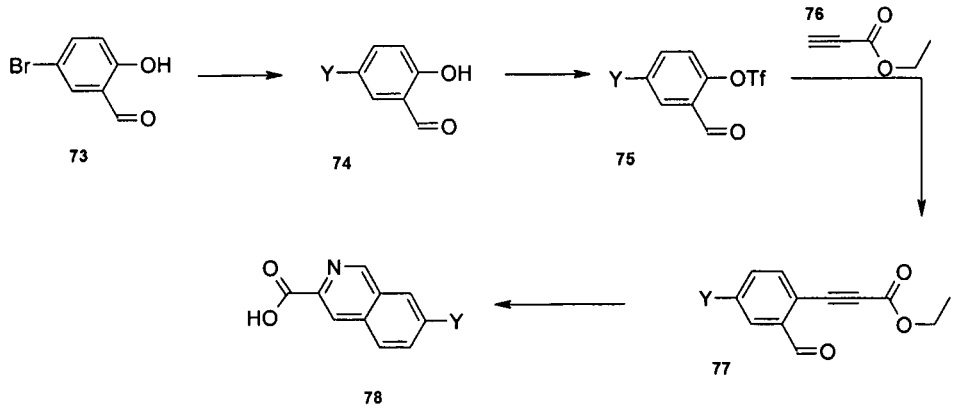
[0174] The preferred intermediate is to be synthesized as described for **19** except **7** and **18** are replaced with ethyl-pyruvate, **70**, and **71**, respectively as described in R.P.Thummel, S.Chirayl, C.Hery, J-L. Lim, T-L Wang, J.Org.Chem., 1993, **58**, 1666-1671. **72** may be further derivatized with the substituted aryl moiety by using standard coupling procedures, such as Suzuki conditions using the appropriately substituted aryl boronic acid to provide for intermediate **72a**.

3,7-Isoquinoline Het-Y:



I-H

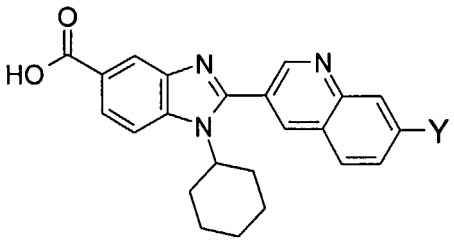
[0175] I-H may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-isoquinoline Het-Y moiety. I-H may be obtained from the intermediate **78** which is provided as shown below.



[0176] The preferred "reversed" 3,7-isoquinoline intermediate is synthesized by reaction of commercial 5-bromosalicylaldehyde **73** with the appropriate

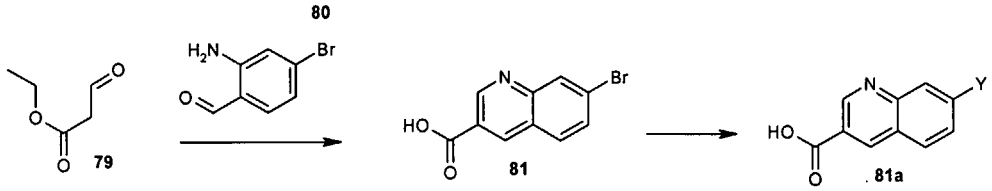
aryl boronic acid under Suzuki conditions. The product, **74**, is then converted to the triflate, **75**, using standard conditions (triflic anhydride, 2,6-lutidine in dichloromethane). This intermediate and commercial ethyl propynoate, **76**, are then used to synthesize the desired isoquinoline by modification of the procedure described in Numata, A., et al., Synthesis, 1999, 306, followed by reduction of the isoquinoline N-oxide with triphenylphospine as described in Katrizky, A.R., Lam, J.N., Heterocycles, 1992, 33, 1011 to afford the intermediate **78**.

Reverse 3,7-Quinoline linker:



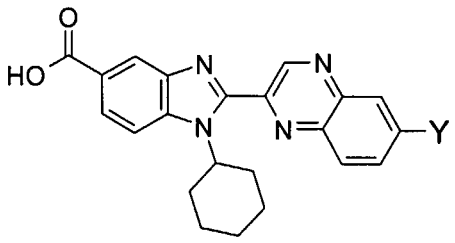
I-I

[0177] I-I may be optionally further modified as per the above Schemes to afford the title compounds with a reverse 3,7-quinoline Het-Y moiety. I-I may be obtained from the intermediate **81** which is provided as shown below.



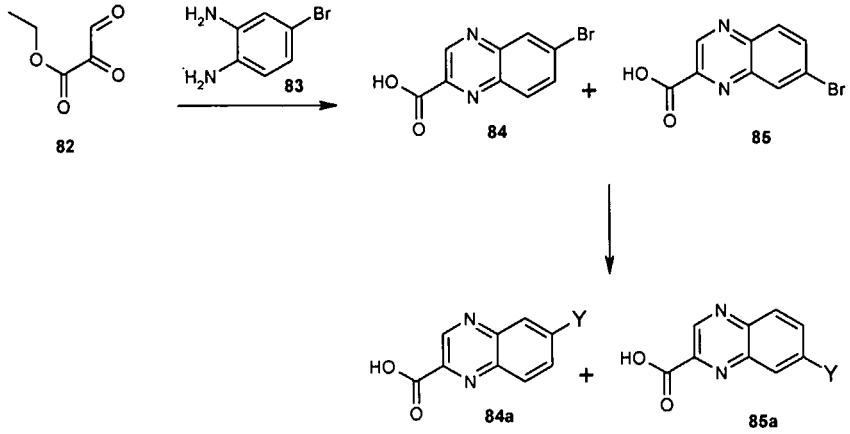
[0178] The preferred intermediate, **81**, is to be synthesized as described for **19** except **7** and **18** are replaced with **79** and **80**, respectively, as described in R.P.Thummel, S.Chirayl, C.Hery, J-L. Lim, T-L Wang, J.Org.Chem., 1993, **58**, 1666-1671 which is then coupled using Suzuki conditions to the appropriately substituted aryl boronic acid to provide the aryl substituted product **81a**.

Reverse Quinoxaline Het-Y:



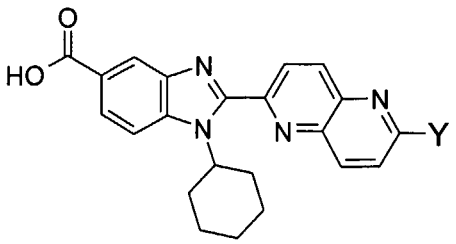
I- J

[0179] I-J may be optionally further modified as per the above Schemes to afford the title compounds with a reverse quinoxaline Het-Y moiety. I-J may be obtained from the intermediate **85** which is provided as shown below.



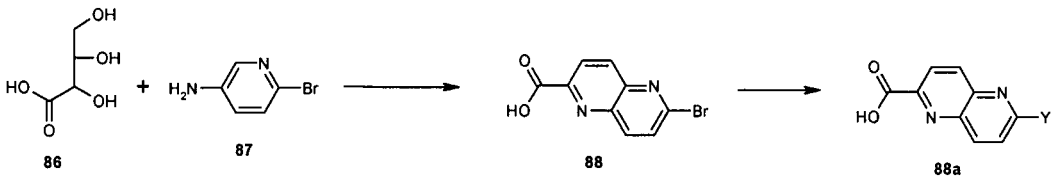
[0180] The preferred intermediate is to be synthesized as described for **36** and **37** except 3,4-diaminobenzoic acid, **34**, and phenylglyoxal, **35**, are replaced with **82** and **83**, respectively as described in F. Roubinek, V. Bydzovsky and Z. Budesinsky, *Coll. Czech. Chem. Commun., **49**, 285, 1984.* The resulting isomers, compounds **84** and **85** are then resolved and then coupled using Suzuki conditions to the appropriate substituted aryl boronic acid to provide the aryl substituted reverse quinoxaline, compounds **84a** and **85a**.

[1,5]-Naphthyridine Het-Y:



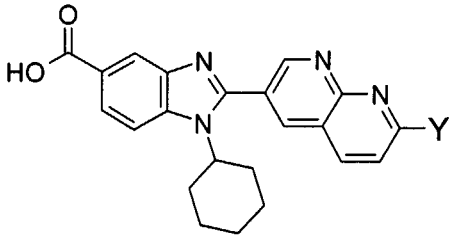
I-K

[0181] I-K may be optionally further modified as per the above Schemes to afford the title compounds with a [1,5]-Naphthyridine Het-Y moiety. I-K may be obtained from the intermediate **88** which is provided as shown below:



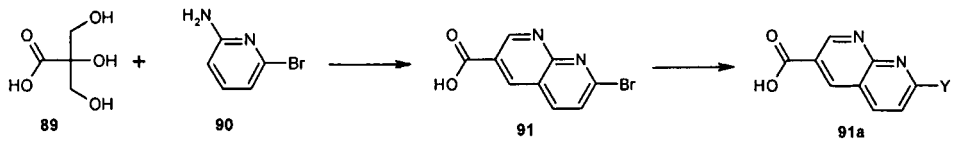
[0182] The preferred intermediate, compound **88**, is to be synthesized using the procedure described by X.Li, Z.Xu, E.F. Erin, M.C. Kozlowski, Tetrahedron Lett., ***43***(20), 3747 (2002) utilizing **87** (synthesis described in V.S.Binz, *Chem.Ber.*, **68**, 1935; 315;321) and **86**. This is then coupled using Suzuki conditions to the appropriate substituted aryl boronic acid to provide the aryl substituted [1,5]-naphthyridine product, compound **88a**.

3,7-Substituted [1,8]-Naphthyridine Het-Y:



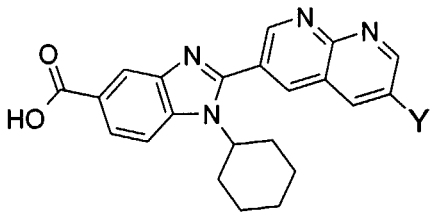
I-L

[0183] I-L may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-substituted [1,8]-naphthyridine Het-Y moiety. I-L may be obtained from the intermediate **91** which is provided as shown below:



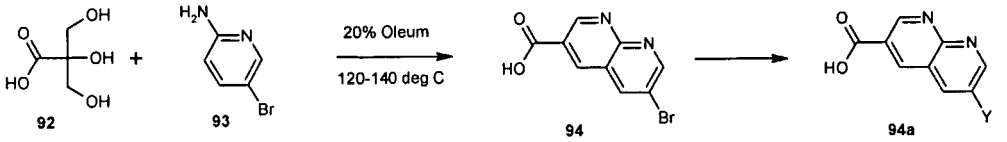
[0184] The preferred intermediate, compound **91**, is synthesized using the procedure described by H. Bock, T.T.H. Van, H. Schoedel, *Monatsh. Chem.*, 127; 4; 1996; 391-396 utilizing **89** (described in Coleman, Glattfeld, *J. Am. Chem. Soc.*, ***66,*** 1944; 1183; 1186) and **90**. The bromo-substituted product is then coupled using Suzuki conditions to the appropriate substituted aryl boronic acid to afford the aryl substituted 3,7-substituted [1,8]-naphthyridine product compound **91a**.

3,6-Substituted [1,8]-Naphthyridine Het-Y:



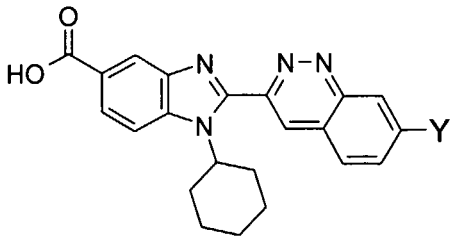
I-M

[0185] I-M may be optionally further modified as per the above Schemes to afford the title compounds with a 3,6-Substituted [1,8]-Naphthyridine Het-Y moiety. I-M may be obtained from the intermediate **94** which is provided as shown below:



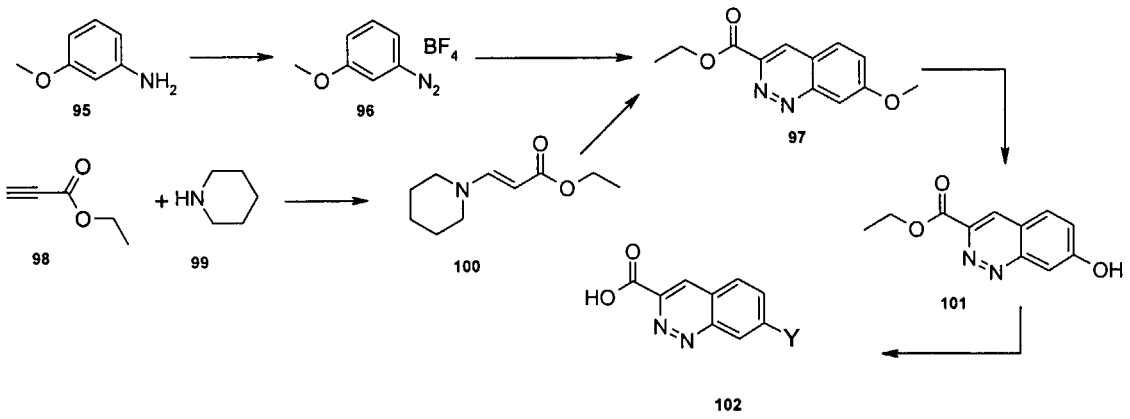
[0186] The preferred intermediate, **94**, is synthesized using the procedure described by H. Bock, T.T.H. Van, H. Schoedel, *Monatsh. Chem.*, 127; 4; 1996; 391-396 utilizing **93** (whose synthesis is described in Coleman, Glattfeld, *J. Am. Chem. Soc.*, ***66,*** 1944; 1183; 1186) and **92**. This is then coupled using Suzuki conditions to the appropriate substituted aryl boronic acid to provide the aryl substituted 3,6-Substituted [1,8]-naphthyridine product, **94a**.

3,7-Cinnoline Het-Y:



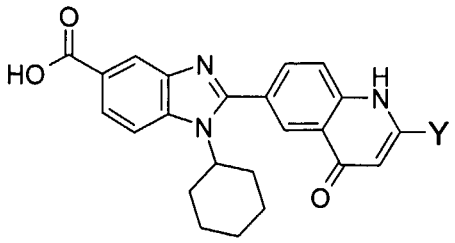
I-N

[0187] I-N may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-Cinnoline Het-Y moiety. I-N may be obtained from the intermediate **102** which is provided as shown below:



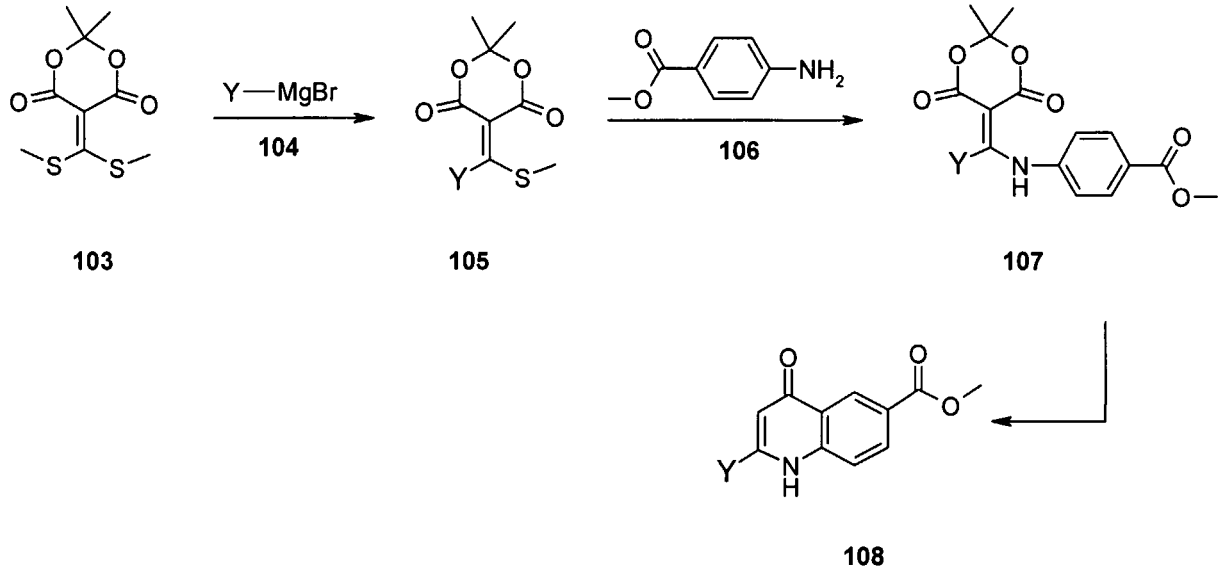
[0188] The preferred 3,7-cinnoline intermediate, **102**, is synthesized by conversion of commercial anisidine **95** to its diazo form **96** (synthesis described in Hanson, P. et al., J. Chem. Soc. Perkin Trans. 2, 2002, 6, 1135.) and then coupled with ethyl (E)-3-piperidinoacrylate **100** to yield the 3-carboxyethyl-7-methoxy-cinnoline **97** as described in Kanner, C.B., Pandit, U.K., Tetrahedron, 1982, 38,3597. The methoxy group is deprotected to the phenol **101** using standard BBr_3 conditions. Intermediate **101** is then converted to the triflate (not shown) using standard conditions (triflic anhydride, 2,6-lutidine in dichloromethane) and finally converted to the preferred intermediate **102** via a Suzuki reaction with the appropriately substituted aryl boronic acid.

2,6-1H-Quinolin-4-one Het-Y:



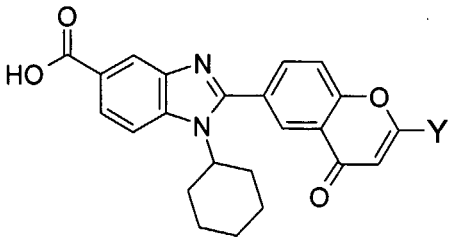
I-O

[0189] I-O may be optionally further modified as per the above Schemes to afford the title compounds with a 2,6-1H-Quinolin-4-one Het-Y moiety. I-O may be obtained from the intermediate **107** which is provided as shown below:



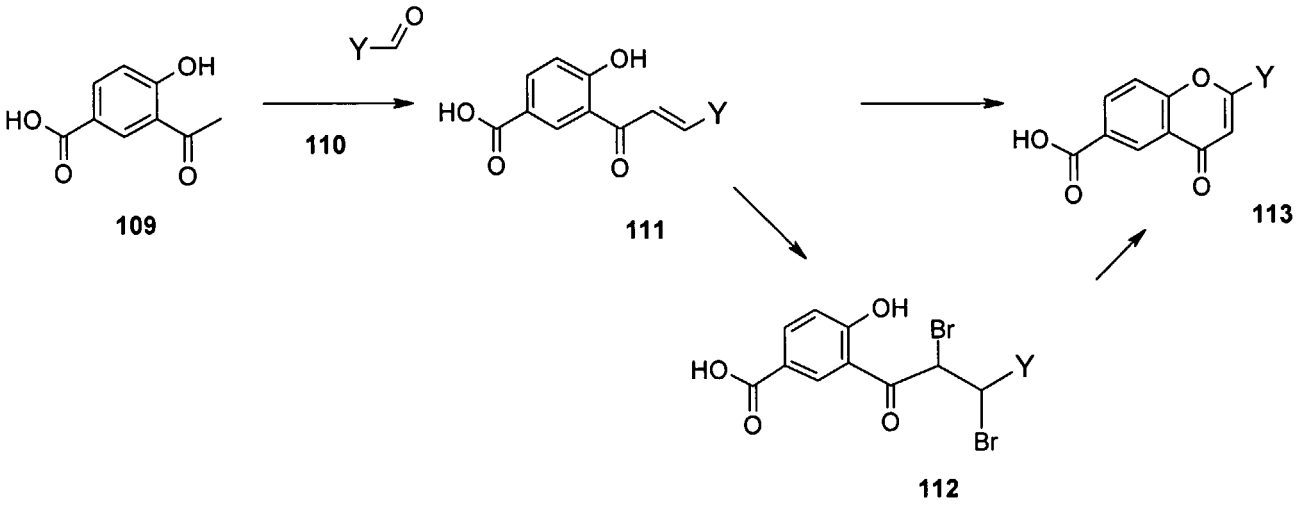
[0190] The key intermediate **108** is synthesized by a variation of the Conrad-Limpach-Knorr synthesis. Commercial starting material **103** is reacted with the appropriate aromatic Grignard-reagent, Compound **104**, (or other appropriate organometallic) to yield compound **105** as described in J.Chem. Soc. Perkin Trans. I 10, 1995; 1209-1214. Subsequent nucleophilic attack of amine **106** yields compound **107** as described in Synthesis 1987, 5, 482-483. **107** is then heated in Dowtherm A at 240 °C to yield compound **108** as described in J.Med. Chem. 38; 22; 1995; 4439-4445 or Eur. J. Med. Chem. Chim. Ther. 32; 7-8; 1997; 547-570.

2,6-Chromen-4-one Het-Y:



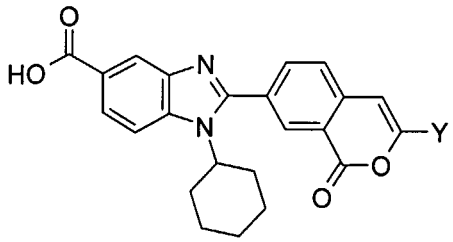
I-P

[0191] I-P may be optionally further modified as per the above Schemes to afford the title compounds with a 2,6-chromen-4-one Het-Y moiety. I-P may be obtained from the intermediate **112** which is provided as shown below.



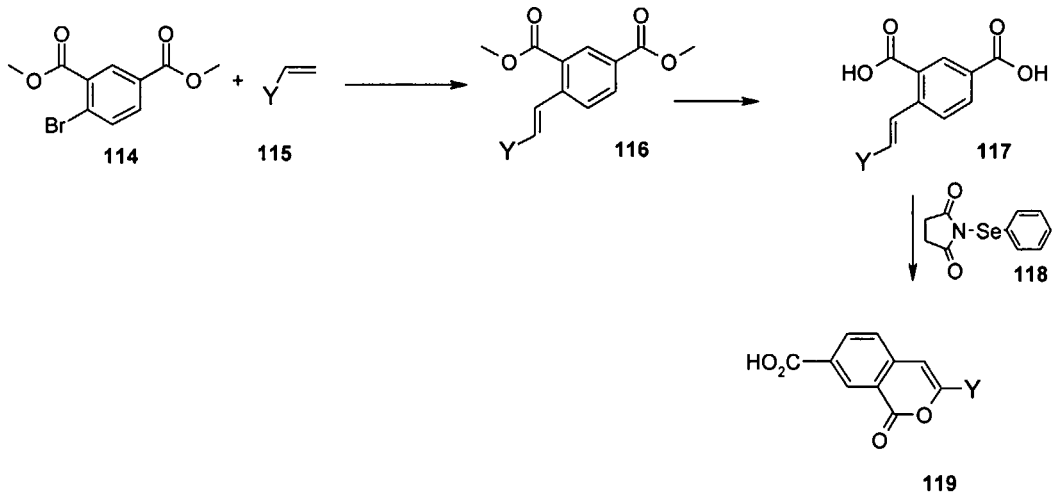
[0192] The preferred intermediate is synthesized by an aldol condensation performed on starting material **109** with the appropriate substituted aldehyde **110** with sodium hydroxide in ethanol, as described in Eur. J. Med. Chem. Chim. Ther. 31; 11;1996; 861-874 or J. Med. Chem. 23;3;1980; 335-338. Subsequent cyclization to **113** is accomplished using selenium dioxide in amyl alcohol at 150 °C or DDQ as described in JACS 77; 1955; 2223 or Eur. J. Med. Chem. Chim. Ther. 13; 1978; 33-39. Alternatively the double-bond of enone **111** is brominated to give **112**, which in turn is cyclized to give **113**, using aqueous potassium hydroxide as catalyst, as described in J. Med. Chem. 23;3;1980; 335-338.

3,7-Isochromen-1-one Het-Y:



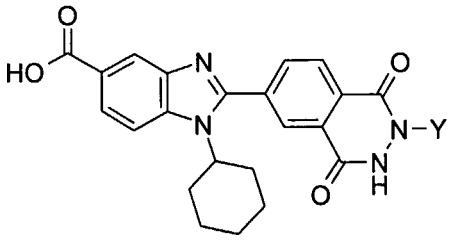
I-Q

[0193] I-Q may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-isochromen-1-one Het-Y moiety. I-Q may be obtained from the intermediate **119** which is provided as shown below.



[0194] The preferred intermediate **119** is synthesized via a modification of Izumi, et al., Heterocycl. Chem. 31;1;1994;145-152. Starting material **114** (described in J. Heterocycl. Chem. 31;1;1994;145-152) is coupled via standard Heck reaction conditions to the appropriate styrene **115** to give **116**. Hydrolysis of the methyl esters of **116** with sodium hydroxide gives the free acid **117**, which is then oxidatively cyclized using selenium reagent **118** to give intermediate **119**.

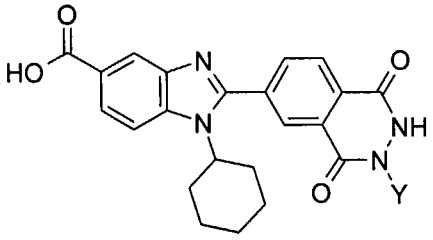
2,6-(2,3-Dihydrophthalazine-1,4-dione) Het-Y:



I-R

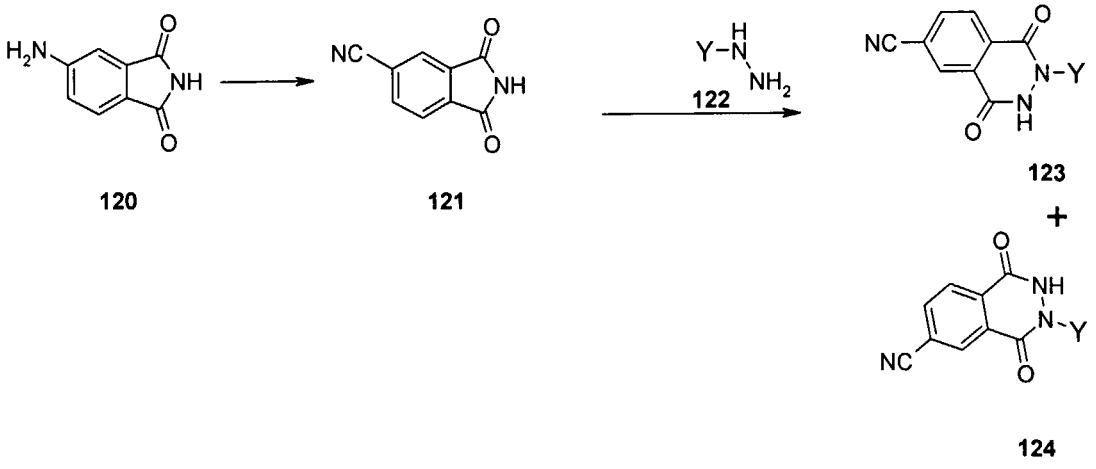
[0195] I-R may be optionally further modified as per the above Schemes to afford the title compounds with a 2,6-(2,3-Dihydrophthalazine-1,4-dione) Het-Y moiety. I-R may be obtained from the intermediate **124** which is provided as shown below:

2,7-(2,3-Dihydrophthalazine-1,4-dione) Het-Y:



I-S

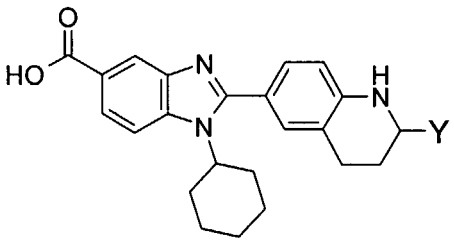
[0196] I-S may be optionally further modified as per the above Schemes to afford the title compounds with a 2,7-(2,3-Dihydrophthalazine-1,4-dione) Het-Y moiety. I-S may be obtained from the intermediate **124** which is provided as shown below.



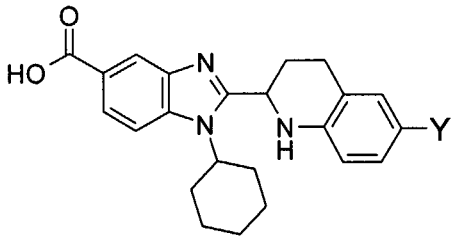
120 **121** **122** **123** **124**

[0197] The preferred intermediates are synthesized via a modification of the procedure described by Watanabe, N., et al., J. Med. Chem. 1998, 41, 3367-3372. Amine **120** is converted to **121** by formation and subsequent nucleophilic displacement with cyanide of the diazonium salt. **121** is then reacted with the appropriate substituted hydrazine **122** to give a mixture of **123** and **124**. This mixture is then resolved via chromatography or crystallization into its pure forms. Intermediate **123** is then utilized to synthesize **I-R** and intermediate **124** is used to synthesize **I-S**.

3,7-tetrahydroquinoline (I-T) andreversed 3,7-tetrahydroquinoline (I-T) Het-Y:



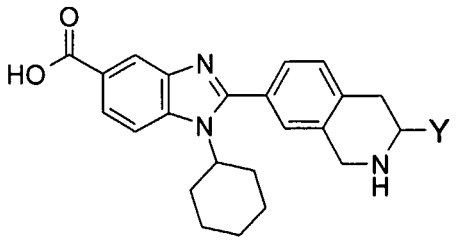
I-T



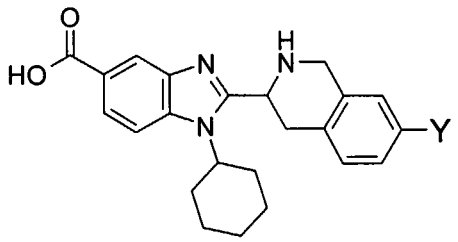
I-U

[0198] I-T and I-U may be optionally further modified as per the above Schemes to afford the title compounds with a 3,7-tetrahydroquinoline (I-T) and reversed 3,7-tetrahydroquinoline (I-T) Het-Y moiety. I-T and I-U may be obtained from by selective catalytic reduction of the aromatic Het-Y molecule with PtO_2 utilizing a modification of the procedure described in Maillard, M.C., et al., J. Med. Chem., 1998, 41, 3048.

3,7-tetrahydroisoquinoline and reversed 3,7-tetrahydroisoquinoline Het-Y:



I-V



I-W

[0199] I-V and I-W may be used in the above Schemes to afford the title compounds with a 3,7-tetrahydroisoquinoline (I-V) and reversed 3,7-tetrahydroisoquinoline (I-W) Het-Y moiety. I-V and I-W may be obtained from selective catalytic reduction of the aromatic Het-Y molecule with PtO_2 utilizing a modification of the procedure described in Maillard, M.C., et al., J. Med. Chem., 1998, 41, 3048.

Utility

[0200] The present invention provides novel compounds possessing antiviral activity, including *Flaviviridae* family viruses such as hepatitis C virus. The compounds of this invention inhibit viral replication by inhibiting the enzymes involved in replication, including RNA dependent RNA polymerase. They may also inhibit other enzymes utilized in the activity or proliferation of *Flaviviridae* viruses.

[0201] Compounds of this invention maybe used alone or in combination with other compounds to treat viruses.

Administration and Pharmaceutical Composition

[0202] In general, the compounds of this invention will be administered in a therapeutically effective amount by any of the accepted modes of administration for

agents that serve similar utilities. The actual amount of the compound of this invention, i.e., the active ingredient, will depend upon numerous factors such as the severity of the disease to be treated, the age and relative health of the subject, the potency of the compound used, the route and form of administration, and other factors. The drug can be administered more than once a day, preferably once or twice a day.

[0203] Therapeutically effective amounts of compounds of Formula I may range from approximately 0.1 to 20 mg per kilogram body weight of the recipient per day, more preferably from about 0.1 to 10 mg/kg/day.

[0204] In general, compounds of this invention will be administered as pharmaceutical compositions by any one of the following routes: oral, systemic (e.g., transdermal, intranasal or by suppository), or parenteral (e.g., intramuscular, intravenous or subcutaneous) administration. The preferred manner of administration is oral using a convenient daily dosage regimen that can be adjusted according to the degree of affliction. Compositions can take the form of tablets, pills, capsules, semisolids, powders, sustained release formulations, solutions, suspensions, elixirs, aerosols, or any other appropriate compositions. Another preferred manner for administering compounds of this invention is inhalation. This is an effective method for delivering a therapeutic agent directly to the respiratory tract, in particular for the treatment of diseases such as asthma and similar or related respiratory tract disorders (see U.S. Patent 5,607,915).

[0205] The choice of formulation depends on various factors such as the mode of drug administration and bioavailability of the drug substance. For delivery via inhalation the compound can be formulated as liquid solution, suspensions, aerosol propellants or dry powder and loaded into a suitable dispenser for administration. There are several types of pharmaceutical inhalation devices-nebulizer inhalers, metered dose inhalers (MDI) and dry powder inhalers (DPI). Nebulizer devices produce a stream of high velocity air that causes the therapeutic agents (which are formulated in a liquid form) to spray as a mist that is carried into the patient's respiratory tract. MDI's typically are formulation packaged with a compressed gas. Upon actuation, the device discharges a measured amount of therapeutic agent by compressed gas, thus affording a reliable

method of administering a set amount of agent. DPI dispenses therapeutic agents in the form of a free flowing powder that can be dispersed in the patient's inspiratory air-stream during breathing by the device. In order to achieve a free flowing powder, the therapeutic agent is formulated with an excipient such as lactose. A measured amount of the therapeutic agent is stored in a capsule form and is dispensed with each actuation.

[0206] Recently, pharmaceutical formulations have been developed especially for drugs that show poor bioavailability based upon the principle that bioavailability can be increased by increasing the surface area i.e., decreasing particle size. For example, U.S. Pat. No. 4,107,288 describes a pharmaceutical formulation having particles in the size range from 10 to 1,000 nm in which the active material is supported on a cross-linked matrix of macromolecules. U.S. Pat. No. 5,145,684 describes the production of a pharmaceutical formulation in which the drug substance is pulverized to nanoparticles (average particle size of 400 nm) in the presence of a surface modifier and then dispersed in a liquid medium to give a pharmaceutical formulation that exhibits remarkably high bioavailability.

[0207] The compositions are comprised of in general, a compound of formula I in combination with at least one pharmaceutically acceptable excipient. Acceptable excipients are non-toxic, aid administration, and do not adversely affect the therapeutic benefit of the compound of formula I. Such excipient may be any solid, liquid, semi-solid or, in the case of an aerosol composition, gaseous excipient that is generally available to one of skill in the art.

[0208] Solid pharmaceutical excipients include starch, cellulose, talc, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, magnesium stearate, sodium stearate, glycerol monostearate, sodium chloride, dried skim milk and the like. Liquid and semisolid excipients may be selected from glycerol, propylene glycol, water, ethanol and various oils, including those of petroleum, animal, vegetable or synthetic origin, e.g., peanut oil, soybean oil, mineral oil, sesame oil, etc. Preferred liquid carriers, particularly for injectable solutions, include water, saline, aqueous dextrose, and glycols.

[0209] Compressed gases may be used to disperse a compound of this invention in aerosol form. Inert gases suitable for this purpose are nitrogen, carbon dioxide, etc.

[0210] Other suitable pharmaceutical excipients and their formulations are described in Remington's Pharmaceutical Sciences, edited by E. W. Martin (Mack Publishing Company, 18th ed., 1990).

[0211] The amount of the compound in a formulation can vary within the full range employed by those skilled in the art. Typically, the formulation will contain, on a weight percent (wt%) basis, from about 0.01-99.99 wt% of a compound of formula I, Ia, Ib, II, or III based on the total formulation, with the balance being one or more suitable pharmaceutical excipients. Preferably, the compound is present at a level of about 1-80 wt%. Representative pharmaceutical formulations containing a compound of formula I, Ia, Ib, II, or III are described below.

EXAMPLES

[0212] In the examples below and the synthetic schemes above, the following abbreviations have the following meanings. If an abbreviation is not defined, it has its generally accepted meaning.

μL	=	microliters
μM	=	micromolar
μg	=	micrograms
NMR	=	nuclear magnetic resonance
AcOH	=	acetic acid
aq.	=	aqueous
boc	=	*t*-butoxycarbonyl
br	=	broad peak
cm	=	centimeters
CSA	=	camphorsulfonic acid
d	=	doublet
δ	=	chemical shift
DCM	=	dichloromethane
dd	=	doublet of doublets

DIEA	=	diisopropylethylamine
DMAP	=	4-*N,N*-dimethylaminopyridine
DMEM	=	Dulbeco's Modified Eagle's Medium
DMF	=	N,N-dimethylformamide
DMSO	=	dimethylsulfoxide
dppp	=	1,3-bis(diphenylphosphino)propane
DTT	=	dithiothreotol
EDTA	=	ethylenediaminetetraacetic acid
eq.	=	equivalents
ESI	=	electrospray ionization
EtOAc	=	ethyl acetate
EtOH	=	ethanol
Fmoc	=	9-fluorenylmethoxycarbonyl
g	=	gram
h	=	hours
HATU	=	O-(7-Azabenzotriazol-1-yl)-N, N, N', N'-tetramethyluronium hexafluorophosphate
HBTU	=	O-Benzotriazol-1-yl-N, N, N', N'-tetramethyluronium hexafluorophosphate
HCV	=	hepatitus C virus
HPLC	=	high performance liquid chromatography
Hz	=	hertz
IPTG	=	isopropyl-β-D-thiogalactopyranoside
IU	=	International Units
IC_{50}	=	inhibitory concentration at 50% inhibition
J	=	coupling constant
L	=	liters
m	=	multiplet
M	=	molar
M+ H^+	=	parent mass spectrum peak plus H^+
M- H^+	=	parent mass spectrum peak minus H^+
MeOH	=	methanol
MeCN	=	methylcyanide
mg	=	milligram
min.	=	minutes
mL	=	milliliter
mM	=	millimolar
mmol	=	millimole
MS	=	mass spectrum
N	=	normal
nm	=	nanometer
nM	=	nanomolar
ng	=	nanogram
NMP	=	1-methyl-2-pyrrolidinone
NTA	=	nitrilotriacetic acid
NTP	=	nucleoside triphosphate

PCR	=	Polymerase chain reaction
Pfp	=	pentafluorophenyl radical
Ph or ø	=	phenyl
ppm	=	parts per million
psi	=	pounds per square inch
PyBroP	=	Bromotris(pyrrolidine)phosphonium hexafluorophosphate
q	=	quartet
Rp-HPLC	=	reversed phase high performance liquid chromatography
s	=	singlet
t	=	triplet
dt	=	Doublet of triplets
t-Bu	=	tertiary-butyl protecting group
TBTU	=	O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium tetrafluoroborate
TC_{50}	=	Toxic concentration at 50% cell toxicity
TEA	=	triethylamine
tetrakis or tetrakis palladium	=	tetrakis(triphenylphosphine)palladium(0)
Tf_2O	=	Trifluorosulfonic anhydride
TFMSA	=	Trifluoromethanesulfonic acid
TFA	=	trifluoroacetic acid
THF	=	tetrahydrofuran
TLC	=	Thin layer chromatography
Tris	=	Tris(hydroxymenthyl)aminomethane
UTP	=	uridine triphosphate
v/v	=	Volume to volume ratio
w/v	=	Weight to volume ratio

[0213] Set forth in the examples below are compounds and intermediates useful for making compounds of the present invention. An overview of the synthetic protocols employed to prepare these compounds is set forth above.

[0214] Unless indicated otherwise the HPLC methods referred to in the Examples correspond to the following procedures.

HPLC Procedure A	-Buffer A consists of 0.1% TFA in purified water -Buffer B consists of 0.1% TFA in acetonitrile -Vydac C18 Protein and Peptide column (250x4.6mm) The column uses a flow rate of 1mL per minute with a gradient of 20% B to 99% B over 20 minutes. (c18 column)
HPLC Procedure B	-Buffer A consists of 0.1% TFA in purified water -Buffer B consists of 0.1% TFA in acetonitrile -Vydac C18 Protein and Peptide column (250x4.6mm) The column uses a flow rate of 2 mL per minute with a gradient of 20% B to 99% B over 10 minutes. (C18 column)
HPLC Procedure C	-Buffer A consists of 0.1% TFA in purified water -Buffer B consists of 0.1% TFA in acetonitrile -Merck KGaA Chromolith Performance RP-18e column (100x4.6mm) The column uses a flow rate of 4 mL per minute with a gradient of 20% B to 99% B over 5 minutes. (Monolithic column)

Example 1

Preparation of 1-Cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic-acid (**Compound 201**)

Step 1: *trans*-3-(2-Dimethylamino-vinyl)-4-nitro-benzoic acid methyl ester (Compound 3)

[0215] A 100 mL flask fitted with a 15 cm Vigreux head was charged with 10 g (49.7 mmol) of 3-methyl-4-nitro-benzoic acid methyl ester, 12.5 mL of DMF and 14.8 g (124.2 mmol) of N,N-dimethylformamide dimethylacetal. The reaction vessel was immersed in a 140 °C oil bath for 18 h under argon while the forming methanol distilled away. Upon cooling to room temperature the dark red content of the flask solidified. The solid was transferred to a 250 mL flask using DMF which was removed by evaporation.

The residue was triturated with petroleum ether to give 11.81g of enamine as dark red solid.

MS: 251.10 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 8.11 (d, 1H, Ar-H^2), 7.80 (d, 1H, Ar-H^5), 7.53-7.50 (dd, 1H, Ar-H^6), 7. 06 (d, 1H, CH=), 5.76 (d, 1H, CH=), 3.93 (s, 3H, OCH_3), 2.93 (s, 6H, $(CH_3)_2N$).

Step 2: 3-Formyl-4-nitro-benzoic acid methyl ester (Compound 4)

[0216] Compound **3** (11.81g 47.2 mmol) and $NaIO_4$ (30.3 g 141.6 mmol) was dissolved in 250 mL THF/H_2O 1:1 at room temperature. The dark red solution was warmed to about 40 °C while heavy precipitation occurred and the color changed to light brown. After 1 h the precipitate was removed by filtration and washed with 200 mL ethyl acetate. The organic layer was washed three times with saturated $NaHCO_3$, once with brine and dried with Na_2SO_4. The solution was evaporated to dryness and the resulting oil was purified on a silicagel pad eluting with DCM-hexane gradient (30% to 60% DCM) to yield after evaporation yellow Compound **4**.

[0217] H^1-NMR ($CDCl_3$): δ(ppm) 10.39 (s, 1H, CHO), 8.57 (d, 1H, J=2.1 Hz, Ar-H^2) 8.40-8.36 (dd, 1H, J=2.1 Hz and 8.4Hz, Ar-H^6), 8.14 (d, 1H, J=8.4Hz, Ar-H^5), 4.00 (s, 3H, OCH_3).

Step 3: 3-Dimethoxymethyl-4-nitro-benzoic acid methyl ester (Compound 5)

[0218] To a solution of Compound **4** (1g, 4.78 mmol) in 20 mL methanol, 0.5 mL 4N HCL/dioxane was added and the mixture was kept at 90 °C for 10 minutes. The reaction mixture was then evaporated to dryness. The white solid material was dissolved in 20 mL methanol and was treated with 0.5 mL 4N HCl again in the same way. The solid was dried under high vacuum overnight to give compound **5** in quantitative yield.

[0219] H^1-NMR ($CDCl_3$): δ(ppm) 8.40 (d, 1H, J=1.8 Hz, Ar-H^2), 8.14-8.10 (dd, 1H, J=8.1 Hz and 1.8Hz, Ar-H^6), 7.81 (d, 1H, J=8.1Hz, Ar-H^5), 5.89 (s, 1H, Ar-CH), 3.96 (s, 3H, ester CH_3), 3.40 (s, 6H, acetal CH_3);

Step 4: 4-Amino-3-dimethoxymethyl-benzoic acid methyl ester (Compound 6)

[0220] 100 mg 10%Pd/C and 1 g Mg_2SO_4 were suspended in 20 mL methanol and were hydrogenated in a Parr apparatus at 30 psi for 15 minutes. The apparatus was opened, and 1.22g (4.78 mmol) of Compound **5** dissolved in 40 mL methanol was added, followed by 2 mL TEA. The mixture was hydrogenated at 30 psi for 30 minutes, the catalyst was removed by means of filtration and the solution was evaporated to dryness. The solid material was dried over P_2O_5/H_3PO_4 overnight to give Compound **6**.

[0221] H^1-NMR (DMSO): δ(ppm) 7.80 (d, 1H, J=2.1Hz, Ar-H^2), 7.62-7.58 (dd, 1H, J=8.4Hz and 2.1Hz, Ar-H^6), 6.64 (d, 1H, J=8.4Hz, Ar-H^5), 5.84 (s, 2H, NH2), 5.32 (s, 1H, Ar-CH), 3.72 (s, 3H, ester CH_3), 3.20 (s, 6H, acetal CH_3).

Step 5: 4-Amino-3-formyl-benzoic acid methyl ester (Compound 7)

[0222] Compound **6** (0.95g, 4.2 mmol) was dissolved at room temperature in 15 mL of a solvent mixture composed of EtOH-acetic acid-water 2:2:1. The strongly colored yellow solution became pale yellow in 5 minutes. The mixture was let stand for an additional 15 minutes before it was evaporated to dryness and further dried in high vacuum overnight to get Compound **7** as a yellow powder.

[0223] MS: 180.05 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 9.88 (s, 1H, CHO), 8.23 (d, 1H, J=2.1Hz, Ar-H^2), 7.96-7.91 (dd, 1H, J=8.7Hz and 2.1Hz, Ar-H^6), 6.64 (d, 1H, J=8.4Hz, Ar-H^5), 3.88 (s, 1H, CH_3).

Step 6: 4-Chloro-3-nitro-benzoic acid ethyl ester (Compound 9)

[0224] 4-chloro-3-nitrobenzoic acid (100 g) was dissolved in 500 mL anhydrous ethanol and 35 mL concentrated sulfuric acid was added dropwise over a period of 5 minutes. The mixture was refluxed overnight then poured on 1 L ice. The precipitate was separated by filtration, washed four times with water and was then air dried. Recrystallization from 275 mL ethanol afforded a pale yellow product.

[0225] H^1-NMR ($CDCl_3$): δ(ppm) 8.49 (d, 1H, J=2.1Hz, Ar-H^2), 8.17-8.13 (dd, 1H, J=8.8 and 2.1 Hz), Ar-H^6), 7.63 (d, 1H, J=8.1 Hz, Ar-H^5), 4.42 (q, 2H, J=7.5Hz, CH_2), 1.42 (t, 3H, J=7.5 Hz, CH_3);

Step 7: 4-Cyclohexylamino-3-nitro-benzoic acid ethyl ester (Compound 10)

[0226] A solution of Compound **9** (22.96g, 100 mmol), cyclohexylamine (15.31g, 154 mmol) and TEA (13.57 g, 134 mmol) in 100 mL acetonitrile was refluxed overnight. The reaction mixture was poured into icy water and the precipitated crystals were collected by means of filtration, washed three times with water then was dried over phosphorous pentoxide in high vacuum to yield Compound **10**.

[0227] MS: 293.16 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 8.85 (d, 1H, J=2.1Hz, Ar-H^2), 8.40 (d, br, 1H, J=6.9Hz, NH), 8.01-7.97 (dd, 1H, J=9.0 and 2.1 Hz), Ar-H^6), 6.86 (d, 1H, J=9.0 Hz, Ar-H^5), 4.34 (q, 2H, J=7.5Hz, CH_2), 3.56 (m, 1H, -CH=), 2.05 (m, 2H), 1.81 (m, 2H), 1.65 (m, 2H), 1.44 (m, 4H), 1.38 (t, 3H, J=7.5 Hz, CH_3);

Step 8: 3-Amino-4-cyclohexylamino-benzoic acid ethyl ester (Compound 11)

[0228] To a solution of 5.84 g (20 mmol) of Compound **10** in 50 mL ethyl acetate and 30 mL methanol, 100 mg of 10% Pd/C was added, and the mixture was hydrogenated at 30 psi for 6 h. The catalyst was removed by filtration through a pad of Celite, the solvent was evaporated to dryness resulting in a dark purple solid which was recrystallized from ether-hexane. The mother liquid was evaporated, and the resulting solid was suspended in hexane and filtered to give additional yield of Compound **11**

[0229] MS: 263.18 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 7.57-7.54 (dd, 1H, J=8.7 and 2.1 Hz, Ar-H^6), 7.39 (d, 1H, J=2.1Hz, Ar-H^2), 6.57 (d, 1H, J=9.0 Hz, Ar-H^5), 4.29 (q, 2H, J=7.2Hz, CH_2), 3.32 (m, 1H, -CH=), 2.05 (m, 2H), 1.77 (m, 2H), 1.66 (m, 2H), 1.42-1.20 (m, 7H);

Step 9: 2-Phenyl-quinoline-6-carboxylic acid (Compound 13, Y = phenyl)

[0230] To a solution of 100 mg (0.56 mmol) of Compound **7** and 67 mg (0.56 mmol) of acetophenone in 7 mL ethanol, 420 µL of a 10% KOH/ethanol (0.75 mmol) solution was added and the mixture was refluxed under argon overnight. The product partially precipitated as bright yellow crystals which were not filtered off. The whole mixture was evaporated to dryness, the residue was triturated with ether to give the

product as potassium salt. The acid was liberated by dissolving in 10 mL water and acidification to pH 4 (about 500 μL 1M HCl). The precipitate was collected by filtration, washed twice with water and dried over phosphorous pentoxide in high vacuum to yield Compound **13**.

[0231] MS: 250.10 ($M+H^+$); H^1-NMR (DMSO): δ(ppm) 8.51-8.48 (m, 2H), 8.22-8.08 (m, 4H), 7.96 (d, 1H, J=8.4 Hz), 7.50-7.40 (m, 3H);

Step 10: 2-Phenyl-quinoline-6-carbonyl chloride (Compound 14, Y = phenyl)

[0232] Compound **13** (100 mg, 0.4 mmol) was suspended in 15 mL of thionyl chloride and refluxed for 1 hr. The mixture was evaporated to dryness and the residue co-evaporated twice with toluene to give Compound **14** as a yellow solid in quantitative yield which was used immediately without further purification.

Step 11: 1-Cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic-acid (Compound 201 or Compound 16, Y = phenyl))

[0233] Compound **14,** prepared from 100 mg (0.4 mmol) of Compound **13,** was dissolved in 4 mL of DMF. Then 105.2 mg (0.4 mmol) Compound **11** was added as a solid, followed by 69 μL (0.4 mmol) of DIEA. The mixture was then evaporated to dryness and the residue dissolved in 30 mL of glacial acetic acid. The solution was refluxed for 3 h and evaporated to dryness. The yellow solid was dissolved again in 15 mL methanol, and 4 mL 1N NaOH was added with stirring at 80 °C for 1 h. The reaction mixture was cooled in an ice bath, acidified with 4 mL 1N HCl and evaporated to dryness to give an oil which was dissolved in 20 mL DMF-water 1:1 containing 0.1% TFA. The solution was applied on a RP-HPLC column to give the pure Compound **201.**

[0234] **Conversion to HCl salt:** The purified title compound was dissolved in 4 mL methanol, 500 μL 4M HCl in dioxane was added followed by 40 mL ether. The white precipitate was separated by filtration and dried in high vacuum overnight.

[0235] MS: 448.20 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.70 (m, 1H), 8.47 (s, 1H), 8.33 (m, 5H), 8.22 (m, 1H), 8.09 (m, 1H), 8.00 (m, 2H), 7.58 (m, 3H), 4.44 (m, 1H), 4.23 (br, 4H), 2.33 (m, 2H), 2.10 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.36 (m, 3H);

Example 2

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (**Compound 229**)

[0236] To a solution of 45 mg (0.1 mmol) Compound **201** in 500 µL DMF 22.8 µL (0.13 mmol) TFA-OPfp and 23 µL (0.13 mmol) DIEA was added. The mixture was stirred at room temperature for 30 minutes. 29.1 mg (0.13 mmol) L-5-hydroxytryptophane dissolved in 500 µL DMF was added to the activated ester solution followed by 40 µL DIEA. The reaction was complete in 1 h. The DMF was evaporated and the residual oil which was dissolved in 20 mL DMF-water 1:1 containing 0.1% TFA. The solution was applied on a RP-HPLC column to give the pure Compound **229** as TFA salt.

[0237] **Conversion to HCl salt:** The purified Compound **229** was dissolved in 4 mL methanol, 1 mL 4M HCl in dioxane was added followed by 40 mL ether. The off-white precipitate was separated by filtration and dried in high vacuum overnight.

[0238] MS: 650.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.52 (d, 1H), 8.93 (d, 1H), 8.71 (d, 1H), 8.49 (d, 1H), 8.35-8.24 (m, 5H), 8.23 (d, 1H), 8.09 (dd, 1H), 7.97 (dd, 1H), 7.63-7.54 (m, 3H), 7.12-7.08 (m, 2H), 6.90 (d, 1H), 6.57 (dd, 1H), 4.46 (m, 1H), 4.44 (m, 1H), 3.32 (m, 2H), 2.33 (m, 2H), 2.10 (m,2H), 1.85 (m, 2H), 1.60 (m, 1H), 1.32 (m, 3H);

Example 3

Preparation of 1-(trans-4-Hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 579)**

Step 1: 3-Nitro-4-(trans-4-hydroxy-cyclohexylamino)-benzoic acid ethyl ester (Compound 579a)

[0239] Compound **9** (689 mg, 3 mmol) was suspended in acetonitrile (5 mL) and then triethylamine was added (1.3 mL, 9 mmol). trans-4-aminocyclohexanol hydrochloride (682 mg, 4.5 mmol) was then added and the reaction refluxed for 12 hours, 2 mL methanol was then added and the reaction further refluxed for another 24 hours.

Water (100 mL) was added and the resulting precipitate filtered, washed 3 times with water and air-dried. The product was used without further characterization in the next step MS: 309.3 ($M+H^+$)

Step 2: 3-Amino-4-(trans-4-hydroxy-cyclohexylamino)-benzoic acid ethyl ester (Compound 579b)

[0240] The product from the previous step (3 mmol) was dissolved in ethyl acetate (60 mL) and methanol (40 mL) and 10% Pd/C (100 mg) was added. The reaction was hydrogenated on a Parr-shaker at 35 psi for 6 ½ hours at ambient temperature. The Pd/C was filtered and the filtrate concentrated. Chromatography (SiO_2, methanol/dichloromethane 3:97 v/v) to yield the title intermediate (265 mg, 0.95 mmol) MS: 279.2 ($M+H^+$)

Step 3: 1-(trans-4-Hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 579)

[0241] Compound **36A Y=Phenyl,** (200 mg, 0.8 mmol) was activated in 8 mL DMF with TBTU (282 mg, 0.88 mmol) and DIEA (0.285 mL, 1.6 mmol) for 30 minutes at room temperature. This solution was then added to Compound **579b** (265 mg, 0.95 mmol) and stirred at ambient temperature for 20 hours. The reaction was concentrated to a residue in-vacuo and then dissolved in acetic acid (20 mL) and refluxed overnight. In the morning, the acetic acid was removed in-vacuo and the crude residue dissolved in a mixture of THF (20 mL), methanol (16 mL) and 2 M NaOH (4 mL) and the solution heated at 60 C overnight. The solution was then concentrated in-vacuo to an aqueous solution and concentrated HCl added until the pH was 5. The resulting precipitate was filtered, washed with water and purified using RP-HPLC column to give the pure title compound.

[0242] **Conversion to HCl salt:** The HPLC purified product was dissolved in 4 mL methanol, 500 µL 4M HCl in dioxane was added followed by 40 mL ether. The resulting precipitate was separated by filtration and dried in high vacuum overnight. Yield: 15.7 mg.

[0243] MS: 465.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.72 (s, 1H), 8.45 (s, 1H), 8.41-8.32 (m, 5 H), 8.19-8.12 (m, 2H), 7.98 (d, 1H, 8.4 Hz), 7.62 (m, 3H), 4.27 (t, 1H, 12 Hz), 2.53-2.36 (m, 3 H), 2.06-1.93 (m, 4 H), 1.29-1.22 (m, 2 H).

Example 4

Preparation of 2-{[1-Cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (**Compound 230**)

Step 1: 2-Methyl-quinoline-6-carboxylic acid (Compound 28)

[0244] Compound **28** was synthesized as described for Compound **13**, using acetone in place of acetophenone.

[0245] MS: 188.06 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.88 (d, 1H, J=8.4Hz), 8.78 (s, 1H), 8.37-8.26 (m, 2H), 7.83-7.80 (m, 1H), 2.88 (s, 3H).

Step 2: 4-Cyclohexylamino-3-[(2-methyl-quinoline-6-carbonyl)-amino]-benzoic acid ethyl ester (Compound 29)

[0246] Compound **29** was synthesized from Compound **28** as described for Compound **25** with quantitative yield.

Step 3: 1-Cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 30)

[0247] Compound **30** was synthesized from Compound **29** as described for Compound **23** with quantitative yield. MS: 414.24 ($M+H^+$).

Step 4: 1-Cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 31)

[0248] Compound **31** was synthesized from Compound **30** as described for Compound **204**. Yield: 77%.

[0249] MS: 386.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.99 (d, 1H, J=8.7Hz), 8.57 (d, 1H, J=1.8Hz), 8.52 (d, 1H, J=8.7Hz), 8.27-8,23 (m, 2H), 8.085 (d, 1H, J=9.0Hz), 7.92-7.88 (m, 2H), 4.28 (m, 1H), 2.94 (s, 3H), 2.30-2.18 (m, 2H), 1.99 (m, 2H), 1.78 (m, 2H), 1.56 (m, 1H), 1.36-1.20 (m, 3H).

Step 4: 2-{[1-Cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (Compound 230)

[0250] Compound **230** was synthesized from Compound **31** as described for Compound **235** Yield: 32%.

[0251] MS: 588.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.47 (s, 1H), 8.92 (d, 1H, J=9.0Hz), 8.79 (d, 1H, J=7.5Hz)8.56 (s, 1H), 8.41 (d, 1H, J=8.7Hz), 8.28-8.21 (m, 2H), 8.10 (d, 1H, J=8.7Hz), 7.88 (d, 2H, J=8.7Hz), 7.08-7.04 (m, 2H), 6.86 (d, 1H, J=1.8Hz), 6.55-6.51 (dd, 1H, J=2.1Hz, 8.7Hz), 4.61 (m, 1H), 4.31 (m, 1H), 2.91 (s, 3H), 2.28-2.24 (m, 2H), 2.01 (m, 2H), 1.80 (m, 2H), 1.56 (m, 1H), 1.32-1.19 (m, 3H).

Example 5

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-hydroxy-propionic acid (**Compound 231**)

[0252] Compound **231** was synthesized from Compound **201** as described for Compound **235**, except L-serine was used instead of L-5-hydroxytryptophane. Yield: 36%.

[0253] MS: 535.26 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.93 (d, 1H, J=7.2Hz), 8.73 (d, 1H, J=8.4Hz), 8.54 (d, 1H, J=2.1Hz), 8.46 (s, 1H), 8.38-8.29 (m, 5H), 8.15-8.11 (m, 2H), 7.73-7.55 (m, 3H), 4.50 (m, 2H), 3.85 (d, 1H, J=5.4Hz), 2.37-2.32 (m, 2H), 2.15 (m, 2H), 1.86 (m, 2H), 1.61 (m, 1H), 1.39-1.30 (m, 3H).

Example 6

Preparation of 6-Amino-2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-hexanoic acid (**Compound 232**)

[0254] Compound **232** was synthesized from Compound **201** as described for Compound **235**, except H-Lys(Boc)-OtBu was used instead of L-5-hydroxytryptophane. In the 3rd step the protected intermediate was treated with a mixture of TFA-anisol 8:2 for 2 hours then the product was precipitated with ether and purified on RP-HPLC. Yield 15%.

[0255] MS: 576.33 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.90 (d, 1H, J=7.8Hz), 8.71 (d, 1H, J=8.7Hz), 8.48 (d, 1H, J=1.8Hz), 8.41 (d, 1H), 8.35-8.32 (m, 4H), 8.22 (d, 1H, J=9.6Hz), 8.12-8.08 (dd, 1H, J=1.8Hz, 8.7Hz), 8.02 (d, 1H, J=8.7Hz), 7.86 (br, 3H), 7.60-7.54 (m, 3H), 4.42 (m, 2H), 2.78 (m, 2H), 2.36-2.27 (m, 2H), 2.11 (m, 2H), 1.90-1.83 (m, 4H), 1.62 (m, 3H), 1.53-1.25 (m, 6H).

Example 7

Preparation of 1-[1-Cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-pyrrolidine-2-carboxylic acid (**Compound 233**)

[0256] Compound **233** was synthesized from Compound **201** as described for Compound **235**, except L-proline was used instead of L-5-hydroxytryptophane. Yield: 15%.

[0257] MS: 545.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.71 (d, 1H), J=9.0Hz), 8.49 (d, 1H), 8.36-8.32 (m, 4H, 8.26 (d, 1H, J=8.7Hz), 8.12-8.08 (dd, 1H, J=1.5Hz, 8.7Hz), 7.95 (m, 1H), 7.65-7.53 (m, 2H), 4.44 (m, 1H), 3.56 (m,1H), 2.30 (m, 3H), 2.11 (m, 2H), 1.92-1.83 (m, 6H), 1.65 (m,1H), 1.37-1.32 (m, 4H).

Example 8

Preparation of 1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 203 or Compound 39, Y=phenyl**)

Step 1: 2-Phenyl-quinoxaline-6-carboxylic acid (compound 36A, Y = phenyl) and 3-Phenyl-quinoxaline-6-carboxylic acid (compound 36B, Y = phenyl)

[0258] To a solution of Compound **34** (850.75 mg, 5 mmol) and 3,4-diaminobenzoic acid in 50 mL of acetic acid, Compound **35** (670.7 mg, 5 mmol) phenylglyoxal was added and was refluxed under argon for 2.5 h. The reaction mixture was evaporated to dryness. The resulting grey solid containing the two isomers in about 2:1 ration was separated by HPLC resulting in 230mg (19%) Compound **36A** and 140 mg (12%) Compound **36B**.

[0259] The major component (Compound **36A**) was also prepared in an alternate manner. Ethanol was used as a solvent in place of acetic acid and the reaction

mixture was stirred overnight at 0 °C. The precipitate formed during the reaction was filtered off, washed with cold ethanol and dried to provide Compound **36A**. Yield (78%).

[0260] **Compound 36A**: MS: 251.10 ($M+H^+$); H^1-NMR (DMSO): δ (ppm) 13.5 (s, 1H), 9.67 (s, 1H,), 8.60 (d, 1H, J=1.5 Hz), 8.38-8.34 (m, 2H), 8.31-8.27 (dd, 1H, J=8.7Hz and 2.1Hz), 8.20 (d, 1H, J=9Hz), 7.65-7.59 (m, 3H);

[0261] **Compound 36B**: MS: 251.10 ($M+H^+$); H^1-NMR (DMSO): δ (ppm) 13.5 (s, 1H), 9.63 (s, 1H,), 8.30 (d, 1H, J=1.2 Hz), 8.38-8.34 (m, 2H), 8.28-8.24 (dd, 1H, J=8.7Hz and 1.8Hz), 8.18 (d, 1H, J=8.7Hz), 7.63-7.57 (m, 3H);

Step 2: 4-Cyclohexylamino-3-[(2-phenyl-quinoxaline-6-carbonyl)-amino]-benzoic acid ethyl ester (compound 37, Y = phenyl)

[0262] The suspension of 250 mg (1 mmol) of Compound **36** in 4 mL of DMF was activated by treatment with 418 mg (1.1 mmol) of HATU and 383 µL (2.2 mmol) of DIEA for 10 minutes at room temperature during which time it remains a suspension. Compound **11** (289 mg, 1.1 mmol) was added and the mixture was stirred at room temperature overnight, becoming a clear solution. The DMF was evaporated and the resulting oil was triturated with water. The solidified material was filtered, washed with water (3x) and dried to give Compound **37** as a yellow solid which was used without further purification. MS: 495.27 ($M+H^+$);

Step 3: 1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 38, Y = phenyl)

[0263] Compound **37** (1 mmol) from the previous step was dissolved in 80 mL glacial acetic acid and was refluxed for 4 h. The acetic acid was evaporated and the resulting oil was dried overnight under high vacuum to give Compound **38** as a semisolid which was used without further purification. MS: 477.25 ($M+H^+$);

Step 4: 1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 203)

[0264] To the solution of 1 mmol of Compound **38** in 40 mL ethanol, 10 mL of 1 M NaOH was added and the mixture was refluxed for 1 h. The reaction mixture was then cooled and evaporated to dryness. The residue was dissolved in 50 mL of water

and acidified with 1M HCl to pH 4. The precipitate was filtered off, washed with water (4x) and dried to give the title compound.

[0265] MS: 449.23 ($M+H^+$); H^1-NMR (DMSO): δ(ppm) 9.73 (s, 1H), 8.51 (d, 1H, J=1.5 Hz), 8.42-8.35 (m, 4H), 8.24-8.16 (m, 2H), 8.03-7.99 (dd, 1H, J=9Hz and 1.5Hz), 7.65-7.61 (m, 3H), 4.41 (m, 1H), 4.5-3.9 (br, 2H), 2.31 (m, 2H), 2.10 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.40-1.20 (m, 3H);

Example 9

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (**Compound 234**)

[0266] Compound **203** (100 mg, 0.22 mmol) was activated in 2mL DMF with 92 mg (0.24 mmol) HBTU and 85µL DIEA for 10 minutes at room temperature. 56 mg 5-hydroxy-L-tryptophane, dissolved in 1 mL DMF was added followed by 44 µL DIEA. The mixture was stirred at room temperature for 1 h, then evaporated to dryness. The oil was purified using RP-HPLC column to give Compound **234.**

[0267] **Conversion to HCl salt:** The purified Compound **234** was dissolved in 4 mL methanol, 500 µL of 4M HCl in dioxane was added followed by 40 mL of ether. The yellow precipitate was separated by filtration and dried in high vacuum overnight. Yield: 76 mg (58 %) off yellow solid.

[0268] MS: 651.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.49 (d, 1H), 9.71 (s, 1H), 8.73 (d, 1H), 8.41-8.31 (m, 5H), 8.18-8.14 (dd, 1H, J=8.4Hz and 1.8Hz), 8.05 (d, 1H, J=9Hz), 7.85 (dd, 1H, J=9Hz and 1.8 Hz), 7.67-7.61 (m, 3H), 7.13-7.08 (m, 2H), 6.90 (d, 1H, J=2.1Hz), 6.59-6.55 (dd, 1HH, J=8.7Hz and 2.4Hz), 4.65 (m, 1H), 4.41 (m, 1H), 3.20 (m, 2H), 2.32 (m, 2H), 2.04 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.44-1.22 (m, 3H).

Example 10

Preparation of 2-{2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 204**)

Step 1: 1-[2-Hydroxy-5-(pyrrolidine-1-carbonyl)-phenyl]-ethanone (Compound 18)

[0269] To a solution of 500 mg (2.8 mmol) of 3-acetyl-4-hydroxy-benzoic acid in 5 mL of DMF, 721.6 µL (4.2 mmol) of TFA-OPfp and 731.5 µL (4.2 mmol) of DIEA were added. The clear solution was stirred at room temperature for 15 minutes, then 467.5 µL (5.6 mmol) of pyrrolidine was added. The mixture was stirred for another hour and was then evaporated to dryness. The oily residue was taken up in 50 mL water-50 mL ethyl acetate mixture, the EtOAc phase was separated, washed twice with 1M HCl, water, saturated $NaHCO_3$, brine and was dried with Na_2SO_4. The EtOAc was evaporated; the oil was purified on an open silica gel column using a toluene/ethyl acetate gradient containing 5% acetic acid to yield 410 mg (51%) Compound **18**.

[0270] MS: 232.12 ($M\text{-}H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 12.02 (s, 1H), 7.99 (d, 1H, J=2.1Hz), 7.69-7.65 (dd, 1H, J=2.1Hz, 8.7Hz), 6.97 (d, 1H, J=8.7Hz), 3.47-3.32 (m, 4H), 2.65 (s, 3H), 1.90-1.83 (br, 4H).

Step 2: 2-[2-Hydroxy-5-(pyrrolidine-1-carbonyl)-phenyl]-quinoline-6-carboxylic acid (Compound 19)

[0271] Compound **18** (410 mg, 1.75 mmol) and Compound **7** (315 mg, 1.75 mmol) were dissolved in 30 mL of ethanol, 2.45 mL of a 10% KOH/ethanol solution was added and the mixture was refluxed overnight under argon. The ethanol was evaporated, the residue dissolved in water, and acidified with 3 mL of 1M HCl. The formed gel was solidified by addition of 30 mL of ethyl acetate and 30 mL of a saturated NaCl solution. The solid was filtered, awashed with water, and dried. Yield 302 mg (48%) Compound **19**.

[0272] MS: 363.15 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 13.28 (br, 1H), 8.72 (m, 2H), 8.50 (m, 1H), 8.37 (s, 1H), 8.25 (m, 1H), 8.14 (d, 1H, J=8.7Hz), 7.58 (m, 1H), 7.02 (d, 1H, J=8.7Hz), 3.51 (m, 4H), 1.85 (m, 4H).

Step 3: 2-[2-Hydroxy-5-(pyrrolidine-1-carbonyl)-phenyl]-quinoline-6-carboxylic acid methyl ester (Compound 20)

[0273] To the solution of 295 mg (0.81 mmol) of Compound **19** in 3 mL of methanol, 1 mL of 4M HCl/dioxane was added, and the mixture was heated at 60 °C overnight. The reaction mixture was then evaporated to dryness to give Compound **20** in quantitative yield. MS: 377.18 ($M+H^+$).

Step 4: 2-[5-(Pyrrolidine-1-carbonyl)-2-trifluoromethanesulfonyloxy-phenyl]-quinoline-6-carboxylic acid methyl ester (Compound 21)

[0274] Compound **20** described in the previous step (0.81 mmol) and 10 mg of DMAP were dissolved in 10 mL of DCM. Then 1 mL of pyridine was added, followed by 450 μL (2.67mmol) of triflic anhydride (drop-wise), and the mixture was stirred overnight. The reaction mixture was evaporated and purified on silicagel using toluene-ethyl acetate (10-50%) gradient. Yield: 320 mg (77%) Compound **21**.

[0275] MS: 509.11 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.78-8.74 (m, 2H), 8.29-8.25 (dd, 1H, J=2.1Hz, 9.0Hz), 8.18 (d, 1H, J=8.7 Hz), 8.1 (d, 1H, J=2.1Hz), 8.03 (d, 1H, J=8.7Hz), 7.85-7.81 (dd, 1H, J=2.1Hz, J=2.1Hz, 8.4Hz), 7.67 (d, 1H, J=8.4Hz), 3.94 (s, 3H), 3.51-3.41 (m, 4H), 1.9-1.82 (m, 4H); F^{19}-NMR: δ -74.58.

Step 5: 2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinoline-6-carboxylic acid methyl ester (Compound 23)

[0276] Compound **21** (320 mg, 0.63 mmol), 4-chloro-phenylboronic acid (Compound **22,** 148 mg, 0.94 mmol), 500 mg (2.35 mmol) of K_3PO_4, 27 mg (0.63 mmol) of LiCl and 36.5 mg (0.031 mmol) of $Pd(PPh_3)_4$ were dissolved in 30 mL dioxane (degassed). The mixture was refluxed under argon overnight. The black solution was filtered through a Celite pad, and evaporated to dryness to give Compound **23** as yellow oil which was used without further purification. MS: 471.16 ($M+H^+$).

Step 6: 2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinoline-6-carboxylic acid (Compound 24)

[0277] Compound **23** from the previous step (0.63 mmol) was dissolved in 15 mL methanol, and 5 mL of 1M NaOH were added. The solution was refluxed for 2 hours, then evaporated. The residue was then dissolved in water, acidified with 5 mL of

1M HCl, and the precipitate was filtered off, washed three times with water and dried to yield 276 mg (96%) of Compound **24**.

[0278] MS: 455.12 ($M+H^+$); H^1-NMR (DMSO- d_6): δ(ppm) 13.1 (br, 1H), 8.59 (d, 1H, J=1.8Hz), 8.33 (d, 1H, J=8.4Hz), 8.20-8.17 (dd, 1H, J=2.1Hz, 9.0Hz), 8.04 (d, 1H, J=8.7Hz), 7.87 (d, 1H, J=1.8Hz), 7.74-7.71 (dd, 1H, J=1.8Hz, 8.1Hz), 7.55-7.51 (d, 1H, J=8.4Hz), 7.32-7.3 (m, 2H), 7.17-7.13 (m, 3H), 3.51-3.47 (m, 4H), 1.88-1.83 (m, 4H).

Step 7: 3-({2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinoline-6-carbonyl}-amino)-4-cyclohexylamino-benzoic acid ethyl ester (Compound 25)

[0279] Compound **24** (270 mg, 0.59 mmol) in 4 mL of DMF was activated with 246.6 mg (0.65 mmol) of HATU and 226 µL (1.30 mmol) of DIEA at room temperature for 15 minutes. Compound **11** (170 mg, 0.65 mmol) was added as solid and the mixture was stirred overnight. The DMF was evaporated; the remaining oil was solidified by trituration with water. The solid Compound **25** was filtered off, dried and used without further purification. MS: 701.34 ($M+H^+$).

Step 8: 2-{2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 27 Q=ethyl)

[0280] The compound from the previous step (0.59 mmol) was dissolved in 80 mL acetic acid and refluxed for 2.5 hours. The acetic acid was evaporated, the residue was dried to give Compound **204** in quantitative yield. MS: 683.33 ($M+H^+$).

Step 9: 2-{2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 204)

[0281] Compound **27 Q=ethyl** (0.59 mmol), from the previous step, was dissolved in a mixture of 25 mL of ethanol and 5 mL of 1M NaOH and was refluxed for 2 hours. The reaction mixture was then evaporated to dryness. The residue was dissolved in 30 mL water, acidified with 1M HCl to pH 4. The precipitate that formed was filtered off, washed four times with water and dried. Yield 315 mg (73%). The title compound maybe further purified using RP-HPLC.

Conversion to HCl salt: The purified Compound **204** was dissolved in 4 mL methanol, 1 mL 4M HCl in dioxane was added followed by 40 mL ether. The off-white precipitate was separated by filtration and dried in high vacuum overnight. Yield: 28.3 mg solid.

[0282] MS: 655.26 ($M+H^+$); H^1-NMR (DMSO- d_6): δ(ppm) 8.41-8.38 (m, 2H), 8.32 (d, 1H, J=1.5Hz), 8.27-8.19 (m, 2H), 8.10-8.06 (dd, 1H, J=1.8Hz, 8.7Hz), 8.02-7.98 (dd, 1H, J=1.5Hz, 8.7Hz), 7.92 (d, 1H, J=1.8Hz), 7.77-7.74 (dd, 1H, J=2.1Hz, 8.1Hz), 7.58 (d, 1H, J-7.8Hz), 7.36-7.33 (m, 2H), 7.25-7.19 (m, 3H), 4.43 (m, 1H), 3.51 (m, 4H), 3.33 (m, 2H), 2.08 (m, 2H), 1.87 (m, 6H), 1.61 (m, 1H), 1.32 (m, 3H).

Example 11

Preparation of 1-Cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 205**)

Step 1: 4-Cyclohexylamino-3-[(3-phenyl-quinoxaline-6-carbonyl)-amino]-benzoic acid ethyl ester (Compound 41)

[0283] The solution of 238 mg (0.95 mmol) Compound **37** in 5 mL DMF was activated by treatment with 398 mg (1.05 mmol) HATU and 365 µL (2.1 mmol) DIEA for 10 minutes at room temperature. Compound **11** (275 mg, 1.1 mmol) was added and the mixture was stirred at room temperature overnight. The DMF was evaporated, the resulting oil was triturated with water, the solidified material filtered off, washed with water (3x) and dried to give Compound **41** as a 92% pure yellow solid which was used without further purification. MS: 495.26 ($M+H^+$);

Step 2: 1-Cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 42)

[0284] Compound **41** (0.95 mmol) from the previous step was refluxed in 80 mL acetic acid for 3.5 h. The mixture was then evaporated to dryness and dried overnight under high vacuum to yield Compound **42** in quantitative yield. It was not further purified before saponification.

Step 3: 1-Cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 205)

[0285] To the solution of Compound **42** (0.95 mmol) in 25 mL ethanol 5 mL, 1 M NaOH was added and the mixture was refluxed for 1 h. It was then cooled and evaporated to dryness. The residue was dissolved in 50 mL water, acidified with 1M HCl to pH 4. The precipitate was filtered off, washed with water (4x) and dried to give 345 mg (81%) of the title compound which maybe further purified by RP-HPLC.

[0286] MS: 448.19 ($M-H^+$); H^1-NMR (DMSO-): δ(ppm) 9.72 (s, 1H), 8.48 (d, 1H, J=1.8 Hz), 8.39-8.34 (m, 4H), 8.20-8.11 (m, 2H), 8.01-7.97 (dd, 1H, J=8.7Hz and 1.5Hz), 7.63-7.60 (m, 3H), 4.41 (m, 1H), 4.5-3.9 (br, 2H), 2.31 (m, 2H), 2.10 (m, 2H), 1.85 (m, 2H), 1.60 (m, 1H), 1.40-1.20 (m, 3H);

Example 12

Preparation of 2-[(2-{2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-3-(5-hydroxy-1H-indol-3-yl)-propionic acid **(Compound 235)**

[0287] Compound **204** (100 mg, 0.15 mmol) in 2 mL DMF was activated with 64 mg (0.17 mmol) HBTU and 58 µL (0.33 mmol) DIEA at room temperature for 10 minutes. Then 40 mg (0.18 mmol) 5-hydroxytryptophane and 32 µL (0.25 mmol) DIEA, dissolved in 1 mL DMF, was added and the mixture was stirred for 1 h. The DMF was evaporated; the residue was purified with RP-HPLC.

[0288] **Conversion to HCl salt:** The purified Compound **235** was dissolved in 4 mL methanol, 1 mL 4M HCl in dioxane was added followed by 40 mL ether. The off-white precipitate was separated by filtration and dried in high vacuum overnight. Yield: 44.1 mg (32%).

[0289] MS: 856.23 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.51 (d, 1H, J=1.8Hz), 8.89 (d, 1H, J=4.8Hz), 8.41-8.38 (m, 2H), 8.33 (d, 1H, J=1.5Hz), 8.28-8.19 (m, 2H), 8.10-8.07 (dd, 1H, J=1.5Hz, 8.1Hz), 7.96-7.91 (m, 2H), 7.78-7.74 (dd, 1H, J=1.8Hz, 8.1Hz), 7.58 (d, 1H, J=7.8Hz), 7.37-7.34 (m, 2H), 7.26-7.19 (m, 3H), 7.10 (m, 2H), 6.89 (d, 1H, J=1.8Hz), 6.58-6.55 (dd, 1H, J=2.1Hz, 8.7Hz), 4.65 (m. 1H), 4.43 (m, 1H), 3.51 (m,4H), 2.33 (m, 2H), 2.08 (m, 2H), 1.87 (m, 6H), 1.61 (m, 1H), 1.32 (m, 3H).

Example 13

Preparation of 2-{[1-Cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (**Compound 236**)

[0290] Compound **205** (100 mg, 0.22 mmol) was activated in 2mL of DMF with 92 mg (0.24 mmol) of HBTU and 85 μL of DIEA for 10 minutes at room temperature. 5-hydroxy-L-tryptophane(56 mg) dissolved in 1 mL DMF was added, followed by 44 μL of DIEA. The mixture was stirred at room temperature for 1 h, then was evaporated to dryness. The oil was purified using RP-HPLC column to give the pure Compound **236.**

[0291] **Conversion to HCl salt:** The purified Compound **236** was dissolved in 4 mL methanol, 500 μL 4M HCl in dioxane was added followed by 40 mL ether. The dark gray precipitate was separated by filtration and dried in high vacuum overnight. Yield: 87 mg (55 %) of grayish brown solid.

[0292] MS: 649.22 ($M-H^+$); H^1-NMR (DMSO- d_6): δ(ppm) 10.54 (d, 1H, J-2.1HZ), 9.75 (s, 1H), 8.99 (d, 1H, J=7.5Hz), 8.58 (d, 1H, J=1.8Hz), 8.41-8.36 (m, 4H), 8.28-8.25 (d, 1H, J=9.0Hz), 8.18-8.14 (dd, 1H, J=1.8Hz, 8.7Hz), 8.02-7.99 (dd, 1H, 1.8Hz, 8.7Hz), 7.65-7.60 (m, 3H), 7.12-7.08 (m, 2H), 6.90 (m, 1H), 6.59-6.55 (dd, 1H, J=2.4Hz, 8.7Hz), 4.67 (m, 1H), 4.44 (m, 1H), 3.22 (m, 2H), 2.30 (m, 2H), 2.12 (m, 2H), 1.85 (m, 2H), 1.58 (m, 1H), 1.36-1.25 (m, 3H);

Example 14

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-pentanedioic acid (**Compound 237**)

[0293] Compound **237** was synthesized from Compound **201** as described for Compound **235**, using L-glutamic acid dimethylester in place of L-5-hydroxytryptophane. In the 3rd step the protected intermediate was treated with aqueous sodium hydroxide for a 15% yield of the title compound

[0294] MS: 577.17 ($M+H^+$); H^1-NMR (DMSO d_6): δ(ppm) 8.72-8.64 (m, 2H), 8.38-8.25 (m, 6H), 8.06-8.02 (m, 2H), 7.89-7.86 (dd, 1H, J=1.5Hz, 8.7Hz), 7.60-

7.53 (m, 3H)4.48-4.38 (m, 2H), 2.42-2.28 (m, 4H), 2.16-1.96 (m, 4H), 1.88-1.83 (m, 2H), 1.62 (m, 1H), 1.4-1.22 (m, 3H).

Example 15

Preparation of 1-Cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 206**)

Step 1: 3-Phenyl-quinoline-6-carboxylic acid (Compound 206a)

[0295] The title intermediate was synthesized as described for Compound **13**, using phenylacet-aldehyde instead of acetophenone. Yield: 68%.

[0296] MS: 248.09 ($M-H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.20 (s, 1H), 8.79 (d, 2H), 8.20-8.00 (m, 2H), 7.95-7.00 (m, 5H).

Step 2: 4-Cyclohexylamino-3-[(3-phenyl-quinoline-6-carbonyl)-amino]-benzoic acid ethyl ester (Compound 206b)

[0297] The title intermediate was synthesized from the product of the previous step as described for Compound **25** with quantitative yield.

Step 3: 1-Cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 206c)

[0298] The title intermediate was synthesized from the product of the previous step as described for compound **27 Q=ethyl** with quantitative yield. MS: 476.26 ($M+H^+$).

Step 4: 1-Cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid

The title compound was synthesized from the product of the previous step as described for Compound **204**. Yield: 91%.

[0299] MS: 448.22 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.50 (d, 1H, J=2.4Hz), 9.05 (d, 1H, J=1.8Hz), 8.55 (d, 1H, J=1.5Hz), 8.39-8.34 (m, 2H), 8.24-8.21 (d, 1H, J=8.7Hz), 8.16-8.12 (dd, 1H, J=9.0Hz, 1.5Hz), 8.03-7.94 (m, 3H), 7.61-7.47 (m, 3H),4.44 (m, 1H), 2.35-2.26 (m, 2H), 2.16-2.08 (m, 2H), 1.86-1.82 (m, 2H), 1.60 (m, 1H), 1.43-1.25 (m, 3H).

Example 16

Preparation of 2-{[1-Cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (**Compound 238**)

[0300] The title compound was synthesized from Compound **206** as described for Compound **235** Yield: 19%.

[0301] MS: 650-31 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.52 (s, 1H), 9.49 (d, 1H, J=1.8Hz), 9.01 (s, 1H), 8.95-8.92 (d, 1H, J=7.5Hz), 8.56 (s, 1H), 8.39-8.33 (m, 2H), 8.25-8.22 (d, 1H, J=9.0Hz), 8.15-8.12 (d, 1H, J=8.7Hz), 7.99-7.94 (m, 3H), 7.61-7.47 (m, 3H), 7.11-7.03 (m, 2H), 6.89 (m, 1H), 6.58-6.55 (m, 1H), 4.70-4.62 (m, 1H), 4.44 (m, 2H), 3.21 (m, 1H), 2.34-2.31 (m, 2H), 2.10 (m, 2H), 1.86-1.82 (m, 2H), 1.59 (m, 1H), 1.45-1.30 (m, 3H).

Example 17

Preparation of 2-[(2-(2-phenyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid (**Compound 310**)

[0302] The general procedure described for Compound **242** was used with Fmoc-Ala Wang resin (167mg, 0.6mmol/g), producing 10.2mg of the title compound. (10% yield). MS: 520.26 ($M+H^+$) HPLC Procedure A, retention time = 12.52min.

Example 18

Preparation of 3-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid (**Compound 239**)

[0303] The general procedure described for Compound **242** was used with with Fmoc-β-Ala Wang resin (167mg, 0.6mmol/g), producing 21mg of the title compound (39% yield).

[0304] MS: 520.26 ($M+H^+$) HPLC Procedure A, retention time = 12.25min.

Example 19

Preparation of 3-Biphenyl-4-yl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid (**Compound 240**)

[0305] The general procedure described for Compound **242** was used with Fmoc-Bip Wang resin (125mg, 0.8mmol/g), producing 33mg of the title compound (51% yield).

[0306] MS: 672.33 ($M+H^+$) HPLC Procedure A, retention time = 16.33min.

Example 20

Preparation of 3-(4-Benzoyl-phenyl)-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid **(Compound 241)**

[0307] The general procedure described for Compound **242** was used with Fmoc-Bpa Wang resin (125mg, 0.8mmol/g), producing 37mg of the title compound (50% yield).

[0308] MS: 700.32 ($M+H^+$) HPLC Procedure A, retention time = 15.46min.

Example 21

Preparation of 3-Cyclohexyl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid (**Compound 242**)

[0309] Fmoc protected amino acids on Wang resins (0.1mmol) were added to a reaction vessel. The resin was then stirred for 1 hour with a 20% solution of piperidine in DMF. The resins were rinsed 6 times with DMF. A solution of Compound **203** (0.5mmol in 6mL DMF), preactivated with HATU (0.496 mmol) and DIEA (1.0 mmol), was added to the resin and mixed for 16 hours. The resins were then washed with DMF (5mL 3 times), dichloromethane (5mL 3 times), and diethylether (5mL 3 times). The desired compound was cleaved from the resin with 2% water in TFA and converted to the HCl salt by dissolving in 0.8 mL methanol and adding 1 mL 4M HCl in dioxane

followed by 40mL ether. The compound was centrifuged down, the solvent decanted off, and the solid dried to yield the final compound.

[0310] This general procedure was followed with Fmoc-Cys Wang resin (167mg, 0.6mmol/g), producing 25mg of the title compound (46% yield). MS: 600.29 ($M-H^+$) HPLC Procedure A, retention time = 15.76min.

Example 22

Preparation of Cyclohexyl-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid (**Compound 243**)

[0311] The general procedure described for Compound **242** was used with Fmoc-Cha Wang resin (250mg, 0.4mmol/g), producing 29mg of the title compound (48% yield). MS: 586.27 ($M-H^+$) HPLC Procedure A, retention time = 14.94min.

Example 23

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-succinic acid (**Compound 244**)

[0312] The general procedure described for Compound 242 was used with Fmoc-Asp Wang resin (125mg, 0.8mmol/g), producing 28mg of the title compound (50% yield). MS: 562.20 ($M-H^+$) HPLC Procedure A, retention time = 12.08min.

Example 24

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-pentanedioic acid (**Compound 245**)

[0313] The general procedure described for Compound **242** was used with Fmoc-Glu Wang resin (111mg, 0.9mmol/g), producing 25mg of the title compound (44% yield). MS: 576.22 ($M-H^+$) HPLC Procedure A, retention time = 12.14min.

Example 25

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-phenyl-propionic acid (**Compound 246**)

[0314] The general procedure described for Compound **242** was used with Fmoc-Phe Wang resin (167mg, 0.6mmol/g), producing 26mg of the title compound (44% yield). MS: 594.24 ($M-H^+$) HPLC Procedure A, retention time = 14.58min.

Example 26

Preparation of {[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid (**Compound 311**)

[0315] The general procedure described for Compound **242** was used with Fmoc-Gly Wang resin (125mg, 0.8mmol/g), producing 30mg of the title compound (55% yield). MS: 504.21 ($M-H^+$) HPLC Procedure A, retention time = 12.32min.

Example 27

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(1H-imidazol-4-yl)-propionic acid (**Compound 247**)

[0316] The general procedure described for Compound **242** was used with Fmoc-His Wang resin (250mg, 0.4mmol/g), producing 30mg of the title compound (51% yield). MS: 584.24 ($M-H^+$) HPLC Procedure A, retention time = 11.16min.

Example 28

Preparation of 1-[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-4-hydroxy-pyrrolidine-2-carboxylic acid (**Compound 248**)

[0317] The general procedure described for Compound **242** was used with Fmoc-Hyp Wang resin (143mg, 0.7mmol/g), producing 23mg of the title compound (50% yield). MS: 560.23 ($M-H^+$) HPLC Procedure A, retention time = 11.58min.

Example 29

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-methyl-pentanoic acid (**Compound 249**)

[0318] The general procedure described for Compound **242** was used with Fmoc-Ile Wang resin (250mg, 0.4mmol/g), producing 23mg of the title compound (54% yield). MS: 560.26 ($M-H^+$) HPLC Procedure A, retention time = 14.34min.

Example 30

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methyl-pentanoic acid (**Compound 513**)

[0319] The general procedure described for Compound **242** was used with Fmoc-Leu Wang resin (111mg, 0.9mmol/g), producing 8.1mg of the title compound (14% yield). MS: 560.25 ($M-H^+$) HPLC Procedure A, retention time = 17.17min.

Example 31

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methylsulfanyl-butyric acid (**Compound 515**)

[0320] The general procedure described for Compound **242** was used with Fmoc-Met Wang resin (111mg, 0.9mmol/g), producing 21mg of the title compound (36% yield). MS: 578.21 ($M-H^+$) HPLC Procedure A, retention time = 15.08min.

Example 32

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-succinamic acid (**Compound 518**)

[0321] The general procedure described for Compound **242** was used with Fmoc-Asn Wang resin (167mg, 0.6mmol/g), producing 22mg of the title compound (36% yield). MS: 561.21 ($M-H^+$) HPLC Procedure A, retention time = 15.04min.

Example 33

Preparation of 4-Carbamoyl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-butyric acid (**Compound 541**)

[0322] The general procedure described for Compound **242** was used with Fmoc-Gln Wang resin (167mg, 0.6mmol/g), producing 27mg of the title compound (47% yield). MS: 575.22 ($M-H^+$) HPLC Procedure A, retention time = 15.02min.

Example 34

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-5-guanidino-pentanoic acid (**Compound 523**)

[0323] The general procedure described for Compound **242** was used with Fmoc-Arg Wang resin (200mg, 0.5mmol/g), producing 53mg of the title compound (87% yield). MS: 605.35 ($M+H^+$) HPLC Procedure A, retention time = 14.84min.

Example 35

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-hydroxy-butyric acid (**Compound 512**)

[0324] The general procedure described for Compound **242** was used with Fmoc-Thr Wang resin (200mg, 0.5mmol/g), producing 26mg of the title compound (47% yield). MS: 548.22 ($M-H^+$) HPLC Procedure A, retention time = 15.45min.

Example 36

Preparation of 2-[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid (**Compound 520**)

[0325] The general procedure described for Compound **242** was used with Fmoc-Tic Wang resin (143mg, 0.7mmol/g), producing 25mg of the title compound (41% yield). MS: 606.22 ($M-H^+$) HPLC Procedure A, retention time = 17.18min.

Example 37

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-methyl-butyric acid (**Compound 517**)

[0326] The general procedure described for Compound **242** was used with Fmoc-Val Wang resin (250mg, 0.4mmol/g), producing 16mg of the title compound (29% yield). MS: 546.23 ($M-H^+$) HPLC Procedure A, retention time = 16.59min.

Example 38

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(4-hydroxy-phenyl)-propionic acid (**Compound 519**)

[0327] The general procedure described for Compound **242** was used with Fmoc-Tyr Wang resin (125mg, 0.8mmol/g), producing 22mg of the title compound (36% yield). MS: 610.22 ($M-H^+$) HPLC Procedure A, retention time = 16.14min.

Example 39

Preparation of 2-[2-(4'-Chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 387**)

[0328] Compound **352** (150 mg, 0.28 mmol), 4-chlorophenyl boronic acid (134 mg, 0.86 mmol), potassium phosphate (452 mg, 2.14 mmol), lithium chloride (12.1 mg, 0,28 mmol) and tetrakis(triphenylphosphine) palladium(0) (34 mg, 0.028 mmol) were combined in 15 mL degassed dioxane and the mixture was refluxed under argon overnight. The dark mixture was filtered through a Celite pad, was evaporated and purified using RP-HPLC to give 31 mg (17%) of the title compound.

[0329] MS: 558.24 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.49-8.40 (m, 3H), 8.34-8.30 (m, 2H), 8.17-8.14 (dd, 1H, J=8.4Hz &1.5Hz), 8.10-8.07 (dd, 1H, J=8.4Hz & 1.2Hz), 7.87-7.84 (m, 1H), 7.68-7.56 (m, 3H), 7.39-7.36 (m, 2H), 7.30-7.27 (d, 1H, J=8.4Hz), 7.24-7.21 (m, 2H), 4.50 (m, 1H), 2.35 (m, 2H), 2.15 (m, 2H), 1.90 (m, 2H), 1.65 (m, 1H), 1.49-1.26 (m, 3H).

Example 40

Preparation of 1-Cyclohexyl-2-[2-(2-pyrid-4-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 369**)

[0330] The title compound was synthesized as described for Compound **387** except pyridine-4-boronic acid was used instead of 4-chlorophenyl-boronic acid.

[0331] MS: 525.26 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.75 (m, 2H), 8.61-8.58 (d, 1H, J=8.4Hz), 8.41 (d, 1H, 1.5Hz), 8.32 (d, 1H, 1.5Hz), 8.13-8.10 (d, 1H, J=8.4 Hz), 8.05-7.90 (m, 4H), 7.82-7.71 (m, 6H), 4.42 (m, 1H), 2.35 (m, 2H), 2.08 (m, 2H), 1.90 (m, 2H), 1.65 (m, 1H), 1.40-1.26 (m, 3H).

Example 41

Preparation of 1-Cyclohexyl-2-{2-[3-(pyrrolidine-1-carbonyl)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid (**Compound 370**)

Step 1: 1-[3-(Pyrrolidine-1-carbonyl)-phenyl]-ethanone (Compound 370a)

[0332] The title intermediate was synthesized as described for Compound **18** except 3-acetylbenzoic acid was used instead of 3-acetyl-4-hydroxy benzoic acid.

[0333] H^1-NMR (DMSO-d_6): δ(ppm) 8.06-8.02 (m, 2H), 7.80-7.77 (m, 1H), 7.63-7.58 (m, 1H), 3.51 (t, 2H, J=6.6Hz), 3.40 (t, 2H, J=6.3Hz), 2.65 (s, 3H), 1.94-1.83 (m, 4H).

Step 2: 1-Cyclohexyl-2-{2-[3-(pyrrolidine-1-carbonyl)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid (Compound 370)

[0334] The title compound was synthesized in four steps as described for Compound **13,** Compound **25,** Compound **27 Q=ethyl** and Compound **204**, respectively, except the product of the previous step was used in the first step, instead of acetophenone.

[0335] MS: 545.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.78-8.75 (d, 1H, J=8.4Hz), 8.55 (d, 1H, J=1.5Hz), 8.50 (s, 1H), 8.47-8.38 (m, 4H), 8.33-8.30 (d, 1H), J=9.0Hz), 8.17-8.14 (dd, 1H, J=8.7Hz & 1.5Hz), 8.10-8.06 (dd, 1H, J=8.7Hz & 1.8Hz), 7.74-7.66 (m, 2H), 4.50 (m, 1H), 2.36 (m, 2H), 2.15 (m, 2H), 1.90 (m, 6H), 1.65 (m, 1H), 1.44-1.20 (m, 3H).

Example 42

Preparation of 2-[2-(2-Bromo-phenyl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 471)**

Step 1: 4-{[1-(2-Bromo-phenyl)-meth-(E)-ylidene]-amino}-benzoic acid methyl ester (Compound 471a)

[0336] 4-aminobenzoic acid methyl ester (1.51g, 10mmol) and 2-bromobenzaldehyde (1.45 mL, 12.5 mmol) were dissolved in 15 mL of methanol. The mixture was let stand overnight. A white precipitate formed and the crystals were filtered off, washed with cold methanol (2x) and dried.

[0337] MS: 318.03 & 320.03 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.81 (s, 1H), 8.22-8.19 (dd, 1H, J=7.8 &1.8Hz), 8.09-8.05 (m, 2H), 7.63-7.60 (dd, 1H, J=7.8&1.2Hz), 7.43-7.30 (m, 2H), 7.24-7.2 (m, 2H), 3.92 (s, 3H), 1.62 (s. 1H).

Step 2: 2-(2-Bromo-phenyl)-4-methyl-quinoline-6-carboxylic acid methyl ester (Compound 471b)

[0338] A suspension of 1.97g (6.1 mmol) of the product of the previous step in 20 mL acetonitrile and a solution of 385 mg (0.61 mmol) of ytterbium-triflate in 20 mL acetonitrile were combined and stirred at room temperature for 10 minutes. Then 1.46 mL (15.3 mmol) of 2-methoxy-propene were added in one portion. The suspension immediately cleared. The mixture was stirred at room temperature overnight. The next day the reaction was quenched by the addition of 20 mL of 2.5 M HCl. The resulting mixture was evaporated and the product purified on a silica pad using hexane-ethyl acetate 10%-30% step gradient to yield 500mg (23%) (See also, Y.Makioka, T.Shindo,Y.Taniguchi, KTakaki, Y.Fujiwara, *Synthesis*, 1995.) MS: 356.05 & 358.05 ($M+H^+$)

Step 3: 2-(2-Bromo-phenyl)-4-methyl-quinoline-6-carboxylic acid (Compound 471c)

[0339] Compound **471b** (500 mg, 1.4mmol) was refluxed in a mixture of 15 mL dioxane and 15 mL 1M aqueous NaOH for 1h then it was evaporated to dryness, the residue dissolved in 50 mL water and acidified with 1M HCl solution to pH 4. The

precipitate was filtered off, washed four times with water and dried. Yield: 361 mg (75%).

[0340] MS: 344.02 & 342.03 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 7.65-7.62 (dd, 1H, J=8.1 & 0.9Hz), 7.60-7.51 (m, 4H), 7.46-41 (m, 1H), 7.27-7.25 (m, 2H), 1.98 (s, 3H).

Step 4: 2-[2-(2-Bromo-phenyl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 471)

[0341] The title compound was synthesized in a one-pot reaction sequence of three steps starting with the product of the previous step as described for Compound **25,** Compound **27 Q=ethyl** and Compound **204**, respectively. Yield: 91%.

[0342] MS: 540.13 & 542.14 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.639 (s, 1H), 8.4-8.34 (m, 2H), 8.3-8.27 (d, 1H, J=8.7Hz), 8.21-8.13 (d, 1H, J=8.7Hz), 8.08-8.05 (d, 1H, J=9.0Hz), 7.88-7.83 (m, 2H), 7.7-7.67 (dd, 1H, J=7.2 & 1.5Hz), 7.64-7.59 (m, 1H), 7.54-7.48 (m, 1H), 4.57 (m, 1H), 2.89 (s, 1H), 2.39 (m, 2H), 2.15 (m, 2H), 1.90 (m, 2H), 1,67 (m, 1H), 1.44 (m, 3H).

Example 43

Preparation of 2-[2-(4'-Chloro-biphen-2-yl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 485**) and 1-Cyclohexyl-2-(4-methyl-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 498**)

[0343] Compound 471 was treated as described for Compound 23. The reaction resulted in two products that were separated using preparative RP-HPLC.

[0344] **Compound 485:** MS: 572.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ (ppm) 8.38 (s, 1H), 8.3 (d, 1H, J=1.2Hz), 8.17-8.05 (m, 3H), 7.96-7.92 (dd, 1H, J=9.0 & 1.5Hz), 7.78-7.74 (m, 1H), 7.63-7.51 (m, 3H), 7.34-7.31 (m, 2H), 7.21-7.18 (m, 3H), 4.46 (m, 1H), 2.59 (s, 3H), 2.33 (m, 2H), 2.05 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.34 (3H).

[0345] **Compound 498:** MS: 462.22 ($M+H^+$); H^1-NMR (DMSO-d_6): δ (ppm) 8.49 (m, 1H), 8.35-8.30 (m, 4H), 8.23 (s, 1H), 8.19-8.16 (d, 1H, J=8.7Hz), 8.13-8.09 (dd, 1H, J=8.7 & 1.8Hz), 8.00-7.97 (dd, 1H, J=8.7Hz), 7.63-7.55 (m, 3H), 4.48 (m, 1H), 2.86 (s, 1H), 2.34 (m, 2H), 2.10 (m, 2H), 1.86 (m, 2H), 1.62 (m, 1H), 1.35 (m, 3H).

Example 44

Preparation of 2-[2-(4'-Chloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 353**)

Step 1: 2-(2-Bromo-phenyl)-quinoline-6-carboxylic acid (Compound 353a)

[0346] The title intermediate was synthesized as described for Compound **13, Y=phenyl** except 2' bromoacetophenone was used instead of acetophenone.

[0347] MS: 326.00 & 328.00 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.72 (d, 1H, J=1.2Hz), 8.65-8.62 (d, 1H, J=8.4Hz), 8.25-8.21 (dd, 1H, J=9,0Hz & 1.8Hz), 8.11-8.09 (d, 1H, J=8.7Hz), 7.83-7.77 (m, 2H), 7.64-7.61 (m, 1H), 7.56-7.51 (m, 1H), 7.46-7.40 (m, 1H).

Step 2: 2-(4'-Chloro-biphen-2-yl)-quinoline-6-carboxylic acid (Compound 353b)

[0348] The title intermediate was synthesized from the product of the previous step, compound **353a**, as described for compound **387**.

[0349] MS: 358.09 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.62 (d, 1H, J=1.2Hz), 8.36-8.33 (d, 1H, J=8.4Hz), 8.24-8.21 (dd, 1H, J=9.0Hz & 1.8Hz), 8.08-8.05 (d, 1H, J=9Hz), 7.81-7.78 (dd, 1H, J=6.3hz & 2.1Hz), 7.14-7.12 (d, 1H, J=8.7Hz), 7.64-7.52 (m, 3H), 7.34-7.31 (m, 2H), 7.18-7.15 (m, 2H).

Step 3: 2-[2-(4'-Chloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (Compound 353)

[0350] The title compound was synthesized from Compound **353b** in two steps as described for Compound **25** and **27 Q=ethyl,** respectively.

[0351] MS: 476.11 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.03 (m, 1H), 8.71-8.69 (dd, 1H, J=7.Hz), 8.43-8.29 (m, 3H), 8.1-8.07 (dd, 1H, J=7.5Hz), 7.93-7.84 (m, 2H), 7.68-7.57 (m, 3H), 7.38-7.2 (m, 5H).

Example 45

Preparation of 2-[2-(4'-Chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 408**)

[0352] The title compound was synthesized using the procedures described in Examples 42 to 43 except in step 1 of Example 42 4-aminobenzoic acid methyl ester was replaced by 4-amino-2-fluorobenzoic acid methyl ester and in the second step methyl-vinyl ether was used.

[0353] MS: 576.19 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.42-8.40 (d, 1H, J=7.8Hz), 8.34-8.31 (m, 2H), 8.13-8. 3 (m, 2H), 7.97-7.94 (dd, 1H, J=8.4 & 1.5Hz), 7.81-7.78 (m, 1H), 7.63-7.51 (m, 3H), 7.35-7.32 (m, 2H), 7.19-7.12 (m, 3H), 4.14 (m, 1H), 2.26 (m, 2H), 1.95 (m, 2H), 1.82 (m, 2H), 1.60 (m, 1H), 1.33 (m, 3H). F^{19}-NMR (DMSO-d_6): δ(ppm) -112.33 (t).

Example 46

Preparation of 2-(2-Biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 388**)

[0354] The title compound was collected as a side product of the synthesis of Compound **408**.

[0355] MS: 541.22 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.39-8.36 (d, 1H, J=7.5Hz), 8.30 (d, 1H, J=1.5Hz), 8.26-8.23 (d, 1H, J=8.7Hz), 8.10-8.04 (m, 2H), 7.96-7.78 (m, 1H), 7.65-7.51 (m, 3H), 7.30-7.26 (m, 3H), 7.18-7.15 (m, 2H), 7.08-7.05 (d, 1H, J=8.7Hz), 4.14 (m, 1H), 2.26 (m, 2H), 1.95 (m, 2H), 1.82 (m, 2H), 1.60 (m, 1H), 1.32 (m, 3H). F^{19}-NMR (DMSO-d_6): δ(ppm) -112.51 (t).

Example 47

Preparation of 2-[2-(4'-Chloro-biphen-2-yl)-8-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 417**)

[0356] The title compound was synthesized using the procedures described in Examples 42 to Example 43 except in step 1 of Example 42 4-aminobenzoic acid

methyl ester was replaced by 4-amino-3-methylbenzoic acid methyl ester and in the second step methyl-vinyl ether was used.

[0357] MS: 572.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.43 (d, 1H, J=8.4Hz), 8.30 (d, 1H, J=1.5Hz), 8.20-8.17 (m, 2H), 7.99 (dd, 1H, J=8.7 and 1.2Hz), 7.88-7.83 (m, 2H), 7.62-7.59 (m, 2H), 7.53-7.50 (m, 1H0, 7.46 (d, 1H, J=8.7Hz), 7.33-7.30 (m, 2H), 7.17-7.14 (m, 2H), 4.46 (m, 1H), 2.51 (s, 3H), 2.35-1.28 (m 10H).

Example 48

Preparation of 2-(2-Biphen-2-yl-8-methyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 379)**

[0358] The title compound was collected as a side product of the synthesis of Compound **417**.

[0359] MS: 538.27 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.33-8.27 (m, 2H), 8.12-8.10 (m, 2H), 7.95 (dd, 1H, J=8.7Hz), 7.86-7.83 (m, 2H), 7.60-7.50 (m, 3H), 7.34 (d, 1H, J=8.7Hz), 7.26-7.13 (m, 5H), 4.44 (m, 1H), 2.62 (s, 3H), 2.35-1.23 (m 10H).

Example 49

Preparation of 1-Cyclohexyl-2-(8-methyl-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 397)**

[0360] The title compound was collected as a side product of the synthesis of Compound **417**.

[0361] MS: 462.22 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.64 (d, 1H, J=8.7Hz), 8.38-8.36 (m, 2H), 8.32-8.29 (m, 2H), 8.21 (m, 1H), 8.13 (d, 1H, J=8.1Hz), 7.97-7.94 (m, 2H), 7.62-7.53 (m, 3H), 4.45 (m, 1H), 2.92 (s, 3H), 2.35-1.23 (m 10H);

Example 50

Preparation of {2-[2-(4'-Chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(4-methyl-piperazin-1-yl)-methanone **(Compound 521)**

[0362] The title compound was synthesized from **Compound 408** and N-methyl-piperazine using standard HBTU activation.

[0363] MS: 329.63 ($M+2H^+$)/2; H^1-NMR (DMSO-d_6): δ(ppm) 10.95 (s, 1H), 8.34-8.28 (m, 2H), 8.06-8.00 (m, 2H), 7.85 (d, 1H, J=1.8Hz), 7.80-7.77 (m,1H), 7.62-7.50 (m, 3H), 7.43-7.39 (dd, 1H, J=8.1Hz & 1.5Hz), 7.35-7.32 (m, 2H), 7.20-7.10 (m, 3H), 4.09 (, 1H), 3.38 (m, 5H), 3.12 (m, 3H), 2.78 (d, 3H, J=4.2Hz), 2.28 (m, 2H), 1.93-1.80 (m, 4H), 1,59 (m, 1H), 1.33 (m, 3H); F^{19}-NMR (DMSO-d_6): δ(ppm) -112.71 (t).

Example 51

Preparation of {2-[2-(4'-Chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(4-hydroxy-piperidin-1-yl)-methanone **(Compound 514)**

[0364] The title compound was synthesized from **Compound 408** and 4-hydroxypiperidine using standard HBTU activation.

[0365] MS: 659.31 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.44-8.36 (m, 2H), 8.11-8.08 (m, 2H), 7.89-7.86 (m, 1H), 7.80 (d, 1H, J-1.2Hz), 7.70-7.67 (m, 2H), 7.62-7.59 (m, 1H), 7.43-7.41 (m, 3H), 7.24-7.18 (, 3H), 4.17 (m, 1H), 3.83 (m, 1H), 3.3 (m, 1H), 2.37 (, 2H), 2.37-1.41 (m, 15H);); F^{19}-NMR (DMSO-d_6): δ(ppm) -112.67 (t).

Example 52

Preparation of [2-(2-Biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazol-5-yl]-(4-methyl-piperazin-1-yl)-methanone **(Compound 522)**

[0366] The title compound was isolated as a side product of Compound **521** synthesis.

[0367] MS: 312.65 ($M+2H^+$)/2 ; H^1-NMR (DMSO-d_6): δ(ppm) 10.76 (s, 1H), 8.30 (d, 1H, J=7.8Hz), 8.22 (d, 1H), J=8.7Hz), 8.05-8.01 (m, 2H), 7.84 (d, 1H, J=1.2Hz), 7.80-7.77 (m, 2H), 7.61-7.50 (m, 3H), 7.42-7.39 (dd, 1H), J=6.9Hz & 1.2Hz), 7.28-7.25 (m, 3H), 7.18-7.14 (m. 2H), 7.05 (d, 1H, J=8.7Hz), 4.1 (m, 1H), 3.38 (m, 2H),

3.12 (m, 3H), 2.79 (d, 3H, J=4.2Hz), 2.28-1.22 (m, 13H); F^{19}-NMR (DMSO-d_6): δ(ppm) -112.77 (t).

Example 53

Preparation of 2-(2-Biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazol-5-yl]-(4-hydroxy-piperidin-1-yl)-methanone **(Compound 410)**

[0368] The title compound was isolated as a side product of Compound **514** synthesis.

[0369] MS: 625.34 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.32 (d, 1H0, J=8.4Hz), 8.21 (d, 1H, J=8.4Hz), 8.04-8.97 (m, 2H), 7.79 (m, 1H0, 7.71 (d, 1H, J=1.2Hz), 7.63-7.50 (m, 3H), 7.32 (dd, 1H0, J=8.4Hz & 1.5Hz), 7.28-7.14 (m, 2H), 7.03 (d, 1H, J=8.7Hz), 4.09 (m, 1H), 3.73 (m, 1H), 3.20 (m, 2H), 2.25-1.33 (m, 16H). F^{19}-NMR (DMSO-d_6): δ(ppm) -112.81 (t).

Example 54

Preparation of 2-[2-(5-Bromo-2-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 354)**

Step 1: 3-Dimethoxymethyl-4-nitro-benzoic acid (Compound 354a)

[0370] To a solution of 5.49 g (21.5 mmol) of Compound **5** in 200 mL of methanol, 50 mL of 1M NaOH were added and the mixture was stirred at room temperature for 2 h. The reaction mixture was then evaporated to dryness, the residue was dissolved in 100 mL water, acidified with 1M HCl to pH 3-4. The precipitate was then filtered off, washed with water (4x), and dried. Yield: 4.96g (95%).

[0371] MS: 240.08 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.49 (d, 1H, J=1.8Hz), 8.21-8.18 (dd, 1H, J=8.4 & 1.8Hz), 7.85-7.82 (d, 1H, J=8.4Hz), 5.90 (s, 1H), 3.41 (s, 6H).

Step 2: 4-Cyclohexylamino-3-(3-dimethoxymethyl-4-nitro-benzoylamino)-benzoic acid ethyl ester (Compound 354b)

[0372] The title intermediate was synthesized from the product of the previous step as described for Compound **25**.

[0373] MS: 486.23 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.93 (s, 1H), 8.23-8.15 (m, 2H), 8.05-8.02 (d, 1H, J=8.1Hz), 7.70-7.67 (m, 2H), 6.78-6.75 (d, 1H, J=8.4Hz), 5.83 (s, 1H), 5.54-5.51 (d, 1H, J=7.5Hz), 4.22 (q, 2H, J=7.2Hz), 3.39-3.34 (m, 7H), 1.92 (m, 2H), 1.73-1.58 (m, 3H), 1.38-1.12 (m, 8H).

Step 3: 1-Cyclohexyl-2-(3-dimethoxymethyl-4-nitro-phenyl)-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 354c)

[0374] To a solution of 1.53 g (3.15 mol) the product of the previous step in 75 mL acetic acid 1.5 g 4A molecular sieves was added and the mixture was refluxed for 2h. TLC indicated a complete and clean reaction. The mixture was evaporated to dryness, dried under high vacuum and was used without further purification.

Step 4: 2-(4-Amino-3-dimethoxymethyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 354d)

[0375] In 20 mL methanol 100 mg of 10% Pd-C was pre-hydrogenated in the presence of 1g $MgSO_4$ at 30 psi for 15 minutes. Compound **354c** (100mg) dissolved in a solution of 20 mL of methanol containing 2 mL triethylamine, was added to the catalyst and the hydrogenation was continued for 30 minutes. The catalyst and the magnesium sulfate were filtered using Celite. The solution was evaporated to dryness and the oily residue was used immediately in the following step.

Step 5: 2-(4-Amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 354e)

[0376] The oily product of the previous step was dissolved in 25 mL ethanol-acetic acid-water 2:2:1 mixture and was let stand for 15 minutes at room temperature. It was evaporated to dryness to get the solid title intermediate, which was pure enough to use in the next step without further purification. MS: 392.25 ($M+H^+$)

Step 6: 2-[2-(5-Bromo-2-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 354)

[0377] The title compound was synthesized from the product of the previous step as described for Compound **19,** followed by purification on RP-HPLC.

[0378] MS: 542.15 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 12.81 (s, 1H), 8.77-8.74 (d, 1H, J=8.7Hz), 8.56-8.53 (d, 1H, J=9.0Hz), 8.41 (m, 2H), 8.30-8.27 (m, 2H), 8.10-8.07 (dd, 1H, J=8.7 & 2.1Hz), 8.03-8.00 (d, 1H, J=8.7Hz), 7.90-7.87 (dd, 2H, J=8.7 & 1.5Hz), 7.57-7.53 (dd, 1H, J=9.0 & 2.4Hz), 7.02-6.99 (d, 1H, J=9.0Hz), 4.39 (m, 1H), 2.33 (m, 2H), 2.02 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.32 (m, 3H).

Example 55

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 356)**

[0379] The title compound was synthesized in seven steps as described for Compound **204** except 2-hydroxy-5-methoxy acetophenone was used instead of Compound **18**.

[0380] MS: 588.23 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.38-8.35 (m, 2H), 8.30 (d, 1H, J=1.5Hz), 8.23 (d, 1H, J=8,7Hz), 8.15 (d, 1H, J=8.7Hz), 8.05 (dd, 1H, J=8.7Hz & 1.5Hz), 7.97 (dd, 1H, J=9Hz & 1.5Hz), 7.45 (d, 1H, J=8.4Hz), 7.31-7.27 (m, 3H), 7.21-7.17 (m, 2H), 7.13-7.10 (m, 2H), 4.41 (m, 1H), 3.87 (s, 3H), 2.34-1.28 (m, 10H);

Example 56

Preparation of 1-Cyclohexyl-2-[2-(4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 499)**

[0381] The title compound was isolated as side product of the synthesis of Compound **356**.

[0382] MS: 554.26 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.34-8.24 (m, 4H), 8.13 (d, 1H, J=8.4Hz), 8.05 (dd, 1H, J=9Hz), 7. 95 (dd, 1H, J=8.4Hz & 1.2Hz), 7.46

(d, 1H, J=8.4Hz), 7.33 (d, 1H, J=2.4Hz), 7.24-7.10 (m, 7H), 4.42 (m, 1H), 3.88 (s, 3H), 2.34-1.28 (m, 10H).

Example 57

Preparation of 1-Cyclohexyl-2-[2-(3-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 486)**

[0383] The title compound was isolated as side product of the synthesis of Compound **356**.

[0384] MS: 478.22 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.68 (d, 1H, J=8.7Hz), 8.43 (d, 1H, J=1.8Hz), 8.33-8.29 (m, 3H), 8.15 (d, 1H, J=9Hz), 8.06 (dd, 1H, J=8.7Hz &1.5Hz), 7.97 (dd, 1H, J=8.7Hz & 1.5Hz), 7.91-7.87 (m, 2H), 7.53-7.48 (m, 1H), 7.12 (dd, 1H, J=8.4Hz, 2.4Hz), 4.43 (m, 1H), 3.89 (s, 3H), 2.35-1.28 (m, 10H).

Example 58

Preparation of 2-[2-(4'-Chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 500)** and 1-Cyclohexyl-2-[2-(3-hydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 474)** and 1-Cyclohexyl-2-[2-(4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 487)**

[0385] To a cold solution of 2.3g (3.7 mmol) of Compound **500a** in 90 mL DCM, 37.2 mL (37.2 mmol) of a solution of 1M PBr_3 in DCM was added. The mixture was stirred overnight then was quenched by addition of 110 mL of methanol. The reaction mixture was evaporated to dryness and triturated with water to give the title compound which was purified by RP-HPLC. After trituration, Compound 500 was sufficient to use in subsequent reactions without further purification. Two side-products (Compound **487**) and (Compound **474**) were also separated and identified from the reaction mixture. .

[0386] **(Compound 500):** MS: 574.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ (ppm) 8.38-8.31 (m, 3H), 8.25 (d, 1H, J=8.7Hz), 8.18 (d, 1H, J=8.7Hz), 8.08 (dd, 1H, J=8.7 & 2.1Hz), 7.99 (dd, 1H, J=8.4 & 1.5Hz), 7.35 (d, 1H, J=8.7Hz), 7. 28 (m, 2H), 7.21 (d, 1H, J=2.7Hz), 7.16 (d, 1H, J=8.7Hz), 7.10 (m. 2H), 7.01 (dd, 1H, J=8.4 & 2.1Hz),4.44 (m, 1H), 2.35-1.03 (m, 10H);

[0387] **(Compound 474):** MS: 464.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ (ppm) 8.68 (d, 1H, J=8.7Hz), 8.47 (d, 1H, J=1.8Hz), 8.34-8.22 (m, 4H), 8.10 (dd, 1H, J=8.7 & 1.8Hz), 8.03 (dd, 1H, J=8.7 & 1.5Hz), 7.76-7.70 (m, 2H), 7.41-7.35 (m, 1H), 6.97-6.94 (m, 1H), 4.44 (m, 1H), 2.35-1.23 (m, 10H);

[0388] **(Compound 487):** MS: 540.25 ($M+H^+$); H^1-NMR (DMSO-d_6): δ (ppm) 8.34-8.24 (m, 4H), 8.15 (d, 1H), 8.05 (dd, 1H), 7.98 (dd, 1H), 7.34 (d, 1H, J=8.7Hz), 7.21 (m, 4H), 7.11-7.08 (m, 3H), 7.01 (dd, 1H, J=8.1 & 2.7Hz), 5.43 (m, 1H), 2.35-1.33 (m, 10H);

Example 59

Preparation of 2-{2-[4'-Chloro-4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 475)**

Step 1: 2-[2-(4'-Chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid methyl ester (Compound 475a)

[0389] To a solution of 2.15g (3.745 mmol) of Compound **500** in 100 mL methanol, 25 mL of 4M HCl in dioxane were added and the mixture was heated at 55 C° for 3 hours. The reaction mixture was then evaporated to dryness and the residual oil triturated with water and dried to yield 1.97g (89%) of the title intermediate, which was used without further purification.

Step 2: 2-{2-[4'-Chloro-4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 475)

[0390] Compound **475a** (100 mg, 0.162 mmol) was dissolved in 2 mL of DMF and treated with 16.8 mg (0.7 mmol) of NaH for 30 min. 1-bromo-2-methoxy ethane (30.5 μL) was added and the mixture was agitated overnight. The next day the reaction mixture was evaporated to dryness, the oily residue dissolved in 3 mL methanol followed by the addition of 1mL 1M NaOH. The mixture was refluxed for 2 h before it was evaporated to dryness. The product was purified by RP-HPLC for a yield of 19.3 mg of the title compound.

[0391] MS: 632.24 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.40-8.34 (m, 2H), 8.32 (d, 1H, J=1.2Hz), 8.23 (d, 1H, J=8.7Hz), 8.15 (d, 1H, J=9.0Hz), 8.07 (dd, 1H, J=9.0 and 1.8Hz), 7.48 (dd, 1H, J=8.4 and 1.2Hz), 7.45 (d, 1H, J=8.4Hz), 7.33-7.29 (m, 3H), 7.23-7.14 (m, 2H), 7.14-7.11 (m, 2H), 4.43 (m, 1H), 4.24 (m, 3H), 3.71 (m, 2H), 3.37 (m, 3H), 2.35-1.30 (m. 10H);

Example 60

Preparation of 1-Cyclohexyl-2-{2-[4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 461)**

[0392] The title compound was isolated as a side product of the synthesis of Compound **475**.

[0393] MS: 598.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.33-8.28 (m, 3H), 8.23 (d, 1H, J=9.0Hz), 8.13-8.03 (m, 2H), 7.95 (dd, 1H, J=8.7Hz, 1.2Hz), 7.45 (d, 1H, J=8.4Hz), 7.34 (d, 1H, J=2.7Hz), 7.24-7.18 (m, 4H), 7.14-7.10 (m, 3H), 4.41 (m, 1H), 4.22 (m , 2H), 3.5-3.3 (m, 5H offset by water), 2.34-1.23 (m, 10H);

Example 61

Preparation of 1-Cyclohexyl-2-{2-[3-(2-methoxy-ethoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 445)**

[0394] The title compound was isolated as a side product of the synthesis of Compound **475**.

[0395] MS: 522.24 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.69 (d, 1H, J=8.7Hz), 8.44 (d, 1H, J=1.8Hz), 8.35-8.29 (m, 3H), 8.17 (d, 1H, J=8.7Hz), 8.08 (dd, 1H, J=8.7 and 1.8Hz), 8.98 (dd, 1H, J=9.0 and 1.8Hz), 7.92-7.89 (m, 2H), 7.52-7.47 (m, 1H), 7.15-7.12 (m, 1H), 4.43 (m, 1H), 4,24 (m, 2H), 3.73 (m, 2H), 3.41-3.34 (m, 3H), 2.36-1.2 (m, 10H);

Example 62

Preparation of 2-{2-[4'-Chloro-4-(2-ethoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 507)**

[0396] The title compound was synthesized as described for Compound 475, except 1-bromo-2-ethoxy ethane was used for alkylation instead of 1-bromo-2-methoxy ethane.

[0397] MS: 646.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.34-8.22 (m, 3H), 8.18 (d, 1H, J=9.0Hz), 8.08 (d, 1H, J=8.4Hz), 8.01 (dd, 1H, J=8.4 and 1.5Hz), 7.91 (dd, 1H, 8.4 and 1.2Hz), 7.40 (m, 1H), 7.29-7.07 (m, 7H), 4.37 (m, 1H), 4,18 (m, 2H), 3.70 (m, 2H), 3.50 (q, 2H, J=1.2Hz), 2.30-1.24 (m, 10H), 1.10 (t, 3H, J=1.2Hz);

Example 63

Preparation of 2-[2-(4-Carboxymethoxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 393)**

[0398] The title compound was synthesized as described for Compound **475**, except *tert*-butyl bromoacetate was used for alkylation instead of 1-bromo-2-methoxy ethane. The *tert*-butyl group was removed in a separate step before saponification by a 1 h treatment with TFA.

[0399] MS: 630.16 ($M-H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.41-8.38 (m, 2H), 8.32 (d, 1H, J=1.5Hz), 8.25-8.18 (m, 2H), 8.09 (dd, 1H, J=8.4 and 1.8Hz), 8.00 (dd, 1H, J=8.7 and 1.5hz), 7.47 (d, 1H, J=8.4Hz), 7.32-7.29 (m, 3H), 7.23-7.11 (m, 4H), 4.83 (s, 2H), 4.44 (m, 1H), 2.35-1.3 (m, 10H);

Example 64

Preparation of 2-[2-(4-Carboxymethoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 375)**

[0400] The title compound was isolated as a side product of the synthesis of Compound **393**.

[0401] MS: 596.20 ($M-H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.35-8.29 (m, 3H), 8.25 (d, 1H, J=8.7Hz), 8.15 (dd, 1H, J=9.0Hz), 8.07 (dd, 1H, J=9.0Hz), 7.97 (dd,

1H, 7.2 and 1.8Hz), 7.46 (d, 1H, J=8.4Hz), 7.31 (d, 1H, J=2.7Hz), 7.25-7.11 (m, 8H), 4.82 (s, 2H), 4.42 (m, 1H), 2.43-1.30 (m, 10H);

Example 65

Preparation of 2-[2-(3-Carboxymethoxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 359)**

[0402] The title compound was isolated as a side product of the synthesis of Compound **393**.

[0403] MS: 520.17 ($M-H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.70 (d, 1H, J=8.7Hz), 8.45 (d, 1H), 8.32 (m, 3H), 8.19 (d, 1H, J=9.0Hz), 8.09 (dd, 1H), 8.00-7.87 (m, 3H), 7.50 (m, 1H), 7.11 (m, 1H), 4.83 (s, 2H), 4.44 (m, 1H), 2.35-1.30 (m, 10H);

Example 66

Preparation of 2-{2-[4'-Chloro-4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 447)**

[0404] The title compound was synthesized as described for Compound **475**, except 1,3-dibromopropane was used for alkylation instead of 1-bromo-2-methoxy ethane. The resulting 3-bromopropyl derivative was treated *in situ* with an excess of pyrrolidine to give the final product.

[0405] MS: 685.34 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.74 (m, 1H), 8.39-8.36 (m, 2H), 8.32 (d, 1H, J=1.5Hz), 8.25 (d, 1H, J=8.7Hz), 8.18 (d, 1H, J=8.7Hz), 8.07 (dd, 1H, J=8.4 and 1.8Hz), 8.98 (dd, 1H, J=9.0 and 1.6Hz), 7.47 (d, 1H, J=8.7Hz), 7.35-7.29 (m, 3H), 7.23-7.18 (m 2H), 7.14-7.11 (m, 2H), 4.42 (m, 1H), 4.21 (m, 2H), 3.56 (m, 2H), 3.33 (m, 2H), 3.02 (m, 2H), 2.35-1.28 (m, 16H);

Example 67

Preparation of 1-Cyclohexyl-2-{2-[4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 430)**

[0406] The title compound was isolated as a side product of the synthesis of Compound **447**.

[0407] MS: 651.36 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.70 (m, 1H), 8.34-8.23 (m, 4H), 8.13 (d, 1H, J=8.4Hz), 8.06 (dd, 1H, J=8.7 and 1.8Hz), 7.96 (dd, 1H, J=8.7 and 1.5Hz), 7.47 (d, 1H, J=8.7Hz), 7.35 (d, 1H, J=2.7Hz), 7.26-7.18 (m, 4H), 7.14-7.09 (m, 3H), 4.41 (m, 1H), 4.21 (m, 2H), 3.58 (m, 2H), 3.34 (m, 2H), 3.02 (m, 2H), 2.35-1.23 (m, 16H);

Example 68

Preparation of 1-Cyclohexyl-2-{2-[3-(3-pyrrolidin-1-yl-propoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 414)**

[0408] The title compound was isolated as a side product of the synthesis of Compound **447**.

[0409] MS: 575.32 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.70 (m, 1H), 8.68 (d, 1H, J=8.7Hz), 8.42 (d, 1H), 8.30 (m, 3H), 8.14 (d, 1H, J=8.4Hz), 8.07 (dd, 1H, J=8.4Hz), 7.97-7.90 (m, 3H), 7.71 (m, 1H), 7.13 (m, 1H), 4.41 (m, 1H), 4.22 (m, 2H), 3.59 (m, 2H), 3.36 (m, 2H), 3.042 (m, 2H), 2.43-1.23 (m, 16H);

Example 69

Preparation of 2-{2-[4'-Chloro-4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 376)**

[0410] The title compound was synthesized as described for Compound **475**, except 2-bromo-1-pyrrolidin-1-yl-ethanone was used for alkylation instead of 1-bromo-2-methoxy ethane.

[0411] MS: 685.34 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.37-8.34 (m, 3H), 8.20 (d, 1H, J=8.4Hz), 8.12-8.03 (m, 2H), 7.94 (dd, 1H, J=8.7 and 1.2Hz), 7.43 (d, 1H, J=8.7Hz), 7.31-7.28 (m, 3H), 7.20-7.11 (m, 4H), 4.87 (s, 2H), 4.41 (m, 1H), 3.49 (m, 2H), 3.33 (m, 2H), 2.35-1.23 (m, 14H);

Example 70

Preparation of 1-cyclohexyl-2-{2-[4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 360)**

[0412] The title compound was isolated as a side product of the synthesis of Compound **376**.

[0413] MS: 651.34 (M+H+); H1-NMR (DMSO-d_6): δ (ppm) 8.30-8.25 (m, 3H), 8.20 (d, 1H, J=8.4Hz), 8.05 (m, 2H), 7.192 (dd, 1H, J=8.4 and 1.5Hz), 7.43 (d, 1H, J=8.4Hz), 7.30 (d,1H, J=2.7Hz), 7.24-7.08 (m, 8H), 4.87 (s, 2H), 4.40 (m, 1H), 3.49 (m, 2H), 3.34 (m, 2H), 2.34-1.23 (m, 14H);

Example 71

Preparation of 1-cyclohexyl-2-{2-[3-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 503)**

[0414] The title compound was isolated as a side product of the synthesis of Compound **376**.

[0415] MS: 575.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.66 (d, 1H, J=8.7hz), 8.41 (d, 1H, J=1.8Hz), 8.30-8.26 (m, 3H), 8.12-8.04 (m, 2H), 7.96-7.87 (m, 3H), 7.49 (m, 1H), 7.10 (dd, 1H, J=7.8 and 2.1Hz), 4.87 (s, 2H), 4.42 (m, 1H), 3.41 (m, 2H), 3.35 (m, 2H), 2.35-1.23 (m, 14H);

Example 72

Preparation of 2-[2-(4-Carboxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 415)**

Step 1: 2-[2-(4'-Chloro-4-trifluoromethanesulfonyloxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid methyl ester (Compound 415a)

[0416] To a solution of 1g (1.7mmol) of Compound **475a** in 20 mL of DCM, 550 µL (6.8mmol) of pyridine, and 21 mg (0.17 mmol) of DMAP were added and the entire mixture was cooled to 0 °C. Dropwise, 860 µL of Tf_2O was added. The reaction was then stirred at room temperature for 1 h. Finally the reaction mixture was evaporated, and the product dissolved in ethyl acetate, washed with cold water (2x), brine (2x) , dried

with Na_2SO_4 and evaporated again to give the title intermediate as a white solid foam in quantitative yield.

Step 2: 2-[2-(4-Carboxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid methyl ester (Compound 415b)

[0417] A mixture of 1.334g (1.85 mmol) of the product from the previous step, 350 μL of acetic anhydride, 288 mg (5.55 mmol) of LiO(O)CH, 235 mg (5.55 mmol) of LiCl, 644 μL (3.7 mmol) of DIEA and 54 mg (92.5 μmol) of Pd Cl_2(dppp) in DMF was heated under Ar at 80 °C overnight. The solvent was evaporated and the residue triturated with water to give 1g of the crude title intermediate, which was not isolated and was used as is in the following steps.

Step 3: 2-[2-(4-Carboxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 415)

[0418] The crude product from the previous step (250 mg) was saponified with 5 eq. of aq. 1M NaOH in methanol for 1h at 55 °C. The reaction mixture was evaporated and the product purified with RP-HPLC to give the title compound as a yellow solid.

[0419] MS: 600.14 ($M-H^+$); H^1-NMR (DMSO-d_6): δ (ppm) 8.41-8.38 (m, 2H), 8.34-8.28 (m, 3H), 8.23 (d, 1H, J=8.4Hz), 8.14 (dd, 1H, J=8.1 and 1.8Hz), 8.09 (dd, 1H, J=8.4 and 1.8Hz), 8.00 (dd, 1H, J=7.2Hz), 7.67 (d, 1H, J=7.8Hz), 7.37 (m, 2H), 7.26-7.20 (m, 3H), 4.43 (m 1H), 2.31-1.32 (m, 10H).

Example 73

Preparation of 2-{2-[4'-Chloro-4-(2-dimethylamino-ethylcarbamoyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 491)**

[0420] Crude Compound **415b** (250 mg, 0.4 mmol) in 2 mL DMF was pre-activated with 193 mg (0.5mmol) of HATU and 174 μL (1 mmol) of DIEA for 15 min at room temperature. N^1,N^1-dimethyl-ethane-1,2-diamine (100 μL, 0.9 mmol) was added and stirred overnight. The next day the reaction mixture was evaporated to dryness and triturated with water. The wet solid was dissolved in 5 mL methanol and was saponified

as described for Compound **415** to give, after RP-HPLC purification, 8.5 mg of the title compound.

[0421] MS: 672.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.10 (m, 1H), 9.04 (m, 1H), 8.40-8.36 (m, 2H), 8.31-8.29 (m, 2H), 8.23 (d, 1H, J=8.7Hz), 8.16-8.04 (m, 3H), 7.94 (dd, 1H, J=8.7 and 1.2Hz), 7.65 (d, 1H, J=7.8Hz), 7.36 (m, 2H), 7.22 (m, 3H), 4.41 (m, 1H), 3.69 (m, 2H), 3.31 (m, 2H), 2.84 (s, 6H), 2.36-1.23 (m, 10H).

Example 74

Preparation of 1-Cyclohexyl-2-{2-[4-(2-dimethylamino-ethylcarbamoyl)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid **(Compound 504)**

[0422] The title compound was isolated as a side product of the synthesis of Compound **491**.

[0423] MS: 638.31 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.99 (m, 1H), 9.00 (m, 1H), 8.33-8.28 (m, 4H), 8.25 (d, 1H, J=8.7Hz), 8.14-8.04 (m, 3H), 7.94 (dd, 1H, J=9.0Hz), 7.66 (d, 1H, J=8.1Hz), 7.30-7.27 (m, 3H), 7.21-1.13 (m, 3H), 4.41 (m, 1H), 3.68 (m, 2H), 3.31 (m, 2H), 2.83 (s, 6H), 2.35-1.23 (m, 10H).

Example 75

Preparation of 2-{2-[4-(Carbamoylmethyl-carbamoyl)-4'-chloro-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 361)**

[0424] The title compound was synthesized as described for Compound **491**, except glycine-amide was used instead of N^1,N^1-dimethyl-ethane-1,2-diamine.

[0425] MS: 658.24 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.92 (m, 1H), 8.41-8.23 (m, 5H), 8.14-8.04 (m, 3H), 7.95 (dd, 1H, J=8.4 and 1.5Hz), 7.65 (d, 1H, J=8.4Hz), 7.43-7.35 (m, 3H), 7.26-7.20 (m, 3H), 7.06 (m, 1H), 4.42 (m, 1H), 3.86 (m, 2H), 2.35-1.23 (m, 10H).

Example 76

Preparation of 2-{2-[4-(Carbamoylmethyl-carbamoyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 377)**

[0426] The title compound was isolated as a side product of the synthesis of Compound **361**.

[0427] MS: 624.24 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.90 (m, 1H), 8.33-8.25 (m, 4H), 8.12-8.04 (m, 3H), 7.95 (d, 1H, J=9.0Hz), 7.64 (d, 1H, J=8.1Hz), 7.42 (m, 1H), 7.28 (m, 2H), 7.22-7.06 (m, 3H), 4.42 (m, 1H), 3.87 (m, 2H), 2.35-1.23 (m, 10H).

Example 77

Preparation of 2-[2-(4'-chloro-4-methylcarbamoyl-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 378)**

[0428] The title compound was synthesized as described for Compound **491**, except methyl amine was used instead of N^1,N^1-dimethyl-ethane-1,2-diamine.

[0429] MS: 615.25 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.70 (d, 1H, J=9.3Hz), 8.46 (d, 1H, J=1.5Hz), 8.39 (m, 1H), 8.34-8.31 (m, 3H), 8.27-8.19 (m, 2H), 8.10-7.99 (m, 3H), 7.64-7.55 (m, 3H), 7.35 (d, 1H, J=8.4 Hz), 7.27-7.19 (m, 1H), 4.44 (m, 1H), 2.83 (d, 3H), 2.35-1.23 (m, 10H).

Example 78

Preparation of 1-cyclohexyl-2-[2-(4-methylcarbamoyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 362)**

[0430] The title compound was isolated as a side product of the synthesis of Compound **378**.

[0431] MS: 581.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.65 (m, 1H), 8.36-8.25 (m, 5H), 8.15 (d, 1H, J=9.0Hz), 8.08-8.04 (m, 2H0, 7.97 (dd, 1H, J=8.7 and 1.8Hz), 7.62 (d, 1H, J=7.8Hz), 7.30-7.15 (m, 6H), 4.43 (m, 1H), 2.84 (d, 3H), 2.35-1.23 (m, 10H).

Example 79

Preparation of 2-(2-biphen-2-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 395)**

[0432] The title compound was isolated as a side product of the synthesis of Compound **378**.

[0433] MS: 524.22 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.40 (d, 1H, J=1.8Hz), 8.34-8.28 (m, 3H), 8.23 (d, 1H, J=8.7Hz), 8.10 (dd, 1H, J=8.4 and 1.7Hz), 8.02 (dd, 1H, J=8.7 and 1.2Hz), 7.81 (dd, 1H, J=7.8 and 1.5Hz), 7.63-7.52 (m, 3H), 7.28-7.14 (m, 6H), 4.44 (m, 1H), 2.35-1.29 (m, 10H).

Example 80

Preparation of Cyclohexyl-2-(2,3-diphenylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid (**Compound 406**)

Step 1: 3,4-Bis-tert-butoxycarbonylaminobenzoic acid (Compound 406a)

[0434] A solution of 2 g (13.15 mmol) of 3,4-diaminobenzoic acid, 8.61 g (39.45 mmol) of $(BOC)_2O$, and 2.04 g (15.78 mmol) of DIEA in 15 mL anhydrous DMF was stirred at room temperature overnight and then poured into 150 mL H_2O. The pH of the mixture was adjusted to pH 5 or 6 followed by extraction with 3x100 mL EtOAc. The organic layer was washed with 300 mL H_2O, dried (Na_2SO_4) and the solvent was evaporated. The residue was purified on silica gel using hexane and EtOAc to yield 3 g white solid. MS: 351.17 ($M-H^+$).

Step 2: 1-Cyclohexyl-2-(3,4-diaminophenyl)-1H-benzimidazole-5-carboxylic acid (Compound 406b)

[0435] A solution of 1 g (2.84 mmol) of the product of the previous step, 0.91 g (2.84 mmol) of TBTU and 0.73 g (5.68 mmol) of DIEA in 10 mL anhydrous DMF was allowed to stand at room temperature for 15 min. To this solution was added 0.90 g (3.41 mmol) of Compound **11**, and the solution was allowed to stand at room temperature overnight. The solution was then poured into 100 mL H_2O, stirred for 30 min, filtered and dried. The solution of the solids thus obtained, in 50 mL 1M HCl and 25 mL EtOH, was

refluxed at 110°C overnight. The solvents were removed and the residue was treated with 14 mL 2 M NaOH in 70 mL of MeOH at 60°C overnight. The MeOH was evaporated, the residue was diluted with 70 mL H_2O and acidified to pH 6. The precipitate was filtered, washed with H_2O and dried yielding 0.95 g brown solid. MS: 351.20 ($M+H^+$).

Step 3: 1-Cyclohexyl-2-(2,3-diphenylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid (Compound 406)

[0436] A solution of 100 mg (0.29 mmol) of Compound **406b** and 74 mg (0.35 mmol) of benzil was stirred at room temperature overnight. The solvent was evaporated and the residue was purified on preparative HPLC yielding 10 mg.

[0437] MS: 523.25 ($M-H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.44-8.32 (m, 3H), 8.18-8.12 (m, 2H), 7.97-7.90 (m, 2H), 7.79 (t, 1H, J=7.5Hz), 7.77-7.60 (m, 1H), 7.53-7.50 (m, 3H), 7.44-7.35 (m, 4H), 4.42 (m, 1H), 2.40-2.20 (m, 2H), 2.09-2.06 (m, 2H), 1.86 (m, 2H), 1.62 (m, 2H), 1.39-1.23 (m, 3H).

Example 81

Preparation of 2-[2,3-Bis-(4-bromophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 371)**

[0438] Prepared as described for Compound **406** using 4,4'-dibromobenzil in place of benzil.

[0439] MS: 683.04 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.42-8.30 (m, 3H), 7.88-7.81 (m, 3H), 7.65-7.60 (m, 4H), 7.49-7.44 (m, 4H), 4.38 (m, 1H), 2.34-2.27 (m, 2H), 2.08-2.04 (m, 2H), 1.91-1.83 (m, 2H), 1.61 (m, 1H), 1.42-1.23 (m, 3H).

Example 82

Preparation of 1-Cyclohexyl-2-(2,3-di-*p*-tolylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid **(Compound 389)**

[0440] Prepared as described for Compound **406** using 4,4'-dimethylbenzil in place of benzil.

[0441] MS: 553.26 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.38-8.31 (m, 3H), 8.10 (t, 2H, J=10.5Hz), 7.93 (d, 1H, J=8.4Hz), 7.42 (dd, 4H, J=2.7Hz and 7.8Hz),

7.19 (d, 4H, J=7.8Hz) 4.40 (m, 1H), 2.41-2.31 (m, 8H), 2.07 (m, 2H), 1.83 (m, 2H), 1.61 (m, 1H), 1.23 (m, 3H).

Example 83

Preparation of 2-[2,3-Bis-(4-fluorophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (**Compound 409**)

[0442] Prepared as described for Compound **406** using 4,4'-difluorobenzil in place of benzil.

[0443] MS: 561.19 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.44 (s, 1H), 8.35(t, 2H, J=9Hz), 8.15 (m, 2H), 7.59-7.54 (m, 4H), 7.28-7.22 (m, 4H), 4.40 (m, 1H), 2.30 (m, 2H), 2.07 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.43-1.23 (m, 3H).

Example 84

Preparation of 2-[2,3-Bis-(3-methoxyphenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (**Compound 425**)

[0444] Prepared as described for Compound **406** using 3,3'-dimethoxybenzil in place of benzil.

[0445] MS: 585.25 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.40-8.31 (m, 4H), 8.15 (d, 1H, J=8.4Hz), 8.06 (d, 1H, J=4.2Hz), 7.92 (d, 1H, J=8.4Hz), 7.30 (t, 2H, J=8.1Hz), 7.07(m, 3H), 6.99 (d, 2H, J=8.1Hz), 4.39 (m, 1H), 3.67 (s, 3H), 3.66(s, 3H), 2.35-2.26(m, 2H), 2.08-2.04 (m, 2H), 1.87-1.84 (m, 2H), 1.62 (m, 1H), 1.34-1.23 (m, 3H).

Example 85

Preparation of 2-[2,3-Bis-(4-methoxyphenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (**Compound 441**)

[0446] Prepared as described for Compound **406** using 4,4'-dimethoxybenzil in place of benzil.

[0447] MS: 585.25 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.39 (s, 1H), 8.32 (d, 2H, J=9H), 8.13 (m, 2H), 7.96 (m, 1H), 7.84 (dd, 1H, J=0.9Hz and 9Hz), 7.51

(m, 4H), 6.96 (dd, 4H, J=3Hz, 9Hz), 4.42 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.35-2.27 (m, 2H), 2.09-2.06 (m, 2H), 1.87-1.83 (m, 2H), 1.65-1.61 (m, 1H), 1.38-1.23 (m, 3H).

Example 86

Preparation of 2-[2,3-Bis-(4-dimethylaminophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 458)**

[0448] Prepared as described for Compound **406** using 4,4'-dimethylaminobenzil in place of benzil.

[0449] MS: 306.17 ($M/2+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.32 (m, 2H), 8.22-8.15 (m, 3H), 8.02-7.96 (m, 3H), 7.49-7.44 (m, 4H), 6.73 (d, 4H, J=9Hz), 4.43 (m, 1H), 2.97 (s, 6H), 2.96 (s, 6H), 2.35-2.27 (m, 2H), 2.09-2.06 (m, 2H), 1.91-1.83 (m, 2H), 1.61 (m, 1H), 1.38-1.23 (m, 3H).

Example 87

Preparation of 1-Cyclohexyl-2-{2-[3',4'-dimethoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid **(Compound 419)**

Step 1: 3-Acetyl-4-iodobenzoic acid methyl ester (Compound 419a)

[0450] A suspension of 1.45 g (7.56 mmol) of 3-acetyl-4-aminobenzoic acid methyl ester in 15 mL of 6N HCl and 3 mL MeOH was stirred and cooled to 0°C. (See Padwa, A.; *et al. J.Org Chem.* **1997**, 62, 4088-4096). A solution of 0.63 g (9.07 mmol) of $NaNO_2$ in 5 mL H_2O was added dropwise to the suspension while stirring. The resulting solution was stirred at 0°C for 15 min. A solution of 3.77 g of KI in 25 mL H_2O was added dropwise to this solution. The flask was removed from the cooling bath and stirred overnight. The mixture was extracted with 3x50 mL EtOAc. The organic layer was washed with 10% $Na_2S_2O_3$ solution until all I_2 was removed. A pale yellow solution was obtained which was dried (Na_2SO_4) and concentrated. The residue was purified on silica gel using hexane and EtOAc as eluent yielding 2 g yellow solid.

Step 2: 3-Acetyl-4-iodobenzoic acid (Compound 419b)

[0451] A solution of 2 g of the product from the previous step (6.58 mmol) in a mixture of 66 mL MeOH and 33 mL 2 N aqueous NaOH was heated at 60°C

overnight. The MeOH was evaporated and the residue was acidified by the addition of 70 mL of 1 N aqueous HCl. The resulting emulsion was extracted with 3x50 mL EtOAc, the organic layer was washed with 50 mL of H_2O, dried (Na_2SO_4) and the solvent was evaporated to yield 1.92 g of a yellow solid.

Step 3: 1-[2-Iodo-5-(pyrrolidine-1-carbonyl)phenyl]ethanone (Compound 419c)

[0452] A solution of 1.92 g (6.62 mmol) of the product from the previous step, 1.61 g (15.88 mmol) of Et_3N and 3.01 g (7.94 mmol) of HBTU in 10 mL anhydrous DMF was allowed to stand at room temperature for 15 min. Pyrrolidine (2 mL) was added and the solution was allowed to stand at room temperature overnight. The volatiles were removed and the residue was purified on silica gel using hexane and EtOAc as eluent yielding 1.6 g yellow oil. MS: 343.99 ($M+H^+$)

Step 4: 1-Cyclohexyl-2-{2-[iodo-5-(pyrrolidine-1-carbonyl)phenyl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 419d)

[0453] A mixture of 1.03 g (3 mmol) compound **419c** 1.41 g (3.6 mmol) Compound **354e** and 5.1 mL 10% KOH in EtOH in 50 mL anhydrous EtOH was heated at 55°C for 30 min. The solvent was evaporated, the residue was dissolved in 50 mL H_2O and the solution was extracted with 3x50 mL EtOAc. The organic layers were washed with 50 mL H_2O, dried over Na_2SO_4 and the solvent was evaporated. The residue was purified on silica gel using first hexane/EtOAc and then CH_2Cl_2/MeOH as the eluent to yield 1.09 g yellow solid. MS: 699.22 ($M+H^+$).

Step 5: 1-Cyclohexyl-2-{2-[3',4'-dimethoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid (Compound 419)

[0454] A mixture of 50 mg (0.07 mmol)) of the product from the previous step, 20 mg (0.11 mmol) of 3,4-dimethoxyphenylboronic acid, 8 mg (0.007 mmol) of $Pd(PPh_3)_4$ and 1.25 mL of saturated aqueous $NaHCO_3$ in 2.5 mL degassed toluene was stirred at 80 °C, under Ar, overnight. The mixture was filtered through Celite, the solvents were evaporated and the residue was hydrolyzed in 2.5 mL MeOH and 0.35 mL 2 N aqueous NaOH at 65°C for 2.5 h. The mixture was acidified with 1 mL 4 N HCl in

dioxane and the solvents were removed. The residue was purified by HPLC yielding 10 mg.

[0455] MS: 681.31 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.47-8.30 (m, 4H), 8.16-8.08 (m, 2H), 7.91 (d, 1H, J=1.5Hz), 7.75 (m, 1H), 7.63 (d, 1H, J=8.1Hz), 7.24 (d, 1H, J=8.7Hz), 6.87-6.80 (m, 3H), 6.68 (m, 1H), 4.40 (m, 1H), 3.56 (s, 3H), 3.55 (m, 4H), 3.54 (s, 3H), 2.30 (m, 2H), 2.17 (m, 2H), 1.88 (m, 4H), 1.59 (s, 1H), 1.25 (m, 3H).

Example 88

Preparation of 1-cyclohexyl-2-{2-[4'-nitro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid (**Compound 435**)

[0456] The title compound (5.2 mg yield) was prepared as described for Compound **419** using 4-nitrophenylboronic acid in place of 3,4-dimethoxyphenylboronic acid.

[0457] MS: 666.27 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.46 (m, 3H), 8.35 (d, 1H, J=1.2Hz), 8.26 (d, 1H), 8.20-7.98 (m, 5H), 7.81 (m, 1H), 7.48 (d, 2H, J=9Hz), 7.40 (d, 1H, J=8.7Hz), 3.55 (m, 4H), 2.38 (m, 2H), 2.15 (m, 2H), 1.89 (m, 4H), 1.63 (m, 1H), 1.30 (m, 3H).

Example 89

Preparation of 6-(5-carboxy-1-cyclohexyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid (**Compound 402**)

Step 1: 6-(1-Cyclohexyl-5-ethoxycarbonyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid (Compound 402a)

[0458] A solution of 500 mg (1.28 mmol) of Compound **354e**, 255 mg (2.56 mmol) of pyruvic acid and 436 mg (5.16 mmol) of piperidine in 25 mL anhydrous MeOH was heated at 55°C overnight. The solvent was evaporated, the residue was dissolved in H_2O and neutralized. The precipitate was filtered, washed with H_2O and dried yielding 600 mg white solid.

[0459] MS: 442.18 ($M-H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.76 (d, 1H, J=8.4Hz), 8.50 (d, 1H, J=1.5Hz), 8.38-8.32 (m, 2H), 8.22 (d, 1H, J=8.4Hz), 8.16-8.13 (m,

2H), 7.95 (dd, 1H, J=1.8Hz and 9hz), 4.36 (q, 2H, J=7.2Hz), 2.31 (m, 2H), 2.07 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.37 (t, 3H, J=6.9Hz), 1.32 (m, 3H).

Step 2: 6-(5-Carboxy-1-cyclohexyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid (Compound 402)

[0460] A solution of 90 mg (0.2 mmol) of Compound **402a** and 1 mL 2 N aq. NaOH in 4 mL MeOH was heated overnight at 55°C. The solvent was evaporated, the residue was dissolved in H_2O and neutralized. The precipitate was filtered, washed with H_2O and dried. The product was purified by HPLC to yield 34 mg.

[0461] MS: 416.17 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 9.23 (s, 1H), 8.76 (d, 1H, J=8.7Hz), 8. 48 (s, 1H), 8.36 (d, 1H, J=8.7Hz), 8.30-8.21 (m, 2H), 8.12 (t, 2H, J=8.4 Hz), 8.95 (d, 1H, J=8.7Hz), 4.32 (m, 1H), 2.30 (m, 2H), 2.06 (m, 2H), 1.85 (m, 2H), 1.63 (m, 1H), 1.35 (m, 3H).

Example 90

Preparation of 2-[2-(1-Carbamoylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound **497**)

Step 1: 2-[2-(1-Carbamoylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 497a)

[0462] A solution of 100 mg (0.23 mmol) of Compound **402a**, 86 mg (0.69 mmol) of L-alaninamide, 322 mg (0.69 mmol) of PyBroP, 84 mg (0.69 mmol) DMAP and 89 mg (0.69 mmol) DIEA in 5 mL anhydrous CH_2Cl_2 was stirred at room temperature for 24 h. To this solution was added 214 mg (0.92 mmol) of CSA. The solution was stirred for another 24 h, diluted with 10 mL CH_2Cl_2 and washed with 10 mL H_2O. The solvent was dried and evaporated. The residue was chromatographed on silica gel using first hexane/EtOAc then CH_2Cl_2/MeOH as eluent yielding 50 mg yellow oil. MS: 514.28 ($M+H^+$).

Step 2: 2-[2-(1-Carbamoylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound 497)

[0463] A solution of 50 mg (0.1 mmol) of the product from the previous step in 2.5 mL THF, 2 mL MeOH and 0.5 mL 2 N aq. NaOH was allowed to stand at

room temperature overnight. The solvents were removed, the residue was dissolved in 1 mL H_2O, and the solution was neutralized with 1 M aq. HCl. The precipitate was purified by HPLC to yield 7 mg of the title compound.

[0464] MS: 486.24 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 8.76 (d, 1H, J=8.4Hz), 8.61-8.51 (m, 3H), 8.40-8.32 (m, 3H), 8.20 (d, 1H, J=8.4Hz), 4.70 (m, 2H), 2.47 (m, 2H), 2.67 (m, 2H), 2.00 (m, 2H), 1.75 (m, 1H), 1.60 (d, 3H, J=6.9Hz), 1.45 (m, 3H).

Example 91

Preparation of 2-[2-(1-Carbamoyl-2-methylpropylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 511)**

[0465] The title compound (5 mg yield) was prepared as described for Compound **497a** using L-valinamide in place of L-alaninamide, and hydrolyzed as described for Compound **497**.

[0466] MS: 514.28 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 8.72 (d, 1H, J=9Hz), 8.52-8.47 (m, 3H), 8.40-8.36 (m, 1H), 8.19-8.14 (m, 2H), 7.99 (d, 1H, J=8.4Hz), 4.58 (m, 2H), 2.44 (m, 2H), 2.29 (m, 1H), 2.19 (m, 2H), 2.02 (m, 3H), 1.74 (m, 1H), 1.44 (m, 3H), 1.10 (m, 6H).

Example 92

Preparation of 2-{2-[1-Carbamoyl-2-(1H-imidazol-2-yl)ethylcarbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 368)**

[0467] The title compound (8 mg yield) was prepared as described for Compound **497a** using L-histidinamide in place of L-alaninamide and hydrolyzed as described for Compound **497**.

[0468] MS: 552.25 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 8.80 (d, 1H, J=1.5Hz), 8.71 (d, 1H, J=8.7Hz), 8.49-8.45 (m, 3H), 8.32 (d, 1H, J=8.7Hz), 8.21 (m, 2H), 8.15 (dd, 1H, J=1.8Hz and 8.7Hz), 7.97 (s, 1H), 7.40 (d, 1H, J=1.2Hz), 5.05-5.01(m, 1H), 4.53 (m, 1H), 3.54 (dd, 1H, J=5.4Hz and 15.3Hz), 3.52 (t, 1H, J=8.4Hz), 2.46 (m, 2H), 2.17 (m, 2H), 1.98 (m, 2H), 1.74 (m, 1H), 1.45-1.36 (m, 3H).

Example 93

Preparation of 2-[2-(1-Carbamoyl-2-hydroxyethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 385)**

[0469] The title compound (5 mg yield) was prepared as described for Compound **497a** using L-serinamide in place of L-alaninamide and hydrolyzed as described for Compound **497**.

[0470] MS: 502.23 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 8.73 (d, 1H, J=8.4Hz), 8.51 (m, 2H,), 8.40 (d, 1H, J=8.7Hz), 8.26 (s, 2H), 8.17 (d, 1H, J=9.3), 7.97 (s, 1H), 4.72 (t, 1H, J=4.5Hz), 4.59 (m, 1H), 4.02 (m, 2H), 3.00 (s, 1H), 2.86 (s, 1H), 2.46 (m, 2H), 2.20 (m, 2H), 1.98 (m, 2H), 1.75 (m, 1H), 1.43 (m, 3H).

Example 94

Preparation of 2-[2-(1-Carbamoyl-2-phenylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 542)**

[0471] The title compound (5 mg yield) was prepared as described for Compound **497a** using L-phenylalaninamide in place of L-alaninamide and hydrolyzed as described for Compound **497**.

[0472] MS: 562.27 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 9.06 (d, 1H, J=8.1Hz), 8.72 (d, 1H, J=8.4Hz), 8.50 (m, 2H), 8.32 (m, 2H), 8.17 (dd, 1H, J=1.8Hz and 8.7Hz), 7.34-7.19 (m, 5H), 4.61 (m, 1H), 3.34 (d, 2H, obscured by residual solvent), 3.22 (m, 1H), 2.46 (m, 2H), 2.25 (m, 2H), 2.00 (m, 2H), 1.77 (m, 1H), 1.44 (m, 3H).

Example 95

Preparation of 2-[2-(4-Chlorophenylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 510)**

Step 1: 2-[2-(4-Chlorophenylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 510a)

[0473] The title compound was prepared as described for Compound **497a** using 4-chloroaniline in place of L-alaninamide yielding 91 mg yellow solid. MS: 553.23 ($M+H^+$).

Step 2: 2-[2-(4-Chlorophenylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound 510)

[0474] The 91 mg of the product from the previous step was hydrolyzed as described for Compound **497** yielding 16 mg of the title compound.

[0475] MS: 525.18 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 10.97 (s, 1H), 8.83 (d, 1H, J=8.7), 8.46 (m, 2H), 8.32 (m, 2H), 8.19 (dd, 1H, J=1.8Hz and 8.7Hz), 8.10 (d, 1H, J=8.7Hz), 8.02 (m, 2H), 7.94 (dd, 1H, J=1.5Hz and 8.4Hz), 7.48 (m, 1H), 4.41 (m, 1H), 2.32 (m, 2H), 2.06 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.36 (m, 3H).

Example 96

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-1H-indole-6-carboxylic acid (Compound **536**)

Step 1: 2-Amino-5-bromo-benzaldehyde (Compound 536a)

[0476] The title intermediate was synthesized as described for Compound **7** in five steps starting from 5-bromo-2-nitrotoluene instead of 3-methyl-4-nitrobenazoic acid methyl ester.

MS: 199.97 & 201.97 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 9.75 (s, 1H), 7.71 (s, 1H), 7.39 (d, 1H, J=9.3Hz), 7.22 (s, 2H), 6.72 (d, 1H, J=9.3Hz);

Step 2: 6-Bromo-2-(4'-chloro-4-methoxy-biphen-2-yl)-quinoline (Compound 536c)

[0477] The title intermediate was synthesized from the product of the previous reaction and Compound **525a** using the procedure described for Compound **13** (y= phenyl) in 44% yield.

[0478] MS: 424.03 & 426.03 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 8.20 (d, 1H, J=2.1Hz), 8.10 (d, 1H, J=9.0Hz), 7.93-7.83 (m , 2H), 7.40 (d, 1H, J=8.4Hz), 7.26-7.23 (m, 3H0, 7.16-7.03 (m, 4H), 3.85 (s, 3H);

Step 3: 2-Boronic acid derivative of 3-Cyclohexyl-1H-indole-6-carboxylic acid methyl ester (Compound 536e)

[0479] Compound **536d** (1g, 3 mmol) (See International Patent Application Publication Number WO 03/010141), 890 mg (9 mmol) of potassium acetate, 105 mg (0.15 mmol) of dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct and 6.7 g (30 mmol) of bis(neopentyl glycolato)diboron were dissolved in 20mL of DMSO and the mixture was heated overnight at 95 °C. The crude product was precipitated by addition of 30 mL water. It was purified on a silicagel pad using toluene-ethyl acetate solvent gradient elution to yield 391mg (43%) of the title compound.

[0480] H^1-NMR ($CDCl_3$): δ(ppm) 11.06 (s, 1H), 8.01 (d, 1H, J=1.5Hz), 7.78 (d, 1H, J=8.4Hz), 7.47 (dd, 1H, J=8.4 and 1.8Hz), 3.81 (s, 3H), 1.98-1.33 (m, 11H).

Step 4: 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-1H-indole-6-carboxylic acid (Compound 536)

[0481] A mixture of 106g (0.25 mmol) of Compound **536c**, 180 mg (0.6 mmol) of Compound **536e,** 58 mg (0.05 mmol) of tetrakis-(triphenylphosphino) palladium, 6 mL of toluene, 1.5 mL of methanol and 600 µL of saturated sodium bicarbonate was heated under Ar overnight at 80 °C. The reaction mixture was then evaporated to dryness, the semi-solid dissolved in 5 mL ethanol, 3 mL 1M NaOH was added and was heated at 85 °C for 30 minutes. The reaction mixture was then evaporated to dryness. The pure title compound was isolated using RP-HPLC to yield 27.5 mg (19%) yellow solid.

[0482] MS: 587.23 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 11.66 (s, 1H), 8.39 (d, 1H, J=8.4Hz), 8.20 (d, 1H, J=8.7Hz), 8.12 (d, 1H, J=1.5Hz), 8.00-7.95 (m, 2H), 7.86 (d, 1H, J=8.4Hz), 7.59 (, dd, 1H, J=8.7 and 1.5Hz), 4.47 (d, 1H, J=8.7Hz), 7.34-7.28 (m, 3H), 7.22-7.18 (m, 2H), 7.14-7.11 (m, 2H), 3.88 (s, 3H), 2.96 (m, 1H), 2.05-1.22 (m, 10H).

Example 97

Preparation of 1-Cyclohexyl-2-(2-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 405**)

Step 1: 4-methyl-3-nitro-benzoic acid methyl ester (Compound 405a)

[0483] 4-Methyl-3-nitro benzoic acid (12.5 g, 69mmol) was dissolved in anhydrous methanol (500 mL) in a 1L flask. HCl gas was then bubbled through the solution until saturation (3 h). The HCl source was then removed, and the reaction was stirred at room temperature overnight. The reaction was then concentrated to dryness and dried over phosphorus pentoxide overnight to yield 13.34g (99%) of product which was 99% pure by QC HPLC.

[0484] H^1-NMR ($CDCl_3$): δ(ppm) 8.59 (d, 1H, Ar-H^2), 8.13 (dd, 1H, Ar-H^6), 7.43 (d, 1H, Ar-H^5), 3.96 (s, 3H, OCH_3), 2.67 (s, 3H, CH_3)

Step 2: *trans*-4-(2-Dimethylamino-vinyl)-3-nitro-benzoic acid methyl ester (Compound 405b)

[0485] A 100 mL flask fitted with a 15 cm Vigreux head was charged with 10 g (49.7 mmol) of the product from the previous step, 16.9 mL of DMF, and 21.2g (196.0 mmol) of N,N-dimethylformamide dimethylacetal. The reaction vessel was immersed in a 140 C° oil bath for 18 h under Ar while the forming methanol was distilled away. Upon cooling to room temperature the dark red content of the flask solidified. The solid was transferred to a 250 mL flask using DMF, which was subsequently removed by evaporation. The residue was triturated with petroleum ether to give 16.16g (95%) enamine as dark red solid which was 98.4% pure based on QC HPLC.

[0486] H^1-NMR ($CDCl_3$): δ(ppm) 8.48 (d, 1H, Ar-H^2), 7.88 (dd, 1H, Ar-H^6), 7.45 (d, 1H, Ar-H^5), 7. 15 (d, 1H, CH=), 5.91 (d, 1H, CH=), 3.90 (s, 3H, OCH_3), 2.95 (s, 6H, $(CH_3)_2N$)

Step 3: 4-Formyl-3-nitro-benzoic acid methyl ester (Compound 405c)

[0487] The product from the previous step (16.10g, 64.3 mmol) and $NaIO_4$ (41 g, 191.7 mmol) was dissolved in 250 mL of 1:1 THF/H_2O at room temperature. The dark red solution was warmed to about 40 °C while heavy precipitation occurred and the

solution color changed to light brown. After 1 h, the precipitate was removed by filtration and was washed with 400 mL ethyl acetate. The organic layer was washed three times with saturated $NaHCO_3$, once with brine and dried with Na_2SO_4. The solution was evaporated to dryness and the resulting oil was purified on a silicagel pad eluting with ethyl acetate-hexane gradient (30% to 40% ethyl acetate) to yield 11.07g (83%) of the title intermediate as a yellow solid after evaporation.

[0488] H^1-NMR ($CDCl_3$): δ(ppm) 10.45 (s, 1H, CHO), 8.75 (d, 1H, Ar-H^2) 8.41 (dd, 1H, Ar-H^6), 8.01 (d, 1H, Ar-H^5), 4.02 (s, 3H, OCH_3)

Step 4: 4-Dimethoxymethyl-3-nitro-benzoic acid methyl ester (Compound 405d)

[0489] To a solution of 11g (52.6 mmol) of the product from the previous step in 220 mL methanol 5.5 mL 4N HCL/dioxane was added. The mixture was kept at 90 °C for 10 minutes before it was evaporated to dryness. The white solid material was dissolved in 20 mL methanol again and was treated with 5.5 mL 4N HCl in the same way 2 more times. The solid was dried in high vacuum overnight to give 12.46g (93%) reddish oil of the title intermediate (76%).

[0490] H^1-NMR ($CDCl_3$): δ(ppm) 8.43 (d, 1H, Ar-H^2), 8.23 (dd, 1H, Ar-H^6), 7.87 (d, 1H, Ar-H^5), 5.93 (s, 1H, Ar-CH), 3.97 (s, 3H, ester CH_3), 3.41 (s, 6H, acetal CH_3)

Step 5: 3-Amino-4-dimethoxymethyl-benzoic acid methyl ester (Compound 405e)

[0491] Mg_2SO_4 (1 g) and 100 mg of 10% Pd/C were suspended in 20 mL methanol and were hydrogenated in a Parr apparatus at 30 psi for 20 minutes. The apparatus was opened and 1.22g (4.78 mmol) of the product from the previous step dissolved in 20 mL methanol was added followed by 2 mL TEA. The mixture was hydrogenated at 30 psi for 45 minutes, the catalyst was removed by filtration and the solution was evaporated to dryness. The solid material was dried over P_2O_5 overnight to give 84mg (95.4%) of the title intermediate.

[0492] H^1-NMR ($CDCl_3$): δ(ppm) 7.37 (d, 2H, Ar-H^{5+6}), 7.31 (d, 1H, Ar-H^2), 5.34 (s, 1H, Ar-CH), 4.36 (s, 2H, NH2), 3.88 (s, 3H, ester CH_3), 3.33 (s, 6H, acetal CH_3)

Step 6: 3-Amino-4-formyl-benzoic acid methyl ester (Compound 53)

[0493] The product from the previous step (100mg, 0.44mmol) was dissolved at room temperature in a 15 mL solvent mixture composed of 2:2:1 EtOH-acetic acid-water. The strong yellow solution became pale yellow in 5 minutes. The mixture was let stand for an additional 15 minutes then was evaporated to dryness and was further dried in high vacuum overnight to get 75mg (94%) of the title intermediate as a yellow powder.

[0494] H^1-NMR ($CDCl_3$): δ(ppm) 9.92 (s, 1H, CHO), 7.55 (d, 1H, Ar-H^2), 7.34 (m, 2H, Ar-H^{5+6}), 3.91 (s, 1H, CH_3)

Step 7: 2-Phenyl-quinoline-7-carboxylic acid (Compound 405f)

[0495] To a solution of 500 mg (2.8 mmol) of the product from the previous step, 340 mg (2.8 mmol) of acetophenone in 20 mL ethanol, 2.1 mL of a 10% KOH/ethanol solution was added and the mixture was refluxed under argon overnight. The product partially precipitated as dull tan crystals which were not filtered off. The whole mixture was evaporated to dryness; the residue was triturated with ether to give the product as a potassium salt. The acid was obtainedby dissolving the potassium salt in 25 mL water and acidifying to pH 4. The precipitate was collected by filtration, washed twice with water and dried over phosphorous pentoxide in high vacuum to yield 261 mg (54%) the title intermediate MS: 250.32 ($M+H^+$)

Step 8: 4-Cyclohexylamino-3-[(2-phenyl-quinoline-7-carbonyl)-amino]-benzoic acid ethyl ester (Compound 405g)

[0496] To a solution of 250 mg (1.0mmol) of the product from the previous step and 418 mg HATU (1.1mmol) in DMF (5 mL), 0.383 mL (2.2mmol) of DIEA was added. The reaction was stirred at room temperature for 15 minutes before 289mg (1.1mmol) of Compound **11** was added. The reaction was complete after stirring at room temperature for 1 hour. After being evaporated to dryness, the reaction mixture was dissolved in ethyl acetate, and washed with water (2x 100mL), brine (1x 100mL), dried over sodium sulfate, and evaporated to an oil residue which was then dried over phosphorus pentoxide overnight to produce 200 mg (46% yield) of the title intermediate.

Step 9: 1-Cyclohexyl-2-(2-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 405)

[0497] The product from the previous step (200mg, 0.4mmol) was dissolved in 30 mL of glacial acetic acid. The solution was refluxed for 4 h, then evaporated to dryness. The yellow solid was dissolved again in 20 mL ethanol, and 4 mL 1N NaOH was added with stirring at 80 °C for 1 h. The reaction mixture was then evaporated to dryness. The solid was dissolved in 20mL water, cooled in an ice bath, acidified with 4 mL 1N HCl after which the precipitate was filtered and washed with water. The solid was dried over phosphorus pentoxide overnight to yield 25mg of the title compound.

[0498] MS: 448.27 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.64 (d, 1H), 8.44 (s, 1H), 8.30 (m, 5H), 8.18 (d, 1H), 7.95 (dd, 1H), 7.90 (dd, 1H), 7.55 (m, 3H), 3.40 (m, 4H), 2.32 (dd, 2H), 2.08 (d, 2H), 1.85 (d, 2H), 1.62 (d, 1H)

Example 98

Preparation of 1-cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 351)**

Step 1: 3-Phenyl-quinoline-7-carboxylic acid (Compound 351a)

[0499] Following the same reaction procedure and workup for Compound **405f**, 500mg (2.8mmol) of Compound **53** was reacted with 340mg (2.8mmol) phenylacetaldehyde to produce 603mg (87% yield) of the title intermediate.

[0500] MS: 250.17 ($M+H^+$); H^1-NMR (DMSO): δ(ppm) 9.35 (d, 1H), 8.72 (s, 1H), 8.58 (s, 1H), 8.12 (m, 2H); 7.90 (d, 2H), 7.55 (m, 3H);

Step 2: 4-Cyclohexylamino-3-[(3-phenyl-quinoline-7-carbonyl)-amino]-benzoic acid ethyl ester (Compound 351b)

[0501] Following the same reaction procedure and workup as for Compound **405g**, 250mg (1mmol) of the product from the previous step was reacted with 289mg (1.1mmol) of Compound **11**, using 418mg (1.1mmol) of HATU and 0.383 mL of DIEA to produce 448mg (91% yield) of the title intermediate. MS: 494.29 ($M+H^+$)

Step 3: 1-Cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 351)

[0502] Following the same reaction procedure and workup as for Compound **405**, 450mg (0.9mmol) of the product from the previous step was cyclized with 40 mL acetic acid and saponified with 35mL EtOH and 7mL 1M NaOH to produce 70mg (17% yield) of the title compound.

[0503] MS: 448.23 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.49 (d, 1H), 9.0 (d, 1H), 8.56 (s, 1H), 8.39 (m, 2H), 8.26 (d, 1H), 8.05 (m, 5H), 7.55 (m, 3H), 2.30 (m, 3H), 2.12 (d, 3H), 1.86 (d, 3H), 1.62 (d, 2H), 1.34 (m, 5H)

Example 99

Preparation of 2-{[1-cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid (**Compound 516**)

[0504] To a solution of 50 mg (0.11 mmol) of Compound **351** in 2 mL DMF, 46mg (0.12mmol) of HATU and 40 µL (0.24 mmol) of DIEA were added. The mixture was stirred at room temperature for 30 minutes and 27 mg (0.12 mmol) of L-5-hydroxytryptophane was added to the activated ester solution. The reaction was complete in 1 h. The DMF was evaporated and the residual oil which was dissolved in 20 mL 1:1 DMF-water containing 0.1% TFA. The solution was applied on a RP-HPLC column to give the pure title compound as TFA salt.

[0505] **Conversion to HCl salt:** The purified Compound **516** was dissolved in 0.8 mL methanol, 1 mL 4M HCl in dioxane was added followed by 40 mL ether. The off-white precipitate was centrifuged down and the ether was decanted off. Yield: 15 mg (25 %) beige solid.

[0506] MS: 648.24 ($M-H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 10.50 (d, 1H), 9.45 (s, 1H), 8.92 (s, 1H), 8.52 (s, 1H), 8.39-8.30 (m, 3H), 8.23 (m, 1H), 7.98 (m, 4H), 7.54 (m, 3H), 7.08 (m, 3H), 6.87 (m, 3H), 6.56 (d, 1H), 4.65 (m, 1H), 4.36 (m, 1H), 2.32 (m, 2H), 2.10 (m,2H), 1.84 (d, 2H), 1.95(m, 1H), 1.29 (m, 4H);

Example 100

Preparation of 1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid morpholin-4-ylamide **(Compound 574)**

[0507] A solution of Compound **203** (0.25 mmol) in 3 mL DMF was preactivated with HATU (0.246 mmol) and DIEA (0.5 mmol). To the solution, the desired amine was added (0.1 mmol) and the reaction was stirred for 16 hours. The completed reaction was then purified via RP-HPLC, and converted to the HCl salt by evaporating to dryness, dissolving in 0.8 mL methanol and adding 1 mL 4M HCl in dioxane followed by 40 mL ether. The compound was centrifuged down, the solvent decanted off, and the solid dried to yield the final compound.

[0508] Using this general procedure with morpholin-4-ylamine (9.8ul), produced 15 mg of the title compound (58% yield). MS: 533.32 ($M+H^+$) HPLC Procedure A, retention time = 12.87min.

Example 101

Preparation of 2-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-ethanesulfonic acid **(Compound 524)**

[0509] The general procedure described for Compound **574** was used with 2-amino-ethanesulfonic acid (12.5mg), producing 28mg of the title compound (98% yield). MS: 556.28 ($M+H^+$) HPLC Procedure A, retention time = 11.36min.

Example 102

Preparation of 1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (7-hydroxy-naphthalen-1-yl)-amide **(Compound 575)**

[0510] The general procedure described for Compound **574** was used with 8-amino-naphthalen-2-ol (15.9mg), producing 5 mg of the title compound (20% yield). MS: 590.25 ($M+H^+$) HPLC Procedure A, retention time = 15.31min.

Example 103

Preparation of 1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (5-hydroxy-naphthalen-1-yl)-amide **(Compound 576)**

[0511] The general procedure described for Compound **574** was used with 5-amino-naphthalen-1-ol (15.9mg), producing 7 mg of the title compound (25% yield). MS: 590.24 ($M+H^+$) HPLC Procedure A, retention time = 15.26min.

Example 104

Preparation of 6-{[1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-naphthalene-2-carboxylic acid **(Compound 526)**

[0512] The general procedure described for Compound **574** was used with 6-amino-naphthalene-2-carboxylic acid (18.7mg), producing 15 mg of the title compound (53% yield). MS: 618.30 ($M+H^+$) HPLC Procedure A, retention time = 16.24min.

Example 105

Preparation of 1-Cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (4-methyl-2-oxo-2H-chromen-7-yl)-amide **(Compound 577)**

[0513] The general procedure described for Compound **574** was used with 7-Amino-4-methyl-chromen-2-one (17.5mg), producing 8mg of the title compound (27% yield). MS: 606.29 ($M+H^+$) HPLC Procedure A, retention time = 19.22min.

Example 106

Preparation of 1-Cyclohexyl-2-(2-phenyl-1,2,3,4-tetrahydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 215)**

[0514] A solution of Compound **203** (100mg, 0.23mmol) and platinum oxide (12mg, 0.048mmol) in methanol (5mL) was hydrogenated at 40 psi for 3 h. The reaction was evaporated to dryness, and purified via HPLC. The resulting compound was then converted to the HCl salt using the standard method, yielding 40 mg (37% yield) of the title compound.

[0515] MS: 452.25 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.31 (d, 1H, J=9), 8.22 (d, 1H, J=1.5), 8.044 (dd, 1H, J=9.1,1.5), 7.36 (m, 7H), 6.865 (d, 1H, J=9), 4.58 (m, 2H), 2.86 (m, 1H), 2.66 (m, 1H), 2.33 (m, 2H), 2.07 (m, 3H), 1.90 (m, 3H), 1.66 (m, 1H), 1.41 (m, 3H).

Example 107

Preparation of 2-[2-(2-Bromo-phenyl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 424)**

Step 1: 1-(2-Bromo-phenyl)-2-phenyl-ethanol (Compound 424a)

[0516] A mixture of 2-bromobenzaldehyde (1mL, 5.4mmol) in diethylether (2mL) was added to a flame dried flask, and flushed with argon. The temperature was reduced to -10 °C and benzylmagnesium chloride was slowly added to the flask via syringe. The reaction was stirred at -10 °C for 1 hour and then stirred at room temperature for 16 hours. The reaction was the poured over ice and acidified to pH 3. It was then extracted with ether (3x40mL). The organic layers were combined, evaporated, and the resulting residue was purified via silica gel chromatography to produce 520mg (33% yield) of the title intermediate.

[0517] H^1-NMR ($CDCl_3$): δ(ppm) 7.54 (dd, 2H), 7.33 (m, 1H), 7.25 (m, 3H), 7.12 (m, 2H), 5.22 (m, 1H), 3.18 (dd, 3.18, J=2.7,13.8), 2.715 (dd, 1H, J=13.8, 9)

Step 2: 1-(2-Bromo-phenyl)-2-phenyl-ethanone (Compound 424b)

[0518] To a flame dried flask, Dess-Martin periodinane (1.23g, 2.9mmol) and dichloromethane (30mL) were added. The mixture was cooled to 0 °C, and the product of the previous reaction (520mg, 1.8mmol) was added and stirred for 1 hour at the reduced temperature before being stirred for 48 hours at room temperature. The reaction was then evaporated to an oil, and purified on silica gel to produce the title intermediate (385mg, 78% yield).

[0519] H^1-NMR ($CDCl_3$): δ(ppm) 7.58 (m, 1H), 7.26 (m, 8H), 4.23 (s, 2H)

Step 3: 3-(2-Bromo-phenyl)-2-phenyl-quinoline-6-carboxylic acid (Compound 424c)

[0520] Following the same reaction procedure and workup as for Compound **405f** (235mg, 1.31mmol) of Compound **53** was reacted with the product of the previous reaction, Compound **424b** (360mg, 1.31mmol), in ethanol (12mL) using 10% w/v KOH in ethanol (1.1 mL) to produce the title compound (210mg, 40% yield).

[0521] MS: 403.22 ($M-H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.69 (s, 1H), 8.28 (d, 1H, J=8.7), 8.04 (s, 1H, J=8.7), 7.93 (s, 1H); 7.542 (d, 1H, J=7.2), 7.40 (m, 3H), 7.25 (m, 4H)

Step 4: 3-{[2-(2-Bromo-phenyl)-3-phenyl-quinoline-6-carbonyl]-amino}-4-cyclohexylamino-benzoic acid ethyl ester (Compound 424d)

[0522] Using the same reaction procedure and workup as for Compound **405g,** the product of the previous reaction, Compound **424c** (200mg, 0.495mmol), HATU (207mg, 0.545mmol), DIEA (141mg, 1.09mmol), Compound **11** (143mg, 0.545mmol) and DMF (4mL) were used to produce of the title intermediate (250mg, 78%yield). MS 649.57 ($M+H^+$)

Step 5: 2-[2-(2-Bromo-phenyl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 424)

[0523] Using the same reaction procedure and workup as for Compound **405**, the product of the previous reaction (250mg, 0.39mmol) was reacted with acetic acid (30mL), and 1M NaOH (4mL) to produce the title compound (60mg, 25% yield).

[0524] MS 602.15; H^1-NMR (DMSO-d_6): δ(ppm) 8.71 (s, 1H), 8.53 (s, 1H), 8.31 (m, 2H), 8.13 (m, 2H), 7.98 (dd, 1H, J=1.5, 8.4), 7.585 (d, 1H, J=7.8), 7.46 (m, 2H), 7.3 (m, 6H), 4.47 (m, 1H), 2.35 (m, 3H), 2.09 (m, 2H), 1.86 (m, 2H), 1.63 (m, 1H), 1.37 (m, 3H)

Example 108

Preparation of 2-[2-(4'-Chloro-biphen-2-yl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 440**)

[0525] Compound **424** (50mg, 0.083mmol), 4-chlorophenylboronic acid (20mg, 0.125mmol), and CsF (143mg, 0.94mmol) were added to degassed dioxane (6mL). A solution of 2-(dicyclohexylphosphino)biphenyl (5mg, .0125mmol) and palladium acetate (2mg, .0083mmol) in degassed dioxane (3mL) was added to the reaction solution. The reaction was then refluxed under argon for 3 hours. The reaction was then evaporated to dryness and purified via HPLC resulting in the title compound (4mg, 10% yield).

[0526] MS 634.18; H^1-NMR (DMSO-d_6): δ(ppm) 8.40 (d, 2H, J=4.8), 8.30 (d, 2H, J=8.7), 8.09 (m, 2H), 7.9 (d, 1H, J=8.7), 7.3 (d, 1H, J=7.2), 7.54 (m, 2H), 7.20 (m, 2H), 7.08 (dd, 4H, J=13.8, 7.8), 6.61 (d, 2H, J=6.9), 6.47 (d, 2H, J=8.4), 2.34 (m, 2H), 2.05 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.38 (m, 3H)

Example 109

Preparation of 2-(2-biphenyl-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 390**)

[0527] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-biphenyl-4-yl-ethanone (51mg, 0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (15mg, 10% yield).

[0528] MS: 524.24 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.71 (d, 1H, J=9), 8.39 (m, 6H), 8.2 (d, 1H, J=8.7), 8.19 (d, 1H, J=9), 8.0 (d, 1H, J=9), 7.9 (d, 2H, J=8.1), 7.79 (d, 2H, J=7.5), 7.52 (m, 2H), 7.42 (m, 1H), 3.56 (s, 1H), 2.45 (m, 2H), 2.10 (m, 2H), 1.86 (m, 2H), 1.62 (s, 1H), 1.34 (m, 3H)

Example 110

Preparation of 1-cyclohexyl-2-[2-(2,4-dimethyl-thiazol-5-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 426**)

[0529] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2,4-dimethyl-thiazol-5-yl)-ethanone (40mg, 0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (14mg, 12% yield).

[0530] MS: 483.19 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.61 (m, 1H), 8.37 (m, 1H), 8.26 (m, 1H), 8.0 (m, 5H), 4.38 (s, 1H), 2.72 (s, 3H), 2.66 (s, 3H), 2.28 (m, 2H), 2.02 (m, 2H), 1.82 (m, 2H), 1.62 (m, 1H), 1.30 (m, 3H)

Example 111

Preparation of 1-cyclohexyl-2-(2-pyrazin-2-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 442**)

[0531] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256 mmol) was reacted with 1-pyrazin-2-yl-ethanone (32 mg, 0.256 mmol) in ethanol (2 mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (15mg, 10% yield).

[0532] MS: 450.20 ($M+H^+$); H^1-NMR (DMSO-d_6): 9.79 (d, 1H, J=1.5), 8.84 (m, 3H), 8.62 (d, 1H, J=8.7), 8.53 (d, 1H, J=1.5), 8.40 (d, 1H, J=8.4), 8.34 (d, 1H, J=1.5), 8.22 (d, 1H, J=8.7), 8.15 (dd, 1H, J=9, 2.1), 8.01 (dd, 1H, J=8.4, 1.2), 2.33 (m, 2H), 2.10 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.35 (m, 3H)

Example 112

Preparation of 1-cyclohexyl-2-[2-(5-methyl-2-phenyl-thiophen-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 472**)

[0533] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(5-methyl-2-phenyl-thiophen-3-yl)-ethanone (56mg, 0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (8mg, 6% yield). MS: 544.27 ($M+H^+$) HPLC Procedure A, retention time = 17.05min.

Example 113

Preparation of 1-cyclohexyl-2-(2-pyridin-3-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 355**)

[0534] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-pyridin-3-yl-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (19mg, 17% yield). MS: 449.21 ($M+H^+$) HPLC Procedure A, retention time = 7.96min.

Example 114

Preparation of 2-[2-(4-amino-3-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 372**)

[0535] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with N-(4-acetyl-2-bromo-phenyl)-acetamide (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (16mg, 15% yield).

[0536] MS: 541.15 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.80 (d, 1H, J=9), 8.53 (m, 3H), 8.35 (m, 2H), 8.28 (d, 1H, J=9), 8.17 (m, 2H), 8.04 (dd, 1H, J=8.7, 1.2), 6.98 (d, 1H, J=8.7), 4.44 (m, 1H), 2.30 (m, 2H), 2.12 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.35 (m, 3H)

Example 115

Preparation of 2-[2-(2-amino-4-methyl-thiazol-5-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 391**)

[0537] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2-amino-4-methyl-thiazol-5-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (8mg, 9% yield). MS: 484.19 ($M+H^+$); HPLC Procedure A, retention time = 8.57min.

Example 116

Preparation of 1-cyclohexyl-2-[2-(7-hydroxy-benzofuran-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 411**)

[0538] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(7-hydroxy-benzofuran-2-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (19mg, 20% yield). MS: 504.22 ($M+H^+$); HPLC Procedure A, retention time = 12.20min.

Example 117

Preparation of 1-cyclohexyl-2-(2-pyridin-2-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 427**)

[0539] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-pyridin-2-yl-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506μL, 0.64mmol) to produce the title compound (66mg, 61% yield). MS: 449.19 ($M+H^+$); HPLC Procedure A, retention time = 9.85min.

Example 118

Preparation of 1-cyclohexyl-2-(2-pyridin-4-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 443**)

[0540] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-pyridin-4-yl-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (68mg, 62% yield). MS: 449.19 ($M+H^+$); HPLC Procedure A, retention time = 7.98min.

Example 119

Preparation of 1-cyclohexyl-2-[2-(5,6,7,8-tetrahydro-naphthalen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 459**)

[0541] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(5,6,7,8-tetrahydro-naphthalen-2-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in Ethanol (506 μL, 0.64mmol) to produce the title compound (65mg, 60% yield).

[0542] MS: 502.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.76 (m, 1H), 8.54 (s, 1H), 8.39 (m, 4H), 8.10 (m, 4H), 7.36 (m, 1H), 4.45 (m, 1H), 2.84 (m, 4H), 2.35 (m, 2H), 2.14 (m, 2H), 1.80 (m, 6H), 1.62 (m, 1H), 1.34 (m, 3H)

Example 120

Preparation of 1-cyclohexyl-2-[2-(4-imidazol-1-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 473**)

[0543] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(4-imidazol-1-yl-phenyl)-ethanone (0.256mmol) in ethanol (2 mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (75mg, 59% yield). MS: 514.23 ($M+H^+$); HPLC Procedure A, retention time = 8.40min.

Example 121

Preparation of 2-(2-benzo[1,3]dioxol-5-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 412**)

[0544] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-benzo[1,3]dioxol-5-yl-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (30mg, 24% yield).

[0545] MS: 492.21 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.68 (m, 1H), 8.42 (s, 1H), 8.28 (m, 4H), 8.05 (m, 2H), 7.92 (m, 2H), 7.13 (m, 1H), 6.15 (s, 2H), 2.33 (m, 2H), 2.10 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.35 (m, 3H)

Example 122

Preparation of 1-cyclohexyl-2-[2-(4-phenoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 428**)

[0546] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(4-phenoxy-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in Ethanol (506 μL, 0.64mmol) to produce the title compound (42mg, 31% yield).

[0547] MS: 540.25 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.68 (d, 1H), 8.46 (d, 1H), 8.30 (m, 6H), 8.04 (dd, 2H), 7.44 (m, 2H), 7.16 (m, 5H), 4.45 (m, 1H), 2.32 (m, 2H), 2.10 (m, 2H), 1.85 (m, 2H), 1.65 (m, 1H), 1.35 (m, 3H)

Example 123

Preparation of 1-cyclohexyl-2-[2-(6-methyl-naphthalen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 444**)

[0548] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(6-methyl-naphthalen-2-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (23mg, 18% yield).

[0549] MS: 512.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.85 (s, 1H), 8.73 (d, 1H), 8.46 (d, 3H), 8.34 (m, 2H), 8.20 (d, 1H), 8.10 (dd, 1H), 8.02 (m, 3H), 7.57 (s, 1H), 7.44 (1H), 2.32 (m, 2H), 2.08 (m, 2H), 1.85 (m, 2H), 1.64 (m, 1H), 1.36 (m, 3H)

Example 124

Preparation of 1-cyclohexyl-2-[2-(2-hydroxy-naphthalen-1-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 460**)

[0550] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2-hydroxy-naphthalen-1-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (7mg, 6% yield). MS: 514.23 ($M+H^+$); HPLC Procedure A, retention time = 12.20min.

Example 125

Preparation of 1-cyclohexyl-2-(2-naphthalen-1-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 357**)

[0551] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-naphthalen-1-yl-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (4mg, 4% yield).

[0552] MS: 498.24 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.82 (d, 1H), 8.59 (d, 1H), 8.36 (m, 2H), 8.24 (d, 1H), 8.10 (m, 6H), 7.81 (d, 1H), 7.70 (m, 1H), 7.57 (m, 2H), 4.49 (m, 1H), 3.55 (s, 1H), 2.31 (m, 2H), 2.10 (m, 2H), 1.82 (m, 2H), 1.62 (m, 1H), 1.36 (m, 3H)

Example 126

Preparation of 1-cyclohexyl-2-[2-(4-piperazin-1-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 488**)

[0553] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(4-piperazin-1-yl-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (120mg, 91% yield). MS: 532.21 ($M+H^+$); HPLC Procedure A, retention time = 7.78min.

Example 127

Preparation of 2-[2-(4-acetylamino-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 501**)

[0554] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with N-(4-acetyl-phenyl)-acetamide (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (19mg, 15% yield). MS: 505.26 ($M+H^+$); HPLC Procedure A, retention time = 9.94min.

Example 128

Preparation of 2-[2-(4-amino-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 358**)

[0555] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(4-amino-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (14mg, 10% yield). MS: 463.23 ($M+H^+$); HPLC Procedure A, retention time = 8.62min.

Example 129

Preparation of 2-[2-(3-carbamoyl-4-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 374**)

[0556] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 5-acetyl-2-hydroxy-benzamide (0.256mmol) in ethanol (2mL) using 10% w/v KOH in Ethanol (506 μL, 0.64mmol) to produce the title compound (13mg, 10% yield). MS: 507.24 ($M+H^+$); HPLC Procedure A, retention time = 10.36min.

Example 130

Preparation of 1-Cyclohexyl-2-[2-(3-hydroxy-propyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 392**)

[0557] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 5-hydroxy-pentan-2-one (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (96mg, 90% yield). MS: 430.23 ($M+H^+$); HPLC Procedure A, retention time = 6.84min, 82.48% purity.

Example 131

Preparation of 2-(2-benzofuran-2-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 413**)

[0558] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-benzofuran-2-yl-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (75mg, 62% yield). MS: 488.22 ($M+H^+$); HPLC Procedure A, retention time = 14.35min.

Example 132

Preparation of 1-cyclohexyl-2-[2-(4-morpholin-4-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 429**)

[0559] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(4-morpholin-4-yl-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (37mg, 30% yield). MS: 533.28 ($M+H^+$); HPLC Procedure A, retention time = 10.39min.

Example 133

Preparation of 2-[6-(2-Nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 446**)

[0560] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2-nitro-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (11mg, 10% yield). MS: 493.21 ($M+H^+$); HPLC Procedure A, retention time = 12.72min.

Example 134

Preparation of 2-[2-(4-benzyloxy-2-hydroxy-3-methyl-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 462**)

[0561] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(4-benzyloxy-2-hydroxy-3-methyl-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (73mg, 10% yield). MS: 584.29 ($M+H^+$); HPLC Procedure A, retention time = 18.27min.

Example 135

Preparation of 1-cyclohexyl-2-[2-(2-pyrazol-1-yl-ethyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 476**)

[0562] Following the procedure and workup for Compound 354, Compound 354e (100mg, 0.256mmol) was reacted with 4-pyrazol-1-yl-butan-2-one (0.256mmol) in ethanol (2mL) using 10% w/v KOH in Ethanol (506 μL, 0.64mmol) to produce the title compound (14mg, 50% yield). MS: 466.27 ($M+H^+$); HPLC Procedure A, retention time = 8.41min.

Example 136

Preparation of 1-cyclohexyl-2-(2-dipropylaminomethyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 489**)

[0563] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-dipropylamino-propan-2-one (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (70mg, 58% yield). MS: 485.34 ($M+H^+$); HPLC Procedure A, retention time = 9.20min.

[0564] H^1-NMR (DMSO-d_6): 8.70 (d, 1H), 8.44 (d, 1H), 8.25 (m, 2H), 8.10 (m, 2H), 7.92 (dd, 1H), 7.95 (d, 1H), 4.8 (m, 2H), 3.4 (m, 4H), 3.25 (m, 2H), 2.30 (m, 1H), 2.00 (m, 1H), 1.85 (m, 5H), 1.6 (m, 1H), 1.35 (m, 3H), 0.89 (m, 6H)

Example 137

Preparation of 2-[2-(3-carboxymethyl-2,2-dimethyl-cyclobutyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 502**)

[0565] Following the procedure and workup for Compound **354**, Compound **354e** 100mg, 0.256mmol) was reacted with (3-acetyl-2,2-dimethyl-cyclobutyl)-acetic acid (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (21mg, 16% yield). MS: 512.31 ($M+H^+$); HPLC Procedure A, retention time = 9.07min.

Example 138

Preparation of 2-[2-(7-bromo-5-methoxy-benzofuran-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 394**)

[0566] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(7-bromo-5-methoxy-benzofuran-2-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound, 17% yield).

[0567] MS: 596.12 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.75 (d, 1H), 8.51 (d, 1H), 8.34 (m, 2H), 8.3 (m, 2H), 8.13 (dd, 1H), 8.05 (dd, 1H), 7.96 (s, 1H), 7.31 (m, 2H), 4.40 (m, 1H), 3.83 (s, 1H), 2.30 (m, 2H), 2.15 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.35 (m, 3H)

Example 139

Preparation of 2-{2-[1-(2-chloro-pyridin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 431**)

[0568] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 5-acetyl-1-(2-chloro-pyridin-3-yl)-1H-pyrimidine-2,4-dione (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound 45mg, 31% yield). MS: 593.17 ($M+H^+$); HPLC Procedure A, retention time = 10.02min.

Example 140

Preparation of 2-[2-(5-benzyloxy-2-methyl-benzofuran-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 448**)

[0569] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(5-benzyloxy-2-methyl-benzofuran-3-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (75mg, 49% yield). MS: 608.25 ($M+H^+$); HPLC Procedure A, retention time = 17.24min.

Example 141

Preparation of 2-[2-(6-chloro-9-methyl-9H-carbazol-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 463**)

[0570] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(6-chloro-9-methyl-9H-carbazol-3-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (18mg, 12% yield). MS: 585.21 ($M+H^+$); HPLC Procedure A, retention time = 16.25min.

Example 142

Preparation of 1-cyclohexyl-2-[2-(2,3-dihydro-benzofuran-5-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 478**)

[0571] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2,3-dihydro-benzofuran-5-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in Ethanol (506 μL, 0.64mmol) to produce the title compound (34mg, 28% yield). MS: 490.19 ($M+H^+$); HPLC Procedure A, retention time = 11.50min.

Example 143

Preparation of 1-cyclohexyl-2-[2-(1-phenyl-1H-pyrazol-4-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 449**)

[0572] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(1-phenyl-1H-pyrazol-4-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (69mg, 51% yield). MS: 514.23 ($M+H^+$); HPLC Procedure B, retention time = 6.36min.

Example 144

Preparation of 1-cyclohexyl-2-[2-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 464**)

[0573] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (47mg, 37% yield).

[0574] MS: 542.27 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.73 (d, 1H), 8.49 (d, 1H), 8.32 (m, 2H), 8.23 (d, 1H), 8.12 (dd, 1H), 8.02 (dd, 1H), 7.93 (d, 1H), 7.57 (m, 4H), 7.47 (m, 1H), 4.45 (m, 1H), 2.58 (s, 3H), 2.34 (m, 2H), 2.32 (s, 3H), 2.10 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.36 (m, 3H)

Example 145

Preparation of 1-cyclohexyl-2-{2-[3-(3,4-dichloro-phenyl)-isoxazol-5-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid (**Compound 479**)

[0575] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-[3-(3,4-dichloro-phenyl)-isoxazol-5-yl]-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (21mg, 15% yield). MS: 583.16 ($M+H^+$); HPLC Procedure B, retention time = 8.77min.

Example 146

Preparation of 2-{2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 492**)

[0576] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (75mg, 49% yield). MS: 608.17 ($M+H^+$); HPLC Procedure B, retention time = 8.44min.

Example 147

Preparation of 2-{2-[5-(4-chloro-phenyl)-2-methyl-furan-3-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 505**)

[0577] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-[5-(4-chloro-phenyl)-2-methyl-furan-3-yl]-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (83mg, 59% yield). MS: 562.21 ($M+H^+$); HPLC Procedure B, retention time = 8.99min.

Example 148

Preparation of 2-{2-[3-(4-chloro-phenyl)-5-methyl-isoxazol-4-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 396**)

[0578] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-[3-(4-chloro-phenyl)-5-methyl-isoxazol-4-yl]-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (16mg, 12% yield).

[0579] MS: 563.20 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.59 (d, 1H), 8.46 (d, 1H), 8.35 (d, 1H), 8.24 (m, 2H), 8.06 (m, 2H), 7.53 (s, 4H), 7.46 (d, 1H), 4.48 (m, 1H), 3.55 (s, 1H), 2.72 (s, 3H), 2.30 (m, 2H), 2.10 (m, 2H), 1.83 (m, 2H), 1.62 (m, 1H), 1.34 (m, 3H)

Example 149

Preparation of 2-{2-[2-(4-chloro-phenyl)-4-methyl-thiazol-5-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 416**)

[0580] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-[2-(4-chloro-phenyl)-4-methyl-thiazol-5-yl]-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (27mg, 19% yield). MS: 580.19 ($M+H^+$); HPLC Procedure B, retention time = 9.18min.

Example 150

Preparation of 1-cyclohexyl-2-[2-(1H-pyrrol-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 432**)

[0581] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(1H-pyrrol-3-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (10mg, 8% yield).

[0582] MS: 437.20 ($M+H^+$); H^1-NMR (DMSO-d_6): 12.22 (s, 1H), 8.95 (d, 1H), 8.89 (d, 1H), 8.55 (m 2H), 8.42 (d, 1H), 8.31 (m, 2H), 8.15 (d, 1H), 7.90 (d, 1H), 7.49 (s, 1H), 7.15 (s, 1H), 4.39 (m, 1H), 3.55 (s, 1H), 2.32 (m, 2H), 2.05 (m, 2H), 1.85 (m, 2H), 1.66 (m, 1H), 1.35 (m, 3H)

Example 151

Preparation of 1-Cyclohexyl-2-[2-(1H-pyrrol-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 450**)

[0583] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(1H-pyrrol-2-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (11mg, 9% yield).

[0584] MS: 437.16 ($M+H^+$); H^1-NMR (DMSO-d_6): 12.12 (s, 1H), 8.80 (d, 1H), 8.49 (m, 2H), 8.31 (m, 2H), 8.18 (m, 2H), 7.95 (d, 1H), 7.63 (m, 1H), 7.43 (s, 1H), 6.45 (m, 1H), 4.40 (m, 1H), 3.51 (s, 1H), 2.30 (m, 2H), 2.08 (m, 2H), 1.85 (m, 2H), 1.65 (m, 1H), 1.35 (m, 3H)

Example 152

Preparation of 1-cyclohexyl-2-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 465**)

[0585] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 6-acetyl-4H-benzo[1,4]oxazin-3-one (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (11mg, 8% yield).

[0586] MS: 519.21 ($M+H^+$); H^1-NMR (DMSO-d_6): 10.95 (s, 1H), 8.67 (d, 1H), 8.49 (s, 1H), 8.25 (m, 4H), 8.05 (m, 2H), 7.95 (d, 1H), 7.85 (m, 1H), 7.12 (d, 1H), 4.68 (s, 2H), 4.45 (m, 1H), 2.31 (m, 2H), 2.11 (m, 2H), 1.83 (m, 2H), 1.60 (m, 1H), 1.31 (m, 3H)

Example 153

Preparation of 2-[2-(3-amino-5-phenyl-thiophen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 480**)

[0587] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(3-amino-5-phenyl-thiophen-2-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (19mg, 14% yield). MS: 545.24 ($M+H^+$); HPLC Procedure B, retention time = 8.25min.

Example 154

Preparation of 1-cyclohexyl-2-[2-(5-methoxy-benzofuran-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 493**)

[0588] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(5-methoxy-benzofuran-3-yl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (10mg, 8% yield). MS: 518.24 ($M+H^+$); HPLC Procedure B, retention time = 7.60min.

Example 155

Preparation 1-(trans-2-Hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 578**)

Step 1: 3-Nitro-4-(trans-2-hydroxy-cyclohexylamino)-benzoic acid ethyl ester (Compound 578a)

[0589] Compound **9** (689 mg, 3 mmol) was suspended in acetonitrile (5 mL) and then triethylamine was added (1.3 mL, 9 mmol). trans-2-aminocyclohexanol hydrochloride (682 mg, 4.5 mmol) was then added and the reaction refluxed for 12 hours, 2 mL methanol was then added and the reaction further refluxed for another 24 hours. Water (100 mL) was added and the resulting precipitate filtered, washed 3 times with water and air-dried. The product was used without further characterization in the next step. MS: 309.3 ($M+H^+$)

Step 2: 3-Amino-4-(trans-2-hydroxy-cyclohexylamino)-benzoic acid ethyl ester (Compound 578b)

[0590] The product from the previous step (3 mmol) was dissolved in ethyl acetate (60 mL) and methanol (40 mL) and 10% Pd/C (100 mg) was added. The reaction was hydrogenated on a Parr-shaker at 35 psi for 6 ½ hours at ambient temperature. The Pd/C was filtered and the filtrate concentrated. Chromatography (SiO_2, ethyl acetate/ toluene 6:4 v/v) to yield the title intermediate (230 mg, 0.83 mmol) MS: 279.2 ($M+H^+$)

Step 3: 1-(trans-2-Hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 578)

[0591] Compound **36A Y=Phenyl,** (200 mg, 0.8 mmol) was activated in 8 mL DMF with TBTU (282 mg, 0.88 mmol) and DIEA (0.285 mL, 1.6 mmol) for 30 minutes at room temperature. This solution was then added to Compound **578b** (230 mg, 0.83 mmol) and stirred at ambient temperature for 20 hours. The reaction was concentrated to a residue in-vacuo and then dissolved in acetic acid (20 mL) and refluxed overnight. In the morning, the acetic acid was removed in-vacuo and the crude residue dissolved in a mixture of THF (20 mL), methanol (16 mL) and 2 M NaOH (4 mL) and the solution heated at 60 C overnight. The solution was then concentrated in-vacuo to an aqueous solution and concentrated HCl added until the pH was 5. The resulting precipitate was filtered, washed with water and purified using RP-HPLC column to give the pure title compound.

[0592] Conversion **to HCl salt:** The HPLC purified product was dissolved in 4 mL methanol, 500 μL 4M HCl in dioxane was added followed by 40 mL ether. The resulting precipitate was separated by filtration and dried in high vacuum overnight. Yield: 18.3 mg.

[0593] MS: 465.21 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 9.71 (s, 1H), 8.68 (s, 1H), 8.41-8.32 (m, 5 H), 8.2 (d, 1H, J = 8.7 Hz), 7.98 (d, 1H, 8.7 Hz), 7.62 (m, 3H), 4.33 (m, 2H), 2.36 (m, 1H), 2.06 (m, 2 H), 1.77-1.55 (m, 2 H), 1.29-1.22 (m, 2 H).

Example 156

Preparation of 2-[2-(4-amino-3,5-dichloro-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 363**)

[0594] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256 mmol) was reacted with 1-(4-amino-3,5-dichloro-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (31mg, 25% yield).

[0595] MS: 531.15 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.68 (d, 1H), 8.49 (d, 1H), 8.34 (m, 6H), 8.09 (m, 2H), 4.48 (m, 1H), 3.55 (s, 1H), 2.30 (m, 2H), 2.12 (m, 2H), 1.82 (m, 2H), 1.60 (m, 1H), 1.30 (m, 3H)

Example 157

Preparation of 2-[2-(3-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 482**)

[0596] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(3-bromo-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (15mg, 12% yield).

[0597] MS: 526.12 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.72 (d, 1H), 8.53 (m, 1H), 8.48 (d, 1H), 8.35 (m, 4H), 8.23 (d, 1H), 8.10 (dd, 1H), 8.01 (dd, 1H), 7.74 (m, 1H), 7.55 (m, 1H), 4.45 (m, 1H), 3.51 (s, 1H), 2.30 (m, 2H), 2.10 (m, 2H), 1.83 (m, 2H), 1.64 (m, 1H), 1.33 (m, 3H)

Example 158

Preparation of 1-cyclohexyl-2-[2-(3,5-dimethoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 495**)

[0598] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(3,5-dimethoxy-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (44mg, 35% yield).

[0599] MS: 508.23 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.74 (d, 1H), 8.55 (d, 1H), 8.37 (m, 4H), 8.10 (m, 2H), 7.47 (d, 2H), 6.70 (m, 1H), 4.43 (m, 1H), 3.85 (s, 6H), 3.51 (s, 1H), 2.30 (m, 2H), 2.13 (m, 2H), 1.82 (m, 2H), 1.60 (m, 1H), 1.32 (m, 3H)

Example 159

Preparation of 1-cyclohexyl-2-[2-(3,4-dichloro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 508**)

[0600] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(3,4-dichloro-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (12mg, 10% yield).

[0601] MS: 516.14 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.74 (d, 1H), 8.58 (d, 1H), 8.49 (d, 1H), 8.40 (d, 1H), 8.34 (m, 3H), 8.25 (d, 1H), 8.11 (dd, 1H), 8.03 (dd, 1H), 7.85 (d, 1H), 4.45 (m, 1H), 3.51 (s, 1H), 2.32 (m, 2H), 2.10 (m, 2H), 1.84 (m, 2H), 1.62 (m, 1H), 1.33 (m, 3H)

Example 160

Preparation of 1-cyclohexyl-2-[2-(2,4-dihydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 364**)

[0602] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2,4-dihydroxy-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (9.5mg, 8% yield).

[0603] MS: 480.21 (M+H+); H1-NMR (DMSO-d6): 8.72 (d, 1H), 8.46 (d, 1H), 8.35 (m, 2H), 8.26 (dd, 2H), 8.15 (dd, 1H), 8.03 (d, 2H), 6.47 (dd, 1H), 6.42 (d, 1H), 4.44 (m, 1H), 3.51 (s, 1H), 2.30 (m, 2H), 2.10 (m, 2H), 1.84 (m, 2H), 1.64 (m, 1H), 1.35 (m, 3H)

Example 161

Preparation of 1-cyclohexyl-2-[2-(3,5-dihydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 381**)

[0604] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(3,5-dihydroxy-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 µL, 0.64mmol) to produce the title compound (22mg, 18% yield).

[0605] MS: 480.21 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.66 (d, 1H), 8.46 (d, 1H), 8.32 (m, 1H), 8.25 (m, 2H), 8.11 (m, 2H), 8.01 (m, 1H), 7.15 (d, 2H), 6.41 (m, 1H), 4.46 (m, 1H), 3.51 (s, 1H), 2.32 (m, 2H), 2.15 (m, 2H), 1.84 (m, 2H), 1.62 (m, 1H), 1.32 (m, 3H)

Example 162

Preparation of 1-cyclohexyl-2-[2-(2-hydroxy-5-methyl-3-nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 418**)

[0606] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2-hydroxy-5-methyl-3-nitro-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (40mg, 31% yield).

[0607] MS: 523.24 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.870 (d, 1H, J=9.3), 8.61 (d, 1H, J=9.3), 8.49 (s, 2H), 8.41 (d, 1H, J=8.7), 8.30 (s, 1H), 8.15 (d, 2H, J=7.8), 7.97 (d, 1H, J=9.3), 7.89 (s, 1H), 4.20 (m, 1H), 3.55 (s, 1H), 2.42 (s, 3H), 2.32 (m, 2H), 2.08 (m, 2H), 1.84 (m, 2H), 1.62 (m, 1H), 1.37 (m, 3H)

Example 163

Preparation of 1-cyclohexyl-2-[2-(2-hydroxy-6-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 434**)

[0608] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with 1-(2-hydroxy-6-methoxy-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (75mg, 69% yield).

[0609] MS: 494.24 ($M+H^+$); H^1-NMR (DMSO-d_6): 9.03 (d, 1H, J=9.3), 8.63 (s, 1H), 8.42 (d, 1H, J= 8.1), 8.26 (m, 3H), 8.15 (d, 1H, J=8.4), 7.97 (d, 1H, J=9), 7.40 (m, 1H), 6.74 (m, 2H), 4.42 (m, 1H), 3.81 (s, 3H), 3.55 (s, 1H), 2.32 (m, 2H), 2.07 (m, 2H), 1.86 (m, 2H), 1.61 (m, 1H), 1.36 (m, 3H)

Example 164

Preparation of 1-cyclohexyl-2-[2-(2-hydroxy-4,6-dimethoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 452**)

[0610] Following the procedure and workup for Compound **354**, Compound **354e** (100mg, 0.256mmol) was reacted with -(2-hydroxy-4,6-dimethoxy-phenyl)-ethanone (0.256mmol) in ethanol (2mL) using 10% w/v KOH in ethanol (506 μL, 0.64mmol) to produce the title compound (85mg, 65% yield).

[0611] MS: 524.25 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.98 (d, 1H, J=8.1), 8.59 (s, 1H), 8.40 (d, 1H, J=8.7), 8.33 (m, 2H), 8.24 (d, 1H, J=9), 8.15 (d, 1H, J=8.7), 7.97 (d, 1H, J=8.7), 6.31 (m, 2H), 4.40 (m, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.55 (s, 1H), 2.32 (m, 2H), 2.08 (m, 2H), 1.83 (m, 2H), 1.62 (m, 1H), 1.37 (m, 3H)

Example 165

Preparation of 2-[2-(4'-chloro-biphenyl-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 483**)

[0612] In dried vial with a Teflon lined screw cap, a solution of Compound **482** (156mg, 0.31mmol), 4-chlorophenylboronic acid (73mg, 0.465mmol), and Palladium Tetrakis (37mg, 0.031mmol) in toluene (9mL), methanol (2mL), and saturated sodium bicarbonate in water (900μL) was degassed, flushed with argon, and sealed. The reaction was stirred for 16 h at 90 °C. The completed reaction was then evaporated to dryness, purified via HPLC, and converted to the HCl salt using the standard procedure (as described in Compound **516**) to produce the title compound (73mg, 42% yield).

[0613] MS: 559.23 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.76 (d, 1H, J=9), 8.53 (m, 3H), 8.34 (m, 4H), 8.13 (dd, 1H, J=8.7, 1.8), 8.05 (dd, 1H, J=8.7, 1.5), 7.86 (m, 3H), 7.70 (t, 1H, J=7.8), 7.57 (m, 2H), 4.47 (m, 1H), 3.55 (s, 1H), 2.33 (m, 2H), 2.13 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.36 (m, 3H)

Example 166

Preparation of 2-[2-(4'-cyano-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 365**)

Step 1: 2-[2-(2-Bromo-5-methoxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 365a)

[0614] Following the procedure and workup for Compound **354**, Compound **354e** (2.28g, 5.83mmol) was reacted with 1-(2-bromo-5-methoxy-phenyl)-ethanone (1.335g, 5.83mmol) (the ethanone was prepared by reacting 1-(2-bromo-5-methoxy)benzoic acid with thionyl chloride to give 1-(2-bromo-5-methoxy) benzoyl chloride which is further reacted with dimethyl zinc to give the ethanone) in ethanol

(45mL) using 10% w/v KOH in ethanol (11.57m, 17.5mmol) to the title intermediate (2.80g, 86% yield).

[0615] MS: 557.14 ($M+H^+$); HPLC Procedure C, retention time=2.82min.

Step 2: 2-[2-(2-Bromo-5-methoxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid methyl ester (Compound 365b)

[0616] In a flame dried flask with stir bar, the product of the previous reaction (1.35g, 2.43mmol) was dissolved in anhydrous methanol (70mL) and 4N HCl in dioxane (10mL) was added. The reaction was refluxed at 60°C overnight. The completed reaction was then evaporated to an oil, coevaporated 3 times with 50mL anhydrous methanol, and foamed from acetonitrile to produce the title intermediate (1.38g, 99% yield).

[0617] MS: 573.12 ($M+H^+$); HPLC Procedure C, retention time = 3.25min.

Step 3: 2-[2-(4'-Cyano-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 365)

[0618] In a flame dried vial with a Teflon lined screw cap, a solution of the product of the previous reaction (100mg, 0.175mmol), 4-cyanophenylboronic acid (31mg, 0.2625mmol), and Palladium Tetrakis (20mg, 0.0175mmol) in toluene (6.5mL), methanol (1.6mL), and saturated sodium bicarbonate in water (800ul) was degassed, flushed with argon, and sealed. The reaction was stirred for 16 hours at 90° C. The vial was then cooled to room temperature and 10% w/v KOH in methanol (2mL, 3.5mmol) was added. The reaction was resealed and stirred at 70°C for 1 hour. The completed reaction was then evaporated to dryness, purified via HPLC, and converted to the HCl salt using the standard procedure (as described for Compound **516**) to produce the title compound.

[0619] MS: 579.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.44-8.41 (m, 2H), 8.33 (s, 1H), 8.24-8.18 (m, 2H), 8.09-8.00 (m, 2H), 7.7-7.68 (m, 2H), 7.50 (d, 1H, J=8.7Hz), 7.35-7.21 (m, 5H), 4.42 (m, 1H), 3.89 (s, 3H), 2.33-1.28 (m 10H)

Example 167

Preparation of 2-[2-(4'-carbamoyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 382)**

[0620] In a flame dried vial with a Teflon lined screw cap, a solution of Compound **365b** (100mg, 0.175mmol), 4-amidophenylboronic acid (31mg, 0.2625mmol), and Palladium Tetrakis (20mg, 0.0175mmol) in toluene (6.5mL), methanol (1.6mL), and saturated sodium bicarbonate in water (800ul) was degassed, flushed with argon, and sealed. The reaction was stirred for 16 hours at 90 °C. The vial was then cooled to room temperature and 10% w/v KOH in methanol (2mL, 3.5mmol) was added. The reaction was resealed and stirred at 70°C for 1 hour. The completed reaction was then evaporated to dryness, purified via HPLC, and converted to the HCl salt using the standard procedure (as described for Compound **516**) to produce the title compound.

[0621] MS: 597.30 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.39-8.19 (m, 5H), 8.09 (d, 1H, J=9.3Hz), 7.99 (d, 1H, J=8.4Hz), 7.91 (m, 1H), 7.74-7.71 (m, 2H), 7.50 (d, 1H, J=8.1Hz), 7.33-7.31 (m, 2H), 7.23-7.17 (4H), 4.43 (m, 1H), 3.88 (s, 3H), 2.33-1.33 (m 10H)

Example 168

Preparation of 2-[2-(3'-chloro-4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 366)**

[0622] In dried vial with a Teflon lined screw cap, a solution of Compound **365b** (100mg, 0.175mmol), 4-fluoro-3-chlorophenylboronic acid (61mg, 0.2625mmol), and Palladium Tetrakis (20mg, 0.0175mmol) in toluene (6.5mL), methanol (1.6mL), and saturated sodium bicarbonate in water (800ul) was degassed, flushed with argon, and sealed. The reaction was stirred for 16 hours at 90 °C. The vial was then cooled to room temperature and 10% w/v KOH in methanol (2mL, 3.5mmol) was added. The reaction was resealed and stirred at 70 °C for 1 hour. The completed reaction was then evaporated to dryness, purified via HPLC, and converted to the HCl salt using the standard procedure (as described for Compound **516**) to produce the title compound (7mg, 7% yield).

[0623] MS: 606.20 (M); H^1-NMR (DMSO-d_6): 8.40 (m, 2H), 8.31 (s, 1H), 8.19 (m, 2H), 8.05 (d, 1H, J=9), 7.96 (d, 1H, J=8.1), 7.49 (d, 1H, J=8.4), 7.37 (m,

1H), 7.30 (m, 2H), 7.20 (m, 2H), 6.98 (s, 1H), 4.40 (m, 1H), 3.75 (s, 3H), 3.55 (s, 1H), 2.30 (m, 2H), 2.05 (m, 2H), 1.85 (m, 2H), 1.63 (m, 1H), 1.30 (m, 3H)

Example 169

Preparation of 1-cyclohexyl-2-[2-(4-methoxy-4'-nitro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 383**)

[0624] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-nitrophenylboronic acid (62mg, 0.2625mmol) to produce the title compound (15mg, 14% yield).

[0625] MS: 599.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.40 (m, 2H), 8.29 (s, 1H), 8.10 (m, 5H), 7.97 (m, 1H), 7.53 (d, 1H, J=8.4), 7.36 (m, 4H), 7.24 (m, 1H), 4.40 (s, 1H), 3.90 (s, 3H), 3.55 (s, 1H), 2.30 (m, 2H), 2.06 (m, 2H), 1.84 (m, 2H), 1.62 (s, 1H), 1.32 (m, 3H)

Example 170

Preparation of 1-cyclohexyl-2-[2-(4'-dimethylamino-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 401**)

[0626] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-dimethylaminophenylboronic acid (44mg, 0.2625mmol) to produce the title compound (27mg, 26% yield).

[0627] MS: 597.32 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.34 (m, 4H), 8.16 (d, 1H, J=9.6), 8.06 (d, 1H, J=9.3), 7.96 (m, 1H), 7.42 (d, 1H, J=9), 7.30 (s, 1H), 7.17 (m, 3H), 7.07 (m, 3H), 4.40 (m, 1H), 3.87 (s, 3H), 2.92 (s, 6H), 2.31 (m, 2H), 2.08 (m, 2H), 1.82 (m, 2H), 1.16 (m, 1H), 1.36 (m, 3H)

Example 171

Preparation of 1-cyclohexyl-2-[2-(4-methoxy-3'-nitro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 420**)

[0628] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 3-nitrophenylboronic acid (44mg, 0.2625mmol) to produce the title compound (7mg, 7% yield).

[0629] MS: 599.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.36 (m, 3H), 8.13 (d, 2H, J=9), 8.02 (m, 4H), 7.58 (d, 1H, J=9), 7.50 (m, 2H), 7.37 (m, 2H), 7.24 (m, 1H), 4.37 (m, 1H), 3.90 (s, 3H), 3.55 (s, 1H), 2.28 (m, 2H), 2.06 (m, 2H), 1.85 (m, 2H), 1.61 (m, 1H), 1.34 (m, 3H)

Example 172

Preparation of 1-cyclohexyl-2-[2-(4-methoxy-4'-trifluoromethyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 436**)

[0630] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-trifluoromethylphenylboronic acid (50mg, 0.2625mmol) to produce the title compound (14mg, 12% yield).

[0631] MS: 622.27 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.40 (m, 2H), 8.32 (s, 1H), 8.21 (d, 2H, J=8.4), 8.06 (dd, 1H, J=8.7, 1.5), 8.00 (d, 1H, J=8.7), 7.58 (d, 2H, J=8.7), 7.51 (d, 1H, J=8.4), 7.32 (m, 4H), 7.22 (m, 2H), 4.45 (m, 1H), 3.89 (s, 3H), 3.55 (s, 1H), 2.32 (m, 2H), 2.07 (m, 2H), 1.84 (m, 2H), 1.06 (m, 1H), 1.35 (m, 3H)

Example 173

Preparation of 1-cyclohexyl-2-[2-(2-furan-2-yl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 454**)

[0632] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 2-furanboronic acid (30mg, 0.2625mmol) to produce the title compound (5mg, 5% yield).

[0633] MS: 544.25 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.51 (d, 1H, J=8.4), 8.42 (s, 1H), 8.28 (m, 2H), 8.09 (m, 2H), 7.92 (m, 2H), 7.68 (d, 1H, J=7.8), 7.48 (s, 1H), 7.40 (d, 1H, J=8.4), 7.17 (m, 1H), 6.40 (s, 1H), 6.06 (m, 1H), 4.45 (m, 1H), 3.86 (s, 3H), 2.34 (m, 2H), 2.08 (m, 2H), 1.85 (m, 2H), 1.62 (m, 1H), 1.34 (m, 3H)

Example 174

Preparation of 1-cyclohexyl-2-[2-(4,4'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 468**)

[0634] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-methoxyphenylboronic acid (40mg, 0.2625mmol) to produce the title compound (15mg, 15% yield).

[0635] MS: 584.29 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.37 (m, 4H), 8.20 (d, 1H, J=9.6), 8.10 (d, 1H, J=8.1), 8.00 (d, 1H, J=9), 7.42 (d, 1H, J=8.4), 7.30 (d, 1H, J=1.5), 7.17 (m, 2H), 7.03 (d, 2H, J=8.1), 6.81 (d, 2H, J=8.7), 4.43 (m, 1H), 3.88 (s, 3H), 3.68 (s, 3H), 3.55 (s, 1H), 2.32 (m, 2H), 2.08 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.34 (m, 3H)

Example 175

Preparation of 2-[2-(4'-carboxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 421**)

[0636] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with methyl 4-boronic acid benzoate (47mg, 0.2625mmol) to produce the title compound (22mg, 21% yield).

[0637] MS: 598.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.32 (m, 2H), 8.21 (d, 1H, J=8.7), 8.13 (d, 1H, J=8.7), 8.03 (m, 2H), 7.95 (m, 1H), 7.84 (d, 1H, J=8.7), 7.76 (d, 2H, J=8.4), 7.50 (d, 1H, J=8.4), 7.33 (d, 1H, J=2.4), 7.21 (m, 3H), 4.41 (m, 1H), 3.89 (s, 3H), 3.55 (s, 1H), 2.29 (m, 2H), 2.05 (m, 2H), 1.83 (m, 2H), 1.61 (m, 1H), 1.32 (m, 3H)

Example 176

Preparation of 2-[2-(3'-carboxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 437**

[0638] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with ethyl 3-boronic acid benzoate (51mg, 0.2625mmol) to produce the title compound (26mg, 23% yield).

[0639] MS: 598.27 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.31 (m, 2H), 8.20 (d, 1H, J=8.7), 8.11 (d, 1H, J=9), 8.03 (m, 1H), 7.93 (m, 1H), 7.74 (m, 2H), 7.49 (d, 1H,

J=8.7), 7.31 (m, 3H), 7.19 (m, 3H), 4.40 (m, 1H), 3.89 (s, 3H), 3.55 (s, 1H), 2.29 (m, 2H), 2.04 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.31 (m, 3H)

Example 177

Preparation of 1-Cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 455**)
and
Ethyl 1-Cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 554**)

[0640] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-fluorophenylboronic acid (37mg, 0.2625mmol) to produce both the title compound (9mg, 8% yield), as well as the ester of the same, Compound **554**.

[0641] **Compound 516:** MS: 572.27 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.36 (m, 2H), 8.30 (d, 1H, J=1.8), 8.24 (d, 1H, J=8.7), 8.17 (d, 1H, J=9), 8.07 (dd, 1H, J=8.7, 1.8), 7.98 (dd, 1H, J=8.7, 1.5), 7.45 (d, 1H, J=8.7), 7.31 (d, 1H, J=2.7), 7.13 (m, 6H), 4.41 (m, 1H), 3.87 (s, 3H), 3.55 (s, 1H), 2.33 (m, 2H), 2.06 (m, 2H), 1.84 (m, 2H), 1.62 (m, 1H), 1.32 (m, 3H)

[0642] **Compound 554:** MS: 586.30 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.35 (m, 3H), 8.25 (d, 1H, J=8.7), 8.16 (d, 1H, J=8.7), 8.06 (dd, 1H, J=8.7, 1.8), 7.97 (dd, 1H, J=8.4, 1.5), 7.45 (d, 1H, J=8.7), 7.31 (d, 1H, J=3), 7.14 (m, 6H), 4.41 (m, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.55 (s, 1H), 2.29 (m, 2H), 2.05 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.34 (m, 3H)

Example 178

Preparation of 1-cyclohexyl-2-[2-(4'-hydroxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 469**)

[0643] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-phenolboronic acid (36mg, 0.2625mmol) to produce the title compound (10mg, 8% yield).

[0644] MS: 570.27 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.36 (m, 3H), 8.21 (d, 1H, J=9), 8.10 (dd, 1H, J=8.4, 1.2), 8.00 (dd, 1H, J=8.7, 1.5), 7.56 (m, 1H), 7.40 (d, 1H,

J=8.7), 7.31 (d, 1H, J=2.7), 7.15 (m, 2H), 6.90 (d, 2H, J=8.7), 6.62 (d, 2H, J=8.4), 4.45 (m, 1H), 3.86 (s, 3H), 3.54 (s, 1H), 2.31 (m, 2H), 2.08 (m, 2H), 1.84 (m, 2H), 1.60 (m, 1H), 1.35 (m, 3H)

Example 179

Preparation of 1-cyclohexyl-2-[2-(3',4'-dichloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 403**)

[0645] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175 mmol) was reacted with 3,4-dichlorophenylboronic acid (50mg, 0.2625mmol) to produce the title compound (5mg, 4% yield).

[0646] MS: 622.20 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.40 (d, 1H, J=9), 8.34 (m, 1H), 8.27 (m, 1H), 8.17 (d, 1H, J=8.4), 8.06 (m, 2H), 7.93 (m, 1H), 7.50 (d, 1H, J=8.4), 7.42 (m, 2H), 7.31 (m, 2H), 7.19 (dd, 1H, J=9, 2.7), 6.96 (dd, 1H, J=8.1, 1.2), 4.45 (m, 1H), 3.88 (s, 3H), 2.29 (m, 2H), 2.05 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.31 (m, 3H)

Example 180

Preparation of 2-[2-(3'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 422**)

[0647] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 3-chlorophenylboronic acid (41mg, 0.2625mmol) to produce the title compound (20mg, 17% yield).

[0648] MS: 588.23 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.39 (m, 2H), 8.30 (d, 1H, J=1.8), 8.20 (m, 2H), 8.06 (dd, 1H, J=8.7, 1.8), 7.98 (dd, 1H, J=8.4, 1.5), 7.49 (d, 1H, J=7.5), 7.31 (d, 1H, J=2.7), 7.24 (m, 6H), 6.99 (m, 1H), 4.41 (m, 1H), 3.88 (s, 3H), 3.55 (s, 1H), 2.31 (m, 2H), 2.06 (m, 2H), 1.84 (m, 2H), 1.60 (m, 1H), 1.31 (m, 3H)

Example 181

Preparation of 1-cyclohexyl-2-[2-(4-methoxy-4'-methyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 438**)

[0649] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with *p*-tolylboronic acid (36mg, 0.2625mmol) to produce the title compound (12mg, 12% yield).

MS: 568.30 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.32 (m, 4H), 7.16 (d, 1H, J=9), 8.07 (dd, 1H, J=8.7, 2.1), 7.97 (dd, 1H, J=8.7, 1.8), 7.42 (d, 1H, J=8.7), 7.30 (d, 1H, J=2.7), 7.15 (m, 2H), 7.02 (m, 4H), 4.42 (m, 1H), 3.87 (s, 3H), 3.54 (s, 1H), 2.30 (m, 2H), 2.24 (s, 3H), 2.06 (m, 2H), 1.84 (m, 2H), 1.63 (m, 1H), 1.32 (m, 3H)

Example 182

Preparation of 1-cyclohexyl-2-[2-(4-methoxy-3'-methyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 367**)

Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with *m*-tolylboronic acid (36mg, 0.2625mmol) to produce the title compound (27mg, 27% yield).

[0650] MS: 568.29 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.30 (m, 4H), 8.16 (d, 1H, J=8.7), 8.07 (dd, 1H, J=8.4, 1.8), 7.97 (dd, 1H, J=9, 1.8), 7.44 (d, 1H, J=8.4), 7.32 (d, 1H, J=2.7), 7.16 (m, 2H), 7.04 (m, 3H), 6.78 (d, 1H, J=7.2), 4.41 (m, 1H), 3.87 (s, 3H), 3.55 (s, 1H), 2.29 (m, 2H), 2.20 (s, 3H), 2.06 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.31 (m, 3H)

Example 183

Preparation of 2-[2-(4'-aminomethyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 384**)

[0651] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-aminomethylphenylboronic acid (49mg, 0.2625mmol) to produce the title compound (48mg, 46% yield).

[0652] MS: 583.31 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.31 (m, 3H), 8.14 (d, 1H, J=8.7), 8.05 (dd, 1H, J=8.4, 1.8), 7.95 (dd, 1H, J=8.4, 1.2), 7.70 (m, 1H), 7.58 (m, 1H), 7.43 (d, 1H, J=8.4), 7.45 (d, 2H, J=8.4), 7.28 (d, 1H, J=2.4), 7.17 (m, 4H), 4.40 (m,

1H), 3.87 (s, 3H), 3.55 (s, 1H), 2.30 (m, 2H), 2.05 (m, 2H), 1.83 (m, 2H), 1.64 (m 1H), 1.33 (m, 3H)

Example 184

Preparation of 1-cyclohexyl-2-[2-(4'-ethoxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 456**)

[0653] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-ethoxyphenylboronic acid (44mg, 0.2625mmol) to produce the title compound (17mg, 16% yield).

[0654] MS: 598.32 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.35 (m, 4H), 8.23 (d, 1H, J=8.4), 8.12 (d, 1H, J=9), 8.02 (d, 1H, J=8.7), 7.42 (d, 1H, J=8.7), 7.32 (m, 1H), 7.16 (m, 2H), 7.02 (d, 2H, J=8.7), 6.78 (m, 2H), 4.43 (m, 1H), 3.94 (m, 2H), 3.86 (s, 3H), 3.54 (s, 1H), 2.32 (m, 2H), 2.08 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.34 (m, 3H), 1.27 (m, 3H)

Example 185

Preparation of 1-cyclohexyl-2-[2-(5-methoxy-2-thiophen-2-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (**Compound 470**)

[0655] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 2-thiopheneboronic acid (34mg, 0.2625mmol) to produce the title compound (26mg, 27% yield).

[0656] MS: 598.32 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.48 (m, 2H), 8.34 (m, 2H), 8.27 (d, 1H, J=8.7), 8.12 (d, 1H, J=8.7), 8.04 (d, 1H, J=9), 7.56 (d, 1H, J=8.4), 7.40 (m, 2H), 7.30 (d, 1H, J=2.7), 7.17 (dd, 1H, J=8.4, 2.7), 6.91 (m, 1H), 6.77 (d, 1H, 2.7), 4.46 (m, 1H), 3.86 (s, 3H), 3.55 (s, 1H), 2.31 (m, 2H), 2.11 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.33 (m, 3H)

Example 186

Preparation of 1-cyclohexyl-2-{2-[2-(2,4-dimethoxy-pyrimidin-5-yl)-5-methoxy-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid (**Compound 484**)

[0657] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 2,4-dimethoxypyrimidine-5-boronic acid (34mg, 0.2625mmol) to produce the title compound (8mg, 7% yield).

[0658] MS: 616.30 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.55 (d, 1H, J=9), 8.43 (s, 1H), 8.32 (d, 1H, J=0.9), 8.21 (d, 1H, J=8.7), 8.16 (s, 1H), 8.09 (m, 2H), 8.00 (m, 1H), 7.56 (d, 1H, J=8.7), 7.39 (m, 2H), 7.18 (dd, 1H, J=8.7, 2.7), 4.40 (m, 1H), 3.87 (m, 6H), 3.55 (s, 1H), 3.84 (s, 3H), 2.30 (m, 2H), 2.10 (m, 2H), 1.84 (m, 2H), 1.60 (m, 1H), 1.32 (m, 3H)

Example 187

Preparation of 2-[2-(2-bromo-phenyl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (**Compound 477**)

Step 1: 6-Hydroxy-5-nitronicotinic acid (Compound 477a)

[0659] A solution of 6-hydroxynicotinic acid (10 g, 71.89 mmol) in fuming nitric acid (100 mL) was stirred at 50 °C for 4 h. After evaporation of extra nitric acid, the solid was obtained and it was directly used in the next step reaction. MS: 185.02 ($M + H^+$).

Step 2: Ethyl 6-chloro-5-nitronicotinic ester (Compound 477b)

[0660] A mixture of 6-hydroxy-5-nitronicotinic acid (Compound **477a**) (1.5 g, 8.15 mmol), phosphorus pentachloride (3 g) and phosphoryl chloride (5 mL) was stirred at 100 °C for 2 h. Excess of phosphoryl chloride was removed under reduced pressure and to the residue was added anhydrous EtOH (2 mL) at 0 °C. Water (50 mL) was added. The mixture was extracted with EtOAc. The combined organic phase was washed with water, dried over anhydrous Na_2SO_4 and evaporated to give the title intermediate (1.24 g, 66%). MS: 230.03 ($M + H^+$).

Step 3: 6-Cyclohexylamino-5-nitro-nicotinic acid ethyl ester (Compound 477c)

[0661] A mixture of ethyl 6-chloro-5-nitronicotinic ester (Compound **477b**)(0.83 g, 3.60 mmol), DIEA (0.32 mL, 18.0 mmol) and cyclohexylamine (1.25 mL, 10.93 mmol) in MeCN (15 mL) was stirred at reflux under Ar overnight. After removal of solvent, the residue was purified by chromatography using $CHCl_3$-hexane (2:1) as the eluent to give the title intermediate (1.0 g, 95%). MS: 294.13 ($M + H^+$).

Step 4: 2-[2-(2-Bromo-phenyl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid ethyl ester (Compound 477d)

[0662] (1) A mixture of Compound **477c** (0.18 g, 0.614 mmol) and 5% Pd/C (20 mg) in MeOH was shaken under 40 psi of H_2 for 30 min. The mixture was filtered through Celite and washed with MeOH and DMF. The combined filtrate was evaporated to dryness to give the amine.

[0663] (2) A mixture of Compound **353a** (0.217 g, 0.661 mmol), HBTU (0.26 g, 0.686 mmol) and DIEA (0.267 mL, 1.53 mmol) in DMF (10 mL) was stirred at room temperature for 30 min and then transferred to above amine. The resulting reaction mixture was stirred at room temperature for 6 h and evaporated to dryness.

[0664] (3) To this residue was added AcOH (8 mL) and the solution was stirred at reflux for 2 h. After removal of solvent by evaporation, the residue was purified by chromatography using $CHCl_3$-hexane (10:1) and $CHCl_3$-MeOH (100: 1) as the eluents to give the title intermediate. Total yield was 69%. MS: 557.17 ($M + H^+$).

Step 5: 2-[2-(2-Bromo-phenyl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (Compound 477)

[0665] Compound 477d (0.139 g, 0.25 mmol) was dissolved in MeOH (3 mL) and 2 N aqueous NaOH (1.5 mL) was added. The mixture was stirred at 55 °C for 2 h and then neutralized with 5 N HCl to pH 3 at 0 °C. The precipitates formed was collected by filtration and purified by RP HPLC (15% of buffer B to 95% of buffer B) to give the title compound. Yield 96%.

[0666] MS: 527. 17, 529.17 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.97 (d, 1H, J = 2.1 Hz), 8.67 (d, 1H, J = 8.1 Hz), 8.55 (d, 1H, J = 1.5 Hz), 8.46 (d, 1H, J = 1.5 Hz), 8.26 (d, 1H, J = 8.7 Hz), 8.10 (dd, 1H, J = 1.8, 8.7 Hz), 7.87 (d, 1H, J = 8.4 Hz), 7.81 (dd, 1H, J = 1.2, 8.1 Hz), 7.66 (d, 1H, J = 2.1, 7.5 Hz), 7.57 (dt, 1H, J = 1.2, 7.5 Hz), 7.45 (dt, 1H, J = 1.2, 7.7 Hz), 4.42 (m, 1H), 2.72-2.68 (m, 2H), 2.07-2.00 (m, 2H), 1.83 (m, 5H), 1.65 (m, 1H), 1.30 (m, 4H).

Example 188

Preparation of 2-[2-(4'-chloro-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid **(Compound 490)**

[0667] A mixture of Compound **477d** (0.139 g, 0.25 mmol), 4-chlorobenzeneboronic acid (78 mg, 0.50 mmol) and $Pd(PPh_3)_4$ (20 mg) in toluene (8 mL), MeOH (2 mL) and saturated $NaHCO_3$ (0.8 mL) was stirred under Ar at 70 °C for 16 h. After evaporation of solvent, the residue was dissolved in $CHCl_3$ (30 mL) and filtered. The filtrate was evaporated to dryness. MS: 587.25 ($M + H^+$).

[0668] The residue was hydrolyzed with 2 N aqueous NaOH in MeOH according to procedure described in Compound **477**. Purification was achieved by RP HPLC (15% of buffer B to 95% of buffer B) to give the title compound (0.116 g, 83%).

[0669] MS: 559.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.97 (d, 1H, J = 1.8 Hz), 8.54 (d, 1H, J = 2.1 Hz), 8.43 (d, 1H, J = 8.4 Hz), 8.39 (d, 1H, J = 1.8 Hz), 8.25 (d, 1H, J = 8.7 Hz), 8.11 (dd, 1H, J = 1.8, 9.0 Hz), 7.81 (dd, 1H, J = 2.1, 6.9 Hz), 7.65-7.60 (m, 2H), 7.54 (dd, 1H, J = 2.4, 6.6 Hz), 7.33 (d, 2H, J = 8.4 Hz), 7.24 (d, 1H, J = 8.4 Hz), 7.19 (d, 2H, J = 8.4 Hz), 4.40 (m, 1H), 2.72-2.67 (m, 2H), 2.03-1.99 (m, 2H), 1.83 (m, 5H), 1.65 (m, 1H), 1.29 (m, 4H).

Example 189

Preparation of (4'-chloro-2-{6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzoimidazol-2-yl]-quinolin-2-yl}-biphenyl-4-yl)-pyrrolidin-1-yl-methanone **(Compound 259)**

Step 1: 1-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-ethanone (Compound 259a)

[0670] A mixture of Compound **419c** (0.29 g, 0.845 mmol), 4-chlorobenzeneboronic acid (0.159 g, 1.02 mmol)) and $Pd(PPh_3)_4$ (97 mg) in toluene (25 mL), MeOH (6 mL) and saturated $NaHCO_3$ (2.5 mL) was stirred under Ar at 70 °C for 16 h. After evaporation of solvent, the residue was dissolved in $CHCl_3$ (30 mL) and filtered. The filtrate was evaporated to dryness. The residue was purified by chromatography using $CHCl_3$-MeOH (80:1 to 30:1) as the eluent to give an oil (0.266g, 96%). MS: 328.08 ($M + H^+$).

Step 2: 2-[4'-Chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinoline-6-carboxylic acid (Compound 259e)

[0671] To a mixture of Compound **259a** (0.388 g, 1.184 mmol) and Compound **7** (0.223 g, 1.243 mmol) was added a solution of KOH (0.234 g, 3.55 mmol) in EtOH (18 mL). The reaction mixture was stirred under Ar at 75 °C for 16 h. EtOH (10 mL) was added to make a clean solution, which was neutralized by adding 4 N HCl in dioxane (about 1 mL) to pH 3. After evaporation of solvent, H_2O (15 mL) was added and the precipitates were collected by filtration, washed with water and dried. Yield 0.125g, 89%. MS: 457.12, 458.13 ($M + H^+$).

Step 3: (4'-Chloro-2-{6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzoimidazol-2-yl]-quinolin-2-yl}-biphenyl-4-yl)-pyrrolidin-1-yl-methanone (Compound 259)

[0672] Compound **128** (91 mg, 0.316 mmol) was reduced to the corresponding amine by hydrogenation according to procedures used in the preparation of Compound **477d**.

[0673] The amine was reacted with Compound **259e** (0.125 g, 0.274 mmol) in the presence of HBTU (0.114 g, 0.30 mmol), followed cyclization in AcOH according

to procedures described for the preparation of Compound **477d**. Separation by RP HPLC (from 10% of buffer B to 85% of buffer B) gave the title compound (42 mg, 23%).

[0674] MS: 679.30 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.45 (d, 1H, J = 1.2 Hz), 8.40-8.37 (m, 2H), 8.29 (d, 1H, J = 8.7 Hz), 8.24 (d, 1H, J = 9.0 Hz), 8.10-8.06 (m, 2H), 7.92 (d, 1H, J = 1.8 Hz), 7.76 (dd, 1H, J = 1.8, 8.1 Hz), 7.59 (d, 1H, J = 7.8 Hz), 7.35 (d, 2H, J = 8.4 Hz), 7.24-7.20 (m, 3H), 4.44 (m, 1H), 3.55-3.49 (m, 4H), 2.43-2.2.28 (m, 2H), 2.09-2.06 (m, 2H), 1.92-1.85 (m, 5H), 1.68-1.62 (m, 1H), 1.45-1.29 (m, 4H).

Example 190

Preparation of 2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid **(Compound 539)**

[0675] Compound **477c** (0.104 g, 0.355 mmol) was hydrogenated over 5% Pd/C (11 mg) according to procedure (1) in the preparation of Compound **477d**.

[0676] The amine was then reacted with Compound **259e** (0.13 g, 0.284 mmol) in the presence of HBTU (0.135 g, 0.356 mmol), followed cyclization in AcOH and purification according to procedure (2) and (3) in the preparation of Compound **477d,** resulting in the precursor ester of Compound **539**.

[0677] Hydrolysis of the ester with 2N aqueous NaOH/MeOH to the acid and purification by HPLC to give the title compound (23 mg, 13%).

[0678] MS: 656.30 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.96 (d, 1H, J = 1.8 Hz), 8.53 (d, 1H, J = 2.1 Hz), 8.37-8.34 (m, including d, 2H, J = 8.1 Hz), 8.20 (d, 1H, J = 8.7 Hz), 8.06 (dd, 1H, J = 1.8, 8.4 Hz), 7.90 (d, 1H, J = 1.8 Hz), 7.75 (dd, 1H, J = 1.8, 7.8 Hz), 7.58 (d, 1H, J = 7.5 Hz), 7.36 (d, 2H, J = 8.4 Hz), 7.22-7.18 (m, 3H), 4.40 (m, 1H), 3.51-3.41 (m, 4H), 2.72-2.68 (m, 2H), 2.02-1.98 (m, 2H), 1.87 (m, 5H), 1.65 (m, 1H), 1.29-1.23 (m, 4H).

Example 191

Preparation of {4'-chloro-2-[6-(1-cyclohexyl-1H-benzoimidazol-2-yl)-quinolin-2-yl]-biphenyl-4-yl}-pyrrolidin-1-yl-methanone **(Compound 540)**

[0679] Compound **259e** (50 mg, 0.109 mmol) was reacted with HBTU (62 mg, 0.163 mmol) in DMF (1.5 mL) in the presence of DIEA (38 μL, 0.219 mmol) at room temperature for 30 min. N-cyclohexyl-benzene-1,2-diamine (31.2 mg, 0.164 mmol), (prepared in the manner described for Compound **11** starting with 2-chloro-nitrobenzene instead of 4-chloro-3 nitro benzoic acid) was added and the mixture was stirred at room temperature for 16 h. After evaporation of solvent, to the residue was added AcOH (5 mL) and the mixture was stirred at reflux for 2 h. The solvent was evaporated and the residue was separated by RP HPLC (from 10% of buffer B to 85% of buffer B) to give the title compound (26 mg, 39%).

[0680] MS: 611.28 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.47(s, 1H), 8.40 (d, 1H, J = 8.7 Hz), 8.31-8.28 (m, including d, 2H, J = 8.7 Hz), 8.12 (d, 1H, J = 8.4 Hz), 7.92-7.89 (m, 2H), 7.77 (dd, 1H, J = 1.5, 8.1 Hz), 7.65-7.58 (m, 3H), 7.36 (d, 2H, J = 8.1 Hz), 7.27 (d, 1H, J = 8.1 Hz), 7.21 (d, 2H, J = 8.7 Hz), 4.47 (m, 1H), 3.55-3.49 (m, 4H), 2.37-2.29 (m, 2H), 2.15-2.12 (m, 2H), 1.92-1.83 (m, 5H), 1.68-1.61 (m, 1H), 1.46-1.23 (m, 4H).

Example 192

Preparation of 2-(4'-chloro-4-methoxy-biphen-2-yl)-6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzoimidazol-2-yl]-quinoline **(Compound 525)**

Step 1: 1-(4'-Chloro-4-methoxy-biphen-2-yl)-ethanone (Compound 525a)

[0681] 1-(2-Bromo-5-methoxyphenyl)ethanone (prepared as described in Step 1 of Example 166) (12 g, 52.39 mmol) was reacted with 4-chlorobenzeneboronic acid (9.02, 57.68 mmol) and the catalyst $Pd(PPh_3)_4$ (0.605 g) as described for Compound **477e**. Purification by chromatography using $CHCl_3$-MeOH (80:1) as the eluent gave the title intermediate (12.67 g, 93%). MS: 261.08 ($M + H^+$), 283.07 ($M + Na^+$).

Step 2: 2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinoline-6-carboxylic acid (Compound 525c)

[0682] Compound **7** (3.06 g. 11.72 mmol) was reacted with compound **525a** (2.1 g, 11.72 mmol) and KOH (2.32 g, 35.16 mmol) in EtOH (150 mL) according to the procedure in the preparation of Compound **259e**. Purification by chromatography using $CHCl_3$-MeOH (7:1) as the eluent gave the title intermediate (3.1 g, 91%). MS: 388.07 ($M + H^+$).

Step 3: Preparation of 2-(4'-Chloro-4-methoxy-biphen-2-yl)-6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzoimidazol-2-yl]-quinoline (Compound 525)

[0683] Compound **128** (98 mg, 0.34 mmol) was reduced to the corresponding amine by hydrogenation according to procedure (1) in the preparation of Compound **477d**.

[0684] The amine was reacted with compound **525c** (0.11 g, 0.34 mmol) in the presence of HBTU (0.135 g, 0.356 mmol), followed by cyclization in AcOH according to procedure (2) in the preparation of Compound **477d**. Separation by RP HPLC (from 20% of buffer B to 99% of buffer B) gave the title compound (51 mg, 25%).

[0685] MS: 612.26 ($M + H^+$). ^1H NMR (DMSO-d_6) δ(ppm) 8.54 (d, 1H, J = 1.6 Hz), 8.44-8.37 (m, 3H), 8.29 (d, 1H, J = 8.7 Hz), 8.19 (d, 1H, J = 9.0 Hz), 8.12 (d, 1H, J = 8.7 Hz), 7.48-7.42 (m, 2H), 7.33-7.19 (m, 5H), 7.12 (d, 1H, J = 8.4 Hz), 4.46 (m, 1H), 3.88 (s, 1H), 2.38-2.34 (m, 2H), 2.13-2.09 (m, 2H), 1.88-1.84 (m, 2H), 1.62 (m, 1H), 1.47-1.30 (m, 3H).

Example 193

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid **(Compound 537)**

Step 1: 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid ethyl ester (Compound 537a)

[0686] Compound **477c** (0.225 g, 0.767 mmol) was reduced to the corresponding amine by hydrogenation according to procedure (1) in the preparation of Compound **477d**.

[0687] The amine was reacted with Compound **525c** (0.314 g, 0.805 mmol) in the presence of HBTU (0.32 g, 0.844 mmol) and DIEA (0.47 mL, 2.68 mmol) in DMF (10 mL), followed cyclization in AcOH (10 mL) according to procedure (2) and (3) in the preparation of Compound **477d**. Separation by RP HPLC (from 20% of buffer B to 99% of buffer B) gave the title intermediate (0.19 g, 40%).

Step 2: 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (Compound 537)

[0688] Hydrolysis of the product from the previous reaction (63 mg, 0.102 mmol) with 2N aqueous NaOH/MeOH and purification by HPLC was accomplished using the procedures described for Compound **477** giving the title compound (31 mg, 52%).

[0689] MS: 589.24 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.96 (d, 1H, J = 1.8 Hz), 8.53 (d, 1H, J = 2.1 Hz), 8.36-8.33 (m, 2H), 8.20 (d, 1H, J = 8.4 Hz), 8.06 (dd, 1H, J = 1.8, 9.0 Hz), 7.45 (d, 1H, J = 8.4 Hz), 7.31-7.28 (m, 3H), 7.20-7.11 (m, 4H), 4.44-4.36 (m, 1H), 3.88 (s, 3H), 2.72-2.67 (m, 2H), 2.01-1.97 (m, 2H), 1.82 (m, 2H), 1.65 (m, 1H), 1.29-1.22 (m, 3H).

Example 194

Preparation of 2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid **(Compound 535)** and 2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid ethyl ester **(Compound 538)**

[0690] Compound **537a** (71.8 mg) was dissolved in anhydrous CH_2Cl_2 (8 mL) and 1.0 M BBr_3 in CH_2Cl_2 (4 mL) was added dropwise at –70 °C. The mixture was stirred at –70 °C for 1 h and at room temperature overnight. The mixture was cooled down to -70 °C again and MeOH (2 mL) was added dropwise. To the mixture was added 2 N aqueous NaOH (1 mL) at room temperature and neutralized with 5 N HCl to pH 3. After evaporation of solvent, the dry residue was dissolved in MeOH (10 mL) and filtered off insoluble precipitates. The filtrate was evaporated to dryness. Separation by RP HPLC (form 20% buffer B to 99% buffer B) gave the title compounds.

[0691] **Compound 535:** (25.8 mg)MS: 575.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 9.88 (br s, 1H), 8.96 (d, 1H, J = 1.8 Hz), 8.53 (d, 1H, J = 1.8 Hz), 8.33-8.30 (m, 2H), 8.20 (d, 1H, J = 9.0 Hz), 8.06 (dd, 1H, J = 2.1, 9.0 Hz), 7.33 (d, 1H, J = 8.1 Hz), 7.29-7.25 (m, 2H), 7.19 (d, 1H, J = 2.4 Hz), 7.13-7.08 (m, 3H), 6.99 (dd, 1H, J = 2.7, 8.4 Hz), 4.41 (m, 1H), 3.88 (s, 3H), 2.72-2.68 (m, 2H), 2.01-1.98 (m, 2H), 1.83 (m, 2H), 1.66 (m, 1H), 1.30 (m, 3H).

[0692] **Compound 538:** (10.6 mg): MS: 603.25 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.98 (d, 1H, J = 1.8 Hz), 8.55 (d, 1H, J = 2.1 Hz), 8.33-8.30 (m, 2H), 8.20 (d, 1H, J = 8.7 Hz), 8.06 (dd, 1H, J = 1.8, 8.7 Hz), 7.32 (d, 1H, J = 8.1 Hz), 7.30-7.25 (m, 3H), 7.19 (d, 1H, J = 2.4 Hz), 7.13-7.08 (m, 3H), 6.99 (dd, 1H, J = 2.4, 8.4 Hz), 4.42-4.34 (m, 3H), 2.72-2.67 (m, 2H), 2.02-1.98 (m, 2H), 1.83 (m, 2H), 1.67 (m, 1H), 1.37 (t, 3H, J = 7.2 Hz), 1.29-1.23 (m, 3H).

Example 195

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-5-carboxylic acid **(Compound 571)**

Step 1: 3-Cyclohexylamino-4-nitro-benzoic acid (Compound 571a)

[0693] A mixture of 3-fluoro-4-nitrobenzoic acid (0.35 g, 1.891 mmol) and cyclohexylamine (2.17 mL, 18.91 mmol) in NMP (10 mL) was stirred under Ar at 85 °C for 6 h. The solvent was evaporated under high vacuum. The residue was purified by chromatography using CH_3Cl-MeOH (10:1) as the eluent to give the title intermediate in a quantitative yield. MS: 263.11 ($M - H^+$)

Step 2: 3-Cyclohexylamino-4-nitro-benzoic acid ethyl ester (Compound 571b)

[0694] A solution of the product of the previous step (0.4 g) in anhydrous EtOH (50 mL) was gently bubbled with anhydrous HCl gas for 4 h and the solution was left at room temperature for 16 h. The solvent was evaporated to dryness to give the title intermediate in a quantitative yield. MS: 293.14 ($M + H^+$)

Step 3: 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-5-carboxylic acid (Compound 571)

[0695] The product from the previous step (0.14 g, 0.479 mmol) was reduced to the corresponding amine by hydrogenation according to the preparation of Compound **477d**.

[0696] The amine was reacted with Compound **525c** (0.215 g, 0.552 mmol) in the presence of HBTU (0.22 g, 0.58 mmol) and DIEA (0.17 mL, 0.976 mmol) in DMF (10 mL), followed cyclization in AcOH (10 mL) according to procedure (2) and (3) in the preparation of Compound **477d**.

[0697] Hydrolysis of above ester with 2 N aqueous NaOH/MeOH and purification by HPLC was accomplished as described for Compound **477** to give the title compound (43.2 mg, 15%).

[0698] MS: 588.24 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.48 (s, 1H), 8.42-8.38 (m, 2H), 8.27 (d, 1H, J = 9.0 Hz), 8.10 (dd, 1H, J = 1.8, 9.0 Hz), 8.03 (dd, 1H, J = 1.5, 8.7 Hz), 7.89 (d, 1H, J = 8.7 Hz), 7.46 (d, 1H, J = 8.7 Hz), 7.32 (d, 1H, J = 2.7 Hz), 7.29 (d, 2H, J = 8.7 Hz), 7.25-7.19 (m, 2H), 7.13 (d, 2H, J = 8.7 Hz), 4.52-4.45 (m, 1H), 3.87 (s, 3H), 2.27-2.12 (m, 4H), 1.86 (br s, 2H), 1.67 (br s, 1H), 1.34 (br, 3H).

Example 196

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-ethyl-1H-benzoimidazole-5-carboxylic acid **(Compound 534)**

Step 1: Loading the resin with 4-chloro-3-nitrobenzoic acid (Resin 534a)

[0699] To a solution of 4-chloro-3-nitrobenzoic acid (0.605 g, 3 mmol) in ethanol (15 mL) and water (5 mL) was added dropwise 10% aqueous Cs_2CO_3 to adjust the solution to pH 7. The resulting mixture was evaporated to dryness and co-evaporated with toluene (20 mL) four times. The residue was then dried over P_2O_5 under high vacuum.

[0700] A mixture in anhydrous DMF (8 mL) of Merrifield resin HL (Nova Biochem, 100-200 mesh, loading: 1.34 mmol/g, 1.04 g) and the dry Cs-salt prepared above was gently agitated at 50 °C overnight. The solution was drained and the resin was washed with DMF (5 mL X 5), DMF/H_2O (9:1 v/v, 5 mL X 5), DMF (5 mL X 5), and MeOH (5 mL X 5). The resin was dried under high vacuum. Based on the increase of the resin weight, the loading of substitution was calculated to be 1.30 mmol/g.

Step 2: Amine addition

[0701] A mixture of Resin **534a** (0.308 g, 0.40 mmol), a 2.0 M solution of ethylamine in MeOH (3.9 mL, 7.8 mmol), and DIEA (0.82 mL, 4.68 mmol) in NMP (10 mL) was shaken for 16 h at room temperature. The solution was drained and the resin was washed with DMF (5 mL X 5), MeOH (5 mL X 5), and CH_2Cl_2 (5 mL X 5). The resins was dried under high vacuum.

Step 3: Reduction of the nitro group

[0702] The resin was then suspended in DMF (10 mL) and $SnCl_2 \cdot 2H_2O$ (5.42 g, 24 mmol) was added. The mixture was shaken under Ar at room temperature for 32 h. The solution was drained and the resin was washed with DMF (5 mL X 5), MeOH (5 mL X 5), and CH_2Cl_2 (5 mL X 5). The resin was dried under high vacuum.

Step 4: Formation of the benzimidazole ring

[0703] Compound **525c** (0.38 g, 0.97 mmol) was reacted with HBTU (0.444 g, 1.2 mmol) in anhydrous DMF (5 mL) in the presence of DIEA (0.41 mL, 2.35 mmol) for 30 min. The mixture was then transferred to a suspension of amine-resin in DMF (5 mL). The reaction mixture was shaken at room temperature overnight. The solution was drained and the resin was washed with DMF (5 mL X 5), MeOH (5 mL X 5), and CH_2Cl_2 (5 mL X 5). The resin was dried under high vacuum.

Step 5: Cleavage of the resin

[0704] To the resin was added AcOH (10 mL) and the mixture was refluxed for 3 h. After evaporation of AcOH, TFA (3 mL) and TFMSA (0.3 mL) were

added to the dry resin. The mixture was left at room temperature for 2 h. The resin was filtered off and washed with TFA (3 mL X 3) and MeOH (3 mL X 2). The filtrate was evaporated and the residue was neutralized with ammonium solution. The product was purified by reverse phase HPLC from 20% of Buffer B to 99% of Buffer A.

[0705] MS: 534.16 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.50 (s, 1H), 8.42-8.34 (m, including d, 2H, J = 8.4 Hz), 8.29-8.20 (m, including d, 2H, J = 8.4 Hz), 8.08 (d, 1H, J = 8.4 Hz), 8.02 (d, 1H, J = 9.0 Hz), 7.46 (d, 1H, J = 8.0 Hz), 7.33-7.07 (m, 7H), 4.53 (q, 2H, J = 6.9 Hz), 3.88 (s, 3H), 1.45 (t, 3H, J = 5.7 Hz).

Example 197

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopropyl-1H-benzoimidazole-5-carboxylic acid **(Compound 528)**

[0706] The title compound was prepared from Resin **534a** and cyclopropylamine according to the procedure described in the preparation of Compound **534.**

[0707] MS: 546.16 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.70 (s, 1H), 8.46-8.39 (m, 2H), 8.31 (s, 1H), 8.23 (d, 1H, J = 9.0 Hz), 8.05 (d, 1H, J = 8.4 Hz), 7.90 (d, 1H, J = 2.1, 8.7 Hz), 7.48-7.42 (m, 2H), 7.35-7.28 (m, 2H), 7.25-7.07 (m, 4H), 4.12 (m, 1H), 3.88 (s, 3H), 1.19 (d, 2H, J = 6.6 Hz), 0.76 (br s, 2H).

Example 198

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-isopropyl-1H-benzoimidazole-5-carboxylic acid **(Compound 527)**

[0708] The title compound was prepared from Resin **534a** and isopropylamine according to the procedure described in the preparation of Compound **534**.

[0709] MS: 548.19 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.38 (s, 1H), 8.36 (d, 1H, J = 7.0 Hz), 8.32 (d, 1H, J = 1.5 Hz), 8.24 (d, 1H, J = 8.7 Hz), 8.14 (d, 1H, J = 9.0 Hz), 8.09 (dd, 1H, J = 2.1, 8.7 Hz), 7.99 (dd, 1H, J = 1.5, 8.7 Hz), 7.46 (d, 1H, J =

8.7 Hz), 7.32-7.27 (m, 3H), 7.22-7.18 (m, 2H), 7.14-7.11 (m, 2H), 4.89 (t, 1H, J = 7.2 Hz), 3.88 (s, 3H), 1.69 (d, 6H, J = 7.2 Hz).

Example 199

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(2-dimethylamino-ethyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 533)**

[0710] The title compound was prepared from Resin **534a** and *N,N*-dimethylethyleneamine according to the procedure described in the preparation of Compound **534**.

[0711] MS: 577.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 10.77 (br s, 1H), 8.47 (s, 1H), 8.42 (d, 1H, J = 8.7 Hz), 8.32 (d, 1H, J = 0.9 Hz), 8.26-8.21 (m, 2H), 8.00 (s, 2H), 7.45 (d, 2H, J = 8.4 Hz), 7.32-7.26 (m, 2H), 7.22-7.17 (m, 2H), 7.14-7.11 (m, 2H), 4.88 (t, 2H, J = 7.8 Hz), 3.88 (s, 3H), 3.83 (s, 6H), 3.61 (m, 2H).

Example 200

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopentyl-1H-benzoimidazole-5-carboxylic acid **(Compound 529)**

[0712] The title compound was prepared from Resin **534a** and cyclopentylamine according to the procedure described in the preparation of Compound **534**.

[0713] MS: 574.21 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.39 (d, 1H, J = 8.7 Hz), 8.38 (s, 1H), 8.32 (d, 1H, J = 1.5 Hz), 8.24 (d, 1H, J = 8.7 Hz), 8.10 (dd, 1H, J = 2.1, 8.8 Hz), 8.00 (dd, 1H, J = 1.5, 8.7 Hz), 7.90 (d, 1H, J = 8.4 Hz), 7.45 (d, 1H, J = 8.4 Hz), 7.31-7.28 (m, 3H), 7.23-7.18 (m, 2H), 7.15-7.11 (m, 2H), 5.03 (q, 1H, J = 9.3 Hz), 3.88 (s, 3H), 2.23 (m, 4H), 2.02 (m, 2H), 1.72-1.69 (m, 2H).

Example 201

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-isobutyl-1H-benzoimidazole-5-carboxylic acid **(Compound 530)**

[0714] The title compound was prepared from Resin **534a** and isobutylamine according to the procedure described in the preparation of Compound **534**.

[0715] MS: 562.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.51 (s, 1H), 8.35 (d, 1H, J = 9.0 Hz), 8.32 (s, 1H), 8.22 (br s, 2H), 8.03-7.95 (m, 2H), 7.45 (d, 1H, J = 8.4 Hz), 7.34 (d, 1H, J = 2.7 Hz), 7.29 (d, 2H, J = 8.7 Hz), 7.20 (d, 1H, J = 8.4 Hz), 7.18 (d, 1H, J =8.4 Hz), 7.12 (d, 2H, J = 8.7 Hz), 4.41 (d, 2H, J = 7.8 Hz), 3.88 (s, 3H), 1.98-1.93 (m, 1H), 0.68 (d, 6H, J = 6.9 Hz).

Example 202

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(3-methyl-butyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 532)**

[0716] The title compound was prepared from Resin **534a** and isoamylamine according to the procedure described in the preparation Compound **534**.

[0717] MS: 576.24 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.49 (s, 1H), 8.37 (d, 1H, J = 8.7 Hz), 8.32 (d, 1H, J = 1.2 Hz), 8.25-8.17 (m, 2H), 8.03 (dd, 1H, J = 1.3, 8.4 Hz), 7.94 (d, 1H, J = 8.7 Hz), 7.46 (d, 1H, J = 8.7 Hz), 7.33 (d, 1H, J = 2.7 Hz), 7.28-7.18 (m, including d, 4H, J = 8.4 Hz), 7.10 (d, 2H, J = 8.4 Hz), 4.49 (t, 2H, J = 7.2 Hz), 3.88 (s, 3H), 1.71-1.64 (m, 2H), 1.55-1.46 (m, 1H), 0.78 (d, 6H, J = 6.6 Hz).

Example 203

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(1-ethyl-propyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 564)**

[0718] The title compound was prepared from Resin **534a** and 1-ethylpropylamine according to the procedure described in the preparation of Compound **534**.

[0719] MS: 576.25 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.39 (d, 1H, J = 8.4 Hz), 8.35-8.32 (m, 2H), 8.27 (d, 1H, J = 8.7 Hz), 8.09-8.02 (m, 2H), 7.98 (d, 1H, J = 9.0 Hz), 7.46 (d, 1H, J = 8.7 Hz), 7.33 (d, 1H, J = 3.0 Hz), 7.30 (d, 2H, J = 8.4 Hz), 7.22-7.18 (m, including d, 2H, J = 8.7 Hz), 7.13 (d, 2H, J = 8.4 Hz), 4.35-4.30 (m, 1H), 3.88 (s, 3H), 2.25-2.15 (m, 2H), 2.05-1.96 (m, 2H), 0.70 (t, 6H, J = 7.2Hz).

Example 204

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopropylmethyl-1H-benzoimidazole-5-carboxylic acid **(Compound 531)**

[0720] The title compound was prepared from Resin **534a** and cyclopropylmethylamine according to the procedure described in the preparation of Compound **534**.

[0721] MS: 560.21 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.29 (s, 1H), 8.13 (d, 1H, J = 8.4 Hz), 8.11 (d, 1H, J = 1.2 Hz), 8.01 (m, 2H), 7.81-7.73 (m, 2H), 7.25 (d, 1H, J = 8.4 Hz), 7.46 (d, 1H, J = 8.7 Hz), 7.33 (d, 1H, J = 2.7 Hz), 7.09 (d, 2H, J = 8.7 Hz), 7.00 (d, 1H, J = 8.4 Hz), 6.98 (d, 1H, J =8.4 Hz), 6.92 (d, 2H, J = 8.7 Hz), 4.23 (d, 2H, J = 6.9 Hz), 3.88 (s, 3H), 0.89 (m, 1H), 0.23-0.169 (m, 2H), 0.03-0.02 (m, 2H).

Example 205

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(tetrahydrofuran-2-yl-methyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 566)**

[0722] The title compound was prepared from Resin **534a** and tetrahydrofurfurylamine according to the procedure described in the preparation of Compound **534**.

[0723] MS: 590.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.49 (s, 1H), 8.31 (d, 1H, J = 9.0 Hz), 8.29 (s, 1H), 8.22-8.15 (m, 2H), 7.97-7.89 (m, 2H), 7.45 (d, 1H, J = 8.4 Hz), 7.31 (d, 1H, J = 2.4 Hz), 7.28 (d, 2H, J = 8.4 Hz), 7.19 (d, 1H, J = 8.4 Hz), 7.17 (d, 1H, J = 8.4Hz), 7.11 (d, 2H, J = 8.4 Hz), 4.61-4.42 (m, 2H), 4.22-4.18 (m, 1H), 3.88 (s, 3H), 1.99-1.90 (m, 2H), 1.77-1.1.67 (m, 2H), 1.58-1.49 (m, 2H).

Example 206

Preparation of 1-bicyclo[2.2.1]hept-2-yl-2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]1H-benzoimidazole-5-carboxylic acid **(Compound 568)**

[0724] The title compound was prepared from Resin **534a** and 2-aminonorbornane according to the procedure described in the preparation of Compound **534**.

[0725] MS: 600.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.39 (d, 1H, J = 1.8 Hz), 8.34 (d, 1H, J = 8.7 Hz), 8.29 (s, 1H), 8.20 (d, 1H, J = 8.7 Hz), 8.12 (dd, 1H, J = 1.8, 8.7 Hz), 8.00 (br s, 2H), 7.46 (d, 1H, J = 8.4 Hz), 7.33 (d, 1H, J = 2.7 Hz), 7.29 (d, 2H, J = 8.7 Hz), 7.22-7.18 (m, 2H), 7.15-7.11 (m, 2H), 4.98-4.93 (m, 1H), 3.88 (s, 3H), 3.73-3.65 (m, 2H), 3.49-3.45 (m, 1H), 2.31 (br s, 1H), 2.04-1.93 (m, 1H), 1.86-1.77 (m, 1H), 1.56-1.45 (m, 3H), 1.33-1.30 (m, 1H).

Example 207

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(4-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid**(Compound 543)** (*Cis* or *Trans*)

[0726] The title compound was prepared from Resin **534a** and a mixture of *cis* and *trans* 4-methylcyclohexyl-amine according to the procedure described in the preparation of Compound **534**.

[0727] MS: 602.25 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.36-8.32 (m, 2H), 8.29 (d, 1H, J = 1.5 Hz), 8.19 (d, 1H, J = 8.7 Hz), 8.04 (dd, 1H, J = 1.8, 8.7 Hz), 7.98 (dd, 1H, J = 1.5, 8.7 Hz), 7.91 (d, 1H, J = 8.4 Hz), 7.45 (d, 1H, J = 8.4 Hz), 7.31-7.27 (m, including d, 3H, J = 8.4 Hz), 7.20-7.17 (m, 2H), 7.12 (d, 2H, J = 8.4 Hz), 4.42-4.33 (m, 1H), 3.88 (s, 3H), 2.44-2.34 (m, 2H), 1.97-1.94 (m, 1H), 1.86-1.83 (m, 2H), 1.62 (m, 4H), 1.13 (d, 3H, J = 7.2 Hz).

Example 208

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(4-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 547)** (*Trans* or *Cis)*

[0728] The title compound was prepared from Resin **534a** and a mixture of *cis* and *trans* 4-methylcyclohexyl-amine according to the procedure described in the preparation of Compound **534**.

[0729] MS: 602.25 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.36-8.32 (m, 2H), 8.27 (d, 1H, J = 1.5 Hz), 8.19 (d, 1H, J = 8.7 Hz), 8.07-8.01 (m, 2H), 7.92 (dd, 1H, J = 1.5, 8.7 Hz), 7.45 (d, 1H, J = 8.4 Hz), 7.31-7.27 (m, including d, 3H, J = 9.0 Hz), 7.20-7.17 (m, 2H), 7.12 (d, 2H, J = 8.7 Hz), 4.42-4.33 (m, 1H), 3.88 (s, 3H), 2.44-2.36 (m, 2H), 2.03-1.99 (m, 2H), 1.82-1.78 (m, 2H), 1.62 (m, 2H), 1.06-1.02 (m, 1H), 0.89 (d, 3H, J = 6.6 Hz).

Example 209

Preparation of 2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(3,3,5-trimethyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 555)**

[0730] The title compound was prepared from Resin **534a** and 3,3,5-trimethylcyclohexylamine according to the procedure described in the preparation of Compound **534**.

[0731] MS: 630.28 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.35-8.32 (m, 2H), 8.29 (d, 1H, J = 1.2 Hz), 8.19 (d, 1H, J = 8.7 Hz), 8.10 (d, 1H, J = 9.0 Hz), 8.05 (dd, 1H, J = 1.5, 8.7 Hz), 7.93 (dd, 1H, J = 1.5, 8.7 Hz), 7.45 (d, 1H, J = 8.4 Hz), 7.32 (d, 1H, J = 2.7 Hz), 7.27 (d, 2H, J = 8.7 Hz), 7.23-7.17 (m, 2H), 7.09 (d, 2H, J = 8.4 Hz), 4.71-4.62 (m, 1H), 3.88 (s, 3H), 2.25-2.15 (m, 1H), 1.94-1.87 (m, 2H), 1.63 (br s, 1H), 1.36-1.32 (m, 1H), 1.23-1.08 (m, 2H), 1.03 (s, 3H), 0.89 (d, 3H, J = 7.2 Hz), 0.87 (s, 3H).

Example 210

Preparation of cyclohexyl-2-(4-oxo-2-phenyl-4H-chromen-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 407)**

Step 1: 4-Hydroxy-3-(3-phenyl-acryloyl)-benzoic acid (Compound 407a)

[0732] 3-Acetyl-4-hydroxy-benzoic acid was prepared as described in J. Pfister et al. in *J. Med. Chem.* (1980), **23**, 335-338. To an ice cooled solution of 3-acetyl-4-hydroxy-benzoic acid (4g, 22.2 mmol) and benzaldehyde (2.44 mL, 24 mmol, 1.08 eq.) in 60 mL ethanol was added 20 mL of an 40% KOH solution. The resulting dark red solution was stirred under argon at ambient temperature until the reaction was complete as judged by TLC (2 days). Thereafter, the mixture was slowly poured into excess 6N HCl, and the resulting yellow precipitate was filtered off, washed with water and dried. The crude materials were recrystallized from THF-EtOH to yield 2.43g of a yellow/brown solid (88% yield).

[0733] MS: 267.10 ($M-H^+$); H^1-NMR (d6-DMSO): δ(ppm) 12.88 (br s, 1H), 12.46 (s, 1H), 8.50 (d, 1H, J=2.1Hz), 8.03 (dd, 1H, J=2.1 HZ, J=8.8Hz), 7.85-7.93 (m, 3H), 7.77 (d, 1H, J=15.5Hz), 7-44-7.48 (m, 3H), 7.08 (d, 1H, J=8.8Hz)

Step 2: 4-Oxo-2-phenyl-4H-chromene-6-carboxylic acid (Compound 407b)

[0734] Bromine (216μL, 1.13 eq.) was added to 4-hydroxy-3-(3-phenyl-acryloyl)-benzoic acid (1g, 3.72 mmol) in acetic acid (37.5 mL). After the solution was stirred at ambient temperature for 1 day, 10% aqueous $NaHSO_3$ (62.5 mL) was added slowly. The resulting precipitate was filtered off, washed with water and suspended in ethanol (25mL). MS: 426.93 ($M+H^+$).

[0735] Potassium hydroxide (861 mg, 3.5eq., 13.05 mmol)dissolved in water (12.5mL) was added and stirring was continued for 4h. The reaction mixture was acidified with 2N HCL, and the precipitate formed was filtered off, washed with water, died and recrystallized to give 621 mg (62%) of product.

[0736] MS: 265.08 ($M-H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.57 (d, 1H, J=2.1 Hz), 8.30 (dd, 1H, J=2.1 Hz, J=8.5 Hz), 8.11-8.14 (m, 2H), 7.87 (d, 1H, 8.7 Hz), 7.58-7.89 (m, 3H), 7.12 (s, 1H).

Step 3: 1-Cyclohexyl-2-(4-oxo-2-phenyl-4H-chromen-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 407)

[0737] 4-Oxo-2-phenyl-4H-chromene-6-carboxylic acid (280 mg, 1.05 mmol) was dissolved in DMF (5 mL), and HATU (418 mg, 1.1 eq.) and diisopropyl ethylamine (402μL) were added. After stirring at room temperature for 15 minutes, 3-amino-4-cyclohexylamino-benzoic acid ethyl ester (303 mg, 1.1 eq.) dissolved in 2 mL DMF was added. After stirring overnight, the reaction was evaporated, dissolved in ethyl acetate and washed with water and brine, dried with sodium sulfate, evaporated and dried overnight. The product was then refluxed in acetic acid for 4h, evaporated to dryness, and coevaporated 2 more times with toluene. Saponification proceeds by dissolving the residue in ethanol (10 mL), adding 10 eq. of 1N NaOH solution and stirring at 40 °C for 4hr. The ethanol was evaporated, water was added and acidified. The resulting precipitate was purified via reverse-phase HPLC. Yield: 58 mg

[0738] MS: 465.20 ($M+H^+$); H^1-NMR (MeOD): δ(ppm) 8.64 (d, 1H, J=2.3Hz), 8.49 (s, 1H), 8.30-8.38 (m, 2H), 8.24 (dd, 1H, J=2.3Hz, J=8.8Hz), 8.12-8.17 (m, 3H), 7.59-7.66 (m, 3H), 7.10 (s, 1H), 4.55-4.63 (m, 1H), 2.42-2.50 (m,2H), 2.20-2.24 (m, 2H), 2.00-2.03 (m, 2H), 1.77-1.81 (m, 1H), 1.42-1.49 (m, 3H).

Example 211

Preparation of 1-cyclohexyl-2-(4-oxo-2-phenyl-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 373)**

[0739] 4-Oxo-2-phenyl-1,4-dihydro-quinoline-6-carboxylic acid (298.5 mg, 1.05 mmol), (Compound **481c**),was dissolved in DMF (5 mL), and HATU (440 mg, 1.1 eq.) and diisopropyl ethylamine (402μL) were added. After stirring at room temperature for 15 minutes, 3-amino-4-cyclohexylamino-benzoic acid ethyl ester (303 mg, 1.1 eq.) dissolved in 2 mL DMF was added. After stirring overnight, the reaction was evaporated, dissolved in ethyl acetate and washed with water and brine, dried with sodium sulfate, evaporated and dried overnight. The product was then refluxed in acetic acid for 4hr, evaporated to dryness, and coevaporated 2 more times with toluene. Saponification proceeded by dissolving the residue in ethanol (10 mL), adding 10 eq. of 1N NaOH solution and stirring at 40°C for 4hr. The ethanol was evaporated, and water was added and acidified. The resulting precipitate is purified via reverse-phase HPLC. Yield: 47 mg

[0740] MS: 464.19 ($M+H^+$); H^1-NMR (MeOD): δ(ppm) 8.71 (s, 1H), 8.44 (s, 1H), 8.22-8.25 (m, 2H), 8.15 (s, 1H), 7.86-7.89 (m,2H), 7.61-7.64 (m, 2H), 6.79 (s, 1H), 4.55-4.64 (m, 1H), 2.45-2.53 (m, 2H), 2.19-2.23 (m, 2H), 1.99-2.02 (m, 2H), 1.76-1.80 (m, 2H), 1.41-1.48 (m, 3H).

Example 212

Preparation of 1-cyclohexyl-2-(4-dimethylamino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 481)**

Step 1: 4-Oxo-2-phenyl-1,4-dihydro-quinoline-6-carboxylic acid ethyl ester (Compound 481b)

[0741] 4-Amino-benzoic acid ethyl ester (66g, 0.4mol) and 3-oxo-3-phenyl-propionic acid ethyl ester (0.4 mol, 1 eq.) were dissolved in 500 mL cyclohexane and refluxed for 2 days using a Dean-Stark trap. The solution was filtered, the solvent evaporated and the residue recrystallized to give 4-(2-ethoxycarbonyl-1-phenyl-ethylideneamino)-benzoic acid ethyl ester (Compound **481a**) MS: 340.18 ($M+H^+$). 4-(2-

Ethoxycarbonyl-1-phenyl-ethylideneamino)-benzoic acid ethyl ester was dissolved in diphenyl-methanone (250mL) and heated to 250°C for 4hr. The resulting solution was diluted with diethyl ether and filtered to give 48.6g of the title intermediate as a white crystalline solid.

[0742] MS: 294.13 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 11.98 (br s, 1H), 8.69 (d, 1H, J=1.1 Hz), 8.16 (dd, 1H, J=2.0Hz, J=8.5 Hz), 7.82-7.86 (m, 3H), 7.56-7.61 (m, 3H), 6.42 (s, 1H), 4.35 (q, 2H, J=7.0Hz), 1.36 (t, 3H, J=7.0 Hz)

Step 2: 4-Oxo-2-phenyl-1,4-dihydro-quinoline-6-carboxylic acid (Compound 481c)

[0743] Saponification proceeded with dissolving 26.5g (0.1mol) 4-oxo-2-phenyl-1,4-dihydro-quinoline-6-carboxylic acid ethyl ester in ethanol (100 mL), adding 10 eq. of 1N NaOH solution and stirring at 40°C for 4hr. The ethanol was evaporated, water was added and acidified, and the precipitate filtered. The white product was dried over P_2O_5 to give quantitative amounts of 4-oxo-2-phenyl-1,4-dihydro-quinoline-6-carboxylic acid.

[0744] MS: 266.10 ($M+H^+$); H^1-NMR (d_6-DMSO): δ(ppm) 12.29 (s, 1H), 8.14 (dd, 1H, J-2.0Hz, J=8.8Hz), 7.94 (d, 1H, J-8.8Hz), 7.84-7.89 (m, 2H), 7.55-7.59 (m, 3H), 6.46 (s, 1H).

Step 3: 1-Cyclohexyl-2-(4-oxo-2-phenyl-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester acid (Compound 481d)

[0745] 4-Oxo-2-phenyl-1,4-dihydro-quinoline-6-carboxylic acid (2.78 g, 1.05 mmol) was dissolved in DMF (50 mL), and HATU (1.1 eq.) and diisopropyl ethylamine (2.2 eq, 402μL) were added. After stirring at room temperature for 15 minutes, 3-amino-4-cyclohexylamino-benzoic acid ethyl ester (2.89g, 1.1 eq.) dissolved in 20 mL DMF was added. After stirring overnight, the reaction was evaporated, dissolved in ethyl acetate and washed with water and brine, dried with sodium sulfate, evaporated and dried overnight. The product was then refluxed in acetic acid for 4hr, evaporated to dryness, and coevaporated 2 more times with toluene. The product was recrystallized from methanol to give 4.13 g of product.

[0746] MS: 492.25 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 11.98 (s, 1H), 8.35 (d, 1H, J=1.5 Hz), 8.27 (d, 1H, 1.7 Hz), 7.95-8.02 (m, 3H), 7.82-7.88 (m, 3H), 7.57-

7.69 (m, 3H), 6.43 (s, 1H), 4.29-4.38 (m, 3H), 2.26-2.37 (m, 2H), 1.95-1.99 (m, 2H), 1.84-1.89 (m, 2H), 1.62-1.66 (m, 1H), 1.24-1.42 (m, 6H).

Step 4: 2-(4-Chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (Compound 481e)

[0747] 1-Cyclohexyl-2-(4-oxo-2-phenyl-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid ethyl ester acid (4g, 8.14 mmol) was dissolved in phosphorous oxy chloride and heated at 100°C overnight. After evaporation of the solvent the product was recrystallized from methanol/water to give 3.96g of crude product. Silica gel purification of the title compound proved to be unsatisfactory due to degradation of the product on the column. MS: 510.22 ($M+H^+$).

Step 5: Preparation of 1-Cyclohexyl-2-(4-dimethylamino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (Compound 481)

[0748] 2-(4-Chloro-2-phenyl-quinolin-6-yl)-1-(1-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid ethyl ester was dissolved in 5 mL NMP and 1.1 eq of nucleophile is added. The reaction mixture was heated to 80°C overnight, and subsequently evaporated. Saponification proceeded with dissolving the residue in ethanol (10 mL), adding 10 eq. of 1N NaOH solution and stirring at 40°C for 4hr. The ethanol was evaporated, and the residue purified via reverse-phase HPLC.

[0749] In the synthesis of the title compound 51mg (0.1mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used. The nucleophile used was neat DMF. No NMP was used in this reaction. Yield: 11 mg

[0750] MS: 491.26 ($M+H^+$); H^1-NMR (MeOD): δ(ppm) 8.69 (s, 1H), 8.41 (s, 1H), 8.12-8.30 (m, 2H), 7.87-8.08 (m,4H), 7.62-7.74 (m,3H), 7.20 (s, 1H), 4.40-4.48 (m, 1H), 3.67 (s, 6H), 2.44-2.48 (m, 2H), 1.96-1.99 (m, 2H),1.75-1.79 (m, 1H), 1.30-1.42 (m, 3H).

Example 213

Preparation of 1-cyclohexyl-2-(4-ethoxy-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 494)**

[0751] The title compound was isolated as a side product from the reaction sequence used for the preparation of Compound **481.**Yield: 4 mg

[0752] MS: 492.22 ($M+H^+$),; H^1-NMR (MeOD): δ(ppm) 8.80 (s, 1H), 8.36-8.46 (m, 3H), 8.12-8.17 (m, 4H), 7.71-97 (m, 4H), 4.75 (q, 1H, J=7.0Hz), 4.46-4.57 (m, 1H), 2.42-2.55 (m 2H), 2.13-2.17 (m, 2H), 1.94-1.99 (m, 2H), 1.71-1.76 (m, 1H), 1.69 (t, 3H, J=7.0Hz), 1.38-1.45 (m, 3H)

Example 214

Preparation of 2-[4-(4-chloro-phenylamino)-2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 380)**

[0753] The title compound was prepared using the method described for Compound **481.** In this reaction 102mg (0.2mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used. The nucleophile used was *p*-chlorophenylamine. Yield: 89 mg

[0754] MS: 573.22 ($M+H^+$),; H^1-NMR (MeOD): δ(ppm) 8.98 (d, 1H, J=1.4Hz), 8.27-8.38 (m, 3H), 8.08-8.16 (m, 2H), 7.86-7.96 (m, 2H), 7.54-7.72 (m, 7H), 7.13 (s, 1H), 4.45 (t t, 1H, J=8.0 Hz, J=4.3 Hz), 2.37-2.48 (m, 2H), 2.13-2.17 (m, 2H), 1.94-1.99 (m, 2H), 1.74-1.78 (m, 1H), 1.37-1.49 (m, 3H)

Example 215

Preparation of 1-cyclohexyl-2-[4-(4-hydroxy-butylamino)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 398)**

[0755] In this reaction 102 mg (0.2mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used in the same reaction sequence as that used for Compound **481.** The nucleophile used was 4-amino-butan-1-ol. Yield: 59 mg

[0756] MS: 535.28 ($M+H^+$); H^1-NMR (MeOD): δ(ppm) 8.75 (s, 1H), 8.43 (s, 1H), 8.15-8.24 (m, 2H), 8.07-8.10 (dd, 1H, J=0.9Hz, J=8.8Hz), 7.98-8.03 (m, 3H), 7.67-7.73 (m, 3H), 7.15 (s,1H), 4.34 (m, 1H), 3.75 (tr, 2H, 7.0Hz), 3.67 (tr, 2H, J=5.9 Hz), 2.37-2.45 (m, 2H), 2.07-2.11 (m, 2H), 1.90-1.97 (m, 4H), 1.70-1.79 (m, 3H), 1.28-1.45 (m, 3H)

Example 216

Preparation of 1-cyclohexyl-2-(2-phenyl-4-phenylamino-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 433)**

[0757] In this reaction 102mg (0.2mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used in the same reaction sequence as that used for Compound **481.** The nucleophile used was aniline. Yield: 143 mg.

[0758] MS: 571.30 ($M+H^+$), 539.26; H^1-NMR (d6-DMSO): δ(ppm) 11.10 (bs, 1H), 9.11 (s, 1H), 8.25-8.36 (m, 3H), 8.05 (d,1H, 8.8Hz), 7.88-7.93 (m, 3H), 7.57-7.67 (m, 7H), 7.39-7.45 (m, 1H), 7.03 (s, 1H), 4.24-4.29 (m, 1H), 2.31-2.37 (m, 2H), 2.02-2.04 (m, 2H), 1.84-1.88 (m, 2H), 1.62-1.66 (m, 1H), 1.21-1.43 (m, 3H)

Example 217

Preparation of 1-cyclohexyl-2-[4-(3-imidazol-1-yl-propylamino)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 451)**

[0759] In this reaction 102mg (0.2mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used in the same reaction sequence as that used for Compound **481.** The nucleophile used was 3-imidazol-1-yl-propylamine. Yield: 31 mg.

[0760] MS: 571.30 ($M+H^+$), 286.12 (($M+2H^+$)/2); H^1-NMR (MeOD): δ (ppm) 9.03 (s, 1H), 8.91 (s, 1H), 8.46 (s, 1H), 8.09-8.30 (m, 5H), 8.01-8.04 (m, 2H), 7.68-7.74 (m, 4H), 7.56-7.58 (m, 1H), 7.17 (s, 1H), 4.49 (tr, 2H, J=7.0 Hz), 4.37-4.47 (m, 1H), 3.83 (tr, 2H, J=6.7 Hz), 2.42-2.51 (m, 2H), 2.12-2.16 (2H, m, 2H), 1.95-1.99 (m, 2H), 1.74-1.78 m, 1H), 1.35-1.42 (m, 3H)

Example 218

Preparation of 1-cyclohexyl-2-(4-phenoxy-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 496)**

[0761] In this reaction 51mg (0.1mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used in the same reaction sequence as that used for Compound **481.** The nucleophile used was phenol. Yield: 19 mg.

[0762] MS: 540.25 ($M+H^+$); H^1-NMR (MeOD): δ(ppm) 8.97 (s, 1H), 8.45-8.50 (m, 2H), 8.32 (d, 1H, J= 8.5 Hz), 8.18 (s, 2H), 7.91-7.94 (m, 2H), 7.54-7.65 (m, 5H), 7.41-7.49 (m, 3H), 7.19 (s, 1H), 4.58-4.66 (m, 1H), 2.42-2.49 (m, 2H), 2.17-2.21 (m, 2H), 1.95-2.01 (m, 2H), 1.72-1.84 (m, 1H), 1.41- 1.52 (m, 3H).

Example 219

Preparation of 1-cyclohexyl-2-[4-(7-hydroxy-naphthalen-2-yloxy)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 509)**

[0763] In this reaction 51mg (0.1mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used in the same reaction sequence as that used for Compound **481.** The nucleophile used was naphthalene-2,7-diol. Yield: 6.2 mg.

[0764] MS: 606.28 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.66 (s, 1H), 8.29-8.34 (m, 2H), 8.15-8.18 (m, 1H), 8.03-8.11 (m, 3H), 7.91-7.97 (m, 2H), 7.83 (d, 1H, J=8.8 Hz), 7.65 (bs, 1H), 7.47-7.49 (m, 3H), 7.34 (s, 1H), 7.27-7.31 (m, 1H), 7.14 (bs, 1H), 7.07-7.11 (m, 1H), 4.47-4.49 (m, 2H, OH and CH), 2.32 (q, 2H, J=12.6 Hz), 2.01-2.04 (m, 2H), 1.81-1.84 (m, 2H), 1.58-1.62 (m, 1H), 1.22-1.41 (m, 3H).

Example 220

Preparation of 1-Cyclohexyl-2-(2-phenyl-4-phenylsulfanyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 467)**

[0765] In this reaction 51mg (0.1mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used

in the same reaction sequence as that used for Compound **481.** The nucleophile used was benzenethiol. Yield: 36 mg.

[0766] MS: 556.21 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.48 (s, 1H), 8.28-8.31 (m, 2H), 8.16 (d, 1H, J=8.8Hz), 8.05 (d, 1H, J=8.8Hz), 7.89-7.97 (m,3H), 7.66-7.70 (m,2H), 7.55-7.57 (m, 3H), 7.48-7.53 (m, 4H), 4.43-4.49 (m,1H), 2.30-2.40 (m, 2H), 2.00-2.04 (m, 2H), 1.85-1.88 (m, 2H), 1.62-1.66 (m, 1H), 1.22-1.37 (m, 3H).

Example 221

Preparation of 1-cyclohexyl-2-[2-(2-ethoxy-5-nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 404)**

[0767] 1-(2-Bromo-5-nitro-phenyl)-ethanone (61mg, 0.25mmol) prepared similarly to the procedure described in Meisenheimer, J., Zimmermann P., and v. Kummer, U. *Ann. der. Chem.* 446, pp. 205-228) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol) were dissolved in 500 µL ethanol and 500 µL 10% ethanolic KOH were added. The reaction was stirred at 75°C overnight. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 16 mg (97.33% pure) of product.

[0768] MS: 537.23 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.71 (d, 1H, J=2.9 Hz), 8.62 (d, 1H, J=8.8Hz), 8.41 (d, 1H, J=2.7Hz), 8.37 (dd, 1H, J=3.0Hz, J=9.0 Hz), 8.29-8.33 (m, 2Hz), 8.18 (d, 1H, J=8.5 Hz), 8.04-8.08 (m, 2H), 7.92 (1H, dd, J=1.8 Hz, J=8.5 Hz), 7.44 (d, 1H, 8.4 Hz), 4.31-4.44 (m, 3H), 2.26-2.34 (m,2H), 2.02-2.05 (m, 2H), 1.83-1.86 (m, 2H), 1.61-1.65 (m, 1H), 1.28-1.43 (m, 6H).

Example 222

Preparation of 2-[2,4']biquinolinyl-6-yl-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 423)**

[0769] Methylmagnesium bromide in diethyl ether (2.4mL of 3.0M solution) was dropped onto solid quinoline-4-carboxylic acid (250mg). After stirring for an additional 15 min. the reaction was quenched by addition of methanol. The solution

was separated between ethyl acetate and water, the water extracted two more times with ethyl acetate, the organic phases were dried with sodium sulfate and then evaporated. The crude product (1-quinolin-4-yl-ethanone was used without further purification in the next step.

[0770] MS: 172.07 ($M+H^+$); H^1-NMR ($CDCl_3$): δ(ppm) 9.01 (d, 1H, J=4.5 Hz), 8.42 (d, 1H, J=9Hz), 8.14 (d, 1H, J=9Hz), 7.72-7.78 (m, 1H), 7.59-7.64 (m, 2H), 2.75 (s, 3H))

[0771] (1-Quinolin-4-yl-ethanone (43mg, 0.25mmol) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol)were dissolved in 500 µL ethanol and 500 µL 10% ethanolic KOH were then added. The reaction was stirred at 75°C overnight. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, and the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 24 mg product.

[0772] MS: 499.23 ($M+H^+$); H^1-NMR (MeOD): δ(ppm) 9.33 (d, 1H, J=5.5 Hz), 8.87 (d, 1H, J=8.5 Hz), 8.65 (d, 1H, J= 1.8 Hz), 8.55 (d, 1H, 8.8Hz), 8.48-8.52 (m, 2H), 8.37 (d, 1H, 8.5 Hz), 8.30 (d, 5.5 Hz), 8.16-8.27 (m, 5H), 7.94-7.99(m, 1H), 4.62 (t,t, 1H, J=8.5 Hz, J=3.9Hz), 2.43-2.54 (m (like br q), 2H), 2.22-2.26 (m,, 2H), 1.99-2.03 (m, 2H), 1.76-1.80 (m,, 1H), 1.40-1.53 (m, 3H).

Example 223

Preparation of 2-[2-(4'-chloro-4-nitro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 439)**

[0773] 1-(2-Bromo-5-nitro-phenyl)-ethanone (1g, 4mmol; prepared similarly to the procedure described in Meisenheimer, J., Zimmermann P., and v. Kummer, U. *Ann. der. Chem.* 446, pp. 205-228), p-Chlorophenylboronic acid (768 mg, 1.2 eq.), and tetrakis(triphenylphosphine)-palladium(0) (473 mg, 0.1 eq.), were dissolved in 25 mL toluene, 6mL methanol and 2.5mL sat. sodium bicarbonate solution. After degassing/sonicating the solution, the sealed reaction vessel was heated to 80 °C overnight. The cooled solution was separated between ethyl acetate and water; the

aqueous phase extracted two more times with ethyl acetate, and the organic fractions were combined, dried with sodium sulfate and evaporated. Silica gel chromatography (4:1 hexanes/ethyl acetate) gave 1-(4'-chloro-4-nitro-biphen-2-yl)-ethanone (962mg).

[0774] 1-(4'-Chloro-4-nitro-biphen-2-yl)-ethanone (69mg, 0.25mmol) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol) were dissolved in 500 μL ethanol and 500 μL 10% ethanolic KOH were added. The reaction was stirred at 75°C overnight. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 34 mg product

[0775] MS: 603.20 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.57 (d, 1H, J=2.3 Hz), 8.38-8.45 (m, 2H), 8.34 (d, 1H, J=1.8Hz), 8.24-8.28 (m, 2H), 8.05-8.08 (m, (like d), 2H), 7.91 (dd, 1H, J=1.5, J=8.8 Hz), 7.82 (d, 1H, J=8.5Hz), 7.38-7.43 (m, 2Hz), 7.20-7.27 (m, 3H), 4.34-4.43 (m, 1H), 2.26-2.34 (m, 2H), 2.01-2.05 (m, 2H), 1.83-1.87 (m, 2H), 1.62-1.75 (m, 2H), 1.32-1.43 (m, 3H).

Example 224

Preparation of 6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylquinoxaline (**Compound 258**)

Step 1: 4-Cyclohexylamino-3-nitrobenzonitrile (Compound 127)

[0776] A solution of 1 g (5.48 mmol) 4-chloro-3-nitrobenzonitrile, Compound **126,** and 1.14 g (11.51 mmol) of cyclohexylamine were heated overnight in 5 mL anhydrous DMF. After cooling to room temperature, the solution was added dropwise into 100 mL H_2O stirring vigorously. The solids were collected by filtration and dried under vacuum yielding 1.34 g (100%) bright yellow solids which were used as such without analysis in the next step.

Step 2: Cyclohexyl-[2-nitro-4-(1*H*-tetrazol-5-yl)-phenyl]amine (Compound 128)

[0777] A solution of 1.10 g (4.49 mmol) of 4-cyclohexylamino-3-nitrobenzonitrile, Compound **127,** and 1.11 g (5.39 mmol) of Me_3SnN_3 in 50 mL toluene was refluxed overnight. The crystals were collected by filtration, washed with toluene,

dried, and treated with 50 mL 4M HCl in dioxane for 4 h. The solids were collected by filtration, washed with dioxane, and dried yielding 1.14 g (88%) red solids. MS: 289.15 ($M+H^+$).

Step 3: *N*-1-Cyclohexyl-4-(1*H*-tetrazol-5-yl)-benzene-1,2-diamine (Compound 129)

[0778] The title intermediate was prepared from 1.20 g (4.16 mmol) Compound **128** as described for Compound **11** to yield 0.9 g (83%). MS: 259.18 ($M+H^+$).

Step 4: 6-[1-Cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylquinoxaline (Compound 258)

[0779] The title compound was prepared from 100 mg (0.39 mmol) of Compound **129** and Compound **36A Y=phenyl** as described for compound **38 Y=phenyl** to yield 21 mg.

[0780] MS: 473.25 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 9.73 (s, 1H), 8.46 (d, 2H, J=1.2Hz), 8.42-8.36 (m, 4H), 8.29 (d, 1H, J=5.6Hz), 8.19 (dd, 1H, J=1.2Hz and 5.6Hz), 8.09 (dd, 1H, J=1Hz and 5.8Hz), 7.63 (m, 5H), 4.45 (m, 1H), 2.44-2.35 (m, 2H), 2.12-2.08 (m, 2H), 1.90-1.85 (m, 2H), 1.62 (m, 1H), 1.50-1.29 (m, 3H).

Example 225

Preparation of 1-cyclohexyl-2-(2,3-diphenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid (**Compound 386**)

[0781] The title compound was synthesized in four steps as described for Compound **13,** Compound **25,** Compound **27 Q=ethyl** and Compound **204**, respectively, except deoxybenzoin was used in the first step instead of acetophenone.

[0782] MS: 524.29 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.73 (s, 1H), 8.57 (s, 1H), 8.40-8.37 (m, 2H), 8.31-8.28 (d, 1H, J=8.4Hz), 8.17-8.14 (d,1H, J=8.4Hz), 8.07-8.04 (d, 1H, J=8.4Hz), 7.45-7.29 (m, 10H), 4.46 (m, 1H), 2.34-2.26 (m, 2H), 2.14-2.10 (m, 2H), 1.86-1.82 (m, 2H), 1.60 (m, 1H), 1.43-1.21 (m, 3H).

Example 226

Preparation of 2-(2-benzhydryl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 457**).

[0783] The title compound was synthesized in four steps as described for Compound **13,** Compound **25,** Compound **27, Q=ethyl** and Compound **204**, respectively, except 1,1-diphenylacetone was used in the first step, instead of acetophenone.

[0784] MS: 538.30 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.63-8.60 (d, 1H, J=9.0Hz), 8.47 (d, 1H, J=1.5Hz), 8.34 (d, 1H, J=1.2Hz), 8.29-8.24 (m, 2H), 8.10-8.02 (m, 2H), 7.66-7.63 (d, 1H), J=8.7Hz), 7.36-7.20 (m, 10H), 6.05 (s, 1H), 4.45-4.41 (m, 1H), 2.33-2.28 (m, 2H), 2.1-2.06 (m, 2H), 1.84-1.79 (m 2H), 1.58 (m, 1H), 1.38-1.20 (m, 3H).

Example 227

Preparation of 2-[2-(2-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (**Compound 352**)

[0785] The title compound was synthesized in four steps as described for Compound **13,** Compound **25,** Compound **27 Q=ethyl** and Compound **204**, respectively, except 2'-bromoacetophenon was used in the first step instead of acetophenone.

[0786] MS: 526.14 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.75-8.72 (d, 1H, J=8.7Hz), 8.55 (d, 1H, J=1.5Hz), 8.38 (d, 1H, J=1.2Hz), 8.36-8.33 (d, 1H, J=8.7Hz), 8.26-8.8.22 (d, 1H, J=8.7Hz), 8.17-8.13 (dd, 1H, J=8,7Hz and 1.8Hz), 8.06-8.02 (dd, 1H, J=8.4Hz and 1.5Hz), 7.96-7.93 (d, 1H, J=8.4Hz), 7.87-7.84 (dd, 1H, J=7.8Hz and 0.9Hz), 7.73-7.69 (dd, 1H, J=7.5Hz and 1.8Hz), 7.64-7.59 (m, 1H), 7.53-7.47 (m 1H), 4.49 (m, 1H), 2.40-2.32 (m, 2H), 2.15-2.11 (m, 2H), 1.91-1.87 (m, 2H), 1.66 (m, 1H), 1.42-1.34 (m, 3H).

Example 228

Preparation of 2-{2-[(4-Chlorophenyl) methyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 546)**

Step 1: (4-Chlorophenyl)isopropylamine (Compound 546a)

[0787] A mixture of 1 g (7.84 mmol) of 4-chloroaniline, 0.91 g (15.68 mmol) of acetone, 0.99 g (15.68 mmol) of $NaCNBH_3$, 4 g of $MgSO_4$ in 99 mL anhydrous EtOH and 1 mL AcOH was stirred at room temperature overnight, filtered and the solvent was removed. The residue was dissolved in 50 mL EtOAc, washed with 50 mL H_2O, dried (Na_2SO_4) and evaporated. The residue was purified on silica gel using hexane/EtOAc as eluent to yield 0.86 g colorless oil. MS: 170.08 ($M+H^+$).

Step 2: (4-Chlorophenyl)cyclohexylamine (Compound 546b)

[0788] Prepared as described above using cyclohexanone in place of acetone to yield 1.11 g colorless crystals. MS: 210.12 ($M+H^+$).

Step 3: 2-{2-[(4-Chlorophenyl) methyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 546c)

[0789] A solution of 100 mg (0.23 mmol) Compound **402a** in 1 mL $SOCl_2$ was allowed to stand at room temperature for 10 min and $SOCl_2$ was removed. The residue was dissolved in 5 mL anhydrous CH_2Cl_2; 89 mg (0.69 mmol) DIEA, 84 mg (0.69 mmol) DMAP, 98 mg (0.69 mmol) 4-chloro-N-methylaniline were added; and the solution was vortexed and allowed to stand at room temperature overnight. The solvent was removed and the residue was chromatographed on silica gel using hexane/EtOAc as the eluent to yield 63 mg of yellow oil. MS: 576.24 ($M+H^+$).

Step 4: 2-{2-[(4-Chlorophenyl) methyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound 546)

[0790] A solution of 63 mg (0.11 mmol)of Compound **546c** in 0.55 mL THF, 0.44 mL of EtOH and 0.11 mL of 2 N aq. NaOH was allowed to stand at room temperature overnight. The reaction was quenched with 0.22 mL 1 M aq. HCl. The

solvents were removed and the residue was purified by HPLC to yield 6 mg of the title compound.

[0791] MS: 539.21 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 8.47 (m, 3H), 8.31 (m, 2H), 8.10 (m, 2H), 7.84 (m, 1H), 7.23 (m, 4H), 4.58 (m, 1H), 3.58 (s, 3H), 2.45 (m, 2H), 2.19 (m, 2H), 1.98 (m, 2H), 1.74 (m, 1H), 1.46-1.30 (m, 3H).

Example 229

Preparation of 2-{2-[(4-Chlorophenyl) isopropyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 550)**

Step 1: 2-{2-[(4-Chlorophenyl) isopropyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 550a)

[0792] The title compound was prepared as described for Compound **546c** using Compound **546a** in place of 4-chloro-N-methylaniline. MS: 595.27 ($M+H^+$).

Step 2: 2-{2-[(4-Chlorophenyl) isopropyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound 550)

[0793] The title compound was prepared as described for Compound **546** heating the solution at 50°C for 4 h instead of standing overnight.

[0794] MS: 567.25 ($M+H^+$); ^{1}H-NMR (CD_3OD): δ(ppm) 8.45 (m, 2H), 8.36 (s, 1H), 8.24 (m, 2H), 8.15 (d, 1H, J=9Hz), 8.04 (d, 1H, J=8.4Hz), 7.71 (d, 1H, J=8.4Hz), 7.24 (dd, 4H, J=8.4Hz and 18.3Hz), 5.12 (m, 1H), 4.53 (m, 1H), 2.41 (m, 2H), 2.15 (m, 2H), 1.95 (m, 2H), 1.73 (m, 1H) 1.41 (m, 3H), 1.31 (d, 6H, J=6.6Hz).

Example 230

Preparation of 2-{2-[(4-Chlorophenyl) cyclohexyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 551)**

Step 1: 2-{2-[(4-Chlorophenyl) cyclohexyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 551a)

[0795] The title compound was prepared as described for Compound **546c** using Compound **546b** in place of 4-chloro-N-methylaniline. MS: 635.31 ($M+H^+$).

Step 2: 2-{2-[(4-Chlorophenyl) cyclohexyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound 551)

[0796] The title compound was prepared as described for Compound **550** using 5 eq. of 2 N aq NaOH in place of 1 eq.

[0797] MS: 607.28 ($M+H^+$); ^{1}H-NMR (DMSO-d_6): δ(ppm) 8.46 (d, 1H, J=8.4Hz), 8.25 (s, 2H), 7.96 (m, 3H), 7.68 (d, 1H, J=8.4Hz), 7.26 (s, 4H), 4.61 (m, 1H), 4.34 (m, 1H), 2.29-0.96 (m, 10H).

Example 231

Preparation of 1-Cyclohexyl-2-[2-(4'-ethyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 557)**

[0798] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 4-ethylphenylboronic acid (39mg, 0.2625mmol) to produce the title compound (48mg, 48% yield).

[0799] MS: 582.32 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.38 (d, 1H, J=1.5), 8.31 (m, 3H), 8.17 (d, 1H, J=8.7), 8.07 (dd, 1H, J=8.7, 1.8), 7.98 (dd, 1H, J=8.4, 1.2), 7.43 (d, 1H, J=8.7), 7.31 (d, 1H, J=2.7), 7.17 (m, 2H), 7.05 (m, 4H0, 4.42 (m, 1H), 3.87 (s, 3H), 2.53 (m, 2H), 2.31 (m, 2H), 2.07 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.32 (m, 3H), 1.12 (m, 3H)

Example 232

Preparation of 1-Cyclohexyl-2-[2-(3',4'-difluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 560)**

[0800] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 3,4-difluorophenylboronic acid (42mg, 0.2625mmol) to produce the title compound (26mg, 25% yield).

[0801] MS: 590.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.46 (m, 2H), 8.36 (s, 1H), 8.29 (d, 2H, J=9), 8.11 (dd, 1H, J=8.7, 1.8), 8.05 (dd, 1H, J=9, 1.5), 7.49 (d, 1H, J=8.4), 7.27 (m, 5H), 6.84 (m, 1H), 4.44 (m, 1H), 3.88 (s, 3H), 3.54 (s, 1H), 2.30 (m, 2H), 2.11 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.35 (m, 3H)

Example 233

Preparation of 1-Cyclohexyl-2-[2-(3',5'-dichloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 562)**

[0802] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 3,5-dichlorophenylboronic acid (50mg, 0.2625mmol) to produce the title compound (17mg, 15% yield).

[0803] MS: 622.20 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.48 (d, 1H, J=8.4), 8.44 (s, 1H), 8.32 (s, 1H), 8.22 (m, 2H), 8.05 (m, 2H), 7.53 (d, 1H, J=8.4), 7.42 (m, 2H), 7.33 (d, 1H, J=2.7), 7.20 (dd, 1H, H=8.7, 2.7), 7.11 (m, 2H), 4.40 (m, 1H), 3.89 (s, 3H), 2.30 (m, 2H), 2.08 (m, 2H), 1.84 (m, 2H), 1.60 (m, 1H), 1.32 (m, 3H)

Example 234

Preparation of 1-Cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid amide **(Compound 570)**

[0804] Compound **455** (50mg, 0.087mmol) was dissolved in ammonia saturated methanol (50mL) and placed in a 100mL glass bomb. The reaction was argon flushed, sealed, and stirred at 70°C for 8 days. The reaction was then evaporated to dryness and purified via HPLC to produce the title compound (9mg, 18% yield).

[0805] MS: 571.27 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.37 (m, 3H), 8.29 (m, 2H), 8.09 (m, 2H), 7.55 (s, 1H), 7.46 (2, 1H, J=8.4), 7.32 (d, 1H, J=2.7), 7.20 (m, 2H), 7.12 (m, 4H), 4.44 (s, 1H), 3.88 (s, 3H), 3.55 (s, 1H), 2.34 (m, 2H), 2.10 (m, 2H), 1.84 (m, 2H), 1.60 (m, 1H), 1.35 (m, 3H)

Example 235

Preparation of 1-Cyclohexyl-2-[2-(2'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 544)**

[0806] Following the full procedure and workup for Compound **366**, Compound **365b** (100mg, 0.175mmol) was reacted with 2-fluorophenylboronic acid (37mg, 0.2625mmol) to produce the title compound (9mg, 25% yield).

[0807] MS: 572.26 ($M+H^+$); H^1-NMR (DMSO-d_6): 8.40 (m, 2H), 8.34 (m, 1H), 8.24 (d, 1H, J=8.7), 8.17 (d, 1H, J=9), 8.04 (m, 2H), 7.41 (m, 2H), 7.29 (m, 3H),

7.20 (m, 2H), 7.03 (m, 1H), 4.43 (m, 1H), 3.90 (s, 3H), 3.55 (s, 1H), 2.30 (m, 2H), 2.10 (m, 2H), 1.84 (m, 2H), 1.61 (m, 1H), 1.35 (m, 3H)

Example 236

Preparation of 2-(2-Biphenyl-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 548)**

Step 1: 1-(4-Methoxy-2'-methyl-biphen-2-yl)-ethanone (Compound 548a)

[0808] Following the procedure and workup (without the potassium hydroxide addition) for Compound **366**, 2-bromo, 5-methoxyacetophenone (80mg, 0.35mmol) was reacted with o-tolylboronic acid (71mg, 0.525mmol) to produce the title intermediate (42mg, 50% yield). HPLC Procedure C, retention time = 2.84min.

Step 2: 2-(2-Biphenyl-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (Compound 562)

[0809] Following the procedure and workup for Compound **354** (68mg, 0.17mmol) was reacted with Compound 548a (42mg, 0.17mmol) in ethanol (3mL) using 10% w/v KOH in Ethanol (506 μL, 0.64mmol) to produce the title compound 29mg, 28% yield).

MS: 568.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.43 (d, 1H, J=1.8), 8.34 (m, 4H), 8.09 (m, 2H), 7.43 (d, 1H, J=2.4), 7.32 (d, 1H, J=8.4), 7.14 (m, 6H), 4.45 (m, 1H), 3.90 (s, 3H), 3.55 (s, 1H), 2.30 (m, 2H), 2.11 (m, 2H), 1.96 (s, 3H), 1.83 (m, 2H), 1.60 (m, 1H), 1.30 (m, 3H)

Example 237

Preparation of 1-Cyclohexyl-2-[2-(4,2'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 552)**

Step 1: 1-(4,2'-Dimethoxy-biphen-2-yl)-ethanone (Compound 552a)

[0810] Following the procedure and workup (without the potassium hydroxide addition) for Compound **366**, 2-bromo, 5-methoxyacetophenone (80mg, 0.35mmol) was reacted with 2-methoxyphenylboronic acid (80mg, 0.525mmol) to produce Compound **552a** (40mg, 48% yield). HPLC Procedure C, retention time = 2.37min.

Step 2: 1-Cyclohexyl-2-[2-(4,2'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (Compound 552)

[0811] Following the procedure and workup for Compound **354** (68mg, 0.17mmol) was reacted with Compound **552a** (40mg, 0.17mmol) in ethanol (3mL) using 10% w/v KOH in Ethanol (506 µL, 0.64mmol) to produce the title compound (12mg, 10% yield).

[0812] MS: 584.28 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.50 (m, 2H), 8.37 (m, 2H), 8.27 (d, 1H, J=9), 8.17 (m, 1H), 8.04 (m, 1H), 7.40 (m, 2H), 7.24 (m, 4H), 6.94 (m, 1H), 6.82 (d, 1H, J=8.4), 4.41 (m, 1H), 3.90 (s, 3H), 3.55 (s, 1H), 3.23 (s, 3H), 2.29 (m, 2H), 2.10 (m, 2H), 1.84 (m, 2H), 1.60 (m, 1H), 1.32 (m, 3H)

Example 238

Preparation of 1-Cyclohexyl-2-[2-(2-cyclohexyl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 545)**

Step 1: 1-(2-Cyclohexyl-5-methoxy-phenyl)-ethanone (Compound 545a)

[0813] 2-bromo-5-methoxyacetophenone (500mg, 2.185mmol), Pd(P(*t*-Bu)$_3$)$_2$ (100mg, 0.219mmol), and NMP (15mL) were added to a 25mL, flame dried, Argon filled flask. The flask was sealed and, while stirring, cyclohexyl zinc bromide (5.5mL, 0.5M in THF) was added dropwise. The reaction was stirred at 90°C for 20h. The reaction was then evaporated to dryness and purified via RP-HPLC to produce the title intermediate (50mg, 10% yield). HPLC Procedure C, retention time = 3.12min.

Step 2: 1-Cyclohexyl-2-[2-(2-cyclohexyl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid (Compound 545)

[0814] Following the procedure and workup for Compound **354**, Compound **354e** (86mg, 0.22mmol) was reacted with Compound **545a** (50mg, 0.22mmol) in ethanol (3mL) using 10% w/v KOH in Ethanol (436 µL, 0.66mmol) to produce the title compound (26mg, 21% yield).

[0815] MS: 560.30 ($M+H^+$); H^1-NMR (DMSO-d_6): δ(ppm) 8.78 (d, 1H, J=8.7), 8.59 (s, 1H), 8.31 (m, 3H), 8.17 (m, 1H), 8.04 (d, 1H, J=8.7), 7.85 (d, 1H, J=8.7),

7.41 (d, 1H, J=8.7), 7.06 (m, 2H), 4.48 (m, 1H), 3.78 (s, 3H), 3.55 (m, 2H), 2.7 (m, 1H), 2.34 (m, 2H), 2.12 (m, 2H), 1.87-1.04 (m, 14H)

Example 239

Preparation of 1-Cyclohexyl-2-{2-[4'-fluoro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid **(Compound 549)**

Step 1: 1-Cyclohexyl-2-{2-[4'-fluoro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 549a)

[0816] A mixture of 200 mg (0.29 mmol) Compound **419d** 62 mg (0.44 mmol) 4-fluorophenyl-boronic acid, 32 mg (0.029 mmol) $Pd(PPh_3)_4$ and 2 mL sat. $NaHCO_3$ in 16 mL degassed MeOH was heated at 90°C under Ar overnight. The mixture was evaporated to dryness, the residue was taken up in CH_2Cl_2 and purified on silica gel using CH_2Cl_2/MeOH as eluent to yield 197 mg orange solid.

Step 2: 1-Cyclohexyl-2-{2-[4'-fluoro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid (Compound 549)

[0817] A solution of 197 mg (0.30 mmol) Compound **549a** in 3.75 mL THF, 3 mL MeOH and 0.75 mL 2 N NaOH was stirred at room temperature overnight and then heated at 50°C for 1.5 h. After the addition of 1.5 mL 1 M HCl, the solution was evaporated to dryness and the residue was purified on HPLC to yield 66 mg yellow solid.

[0818] MS: 639.40 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm) 8.43-8.35 (m, 2H), 8.31-8.25 (m, 2H), 8.11 (dd, 1H, J=9Hz and 1.8Hz), 8.04 (dd, 1H, J=8.7Hz and 1.5Hz), 7.93 (d, 1H, J=1.5Hz), 7.76 (dd, 1H, J=8.1Hz and 1.8Hz), 7.61-7.55 (m, 4H), 7.24 (m, 2H), 7.14 (m, 2H), 4.45 (m, 1H), 3.52 (m, 4H), 2.31 (m, 2H), 2.12 (m, 2H), 1.88 (m, 6H), 1.62 (m, 1H), 1.33 (m, 3H) .

Example 240

Preparation of 1-Cyclohexyl-2-{2-[4'-methoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid **(Compound 561)**

Step 1: 1-Cyclohexyl-2-{2-[4'-methoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 561a)

[0819] Prepared as described for Compound **549a** using 4-methoxyphenylboronic acid instead of 4-fluorophenylboronic acid.

Step 2: 1-Cyclohexyl-2-{2-[4'-methoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid (Compound 561)

[0820] Prepared as described for Compound **549** using Compound **561a** instead Compound **549a**.

[0821] MS: 651.32 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm): 8.35-8.27 (m, 3H), 8.15-8.05 (m, 2H), 7.96 (d, 1H, J=8.7Hz), 8.90 (d, 1H, J=1.2Hz), 7.73 (dd, 1H, J=7.8Hz and 1.2Hz), 7.55 (d, 2H, J=8.1Hz), 7.15-7.11 (m, 3H), 6.86 (d, 2H, J=8.4Hz), 4.43 (m, 1H), 3.72 (s, 3H), 3.52 (m, 4H), 2.31 (m, 2H), 2.07 (m, 2H), 1.87 (m, 6H), 1.62 (m, 1H), 1.33 (m, 3H).

Example 241

Preparation of 2-[2-(4'-Chloro-4-fluoro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 563)**

[0822] 1-(2-Bromo-5-fluoro-phenyl)-ethanone (868mg, 4mmol), *p*-chlorophenylboronic acid (768 mg, 1.2 eq.), and tetrakis (triphenylphosphine)palladium(0) (473 mg, 0.1 eq.), were dissolved in 25 mL toluene, 6mL methanol and 2.5mL sat. sodium bicarbonate solution. After degassing/sonicating the solution, the sealed reaction vessel was heated to 80 °C overnight. The cooled solution was separated between ethyl acetate and water; the aqueous phase extracted two more times with ethyl acetate, and the organic fractions were combined, dried with sodium sulfate and evaporated. Silica gel chromatography (5:1 hexanes/ethyl acetate) gave 1-(4'-chloro-4-fluoro-biphen-2-yl)-ethanone (821mg).

[0823] 1-(4'-Chloro-4-fluoro-biphen-2-yl)-ethanone (62mg, 0.25mmol) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol) were dissolved in 500 μL ethanol and 500 μL 10% ethanolic KOH were added. The reaction was stirred at 75°C overnight. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 84 mg product.

[0824] MS: 576.20 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.27-8.35 (m, 3H), 8.18 (8d, 1H, J=8.8 Hz), 8.07 (d, 1H, J=8.5Hz), 8.01 (dd, 1H, J=2.1Hz, 8.8Hz), 8.92 (dd, 1H, J=1.4Hz, 8.5Hz), 7.84 (dd, 1H, J=5.9Hz, 8.5Hz), 7.38-7.47 (m, 2H), 7.31-7.36 (m, 2H), 7.18-7.22 (m,2H), 7.15 (d, 1H, 8.5Hz) 4.36-4.45 (m, 1H), 2.26-2.35 (m, 2H), 2.01-2.05 (m, 2H), 1.83-1.87 (m, 2H), 1.62-1.75 (m,1H), 1.28-1.43 (m, 3H)

Example 242

Preparation of 2-[2-(4-amino-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 569)**

[0825] 1-(4'-Chloro-4-nitro-biphen-2-yl)-ethanone (69mg, 0.25mmol) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol) were dissolved in 500 μL ethanol and 500 μL 10% ethanolic KOH were added. The reaction was stirred at 75°C for 3days. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 18 mg product.

[0826] MS: 563.22 ($M+H^+$); H^1-NMR (d6-acetone): δ(ppm) 8.51-8.59 (m,2H), 8.12-8.34 (m, 5H), 7.90-7.99 (m, 1H), 7.73 (d, 1H, 8.5 Hz), 7.61-7.68 (m, 1H), 7.15-7.36 (m, 5H), 4.70-4.75 (m, 1H), 2.46-2.58 (m, 2H), 2.22-2.30 (m, 2H), 1.92-2.00 (m, 2H), 1.72-1.75 (m, 1H), 1.46-1.55 (m, 3H)

Example 243

Preparation of 1-cyclohexyl-2-[2-(4,4'-dichloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 567)**

Step 1: 1-(4'-chloro-4-chloro-biphen-2-yl)-ethanone (Compound 567a)

[0827] 1-(2-Bromo-5-chloro-phenyl)-ethanone (467mg, 2 mmol; synthesized similarly as described in Example 166 from 2-Bromo-5-chloro-benzoic acid), *p*-chlorophenylboronic acid (384 mg, 1.2 eq.), and tetrakis (triphenylphosphine)palladium(0) (237 mg, 0.1 eq.), were dissolved in 12.5 mL toluene, 3 mL methanol and 1.3 mL sat. sodium bicarbonate solution. After degassing/sonicating the solution, the sealed reaction vessel was heated to 80 °C overnight. The cooled solution was separated between ethyl acetate and water; the aqueous phase extracted two more times with ethyl acetate, and the organic fractions were combined, dried with sodium sulfate and evaporated. Silica gel chromatography (5:1 hexanes/ethyl acetate) gave the title intermediate (438mg).

Step 2: The title Compound

[0828] 1-(4'-Chloro-4-chloro-biphen-2-yl)-ethanone (132 mg, 0.5mmol) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol) were dissolved in 500 µL ethanol and 500 µL 10% ethanolic KOH were added. The reaction was stirred at 75°C overnight. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 132 mg product.

[0829] MS: 592.17 ($M+H^+$); H^1-NMR (d6-acetone): δ(ppm) 8.54-8.55 (m, 2H), 8.19-8.32 (m, 4H), 8.10 (dd, 1H, J=1.0 Hz, 8.5 Hz), 7.88 (d, 1H, 2.0 Hz), 7.62 (dd, 1H, J=2.3 Hz, 8.3 Hz), 7.55 (d, 1H, 8.2 Hz), 7.22-7.33 (m, 5H), 4.73-4.82 (m, 1H), 2.46-2.54 (m, 2H), 2.28-2.32 (m, 2H), 1.94-1.97 (m, 2H), 1.71-1.75 (m, 1H), 1.46-1.55 (m, 3H)

Example 244

Preparation of 2-{2-[8-(4-chloro-phenyl)-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 565)**

Step 1: 1-[8-(4-Chloro-phenyl)-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl]-ethanone (Compound 565a).

[0830] 1-(8-Bromo-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl)- (1.08g, 4mmol), *p* chlorophenylboronic acid (768 mg, 1.2 eq.), and tetrakis (triphenylphosphine)palladium(0) (473 mg, 0.1 eq.), were dissolved in 25 mL toluene, 6mL methanol and 2.5mL of saturated sodium bicarbonate solution. After degassing/sonicating the solution, the sealed reaction vessel was heated to 80 C overnight. The cooled solution was separated between ethyl acetate and water; the aqueous phase extracted two more times with ethyl acetate, and the organic fractions were combined, dried with sodium sulfate and evaporated. Silica gel chromatography (5:1 hexanes/ethyl acetate) was used for purification

Step 2: The title compound

[0831] 1-[8-(4-Chloro-phenyl)-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl]-ethanone (76mg, 0.25mmol) and 2-(4-amino-3-formyl-phenyl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester (98 mg, 0.25mmol) were dissolved in 500 μL ethanol and 500 μL 10% ethanolic KOH were added. The reaction was stirred at 75°C overnight. The reaction was acidified with 4N hydrochloric acid, extracted three times with ethyl acetate, the organic extracts were dried with sodium sulfate and then evaporated. Purification via reverse-phase HPLC gave 132 mg of the title compound.

[0832] MS: 630.23 ($M+H^+$); H^1-NMR (d6-DMSO): δ(ppm) 8.27-8.32 (m, 3H), 8.17 (d, 1H, J=8.8Hz), 8.07 (d, 1H, 8.5Hz), 8.02 (dd, 1H, 1.8Hz, 9.1Hz), 7.41 (s, 1H), 7.29-7.32 (m, 2H), 7.09-7.15 (m, 4H), 4.36-4.45 (m, 1H), 4.22-4.30 (m,2H), 2.26-2.34 (m,2H), 2.17-2.21 (m, 2H), 2.01-2.05 (m, 2H), 1.83-1.86 (m, 2H), 1.62-1.75 (m, 1H), 1.28-1.35 (m, 3H)

Example 245

Preparation of 2-[4-(2-tert-butoxycarbonylamino-ethylamino)-2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid **(Compound 399)**

[0833] In this reaction 51mg (0.1mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester were used. The nucleophile used was (2-amino-ethyl)-carbamic acid tert-butyl ester. Yield: 21 mg

[0834] MS: 606.32 ($M+H^+$); H^1-NMR (CD_3OD): δ(ppm) 8.72 (s,1H), 8.45 (s, 1H), 8.04-8.27 (m, 6H), 7.68-7.76 (m, 4H), 7.33 (s, 1H), 4.36-4.45 (m, 1H), 3.81 (tr, 2H, 5.6 Hz), 3.49 (tr, 2H, 5.6Hz), 2.42-2.48 (m, 2H), 2.14-2.16 (m, 2H), 1.96-2.99 (m, 2H), 1.74-1.80 (m, 1H), 1.35-1.45 (m, 3H), 1.25 (s, 9H)

Example 246

Preparation of 1-Cyclohexyl-2-(4-hydrazino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid **(Compound 466)**

[0835] In this reaction 102mg (0.2mmol) of crude 2-(4-chloro-2-phenyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid ethyl ester was reacted with hydrazine as the nucleophile as described for the preparation of Compound **481**. Yield: 3.7 mg

[0836] MS: 478.20 ($M+H^+$); H^1-NMR (CD_3OD): δ(ppm) 8.74 (s,1H), 8.38-8.44 (m,2H), 8.28-8.31 (m, 1H), 8.05-8.18 (m, 4H), 7.71-7.77 (m, 4H), 4.36-4.45 (m, 1H), 2.44-2.48 (m,2H), 2.10-2.14 (m, 2H), 1.97-2.01 (m, 2H), 1.83-1.86 (m, 2H), 1.75-1.80 (m, 1H), 1.35-1.42 (m, 3H)

Example 247

Preparation of 1-Benzyl-2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid **(Compound 559)**

[0837] The title compound was prepared from resin **534a** and benzylamine according to the procedure described in the preparation of Compound **534**.

[0838] MS (ESI) 596.19 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.45 (s, 1H), 8.35 (s, 1H), 8.26 (d, 1H, J = 8.7 Hz), 8.17 (s, 2H), 7.95 (dd, 1H, J = 1.5, 8.4 Hz),

7.72 (d, 1H, J = 8.7 Hz), 7.45 (d, 1H, J = 7.5 Hz), 7.32-7.26 (m, 6H), 7.18 (d, 2H, J = 8.4 Hz), 7.10 (d, 2H, J = 8.4 Hz), 7.04 (d, 2H, J = 8.41 Hz), 5.81 (s, 2H), 3.87 (s, 3H).

Example 248

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-4-carboxylic acid **(Compound 572)**

Step 1. 2-Cyclohexylamino-3-nitro-benzoic acid ethyl ester

[0839] To a solution of 2-chloro-3-nitrobenzoic acid (0.85 g, 4.22 mmol) in anhydrous EtOH (50 mL) was bubbled with dry hydrogen chloride for 2 h at room temperature and the mixture was then stirred at room temperate overnight. After evaporation of solvent, water (100 mL) was added and the precipitates were collected by filtration and dried to give 2-chloro-3-nitro-benzoic acid ethyl ester.

[0840] The crude 2-chloro-3-nitro-benzoic acid ethyl ester was dissolved in acetonitrile (100 mL) and cyclohexylamine (2.5 mL, 21.83 mmol) was added. The mixture was stirred at reflux overnight. After evaporation of solvent, water (100 mL) was added and the precipitates were collected by filtration and dried to give 2-cyclohexylamino-3-nitro-benzoic acid ethyl ester (1.168 g, 95%). MS: 293.16 ($M + H^+$).

Step 2. 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-4-carboxylic acid Compound 572)

[0841] 2-Cyclohexylamino-3-nitro-benzoic acid ethyl ester (0.165 g, 0.564 mmol) by hydrogenation according to procedure (1) in the preparation of Compound **477d**.

[0842] The amine was reacted with Compound **525c** (0.23 g, 0.592 mmol) in the presence of HBTU (0.135 g, 0.356 mmol), followed cyclization in AcOH according to procedure (2) in the preparation of Compound **477d**. Separation by RP HPLC (from 20% of buffer B to 99% of buffer B) gave the title compound (36 mg, 11%).

[0843] MS: 588.23 ($M + H^+$); ^{1}H NMR (DMSO-d_6) δ(ppm) 8.38 (d, 1H, J = 1.5 Hz), 8.35 (d, 1H, J = 9.0 Hz), 8.21 (d, 1H, J = 8.7 Hz), 8.08 (dd, 1H, J = 1.5, 8.5 Hz), 7.95 (dd, 1H, J = 1.1, 8.0 Hz), 7.77 (d, 1H, J = 7.5 Hz), 7.53 (d, 1H, J = 7.5 Hz), 7.46 (d, 1H, J = 8.7 Hz), 7.36 (d, 1H, J = 2.4 Hz), 7.29-7.25 (m, 2H), 7.22-7.19 (m, 2H), 7.10

(d, 2H, J = 8.1 Hz), 4.74-4.65 (m, 1H), 3.88 (s, 3H), 2.11-2.08 (m, 2H), 1.70-1.66 (m, 2H), 1.55-1.48 (m, 2H), 1.23-1.16 (m, 2H), 0.82-0.73-1.23 (m, 2H).

Example 249

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(2-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid **(Compound 556)**

[0844] The title compound was prepared from resin **534a** and 2-methylcyclopropylamine (a mixture of cis and trans) according to the procedure described in the preparation of Compound **534**. This product is a mixture of cis and trans isomers.

[0845] MS: 602.24 ($M + H^+$).

Example 250

Preparation of 2-[2-(4'-Chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-piperidin-4-yl-1H-benzoimidazole-5-carboxylic acid **(Compound 558)**

[0846] The title compound was prepared from resin **534a** and 4-amino-cyclohexanecarboxylic acid tert-butyl ester according to the procedure described in the preparation of Compound **534**.

[0847] MS: 589.22 ($M + H^+$); ^1H NMR (DMSO-d_6) δ(ppm) 8.36 (d, 1H, J = 8.7 Hz), 8.33-8.29 (m, 3H), 8.20 (d, 1H, J = 8.7 Hz), 8.08 (dd, 2H, J = 2.1, 8.7 Hz), 7.95 (dd, 1H, J = 1.2, 8.4 Hz), 7.46 (d, 1H, J = 8.4 Hz), 7.32-7.28 (m, 3H), 7.22-7.12 (m, 4H), 4.85 (m, 1H), 3.88 (s, 3H), 3.16-3.03 (m, 3H), 2.92-2.82 (m, 3H), 2.24-2.20 (m, 2H).

Example 251

Preparation of 1-Cyclohexyl-2-{2-[5-(pyrrolidine-1-carbonyl)-2-thiophen-2-yl]quinoline-6-yl}-1H-benzimidazole-5-carboxylic acid **(Compound 400)**

Step 1: 1-Cyclohexyl-2-{2-[5-(pyrrolidine-1-carbonyl)-2-thiophen-2-yl]quinoline-6-yl}-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 400a)

[0848] Prepared as described for Compound **402a** using 4-thiopheneboronic acid instead of 4-fluorophenylboronic acid.

Step 2: 1-Cyclohexyl-2-{2-[5-(pyrrolidine-1-carbonyl)-2-thiophen-2-yl]quinoline-6-yl}-1H-benzimidazole-5-carboxylic acid (Compound 400)

[0849] Prepared as described for Compound **402** using Compound **400a** instead of Compound **402a.**

[0850] MS: 627.25 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm): 8.52-8.49 (m, 2H), 8.38-8.29 (m, 3H), 8.16-8.04 (m, 2H), 7.81-7.69 (m, 3H), 7.54-7.44 (m, 2H), 7.00-6.93 (m, 2H), 4.40 (m, 1H), 3.51 (m, 4H), 2.30 (m, 2H), 2.15 (m, 2H), 1.87 (m, 6H), 1.62 (m, 1H), 1.38 (m, 3H).

Example 252

Preparation of 2-{2-[4'-Carboxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid **(Compound 453)**

Step 1: 2-{2-[4'-Carboxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ethyl ester (Compound 453a)

[0851] Prepared as described for Compound **549a** using 4-carboxyphenylboronic acid instead of 4-fluorophenylboronic acid.

Step 2: 2-{2-[4'-Carboxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid (Compound 453)

[0852] Prepared as described for Compound **549** using Compound **453a** instead of Compound **549a**.

[0853] MS: 665.26 ($M+H^+$); ^{1}H-NMR ($DMSOd_6$): δ(ppm): 8.47-8.28 (m, 6H), 8.14-8.06 (m, 2H), 7.97 (d, J=1.8Hz), 7.85-7.78 (m, 2H), 7.68-7.62 (m, 2H), 7.34-7.26 (m, 2H), 4.47 (m, 1H), 3.39 (m, 4H), 2.47 (m, 2H), 2.12 (m, 2H), 1.88 (m, 6H), 1.62 (m, 1H), 1.34 (m, 3H).

BIOLOGICAL EXAMPLES

Example A
Anti-Hepatitis C Activity

[0854] Compounds can exhibit anti-hepatitis C activity by inhibiting HCV polymerase, by inhibiting other enzymes needed in the replication cycle, or by other pathways. A number of assays have been published to assess these activities. A general method that assesses the gross increase of HCV virus in culture is disclosed in U.S. Patent No. 5,738,985 to Miles *et al.* *In vitro* assays have been reported in Ferrari *et al. Jnl. of*

Vir., 73:1649-1654, 1999; Ishii *et al.*, *Hepatology*, 29:1227-1235, 1999; Lohmann *et al.*, *Jnl of Bio. Chem.*, 274:10807-10815, 1999; and Yamashita *et al.*, *Jnl. of Bio. Chem.*, 273:15479-15486, 1998.

[0855] WO 97/12033, filed on September 27, 1996, by Emory University, listing C. Hagedorn and A. Reinoldus as inventors, which claims priority to U.S.S.N. 60/004,383, filed on September 1995, describes an HCV polymerase assay that can be used to evaluate the activity of the of the compounds described herein. Another HCV polymerase assay has been reported by Bartholomeusz, *et. al.*, Hepatitis C Virus (HCV) RNA polymerase assay using cloned HCV non-structural proteins; Antiviral Therapy 1996:1(Supp 4) 18-24.

[0856] Screens that measure reductions in kinase activity from HCV drugs are disclosed in U.S. Patent No. 6,030,785, to Katze *et al.*, U.S. Patent No. Delvecchio *et al.*, and U.S. Patent No. 5,759,795 to Jubin *et al.* Screens that measure the protease inhibiting activity of proposed HCV drugs are disclosed in U.S. Patent No. 5,861,267 to Su *et al.*, U.S. Patent No. 5,739,002 to De Francesco *et al.*, and U.S. Patent No. 5,597,691 to Houghton *et al.*

Example B

Replicon Assay

[0857] A cell line, ET (Huh-lucubineo-ET) was used for screening of compounds of the present invention for HCV replication. The ET cell line was stably transfected with RNA transcripts harboring a I_{389}luc-ubi-neo/NS3-3'/ET replicon with firefly luciferase-ubiquitin-neomycin phosphotransferase fusion protein and EMCV-IRES driven NS3-5B polyprotein containing the cell culture adaptive mutations (E1202G; T1280I; K1846T) (Krieger at al, 2001 and unpublished). The ET cells were grown in DMEM, supplemented with 10% fetal calf serum, 2 mM Glutamine, Penicillin (100 IU/mL)/Streptomycin (100 µg/mL), 1x nonessential amino acids, and 250 µg/mL G418 ("Geneticin"). They are all available through Life Technologies (Bethesda, MD). The cells were plated at 0.5-1.0 x10^4 cells/well in the 96 well plates and incubated for 24 h before adding test compounds. Then the compounds each at 5 and 50 µM were added to the cells. Luciferase activity was measured 48-72 hours later by adding a lysis buffer and the substrate (Catalog number Glo-lysis buffer E2661 and Bright-Glo leuciferase system E2620 Promega, Madison, WI). Cells should not be too confluent during the assay.

Percent inhibition of replication was plotted relative to no compound control. Under the same condition, cytotoxicity of the compounds was determined using cell proliferation reagent, WST-1(Roche, Germany). The compounds showing antiviral activities, but no significant cytotoxicities were chosen to determine IC_{50} and TC_{50}.

Example C

Cloning and expression of recombinant HCV-NS5b

[0858] The coding sequence of NS5b protein was cloned by PCR from $pFKI_{389}luc/NS3\text{-}3'/ET$ as described by Lohmann, V., et al. (1999) *Science* 285, 110-113 using the following primers:

aggacatggatccgcggggtcgggcacgagacag (SEQ. ID. NO. 1)

aaggctggcatgcactcaatgtcctacacatggac (SEQ. ID. NO. 2)

[0859] The cloned fragment was missing the C terminus 21 amino acid residues. The cloned fragment was inserted into an IPTG-inducible expression plasmid that provided an epitope tag (His)6 at the carboxy terminus of the protein.

[0860] The recombinant enzyme was expressed in XL-1 cells and after induction of expression, the protein was purified using affinity chromatography on a nickel-NTA column. Storage condition was 10 mM Tris-HCl pH 7.5, 50 mM NaCl, 0.1 mM EDTA, 1 mM DTT, 20% glycerol at -20 °C.

Example D

HCV-NS5b Enzyme Assay

[0861] The polymerase activity was assayed by measuring incorporation of radiolabeled UTP into a RNA product using a biotinylated, heteropolymeric template, which included a portion of the HCV genome. Typically, the assay mixture (50 μL) contained 10 mM Tris-HCl (pH 7.5), 5 mM $MgCl_2$, 0.2 mM EDTA, 10 mM KCl, 1 unit/μL RNAsin, 1 mM DTT, 10 μM each of NTP, including [^{3}H]-UTP, and 10 ng/μL heteropolymeric template. Test compounds were initially dissolved in 100% DMSO and further diluted in aqueous buffer containing 5% DMSO. Typically, compounds were tested at concentrations between 1 nM and 100 μM. Reactions were started with addition of enzyme and allowed to continue at 37°C for 2 hours. Reactions were quenched with 8 μL of 100 mM EDTA and reaction mixtures (30 μL) were transferred to streptavidin-

coated scintillation proximity microtiter plates (FlashPlates) and incubated at 4°C overnight. Incorporation of radioactivity was determined by scintillation counting.

[0862] Shown in Table IX below are the values for enzyme inhibition measured at compound concentrations of 100 and 33 uM, (%inh@199 and %inh@33, respectively). The percent inhibition values are calculated from the differential incorporation of radioactivity compared to a control reaction without compound:

$$\% \text{ inhibition} = 100 - [(\text{Counts}_{INH} - \text{Counts}_{BKG})/\text{Counts}_{CTRL} - \text{Counts}_{BKG}) \times 100$$

where Counts_{INH} is the signal of the testwell with inhibitor, Counts_{BKG} is the background signal and Counts_{CTRL} is the signal of a testwell without inhibitor.

TABLE IX

Percent Inhibition Data

Cmpd #	%inh@100	%inh@33
203	97.54	74.98
204	100.95	99.68
205	98.95	84.42
206	96.87	94.16
215	100.88	99.25
230	98.22	92.74
231	97.54	66.96
232	80.22	60.45
233	88.16	49.99
234	100.11	98.59
235	99.50	99.07
236	99.25	99.19
237	95.62	79.74
238	98.40	97.60
239	70.15	49.12
240	96.08	95.74
241	98.41	98.00
242	97.00	97.40
243	98.12	95.99
244	97.02	75.71
245	97.38	73.22
246	96.40	95.92
247	94.24	66.78
248	86.78	47.36
249	97.15	94.51
258	97.99	97.03
259	99.36	99.71
310	98.33	83.24

Cmpd #	%inh@100	%inh@33
311	93.27	83.02
351	98.13	94.87
352	98.82	94.18
353	67.52	67.33
354	100.55	97.99
355	89.31	72.35
356	100.47	101.08
357	100.55	98.79
358	95.33	85.08
359	99.60	97.29
360	97.86	97.56
361	98.71	100.00
362	98.43	100.52
363	100.53	98.36
364	100.54	98.60
365	102.60	102.25
366	99.38	97.62
367	100.85	102.67
368	79.47	51.25
369	98.80	96.18
370	99.67	97.76
372	98.17	98.12
373	83.79	39.89
374	98.32	97.62
376	97.19	97.42
377	99.42	99.20
378	100.93	100.39
379	97.78	93.32
380	101.16	97.59
381	98.05	94.33
382	100.73	101.35
384	99.26	95.54
385	76.24	42.63
386	99.90	100.34
387	98.68	99.05
388	98.58	98.73
389	99.55	99.92
390	92.52	79.87
391	97.45	94.13
392	93.53	83.75
393	96.94	97.56
394	100.04	98.90
395	101.21	100.10
396	100.24	100.13
397	99.28	95.57
398	92.05	59.65
399	101.52	95.64
401	101.01	100.40

Cmpd #	%inh@100	%inh@33
403	99.93	99.42
404	101.17	102.42
405	98.89	90.50
406	98.06	97.29
408	98.86	99.29
409	99.86	97.88
410	88.64	84.34
411	91.45	78.12
412	100.15	98.44
413	100.19	95.50
414	96.83	93.43
415	101.59	101.27
416	102.51	100.70
417	97.98	97.75
418	102.87	103.58
419	101.14	100.67
420	98.26	98.26
421	100.12	100.02
422	99.18	98.76
423	101.62	102.46
424	99.09	98.70
425	98.18	96.17
426	101.61	96.59
427	98.37	93.85
428	99.57	98.85
429	100.88	96.25
430	96.65	98.02
431	96.38	95.34
432	96.37	88.94
433	100.50	92.47
434	102.40	104.83
435	101.42	102.36
436	99.29	98.82
437	100.51	100.29
438	99.60	98.71
439	97.03	99.19
440	97.75	99.15
441	98.75	97.35
442	98.23	92.50
443	98.70	87.01
444	100.55	99.55
445	99.64	96.88
446	100.99	96.61
447	94.86	97.83
448	96.03	94.57
449	101.33	99.77
450	99.70	96.48
451	95.64	76.27

Cmpd #	%inh@100	%inh@33
452	102.35	102.39
454	100.56	98.26
455	99.79	100.03
456	99.69	100.26
457	98.33	98.21
458	103.55	100.15
459	99.82	99.54
460	101.72	100.53
461	96.65	97.89
462	101.29	98.24
463	97.17	95.99
464	100.35	99.74
465	100.83	98.78
466	100.12	92.92
467	100.48	96.33
468	99.12	99.33
469	98.24	94.22
470	99.37	100.78
471	99.81	97.79
472	98.07	97.10
473	97.41	99.22
474	100.57	96.95
475	95.91	97.50
476	97.06	97.35
477	95.91	92.43
478	97.15	95.80
479	102.24	99.64
480	103.84	101.37
481	96.74	76.46
482	100.85	100.12
483	99.39	101.50
484	98.30	99.62
485	99.54	98.59
486	97.89	93.46
487	101.00	101.69
488	97.17	91.81
489	96.01	87.01
490	94.33	95.94
491	99.95	98.35
492	100.37	99.19
493	99.96	101.32
494	99.18	94.82
495	100.98	99.76
496	101.35	101.25
497	88.47	65.45
498	100.08	98.48
499	99.74	100.97
500	100.96	101.33

Cmpd #	%inh@100	%inh@33
501	96.82	90.61
502	100.17	99.04
503	96.99	95.76
504	99.97	98.26
505	101.67	99.73
506	99.12	98.92
507	100.68	100.80
508	98.89	98.94
509	100.70	100.44
510	100.14	99.45
511	94.96	78.44
512	97.87	78.89
513	95.91	93.18
514	91.87	89.64
515	88.31	81.94
516	100.07	99.30
517	97.78	81.02
518	97.84	75.95
519	99.11	96.88
520	98.89	94.81
521	91.41	84.85
522	74.23	76.67
523	94.97	87.14
524	93.58	74.09
525	100.63	100.83
526	98.99	96.84
527	100.64	99.42
528	101.32	100.28
529	99.75	99.20
530	98.15	98.17
531	99.26	99.98
532	98.77	99.64
533	89.85	56.75
534	101.02	90.07
535	100.49	100.97
536	98.87	97.55
537	99.76	100.24
538	72.78	56.60
539	102.41	104.03
540	95.05	91.13
541	98.14	76.08
542	98.58	81.13
543	101.90	102.06
544	100.09	101.67
545	101.02	99.18
546	101.72	95.35
547	101.82	102.71
548	100.68	102.77

Cmpd #	%inh@100	%inh@33
549	102.09	100.38
550	101.72	99.13
551	95.68	87.53
552	100.63	101.29
554	82.03	64.68
555	100.85	101.06
556	102.27	102.72
557	101.41	102.52
558	77.35	32.53
559	101.13	101.11
560	100.73	101.03
562	101.41	101.94
563	100.87	100.69
564	101.39	102.31
565	100.47	102.26
566	100.49	99.17
567	97.65	100.79
568	100.49	100.99
569	100.78	100.86

FORMULATION EXAMPLES

[0863] The following are representative pharmaceutical formulations containing a compound of formula I.

Formulation Example 1

Tablet formulation

[0864] The following ingredients are mixed intimately and pressed into single scored tablets.

Ingredient	Quantity per tablet, mg
compound of this invention	400
cornstarch	50
croscarmellose sodium	25
lactose	120
magnesium stearate	5

Formulation Example 2

Capsule formulation

[0865] The following ingredients are mixed intimately and loaded into a hard-shell gelatin capsule.

Ingredient	Quantity per capsule, mg
compound of this invention	200
lactose, spray-dried	148
magnesium stearate	2

Formulation Example 3

Suspension formulation

[0866] The following ingredients are mixed to form a suspension for oral administration.

Ingredient	Amount
compound of this invention	1.0 g
fumaric acid	0.5 g
sodium chloride	2.0 g
methyl paraben	0.15 g
propyl paraben	0.05 g
granulated sugar	25.0 g
sorbitol (70% solution)	13.00 g
Veegum K (Vanderbilt Co.)	1.0 g
flavoring	0.035 mL
colorings	0.5 mg
distilled water	q.s. to 100 mL

Formulation Example 4

Injectable formulation

[0867] The following ingredients are mixed to form an injectable formulation.

Ingredient	Amount
compound of this invention	0.2 mg-20 mg
sodium acetate buffer solution, 0.4 M	2.0 mL
HCl (1N) or NaOH (1N)	q.s. to suitable pH
water (distilled, sterile)	q.s. to 20 mL

Formulation Example 5

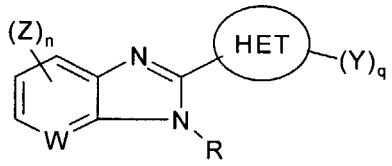
Suppository Formulation

[0868] A suppository of total weight 2.5 g is prepared by mixing the compound of the invention with Witepsol® H-15 (triglycerides of saturated vegetable fatty acid; Riches-Nelson, Inc., New York), and has the following composition:

Ingredient	Amount
Compound of the invention	500 mg
Witepsol® H-15	balance

WHAT IS CLAIMED IS:

1. A compound of formula I:



I

wherein:

W is CH or N;

R is selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -$NR^{12}R^{13}$,

where each R^{12} and R^{13} is independently selected from the group consisting of (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{12} and R^{13} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

Z is selected from the group consisting of

(a) -C(=O)OR^7, wherein R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

(b) -C(=O)NR^8R^9, wherein R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9

together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

(c) tetrazolyl or $-C(O)NHS(O)_2R^4$, wherein R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

(d) $-C(X)-N(R^3)CR^2R^{2'}C(=O)R^1$, wherein X is selected from the group consisting of =O, =S, and $=NR^{11}$, where R^{11} is hydrogen or alkyl, R^1 is selected from the group consisting of $-OR^7$ and $-NR^8R^9$;

wherein R^7, R^8 and R^9 are as defined above;

each R^2 and $R^{2'}$ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic,

or, alternatively, R^2 and $R^{2'}$ as defined are taken together with the carbon atom pendent thereto to form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic group,

or, still further alternatively, one or R^2 or $R^{2'}$ is hydrogen, alkyl or substituted alkyl, and the other is joined, together with the carbon atom pendent thereto, with either the R^7 and the oxygen atom pendent thereto or R^8 and the nitrogen atom pendent thereto to form a heterocyclic or substituted heterocyclic group;

R^3 is selected from the group consisting of hydrogen and alkyl or, when R^2 and $R^{2'}$ are not taken together to form a ring and when $R^2/R^{2'}$ and R^7 or R^8 are not joined to form a heterocyclic or substituted heterocyclic group, then R^3, together with the nitrogen atom pendent thereto, may be taken together with one of R^2 and $R^{2'}$ to form a heterocyclic or substituted heterocyclic ring group;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

each Y is independently selected from the group consisting of halo, cyano, nitro, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, acyl, acyloxy, guanidino, substituted guanidino,

oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

n is an integer equal to 0, 1 or 2;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

2. The compound according to Claim 1, wherein *n* is one.

3. The compound according to Claim 2, wherein Z is 1*H*-tetrazol-5-yl or $-COOR^7$.

4. The compound according to Claim 2, wherein Z is selected from the group consisting of 1*H*-tetrazol-5-yl, -C(=O)OH, and –C(=O)OR" where R" is (C_1-C_6)alkyl.

5. The compound according to Claim 4, wherein Z is selected from the group consisting of carboxy, methyl carboxylate, ethyl carboxylate and 1*H*-tetrazol-5-yl.

6. The compound according to Claim 5, wherein Z is carboxy.

7. The compound according to Claim 2, wherein Z is $-C(=O)NR^8R^9$.

8. The compound according to Claim 7, wherein R^8 is hydrogen and R^9 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic.

9. The compound according to Claim 8, wherein R^9 is substituted alkyl.

10. The compound according to Claim 9, wherein said substituted alkyl comprises 1 to 2 substituents selected from the group consisting of sulfonic acid, carboxy and carboxy ester.

11. The compound according to Claim 10, wherein said substituted alkyl group is selected from the group consisting of $-CH_2CH_2SO_3H$and $-CH_2CH_2COOH$.

12. The compound according to Claim 7, wherein R^9 is aryl or substituted aryl.

13. The compound according to Claim 12, wherein R^9 is substituted aryl.

14. The compound according to Claim 13 wherein R^9 is selected from the group consisting of 7-hydroxynaphth-1-yl, 6-hydroxynaphth-1-yl, 5-hydroxynaphth-1-yl, 4-methyl-2-oxo-2*H*-chromen-7yl, 6-carboxynaphth-2-yl, (4-$HOOCCH_2$-)phenyl, (3,4-dicarboxy)phenyl, 3-carboxyphenyl, and 3-carboxy-4-hydroxyphenyl.

15. The compound according to Claim 7, wherein R^9 is heteroaryl or substituted heteroaryl.

16. The compound according to Claim 15, wherein R^9 is substituted heteroaryl.

17. The compound according to Claim 16, wherein said substituted heteroaryl is selected from the group consisting of 1-phenyl-4-carboxy-1H-pyrazol-5-yl, 5-carboxypyrid-2-yl, 2-carboxypyrazin-3-yl, and 3-carboxythien-2-yl.

18. The compound according to Claim 8, wherein R^9 is heterocyclic.

19. The compound according to Claim 18, wherein said heterocyclic group is N-morpholino.

20. The compound according to Claim 7, wherein R^8 and R^9, together with the nitrogen atom pendent thereto, form a heterocyclic or substituted heterocyclic ring.

21. The compound according to Claim 20, wherein said heterocyclic and substituted heterocyclic rings comprise 4 to 8 membered rings containing 1 to 3 heteroatoms.

22. The compound according to Claim 19, wherein said 1 to 3 heteroatoms comprises 1 to 2 nitrogen atoms.

23. The compound according to Claim 21, wherein said heterocyclic or substituted heterocyclic ring is selected from the group consisting of piperidine, substituted piperidine, piperazine, substituted piperazine, morpholino, substituted morpholino, thiomorpholino and substituted thiomorpholino wherein the sulfur atom of the thiomorpholino or substituted thiomorpholino ring is optionally oxidized to provide for sulfoxide and sulfone moieties.

24. The compound according to Claim 23, wherein said heterocyclic or substituted heterocyclic ring is selected from the group consisting of 4-hydroxypiperidin-1-yl, 1,2,3,4-tetrahydro-3-carboxy-isoquinolin-2-yl, 4-methylpiperizin-1-yl, morpholin-4-yl, and thiomorpholin-4-yl.

25. The compound according to Claim 2, wherein Z is $-C(X)N(R^3)CR^2R^{2'}C(=O)R^1$.

26. The compound according to Claim 25, wherein Z is $-C(O)NHCHR^2C(=O)R^1$.

27. The compound according to Claim 25, wherein R^2 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl.

28. The compound according to Claim 27, wherein R^2 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, and cycloalkyl.

29. The compound according to Claim 28, wherein R^2 is selected from the group consisting of hydrogen, methyl, 1-methylprop-1-yl, *sec*-butyl, hydroxymethyl, 1-hydroxyeth-1-yl, 4-amino-*n*-butyl, 2-carboxyeth-1-yl, carboxymethyl, benzyl, (1*H*-imidazol-4-yl)methyl, (4-phenyl)benzyl, (4-phenylcarbonyl)benzyl, cyclohexylmethyl, cyclohexyl, 5-hydroxy-1*H*-indol-3-yl, 2-methylthioeth-1-yl, *iso*-propyl, carbamoylmethyl, 2-carbamoyleth-1-yl, (4-hydroxy)benzyl, and 3-guanidino-*n*-propyl.

30. The compound according to Claim 29, wherein R^1 is selected from the group consisting of hydroxy, amino, and amino(N-morpholino).

31. The compound according to Claim 2, wherein Z is $-C(O)N(R^3)CHR^2C(=O)R^1$ where R^2 and R^3, together with the carbon atom and nitrogen atom bound thereto respectively, are joined to form a heterocyclic or substituted heterocyclic group.

32. The compound according to Claim 31, wherein said heterocyclic and substituted heterocyclic groups are selected from the group consisting of pyrrolidinyl, 2-carboxy-pyrrolidinyl, 2-carboxy-4-hydroxypyrrolidinyl, and 3-carboxy-1,2,3,4-tetrahydroisoquinolin-3-yl.

33. The compound according to Claim 2, wherein Z is $-C(O)NHS(O)_2R^4$.

34. The compound according to Claim 33, wherein R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl and substituted aryl.

35. The compound according to Claim 34, wherein R^4 is alkyl or aryl.

36. The compound according to Claim 34, wherein R^4 is methyl, trifluoromethyl, phenyl, 4-bromophenyl, 4-nitrophenyl or 4-methylphenyl.

37. The compound according to Claim 1, wherein R is selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

38. The compound according to Claim 37, wherein R is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, and substituted cycloalkyl.

39. The compound according to Claim 38, wherein R is selected from the group consisting of hydrogen, ethyl, *iso*-propyl, *sec*-butyl, 3-methyl-*n*-butyl, cyclopropyl, cyclopentyl, cyclohexyl, cyclopropylmethyl, and 2-(N,N-dimethylamino)eth-1-yl.

40. The compound according to Claim 39, wherein R is cyclohexyl.

41. The compound according to Claim 1, wherein W is N.

42. The compound according to Claim 1, wherein W is CH.

43. The compound according to Claim 1, wherein the heterocyclic or heteroaryl ring of the HET group is a nitrogen-containing heterocyclic or heteroaryl ring.

44. The compound according to Claim 43, wherein the HET group contains 1 to 4 nitrogen ring atoms and optionally 1 to 2 hetero ring atoms selected from the group consisting of -O-, -S-, -S(O)- and $-S(O)_2-$.

45. The compound according to Claim 44, wherein said HET group is selected from the group consisting of quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, pteridinyl, cinnolinyl, [1,8]naphthyridinyl, [1,5]naphthyridinyl, 1,2,3,4-tetrahydroquinolinyl, 1,4-dioxo-1,4-dihydrophthalazinyl, 4-oxo-1,4-dihydroquinolinyl, 4-oxo-1,4-dihydroquinazolinyl, 1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazinyl, and 1,4-dihydroisoquinolinyl.

46. The compound according to Claim 45, wherein said HET group is selected from the group consisting of quinolin-6-yl, isoquinolin-6-yl, quinolin-7-yl, quinoxalin-6-yl, quinazolin-7-yl, pteridin-6-yl, cinnolin-3-yl, [1,8]naphthyridin-3-yl, [1,5]naphthyridin-2-yl,
1,2,3,4-tetrahydroquinolin-6-yl, 1,4-dioxo-1,4-dihydrophthalazin-6-yl, 4-oxo-1,4-dihydroquinolin-6-yl, 4-oxo-1,4-dihydroquinazolin-6-yl, 1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazin-7-yl, and 1,4-dihydroisoquinolin-6-yl.

47. The compound according to Claim 1, wherein the heterocyclic or heteroaryl ring of the HET group is an oxygen-containing heterocyclic or heteroaryl ring.

48. The compound according to Claim 47, wherein the HET group contains 1 to 2 oxygen ring atoms and optionally 1 to 2 hetero ring atoms selected from the group consisting of -S-, -S(O)- and -$S(O)_2$-.

49. The compound according to Claim 47, wherein said HET group is selected from the group consisting of 2-oxo-2*H*-chromenyl, 4-oxo-2*H*-chromenyl, and 4-oxo-4*H*-chromen-6-yl.

50. The compound according to Claim 49, wherein said HET group is selected from the group consisting of 2-oxo-2*H*-chromen-7-yl, 4-oxo-2*H*-chromen-6-yl, 4-oxo-2*H*-chromen-7-yl, and 4-oxo-4*H*-chromen-6-yl.

51. The compound according to Claim 1, wherein HET is naphthyl.

52. The compound according to Claim 1, wherein Y is selected from the group consisting of (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, amino, substituted amino, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, halo, heteroaryl, substituted heteroaryl, substituted heterocyclic, -C(O)$NR^{14}R^{15}$, -OR^{14}, and -SR^{14}.

53. The compound according to Claim 52, wherein at least one Y is selected from the group consisting of amino substituted amino (hydrazine) and mono- and disubstituted amino groups.

54. The compound according to Claim 53, wherein Y is a mono-substituted amino group selected from the group consisting of alkylamino, substituted alkylamino, arylamino, substituted arylamino.

55. The compound according to Claim 53, wherein Y is a disubstituted amino group wherein each substituent is independently selected from alkyl, substituted alkyl, aryl and substituted aryl groups.

56. The compound according to Claim 53, wherein Y is selected from the group consisting of amino, phenylamino, [2-(*t*-butoxycarbonylaminoethyl]amino, N-(4-chlorophenyl)amino, N,N-dimethylamino, 4-hydroxybutylamino, 3-imidazol-1-yl-propylamino, and hydrazino.

57. The compound according to Claim 52, wherein at least one Y is selected from the group consisting of (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, cycloalkyl, and substituted cycloalkyl.

58. The compound according to Claim 57, wherein the substituents for the substituted (C_1-C_{10}) alkyl group is selected from the group consisting of hydroxy, amino, substituted amino, aryl, substituted aryl, heteroaryl and substituted heteroaryl.

59. The compound according to Claim 57, wherein the substituents for the substituted cycloalkyl group are independently selected from the group consisting of carboxymethyl and methyl.

60. The compound according to Claim 58, wherein Y is selected from the group consisting of methyl, 3-hydroxypropyl, (N,N-di-*n*-propyl)aminomethyl, diphenylmethyl (benzhydryl), and 2-(pyrazol-1-yl)eth-1-yl and 3-carboxymethyl-2,2-dimethylcyclobutyl.

61. The compound according to Claim 52, wherein at least one Y is selected from the group consisting of halo, cyano, nitro, carboxy and carboxy esters.

62. The compound according to Claim 52, wherein at least one Y is $-C(O)NR^{14}R^{15}$ where each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl and substituted aryl or where R^{14} and R^{15}, together with the nitrogen atom pendent thereto, form a heterocyclic and substituted heterocyclic group.

63. The compound according to Claim 62, wherein said substituents on the substituted alkyl and substituted aryl are selected from the group consisting of halo, hydroxy, and carbamoyl.

64. The compound according to Claim 63, wherein Y is selected from the group consisting of 1-carbamoylethyl-carbamoyl, 1-carbamoyl-2-(1H-imidazol-2-yl)ethylcarbamoyl, 1-carbamoyl-2-hydroxyethylcarbamoyl, 1-carbamoyl-2-methylpropylcarbamoyl, 4-chlorophenylcarbamoyl, and pyrrolidin-1-ylcarbonyl.

65. The compound according to Claim 52, wherein at least one Y is an aryl group.

66. The compound according to Claim 65, wherein Y is selected from the group consisting of phenyl, naphthalen-1-yl, and 5,6,7,8-tetrahydronaphthalen-2-yl.

67. The compound according to Claim 52, wherein at least one Y is a substituted aryl group.

68. The compound according to Claim 67, wherein the substituted aryl group is substituted with non-aryl groups.

69. The compound according to Claim 67 wherein the substituted aryl group is substituted with a substituent selected from the group consisting of acylamino, amino, substituted amino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkoxy, substituted alkoxy, aryloxy, substituted aryloxy, halo, heterocyclic, substituted heterocyclic, hydroxy, nitro and $-C(O)NR^{14}R^{15}$ where each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl and substituted aryl or where R^{14} and R^{15}, together with the nitrogen atom pendent thereto, form a heterocyclic and substituted heterocyclic group.

70. The compound according to Claim 69, wherein the substituted aryl Y group is selected from the group consisting of 4-acetylaminophenyl, 4-aminophenyl, 4-amino-3-bromophenyl, 4-amino-3,5-dichlorophenyl, 4-benzyloxy-2-hydroxy-3-methylphenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 5-bromo-2-hydroxyphenyl, 3-carbamoyl-4-hydroxyphenyl, 3-carboxymethoxyphenyl, 3,4-dichlorophenyl, 2,4-dihydroxyphenyl, 3,5-dihydroxyphenyl, 4-(N,N-dimethylamino)phenyl, 4-fluorophenyl, 2-furan-2-yl-5-methoxyphenyl, 3-hydroxyphenyl, 2-hydroxy-4-,6-dimethoxyphenyl, 2-hydroxynaphthalen-1-yl, 2-hydroxy-6-methoxyphenyl, 2-hydroxy-5-methyl-3-nitrophenyl, 4-(imidazol-1-yl)phenyl, 3-(2-methoxyethoxy)phenyl, 2-methoxy-5-nitrophenyl, 3-methoxyphenyl, 4-methoxyphenyl, 5-methoxy-2-thiophen-2-ylphenyl, 4-methylphenyl, 4-morpholinophenyl, 6-methylnaphthalen-2-yl, 2-nitrophenyl, 3-(2-oxo-2-pyrrolidin-1-ylethoxy)phenyl, 4-phenoxyphenyl, (4-piperazin-1-yl)phenyl, 3-[pyrrolidin-1-ylcarbonyl]phenyl, 3-[3-(pyrrolidin-1-ylpropoxy)]phenyl. 2-(2,4-dimethoxypyrimidin-5-yl)-4-methoxyphenyl, and 2-(pyrid-4-yl)phenyl.

71. The compound according to Claim 67, wherein the substituted aryl is substituted with one or two aryl or substituted aryl groups further wherein the substituted aryl group is optionally substituted on any of its aryl rings with 1 to 3 substituents selected from the group consisting of acylamino, amino, substituted amino, alkyl, substituted alkyl, alkoxy, substituted alkoxy, aryl, substituted aryl, aryloxy, substituted aryloxy, halo, heterocyclic, substituted heterocyclic, heteroaryl, substituted heteroaryl, hydroxy, nitro and $-C(O)NR^{14}R^{15}$ where each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl and substituted aryl or where R^{14} and R^{15}, together with the nitrogen atom pendent thereto, form a heterocyclic and substituted heterocyclic group.

72. The compound according to Claim 71, wherein the substituted aryl Y groups are selected from the group consisting of biphen-2-yl, biphen-4-yl, 4-amino-4'-chlorobiphen-2-yl, 4'-aminomethyl-4-methoxybiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-(carbamoylmethylcarbamoyl)biphen-2-yl, 4-(carbamoylmethylcarbamoyl)-4'-chlorobiphen-2-yl, 4-carbamoyl-4'-fluorobiphen-2-yl, 4-carbamoyl-4'-nitrobiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carboxy-4'-chlorobiphen-2-yl, 3-carboxy-4'-methoxybiphen-2-yl, 4-carboxy-4'-methoxybiphen-2-yl, 4'-carboxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-carboxymethoxy-biphen-2-yl, 4-carboxymethoxy-4'-chlorobiphen-2-yl, 4'-chlorobiphen-2-yl, 4'-chloro-4-chlorobiphen-2-yl, 4'-chloro-4-(dimethylamino-ethylcarbamoylbiphen-2-yl, 4'-chloro-4-(2-ethoxyethoxy)biphen-2-yl, 3'-chloro-4'-fluoro-4-methoxybiphen-2-yl, 4'-chloro-4-fluorobiphen-2-yl, 4'-chloro-4-hydroxybiphen-2-yl, 3'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-methylcarbamoylbiphen-2-yl, 4'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-(2-methoxy-ethoxy)biphen-2-yl, 4'-chloro-4-nitrobiphen-2-yl, 4'-chloro-4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4'-chloro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-chloro-4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, 4'-cyano-4-methoxybiphen-2-yl, 3',4'-dichloro-4-methoxybiphen-2-yl, 4,4'-dimethoxybiphen-2-yl, 3',4'-dimethoxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-dimethylamino-4-methoxybiphen-2-yl, 4-(2-dimethylamino-ethylcarbamoyl)biphen-2-yl, 4'-ethoxy-4-methoxybiphen-2-yl, 4'-fluoro-4-methoxybiphen-2-yl, 4-hydroxybiphenyl, 4-methoxybiphenyl, 4-methoxy-4'-hydroxybiphen-2-yl, 4-(2-methoxy-ethoxy)biphen-2-yl, 4-methoxy-4'-methylbiphen-2-yl,

4-methoxy-3'-nitrobiphen-2-yl, 4-methoxy-4'-nitrobiphen-2-yl, 4-methylcarbamoylbiphen-2-yl, 3'-methyl-4-methoxybiphen-2-yl, 4'-nitro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, and 4'-trifluoromethyl-4-methoxybiphen-2-yl.

73. The compound according to Claim 52, wherein at least one Y is a heteroaryl group.

74. The compound according to Claim 73, wherein said Y groups are selected from the group consisting of benzo[1,3]dioxol-5-yl, benzofuran-2-yl, 2,3-dihydrobenzofuran-5-yl, pyrazin-2-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, 1*H*-pyrrol-2-yl, 1*H*-pyrrol-3-yl, quinolin-4-yl, 3-oxo-3,4-dihydro-2*H*-benzo[1,4]oxazin-6-yl, and thien-2-yl.

75. The compound according to Claim 52, wherein at least one Y is a substituted heteroaryl group.

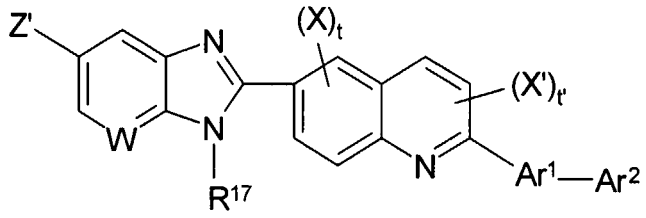
76. The compound according to Claim 75, wherein the substituents on said substituted heteroaryl group are selected from the group consisting of amino, substituted amino, alkyl, substituted alkyl, aryl, substituted aryl, alkoxy, substituted alkoxy, halo, heteroaryl, substituted heteroaryl, hydroxy, nitro and cyano.

77. The compound according to Claim 76, wherein the substituted heteroaryl Y group is selected from the group consisting of 2-amino-4-methylthiazol-5-yl, 3-amino-5-phenylthiophen-2-yl, 5-benzyloxy-2-methylbenzofuran-3-yl, 7-bromo-5-methoxybenzofuran-2-yl, 6-chloro-9-methyl-9*H*-carbazol-3-yl, 5-(4-chlorophenyl)-2-methylfuran-2-yl, 3-(4-chlorophenyl)-5-methylisoxazol-4-yl, 2-(4-chlorophenyl)-4-methylthiazol-5-yl, 1-(2-chloropyrid-3-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl, 3-(3,4-dichlorophenyl)isoxazol-5-yl, 7-hydroxybenzofuran-2-yl, 5-methoxybenzofuran-3-yl, 3,5-dimethyl-1-phenyl-1*H*-pyrazol-4-yl, 2,4-dimethylthiazol-5-yl, 5-methyl-2-phenyl-thiophen-3-yl, and 1-phenyl-1*H*-pyrazol-4-yl.

78. The compound according to Claim 52, wherein the at least one Y is selected from the group consisting of alkoxy, thioalkoxy, substituted alkoxy, substituted thioalkoxy, aryloxy and substituted aryloxy.

79. The compound according to Claim 78, wherein Y is selected from the group consisting of 2-chloro-4-(4-chlorophenyl)phenoxy, ethoxy, 7-hydroxynaphthalen-2-oxy, phenoxy, and phenylsulfanyl.

80. A compound according to formula II:



II

wherein:

W is CH or N;

Z' is selected from the group consisting of carboxy, carboxy ester, and tetrazolyl,

R^{17} is selected from the group consisting of cycloalkyl, cycloalkyl substituted with 1 to 3 alkyl groups, heterocyclic and heterocyclic substituted with 1 to 3 alkyl groups;

X and X' are independently selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, halo, hydroxy, and nitro;

Ar^1 and Ar^2 are independently selected from the group consisting of aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

t is an integer equal to 0, 1 or 2; and

t' is an integer equal to 0 or 1;

and pharmaceutically acceptable salts thereof.

81. The compound according to Claim 80, wherein W is CH.

82. The compound according to Claim 81, wherein R^{17} is cycloalkyl.

83. The compound according to Claim 82, wherein R^{17} is cyclohexyl.

84. The compound according to Claim 80, wherein -Ar^1-Ar^2- are selected from the group consisting of –aryl-aryl, -aryl-substituted aryl, -substituted aryl-aryl, and -substituted aryl-substituted aryl.

85. The compound according to Claim 82, wherein -Ar^1-Ar^2- are selected from the group consisting of biphen-2-yl, biphen-4-yl, 4-amino-4'-chlorobiphen-2-yl, 4'-aminomethyl-4-methoxybiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carbamoyl-4'-fluorobiphen-2-yl, 4-carbamoyl-4'-methoxybiphen-2-yl, 4-carbamoyl-4'-nitrobiphen-2-yl, 4-(carbamoylmethyl-carbamoyl)biphen-2-yl, 4-(carbamoylmethylcarbamoyl)-4'-chlorobiphen-2-yl, 4-carboxy-4'-chlorobiphen-2-yl, 3-carboxy-4'-methoxybiphen-2-yl, 4-carboxy-4'-methoxybiphen-2-yl, 4'-carboxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-carboxymethoxybiphen-2-yl, 4-carboxymethoxy-4'-chlorobiphen-2-yl, 4'-chlorobiphen-2-yl, 4'-chloro-4-chlorobiphen-2-yl, 4'-chloro-4-(dimethylaminoethylcarbamoylbiphen-2-yl, 4'-chloro-4-(2-ethoxyethoxy)biphen-2-yl, 3'-chloro-4'-fluoro-4-methoxybiphen-2-yl, 4'-chloro-4-fluorobiphen-2-yl, 4'-chloro-4-hydroxybiphen-2-yl, 3'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-methylcarbamoylbiphen-2-yl, 4'-chloro-4-methoxybiphen-2-yl, 4'-chloro-4-(2-methoxyethoxy)biphen-2-yl, 4'-chloro-4-nitrobiphen-2-yl, 4'-chloro-4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-yl, 4'-chloro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'_chloro-4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, 4'-cyano-4-methoxybiphen-2-yl, 3',4'_dichloro-4-methoxybiphen-2-yl, 4,4'-dimethoxybiphen-2-yl, 3',4'-dimethoxy-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4'-dimethylamino-4-methoxybiphen-2-yl, 4-(2-dimethylaminoethylcarbamoyl)biphen-2-yl, 4'-ethoxy-4-methoxybiphen-2-yl, 4'-fluoro-4-methoxybiphen-2-yl, 4-hydroxybiphenyl, 4-methoxybiphenyl, 4-methoxy-4'-hydroxybiphen-2-yl, 4-(2-methoxyethoxy)biphen-2-yl, 4-methoxy-4'-methylbiphen-2-yl, 4-methoxy-3'-nitrobiphen-2-yl, 4-methoxy-4'-nitrobiphen-2-yl, 4-methylcarbamoylbiphen-2-yl, 3'-methyl-4-methoxybiphen-2-yl, 4'-nitro-4-(pyrrolidin-1-ylcarbonyl)biphen-2-yl, 4-(2-oxo-2-pyrrolidin-1-ylethoxy)biphen-2-

yl, 4-(3-pyrrolidin-1-ylpropoxy)biphen-2-yl, and 4'-trifluoromethyl-4-methoxybiphen-2-yl.

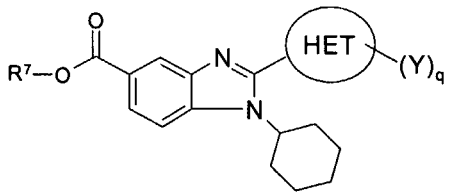
86. The compound according to Claim 80, wherein -Ar^1-Ar^2- are selected from the group consisting of -aryl-heteroaryl, -aryl-substituted heteroaryl, -substituted aryl-heteroaryl, -substituted aryl-substituted heteroaryl, heteroaryl-aryl, heteroaryl-substituted aryl, substituted heteroaryl-aryl, and substituted heteroaryl-substituted aryl.

87. The compound according to Claim 86, wherein -Ar^1-Ar^2- are selected from the group consisting of 2-furan-2-yl-5-methoxyphenyl, 4-(imidazol-1-yl)phenyl, 5-methoxy-2-thiophen-2-ylphenyl, 2-(2,4-dimethoxypyrimidin-5-yl)-4-methoxyphenyl, 2-(pyrid-4-yl)phenyl, 3-amino-5-phenylthiophen-2-yl, 5-(4-chlorophenyl)-2-methylfuran-2-yl, 3-(4-chlorophenyl)-5-methylisoxazol-4-yl, 2-(4-chlorophenyl)-4-methylthiazol-5-yl, 3-(3,4-dichloro-phenyl)isoxazol-5-yl, 3,5-dimethyl-1-phenyl-1*H*-pyrazol-4-yl, 5-methyl-2-phenylthiophen-3-yl, and 1-phenyl-1*H*-pyrazol-4-yl.

88. The compound according to Claim 80, wherein -Ar^1-Ar^2- are selected from the group consisting of -aryl-cycloalkyl, -aryl-substituted cycloalkyl, -substituted aryl-cycloalkyl, -substituted aryl-substituted cycloalkyl, -aryl-heterocyclic, aryl-substituted heterocyclic, substituted aryl-heterocyclic, and substituted aryl-substituted heterocyclic.

89. The compound according to Claim 88, wherein -Ar^1-Ar^2- are selected from the group consisting of (4-piperazin-1-yl)phenyl, 2-cyclohexyl-5-methoxyphenyl, and 4-morpholinophenyl.

90. A compound of formula III:



III

wherein:

R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

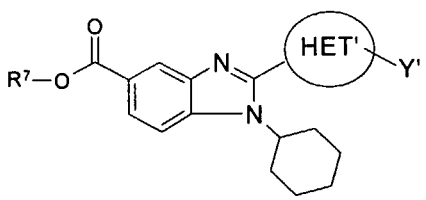
each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

91. A compound of formula IV:



IV

wherein:

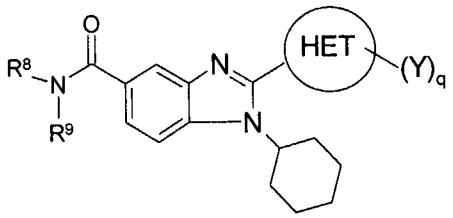
R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

92. A compound of formula V:



V

wherein:

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

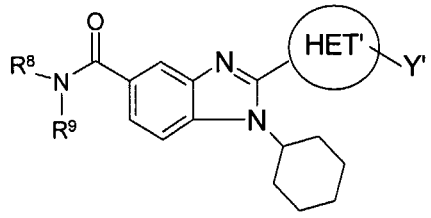
each Y is independently selected from the group consisting of halo, cyano, nitro, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

93. A compound of formula VI:



VI

wherein:

R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted

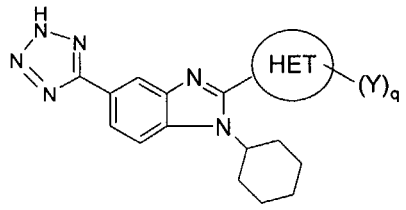
heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

94. A compound of formula VII:



VII

wherein:

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

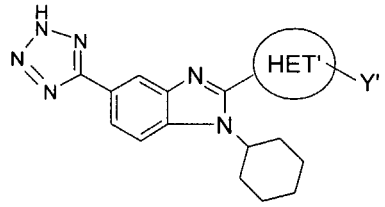
each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl, substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, substituted (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, substituted (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, substituted (C_2-C_{10})alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

95. A compound of formula VIII:



VIII

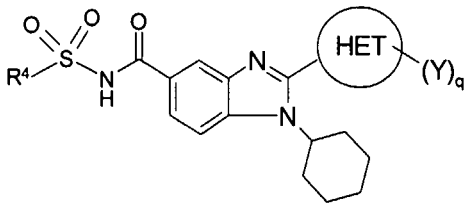
wherein:

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

96. A compound of formula IX:



IX

wherein:

R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

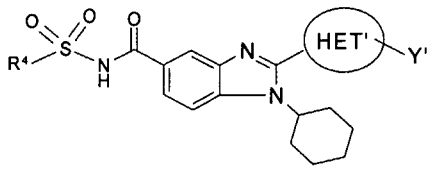
each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

97. A compound of formula X:



X

wherein:

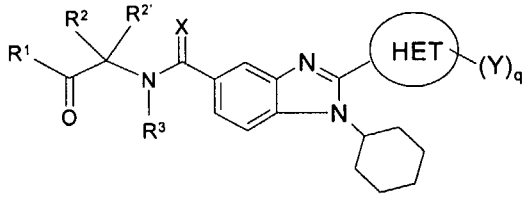
R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

98. A compound of formula XI:



XI

wherein X is selected from the group consisting of =O, =S, and $=NR^{11}$, where R^{11} is hydrogen or alkyl, R^1 is selected from the group consisting of $-OR^7$ and $-NR^8R^9$ where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9

together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

each R^2 and $R^{2'}$ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic,

or, alternatively, R^2 and $R^{2'}$ as defined are taken together with the carbon atom pendent thereto to form a cycloalkyl, substituted cycloalkyl, heterocyclic or substituted heterocyclic group,

or, still further alternatively, one or R^2 or $R^{2'}$ is hydrogen, alkyl or substituted alkyl, and the other is joined, together with the carbon atom pendent thereto, with either the R^7 and the oxygen atom pendent thereto or R^8 and the nitrogen atom pendent thereto to form a heterocyclic or substituted heterocyclic group;

R^3 is selected from the group consisting of hydrogen and alkyl or, when R^2 and $R^{2'}$ are not taken together to form a ring and when $R^2/R^{2'}$ and R^7 or R^8 are not joined to form a heterocyclic or substituted heterocyclic group, then R^3, together with the nitrogen atom pendent thereto, may be taken together with one of R^2 and $R^{2'}$ to form a heterocyclic or substituted heterocyclic ring group;

HET is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, cycloalkyl, cycloalkenyl, heterocyclic, or heteroaryl rings that are optionally substituted with $(Y)_q$; with the proviso that at least one 6-membered ring in the bicycle is heterocyclic or heteroaryl or the bicycle is naphthyl;

each Y is independently selected from the group consisting of halo, cyano, nitro, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, acyl, acyloxy, guanidino, substituted guanidino, oxycarbonylamino, aminocarbonyloxy, aminocarbonylamino, oxycarbonyloxy, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, $-CO_2R^7$, $-NR^{14}R^{15}$, $-NHNR^{14}R^{15}$, $-C(X)NR^{14}R^{15}$, $-OR^{14}$, SR^{14}, $-S(O)R^{14}$, $-S(O)_2R^{14}$, and $-S(O)_2NR^{14}R^{15}$; where X is as defined above;

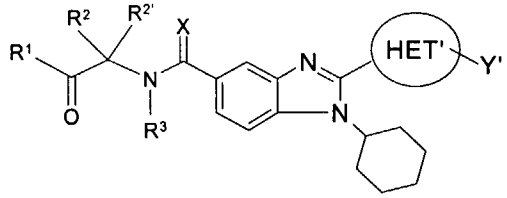
where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl,

heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; s as defined above and each of R^{14} and R^{15} is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl, substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl, substituted $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_{10})$alkenyl, substituted $(C_2\text{-}C_{10})$alkenyl, $(C_2\text{-}C_{10})$alkynyl, substituted $(C_2\text{-}C_{10})$alkynyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or R^{14} and R^{15} may optionally be joined together with the nitrogen atom bound thereto to form a heterocyclic, substituted heterocyclic, heteroaryl or substituted heteroaryl;

q is an integer equal to 1, 2 or 3; and

pharmaceutically acceptable salts or tautomers thereof.

99. A compound of formula XII:



XII

wherein X is selected from the group consisting of =O, =S, and $=NR^{11}$, where R^{11} is hydrogen or alkyl, R^1 is selected from the group consisting of $-OR^7$ and $-NR^8R^9$ where R^7 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic; R^8 and R^9 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocycle or, alternatively, R^8 and R^9 together with the nitrogen atom pendent thereto, form a heterocyclic, a substituted heterocyclic, a heteroaryl or a substituted heteroaryl ring group;

each R^2 and $R^{2'}$ is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic,

or, alternatively, R^2 and $R^{2'}$ as defined are taken together with the carbon atom pendent thereto to form a ring group,

R^3 is selected from the group consisting of hydrogen and alkyl or, when R^2 and $R^{2'}$ are not taken together to form a ring then R^3 may be taken together with one of R^2 and $R^{2'}$ to form a heterocyclic or substituted heterocyclic ring group;

HET' is a fused 6,6-bicycle provided by the fused linkage of any two 6-membered rings selected from aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl, or substituted heteroaryl rings that are optionally substituted with Y; with the proviso that at least one 6-membered ring in the bicycle is aromatic;

Y' is independently selected from the group consisting of alkyl, aryl, heteroaryl, substituted aryl, and substituted heteroaryl; and

pharmaceutically acceptable salts and/or tautomers thereof.

100. A compound selected from the group consisting of

1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic-acid;

1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-phenyl-1,2,3,4-tetrahydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(2-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(5-bromo-2-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-pyridin-3-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-naphthalen-1-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-amino-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3-carboxymethoxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4-(carbamoylmethyl-carbamoyl)-4'-chloro-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methylcarbamoyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-amino-3,5-dichloro-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2,4-dihydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-cyano-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3'-chloro-4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methoxy-3'-methyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-{2-[1-carbamoyl-2-(1H-imidazol-2-yl)ethylcarbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-pyridin-4-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[3-(pyrrolidine-1-carbonyl)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-[2,3-bis-(4-bromophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-[2-(4-amino-3-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-oxo-2-phenyl-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3-carbamoyl-4-hydroxy-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-carboxymethoxy-biphen-2-yl)- quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4'-chloro-4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4-(carbamoylmethyl-carbamoyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methylcarbamoyl-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-(2-biphen-2-yl-8-methyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[4-(4-chloro-phenylamino)-2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3,5-dihydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-carbamoyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methoxy-4'-nitro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-aminomethyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(1-carbamoyl-2-hydroxyethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2,3-diphenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid (;

2-(2-biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2,3-di-p-tolylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid;

2-(2-biphenyl-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(2-amino-4-methyl-thiazol-5-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3-hydroxy-propyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-carboxymethoxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(7-bromo-5-methoxy-benzofuran-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-(2-biphen-2-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{2-[3-(4-chloro-phenyl)-5-methyl-isoxazol-4-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(8-methyl-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[4-(4-hydroxy-butylamino)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid ;

2-[4-(2-*tert*-butoxycarbonylamino-ethylamino)-2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[5-(pyrrolidine-1-carbonyl)-2-thiophen-2-yl]quinoline-6-yl}-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4'-dimethylamino-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

6-(5-carboxy-1-cyclohexyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid;

1-cyclohexyl-2-[2-(3',4'-dichloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-ethoxy-5-nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2,3-diphenylquinoxalin-6-yl)-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-oxo-2-phenyl-4H-chromen-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2,3-bis-(4-fluorophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-(2-biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazol-5-yl]-(4-hydroxy-piperidin-1-yl)-methanone;

1-cyclohexyl-2-[2-(7-hydroxy-benzofuran-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-(2-benzo[1,3]dioxol-5-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-(2-benzofuran-2-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[3-(3-pyrrolidin-1-yl-propoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-carboxy-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{2-[2-(4-chloro-phenyl)-4-methyl-thiazol-5-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-8-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-hydroxy-5-methyl-3-nitro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[3',4'-dimethoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methoxy-3'-nitro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-carboxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2,4']biquinolinyl-6-yl-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(2-bromo-phenyl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2,3-bis-(3-methoxyphenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid ;

1-cyclohexyl-2-[2-(2,4-dimethyl-thiazol-5-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-pyridin-2-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-phenoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-morpholin-4-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-{2-[1-(2-chloro-pyridin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(1H-pyrrol-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-phenyl-4-phenylamino-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-hydroxy-6-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4'-nitro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methoxy-4'-trifluoromethyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3'-carboxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methoxy-4'-methyl-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-nitro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-3-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2,3-bis-(4-methoxyphenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-pyrazin-2-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-pyridin-4-yl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(6-methyl-naphthalen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[3-(2-methoxy-ethoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-[6-(2-Nitro-phenyl)- quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4'-chloro-4-(3-pyrrolidin-1-yl-propoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(5-benzyloxy-2-methyl-benzofuran-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(1-phenyl-1H-pyrazol-4-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(1H-pyrrol-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[4-(3-imidazol-1-yl-propylamino)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-hydroxy-4,6-dimethoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4'-carboxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-furan-2-yl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4'-ethoxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-(2-benzhydryl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2,3-bis-(4-dimethylaminophenyl)quinoxalin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(5,6,7,8-tetrahydro-naphthalen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-hydroxy-naphthalen-1-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-benzyloxy-2-hydroxy-3-methyl-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(6-chloro-9-methyl-9H-carbazol-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-hydrazino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-phenyl-4-phenylsulfanyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4,4'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4'-hydroxy-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(5-methoxy-2-thiophen-2-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(2-bromo-phenyl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(5-methyl-2-phenyl-thiophen-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-imidazol-1-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3-hydroxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4'-chloro-4-(2-methoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-pyrazol-1-yl-ethyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(2-bromo-phenyl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic;

1-cyclohexyl-2-[2-(2,3-dihydro-benzofuran-5-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[3-(3,4-dichloro-phenyl)-isoxazol-5-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3-amino-5-phenyl-thiophen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-dimethylamino-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3-bromo-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphenyl-3-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[2-(2,4-dimethoxy-pyrimidin-5-yl)-5-methoxy-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-4-methyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-piperazin-1-yl-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-dipropylaminomethyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid;

2-{2-[4'-chloro-4-(2-dimethylamino-ethylcarbamoyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(5-methoxy-benzofuran-3-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-ethoxy-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3,5-dimethoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-phenoxy-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(1-carbamoylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-(4-methyl-2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-acetylamino-phenyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(3-carboxymethyl-2,2-dimethyl-cyclobutyl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[3-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-phenyl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4-(2-dimethylamino-ethylcarbamoyl)-biphen-2-yl]-quinolin-6-yl}-1H-benzoimidazole-5-carboxylic acid;

2-{2-[5-(4-chloro-phenyl)-2-methyl-furan-3-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{2-[4'-chloro-4-(2-ethoxy-ethoxy)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3,4-dichloro-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[4-(7-hydroxy-naphthalen-2-yloxy)-2-phenyl-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-chlorophenylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-[2-(1-carbamoyl-2-methylpropylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-[2-(1-carbamoyl-2-phenylethylcarbamoyl)quinolin-6-yl]-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(4-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(2-cyclohexyl-5-methoxy-phenyl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-{2-[(4-chlorophenyl) methyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(4-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid;

2-(2-biphenyl-4-yl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4'-fluoro-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid;

2-{2-[(4-chlorophenyl) isopropyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

2-{2-[(4-chlorophenyl) cyclohexyl carbamoyl]quinolin-6-yl}-1-cyclohexyl-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4,2'-dimethoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

Ethyl 1-cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(3,3,5-trimethyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(2-methyl-cyclohexyl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4'-ethyl-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-piperidin-4-yl-1H-benzoimidazole-5-carboxylic acid;

1-benzyl-2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3',4'-difluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-{2-[4'-methoxy-4-(pyrrolidine-1-carbonyl)biphen-2-yl]quinolin-6-yl}-1H-benzimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(3',5'-dichloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-fluoro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(1-ethyl-propyl)-1H-benzoimidazole-5-carboxylic acid;

2-{2-[8-(4-chloro-phenyl)-3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(tetrahydrofuran-2-yl-methyl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-[2-(4,4'-dichloro-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid;

1-bicyclo[2.2.1]hept-2-yl-2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]1H-benzoimidazole-5-carboxylic acid;

2-[2-(4-amino-4'-chloro-biphen-2-yl)-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazole-5-carboxylic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

2-{[1-cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-hydroxy-propionic acid ;

6-amino-2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-hexanoic acid;

1-[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-pyrrolidine-2-carboxylic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

2-[(2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

2-{[1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-pentanedioic acid;

2-{[1-cyclohexyl-2-(3-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

3-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid;

3-biphenyl-4-yl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid;

3-(4-benzoyl-phenyl)-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid;

3-cyclohexyl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-propionic acid;

cyclohexyl-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-succinic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-pentanedioic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-phenyl-propionic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(1H-imidazol-4-yl)-propionic acid;

1-[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-4-hydroxy-pyrrolidine-2-carboxylic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-methyl-pentanoic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-hydroxy-butyric acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methyl-pentanoic acid;

{2-[2-(4'-chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(4-hydroxy-piperidin-1-yl)-methanone;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methylsulfanyl-butyric acid;

2-{[1-cyclohexyl-2-(3-phenyl-quinolin-7-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-methyl-butyric acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-succinamic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(4-hydroxy-phenyl)-propionic acid;

2-[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid;

{2-[2-(4'-chloro-biphen-2-yl)-7-fluoro-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(4-methyl-piperazin-1-yl)-methanone;

[2-(2-biphen-2-yl-7-fluoro-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazol-5-yl]-(4-methyl-piperazin-1-yl)-methanone;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-5-guanidino-pentanoic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-ethanesulfonic acid;

4-carbamoyl-2-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-butyric acid;

1-cyclohexyl-2-[2-(4'-fluoro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1H-benzoimidazole-5-carboxylic acid amide;

1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid morpholin-4-ylamide;

1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (7-hydroxy-naphthalen-1-yl)-amide;

1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (5-hydroxy-naphthalen-1-yl)-amide;

1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid (4-methyl-2-oxo-2H-chromen-7-yl)-amide;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylquinoxaline;

(4'-chloro-2-{6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzimidazol-2-yl]-quinolin-2-yl}-biphenyl-4-yl)-pyrrolidin-1-yl-methanone;

2-(4'-chloro-4-methoxy-biphen-2-yl)-6-[1-cyclohexyl-5-(1H-tetrazol-5-yl)-1H-benzoimidazol-2-yl]-quinoline;

2-[(2-(2-phenyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid;

{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid;

6-{[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-naphthalene-2-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-isopropyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopropyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopentyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-isobutyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-cyclopropylmethyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(3-methyl-butyl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-(2-dimethylamino-ethyl)-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-1-ethyl-1H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-1H-indole-6-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid;

2-[2-(4'-chloro-4-hydroxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid ethyl ester;

2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-3-cyclohexyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-5-carboxylic acid;

2-[2-(4'-chloro-4-methoxy-biphen-2-yl)-quinolin-6-yl]-3-cyclohexyl-3H-benzoimidazole-4-carboxylic acid;

6-(1-cyclohexyl-5-ethoxycarbonyl-1H-benzimidazol-2-yl)quinoline-2-carboxylic acid;

1-(trans-2-hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-(trans-4-hydroxy-cyclohexyl)-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

{4'-chloro-2-[6-(1-cyclohexyl-1H-benzoimidazol-2-yl)-quinolin-2-yl]-biphenyl-4-yl}-pyrrolidin-1-yl-methanone; and

pharmaceutically acceptable tautomers or salts thereof.

101. A compound selected from the group consisting of

1-cyclohexyl-2-(2-phenyl-pteridin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2- methyl-pteridin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(7-phenyl-cinnolin-3-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(7- methyl-cinnolin-3-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(7-phenyl[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(7-methyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(6-phenyl- [1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(6-methyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-methyl-4-oxo-chromen-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-methyl-4-oxo-chromen-7-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-methyl-1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-methyl-1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4] thiadiazin-7-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-methyl-isoquinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(3-methyl-1,4-dihydro-isoquinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-methyl-quinazolin-7-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-methyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(6-methyl- [1,5]naphthyridin-2-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazole-5-carboxylic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-3-(5-hydroxy-1H-indol-3-yl)-propionic acid;

1-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-7-hydroxy-naphthalene;

1-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-5-hydroxy-naphthalene;

7-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-4-methyl-2-oxo-chromene;

{2-[2-phenyl-quinolin-6-yl]-1-cyclohexyl-1H-benzoimidazol-5-yl}-(morpholin-4-yl)-methanone;

2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-ethanesulfonic acid;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylquinoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methylquinoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-phenylquinoxaline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenylpteridine;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methylpteridine;

3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-phenylcinnoline;

3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-methylcinnoline;

3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-phenyl[1,8]naphthyridine;

3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-7-methyl[1,8]naphthyridine;

3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-6-phenyl[1,8]naphthyridine;

3-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-6-methyl[1,8]naphthyridine;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-phenyl-1,2,3,4-tetrahydroquinoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-1,2,3,4-tetrahydroquinoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-4-oxo-2H-chromene;

7-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-2-oxo-2H-chromene;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-1,4-dioxo-1,2,3,4-tetrahydro-phthalazine;

7-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazine;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-isoquinoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-3-methyl-1,4-dihydro- isoquinoline;

7-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-quinazoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-quinoxaline;

2-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-6-methyl-[1,5]naphthyridine;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-4-oxo-1,4-dihydro-quinoline;

6-[1-cyclohexyl-5-(1*H*-tetrazol-5-yl)-1*H*-benzimidazol-2-yl]-2-methyl-4-oxo-1,4-dihydro-quinazoline;

N-[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine ;

N-[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)- 1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-phenyl-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-phenyl- pteridin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-methyl- pteridin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(7-phenyl-cinnolin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(7-methyl-cinnolin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(7-phenyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(7-methyl -[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(6-phenyl-[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(6-methyl -[1,8]naphthyridin-3-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-phenyl-1,2,3,4-tetrahydroquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(2- methyl-1,2,3,4-tetrahydroquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(3-methyl-4-oxo-2H-chromen-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(3-methyl-2-oxo-2H-chromen-7-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-methyl-1,4-dioxo-1,2,3,4-tetrahydro-phthalazin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(3-methyl-1,1-dioxo-1,4-dihydro-1λ6-benzo[1,2,4]thiadiazin-7-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(3-methyl-isoquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(3-methyl-1,4-dihydro-isoquinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-methyl-quinazolin7-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-methyl-quinoxalin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(6-methyl-[1,5]naphthyridin-2-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(phenylsulfonyl)amine;

N-[1-cyclohexyl-2-(2-methyl-4-oxo-1,4-dihydro-quinazolin-6-yl)-1H-benzoimidazol-5-ylcarbonyl]-N-(methylsulfonyl)amine;

2-[(2-(2-methyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid;

{[1-cyclohexyl-2-(2-methyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid;

2-[(2-(2-methyl-quinolin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid;

{[1-cyclohexyl-2-(2-methyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid;

2-[(2-(3-phenyl-quinoxalin-6-yl)-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid;

{[1-cyclohexyl-2-(3-phenyl-quinoxalin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-acetic acid;

2-[(2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]-propionic acid;

2-[(2-{2-[4'-chloro-4-(pyrrolidine-1-carbonyl)-biphen-2-yl]-quinolin-6-yl}-1-cyclohexyl-1H-benzoimidazole-5-carbonyl)-amino]- acetic acid;

5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-1-phenyl-1H-pyrazole-4-carboxylic acid;

5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}- nicotinic acid;

6-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-naphthalene-2-carboxylic acid;

4-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}- phenylacetic acid;

4-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-phthalic acid;

3-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}- pyrazine-2-carboxylic acid;

5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-2-hydroxy-benzoic acid;

5-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-benzoic acid;

2-{[1-cyclohexyl-2-(2-phenyl-quinolin-6-yl)-1H-benzoimidazole-5-carbonyl]-amino}-thiophene-3-carboxylic acid; and

pharmaceutically acceptable tautomers and salts therof.

102. A pharmaceutical composition comprising a pharmaceutically acceptable diluent and a therapeutically effective amount of a compound of any of Claims 1, 80, or 90-101 or a mixture of two or more of such compounds.

103. A method for treating a viral infection in a mammal mediated at least in part by a virus in the *flaviviridae* family of viruses which method comprises administering to a mammal, that has been diagnosed with said viral infection or is at risk of developing said viral infection, a pharmaceutical composition according to Claim 102.

104. The method according to Claim 103, wherein said virus is hepatitis C virus.

105. The method of Claim 104 in combination with the administration of a therapeutically effective amount of one or more agents active against hepatitis C virus.

106. The method of Claim 105 wherein said active agent against is ribavirin, levovirin, thymosin alpha-1, an inhibitor of NS3 serine protease, and inhibitor of inosine monophosphate dehydrogenase, interferon-alpha, pegylated interferon-alpha, alone or in combination with ribavirin or levovirin.

107. The method of Claim 106 wherein said agent active against HCV is interferon-alpha or pegylated interferon-alpha alone or in combination with ribavirin or levovirin.