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(54) Titre : COMPOSES DE PETITE MOLECULE DE DIPHENYLAMINE MIMETIQUE DU FACTEUR DE CROISSANCE HEMATOPOIETIQUE ET LEURS UTILISATIONS

(54) Title: HEMATOPOIETIC GROWTH FACTOR MIMETIC DIPHENYLAMINE SMALL MOLECULE COMPOUNDS AND THEIR USES

(57) Abrégé/Abstract:
The present embodiments relate to compounds with physiological effects, such as the activation of hematopoietic growth factor receptors. The present embodiments also relate to use of the compounds to treat a variety of conditions, diseases and ailments such as hematopoietic conditions and disorders.

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(54) Title: HEMATOPOIETIC GROWTH FACTOR MIMETIC SMALL MOLECULE COMPOUNDS AND THEIR USES

(57) Abstract: The present embodiments relate to compounds with physiological effects, such as the activation of hematopoietic growth factor receptors. The present embodiments also relate to use of the compounds to treat a variety of conditions, diseases and ailments such as hematopoietic conditions and disorders.

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JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __2___

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HEMATOPOIETIC GROWTH FACTOR MIMETIC DIPHENYLAMINE SMALL MOLECULE COMPOUNDS AND THEIR USES

RELATED APPLICATIONS

FIELD OF THE INVENTION

[0002] The present embodiments relate to compounds with physiological effects, such as the activation of hematopoietic growth factor receptors. The present embodiments also relate to use of the compounds to treat a variety of conditions, diseases and ailments such as hematopoietic conditions and disorders.

BACKGROUND

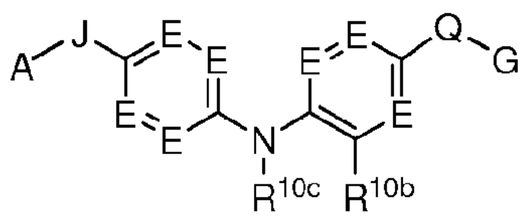
[0003] Hematopoietic growth factor (HGF) represents a family of biological molecules such as glycoproteins with important regulatory functions in the processes of proliferation, differentiation, and functional activation of hematopoietic progenitors and mature blood cells. HGF compounds can be potent regulators of blood cell proliferation and development in the bone marrow. They are able to augment hematopoiesis when bone marrow dysfunction exists. Recombinant DNA technology has made it possible to clone the genes responsible for many of these factors.

[0004] One example of an HGF is the glycoprotein hormone erythropoietin (EPO). EPO is an essential viability and growth factor for the erythrocytic progenitors. EPO is a member of the family of class I cytokines which fold into a compact globular structure consisting of 4 α-helical bundles. Its molecular mass is 30.4 kDa, although it migrates with an apparent size of 34-38 kDa on SDS-polyacrylamide gels. The peptide core of 165 amino acids suffices for receptor-binding and in vitro stimulation of erythropoiesis, while the carbohydrate portion (40% of the total molecule) is required for the in vivo survival of the hormone. The 4 carbohydrate chains of EPO have been analyzed in detail. The 3 complex-type N-linked oligosaccharides at asparagines 24, 38 and 83 appear involved in stabilizing EPO in circulation. EPO is mainly produced by hepatocytes during the fetal stage. After birth, almost all circulating EPO originates from peritubular fibroblast-like cells located in the cortex of the kidneys. Transcription factors of the GATA-family may be important in the

control of the time-specific and tissue-specific expression of the EPO gene. In adults, minor amounts of EPO mRNA are expressed in liver parenchyma, spleen, lung, testis and brain. In brain, EPO exerts neurotrophic and neuroprotective effects, which are separate from the action of circulating EPO on erythropoietic tissues. See e.g., Jelkmann, W., *Internal Medicine* Vol. 43, No.8 (August 2004).

SUMMARY OF THE INVENTION

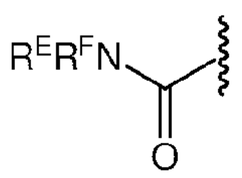
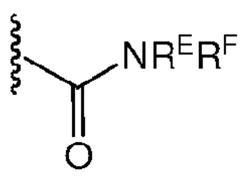
[0005] Some embodiments disclosed herein provide a compound of Formula **VIII**:

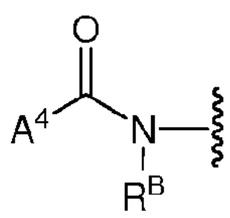
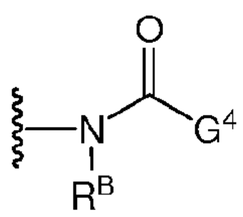


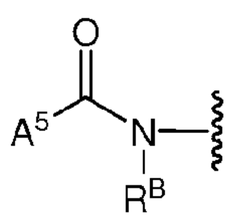
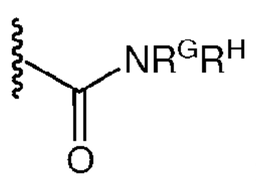
(VIII)

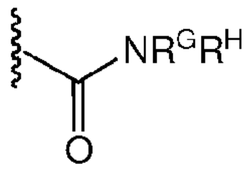
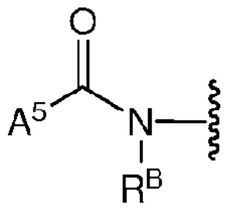
[0006] and pharmaceutically acceptable salts thereof;

[0007] wherein:

[0008] **A–J** is  and **Q–G** is  ;

[0009] or **A–J** is  and **Q–G** is  ;

[0010] or **A–J** is  and **Q–G** is  ;

[0011] or **A–J** is  and **Q–G** is  ;

[0012] each **E** is separately selected from the group consisting of -C**R^{10a}**- and N (nitrogen);

[0013] each **R^{10a}** is separately selected from the group consisting of H (hydrogen), halogen, cyano, C_1-C_6 alkyl optionally substituted with up to five fluoro, C_1-C_6 alkoxy optionally substituted with up to five fluoro, C_2-C_6 alkenyl optionally substituted with up to five fluoro, C_2-C_6 alkynyl optionally substituted with up to five fluoro, C_3-C_7 cycloalkyl

optionally substituted with up to five fluoro, and C_3-C_7 cycloalkenyl optionally substituted with up to five fluoro;

[0014] $\mathbf{R^{10b}}$ is selected from the group consisting of $\mathbf{R^{10bb}}$, H (hydrogen), halogen, cyano, C_1-C_6 alkyl optionally substituted with up to five fluoro, C_1-C_6 alkoxy optionally substituted with up to five fluoro, C_2-C_6 alkenyl optionally substituted with up to five fluoro, C_2-C_6 alkynyl optionally substituted with up to five fluoro, C_3-C_7 cycloalkyl optionally substituted with up to five fluoro, and C_3-C_7 cycloalkenyl optionally substituted with up to five fluoro;

[0015] $\mathbf{R^{10c}}$ is selected from the group consisting of H (hydrogen), $\mathbf{R^U}SO_2$-, $\mathbf{R^U}C(=O)$-, C_1-C_6 alkyl optionally substituted with up to five fluoro, and C_3-C_7 cycloalkyl optionally substituted with up to five fluoro, or $\mathbf{R^{10c}}$ is $\mathbf{R^{10cc}}$ when $\mathbf{R^{10b}}$ is $\mathbf{R^{10bb}}$;

[0016] $\mathbf{R^{10cc}}$ and $\mathbf{R^{10bb}}$ together with the atoms to which they are attached is a five-membered heteroaryl optionally substituted with one or more substituents each separately selected from the group consisting of halogen, cyano, C_1-C_6 alkyl optionally substituted with up to five fluoro, C_1-C_6 alkoxy optionally substituted with up to five fluoro, C_1-C_6 alkylC(=O)- and C_3-C_7 cycloalkylC(=O)-;

[0017] $\mathbf{A^4}$ is selected from the group consisting of C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, $-(CH_2)_m\mathbf{NR^PR^L}$, heterocycle, polycyclic heterocyclyl, aryl, and heteroaryl, said C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, heterocycle, polycyclic heterocyclyl, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$;

[0018] $\mathbf{G^4}$ is selected from the group consisting of polycyclic heterocyclyl, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$;

[0019] $\mathbf{A^5}$ is selected from the group consisting of polycyclic heterocyclyl, aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$;

[0020] each $\mathbf{R^B}$ is separately selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_6 alkenyl, and an optionally substituted C_3-C_7 cycloalkyl;

[0021] each $-N\mathbf{R}^{E}\mathbf{R}^{F}$ is separately selected, wherein each $\mathbf{R}^{E}$ is independently selected from the group consisting of hydrogen and an optionally C_1-C_6 alkyl, and each $\mathbf{R}^{F}$ is independently selected from the group consisting of aryl and heteroaryl, said aryl and heteroaryl in the definition of $\mathbf{R}^{F}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, $-C(=O)N\mathbf{R}^{N}\mathbf{R}^{O}$, $-OC(=O)N\mathbf{R}^{N}\mathbf{R}^{O}$, $-NHC(=O)N\mathbf{R}^{N}\mathbf{R}^{O}$, $-O(CH_2)_qN\mathbf{R}^{N}\mathbf{R}^{O}$, $-NH(CH_2)_qN\mathbf{R}^{N}\mathbf{R}^{O}$ $-(CH_2)_pN\mathbf{R}^{N}\mathbf{R}^{O}$, an optionally substituted aryl and an optionally substituted heteroaryl, and said aryl and heteroaryl in the definition of $\mathbf{R}^{F}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0022] $\mathbf{R}^{G}$ is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_3-C_8 cycloalkenyl, C_1-C_6 heteroalkyl, C_1-C_6 heteroalkenyl, C_1-C_6 heteroalkynyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R}^{4}$, $\mathbf{R}^{5}$, and $\mathbf{R}^{6}$, said aryl and heteroaryl in the definition of $\mathbf{R}^{G}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle, or $\mathbf{R}^{G}$ is $-O\mathbf{R}^{L}$ or $-N\mathbf{R}^{P}\mathbf{R}^{L}$;

[0023] $\mathbf{R}^{H}$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, and C_1-C_3 haloalkyl, or $-N\mathbf{R}^{G}\mathbf{R}^{H}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0024] each $\mathbf{R}^{1}$ is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0025] each $\mathbf{R}^{2}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mO\mathbf{R}^{I}$, $-(CH_2)_mO\mathbf{R}^{I}$, $-N\mathbf{R}^{J}\mathbf{R}^{K}$, $-(CH_2)_mS\mathbf{R}^{I}$, $-C(=O)\mathbf{R}^{L}$, $-(CH_2)_m\mathbf{R}^{L}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and an optionally substituted C_3-C_7 cycloalkyl where said C_3-C_7 cycloalkyl is further optionally fused with aryl or heteroaryl;

[0026] each $\mathbf{R}^{3}$ is separately selected from the group consisting of halogen, $-(CH_2)_mO\mathbf{R}^{G}$, $-N\mathbf{R}^{L}C(=O)\mathbf{R}^{M}$, $-N\mathbf{R}^{L}C(=O)O\mathbf{R}^{M}$, $-N\mathbf{R}^{L}C(=O)N\mathbf{R}^{N}\mathbf{R}^{O}$, $-N\mathbf{R}^{N}\mathbf{R}^{O}$,

-$(CH_2)_mS(O)_{0-2}\mathbf{R^M}$, -$(CH_2)_mNHS(O)_{0-2}\mathbf{R^M}$, –$(CH_2)_mNO_2$, –$(CH_2)_mCN$, –$(CH_2)_m\mathbf{R^P}$, C_1-C_6 alkyl C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^3}$ are each optionally substituted with halogen, hydroxy, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, –C(=O)$\mathbf{OR^M}$, or –$\mathbf{NR^JR^K}$;

[0027] each $\mathbf{R^4}$ is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0028] each $\mathbf{R^5}$ is separately selected from the group consisting of halogen, -$O(CH_2)_mO\mathbf{R^I}$, -$(CH_2)_mO\mathbf{R^I}$, –$\mathbf{NR^JR^K}$, –$(CH_2)_mS\mathbf{R^I}$, -$(CH_2)_mC(=O)\mathbf{R^L}$, –$(CH_2)_m\mathbf{R^L}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0029] each $\mathbf{R^6}$ is separately selected from the group consisting of halogen, -$(CH_2)_mO\mathbf{R^G}$, -$\mathbf{NR^L}C(=O)\mathbf{R^M}$, -$\mathbf{NR^L}C(=O)O\mathbf{R^M}$, -$\mathbf{NR^L}C(=O)N\mathbf{R^NR^O}$, -$\mathbf{NR^NR^O}$, –$(CH_2)_mS(O)_{0-2}\mathbf{R^M}$, -$(CH_2)_mNHS(O)_{0-2}\mathbf{R^M}$, –$(CH_2)_mNO_2$, –$(CH_2)_mCN$, –$(CH_2)_m\mathbf{R^P}$, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^6}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, -C(=O)$\mathbf{OR^M}$, or –$\mathbf{NR^JR^K}$;

[0030] each $\mathbf{R^I}$ is separately selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl;

[0031] each –$\mathbf{NR^JR^K}$ is separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, –$(CH_2)_mO\mathbf{R^{JA}}$, –$(CH_2)_mN\mathbf{R^{JB}R^{JC}}$, –$(CH_2)_m\mathbf{R^R}$, C_3-C_7 cycloalkyl, heterocycle, aryl and heteroaryl, said C_3-C_7 cycloalkyl, heterocycle, aryl and heteroaryl in the definition of $\mathbf{R^J}$ and $\mathbf{R^K}$ are each independently optionally substituted with one or more substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6

haloalkyl, C_1-C_6 alkoxy, aryl and heteroaryl, said aryl and heteroaryl substituent off of $\mathbf{R^J}$ and $\mathbf{R^K}$ are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or -$(CH_2)_m$N$\mathbf{R^{KA}R^{KB}}$; or –N$\mathbf{R^JR^K}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0032] each $\mathbf{R^{JA}}$ is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0033] each –N$\mathbf{R^{JB}R^{JC}}$ is separately selected, wherein $\mathbf{R^{JB}}$ and $\mathbf{R^{JC}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0034] each –N$\mathbf{R^{KA}R^{KB}}$ is separately selected, wherein $\mathbf{R^{KA}}$ and $\mathbf{R^{KB}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0035] each $\mathbf{R^M}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, and –$(CH_2)_m\mathbf{R^P}$;

[0036] each –N$\mathbf{R^NR^O}$ is separately selected, wherein $\mathbf{R^N}$ and $\mathbf{R^O}$ are each independently selected from the group consisting of hydrogen, –$(CH_2)_m$N$\mathbf{R^{NA}R^{NB}}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of $\mathbf{R^N}$ and $\mathbf{R^O}$ are each independently optionally substituted with one or more substituents selected from the group consisting of -$(CH_2)_m$N$\mathbf{R^{OA}R^{OB}}$, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, aryl and heteroaryl, said aryl and heteroaryl substituent off of $\mathbf{R^N}$ and $\mathbf{R^O}$ are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or -N$\mathbf{R^{NA}R^{NB}}$,

[0037] each –N$\mathbf{R^{NA}R^{NB}}$ is separately selected, wherein $\mathbf{R^{NA}}$ and $\mathbf{R^{NB}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0038] each –N$\mathbf{R^{OA}R^{OB}}$ is separately selected, wherein $\mathbf{R^{OA}}$ and $\mathbf{R^{OB}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0039] each $\mathbf{R^P}$ is independently selected from the group consisting of hydrogen and C_1-C_6 alkyl;

[0040] each $\mathbf{R^L}$ is independently selected from the group consisting of C_3-C_7 cycloalkyl, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, $-(CH_2)_mOR^{LA}$, $-(CH_2)_mNR^{LB}R^{LC}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of $\mathbf{R^L}$ are each independently optionally substituted with one or more substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-(CH_2)_mNR^{LD}R^{LE}$, aryl and heteroaryl, said aryl and heteroaryl substituent off of $\mathbf{R^L}$ are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-(CH_2)_mNR^{LF}R^{LG}$;

[0041] each $\mathbf{R^{LA}}$ is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0042] $\mathbf{R^{LB}}$ and $\mathbf{R^{LC}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl, said C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl each optionally substituted with one or more halogen, cyano, or $-(CH_2)_mC(=O)OH$; or $-NR^{LB}R^{LC}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0043] each $-NR^{LD}R^{LE}$ is separately selected, wherein $\mathbf{R^{LD}}$ and $\mathbf{R^{LE}}$ are each independently selected from the group consisting of hydrogen, aryl, heteroaryl, and optionally substituted C_1-C_6 alkyl, said aryl and heteroaryl in the definition of $\mathbf{R^{LD}}$ and $\mathbf{R^{LE}}$ are each optionally substituted with C_1-C_6 alkyl or C_1-C_6 alkoxy; or $-NR^{LD}R^{LE}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0044] each $-NR^{LF}R^{LG}$ is separately selected, wherein $\mathbf{R^{LF}}$ and $\mathbf{R^{LG}}$ are each independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl; or $-NR^{LF}R^{LG}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

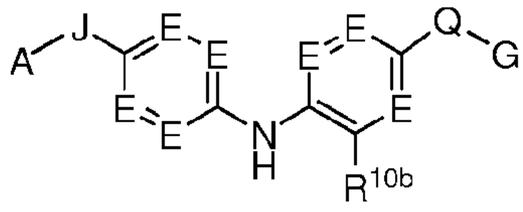
[0045] $\mathbf{R^R}$ is selected from the group consisting of C_1-C_6 alkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

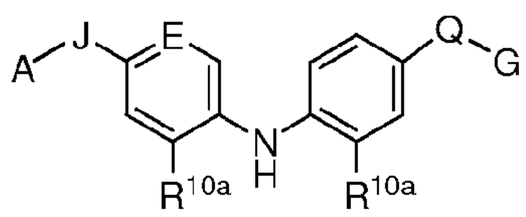
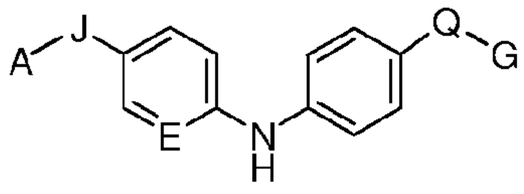
[0046] $\mathbf{R^U}$ is selected from the group consisting of C_3-C_7 cycloalkyl C_1-C_6 alkyl optionally substituted with up to 5 fluoro, and an optionally substituted heteroaryl;

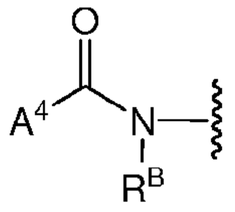
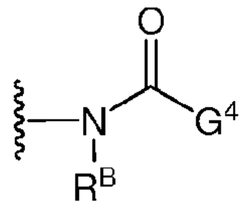
[0047] each **m** is independently 0, 1, 2, or 3;

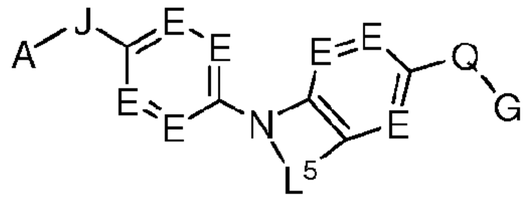
[0048] each **p** is independently 0, 1, 2, 3, 4, 5, or 6; and

[0049] each **q** is independently 1, 2, 3, 4, 5, or 6.

[0050] Some embodiments disclosed herein provide a compound of Formula **VIII** having the formula **VIIIa:**  (**VIIIa**), and pharmaceutically acceptable salts thereof.

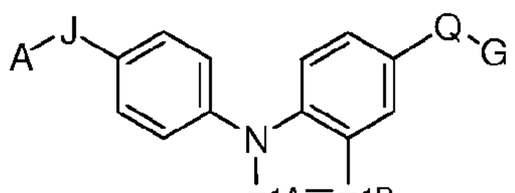
[0051] Some embodiments disclosed herein provide a compound of Formula **VIIIa** having the formula **VIIIaa:**  (**VIIIaa**), and pharmaceutically acceptable salts thereof, and having the formula **VIIIab:**  (**VIIIab**), and pharmaceutically acceptable salts thereof.

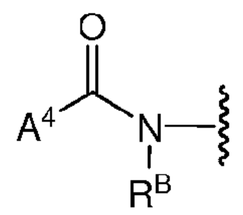
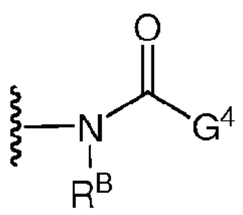
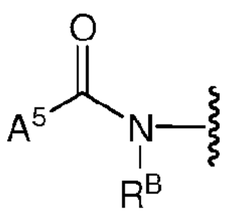
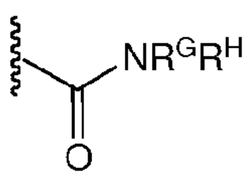
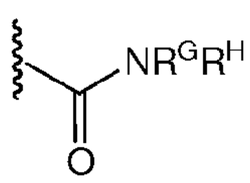
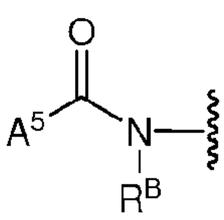
[0052] Some embodiments disclosed herein provide a compound of Formula **VIIIaa**, wherein **A–J** is  and **Q–G** is  , $\mathbf{A^4}$ is selected from the group consisting of aryl and heteroaryl, where at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), and said aryl and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, and $\mathbf{G^4}$ is selected from the group consisting of aryl and heteroaryl, where at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), and said aryl and heteroaryl are each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$.

[0053] Some embodiments disclosed herein provide a compound of Formula **VIII** having the formula **VIIIb:**  (**VIIIb**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{L^5}$ is $\mathbf{E^1}$=$\mathbf{E^1}$ or $\mathbf{E^2}$-$\mathbf{E^2}$, each $\mathbf{E^1}$ is separately selected from the group consisting of -C$\mathbf{R^{10dd}}$- and N (nitrogen), each $\mathbf{R^{10dd}}$ is separately selected from the group consisting of H (hydrogen), halogen, cyano, C_1-C_6 alkyl optionally substituted with up to five fluoro, C_1-C_6 alkoxy optionally substituted with up to five fluoro, C_1-C_6 alkylC(=O)-

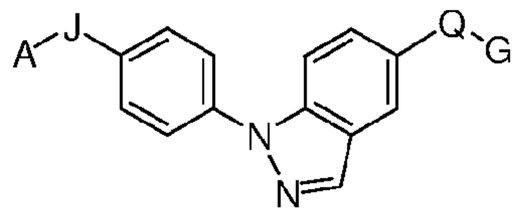
and C_3-C_7 cycloalkylC(=O)-, each $\mathbf{E^2}$ is separately selected from the group consisting of -$\mathbf{CR^7R^8}$- and $\mathbf{NR^9}$, $\mathbf{R^7}$ and $\mathbf{R^8}$ are each independently selected from the group consisting of hydrogen, –OH, and C_1-C_6 alkyl optionally substituted with up to five fluoro, or optionally $\mathbf{CR^7R^8}$ is -C(=O)-, and, $\mathbf{R^9}$ is selected from the group consisting of hydrogen, C_3-C_7cycloalkylC(O)- and C_1-C_6 alkylC(O)-, and C_1-C_6 alkyl optionally substituted with up to five fluoro.

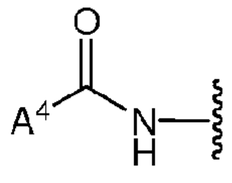
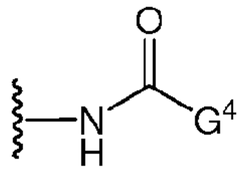
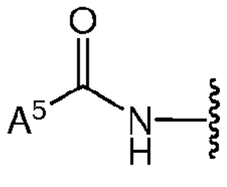
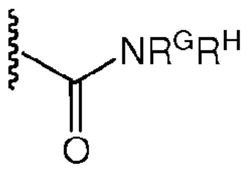
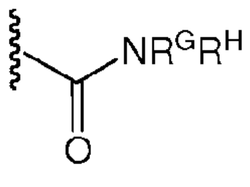
[0054] Some embodiments disclosed herein provide a compound of Formula

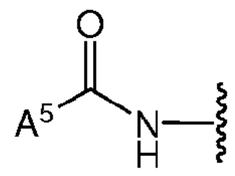


VIIIb having the formula **VIIIbb:** (**VIIIbb**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{E^{1A}}$ is N (nitrogen) and $\mathbf{E^{1B}}$ is -CH-, or $\mathbf{E^{1A}}$ is -CH- and $\mathbf{E^{1B}}$ is -CH-, or $\mathbf{E^{1A}}$ is -CH- and $\mathbf{E^{1B}}$ is N (nitrogen); and **A–J** is  and **Q–G** is  , or **A–J** is  and **Q–G** is  , or **A–J** is  and **Q–G** is  .

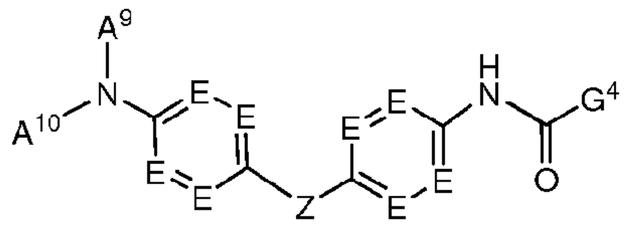
[0055] Some embodiments disclosed herein provide a compound of Formula



VIIIbb having the formula **VIIIbbb:** (**VIIIbbb**), and pharmaceutically acceptable salts thereof, wherein **A–J** is  and **Q–G** is  , or **A–J** is  and **Q–G** is  , or **A–J** is  and

Q–G is  , $\mathbf{A^4}$ is selected from the group consisting of C_5-C_7 cycloalkenyl, C_3-C_6 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, -$N\mathbf{R^P R^L}$, heterocycle, aryl, and heteroaryl, said C_5-C_7 cycloalkenyl, C_3-C_6 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, each $\mathbf{R^1}$ is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl, each $\mathbf{R^2}$ is separately selected from the group consisting of -$O(CH_2)_m\mathbf{O R^I}$, -$(CH_2)_m\mathbf{O R^I}$, –$N\mathbf{R^J R^K}$, –$(CH_2)_m\mathbf{S R^I}$, -$C(=O)\mathbf{R^L}$, and –$(CH_2)_m\mathbf{R^L}$, each $\mathbf{R^3}$ is separately selected from the group consisting of -$(CH_2)_m\mathbf{O R^G}$, -$N\mathbf{R^L}C(=O)\mathbf{R^M}$, -$N\mathbf{R^L}C(=O)\mathbf{O R^M}$, -$N\mathbf{R^L}C(=O)N\mathbf{R^N R^O}$, -$N\mathbf{R^N R^O}$, -$(CH_2)_m S(O)_{0\text{-}2}\mathbf{R^M}$, -$(CH_2)_m NHS(O)_{0\text{-}2}\mathbf{R^M}$, –$(CH_2)_m NO_2$, –$(CH_2)_m CN$, –$(CH_2)_m\mathbf{R^P}$, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^3}$ are each optionally substituted with halogen, hydroxy, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, –$C(=O)\mathbf{O R^M}$, or –$N\mathbf{R^J R^K}$, $\mathbf{G^4}$ is selected from the group consisting of aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, each $\mathbf{R^4}$ is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 heteroalkyl, each $\mathbf{R^5}$ is separately selected from the group consisting of halogen, -$(CH_2)_m$OH, –$N\mathbf{R^J R^K}$, and -$(CH_2)_m C(=O)\mathbf{R^L}$, each $\mathbf{R^L}$ is independently selected from the group consisting of -OH, C_1-C_6 alkyl, and C_1-C_6 alkoxy, each $\mathbf{R^6}$ is separately selected from the group consisting of -$N\mathbf{R^L}C(=O)\mathbf{R^M}$, -$N\mathbf{R^L}C(=O)\mathbf{O R^M}$, -$N\mathbf{R^L}C(=O)N\mathbf{R^N R^O}$, -$N\mathbf{R^N R^O}$, -$(CH_2)_m\mathbf{R^P}$, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^6}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, -$C(=O)\mathbf{O R^M}$, or –$N\mathbf{R^J R^K}$, $\mathbf{R^G}$ within the definition of –$N\mathbf{R^G R^H}$ is heteroaryl optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, and $\mathbf{R^H}$ within the definition of –$N\mathbf{R^G R^H}$ is hydrogen.

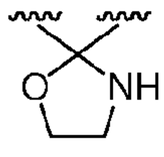
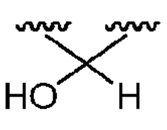
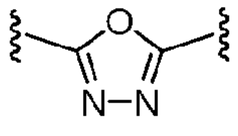
[0056] Some embodiments disclosed herein provide a compound of Formula **IX**:



(IX)

[0057] and pharmaceutically acceptable salts thereof;

[0058] wherein:

[0059] **Z** is  ,  ,  , or -C(=$\mathbf{E}^3$)-;

[0060] each **E** is separately selected from the group consisting of -C$\mathbf{R}^{10a}$- and N (nitrogen);

[0061] each $\mathbf{R}^{10a}$ is separately selected from the group consisting of H (hydrogen), halogen, C_1-C_6 alkyl optionally substituted with up to five fluoro, and C_1-C_6 alkoxy optionally substituted with up to five fluoro;

[0062] $\mathbf{E}^3$ is O (oxygen), N-NH$\mathbf{R}^{Q}$ or N-O$\mathbf{R}^{Q}$ where $\mathbf{R}^{Q}$ in the definition of $\mathbf{E}^3$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, -$(CH_2)_m\mathbf{R}^{RA}$, and -C(=O)$(CH_2)_m\mathbf{R}^{RA}$;

[0063] $\mathbf{R}^{RA}$ is selected from the group consisting of C_1-C_6 alkyl, aryl, and heteroaryl;

[0064] $\mathbf{A}^9$ is hydrogen or C_1-C_6 alkyl;

[0065] $\mathbf{A}^{10}$ is selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, -C(=O)$\mathbf{R}^{A}$, -C(=O)C(=O)$\mathbf{R}^{A}$,-$(CH_2)\mathbf{R}^{B}$, -(CH_2)O$\mathbf{R}^{B}$;

[0066] $\mathbf{R}^{A}$ is selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, heterocycle, polycyclic heterocyclyl, aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R}^1$, $\mathbf{R}^2$, and $\mathbf{R}^3$;

[0067] $\mathbf{R}^{B}$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, and heteroaryl;

[0068] $\mathbf{G}^4$ is selected from the group consisting of polycyclic heterocyclyl, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R}^4$, $\mathbf{R}^5$, and $\mathbf{R}^6$;

[0069] each $\mathbf{R}^1$ is separately selected from the group consisting of halogen, cyano, C_1-C_6 heteroalkyl, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, optionally substituted C_3-C_7 cycloalkenyl, an

optionally substituted C_1-C_6 haloalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0070] each $\mathbf{R^2}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, $-(CH_2)_mSR^I$, $-C(=O)R^L$, $-(CH_2)_mR^L$, C_1-C_6 heteroalkyl, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_3-C_7 cycloalkyl where said C_3-C_7 cycloalkyl is further optionally fused with aryl or heteroaryl;

[0071] each $\mathbf{R^3}$ is separately selected from the group consisting of halogen, $-(CH_2)_mOR^G$, $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mS(O)_{0-2}R^M$, $-(CH_2)_mNHS(O)_{0-2}R^M$,$-(CH_2)_mCN$, $-(CH_2)_mR^P$, C_1-C_6 alkyl C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^3}$ are each optionally substituted with halogen, hydroxy, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-C(=O)OR^M$, or $-NR^JR^K$;

[0072] each $\mathbf{R^4}$ is separately selected from the group consisting of halogen, cyano, C_1-C_6 heteroalkyl, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0073] each $\mathbf{R^5}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, $-(CH_2)_mSR^I$, $-(CH_2)_mC(=O)R^L$, $-(CH_2)_mR^L$, C_1-C_6 heteroalkyl, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_3-C_7 cycloalkyl, and an optionally substituted C_1-C_6 haloalkyl;

[0074] each $\mathbf{R^6}$ is separately selected from the group consisting of halogen, $-(CH_2)_mOR^G$, $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mS(O)_{0-2}R^M$, $-(CH_2)_mNHS(O)_{0-2}R^M$,$-(CH_2)_mCN$, $-(CH_2)_mR^P$, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^6}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-C(=O)OR^M$, or $-NR^JR^K$;

[0075] $\mathbf{R^G}$ is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_3-C_8 cycloalkenyl, C_1-C_6 heteroalkyl, C_1-C_6 heteroalkenyl, C_1-C_6 heteroalkynyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{R^G}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle, or $\mathbf{R^G}$ is -$\mathbf{OR^L}$ or -$\mathbf{NR^PR^L}$;

[0076] each $\mathbf{R^I}$ is separately selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl;

[0077] each –$\mathbf{NR^JR^K}$ is separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, –$(CH_2)_m\mathbf{OR^{JA}}$, –$(CH_2)_m\mathbf{NR^{JB}R^{JC}}$, –$(CH_2)_m\mathbf{R^R}$, C_3-C_7 cycloalkyl, heterocycle, aryl and heteroaryl, said C_3-C_7 cycloalkyl, heterocycle, aryl and heteroaryl in the definition of $\mathbf{R^J}$ and $\mathbf{R^K}$ are each independently optionally substituted with one or more substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, aryl and heteroaryl, said aryl and heteroaryl substituent off of $\mathbf{R^J}$ and $\mathbf{R^K}$ are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or -$(CH_2)_m\mathbf{NR^{KA}R^{KB}}$; or –$\mathbf{NR^JR^K}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0078] each $\mathbf{R^{JA}}$ is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0079] each –$\mathbf{NR^{JB}R^{JC}}$ is separately selected, wherein $\mathbf{R^{JB}}$ and $\mathbf{R^{JC}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0080] each –$\mathbf{NR^{KA}R^{KB}}$ is separately selected, wherein $\mathbf{R^{KA}}$ and $\mathbf{R^{KB}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0081] each $\mathbf{R^M}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, and –$(CH_2)_m\mathbf{R^P}$;

[0082] each $-NR^NR^O$ is separately selected, wherein R^N and R^O are each independently selected from the group consisting of hydrogen, $-(CH_2)_mNR^{NA}R^{NB}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of R^N and R^O are each independently optionally substituted with one or more substituents selected from the group consisting of $-(CH_2)_mNR^{OA}R^{OB}$, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, aryl and heteroaryl, said aryl and heteroaryl substituent off of R^N and R^O are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-NR^{NA}R^{NB}$,

[0083] each $-NR^{NA}R^{NB}$ is separately selected, wherein R^{NA} and R^{NB} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0084] each $-NR^{OA}R^{OB}$ is separately selected, wherein R^{OA} and R^{OB} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0085] R^P is selected from the group consisting of hydrogen and C_1-C_6 alkyl;

[0086] each R^L is independently selected from the group consisting of C_3-C_7 cycloalkyl, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, $-(CH_2)_mOR^{LA}$, $-(CH_2)_mNR^{LB}R^{LC}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of R^L are each independently optionally substituted with one or more substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-(CH_2)_mNR^{LD}R^{LE}$, aryl and heteroaryl, said aryl and heteroaryl substituent off of R^L are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-(CH_2)_mNR^{LF}R^{LG}$;

[0087] each R^{LA} is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0088] R^{LB} and R^{LC} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl, said C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl each optionally substituted with one or more halogen, cyano, or $-(CH_2)_mC(=O)OH$; or $-NR^{LB}R^{LC}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

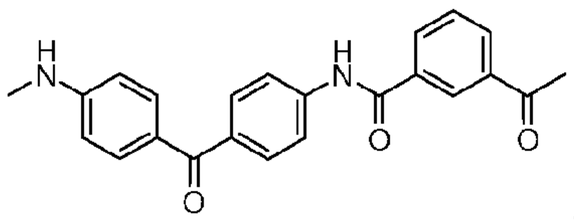
[0089] each $-NR^{LD}R^{LE}$ is separately selected, wherein R^{LD} and R^{LE} are each independently selected from the group consisting of hydrogen, aryl, heteroaryl, and optionally substituted C_1-C_6 alkyl, said aryl and heteroaryl in the definition of R^{LD} and R^{LE}

are each optionally substituted with C_1-C_6 alkyl or C_1-C_6 alkoxy; or $-NR^{LD}R^{LE}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0090] each $-NR^{LF}R^{LG}$ is separately selected, wherein R^{LF} and R^{LG} are each independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl; or $-NR^{LF}R^{LG}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0091] R^R is selected from the group consisting of C_1-C_6 alkyl, an optionally substituted aryl, and an optionally substituted heteroaryl; and

[0092] each **m** is independently 0, 1, 2, or 3, having the proviso that a compound of Formula **IX** is not selected from the group consisting of: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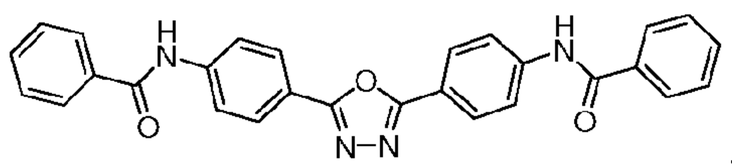
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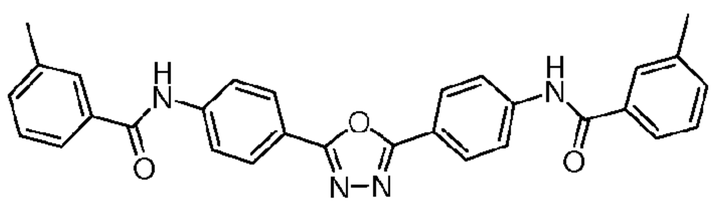
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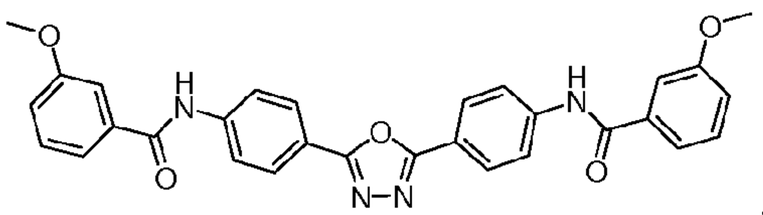
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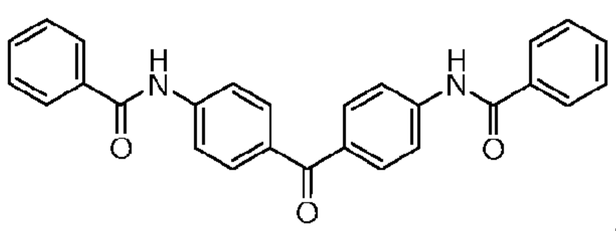
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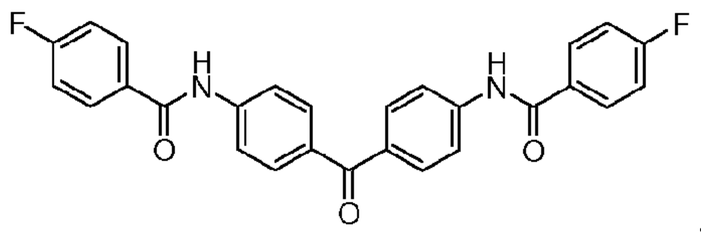
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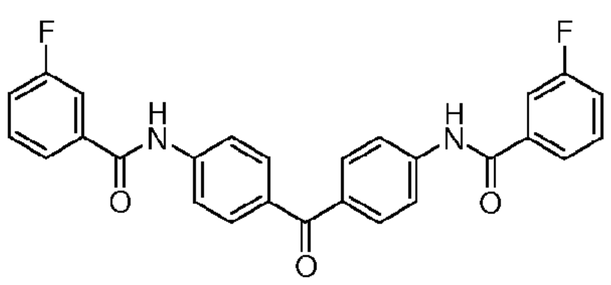
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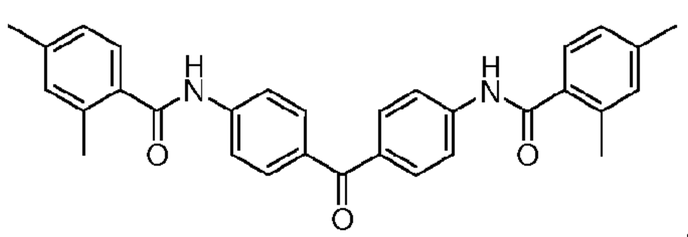
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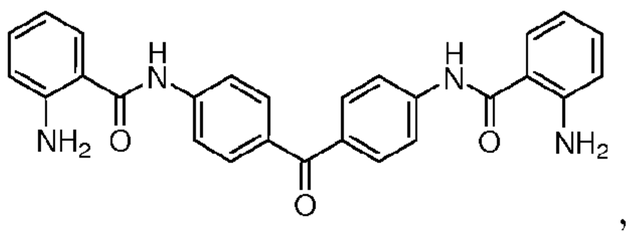
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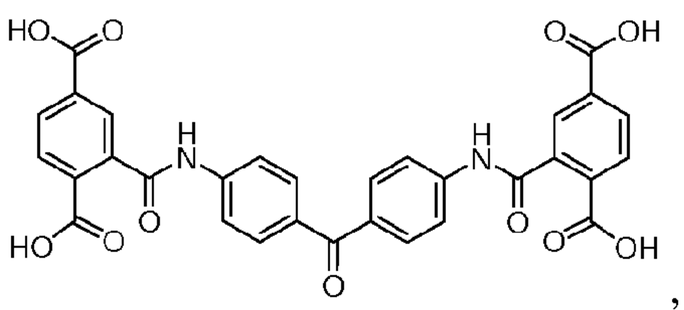
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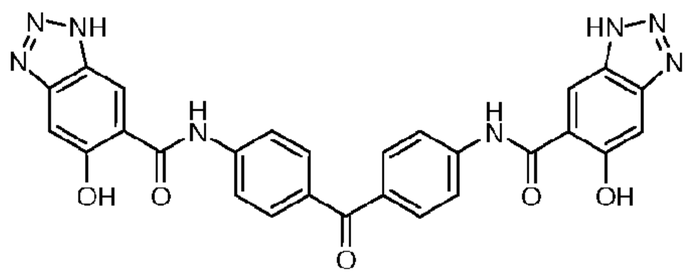
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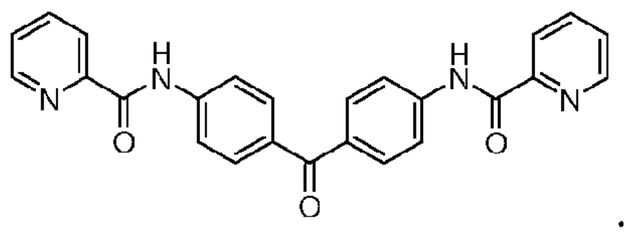
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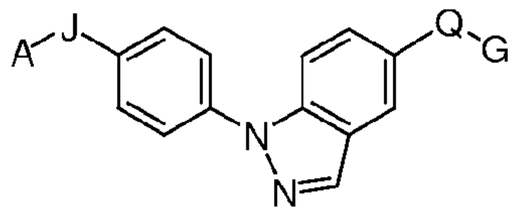
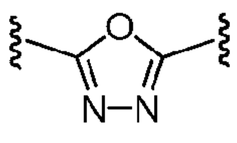
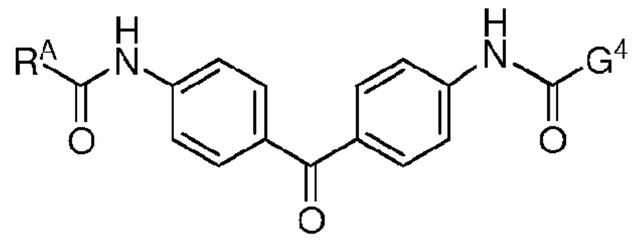
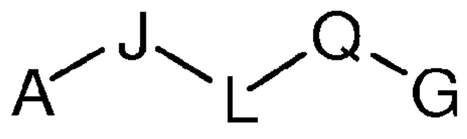
[0093] Some embodiments disclosed herein provide a compound of Formula **IX** having the formula **IXa:**  (**IXa**), and pharmaceutically acceptable salts thereof, wherein **Z** is  , or -C(=O)-, $\mathbf{R^A}$ is selected from the group consisting of heterocycle, polycyclic heterocyclyl, aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, each $\mathbf{R^1}$ is separately selected from the group consisting of chloro, cyano, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, and C_1-C_6 haloalkyl, each $\mathbf{R^2}$ is separately selected from the group consisting of $-O(CH_2)_mO\mathbf{R^I}$, $-(CH_2)_mO\mathbf{R^I}$, $-N\mathbf{R^J}\mathbf{R^K}$, $-(CH_2)_mS\mathbf{R^I}$, $-C(=O)\mathbf{R^L}$, and $-(CH_2)_m\mathbf{R^L}$, and each $\mathbf{R^3}$ is separately selected from the group consisting of $-(CH_2)_mO\mathbf{R^G}$, $-N\mathbf{R^L}C(=O)\mathbf{R^M}$, $-N\mathbf{R^L}C(=O)O\mathbf{R^M}$, $-N\mathbf{R^L}C(=O)N\mathbf{R^N}\mathbf{R^O}$, $-N\mathbf{R^N}\mathbf{R^O}$, $-(CH_2)_mS(O)_{0\text{-}2}\mathbf{R^M}$, $-(CH_2)_mNHS(O)_{0\text{-}2}\mathbf{R^M}$, $-(CH_2)_mCN$, $-(CH_2)_m\mathbf{R^P}$, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^3}$ are each optionally substituted with halogen, hydroxy, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-C(=O)O\mathbf{R^M}$, or $-N\mathbf{R^J}\mathbf{R^K}$.

[0094] Some embodiments disclosed herein provide a compound of Formula **IXa** having the formula **IXaa:**  (**IXaa**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{G^4}$ is selected from the group consisting of polycyclic heterocyclyl, aryl, and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, each $\mathbf{R^4}$ is separately selected from the group consisting of chloro, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl, each $\mathbf{R^5}$ is separately selected from the group consisting of $-O(CH_2)_mO\mathbf{R^I}$, $-(CH_2)_mO\mathbf{R^I}$, $-N\mathbf{R^J}\mathbf{R^K}$, $-(CH_2)_mS\mathbf{R^I}$, $-(CH_2)_mC(=O)\mathbf{R^L}$, $-(CH_2)_m\mathbf{R^L}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally

substituted C_2-C_6 alkenyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl, each $\mathbf{R^6}$ is separately selected from the group consisting of $-(CH_2)_mOR^G$, $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mS(O)_{0-2}R^M$, $-(CH_2)_mNHS(O)_{0-2}R^M$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, $-(CH_2)_mR^P$, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^6}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-C(=O)OR^M$, or $-NR^JR^K$.

[0095] Some embodiments disclosed herein provide a compound of Formula **IXa**, wherein each $\mathbf{R^1}$ is separately selected from the group consisting of cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl, each $\mathbf{R^2}$ is separately selected from the group consisting of $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, $-(CH_2)_mSR^I$, $-C(=O)R^L$, and $-(CH_2)_mR^L$, each $\mathbf{R^3}$ is separately selected from the group consisting of $-(CH_2)_mOR^G$, $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mS(O)_{0-2}R^M$, $-(CH_2)_mNHS(O)_{0-2}R^M$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, $-(CH_2)_mR^P$, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^3}$ are each optionally substituted with halogen, hydroxy, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-C(=O)OR^M$, or $-NR^JR^K$, each $\mathbf{R^4}$ is separately selected from the group consisting of cyano, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 heteroalkyl, each $\mathbf{R^5}$ is separately selected from the group consisting of $-(CH_2)_mOH$, $-NR^JR^K$, and $-(CH_2)_mC(=O)R^L$, each $\mathbf{R^L}$ is independently selected from the group consisting of -OH, C_1-C_6 alkyl, and C_1-C_6 alkoxy, and each $\mathbf{R^6}$ is separately selected from the group consisting of $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mR^P$, heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl, said heterocycle, aryl, polycyclic heterocyclyl, and heteroaryl in the definition of $\mathbf{R^6}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, $-C(=O)OR^M$, or $-NR^JR^K$.

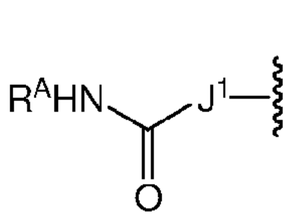
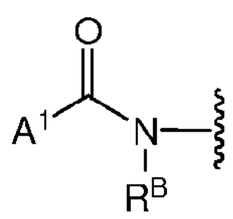
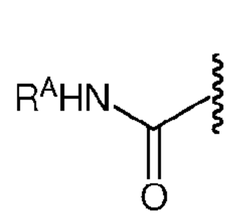
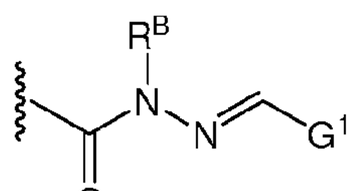
[0096] Some embodiments disclosed herein provide a compound of Formula **I**:

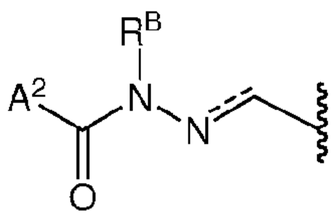
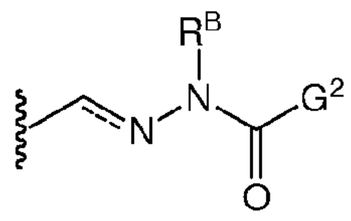


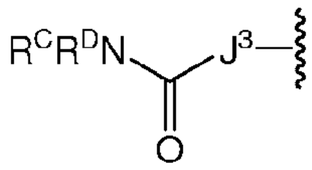
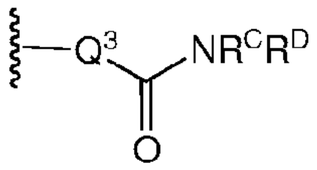
(I)

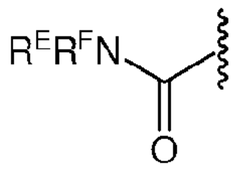
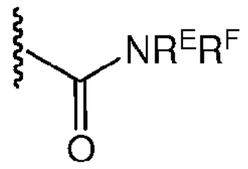
and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof;

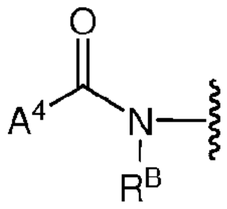
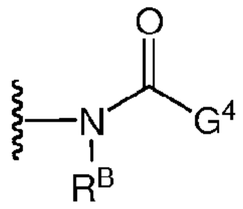
[0097] wherein:

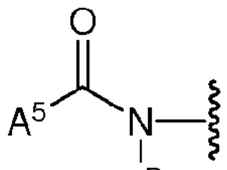
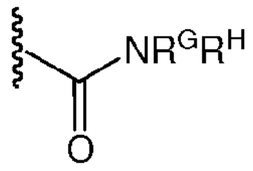
[0098] **A–J** is  ,  , or  and **Q–G** is  ;

[0099] or **A–J** is  and **Q–G** is  ;

[0100] or **A–J** is  and **Q–G** is  ;

[0101] or **A–J** is  and **Q–G** is  ;

[0102] or **A–J** is  and **Q–G** is  ;

[0103] or **A–J** is  and **Q–G** is  ;

[0104] $\mathbf{A^1}$ is selected from the group consisting of C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, $-(CH_2)_mNR^PR^L$, heterocycle, aryl, and heteroaryl, said C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^1}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0105] $\mathbf{J^1}$ is selected from the group consisting of $-(CH_2)_rN\mathbf{R^B}C(=O)(CH_2)_m-$ and $-(CH_2)_rN\mathbf{R^B}(CH_2)_m-$, and $-(CH_2)_r-$;

[0106] $\mathbf{G^1}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^1}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0107] $\mathbf{A^2}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^2}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0108] $\mathbf{G^2}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^2}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0109] $\mathbf{J^3}$ is selected from the group consisting of an optionally substituted aryl, $-(CH_2)_mN\mathbf{R^B}C(=O)(CH_2)_m-$, $-(CH_2)_rO(CH_2)_m-$, $-(CH_2)_rN\mathbf{R^B}(CH_2)_m-$, and $-(CH=CH)_m-$;

[0110] $\mathbf{Q^3}$ is selected from the group consisting of an optionally substituted aryl, $-(CH_2)_rN\mathbf{R^B}C(=O)(CH_2)_m-$, $-(CH_2)_rO(CH_2)_m-$, $-(CH_2)_rN\mathbf{R^B}(CH_2)_m-$, and $-(CH=CH)_r-$;

[0111] $\mathbf{A^4}$ is selected from the group consisting of C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, $-(CH_2)_mN\mathbf{R^P}\mathbf{R^L}$, heterocycle, aryl, and heteroaryl, said C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, and said aryl and heteroaryl in the definition of $\mathbf{A^4}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0112] $\mathbf{G^4}$ is selected from the group consisting of C_3-C_7 cycloalkenyl, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^4}$ are each further

optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0113] $\mathbf{A^5}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^5}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0114] $\mathbf{R^A}$ is selected from the group consisting of $-(CH_2)_p\mathbf{R^L}$, $-(CH_2)_p\mathbf{OR^L}$, $-SO_2\mathbf{R^L}$, $-C(=O)\mathbf{R^L}$, $-C(=O)N\mathbf{R^N R^O}$, $-(CH_2)_pN\mathbf{R^N R^O}$, an aryl and an heteroaryl, said aryl and heteroaryl in the definition of $\mathbf{R^A}$ are each optionally substituted with halogen, cyano, C_1-C_6 haloalkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, $-C(=O)N\mathbf{R^N R^O}$, $-OC(=O)N\mathbf{R^N R^O}$, $-NHC(=O)N\mathbf{R^N R^O}$, $-O(CH_2)_qN\mathbf{R^N R^O}$, $-NH(CH_2)_qN\mathbf{R^N R^O}$, $-(CH_2)_pN\mathbf{R^N R^O}$, an optionally substituted aryl and an optionally substituted heteroaryl, and said aryl and heteroaryl in the definition of $\mathbf{R^A}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0115] each $\mathbf{R^B}$ is separately selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_6 alkenyl, and an optionally substituted C_3-C_7 cycloalkyl;

[0116] each $-N\mathbf{R^C R^D}$ is separately selected, wherein each $\mathbf{R^C}$ is independently selected from the group consisting of hydrogen and an optionally C_1-C_6 alkyl, and each $\mathbf{R^D}$ is independently selected from the group consisting of aryl and heteroaryl, said aryl and heteroaryl in the definition of $\mathbf{R^D}$ are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, $-C(=O)N\mathbf{R^N R^O}$, $-OC(=O)N\mathbf{R^N R^O}$, $-NHC(=O)N\mathbf{R^N R^O}$, $-O(CH_2)_qN\mathbf{R^N R^O}$, $-NH(CH_2)_qN\mathbf{R^N R^O}$ $-(CH_2)_pN\mathbf{R^N R^O}$, an optionally substituted aryl and an optionally substituted heteroaryl, and said aryl and heteroaryl in the definition of $\mathbf{R^D}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0117] each $-N\mathbf{R^E R^F}$ is separately selected, wherein each $\mathbf{R^E}$ is independently selected from the group consisting of hydrogen and an optionally C_1-C_6 alkyl, and each $\mathbf{R^F}$ is independently selected from the group consisting of aryl and heteroaryl, said aryl and heteroaryl in the definition of $\mathbf{R^F}$ are each optionally substituted with halogen, cyano, C_1-C_6

alkyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, $-C(=O)NR^NR^O$, $-OC(=O)NR^NR^O$, $-NHC(=O)NR^NR^O$, $-O(CH_2)_qNR^NR^O$, $-NH(CH_2)_qNR^NR^O$ $-(CH_2)_pNR^NR^O$, an optionally substituted aryl and an optionally substituted heteroaryl, and said aryl and heteroaryl in the definition of R^F are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0118] R^G within the definition of $-NR^GR^H$ is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_3-C_8 cycloalkenyl, C_1-C_6 heteroalkyl, C_1-C_6 heteroalkenyl, C_1-C_6 heteroalkynyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of R^4, R^5, and R^6, said aryl and heteroaryl in the definition of R^G are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle, or R^G is $-OR^L$ or $-NR^PR^L$;

[0119] R^H within the definition of $-NR^GR^H$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_7 cycloalkyl, and C_1-C_3 haloalkyl, or $-NR^GR^H$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0120] each R^1 is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0121] each R^2 is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, $-(CH_2)_mSR^I$, $-C(=O)R^L$, $-(CH_2)_mR^L$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and an optionally substituted C_3-C_7 cycloalkyl where said C_3-C_7 cycloalkyl is further optionally fused with aryl or heteroaryl;

[0122] each R^3 is separately selected from the group consisting of halogen, $-(CH_2)_mOR^G$, $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mS(O)_{0-2}R^M$, $-(CH_2)_mNHS(O)_{0-2}R^M$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, $-(CH_2)_mR^P$, C_1-C_6 alkyl C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, heterocycle, aryl, and heteroaryl, said heterocycle, aryl and heteroaryl in the definition of R^3

are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-NR^JR^K$;

[0123] each R^4 is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0124] each R^5 is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, $-(CH_2)_mSR^I$, $-C(=O)R^L$, $-(CH_2)_mR^L$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0125] each R^6 is separately selected from the group consisting of halogen, $-(CH_2)_mOR^G$, $-NR^LC(=O)R^M$, $-NR^LC(=O)OR^M$, $-NR^LC(=O)NR^NR^O$, $-NR^NR^O$, $-(CH_2)_mS(O)_{0-2}R^M$, $-(CH_2)_mNHS(O)_{0-2}R^M$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, $-(CH_2)_mR^P$, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, and heteroaryl, said heterocycle, aryl and heteroaryl in the definition of R^6 are each optionally substituted with halogen, cyano, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-NR^JR^K$;

[0126] each R^I is separately selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl;

[0127] each $-NR^JR^K$ is separately selected, wherein R^J and R^K are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, $-(CH_2)_mOR^{JA}$, $-(CH_2)_mNR^{JB}R^{JC}$, $-(CH_2)_mR^R$, C_3-C_7 cycloalkyl, heterocycle, aryl and heteroaryl, said C_3-C_7 cycloalkyl, heterocycle, aryl and heteroaryl in the definition of R^J and R^K are each independently optionally substituted with one or more substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, aryl and heteroaryl, said aryl and heteroaryl substituent off of R^J and R^K are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-(CH_2)_mNR^{KA}R^{KB}$; or $-NR^JR^K$ is an optionally substituted non-aromatic

heterocycle linked through a ring nitrogen atom; or $-NR^JR^K$ is an optionally substituted C_1-C_6 alkylideneamino;

[0128] each R^{JA} is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0129] each $-NR^{JB}R^{JC}$ is separately selected, wherein R^{JB} and R^{JC} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0130] each $-NR^{KA}R^{KB}$ is separately selected, wherein R^{KA} and R^{KB} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0131] each R^M is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, and $-(CH_2)_mR^P$;

[0132] each $-NR^NR^O$ is separately selected, wherein R^N and R^O are each independently selected from the group consisting of hydrogen, $-(CH_2)_mNR^{NA}R^{NB}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of R^N and R^O are each independently optionally substituted with one or more substituents selected from the group consisting of $-(CH_2)_mNR^{OA}R^{OB}$, halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, aryl and heteroaryl, said aryl and heteroaryl substituent off of R^N and R^O are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or $-NR^{NA}R^{NB}$,

[0133] each $-NR^{NA}R^{NB}$ is separately selected, wherein R^{NA} and R^{NB} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0134] each $-NR^{OA}R^{OB}$ is separately selected, wherein R^{OA} and R^{OB} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0135] R^P is selected from the group consisting of hydrogen and C_1-C_6 alkyl;

[0136] R^L is selected from the group consisting of C_3-C_7 cycloalkyl, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, $-(CH_2)_mOR^{LA}$, $-(CH_2)_mNR^{LB}R^{LC}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of R^L are each independently optionally substituted with one or more substituents selected from the group

consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, -$(CH_2)_m$N$\mathbf{R^{LD}R^{LE}}$, aryl and heteroaryl, said aryl and heteroaryl substituent off of $\mathbf{R^L}$ are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or -$(CH_2)_m$N$\mathbf{R^{LF}R^{LG}}$;

[0137] $\mathbf{R^{LA}}$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0138] $\mathbf{R^{LB}}$ and $\mathbf{R^{LC}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl; or –N$\mathbf{R^{LB}R^{LC}}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0139] each –N$\mathbf{R^{LD}R^{LE}}$ is separately selected, wherein $\mathbf{R^{LD}}$ and $\mathbf{R^{LE}}$ are each independently selected from the group consisting of hydrogen, aryl, heteroaryl, and optionally substituted C_1-C_6 alkyl, said aryl and heteroaryl in the definition of $\mathbf{R^{LD}}$ and $\mathbf{R^{LE}}$ are each optionally substituted with C_1-C_6 alkyl or C_1-C_6 alkoxy; or –N$\mathbf{R^{LD}R^{LE}}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0140] each –N$\mathbf{R^{LF}R^{LG}}$ is separately selected, wherein $\mathbf{R^{LF}}$ and $\mathbf{R^{LG}}$ are each independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl; or -N$\mathbf{R^{LF}R^{LG}}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0141] **L** is selected from the group consisting of -O(CH_2)$_p$O-, C_1-C_7 alkyl, C_1-C_7 heteroalkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, an optionally substituted heterocycle, an optionally substituted aryl, and an optionally substituted heteroaryl, or **L** is selected from the group consisting of $\mathbf{L^1}$–$\mathbf{L^2}$, $\mathbf{L^1}$-O–$\mathbf{L^2}$, $\mathbf{L^1}$–S–$\mathbf{L^2}$, $\mathbf{L^1}$–N$\mathbf{R^9}$–$\mathbf{L^2}$, $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$, $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$–$\mathbf{L^4}$, $\mathbf{L^1}$-C(=E)–$\mathbf{L^2}$, and $\mathbf{L^1}$–C$\mathbf{R^7R^8}$–$\mathbf{L^2}$;

[0142] $\mathbf{L^1}$ is selected from the group consisting of an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle;

[0143] $\mathbf{L^2}$ is selected from the group consisting of an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle;

[0144] $\mathbf{L^3}$ is selected from the group consisting of an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle;

[0145] $\mathbf{L^4}$ is an optionally substituted aryl;

[0146] **E** is O (oxygen), N-NH$\mathbf{R^Q}$ or N-O$\mathbf{R^Q}$ where $\mathbf{R^Q}$ in the definition of **E** is selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_6 alkenyl, -$(CH_2)_m\mathbf{R^R}$, and -C(=O)$(CH_2)_m\mathbf{R^R}$;

[0147] $\mathbf{R^R}$ is selected from the group consisting of C_1-C_6 alkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0148] $\mathbf{R^7}$ and $\mathbf{R^8}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, and –OH; or $C\mathbf{R^7R^8}$ is a three - to eight- membered optionally substituted carbocycle, which optionally has one to three additional hetero atoms incorporated in the ring;

[0149] $\mathbf{R^9}$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_3-C_7cycloalkylC(O)- and C_1-C_6 alkylC(O)-;

[0150] each **m** is independently 0, 1, 2, or 3;

[0151] each **p** is independently 0, 1, 2, 3, 4, 5, or 6;

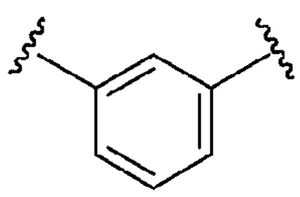
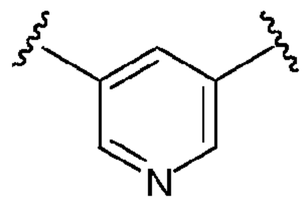
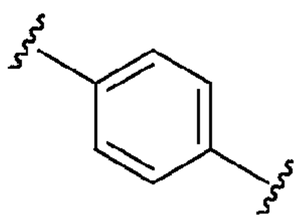
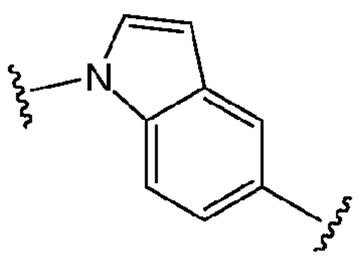
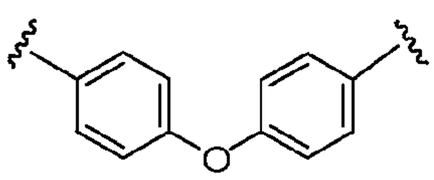
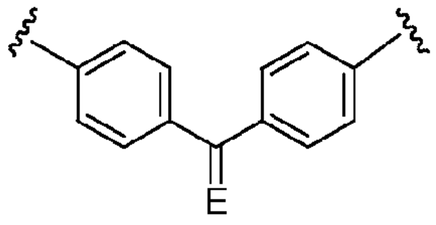
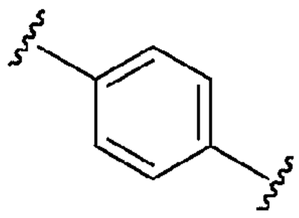
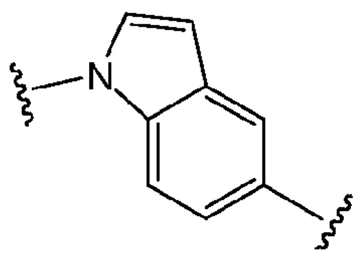
[0152] each **q** is independently 1, 2, 3, 4, 5, or 6;

[0153] each **r** is independently 1, 2, 3, or 4; and

[0154] any bond represented by a dashed and solid line represents a bond selected from the group consisting of a single bond and a double bond.

[0155] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{R^1}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^2}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^I}$, $-N\mathbf{R^JR^K}$, and $-(CH_2)_mS\mathbf{R^I}$; $\mathbf{R^3}$ can be selected from the group consisting of $-(CH_2)_m\mathbf{R^P}$, $-(CH_2)_mO\mathbf{R^M}$, and $-N\mathbf{R^NR^O}$; $\mathbf{R^4}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^5}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^I}$, $-N\mathbf{R^JR^K}$, and $-(CH_2)_mS\mathbf{R^I}$; $\mathbf{R^6}$ can be selected from the group consisting of $-(CH_2)_m\mathbf{R^P}$, $-(CH_2)_mO\mathbf{R^M}$, and $-N\mathbf{R^NR^O}$; $\mathbf{R^I}$ can be selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkyl; each $-N\mathbf{R^JR^K}$ can be separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ can each be independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkyl; or $-N\mathbf{R^JR^K}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-N\mathbf{R^JR^K}$ can be an optionally substituted C_1-C_6 alkylideneamino; each $\mathbf{R^M}$ can be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_m\mathbf{R^P}$; $\mathbf{R^L}$ canbe selected from the group consisting of hydrogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, and an optionally substituted aryl or an optionally substituted heteroaryl; and **m** can be 0, 1, or 2.

[0156] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{G^1}$ can be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^1}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{A^2}$ can be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^2}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{G^2}$ can be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^2}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{A^4}$ can be selected from the group consisting of C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, $-(CH_2)_m\mathbf{NR^PR^L}$, heterocycle, aryl, and heteroaryl, said C_3-C_7 cycloalkenyl, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkenyl, heterocycle, aryl, and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^4}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{G^4}$ can be selected from the group consisting of C_3-C_7 cycloalkenyl, aryl, and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^4}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{A^5}$ canbe selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^5}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{R^1}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^2}$ can be selected from the group consisting of $-(CH_2)_m\mathbf{OR^I}$ and $-\mathbf{NR^JR^K}$; $\mathbf{R^3}$ can be $-\mathbf{R^P}$; $\mathbf{R^4}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^5}$ can be selected from the group consisting of $-(CH_2)_m\mathbf{OR^I}$ and $-\mathbf{NR^JR^K}$; $\mathbf{R^6}$ can be $-\mathbf{R^P}$; and $\mathbf{R^L}$ can be selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, an optionally substituted aryl and an optionally substituted heteroaryl.

[0157] Some embodiments disclosed herein provide a compound of Formula **I**, wherein **L** can be selected from the group consisting of an optionally substituted  , an optionally substituted  , an optionally substituted  , an optionally substituted  ,  , and  ; and **E** can be O (oxygen), N-NH$\mathbf{R^Q}$ or N-O$\mathbf{R^Q}$ where $\mathbf{R^Q}$ in the definition of **E** can be selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, -$\mathbf{R^R}$, and -C(=O)$\mathbf{R^R}$. In some embodiments, **L** can be selected from the group consisting of an optionally substituted  and an optionally substituted  ; each $\mathbf{R^1}$ can be separately selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^2}$ can be separately selected from the group consisting of halogen, -$(CH_2)_m$O$\mathbf{R^I}$, and -N$\mathbf{R^B R^C}$, where $\mathbf{R^I}$ in the definition of can be $\mathbf{R^2}$ selected from the group consisting of hydrogen, and C_1-C_6 alkyl; each $\mathbf{R^3}$ can be fluoro; each –N$\mathbf{R^J R^K}$ canbe separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ can each be independently selected from the group consisting of hydrogen and C_1-C_6 alkyl; or -N$\mathbf{R^J R^K}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each $\mathbf{R^4}$ can be separately selected selected from the group consisting of chloro, fluoro, and an optionally substituted C_1-C_6 alkyl; each $\mathbf{R^5}$ can be separately selected from the group consisting of -OCH_2CH_2O$\mathbf{R^I}$, -$(CH_2)_m$O$\mathbf{R^I}$, and –N$\mathbf{R^J R^K}$, where $\mathbf{R^I}$ in the definition of canbe $\mathbf{R^5}$ selected from the group consisting of hydrogen, and C_1-C_6 alkyl; and each $\mathbf{R^6}$ can be separately selected from the group consisting an optionally substituted aryl and an optionally substituted heteroaryl.

[0158] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{A^1}$, $\mathbf{A^2}$, $\mathbf{A^4}$, and $\mathbf{A^5}$ can each be selected from the group consisting of phenyl, naphthyl, benzo[*d*][1,3]dioxolyl, indolyl, and benzo[d]imidazolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$ and $\mathbf{R^2}$; each $\mathbf{R^1}$ can be separately selected from the group consisting of phenyl, pyrrolyl, and imidazolyl, each optionally substituted with a substituent selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylHN– and (C_1-C_6 alkyl)$_2$N–; each $\mathbf{R^2}$ can be separately selected from the group consisting of bromo, chloro, fluoro, $-(CH_2)_m\mathbf{OR^I}$, $-(CH_2)_m\mathbf{R^L}$, and $-\mathbf{NR^JR^K}$, where each $\mathbf{R^I}$ in the definition of $\mathbf{R^2}$ can be separately selected from the group consisting of hydrogen and C_1-C_6 alkyl; each $-\mathbf{NR^JR^K}$ can be separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ can each be independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl optionally substituted with up to 3 fluoro; or $-\mathbf{NR^JR^K}$ can be a morpholinyl, piperazinyl, pyrrolidinyl, and piperidinyl, each optionally substituted with one or more oxo; each $\mathbf{R^L}$ can be separately selected from the group consisting aryl and heteroaryl, each optionally substituted with one or more substituents each separately selected from the group consisting of halogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, and C_1-C_6 alkoxy optionally substituted with up to 5 fluoro; $\mathbf{G^1}$, $\mathbf{G^2}$, and $\mathbf{G^4}$ can each be selected from the group consisting of: phenyl, naphthyl, benzo[*d*][1,3]dioxolyl, indolyl, and benzo[*d*]imidazolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$ and $\mathbf{R^5}$; each $\mathbf{R^4}$ can be separately selected from the group consisting of phenyl, pyrrolyl, and imidazolyl, each optionally substituted with a substituent selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylHN– and (C_1-C_6 alkyl)$_2$N–; and each $\mathbf{R^5}$ can be separately selected from the group consisting of bromo, chloro, fluoro, $-(CH_2)_m\mathbf{OR^I}$, and $-\mathbf{NR^JR^K}$, where each $\mathbf{R^I}$ in the definition of $\mathbf{R^5}$ can be separately selected from the group consisting of hydrogen and C_1-C_6 alkyl.

[0159] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{A^2}$ can be selected from the group consisting of phenyl, naphthyl, and, indolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$ and $\mathbf{R^2}$; each $\mathbf{R^1}$ can be separately selected from the group consisting of phenyl, pyrrolyl, and imidazolyl, each optionally substituted with a substituent selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylHN– and (C_1-C_6 alkyl)$_2$N–; each $\mathbf{R^2}$ can be separately selected from the group consisting of bromo, chloro, fluoro, $-(CH_2)_m\mathbf{OR^I}$, $-(CH_2)_m\mathbf{R^L}$, and $-\mathbf{NR^JR^K}$, where each $\mathbf{R^I}$ in the definition of $\mathbf{R^2}$ can be separately selected from the group consisting of

hydrogen and C_1-C_6 alkyl; each –N$\mathbf{R^J R^K}$ can be separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ can each be independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl optionally substituted with up to 3 fluoro; or –N$\mathbf{R^J R^K}$ can be a morpholinyl, piperazinyl, pyrrolidinyl, and piperidinyl, each optionally substituted with one or more oxo; each $\mathbf{R^L}$ can be separately selected from the group consisting aryl and heteroaryl, each optionally substituted with one or more substituents each separately selected from the group consisting of halogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, and C_1-C_6 alkoxy optionally substituted with up to 5 fluoro; $\mathbf{G^2}$ can be selected from the group consisting of: phenyl, naphthyl, and, indolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$ and $\mathbf{R^5}$; each $\mathbf{R^4}$ can be separately selected from the group consisting of phenyl, pyrrolyl, and imidazolyl, each optionally substituted with a substituent selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylHN– and $(C_1$-C_6 alkyl$)_2$N–; and each $\mathbf{R^5}$ can be separately selected from the group consisting of bromo, chloro, fluoro, -$(CH_2)_m$O$\mathbf{R^I}$, and –N$\mathbf{R^J R^K}$, where each $\mathbf{R^I}$ in the definition of $\mathbf{R^5}$ can be separately selected from the group consisting of hydrogen and C_1-C_6 alkyl.

[0160] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{A^1}$, $\mathbf{A^2}$, $\mathbf{A^4}$, and $\mathbf{A^5}$ can each be selected from the group consisting of selected from the group consisting of a phenyl, naphthyl, benzo[d][1,3]dioxolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$; and $\mathbf{G^1}$, $\mathbf{G^2}$, and $\mathbf{G^4}$ can each be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$ and each optionally fused with a nonaromatic heterocycle or carbocycle.

[0161] Some embodiments disclosed herein provide a compound of Formula **I**, wherein **L** can be selected from the group consisting of aryl, and heteroaryl, each substituted with one or more substituents each individually selected from the group consisting of alkyl, cycloalkyl, alkoxy, alkenylO–, arylC(=O)–, arylC(=O)NH–, arylNHC(=O)–, aryl$(CH_2)_{0-3}$O$(CH_2)_{0-3}$–, aryl$(CH_2)_{0-3}$NH$(CH_2)_{0-3}$–, HO$(CH_2)_{1-3}$NH–, HO$(CH_2)_{1-3}$O–, HO$(CH_2)_{1-3}$–, HO$(CH_2)_{1-3}$O$(CH_2)_{1-3}$–, and amino.

[0162] Some embodiments disclosed herein provide a compound of Formula **I**, wherein **L** can be $\mathbf{L^1}$–$\mathbf{L^2}$, or $\mathbf{L^1}$-O–$\mathbf{L^2}$, or $\mathbf{L^1}$–N$\mathbf{R^9}$–$\mathbf{L^2}$, or $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$, or $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$–$\mathbf{L^4}$, or $\mathbf{L^1}$-C(=E)–$\mathbf{L^2}$.

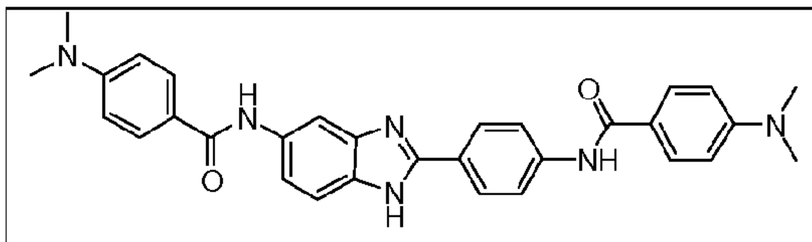
[0163] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{L^1}$ can be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents each individually selected from the group consisting of alkyl, cycloalkyl, alkoxy, alkenylO–, arylC(=O)–, arylC(=O)NH–, arylNHC(=O)–, aryl$(CH_2)_{0-3}O(CH_2)_{0-3}$–, aryl$(CH_2)_{0-3}NH(CH_2)_{0-3}$–, HO$(CH_2)_{1-3}$NH–, HO$(CH_2)_{1-3}$O–, HO$(CH_2)_{1-3}$–, HO$(CH_2)_{1-3}O(CH_2)_{1-3}$–, and amino.

[0164] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{L^2}$ can be selected from the group consisting of aryl, heteroaryl, and heterocyclyl, each substituted with one or more substituents each individually selected from the group consisting of alkyl, cycloalkyl, alkoxy, alkenylO–, arylC(=O)–, arylC(=O)NH–, arylNHC(=O)–, aryl$(CH_2)_{0-3}O(CH_2)_{0-3}$–, aryl$(CH_2)_{0-3}NH(CH_2)_{0-3}$–, HO$(CH_2)_{1-3}$NH–, HO$(CH_2)_{1-3}$O–, HO$(CH_2)_{1-3}$–, HO$(CH_2)_{1-3}O(CH_2)_{1-3}$–, and amino.

[0165] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{L^3}$ can be selected from the group consisting of aryl, heteroaryl, and heterocyclyl, each substituted with one or more substituents each individually selected from the group consisting of alkyl, cycloalkyl, alkoxy, alkenylO–, arylC(=O)–, arylC(=O)NH–, arylNHC(=O)–, aryl$(CH_2)_{0-3}O(CH_2)_{0-3}$–, aryl$(CH_2)_{0-3}NH(CH_2)_{0-3}$–, HO$(CH_2)_{1-3}$NH–, HO$(CH_2)_{1-3}$O–, HO$(CH_2)_{1-3}$–, HO$(CH_2)_{1-3}O(CH_2)_{1-3}$–, and amino.

[0166] Some embodiments disclosed herein provide a compound of Formula **I**, wherein $\mathbf{L^4}$ can be aryl substituted with one or more substituents each individually selected from the group consisting of alkyl, cycloalkyl, alkoxy, alkenylO–, arylC(=O)–, arylC(=O)NH-, arylNHC(=O)–, aryl$(CH_2)_{0-3}O(CH_2)_{0-3}$–, aryl$(CH_2)_{0-3}NH(CH_2)_{0-3}$–, HO$(CH_2)_{1-3}$NH–, HO$(CH_2)_{1-3}$O–, HO$(CH_2)_{1-3}$–, HO$(CH_2)_{1-3}O(CH_2)_{1-3}$–, and amino.

[0167] Some embodiments disclosed herein provide a compound of Formula **I**, having the proviso that a compound for Formula **I** is not selected from the group consisting of: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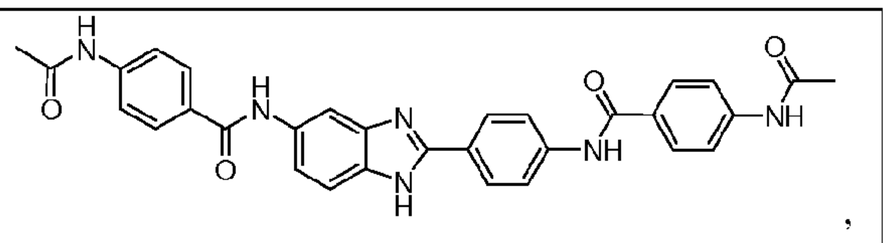
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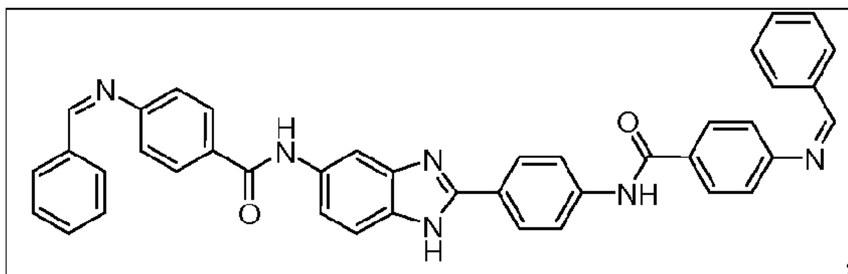
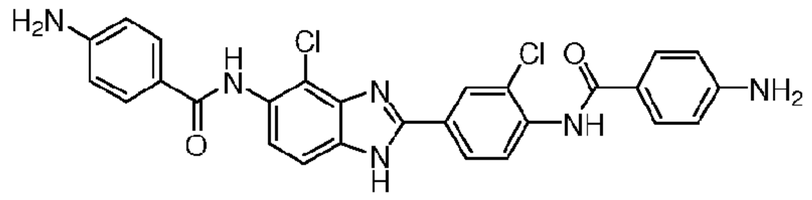
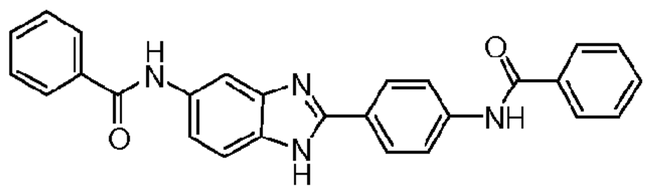
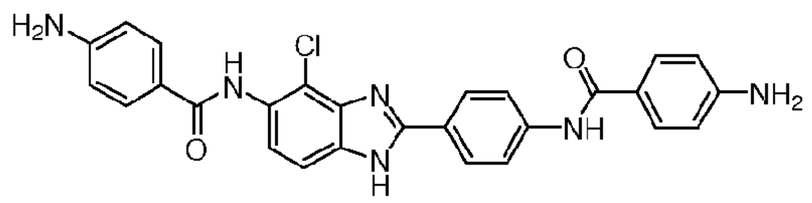
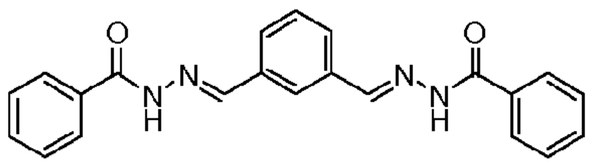
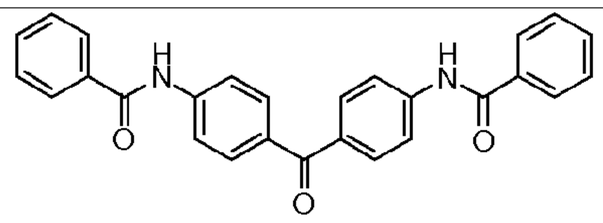
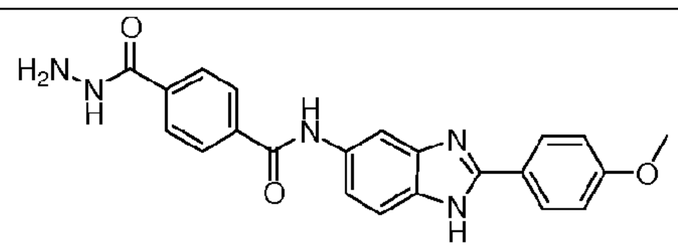
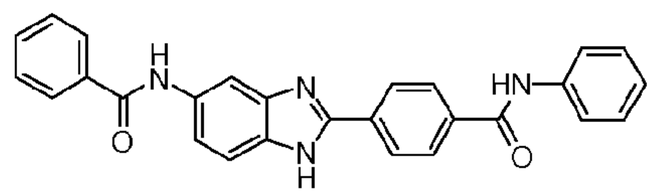
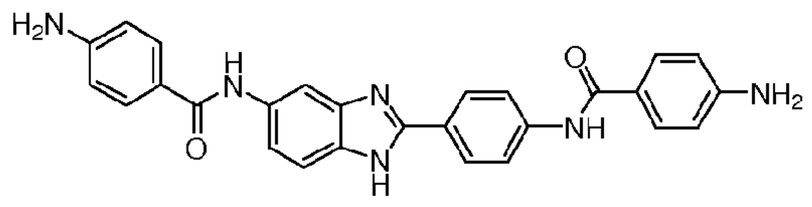
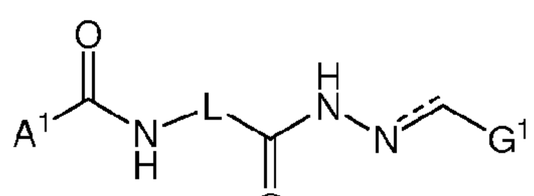
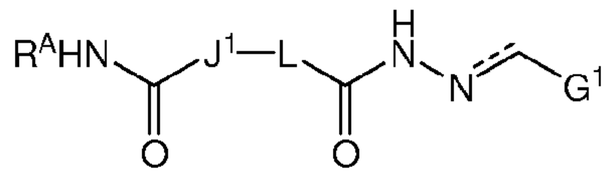
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
and	 .

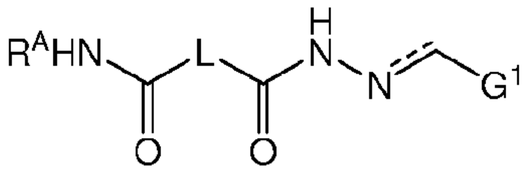
[0168] Some embodiments disclosed herein provide a compound of Formula **I**



having the formula **Ia:** (**Ia**), and pharmaceutically

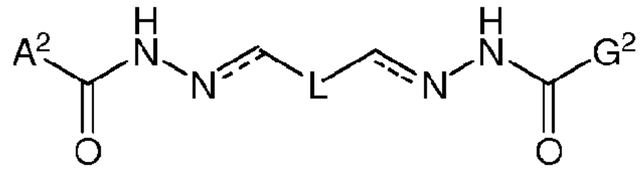


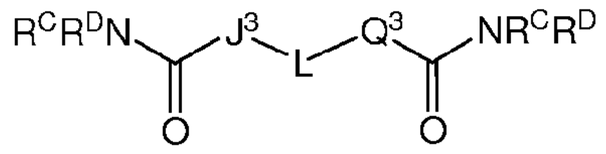
acceptable salts thereof, having the formula **Ib:** (**Ib**), and pharmaceutically acceptable salts thereof, or having the formula **Ic:**



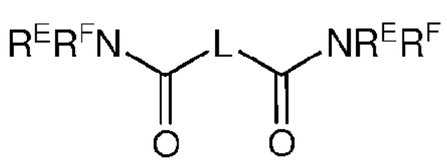
(**Ic**), and pharmaceutically acceptable salts thereof.

[0169] Some embodiments disclosed herein provide a compound of Formula **Ia**, **Ib**, **Ic**, or **Id**, wherein **L** can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl.

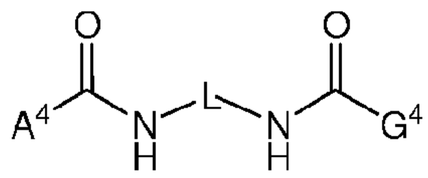
[0170] Some embodiments disclosed herein provide a compound of Formula **I** having the formula **Id:**  (**Id**), and pharmaceutically acceptable salts thereof.

[0171] Some embodiments disclosed herein provide a compound of Formula **I** having the structure of Formula **Ie:**  (**Ie**) and pharmaceutically acceptable salts thereof.

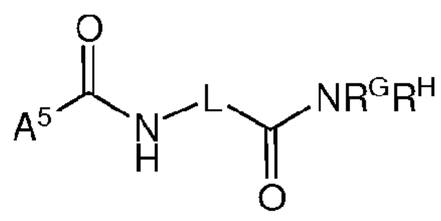
[0172] Some embodiments disclosed herein provide a compound of Formula **Ie**, wherein **L** can be selected from the group consisting of -O$(CH_2)_p$O-, an optionally substituted aryl, and an optionally substituted heteroaryl, or **L** is $\mathbf{L^1}$-$\mathbf{L^2}$; $\mathbf{J^3}$ can be selected from the group consisting of an optionally substituted aryl, -$(CH_2)_m$N$\mathbf{R^B}$C(=O)–, -$(CH_2)_r$O–, and –$(CH{=}CH)_m$–; $\mathbf{Q^3}$ can be selected from the group consisting of an optionally substituted aryl, -$(CH_2)_r$N$\mathbf{R^B}$C(=O)–, -$(CH_2)_r$O–, and –$(CH{=}CH)_r$–; $\mathbf{L^1}$ can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl; and $\mathbf{L^2}$ can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl. In some embodiments, **L** can be -O$(CH_2)_p$O-.

[0173] Some embodiments disclosed herein provide a compound of Formula **I** having the structure of Formula **If:**  (**If**), and pharmaceutically acceptable salts thereof.

[0174] Some embodiments disclosed herein provide a compound of Formula **If**, wherein **L** can be selected from the group consisting of C_4-C_6 cycloalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl, or **L** is $\mathbf{L^1}$-$\mathbf{L^2}$; $\mathbf{L^1}$ can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl; and $\mathbf{L^2}$ can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl.

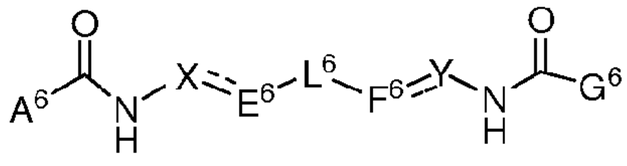
[0175] Some embodiments disclosed herein provide a compound of Formula **I** having the structure of Formula **Ig:**  (**Ig**), and pharmaceutically acceptable salts thereof.

[0176] Some embodiments disclosed herein provide a compound of Formula **Ig**, wherein **L** can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl, or **L** can be selected from the group consisting of $\mathbf{L^1}$–$\mathbf{L^2}$, $\mathbf{L^1}$-O–$\mathbf{L^2}$, $\mathbf{L^1}$–S–$\mathbf{L^2}$, $\mathbf{L^1}$–N$\mathbf{R^9}$–$\mathbf{L^2}$, $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$, $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$–$\mathbf{L^4}$, $\mathbf{L^1}$-C(=E)–$\mathbf{L^2}$, and $\mathbf{L^1}$–C$\mathbf{R^7R^8}$–$\mathbf{L^2}$; $\mathbf{L^1}$ can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl; $\mathbf{L^2}$ can be selected from the group consisting of an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle; $\mathbf{L^3}$ can be selected from the group consisting of an optionally substituted aryl, and an optionally substituted heteroaryl; and $\mathbf{L^4}$ is an optionally substituted aryl.

[0177] Some embodiments disclosed herein provide a compound of Formula **I** having the structure of Formula **Ih:**  (**Ih**), and pharmaceutically acceptable salts thereof.

[0178] Some embodiments disclosed herein provide a compound of Formula **Ih**, wherein **L** can be selected from the group consisting of an optionally substituted aryl or **L** can be selected from the group consisting of $\mathbf{L^1}$–$\mathbf{L^2}$, and $\mathbf{L^1}$–$\mathbf{L^2}$–$\mathbf{L^3}$; $\mathbf{L^1}$ can be an optionally substituted heteroaryl; $\mathbf{L^2}$ can be selected from the group consisting of an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle; and $\mathbf{L^3}$ can be an optionally substituted heterocycle.

[0179] Some embodiments disclosed herein provide a compound of Formula **II**:



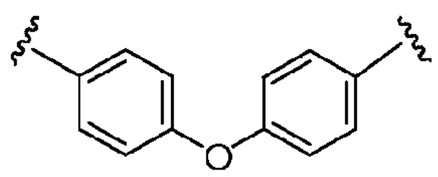
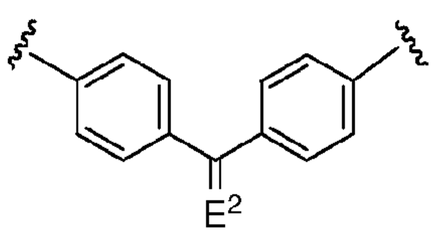
(**II**)

and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof;

wherein:

[0180] $\mathbf{A^6}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{11}}$, $\mathbf{R^{12}}$, and $\mathbf{R^{13}}$, said aryl and heteroaryl in the definition of $\mathbf{A^6}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0181] $\mathbf{G^6}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{14}}$, $\mathbf{R^{15}}$, and $\mathbf{R^{16}}$, said aryl and heteroaryl in the definition of $\mathbf{G^6}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0182] $\mathbf{L^6}$ is an optionally substituted aryl, or an optionally substituted heteroaryl; where the aryl and heteroaryl in the definition of $\mathbf{L^6}$ are optionally fused with a nonaromatic heterocycle or a nonaromatic carbocycle; or $\mathbf{L^6}$ is selected from the group consisting of an optionally substituted  , and an optionally substituted 

;

[0183] $\mathbf{E^2}$ is O (oxygen) or N-O$\mathbf{R^D}$ where $\mathbf{R^D}$ in the definition of $\mathbf{E^2}$ is selected from the group consisting of hydrogen and an optionally substituted C_1-C_6 alkyl;

[0184] each $\mathbf{R^{11}}$ is separately selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0185] each $\mathbf{R^{12}}$ is separately selected from the group consisting of $-O(CH_2)_mO\mathbf{R^A}$, $-(CH_2)_mO\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, and $-(CH_2)_mS\mathbf{R^A}$;

[0186] each $\mathbf{R^{13}}$ is separately selected from the group consisting of $-(CH_2)_mO\mathbf{R^D}$, $-N\mathbf{R^E}\mathbf{R^F}$, $-S(O)_{0\text{-}2}\mathbf{R^D}$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, and $-(CH_2)_m\mathbf{R^G}$;

[0187] each $\mathbf{R^{14}}$ is separately selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally

substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted aryl, and an optionally substituted heteroaryl;

[0188] each $\mathbf{R^{15}}$ is separately selected from the group consisting of $-O(CH_2)_mOR^A$, $-(CH_2)_mOR^A$, $-NR^BR^C$, and $-(CH_2)_mSR^A$;

[0189] each $\mathbf{R^{16}}$ is separately selected from the group consisting of $-(CH_2)_mOR^D$, $-NR^ER^F$, $-(CH_2)_mS(O)_{0-2}R^D$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, and $-(CH_2)_mR^G$;

[0190] $\mathbf{E^6}$ is CR^{17} when the dashed line between $\mathbf{E^6}$ and **X** represents a double bond; or $\mathbf{E^6}$ is $CR^{17}R^{17}$ when the dashed line between $\mathbf{E^6}$ and **X** represents a single bond;

[0191] $\mathbf{F^6}$ is CR^{18} when the dashed line between $\mathbf{F^6}$ and **Y** represents a double bond; or $\mathbf{F^6}$ is $CR^{18}R^{18}$ when the dashed line between $\mathbf{F^6}$ and **Y** represents a single bond;

[0192] each $\mathbf{R^{17}}$ is independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_1-C_4 alkoxy, an optionally substituted C_3-C_7 cycloalkyl, and an optionally substituted C_1-C_4 alkyl;

[0193] each $\mathbf{R^{18}}$ is independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_1-C_4 alkoxy, an optionally substituted C_3-C_7 cycloalkyl, and an optionally substituted C_1-C_4 alkyl;

[0194] $\mathbf{R^A}$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl;

[0195] each $-NR^BR^C$ is separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ are each independently selected from the group consisting of hydrogen, $-SO_2R^H$, $-C(=O)R^H$, $-C(=O)NR^ER^F$, heterocycle, C_1-C_6 alkyl, C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl, where the C_1-C_6 alkyl in the definition of $\mathbf{R^B}$ and $\mathbf{R^C}$ is optionally substituted with an optionally substituted aryl or an optionally substituted heteroaryl and where the C_3-C_7 cycloalkyl and the heterocycle in the definition of $\mathbf{R^B}$ and $\mathbf{R^C}$ are optionally fused with an aryl or heteroaryl; or $-NR^BR^C$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-NR^BR^C$ is an optionally substituted C_1-C_6 alkylideneamino;

[0196] each $\mathbf{R^D}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally

substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_m\mathbf{R^G}$;

[0197] each $-N\mathbf{R^E}\mathbf{R^F}$ is separately selected, wherein $\mathbf{R^E}$ and $\mathbf{R^F}$ are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_m\mathbf{R^G}$; or $-N\mathbf{R^E}\mathbf{R^F}$ is an optionally substituted C_1-C_6 alkylideneamino; or $-N\mathbf{R^E}\mathbf{R^F}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;$\mathbf{R^G}$ is selected from an optionally substituted aryl and an optionally substituted heteroaryl;

[0198] $\mathbf{R^H}$ is selected from the group consisting of hydrogen, C_1-C_3 alkyl, an optionally substituted C_1-C_3 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_3 haloalkyl, and an optionally substituted aryl or heteroaryl;

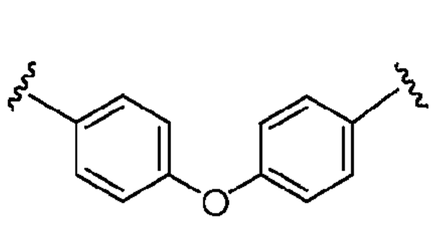
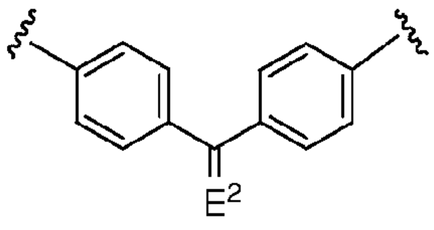
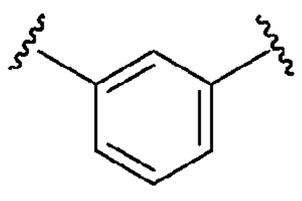
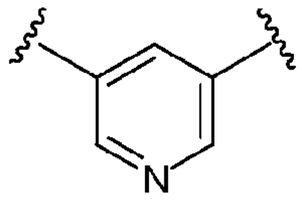
[0199] **X** and **Y** are independently selected from N (nitrogen), NH, $C\mathbf{R^{19}}$, and $C\mathbf{R^{19}}\mathbf{R^{20}}$;

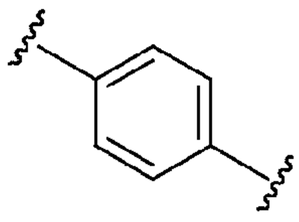
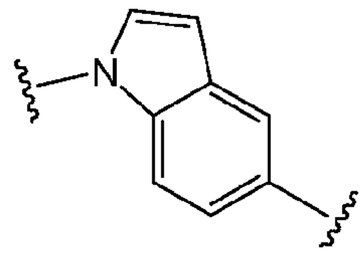
[0200] each $\mathbf{R^{19}}$ and $\mathbf{R^{20}}$ are independently selected from the group consisting of hydrogen and an optionally substituted C_1-C_4 alkyl;

[0201] each **m** is independently 0, 1, or 2; and

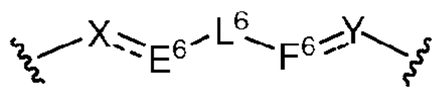
[0202] any bond represented by a dashed and solid line represents a bond selected from the group consisting of a single bond and a double bond.

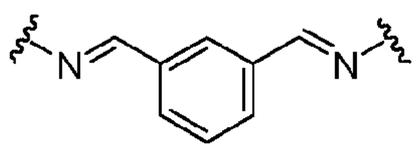
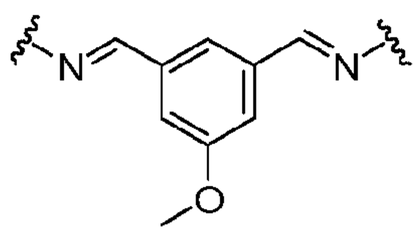
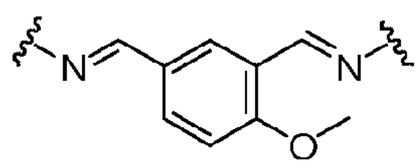
[0203] Some embodiments disclosed herein provide a compound of Formula **II**, wherein $\mathbf{A^6}$ can be selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{11}}$, $\mathbf{R^{12}}$, and $\mathbf{R^{13}}$, said aryl and heteroaryl in the definition of $\mathbf{A^6}$ can each be further optionally fused with a nonaromatic heterocycle or carbocycle; $\mathbf{L^6}$ can be selected from the group consisting of

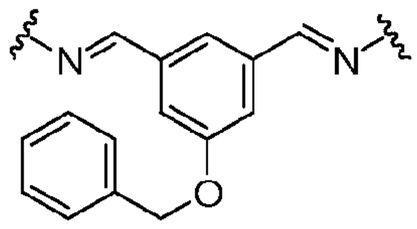
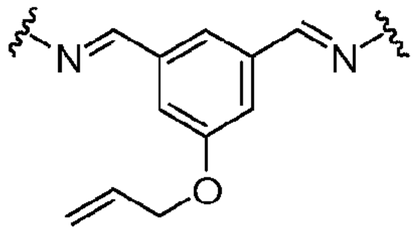
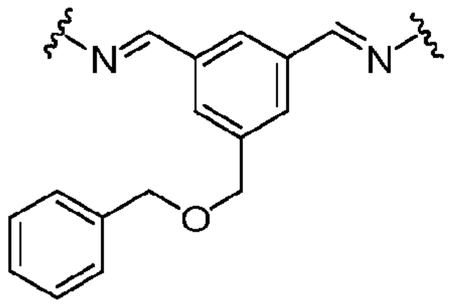

, 
, an optionally substituted 
, an optionally substituted 
, an optionally substituted

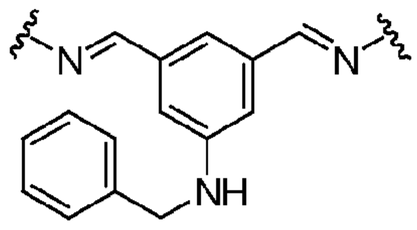
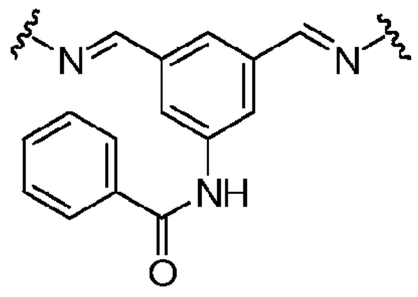
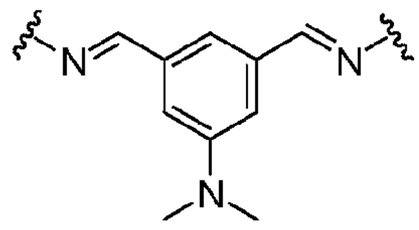

, and an optionally substituted 
; $\mathbf{E^2}$ can be O (oxygen) or N-O$\mathbf{R^D}$ where $\mathbf{R^D}$ in the definition of $\mathbf{E^2}$ can be selected from the group consisting of hydrogen and an optionally substituted C_1-C_6 alkyl; $\mathbf{G^6}$ can be selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{14}}$, $\mathbf{R^{15}}$, and $\mathbf{R^{16}}$, said aryl and heteroaryl in the definition of $\mathbf{G^6}$ can each be further optionally fused with a nonaromatic heterocycle or carbocycle; each $\mathbf{R^{11}}$ can be separately selected from the group consisting of fluoro, an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^{12}}$ can be separately selected from the group consisting of -O$(CH_2)_m$O$\mathbf{R^A}$, -$(CH_2)_m$O$\mathbf{R^A}$, and –N$\mathbf{R^B}\mathbf{R^C}$, where $\mathbf{R^A}$ in the definition of can be $\mathbf{R^{12}}$ selected from the group consisting of hydrogen, and C_1-C_6 alkyl; each $\mathbf{R^{13}}$ can be separately selected from the group consisting of –O$\mathbf{R^D}$, -N$\mathbf{R^E}\mathbf{R^F}$, –S$(O)_2\mathbf{R^D}$, –CN, and –$\mathbf{R^G}$; each –N$\mathbf{R^B}\mathbf{R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, C_3-C_7 cycloalkyl, C_1-C_6 alkyl, and C_1-C_6 haloalkyl, where the C_1-C_6 alkyl in the definition of $\mathbf{R^B}$ and $\mathbf{R^C}$ can be optionally substituted with an optionally substituted aryl or an optionally substituted heteroaryl, and where the C_3-C_7 cycloalkyl in the definition of $\mathbf{R^B}$ and $\mathbf{R^C}$ can be optionally fused with an optionally substituted aryl; or -N$\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; $\mathbf{R^H}$ can be selected from the group consisting of hydrogen, C_1-C_3 alkyl, an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^{14}}$ can be separately selected selected from the group consisting of chloro, fluoro, an optionally substituted C_1-C_6 alkyl, an optionally substituted aryl, and an optionally substituted heteroaryl; each $\mathbf{R^{15}}$ can be separately selected from the group consisting of-O$(CH_2)_m$O$\mathbf{R^A}$, -$(CH_2)_m$O$\mathbf{R^A}$, and –N$\mathbf{R^B}\mathbf{R^C}$, where $\mathbf{R^A}$ in the definition of $\mathbf{R^{15}}$ can be selected from the group consisting of hydrogen, and C_1-C_6 alkyl; and each $\mathbf{R^{16}}$ can be separately selected from the group consisting of –O$\mathbf{R^D}$, -N$\mathbf{R^E}\mathbf{R^F}$, -S$(O)_2\mathbf{R^D}$, –CN, and -$\mathbf{R^G}$. In some embodiments, $\mathbf{A^6}$ can be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{11}}$, $\mathbf{R^{12}}$, and $\mathbf{R^{13}}$, said aryl in the definition of $\mathbf{A^6}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{G^6}$ can be selected from the group

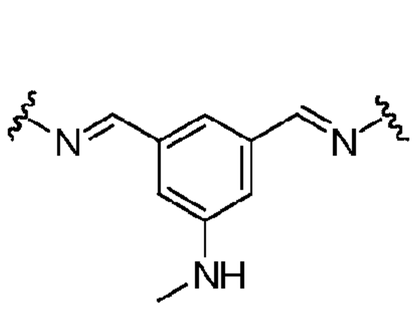
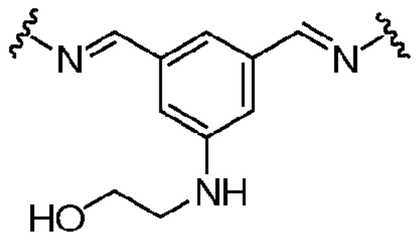
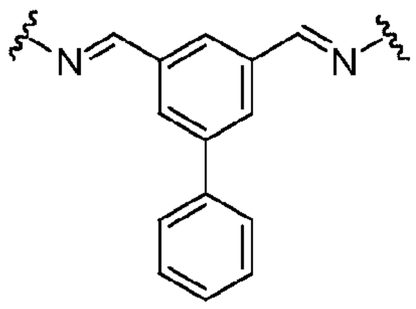
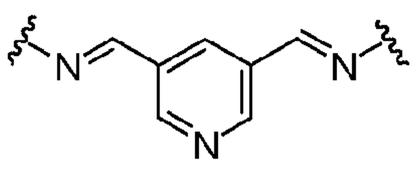
consisting of aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{14}}$, $\mathbf{R^{15}}$, and $\mathbf{R^{16}}$, said aryl and heteroaryl in the definition of $\mathbf{G^6}$ can each be further optionally fused with a nonaromatic heterocycle or carbocycle; each $\mathbf{R^{11}}$ can be separately selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^{12}}$ can be separately selected from the group consisting of $-(CH_2)_m\mathbf{OR^A}$, and $-\mathbf{NR^BR^C}$, where $\mathbf{R^A}$ in the definition of $\mathbf{R^{12}}$ can be selected from the group consisting of hydrogen, and C_1-C_6 alkyl; each $\mathbf{R^{13}}$ can be fluoro; each $-\mathbf{NR^BR^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, $-C(=O)\mathbf{R^H}$, and C_1-C_6 alkyl; or $-\mathbf{NR^BR^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each $\mathbf{R^{14}}$ can be separately selected selected from the group consisting of chloro, fluoro, an optionally substituted C_1-C_6 alkyl, an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^{15}}$ can be separately selected from the group consisting of $-OCH_2CH_2\mathbf{OR^A}$, $-(CH_2)_m\mathbf{OR^A}$, and $-\mathbf{NR^BR^C}$, where $\mathbf{R^A}$ in the definition of can be $\mathbf{R^{15}}$ selected from the group consisting of hydrogen, and C_1-C_6 alkyl; and each $\mathbf{R^{16}}$ can be fluoro.

[0204] Some embodiments disclosed herein provide a compound of Formula **II**, wherein  is selected from the group consisting of:

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,


, 
, 
, and 
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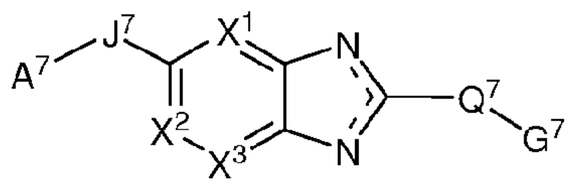
[0205] Some embodiments disclosed herein provide a compound of Formula **II**, wherein $\mathbf{A^6}$ can be selected from the group consisting of phenyl, naphthyl, benzo[*d*][1,3]dioxolyl, indolyl, and benzo[*d*]imidazolyl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{11}}$ and $\mathbf{R^{12}}$; each $\mathbf{R^{11}}$ can be separately selected from the group consisting of phenyl, pyrrolyl, and imidazolyl, each optionally substituted with a substituent selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylHN– and (C_1-C_6 alkyl)$_2$N–; each $\mathbf{R^{12}}$ can be separately selected from the group consisting of bromo, chloro, fluoro, $-(CH_2)_m\mathbf{OR^A}$, and $-\mathbf{NR^BR^C}$, where each $\mathbf{R^A}$ in the definition of $\mathbf{R^{12}}$ can be separately selected from the group consisting of hydrogen and C_1-C_6 alkyl; each $-\mathbf{NR^BR^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, $-C(=O)\mathbf{R^H}$, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, and an optionally substituted C_3-C_7 cycloalkyl further optionally fused with phenyl; or $-\mathbf{NR^BR^C}$ can be a morpholinyl, piperazinyl, pyrrolidinyl, and piperidinyl, each optionally substituted with one or more oxo; each $\mathbf{R^H}$ can be separately selected from the group consisting aryl and heteroaryl, each optionally substituted with one or more substituents each separately selected from the group consisting of halogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, and C_1-C_6 alkoxy optionally substituted with up to 5 fluoro; $\mathbf{G^6}$ canbe selected from the group consisting of: phenyl, naphthyl, benzo[*d*][1,3]dioxolyl, indolyl, and benzo[d]imidazolyl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{14}}$ and $\mathbf{R^{15}}$; each $\mathbf{R^{14}}$ can be separately selected from the group consisting of phenyl, pyrrolyl, and imidazolyl, each optionally substituted with a substituent selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylHN– and (C_1-C_6 alkyl)$_2$N–; and each $\mathbf{R^{15}}$ can be separately selected from the group consisting of bromo, chloro, fluoro, $-(CH_2)_m\mathbf{OR^A}$, and $-\mathbf{NR^BR^C}$, where each $\mathbf{R^A}$ in

the definition of $\mathbf{R^{15}}$ can be separately selected from the group consisting of hydrogen and C_1-C_6 alkyl.

[0206] Some embodiments disclosed herein provide a compound of Formula **III**:



(III)

and pharmaceutically acceptable salts, esters stereoisomers, tautomers or prodrugs thereof;

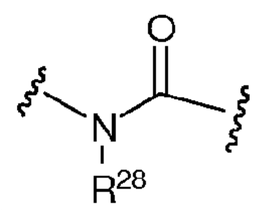
wherein:

[0207] $\mathbf{A^7}$ is selected from the group consisting of aryl, heteroaryl, isoindolinyl, indenyl, dihydroindenyl, tetrahydroisoquinolinyl, and tetrahydronaphthalenyl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$, said aryl and heteroaryl in the definition of $\mathbf{A^7}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; or $\mathbf{A^7}$ is C_3-C_7 cycloalkyl optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$, said C_3-C_7 cycloalkyl in the definition of $\mathbf{A^7}$ is fused with an optionally substituted aryl or optionally substituted heteroaryl;

[0208] each $\mathbf{R^{21}}$ is independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle;

[0209] each $\mathbf{R^{22}}$ is independently selected from the group consisting of $-(CH_2)_mOR^A$, $-O(CH_2)_mOR^A$, $-C(=O)OR^A$, $-O(CH_2)_oNR^BR^C$, $-(CH_2)_mNR^BR^C$, $-C(=O)NR^BR^C$, and $-(CH_2)_mSR^A$;

[0210] each $\mathbf{R^{23}}$ is independently selected from the group consisting of phenyl, $-NHC(=NH)NH_2$, $-(CH_2)_mOR^D$, $-C(=NNR^BR^C)H$, $-NR^LC(=O)NR^BR^C$, $-C(=O)NR^DN(=CHR^G)$, $-(CH_2)_mS(O)_{0-2}R^D$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, and $-(CH_2)_mR^G$, said phenyl in the definition of $\mathbf{R^{23}}$ is substituted with one or more substituents selected from the group consisting of halogen, cyano, C_1-C_3 alkyl, an optionally substituted C_1-C_3 alkoxy, $-O(CH_2)_mOR^A$, $-(CH_2)_mNR^BR^C$;

[0211] $\mathbf{J^7}$ is selected from the group consisting of $-(CH_2)_n[NHC(=O)](CH_2)_o[NHC(=O)](CH_2)_p-$, $-(CH_2)_n[NHC(=O)](CH_2)_o[NH]_q-$, $-NH[C(=O)][C(=O)]NH-$ and  ; ;

[0212] $\mathbf{Q^7}$ is selected from the group consisting of O (oxygen), $-N\mathbf{R^{28}}-$, aryl, and arylamido; or $\mathbf{Q^7}$ is null;

[0213] each $\mathbf{R^{28}}$ is independently selected from the group consisting of hydrogen and an optionally substituted C_1-C_4 alkyl;

[0214] $\mathbf{G^7}$ is selected from the group consisting aryl, heteroaryl, and heterocycle, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$, said aryl and heteroaryl in the definition of $\mathbf{G^7}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0215] each $\mathbf{R^{24}}$ is independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, and an optionally substituted heterocycle;

[0216] each $\mathbf{R^{25}}$ is independently selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-O(CH_2)_mO\mathbf{R^A}$, $-C(=O)O\mathbf{R^A}$, $-O(CH_2)_oN\mathbf{R^B}\mathbf{R^C}$, $-(CH_2)_mN\mathbf{R^B}\mathbf{R^C}$, $-(CH_2)_mC(=O)N\mathbf{R^B}\mathbf{R^C}$, $-C(=NN\mathbf{R^B}\mathbf{R^C})H$, and $-(CH_2)_mS\mathbf{R^A}$;

[0217] each $\mathbf{R^{26}}$ is independently selected from the group consisting of phenyl, $-NHC(=NH)NH_2$, $-(CH_2)_mO\mathbf{R^D}$, $-C(=NN\mathbf{R^B}\mathbf{R^C})H$, $-N\mathbf{R^L}C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-C(=O)N\mathbf{R^D}N(=CH)\mathbf{R^G}$, $-(CH_2)_mS(O)_{0-2}\mathbf{R^D}$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, $-(CH_2)_m\mathbf{R^G}$, said phenyl in the definition of $\mathbf{R^{23}}$ is substituted with $-(CH_2)_mN\mathbf{R^B}\mathbf{R^C}$;

[0218] $\mathbf{X^1}$, $\mathbf{X^2}$, and $\mathbf{X^3}$ are each independently selected from N (nitrogen) and $C\mathbf{R^{27}}$;

[0219] $\mathbf{R^{27}}$ is selected from the group consisting of hydrogen, halogen, and an optionally substituted C_1-C_4 alkyl;

[0220] $\mathbf{R^A}$ is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, and C_1-C_6 haloalkyl;

[0221] each $-NR^BR^C$ is separately selected, wherein R^B and R^C are each independently selected from the group consisting of hydrogen, $-SO_2R^H$, $-C(=O)R^H$, $-(CH_2)_nOR^H$, $-(CH_2)_mR^I$, $-(CH_2)_mR^J$, $-(CH_2)_nC(=O)NR^ER^F$, $-(CH_2)_nNR^ER^F$, $-SO_2NR^ER^F$, heterocycle, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_3-C_7 cycloalkyl, and C_1-C_6 heterohaloalkyl where the C_3-C_7 cycloalkyl and the heterocycle are each optionally fused with an optionally substituted aryl or optionally substituted heteroaryl; or $-NR^BR^C$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom, said optionally substituted non-aromatic heterocycle is optionally fused with an optionally substituted aryl or optionally substituted heteroaryl;

[0222] each R^D is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_mR^I$;

[0223] each $-NR^ER^F$ is separately selected, wherein R^E and R^F are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted heterocycle, and $-(CH_2)_mR^G$; or $-NR^ER^F$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;or $-NR^ER^F$ is C_1-C_6 alkylideneamino substituted with an optionally substituted aryl;

[0224] each R^G is independently selected from an optionally substituted aryl and an optionally substituted heteroaryl;

[0225] each R^H is independently selected from the group consisting of hydrogen, C_1-C_3 alkoxy, C_1-C_3 alkyl, C_1-C_3 haloalkyl, an optionally substituted aryl and an optionally substituted heteroaryl;

[0226] each R^I is independently selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl;

[0227] each R^J is independently selected from the group consisting of aryl and heteroaryl, each substituted with one or more $-NR^ER^F$;

[0228] each R^L is independently selected from the group consisting of C_3-C_7 cycloalkyl, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, $-(CH_2)_mOR^{LA}$, $-(CH_2)_mNR^{LB}R^{LC}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of R^L are each independently optionally substituted with one or more substituents

selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, -$(CH_2)_m$N$\mathbf{R^{LD}R^{LE}}$, aryl and heteroaryl, said aryl and heteroaryl substituent off of $\mathbf{R^L}$ are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or -$(CH_2)_m$N$\mathbf{R^{LF}R^{LG}}$;

[0229] each $\mathbf{R^{LA}}$ is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0230] $\mathbf{R^{LB}}$ and $\mathbf{R^{LC}}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl; or –N$\mathbf{R^{LB}R^{LC}}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0231] each –N$\mathbf{R^{LD}R^{LE}}$ is separately selected, wherein $\mathbf{R^{LD}}$ and $\mathbf{R^{LE}}$ are each independently selected from the group consisting of hydrogen, aryl, heteroaryl, and optionally substituted C_1-C_6 alkyl, said aryl and heteroaryl in the definition of $\mathbf{R^{LD}}$ and $\mathbf{R^{LE}}$ are each optionally substituted with C_1-C_6 alkyl or C_1-C_6 alkoxy; or –N$\mathbf{R^{LD}R^{LE}}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0232] each –N$\mathbf{R^{LF}R^{LG}}$ is separately selected, wherein $\mathbf{R^{LF}}$ and $\mathbf{R^{LG}}$ are each independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl; or -N$\mathbf{R^{LF}R^{LG}}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0233] each **m** is independently 0, 1, or 2;

[0234] each **n** is independently 0, 1, 2, 3, or 4;

[0235] each **o** is independently 1, 2, or 3;

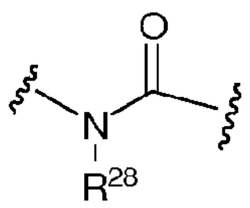
[0236] each **p** is independently 0, 1, 2, or 3;

[0237] each **q** is independently 0 or 1; and

[0238] any bond represented by a dashed and solid line represents a bond selected from the group consisting of a single bond and a double bond.

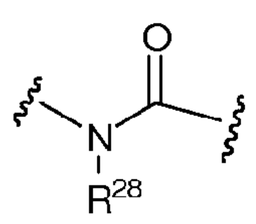
[0239] Some embodiments disclosed herein provide a compound of Formula **III**, wherein $\mathbf{A^7}$ can be selected from the group consisting of phenyl, pyridinyl, pyrimidinyl, imidazolyl, isoxazolyl, thienyl, indolyl, and benzimidazolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$, said aryl and heteroaryl in the definition of $\mathbf{A^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{G^7}$ can be selected from the group consisting aryl, heteroaryl, and heterocycle, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$, said

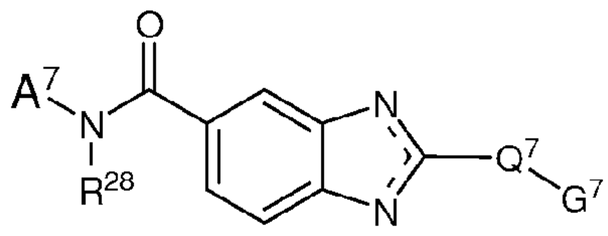
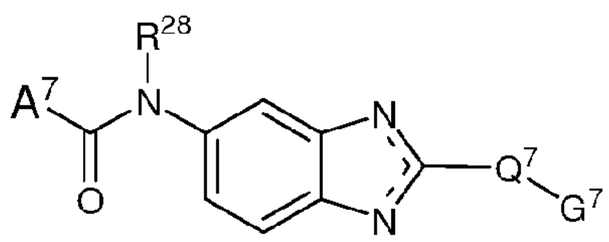
aryl and heteroaryl in the definition of $\mathbf{G^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{R^{21}}$ can be selected from the group consisting of fluorine and chlorine; $\mathbf{R^{22}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-N\mathbf{R^B}\mathbf{R^C}$, and $-(CH_2)_mS\mathbf{R^A}$; $\mathbf{R^{23}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^D}$, and $-C(=O)N\mathbf{R^D}N(=CH\mathbf{R^G})$; $\mathbf{R^{25}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-N\mathbf{R^B}\mathbf{R^C}$; each $\mathbf{R^A}$ can be independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkyl; each $-N\mathbf{R^B}\mathbf{R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl; or $-N\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-N\mathbf{R^B}\mathbf{R^C}$ is an optionally substituted C_1-C_6 alkylideneamino; $\mathbf{J^7}$ can be

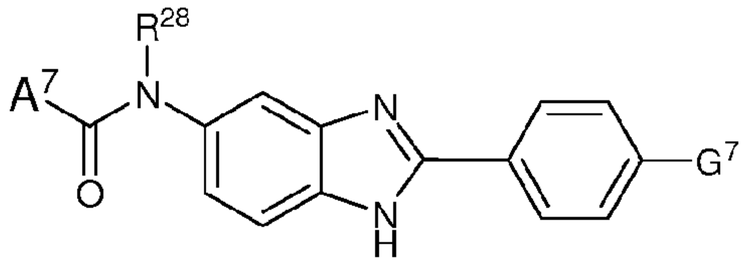


; each $\mathbf{R^{28}}$ can be independently selected from the group consisting of hydrogen and an optionally substituted C_1-C_3 alkyl, with the proviso when $\mathbf{A^7}$ and $\mathbf{G^7}$ are a phenyl then at least one of $\mathbf{R^{22}}$, $\mathbf{R^{23}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-(CH_2)_mO\mathbf{R^D}$, $-N\mathbf{R^B}\mathbf{R^C}$, $-C(=O)N\mathbf{R^D}N(=CH\mathbf{R^G})$, $-N\mathbf{R^E}\mathbf{R^F}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, and an optionally substituted phenyl.

[0240] Some embodiments disclosed herein provide a compound of Formula **III**, wherein $\mathbf{A^7}$ can be selected from the group consisting of phenyl, pyridinyl, pyrimidinyl, imidazolyl, isoxazolyl, thienyl, indolyl, and benzimidazolyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$, said aryl and heteroaryl in the definition of $\mathbf{A^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{G^7}$ can be selected from the group consisting aryl, heteroaryl, and heterocycle, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$, said aryl and heteroaryl in the definition of $\mathbf{G^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{R^{21}}$ can be selected from the group consisting of C_1-C_6 alkyl, fluorine, and chlorine; $\mathbf{R^{22}}$ can be selected from the group consisting of $-NHC(=O)\mathbf{R^E}\mathbf{R^F}$, $-(CH_2)_mO\mathbf{R^A}$, and $-N\mathbf{R^B}\mathbf{R^C}$; $\mathbf{R^{23}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^D}$, and

-C(=O)N$\mathbf{R^D}$N(=CH$\mathbf{R^G}$); $\mathbf{R^A}$ can be selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; each -N$\mathbf{R^B}\mathbf{R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl; or -N$\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or -N$\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted C_1-C_6 alkylideneaminyl; and $\mathbf{J^7}$ can be  , with the proviso when $\mathbf{A^7}$ and $\mathbf{G^7}$ are a phenyl then at least one of $\mathbf{R^{22}}$, $\mathbf{R^{23}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$ can be selected from the group consisting of $-(CH_2)_mOR^A$, $-(CH_2)_mOR^D$, $-NR^BR^C$, -NHC(=O)$\mathbf{R^E}\mathbf{R^F}$, -C(=O)N$\mathbf{R^D}$N(=CH$\mathbf{R^G}$), and an optionally substituted phenyl.

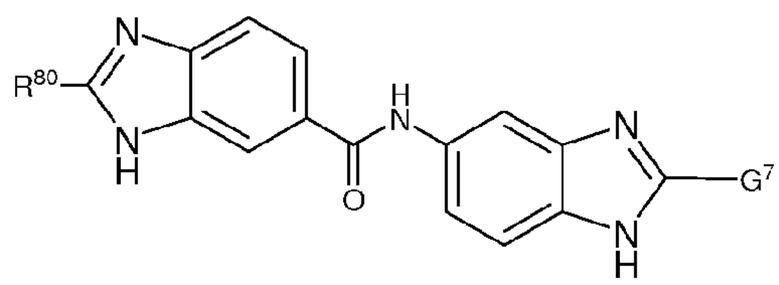
[0241] Some embodiments disclosed herein provide a compound of Formula **III** having the structure of Formula **IIIaa:**  (**IIIaa**), and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof, or having the formula **IIIab:**  (**Ib**), and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof.

[0242] Some embodiments disclosed herein provide a compound of Formula **IIIab** having the structure of Formula **IIIabb:**  (**IIIabb**), and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof, wherein $\mathbf{A^7}$ can be aryl substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$; each $\mathbf{R^{21}}$ canbe independently selected from the group consisting of halogen, cyano, C_1-C_6 alkyl, and C_1-C_6 alkoxy; each $\mathbf{R^{22}}$ can be independently selected from the group consisting of $-(CH_2)_mOR^A$, $-O(CH_2)_mOR^A$ and $-(CH_2)_mNR^BR^C$; each $\mathbf{R^{23}}$ can be phenyl substituted with

-$(CH_2)_mNR^BR^C$; $\mathbf{G^7}$ can be heterocycle substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$; each $\mathbf{R^{24}}$ can be independently selected from the group consisting of halogen, cyano, C_1-C_6 alkyl, and C_1-C_6 alkoxy; each $\mathbf{R^{25}}$ can be independently selected from the group consisting of $-(CH_2)_mOR^A$, $-O(CH_2)_mOR^A$; each $\mathbf{R^{26}}$ can be phenyl substituted with one or more $-(CH_2)_mNR^BR^C$; $\mathbf{R^B}$ can be hydrogen; $\mathbf{R^C}$ can be $-C(=O)R^H$; and $\mathbf{R^H}$ can be an optionally substituted aryl.

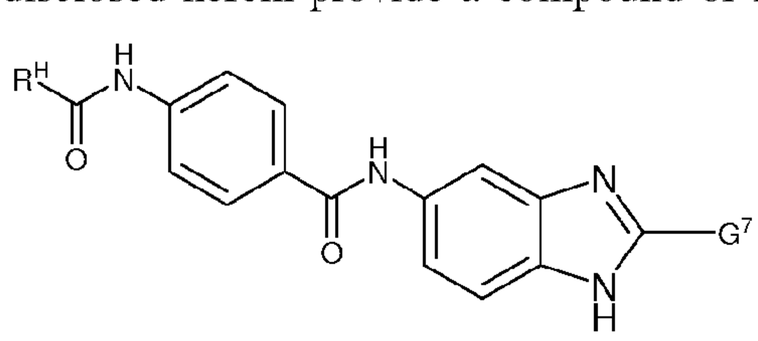
[0243] Some embodiments disclosed herein provide a compound of Formula **IIIabb**, wherein $\mathbf{A^7}$ can be phenyl substituted with one or more substituents selected from the group consisting of $\mathbf{R^{22}}$; each $\mathbf{R^{22}}$ can be independently selected from the group consisting of $-(CH_2)_mOR^A$, and $-O(CH_2)_mOR^A$; each $\mathbf{R^A}$ can be independently selected from the group consisting of hydrogen, C_1-C_3 alkyl, and C_1-C_3 haloalkyl; $\mathbf{G^7}$ can be piperidinyl substituted with one or more substituents selected from the group consisting of $\mathbf{R^{26}}$; each $\mathbf{R^{26}}$ can be phenyl substituted with $-NHC(=O)R^H$; and $\mathbf{R^H}$ can be an optionally substituted phenyl.

[0244] Some embodiments disclosed herein provide a compound of Formula **III** having the structure of Formula **IIIb:**



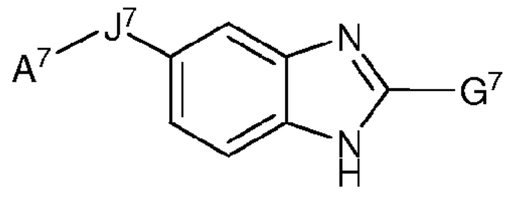
(**IIIb**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{R^{80}}$ can be selected from the group consisting of hydrogen, $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$.

[0245] Some embodiments disclosed herein provide a compound of Formula **III** having the structure of Formula **IIIc:**

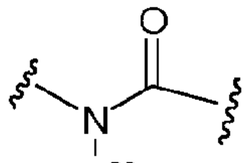


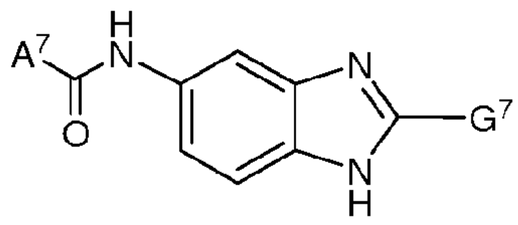
(**IIIc**), and pharmaceutically acceptable salts thereof.

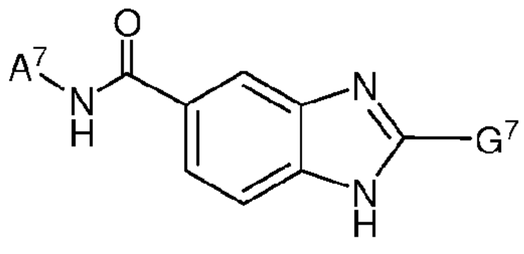
[0246] Some embodiments disclosed herein provide a compound of Formula **III** having the structure of Formula **IIId:**



(**IIId**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{A^7}$ can be selected from the group consisting of aryl and heteroaryl, each substituted with one or more substituents selected from

the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$, said aryl and heteroaryl in the definition of $\mathbf{A^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; or $\mathbf{A^7}$ can be C_3-C_7 cycloalkyl optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$, said C_3-C_7 cycloalkyl in the definition of $\mathbf{A^7}$ can be fused with an optionally substituted aryl or optionally substituted heteroaryl; $\mathbf{J^7}$ can be selected from the group consisting of $-(CH_2)_n[NHC(=O)](CH_2)_oNHC(=O)(CH_2)_p-$, $-(CH_2)_n[NHC(=O)](CH_2)_o[NH]_q-$, and 
; and $\mathbf{G^7}$ can be selected from the group consisting of a aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$, said aryl and heteroaryl in the definition of $\mathbf{G^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle.

[0247] Some embodiments disclosed herein provide a compound of Formula **IIId** having the structure of Formula **IIIda:**  (**IIIda**), and pharmaceutically acceptable salts, esters, or prodrugs thereof, wherein $\mathbf{A^7}$ can be selected from the group consisting of phenyl, indolyl, pyridinyl, pyrimidinyl, thienyl, benzothiofuranyl, naphthalenyl, and tetrahydronaphthalenyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$; and $\mathbf{G^7}$ can be selected from the group consisting of a aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$, said aryl and heteroaryl in the definition of $\mathbf{G^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle.

[0248] Some embodiments disclosed herein provide a compound of Formula **IIId** having the structure of Formula **IIIdb:**  (**IIIdb**), and pharmaceutically acceptable salts, esters, or prodrugs thereof, wherein $\mathbf{A^7}$ can be selected

from the group consisting of phenyl, indolyl, pyridinyl, pyrimidinyl, thienyl, benzothiofuranyl, naphthalenyl, and tetrahydronaphthalenyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{21}}$, $\mathbf{R^{22}}$, and $\mathbf{R^{23}}$; and $\mathbf{G^7}$ can be selected from the group consisting of a aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$, said aryl and heteroaryl in the definition of $\mathbf{G^7}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle.

[0249] Some embodiments disclosed herein provide a compound of Formula **IIIda** or Formula **IIIdb**, wherein $\mathbf{G^7}$ can be selected from the group consisting of phenyl, naphthyl, indolyl, dihydrobenzofuranyl, 1,4-benzodioxanyl, benzotriazolyl, benzimidazolyl, benzofuranyl, and 2,1,3-benzoxadiazolyl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{24}}$, $\mathbf{R^{25}}$, and $\mathbf{R^{26}}$. In some embodiments, $\mathbf{R^{21}}$ can be selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, and an optionally substituted C_3-C_7 cycloalkyl; $\mathbf{R^{22}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-O(CH_2)_mO\mathbf{R^A}$, and $-N\mathbf{R^B}\mathbf{R^C}$; $\mathbf{R^{23}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^D}$, $-(CH_2)_mS(O)_{0\text{-}2}\mathbf{R^D}$, and $-(CH_2)_m\mathbf{R^G}$; $\mathbf{R^{24}}$ can be selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_3-C_7 cycloalkyl; $\mathbf{R^{25}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-O(CH_2)_mO\mathbf{R^A}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-C(=NN\mathbf{R^B}\mathbf{R^C})H$, $-N\mathbf{R^B}\mathbf{R^C}$; $\mathbf{R^{26}}$ can be selected from the group consisting of $-(CH_2)_mO\mathbf{R^D}$, $-(CH_2)_m\mathbf{R^G}$; $\mathbf{R^A}$ can be selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, and C_1-C_6 haloalkyl; each $-N\mathbf{R^B}\mathbf{R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, $-SO_2\mathbf{R^H}$, $-C(=O)\mathbf{R^H}$, $-(CH_2)_nO\mathbf{R^H}$, $-(CH_2)_m\mathbf{R^I}$, $-(CH_2)_m\mathbf{R^J}$, $-(CH_2)_nC(=O)N\mathbf{R^E}\mathbf{R^F}$, $-(CH_2)_nN\mathbf{R^E}\mathbf{R^F}$, $-SO_2N\mathbf{R^E}\mathbf{R^F}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_3-C_7 cycloalkyl, and C_1-C_6 heterohaloalkyl where the alkyl and the heteroalkyl are optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted heterocyle; each $\mathbf{R^D}$ can be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, and $-(CH_2)_m\mathbf{R^I}$; each $-N\mathbf{R^E}\mathbf{R^F}$ can be separately selected, wherein $\mathbf{R^E}$ and $\mathbf{R^F}$ can each be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, and $-(CH_2)_m\mathbf{R^G}$; or $-N\mathbf{R^E}\mathbf{R^F}$ can be an optionally substituted C_1-C_6 alkylideneamino; or $-N\mathbf{R^E}\mathbf{R^F}$ can be an optionally substituted heterocyle;

each $\mathbf{R^G}$ can be independently selected from from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^H}$ can be independently selected from the group consisting of hydrogen, C_1-C_3 alkoxy, C_1-C_3 alkyl, C_1-C_3 haloalkyl, an optionally substituted aryl and optionally substituted heteroaryl; each $\mathbf{R^I}$ can be independently selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^J}$ can be independently selected from the group consisting of aryl and heteroaryl, each substituted with one or more $-N\mathbf{R^E}\mathbf{R^F}$; each **m** can be independently 0, 1, or 2; and each **n** can be independently 0, 1, 2, 3, or 4.

[0250] Some embodiments disclosed herein provide a compound of Formula **III** having the proviso that a compound of Formula **III** is not selected from the group consisting of:

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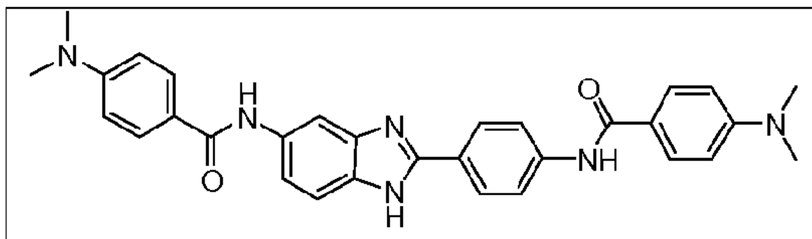
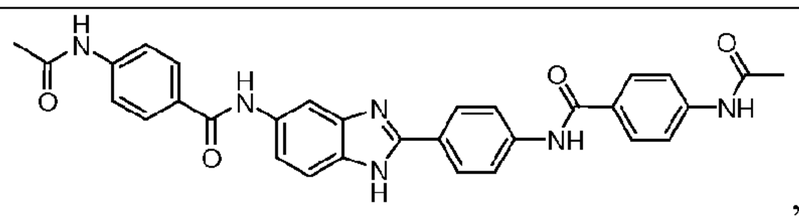
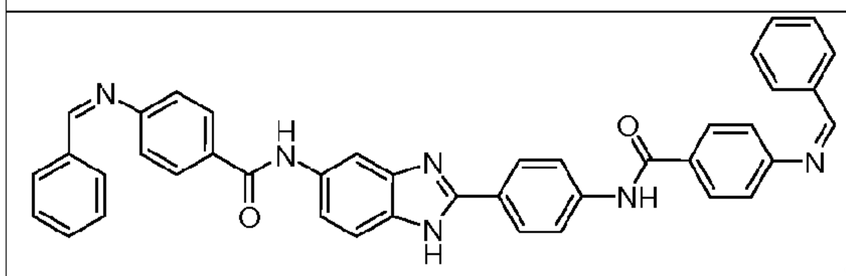
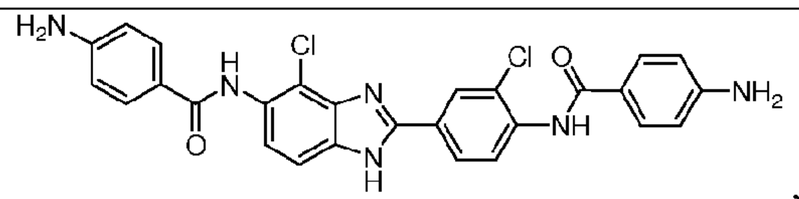
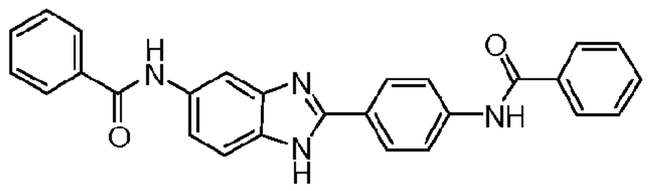
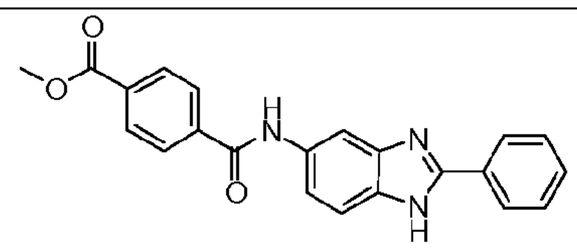
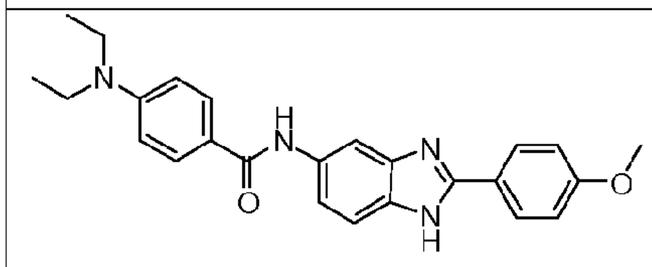
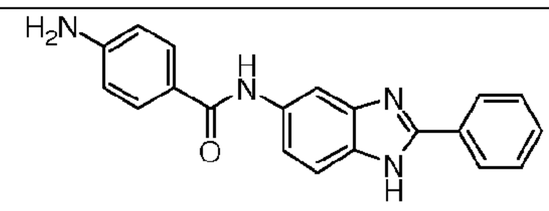
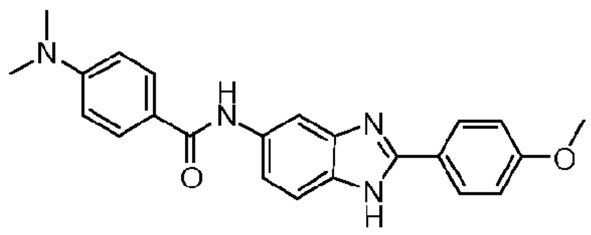
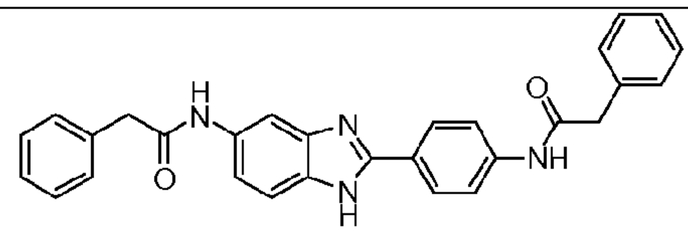
<tr><td>  ,</td><td>  ,</td></tr>
<tr><td>  ,</td><td>  ,</td></tr>
<tr><td>  ,</td><td>  ,</td></tr>
<tr><td>  ,</td><td>  ,</td></tr>
<tr><td>  ,</td><td>  ,</td></tr>
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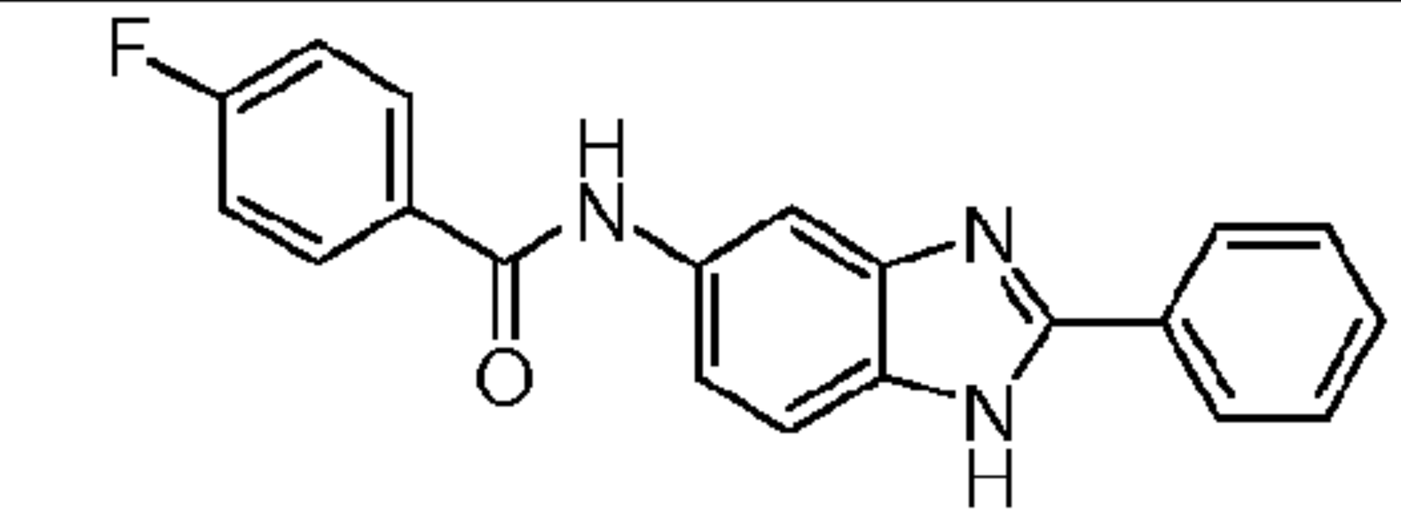
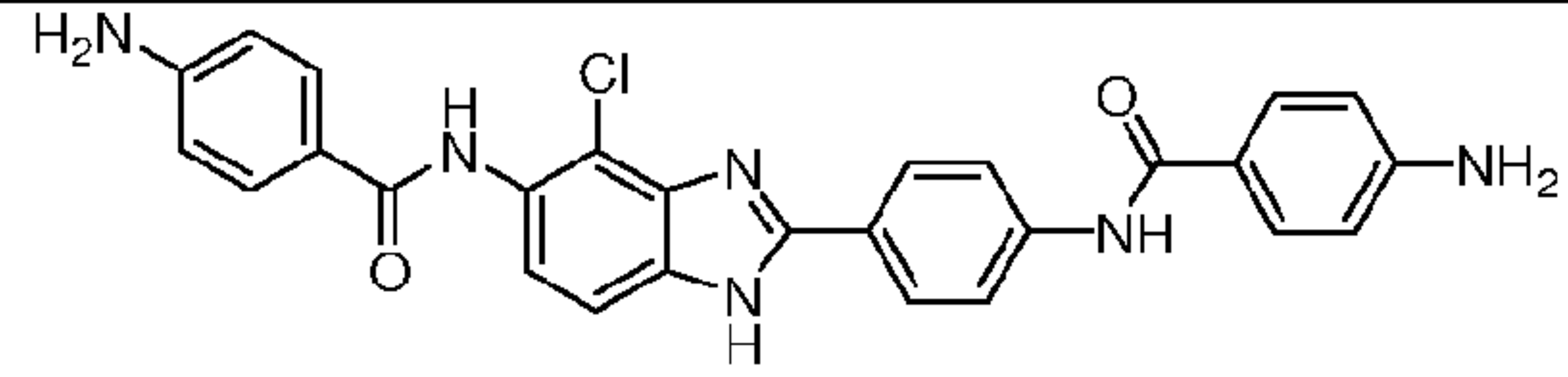
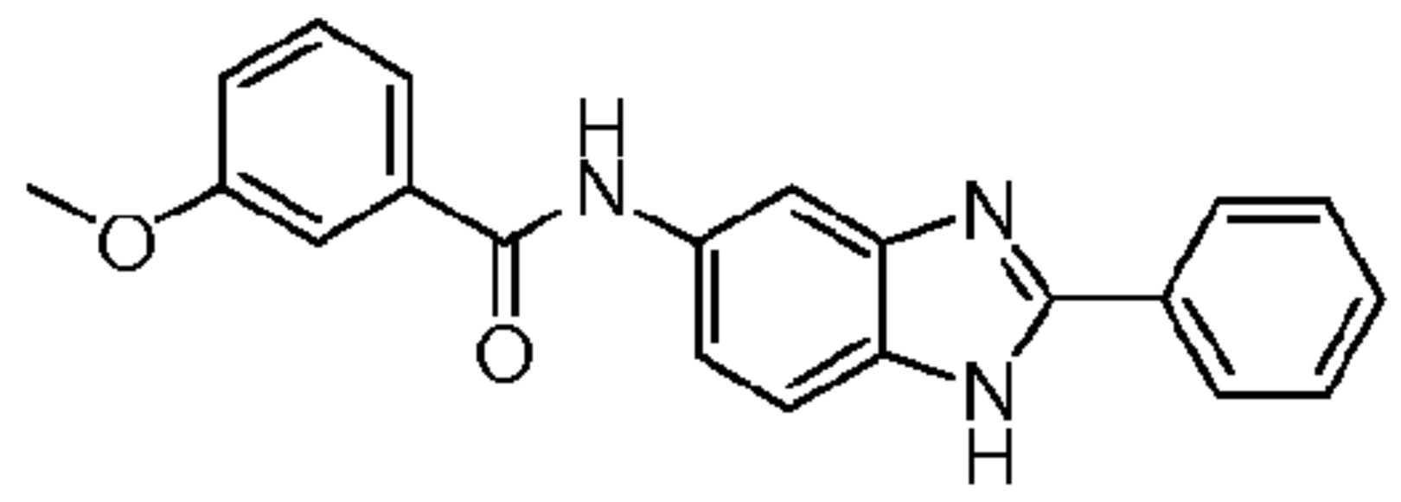
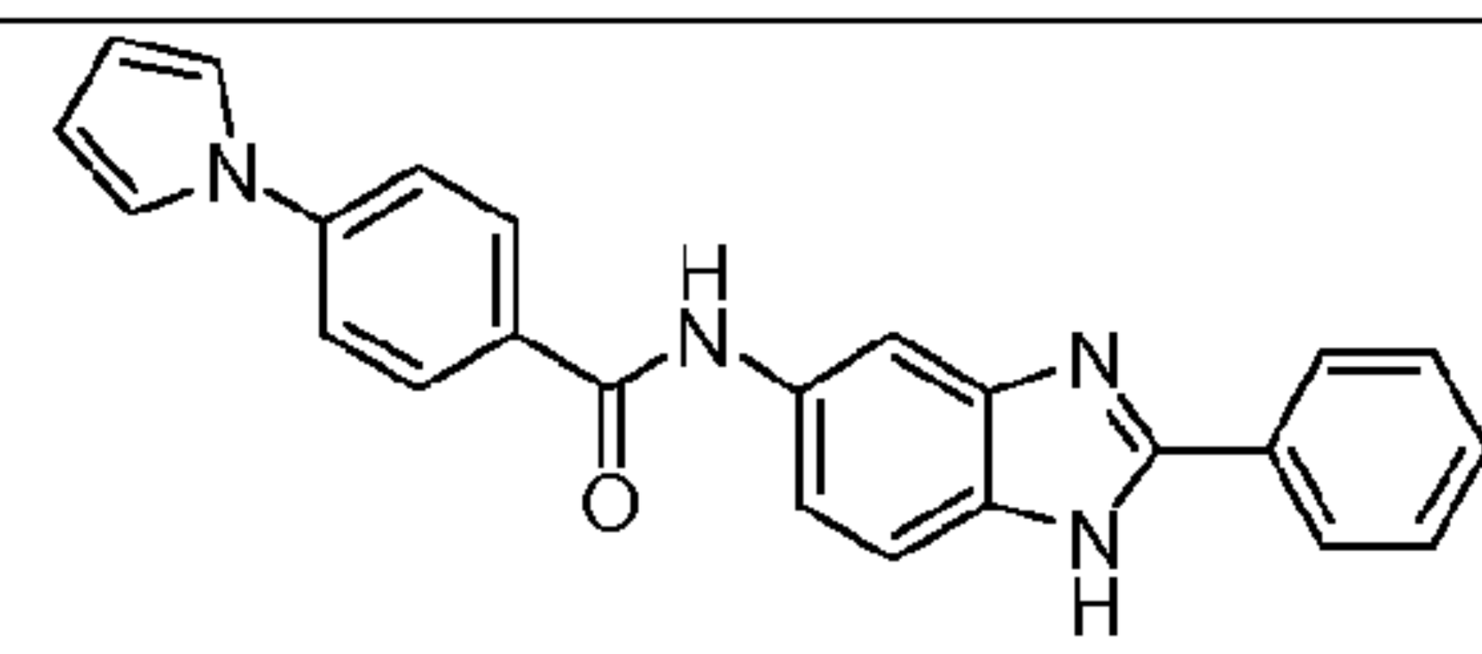
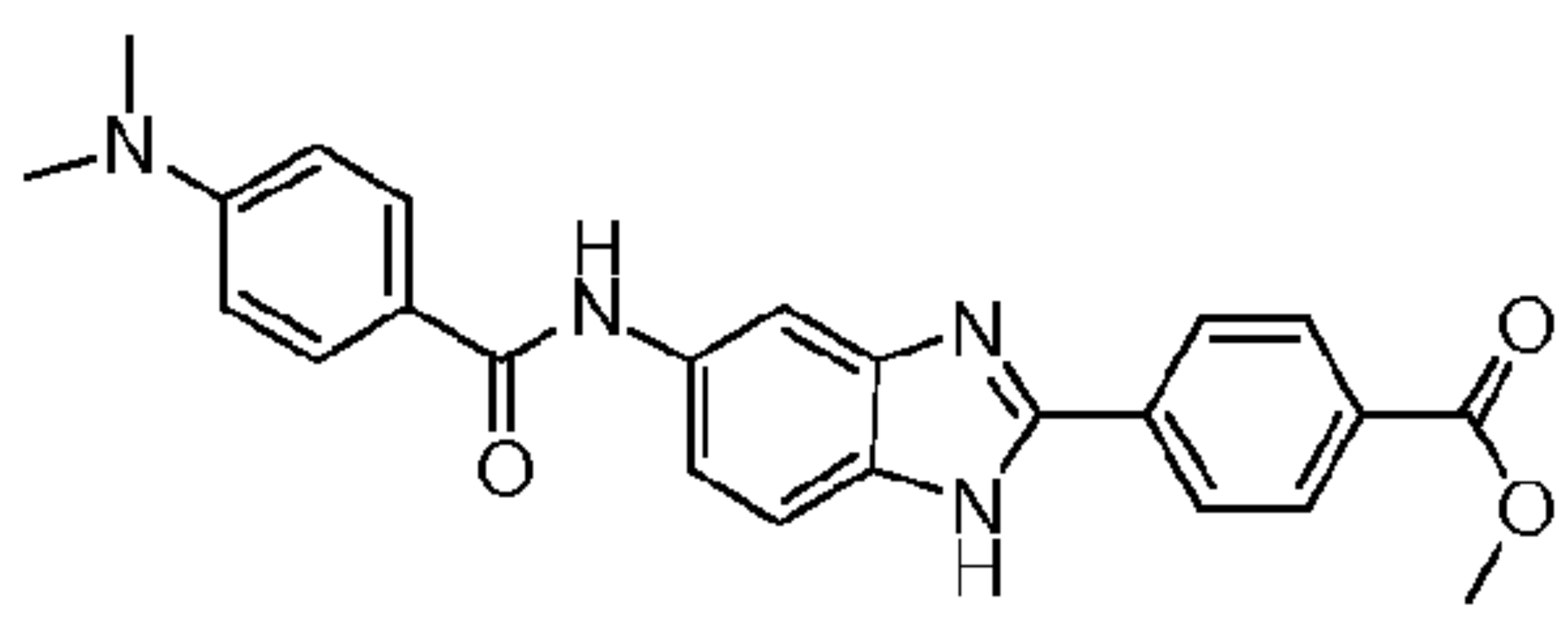
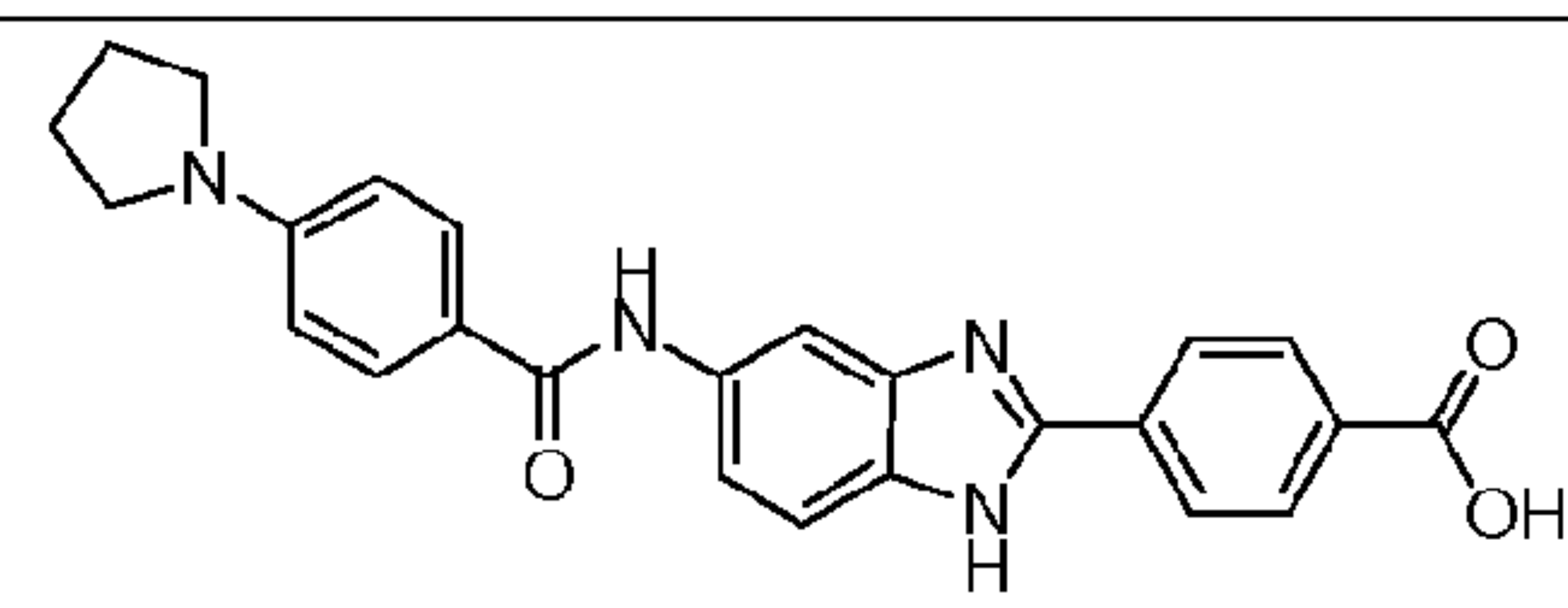
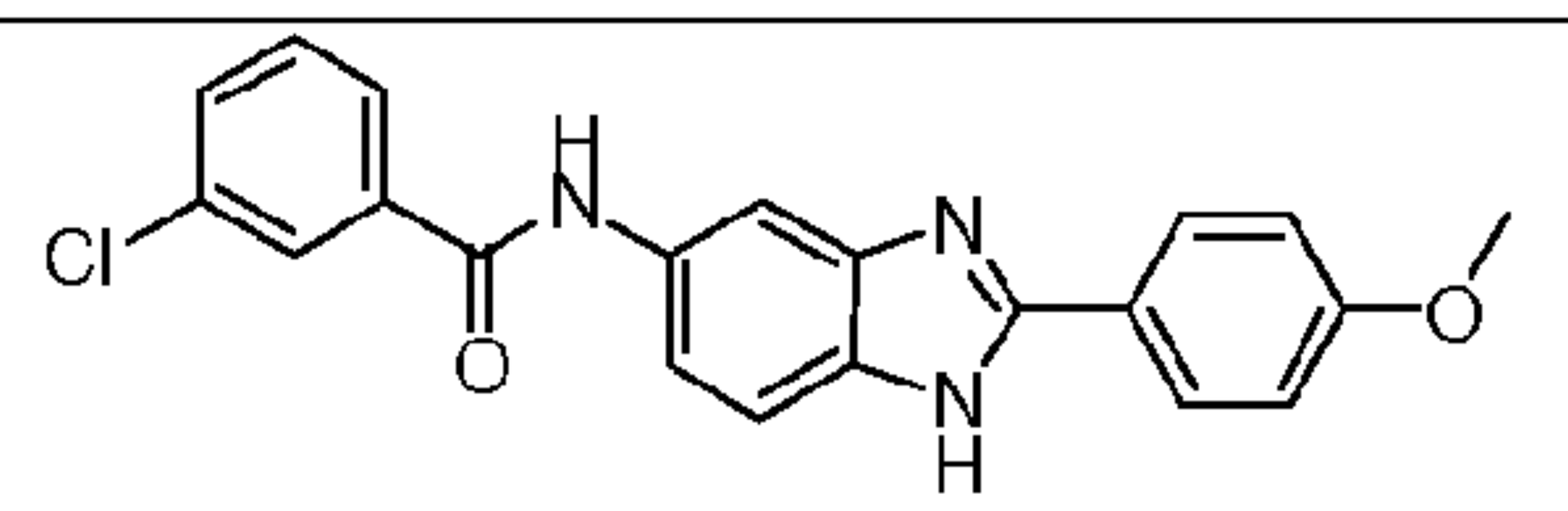
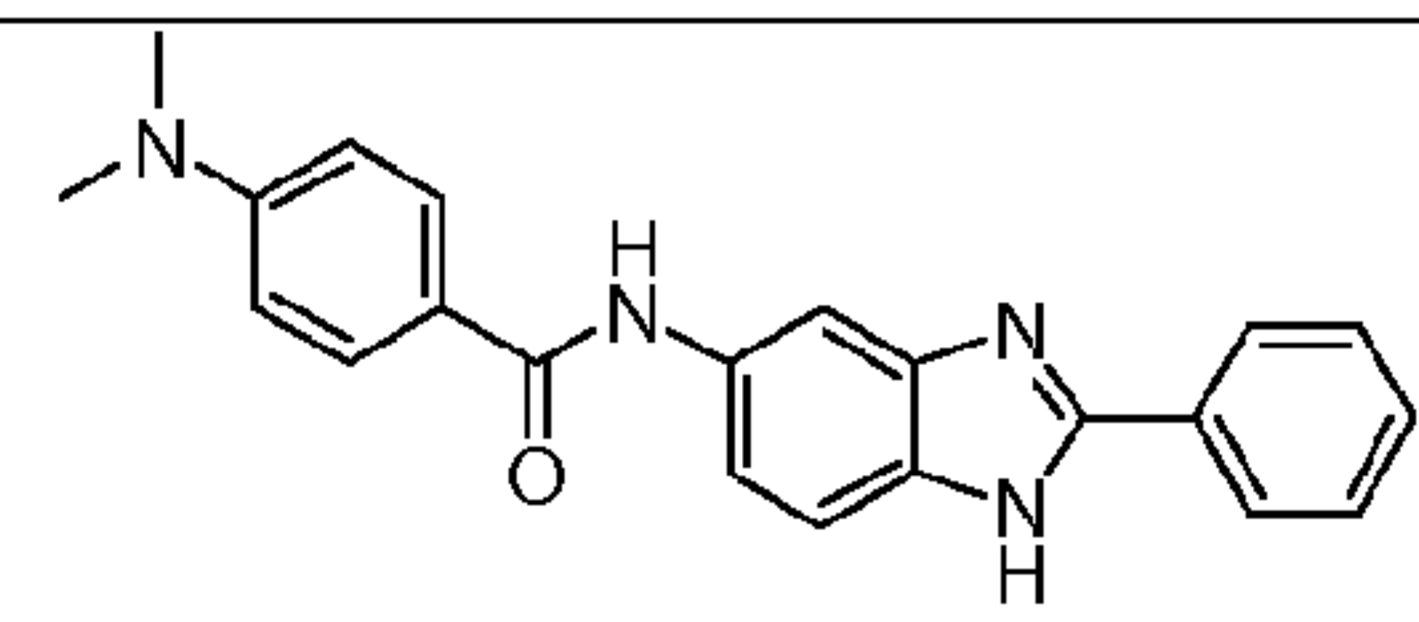
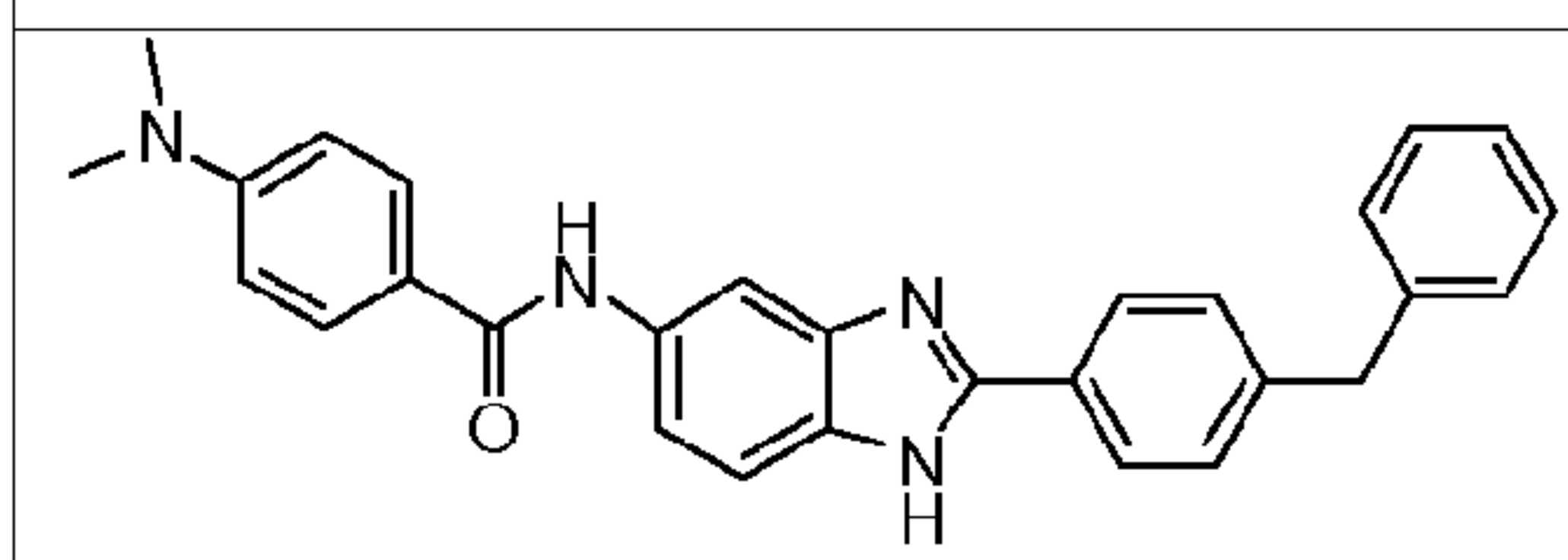
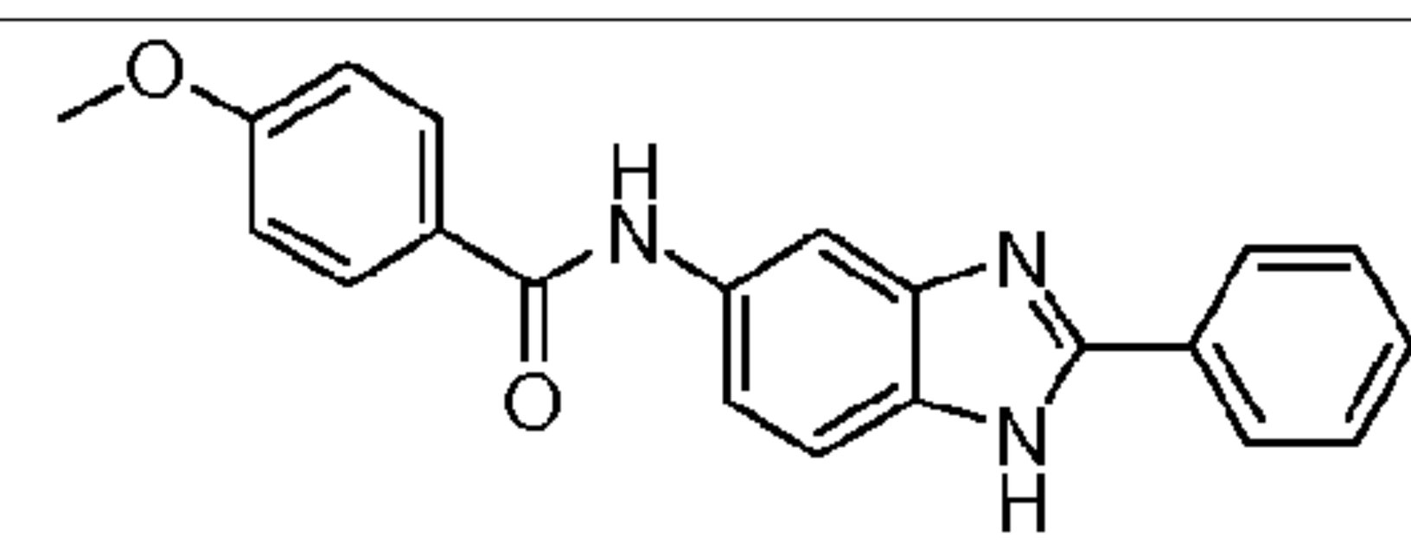
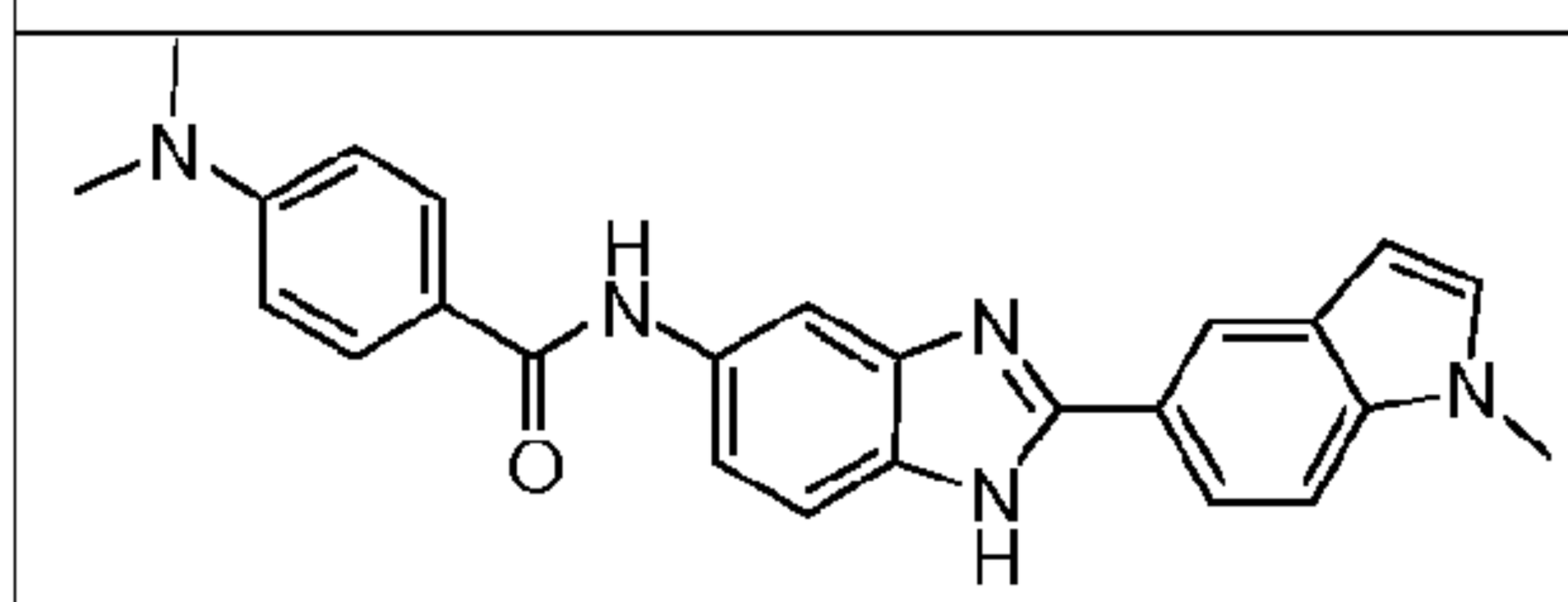
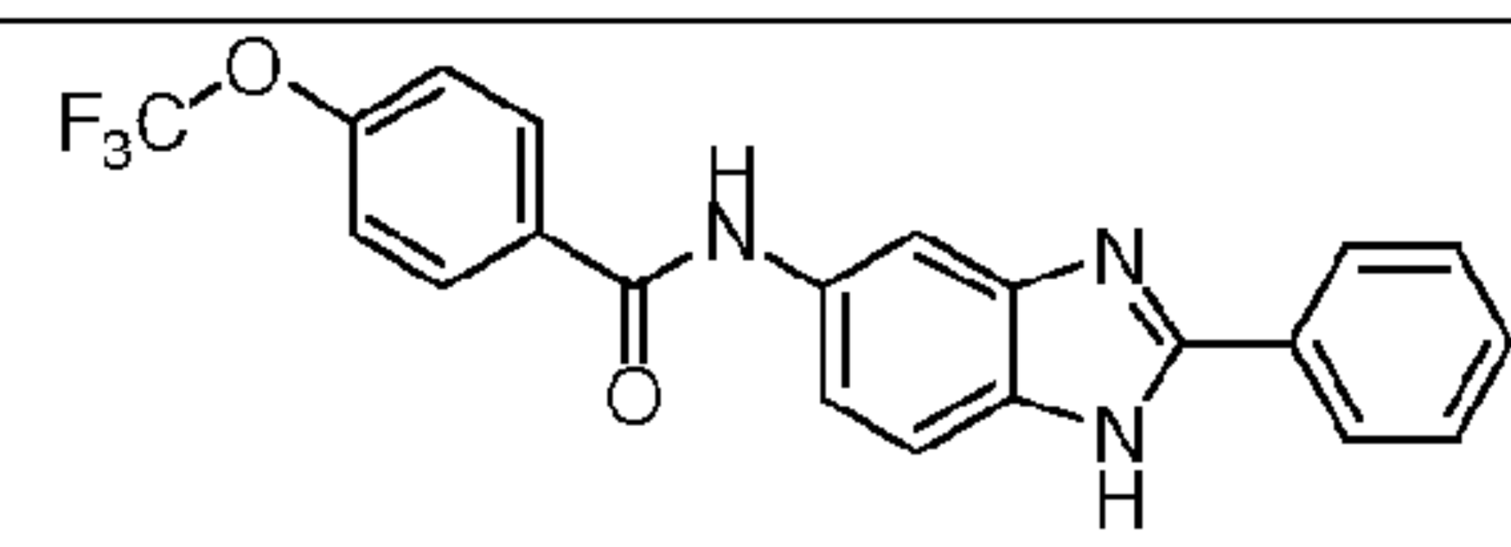
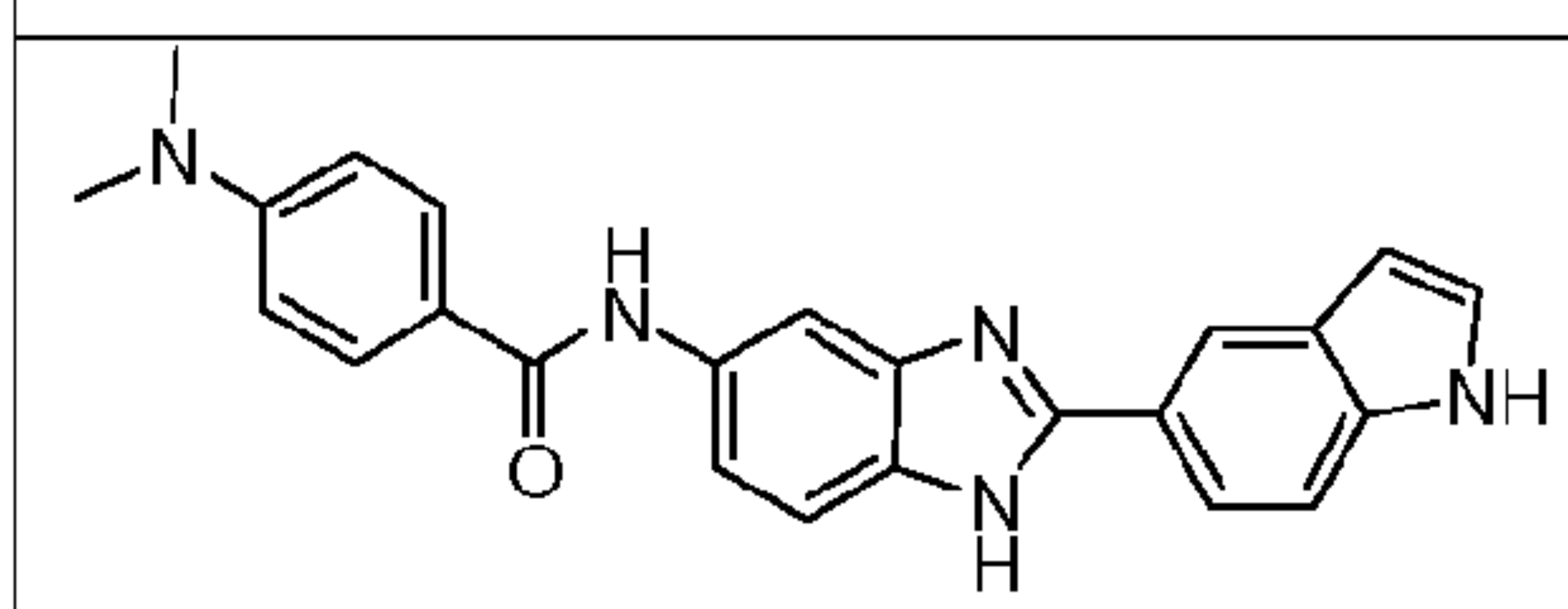
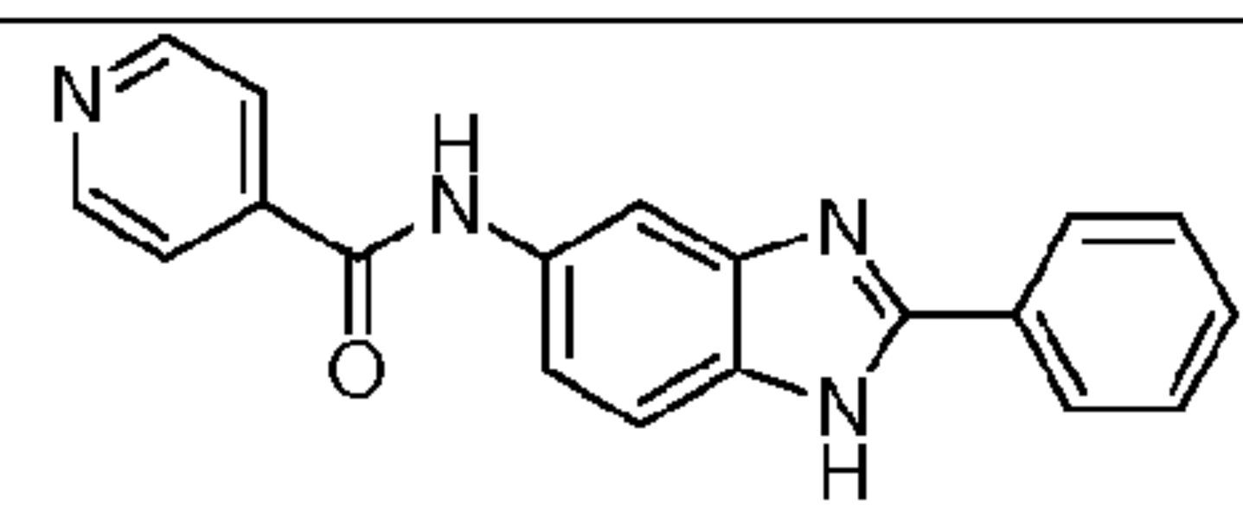
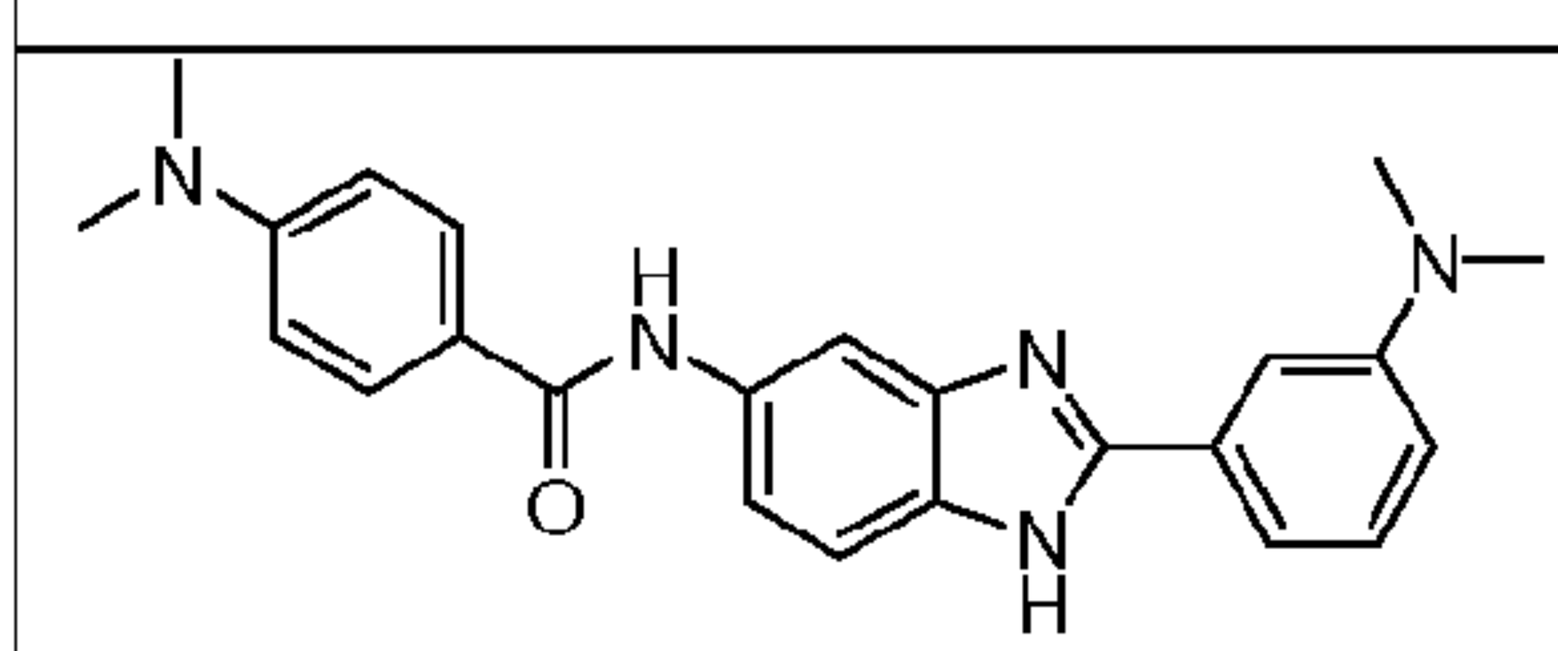
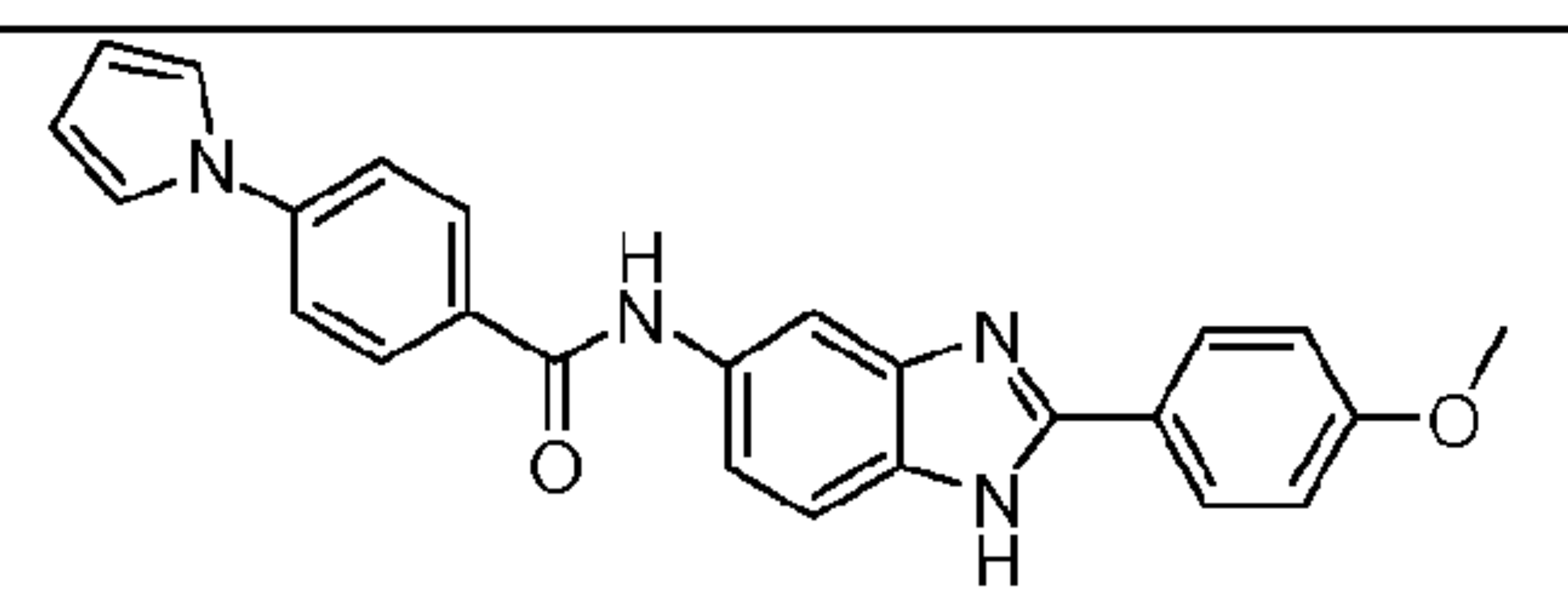
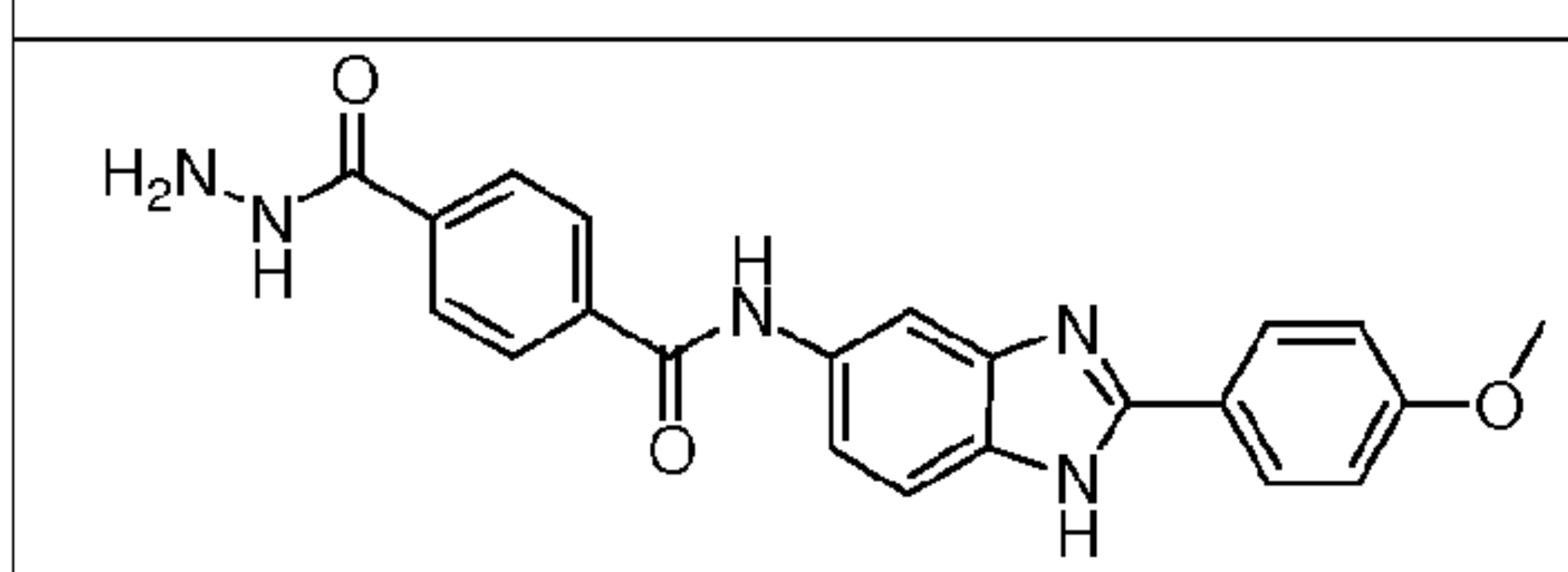
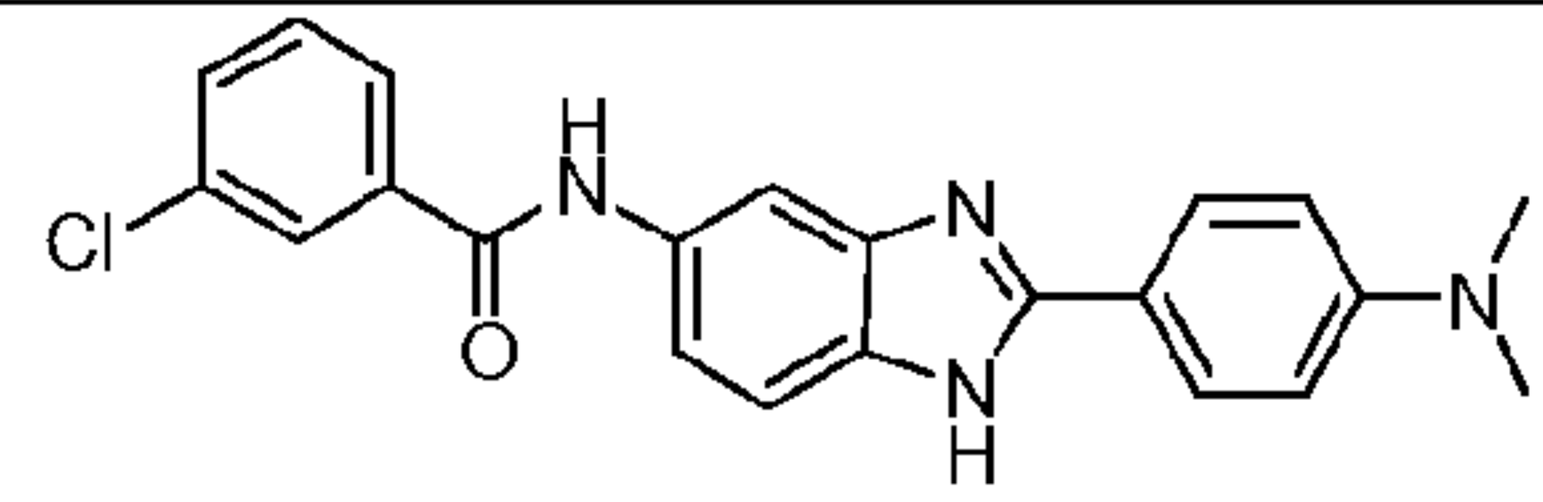
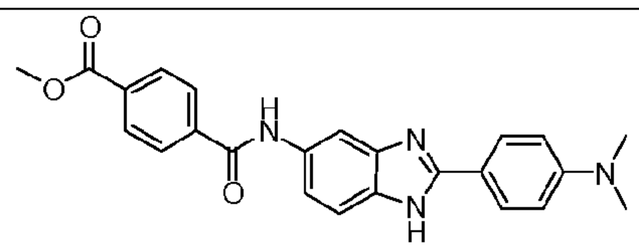
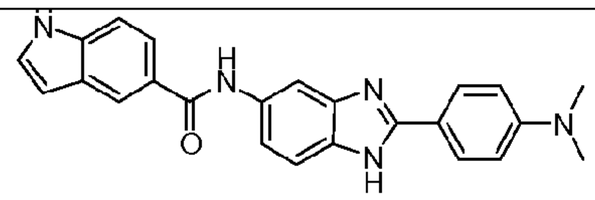
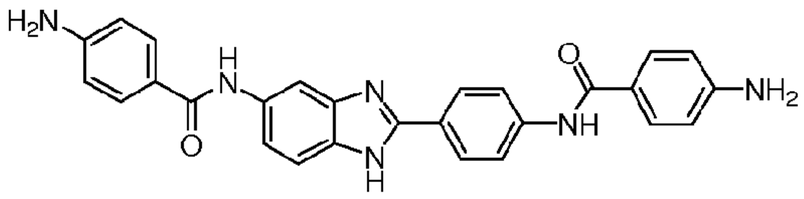
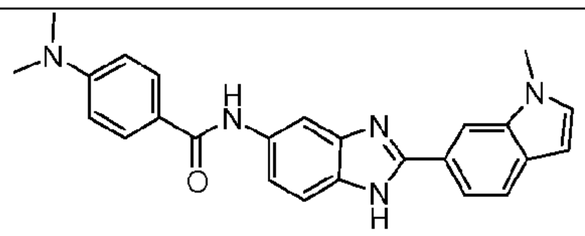
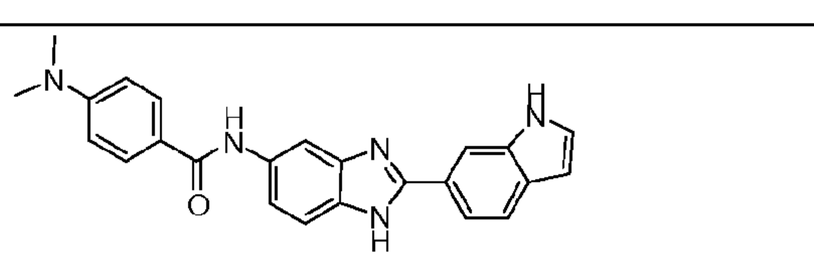
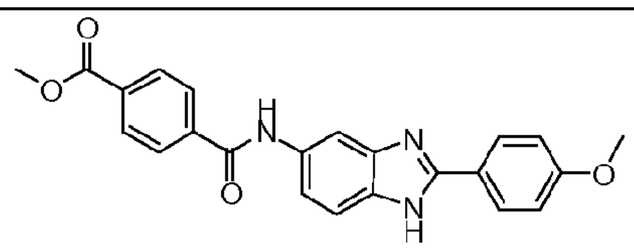
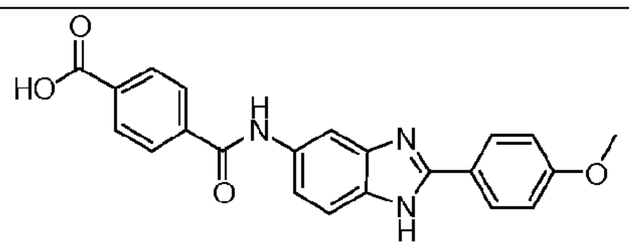
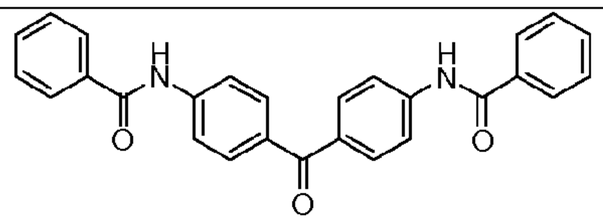
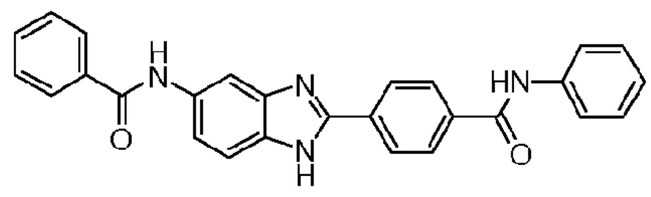
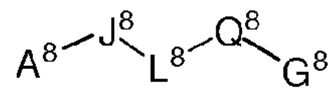
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
and	 .

[0251] Some embodiments disclosed herein provide a compound of Formula **IV**:

 (**IV**)

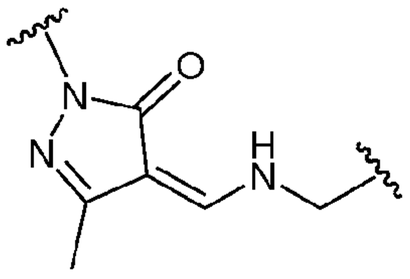
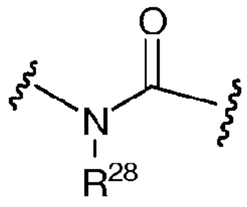
and pharmaceutically acceptable salts, esters stereoisomers, tautomers or prodrugs thereof;

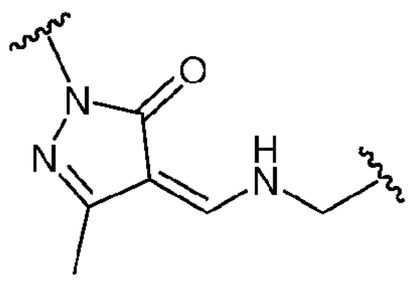
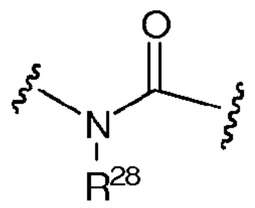
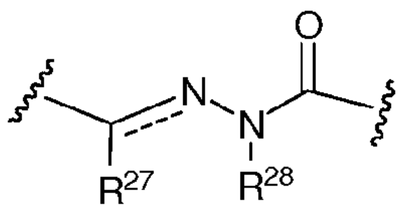
wherein:

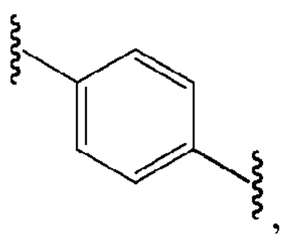
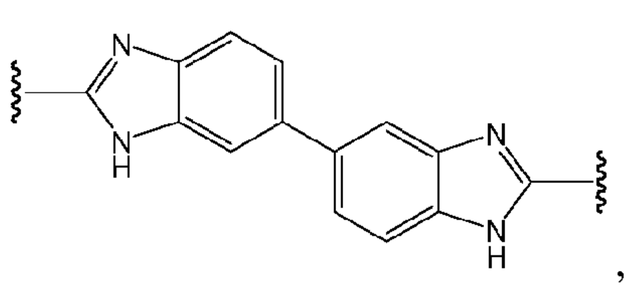
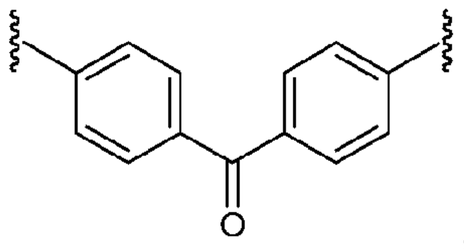
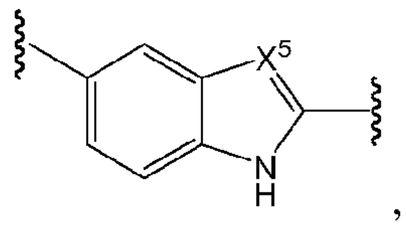
[0252] $\mathbf{A^8}$ is selected from the group consisting of heterocycle, aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{31}}$, $\mathbf{R^{32}}$, and $\mathbf{R^{33}}$, said aryl and heteroaryl in the definition of $\mathbf{A^8}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

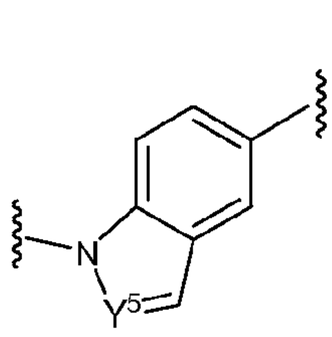
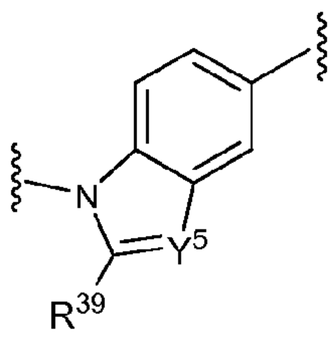
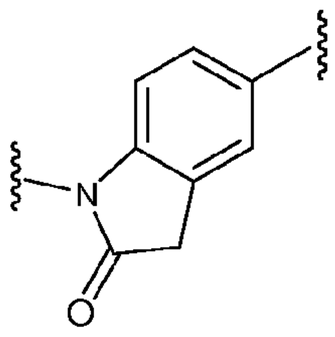
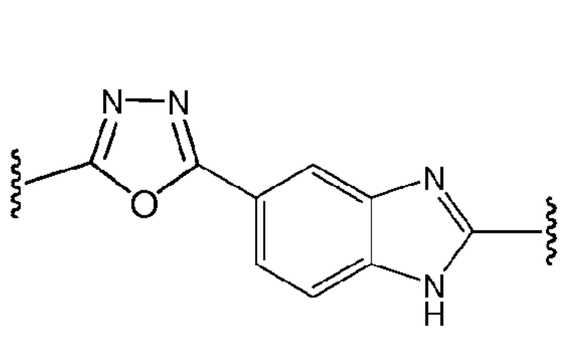
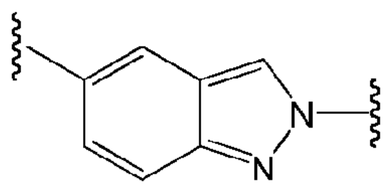
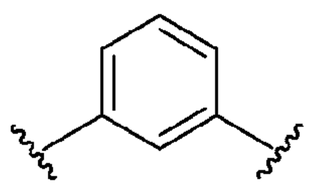
[0253] $\mathbf{G^8}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of

$\mathbf{R^{34}}$, $\mathbf{R^{35}}$, and $\mathbf{R^{36}}$, said aryl and heteroaryl in the definition of $\mathbf{G^8}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0254] $\mathbf{J^8}$ is selected from the group consisting of aryl, heteroaryl, heterocycle, -C(=O)–, -(CH=CH)–, -OC(=O)–, –NHC(=O)NH–, –NHC(=S)NH–, $–S(=O)_2-NH_2–$, -OC(=S)–, –NHC(=S)–, $-(CH_2)_nNH–$, $-(CH_2)_n[NHC(=O)](CH_2)_oNHC(=O)(CH_2)_p–$, $-(CH_2)_n[NHC(=O)](CH_2)_o[NH]_q–$,  , and  ; or $\mathbf{J^8}$ is null;

[0255] $\mathbf{Q^8}$ is selected from the group consisting of aryl, heteroaryl, heterocycle, -C(=O)–, -(CH=CH)–, -OC(=O)–, –NHC(=O)NH–, –NHC(=S)NH–, $–S(=O)_2-NH_2–$, -OC(=S)–, –NHC(=S)–, $-(CH_2)_nNH–$, $-(CH_2)_n[NHC(=O)](CH_2)_oNHC(=O)(CH_2)_p–$, $-(CH_2)_n[NHC(=O)](CH_2)_o[NH]_q–$,  ,  and  ; or $\mathbf{Q^8}$ is null;

[0256] $\mathbf{L^8}$ is selected from the group consisting of  ,  ,  ,  ,







, and ;

[0257] $\mathbf{X^5}$ is selected from the group consisting of N (nitrogen) and $C\mathbf{R^{39}}$;

[0258] $\mathbf{Y^5}$ is selected from the group consisting of N (nitrogen) and $C\mathbf{R^{40}}$;

[0259] each $\mathbf{R^{27}}$ is independently selected from the group consisting of hydrogen, halogen, and an optionally substituted C_1-C_4 alkyl;

[0260] each $\mathbf{R^{28}}$ is independently selected from the group consisting of hydrogen and an optionally substituted C_1-C_4 alkyl;

[0261] each $\mathbf{R^{31}}$ is independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0262] each $\mathbf{R^{32}}$ is independently selected from the group consisting of halogen, $-(CH_2)_mO\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, and $-(CH_2)_mS\mathbf{R^A}$;

[0263] each $\mathbf{R^{33}}$ is independently selected from the group consisting of halogen, -C(=O)OH, $-(CH_2)_mO\mathbf{R^D}$, $-N\mathbf{R^E}\mathbf{R^F}$, $-N\mathbf{R^L}C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-(CH_2)_mS(O)_{0\text{-}2}\mathbf{R^D}$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, and $-(CH_2)_m\mathbf{R^G}$;

[0264] each $\mathbf{R^{34}}$ is independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0265] each $\mathbf{R^{35}}$ is independently selected from the group consisting of halogen, C(=O)OH, $-(CH_2)_mO\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, and $-(CH_2)_mS\mathbf{R^A}$;

[0266] each $\mathbf{R^{36}}$ is independently selected from the group consisting of halogen, $-(CH_2)_mOR^D$, $-NR^ER^F$, $-NR^LC(=O)NR^BR^C$, $-(CH_2)_mS(O)_{0-2}R^D$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, and $-(CH_2)_mR^G$;

[0267] each $\mathbf{R^{39}}$ and $\mathbf{R^{40}}$ are independently selected from the group consisting of hydrogen, halogen, –OH, $-NHR^B$, and an optionally substituted C_1-C_4 alkyl;

[0268] each $\mathbf{R^A}$ is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl;

[0269] each $-NR^BR^C$ is separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ are each independently selected from the group consisting of hydrogen, $-SO_2R^H$, $-C(=O)R^H$, $-C(=O)C(=O)R^H$, $-(CH_2)_mC(=O)OR^H$, $-C(=O)NR^ER^F$, $-(CH_2)_mR^G$, $-(CH_2)_mOR^H$, $-(CH_2)_mR^H$, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_2-C_6 alkenyl, non-aromatic heterocycle, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl where the C_3-C_7 cycloalkyl and the non-aromatic heterocycle are optionally fused with an an optionally substituted aryl or an optionally substituted heteroaryl; or $-NR^BR^C$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-NR^BR^C$ is an optionally substituted C_1-C_6 alkylideneamino;

[0270] each $\mathbf{R^D}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_mR^G$

[0271] each $-NR^ER^F$ is separately selected, wherein $\mathbf{R^E}$ and $\mathbf{R^F}$ are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_mR^G$; or $-NR^ER^F$ is an optionally substituted C_1-C_6 alkylideneaminyl; or $-NR^ER^F$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0272] each $\mathbf{R^G}$ is independently selected from an optionally substituted aryl and an optionally substituted heteroaryl;

[0273] $\mathbf{R^H}$ is selected from the group consisting of hydrogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_3-C_7 cycloalkyl, and an optionally substituted aryl or an optionally substituted heteroaryl;

[0274] each $\mathbf{R^L}$ is independently selected from the group consisting of C_3-C_7 cycloalkyl, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy,

-$(CH_2)_mOR^{LA}$, -$(CH_2)_mNR^{LB}R^{LC}$, aryl and heteroaryl, said aryl and heteroaryl in the definition of R^L are each independently optionally substituted with one or more substituents selected from the group consisting of halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, -$(CH_2)_mNR^{LD}R^{LE}$, aryl and heteroaryl, said aryl and heteroaryl substituent off of R^L are each optionally substituted with one or more halo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or -$(CH_2)_mNR^{LF}R^{LG}$;

[0275] each R^{LA} is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

[0276] R^{LB} and R^{LC} are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkenyl; or –$NR^{LB}R^{LC}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0277] each –$NR^{LD}R^{LE}$ is separately selected, wherein R^{LD} and R^{LE} are each independently selected from the group consisting of hydrogen, aryl, heteroaryl, and optionally substituted C_1-C_6 alkyl, said aryl and heteroaryl in the definition of R^{LD} and R^{LE} are each optionally substituted with C_1-C_6 alkyl or C_1-C_6 alkoxy; or –$NR^{LD}R^{LE}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0278] each –$NR^{LF}R^{LG}$ is separately selected, wherein R^{LF} and R^{LG} are each independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl; or -$NR^{LF}R^{LG}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0279] each –$NR^{LF}R^{LG}$ is separately selected, wherein R^{LF} and R^{LG} are each independently selected from the group consisting of hydrogen, and C_1-C_6 alkyl; or -$NR^{LF}R^{LG}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0280] each **m** is independently 0, 1, or 2;

[0281] each **n** is independently 0, 1, 2, 3, or 4;

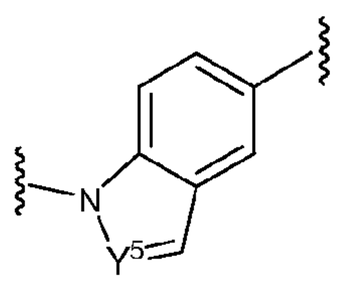
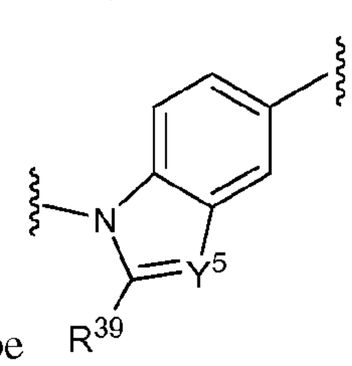
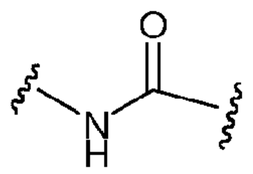
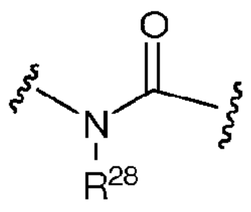
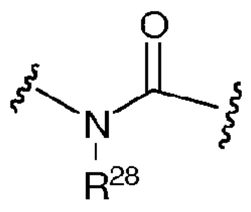
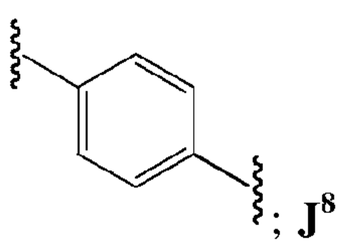
[0282] each **o** is independently 1, 2, or 3;

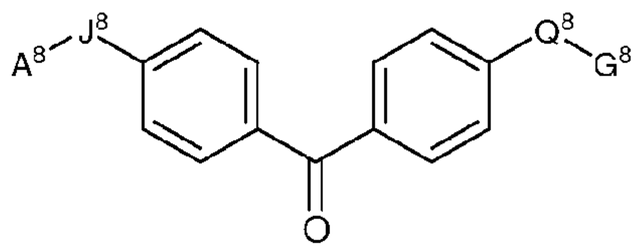
[0283] each **p** is independently 0, 1, 2, or 3;

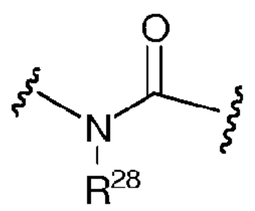
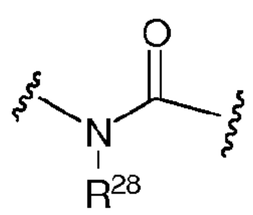
[0284] each **q** is independently 0 or 1; and

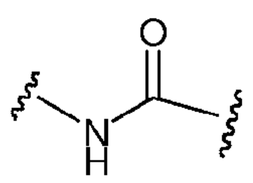
[0285] any bond represented by a dashed and solid line represents a bond selected from the group consisting of a single bond and a double bond.

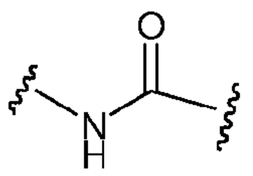
[0286] Some embodiments disclosed herein provide a compound of Formula **IV**, wherein J^8 and Q^8 can each be null. Some embodiments disclosed herein provide a compound of Formula **IV**, wherein A^8 can be aryl substituted with one or more substituents

selected from the group consisting of $\mathbf{R^{31}}$, $\mathbf{R^{32}}$, and $\mathbf{R^{33}}$; $\mathbf{J^8}$ can be -NHC(=O)–; $\mathbf{L^8}$ can be  ; $\mathbf{Q^8}$ can be null; and $\mathbf{G^8}$ can be aryl substituted with one or more substituents selected from the group consisting of $\mathbf{R^{34}}$, $\mathbf{R^{35}}$, and $\mathbf{R^{36}}$. Some embodiments disclosed herein provide a compound of Formula **IV**, wherein $\mathbf{A^8}$ can be aryl substituted with one or more $\mathbf{R^{32}}$; $\mathbf{J^8}$ can be -C(=O)–; $\mathbf{L^8}$ can be  ; $\mathbf{Q^8}$ can be  ; and $\mathbf{G^8}$ can be aryl substituted with one or more $\mathbf{R^{35}}$. Some embodiments disclosed herein provide a compound of Formula **IV**, wherein $\mathbf{A^8}$ can be heteroaryl substituted with one or more substituents selected from the group consisting of $\mathbf{R^{31}}$, $\mathbf{R^{32}}$, and $\mathbf{R^{33}}$; $\mathbf{G^8}$ can be heteroaryl substituted with one or more substituents selected from the group consisting of $\mathbf{R^{34}}$, $\mathbf{R^{35}}$, and $\mathbf{R^{36}}$; $\mathbf{J^8}$ can be  ; and $\mathbf{Q^8}$ can be  . Some embodiments disclosed herein provide a compound of Formula **IV**, wherein $\mathbf{L^8}$ can be  ; $\mathbf{J^8}$ can be -C(=O)–; $\mathbf{Q^8}$ can be –C(=O)NH–; $\mathbf{A^8}$ can be aryl substituted with $\mathbf{R^{32}}$; $\mathbf{G^8}$ can be aryl substituted with $\mathbf{R^{35}}$; $\mathbf{R^{32}}$ can be $-N\mathbf{R^B}\mathbf{R^C}$, and $\mathbf{R^{35}}$ can be $-N\mathbf{R^B}\mathbf{R^C}$.

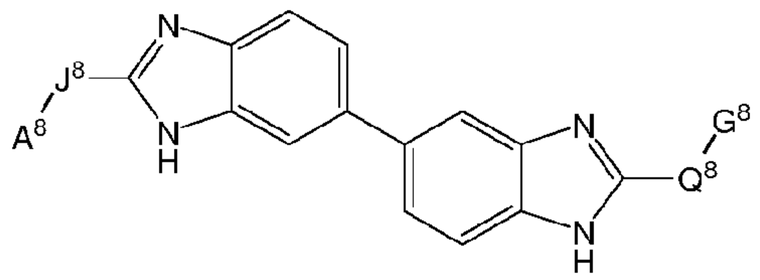
[0287] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVa:**  (**IVa**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{J^8}$ can be selected from the group

consisting -OC(=O)–, –S(=O)$_2$-NH$_2$–, -(CH$_2$)$_n$NH–, and  ; and **Q^8** can be selected from the group consisting -OC(=O)–, –S(=O)$_2$-NH$_2$–, -(CH$_2$)$_n$NH–, and  . Some embodiments disclosed herein provide a compound of Formula **IVa**,



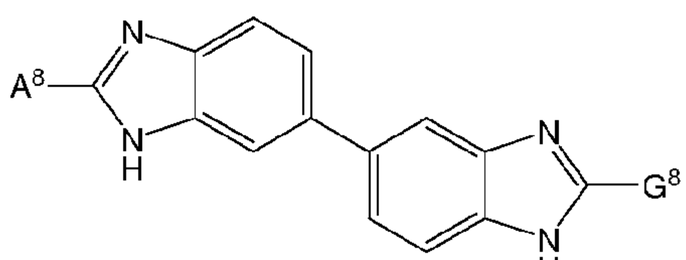
wherein **J^8** can be selected from the group consisting of –S(=O)$_2$-NH$_2$– and ; and **Q^8** can be selected from the group consisting –S(=O)$_2$-NH$_2$–,and  .

[0288] Some embodiments disclosed herein provide a compound of Formula **IV**



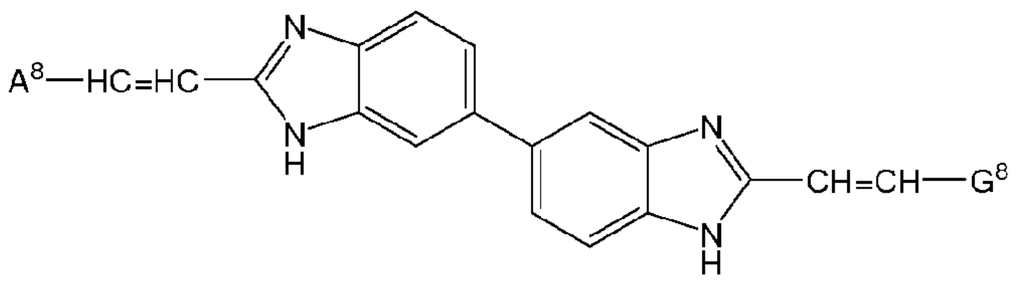
having the structure of Formula **IVb:** (**IVb**), and pharmaceutically acceptable salts thereof, wherein **J^8** can be -CH=CH–; or **J^8** can be null; and **Q^8** can be -CH=CH–; or **Q^8** can be null.

[0289] Some embodiments disclosed herein provide a compound of Formula **IVb**



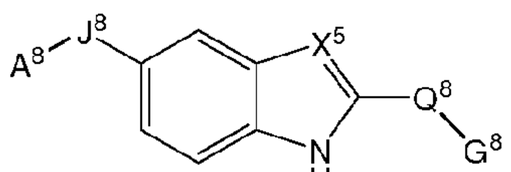
having the structure of Formula **IVba:** (**IVba**), and pharmaceutically acceptable salts thereof.

[0290] Some embodiments disclosed herein provide a compound of Formula **IVb** having the structure of Formula **IVbc:**

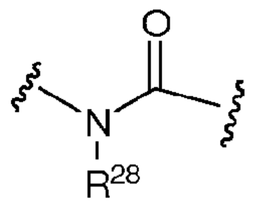


(**IVba**), and pharmaceutically acceptable salts thereof.

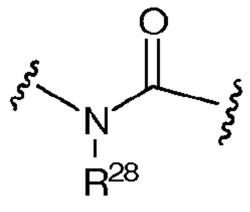
[0291] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVc:**



(**IVc**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{J^8}$ can be selected from the group consisting of -OC(=O)–, –NHC(=O)NH–, -S(=O)$_2$-NH$_2$–, and

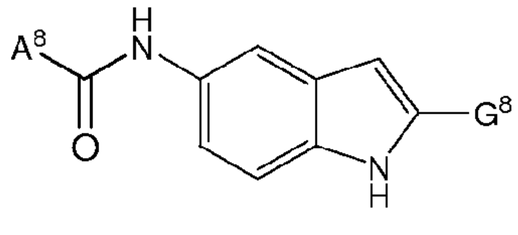


; or $\mathbf{J^8}$ can be null; $\mathbf{Q^8}$ can be selected from the group consisting of -OC(=O)–, –NHC(=O)NH–, -S(=O)$_2$-NH$_2$–, and

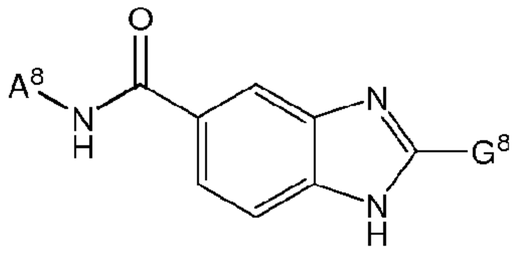


; or $\mathbf{Q^8}$ can be null.

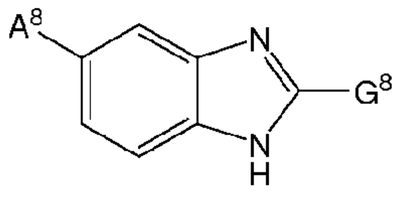
[0292] Some embodiments disclosed herein provide a compound of Formula **IVc** having the structure of Formula **IVca:**



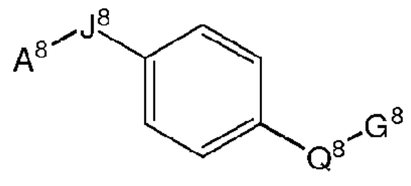
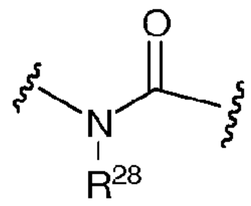
(**IVca**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVcb:**

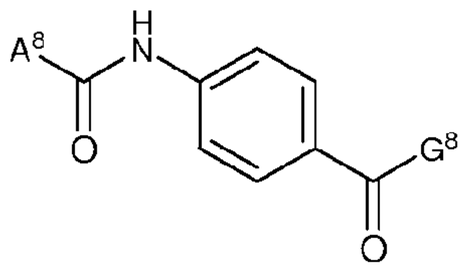
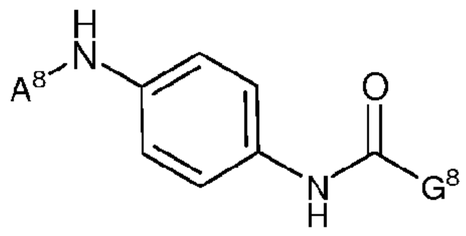
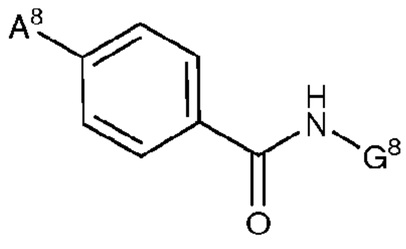
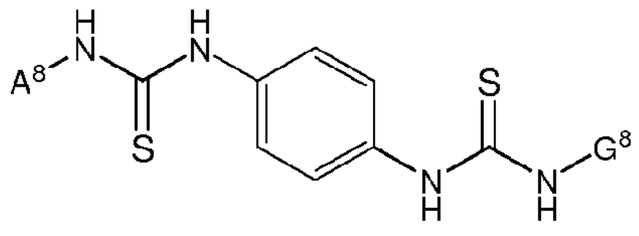


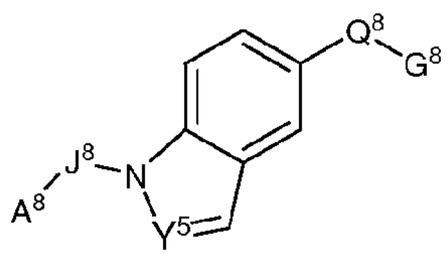
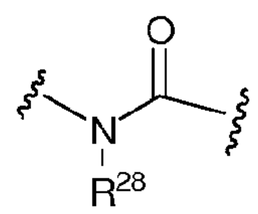
(**IVcb**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVcc:**

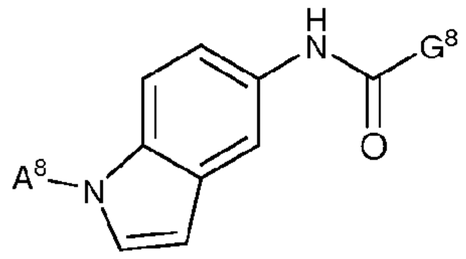
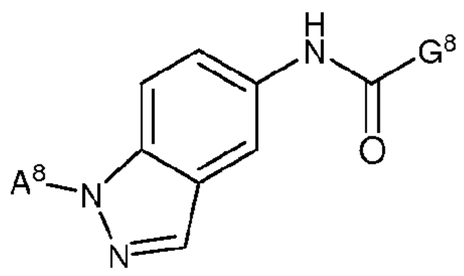
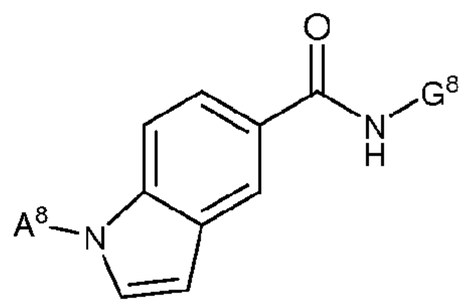


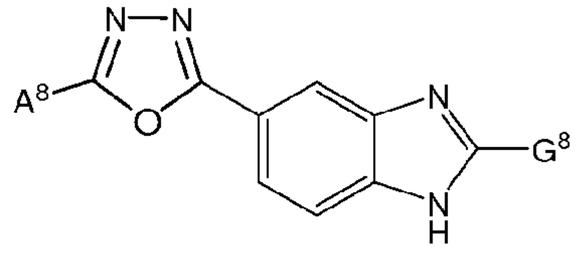
(**IVcc**), and pharmaceutically acceptable salts thereof.

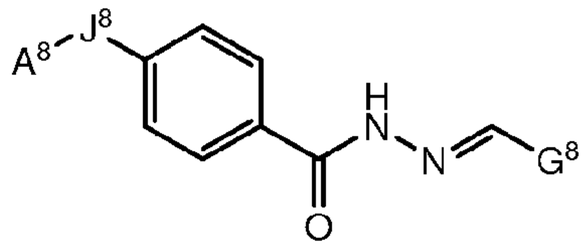
[0293] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVd:**  (**IVd**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{J^8}$ can be selected from the group consisting of -C(=O)–, -$(CH_2)_n$NH–, -NHC(=S)NH-, and  ; or $\mathbf{J^8}$ can be null; $\mathbf{Q^8}$ can be selected from the group consisting of -C(=O)–, –NHC(=S)NH–, and .

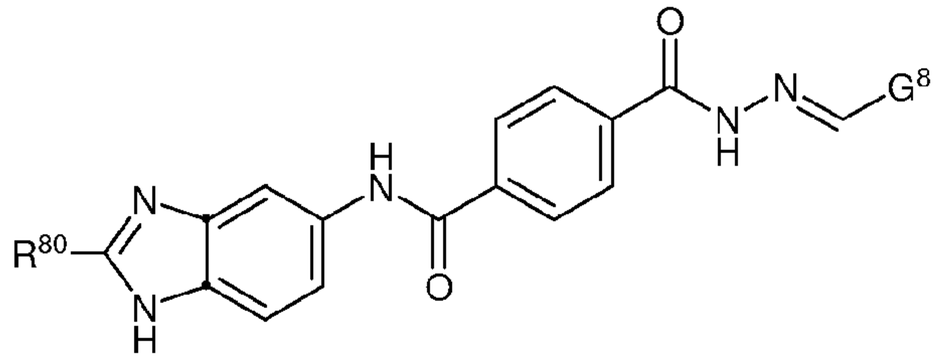
[0294] Some embodiments disclosed herein provide a compound of Formula **IVd** having the structure of Formula **IVda:**  (**IVda**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVdb:**  (**IVdb**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVdc:**  (**IVdc**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVde:**  (**IVde**), and pharmaceutically acceptable salts thereof.

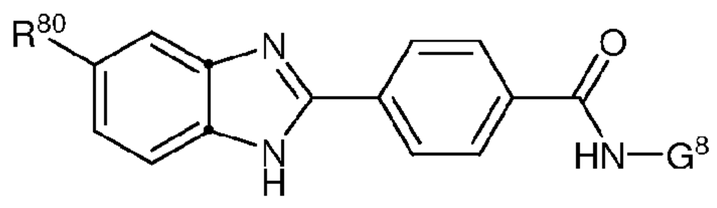
[0295] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVe:**  (**IVe**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{J^8}$ can be null; and $\mathbf{Q^8}$ can be  .

[0296] Some embodiments disclosed herein provide a compound of Formula **IVe** having the structure of Formula **IVea:**  (**IVea**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVeb:**  (**IVeb**), and pharmaceutically acceptable salts thereof, or having the structure of Formula **IVec:**  (**IVec**), and pharmaceutically acceptable salts thereof.

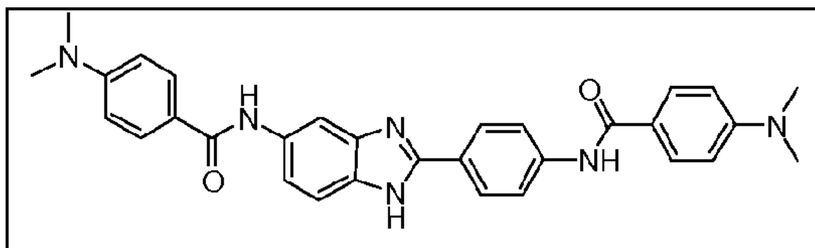
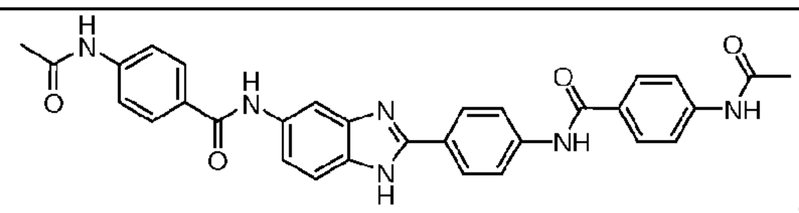
[0297] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVf:**  (**IVf**), and pharmaceutically acceptable salts thereof.

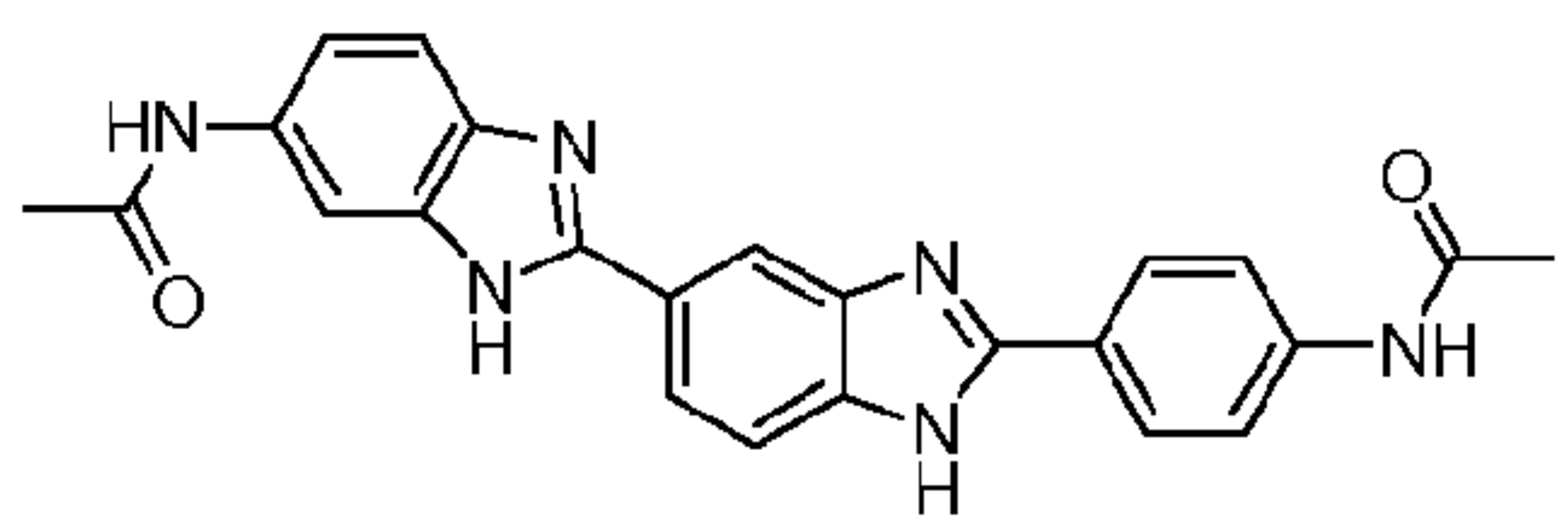
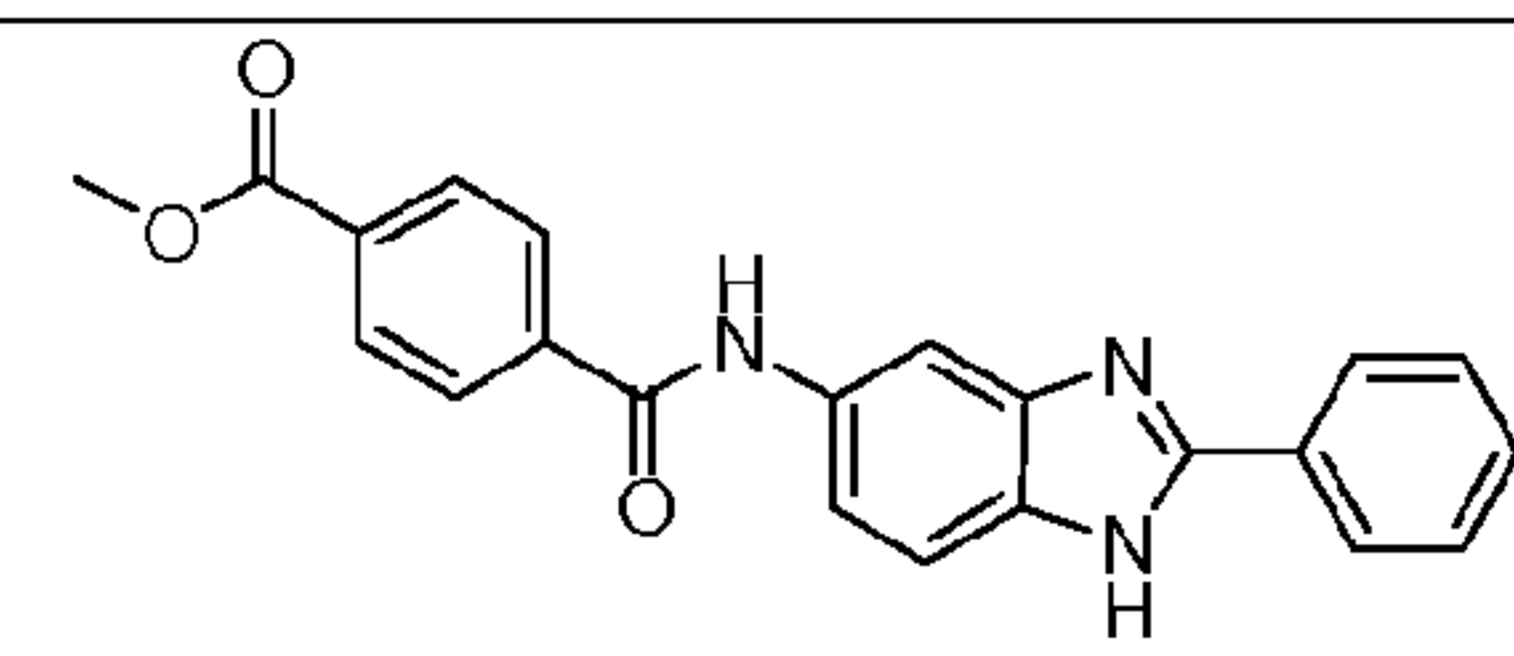
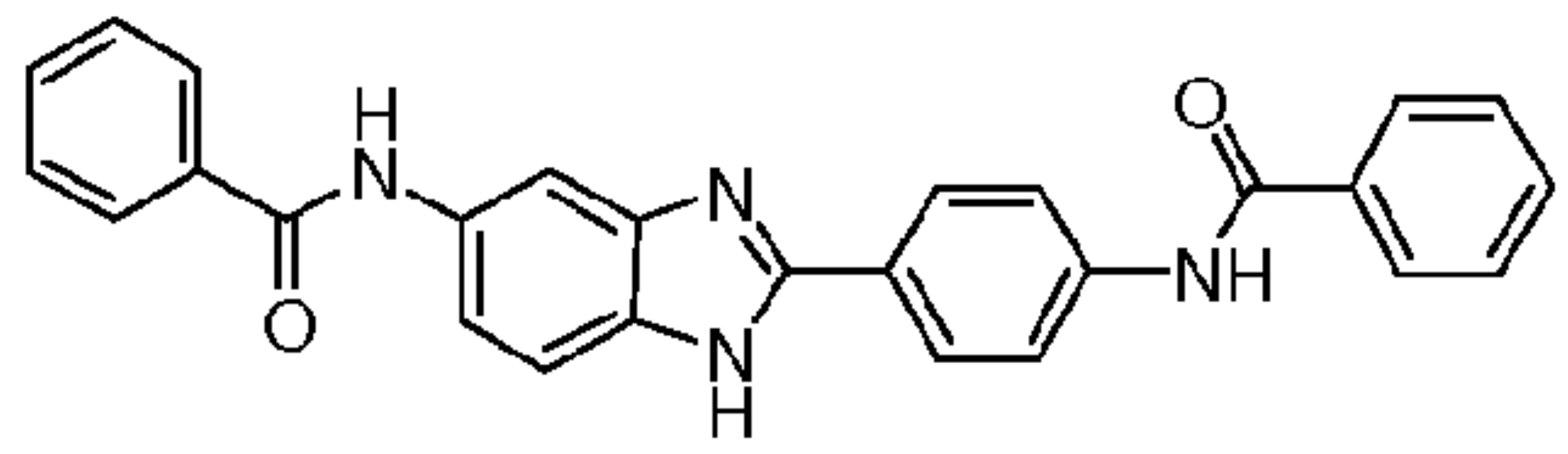
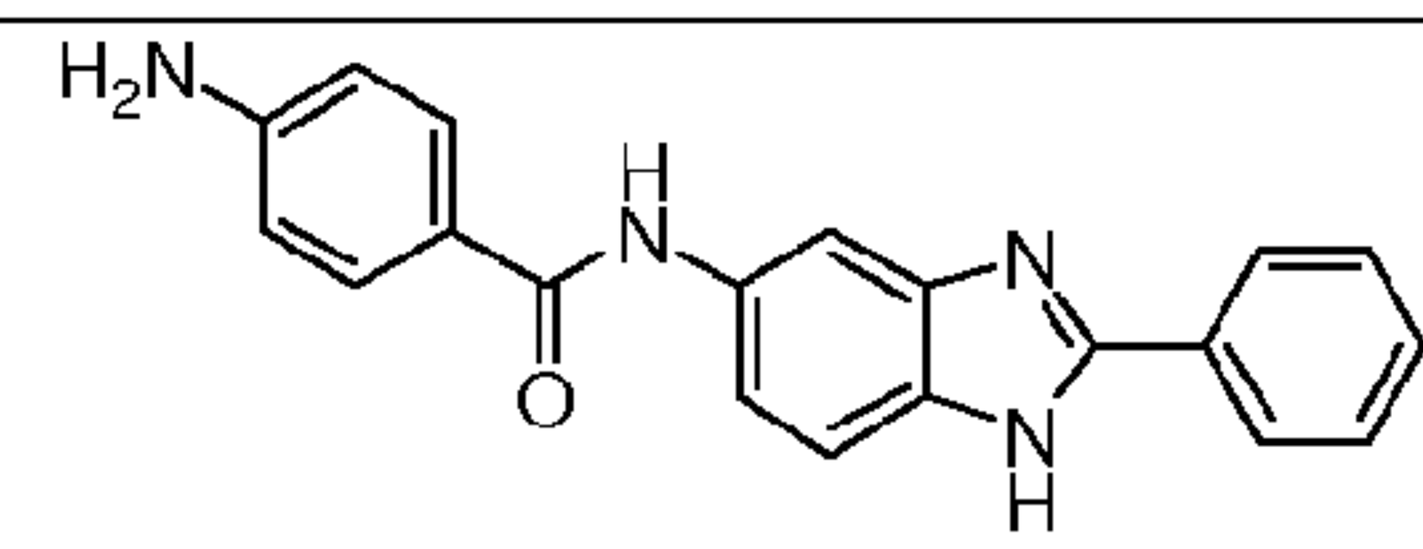
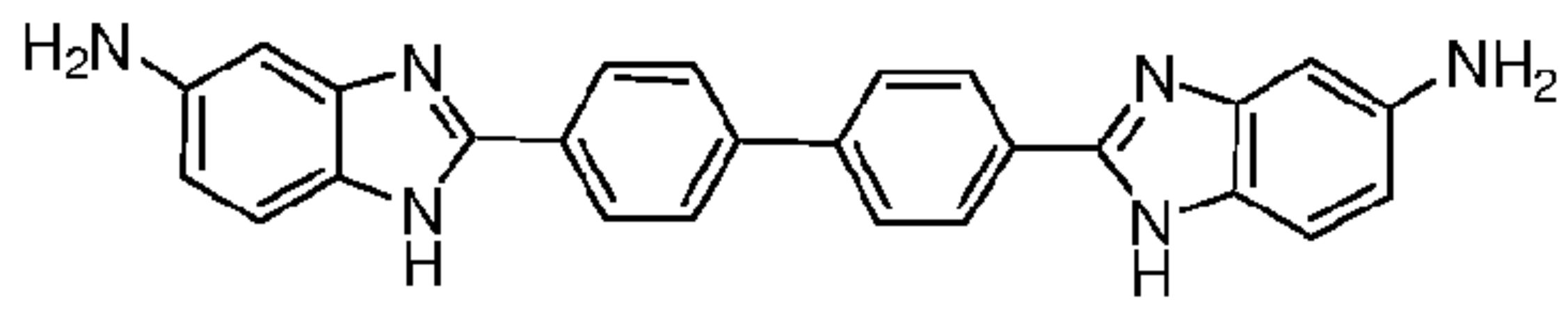
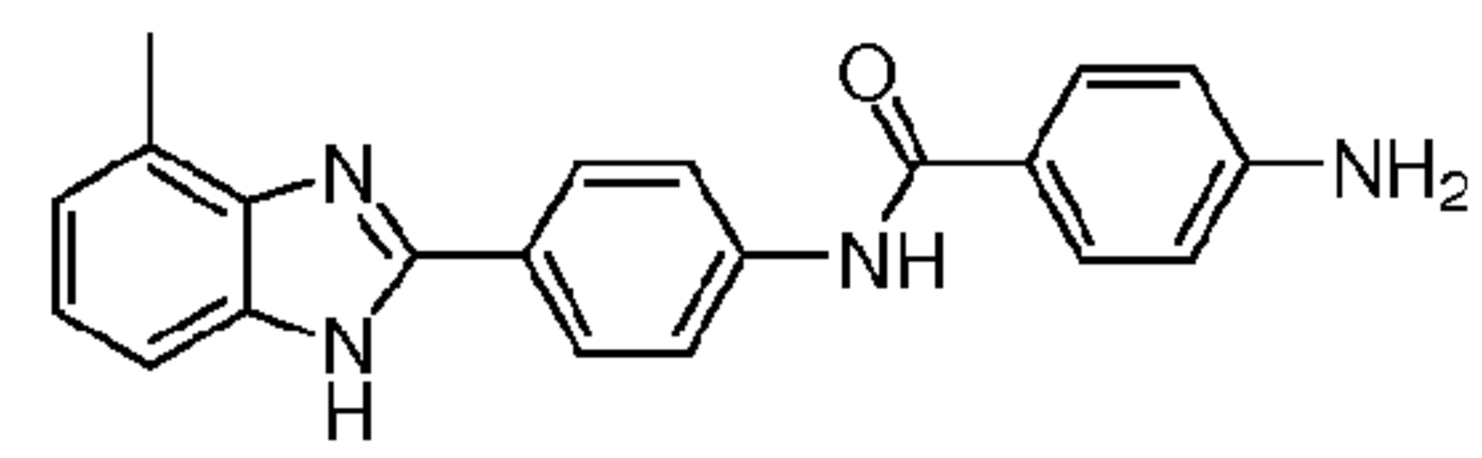
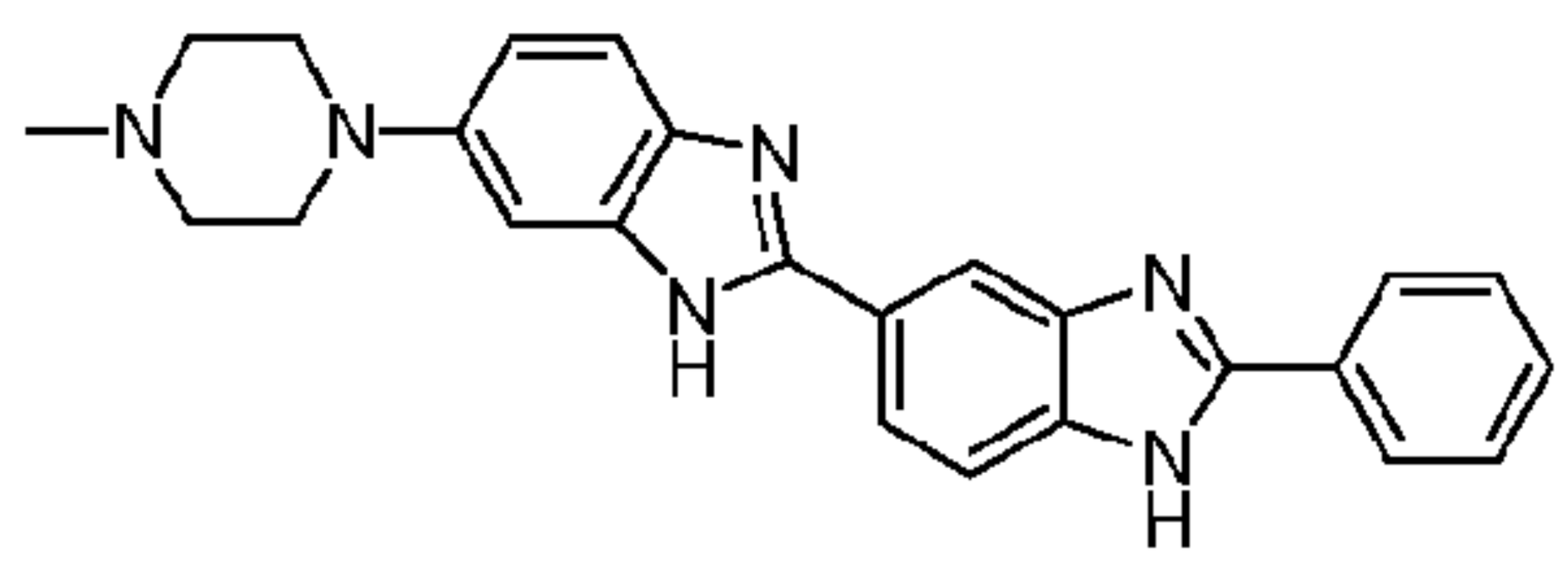
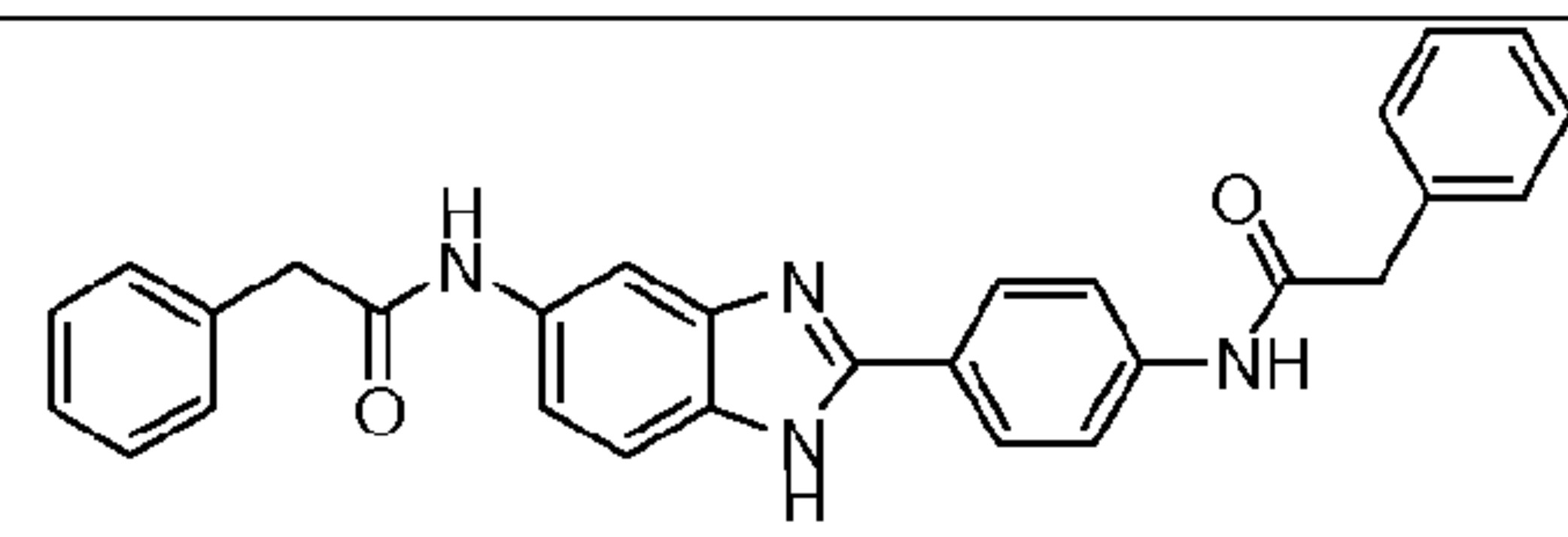
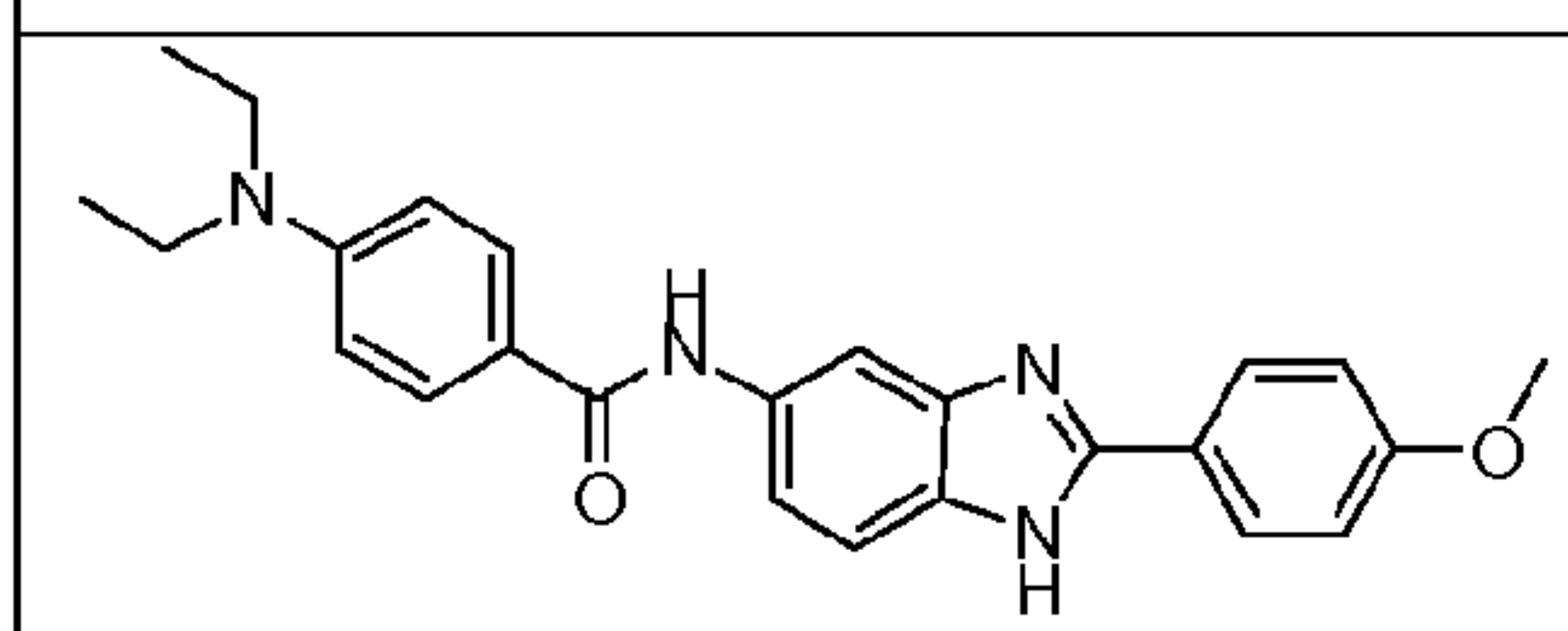
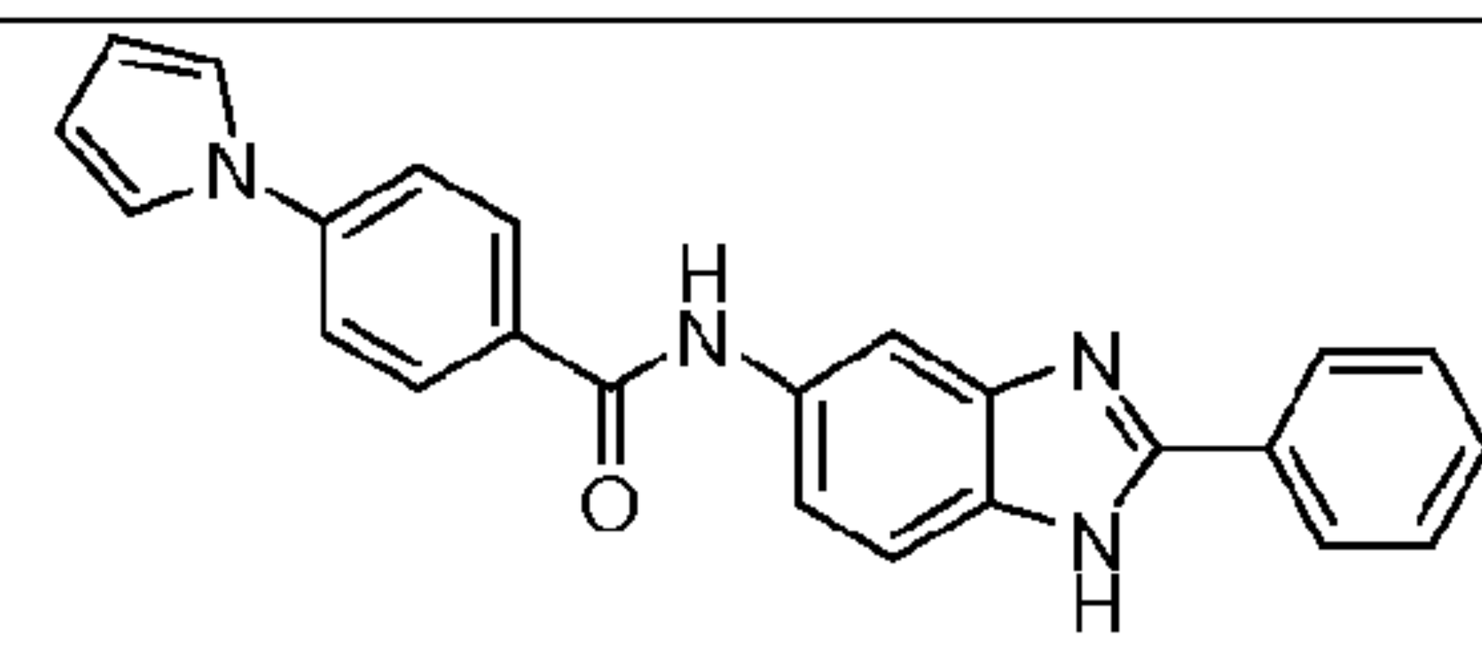
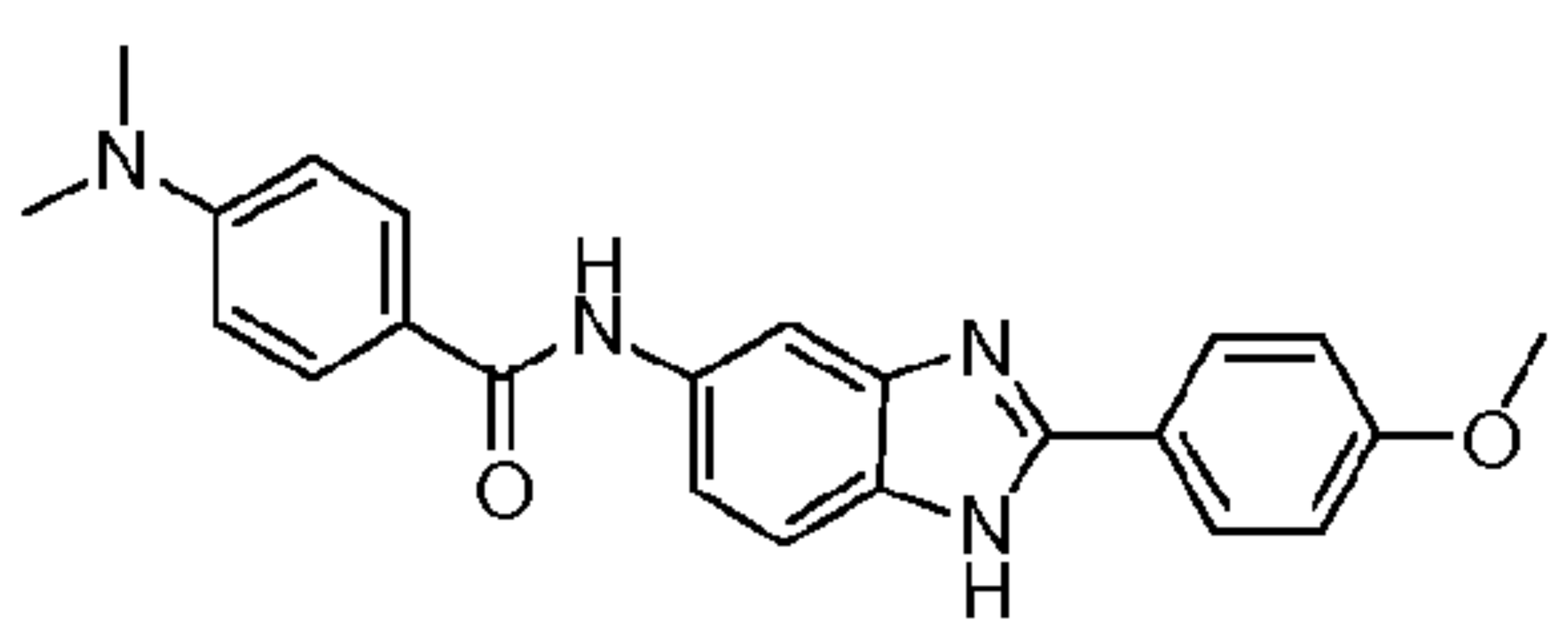
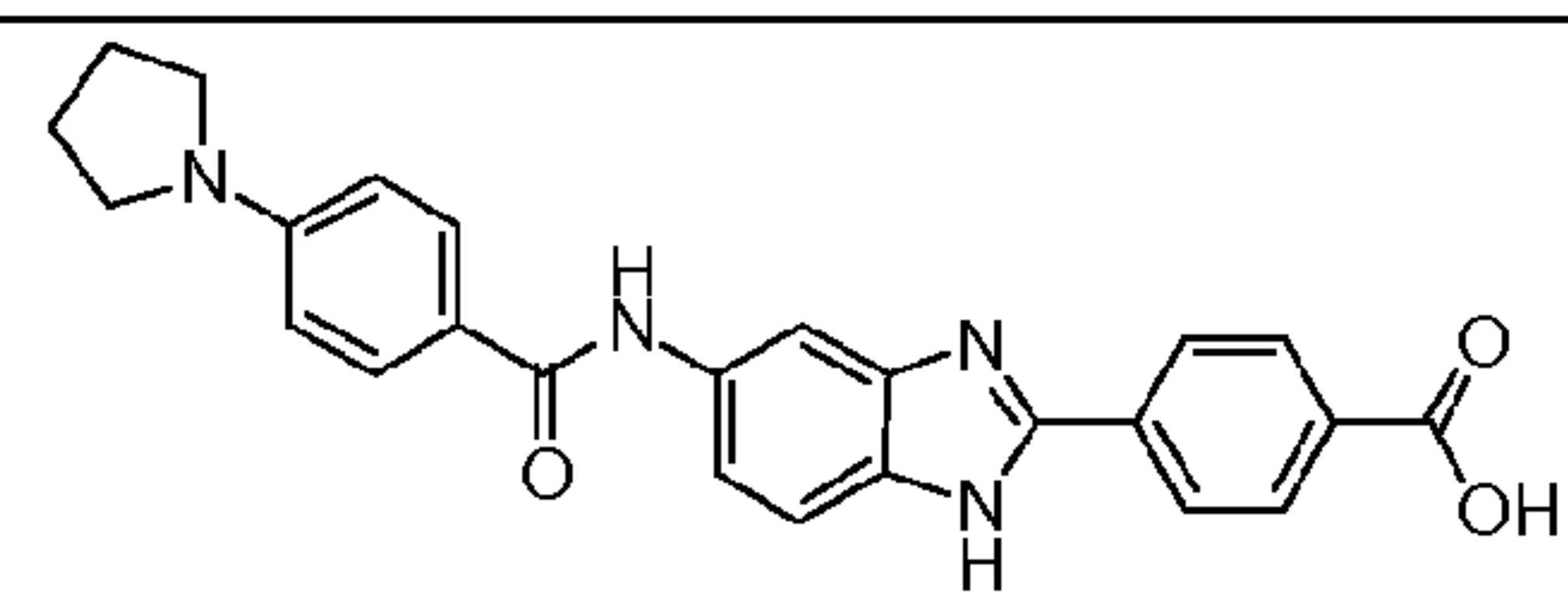
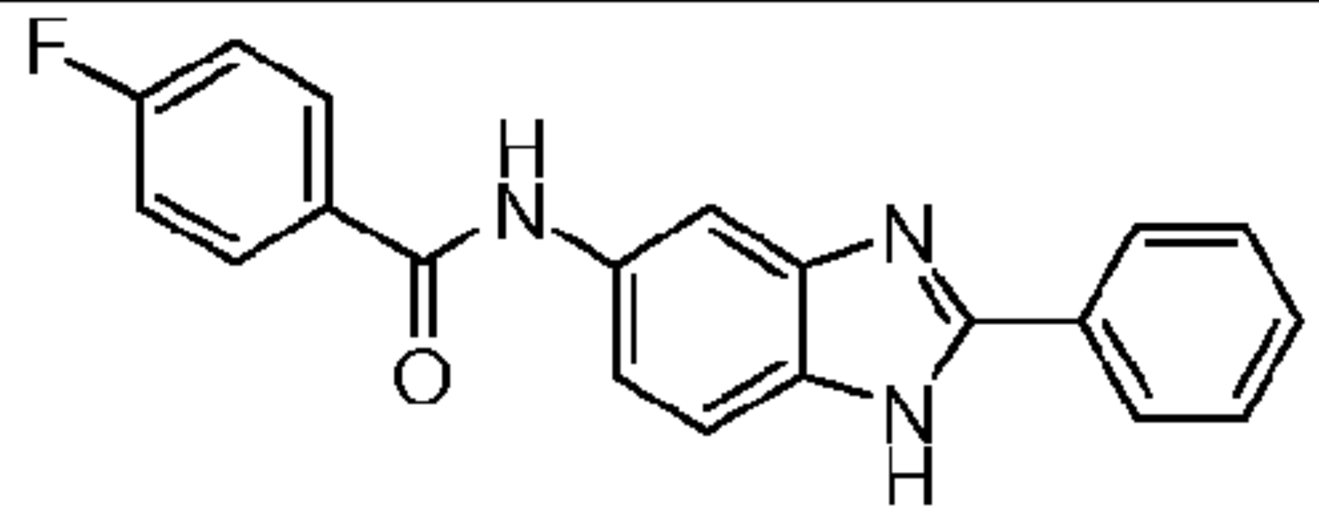
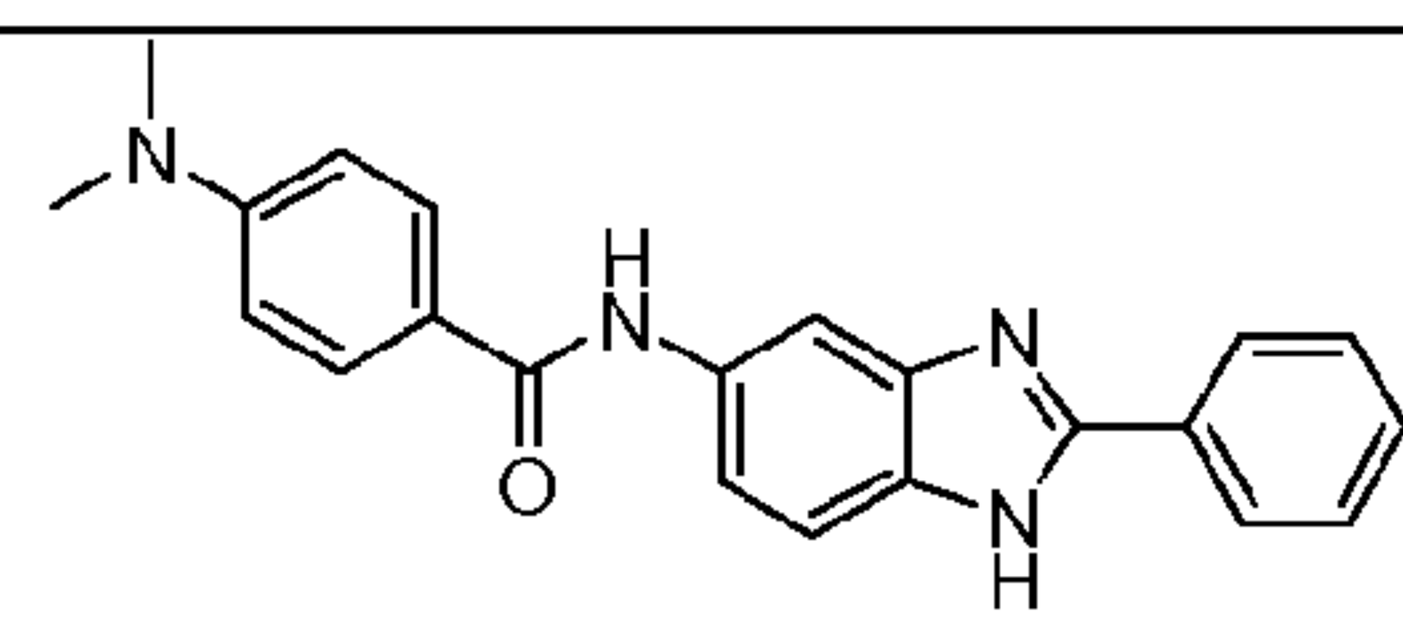
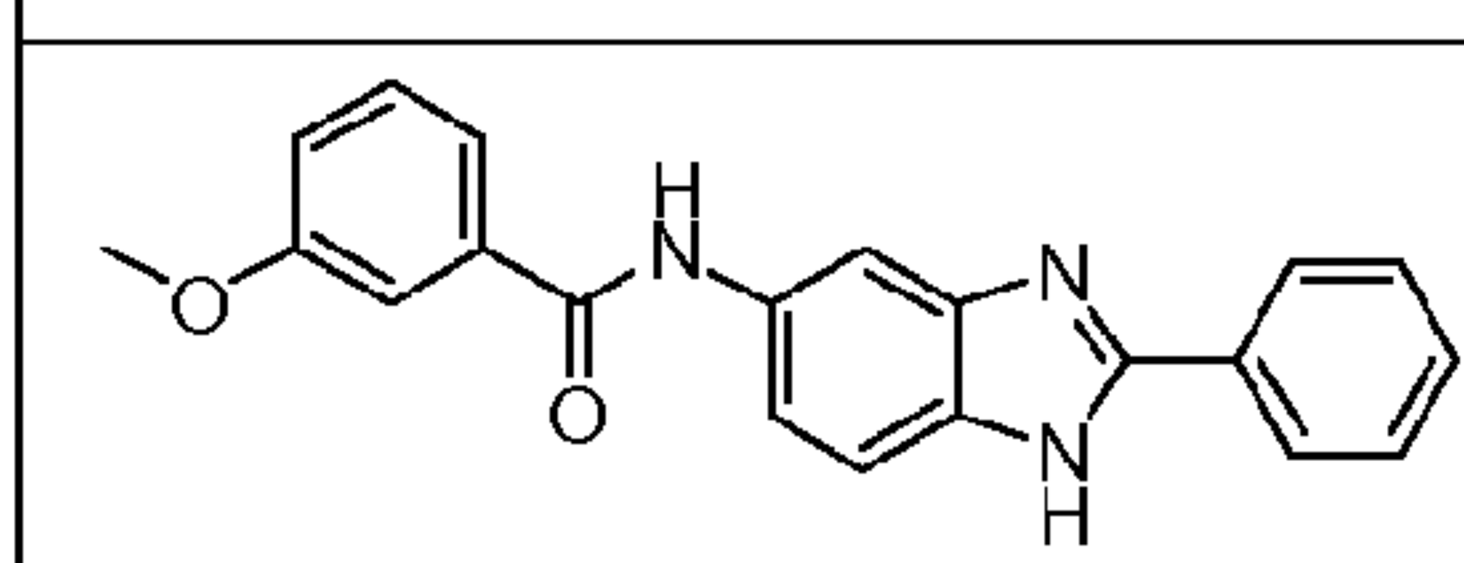
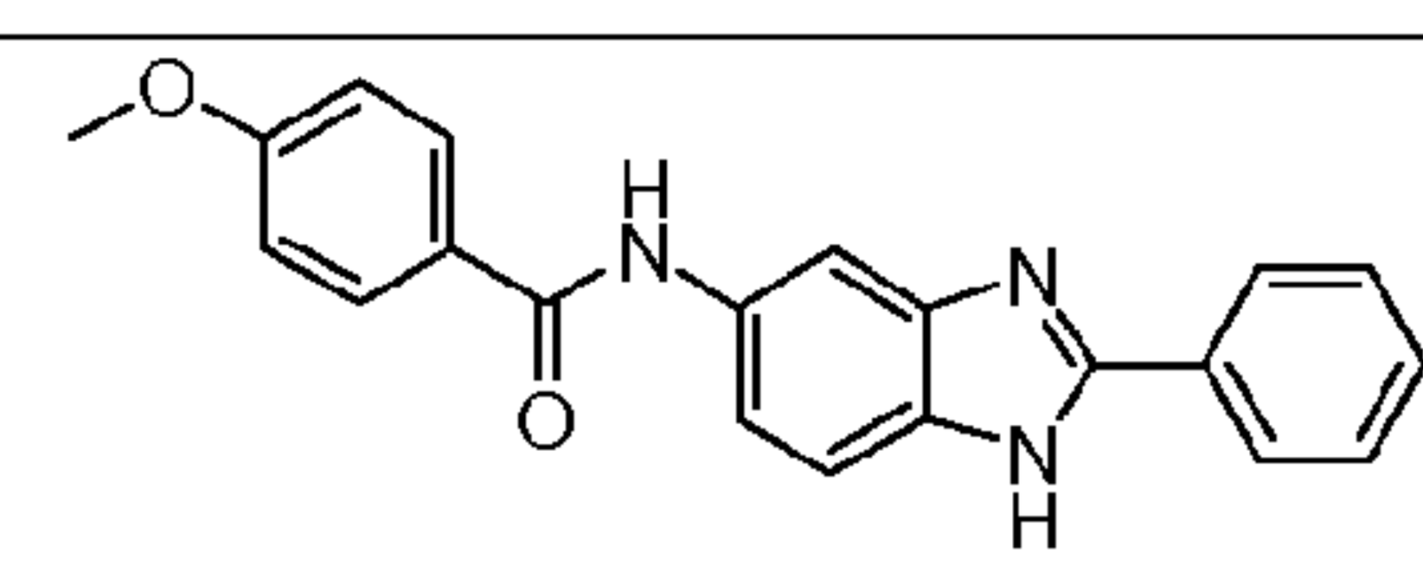
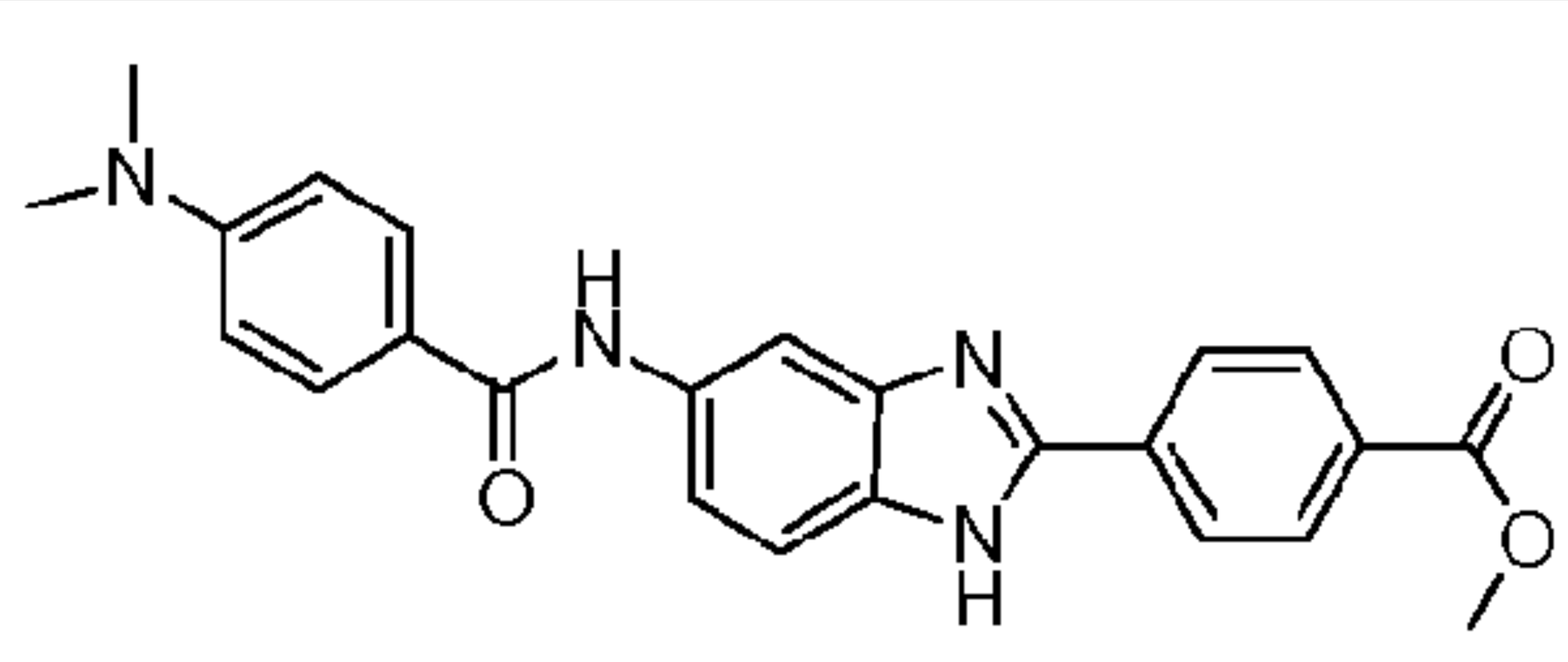
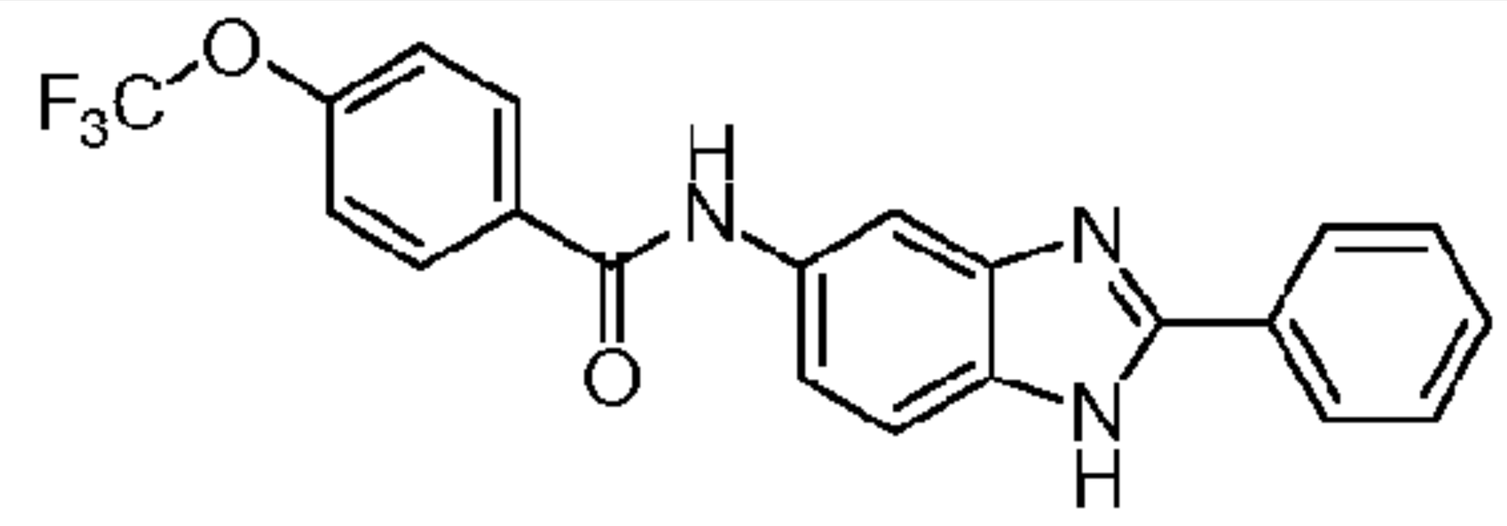
[0298] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVg:**  (**IVg**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{J^8}$ can be selected from the group consisting of $-(CH_2)_n[NHC(=O)](CH_2)_oNHC(=O)(CH_2)_p-$ and $-(CH_2)_n[NHC(=O)](CH_2)_o[NH]_q-$.

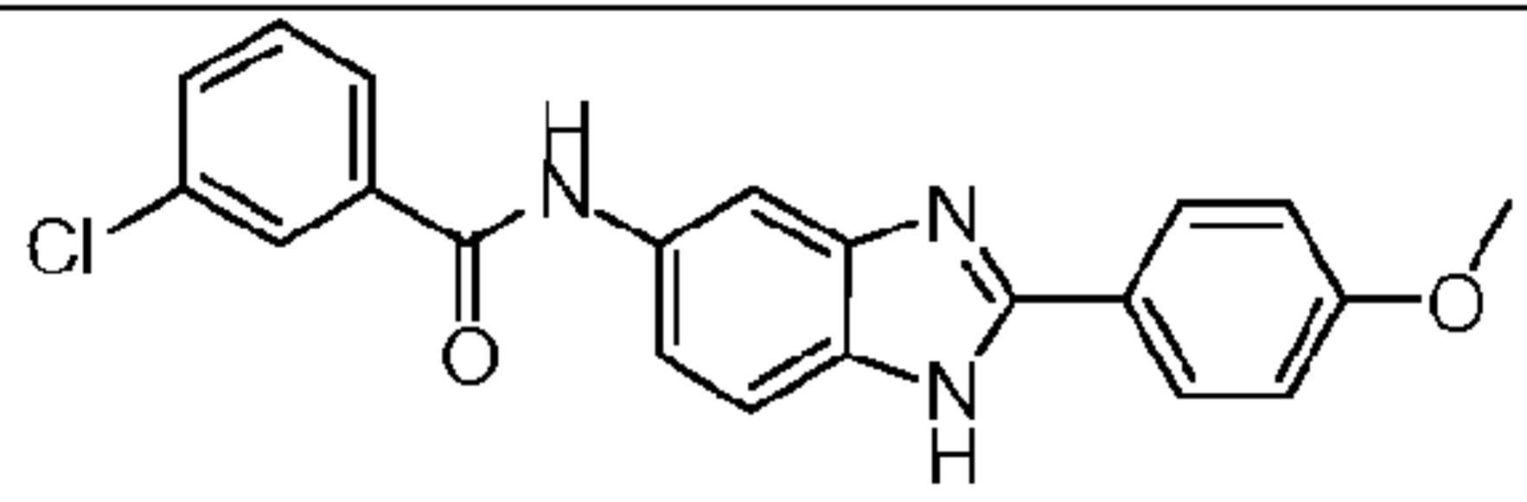
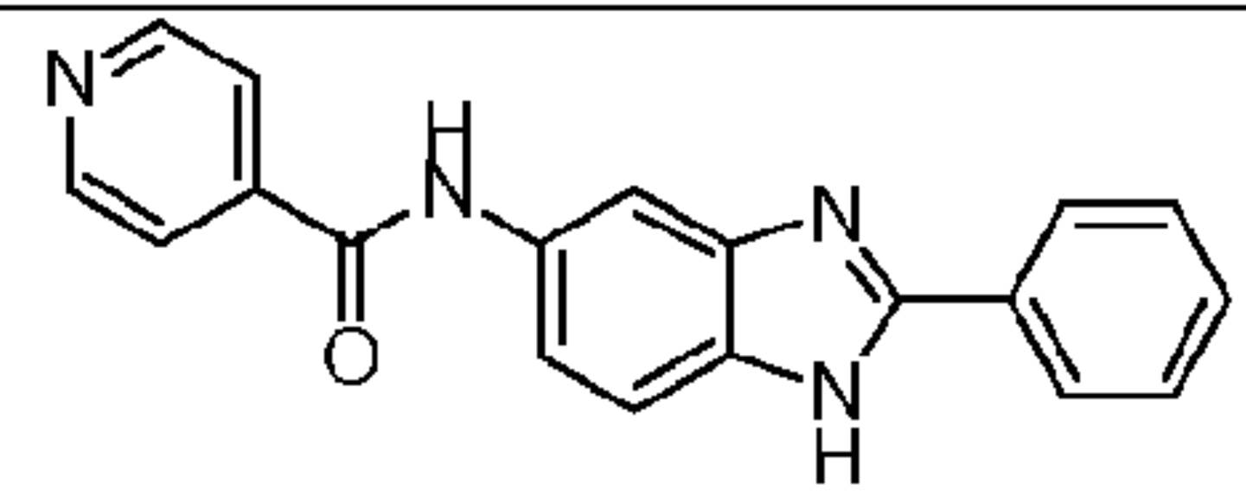
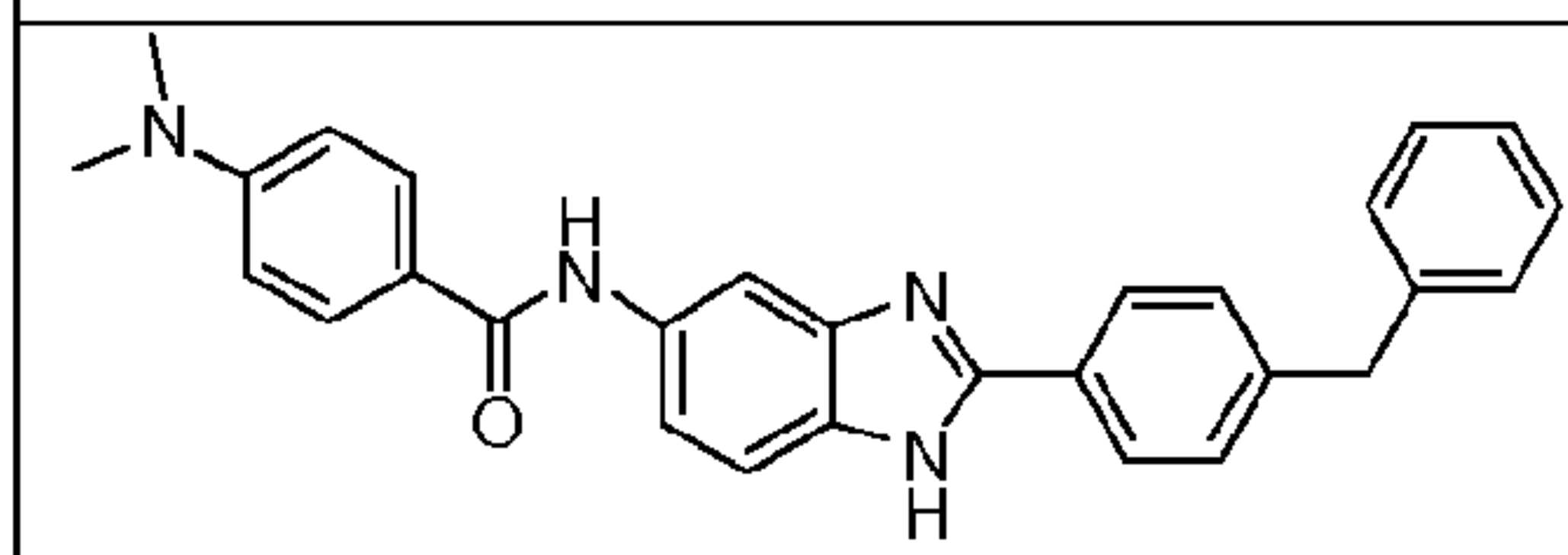
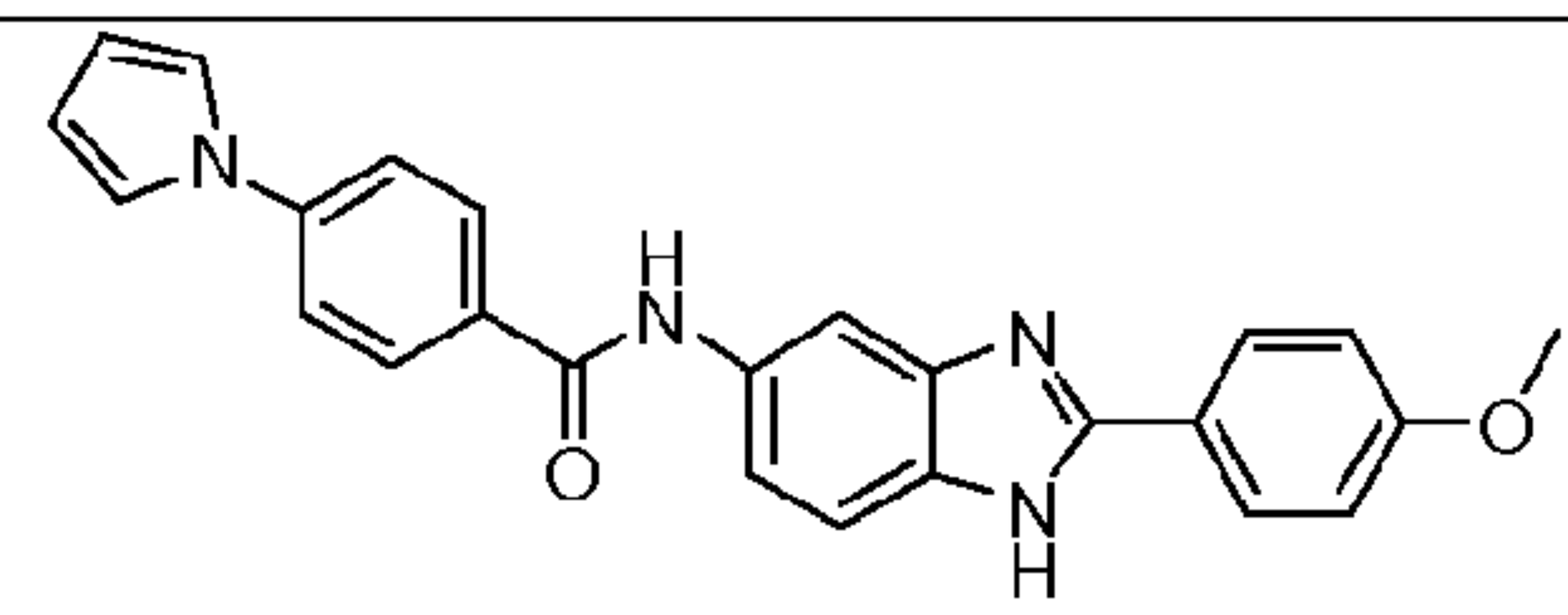
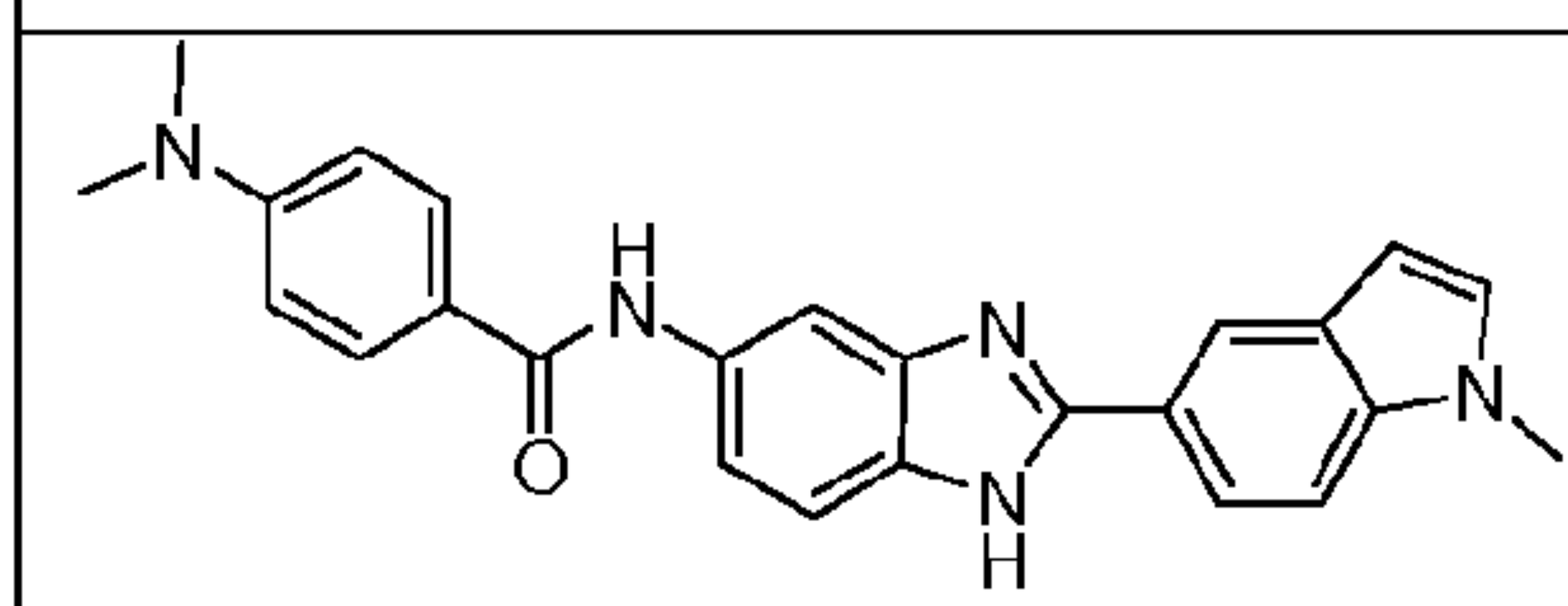
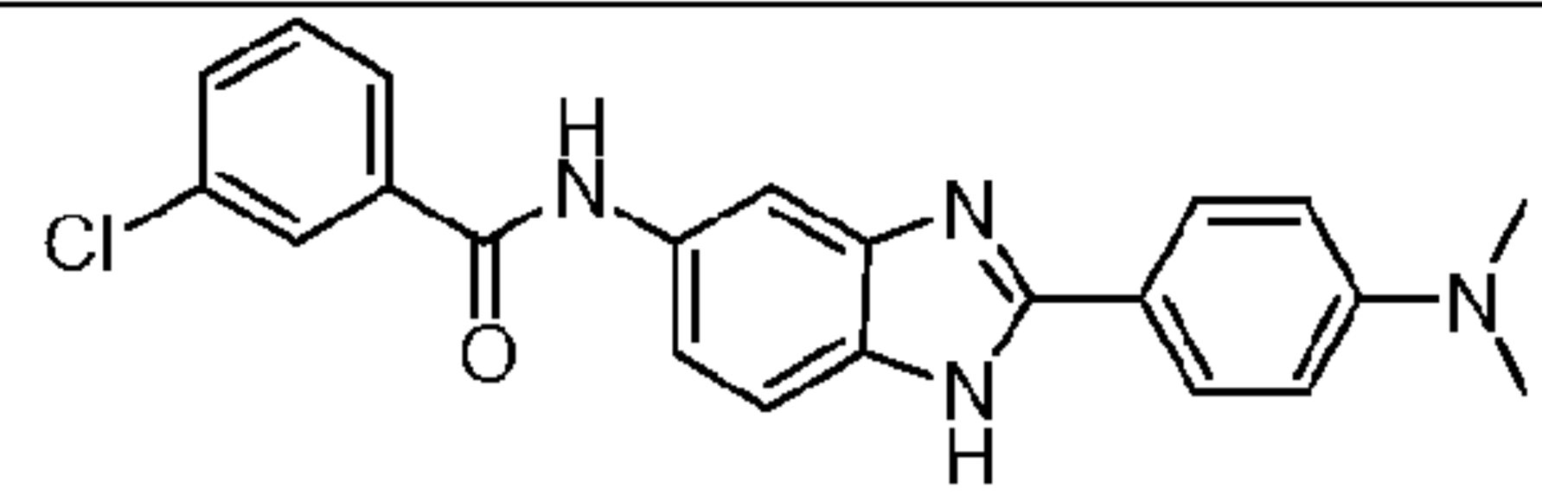
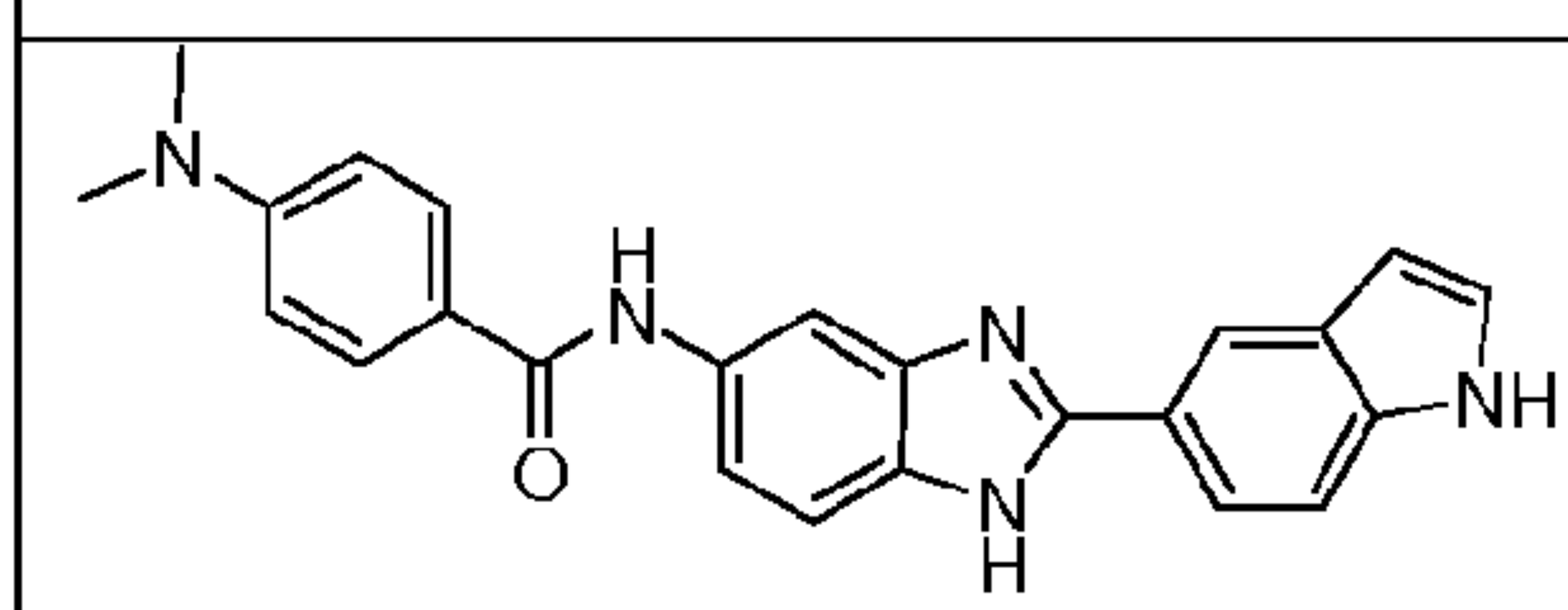
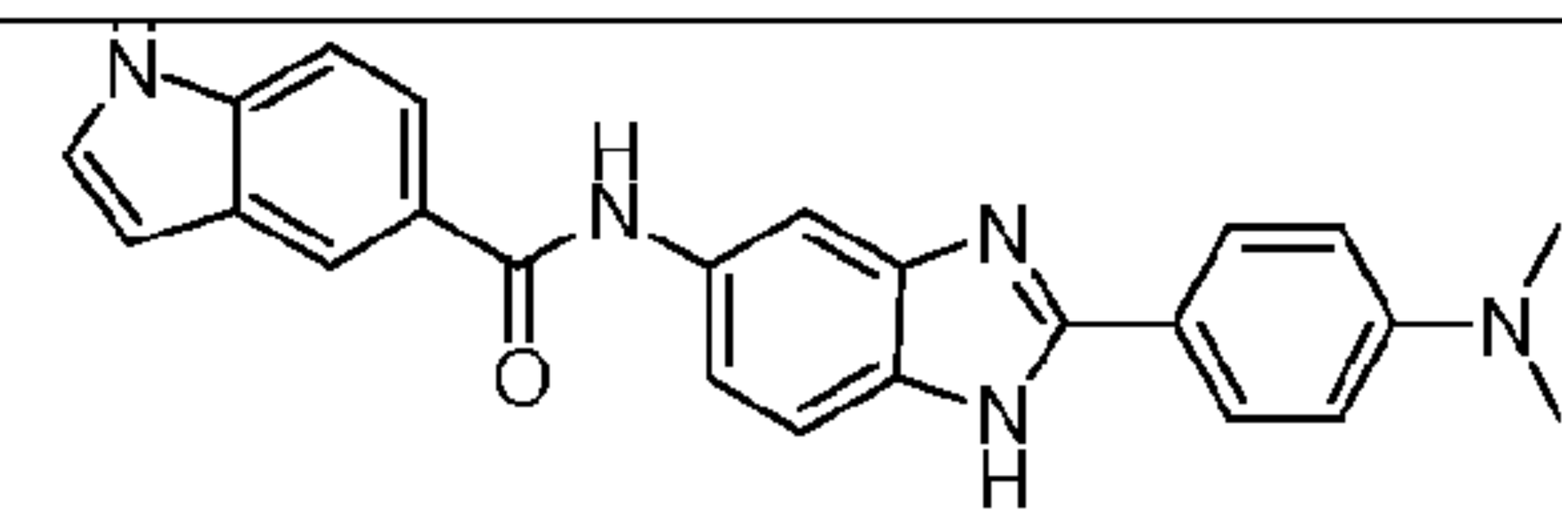
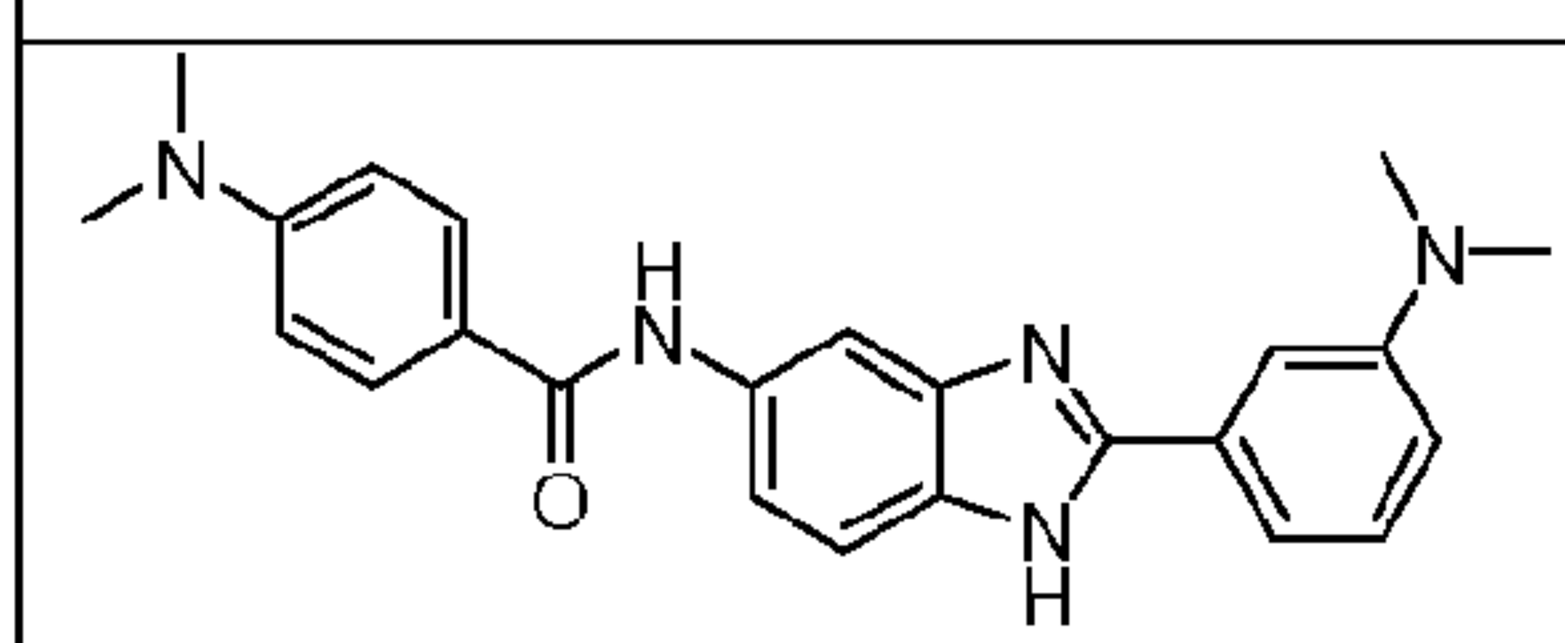
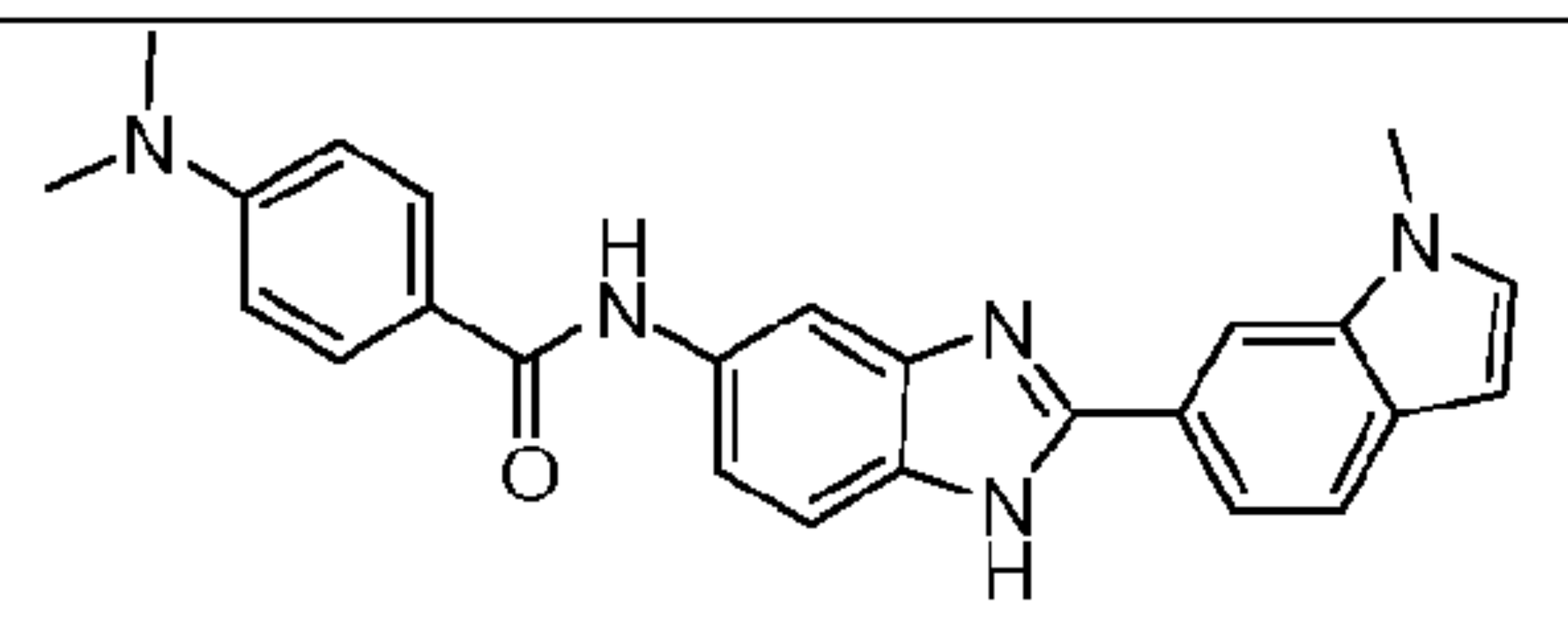
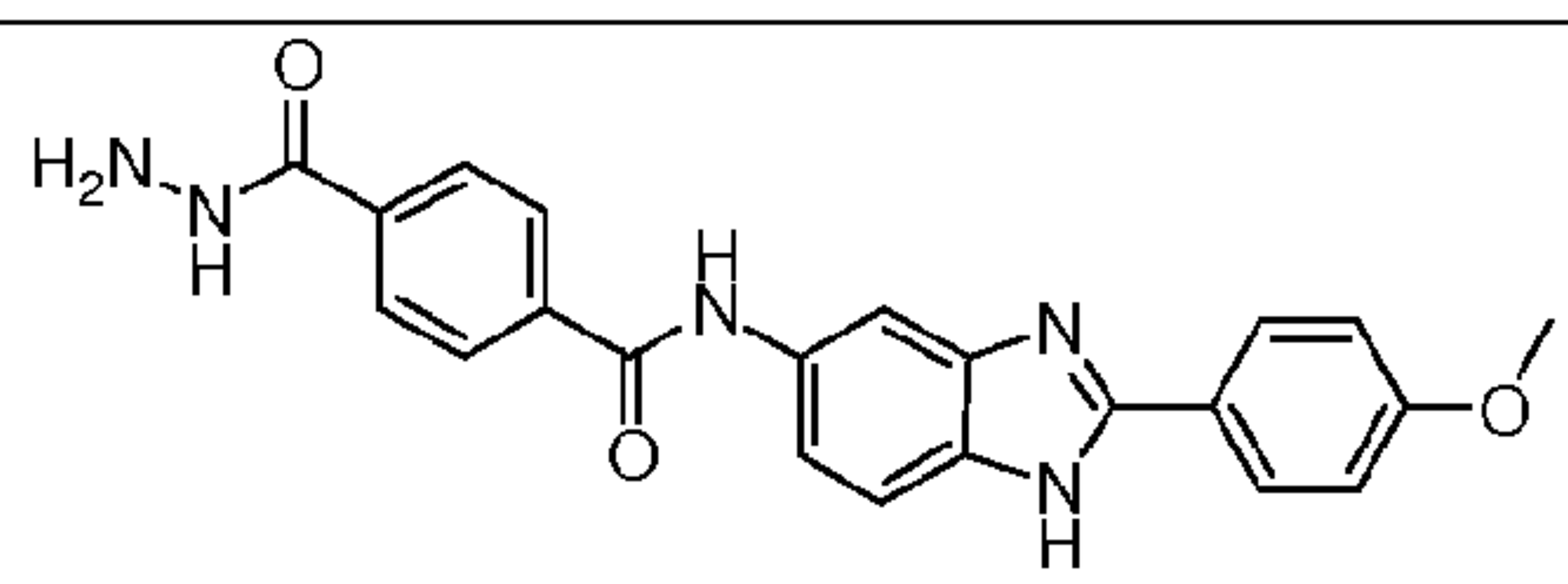
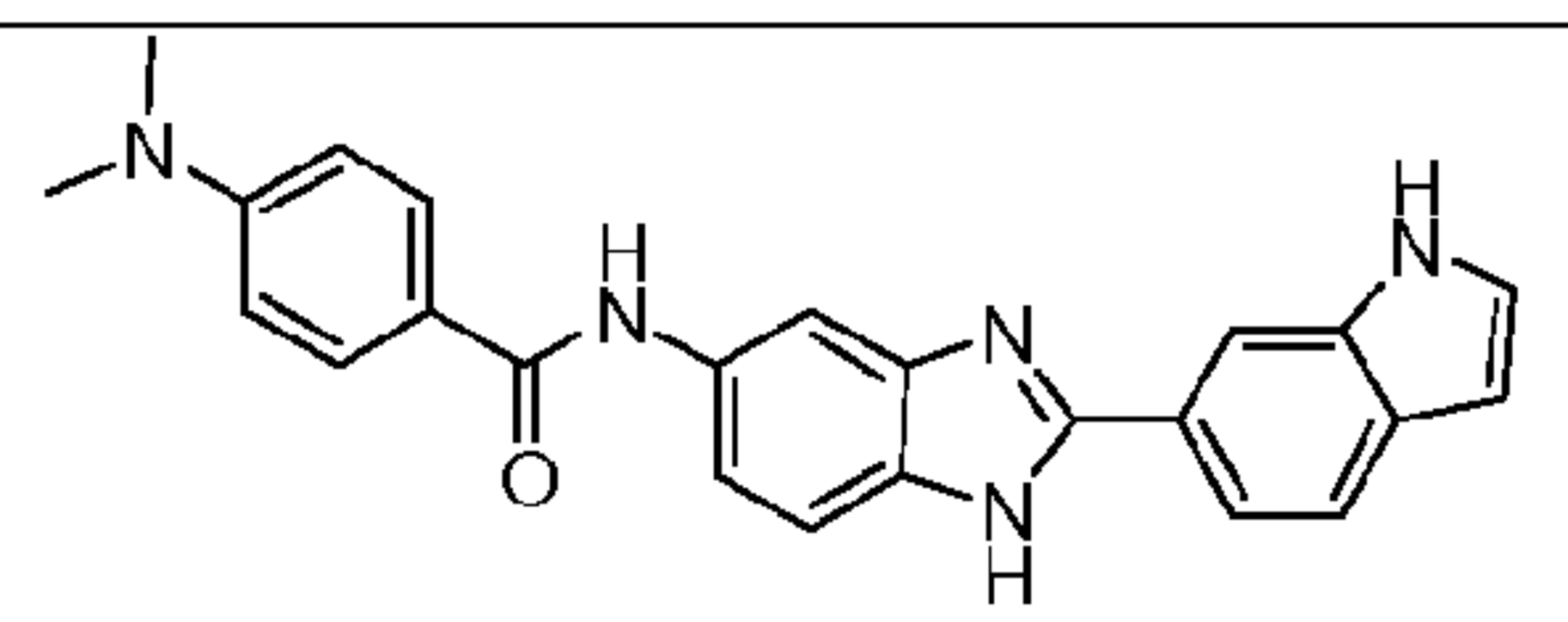
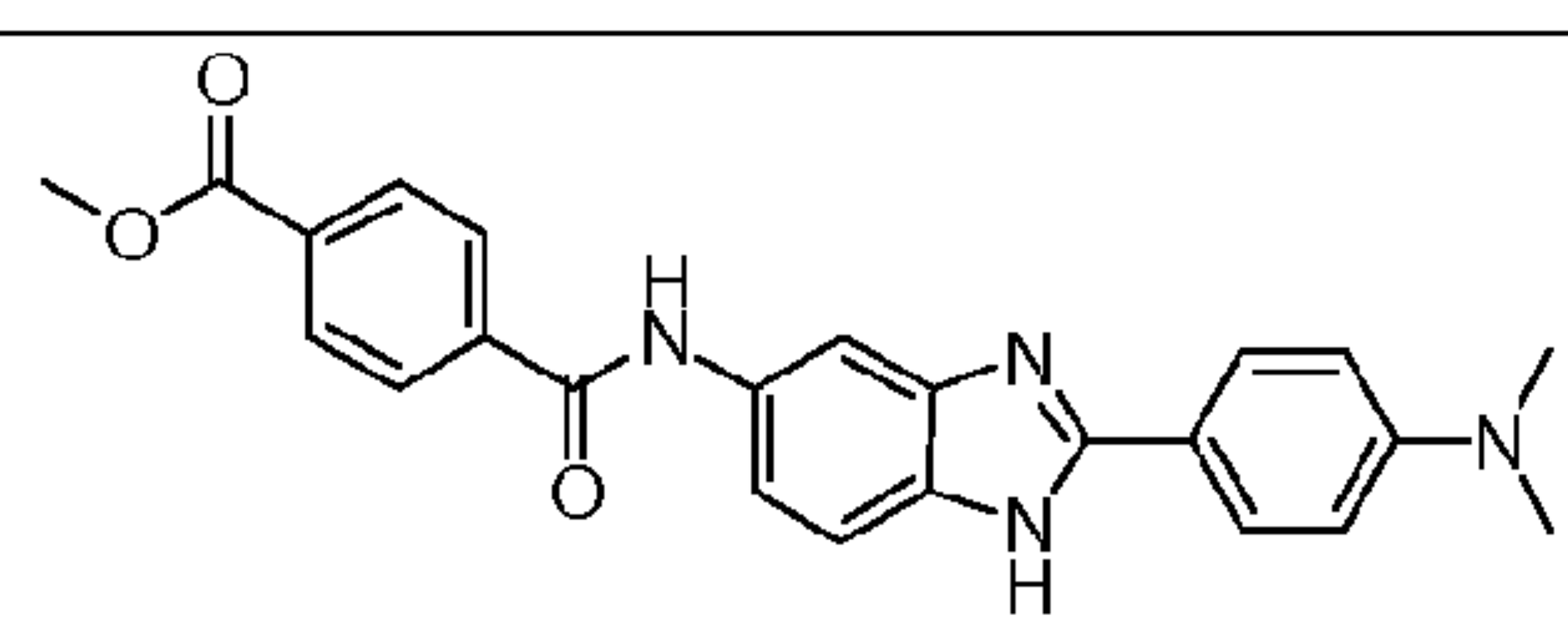
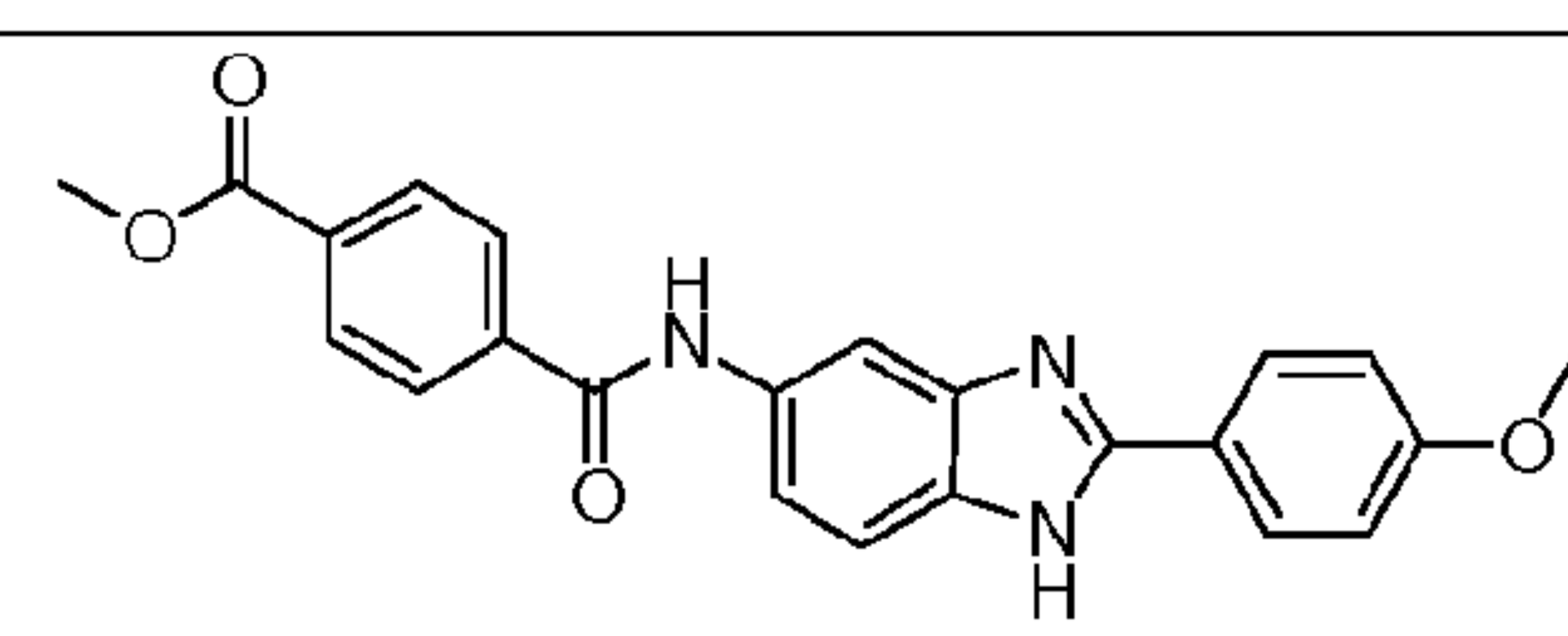
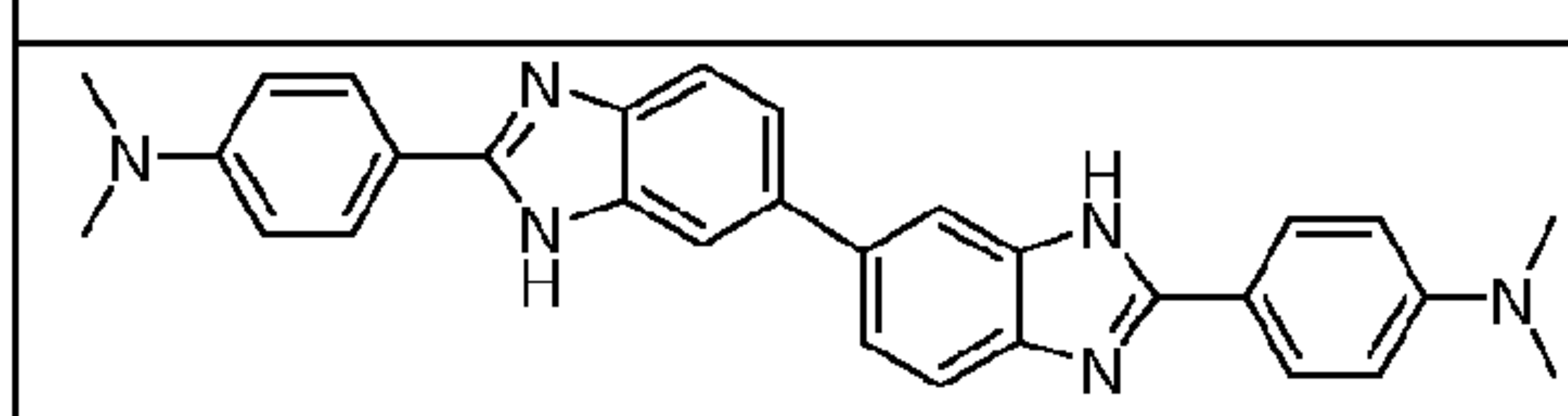
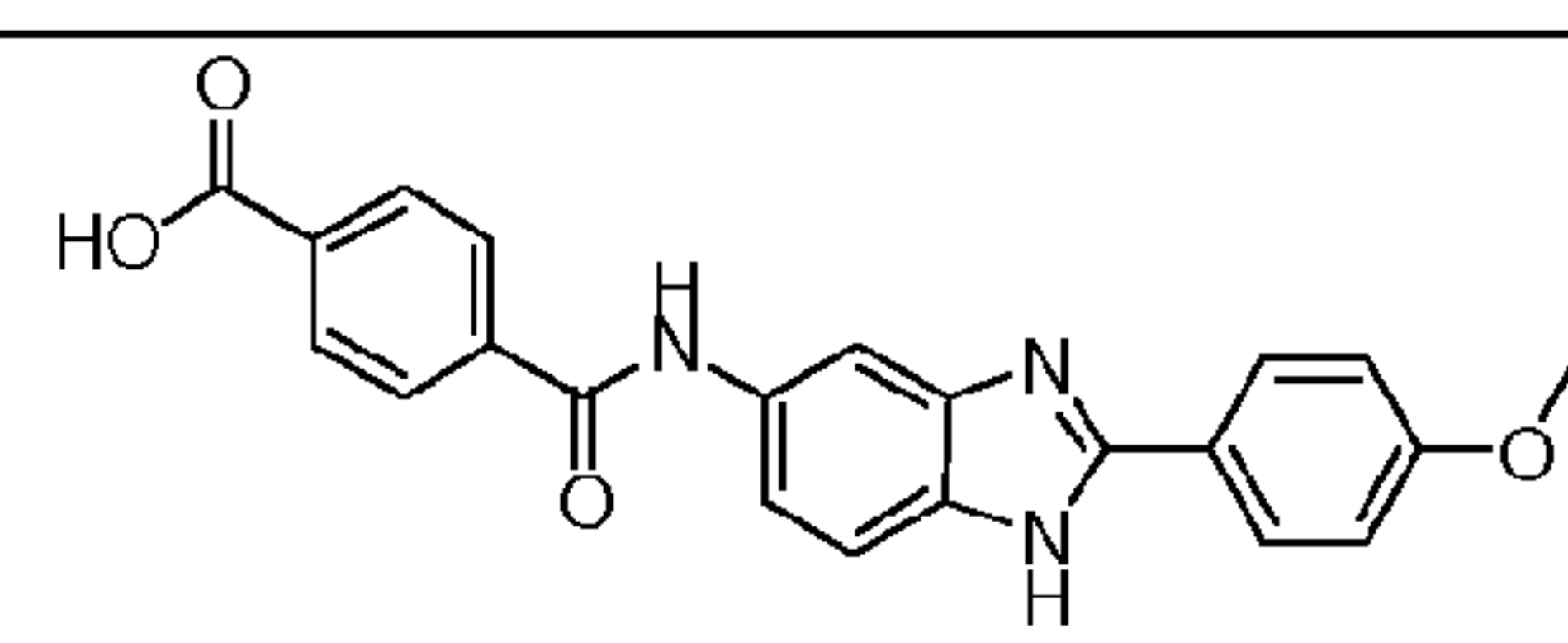
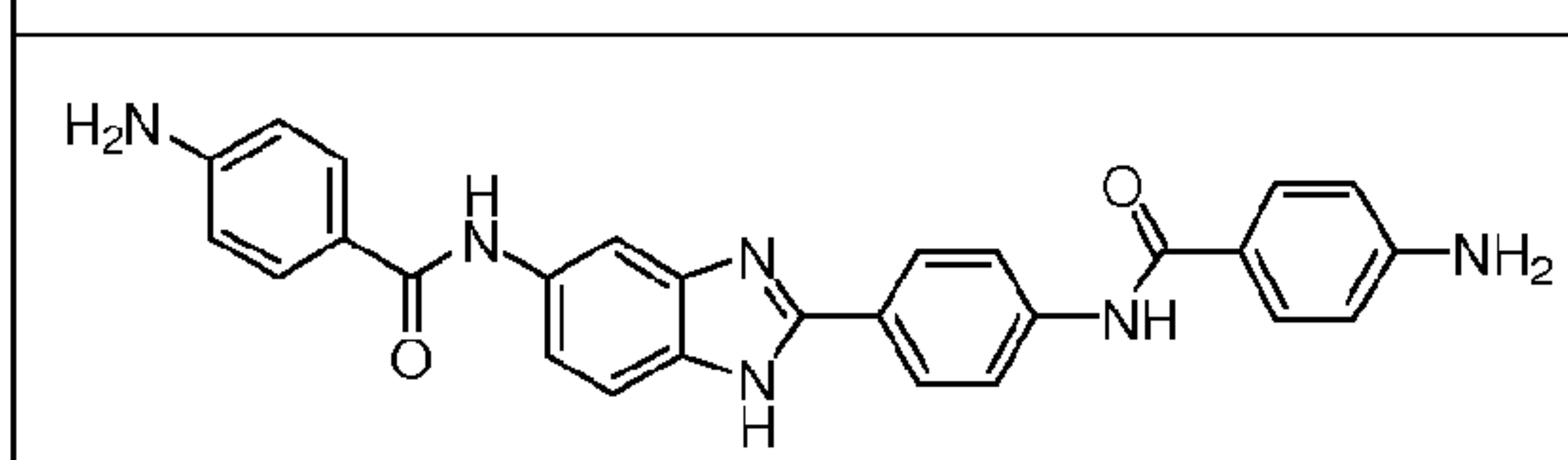
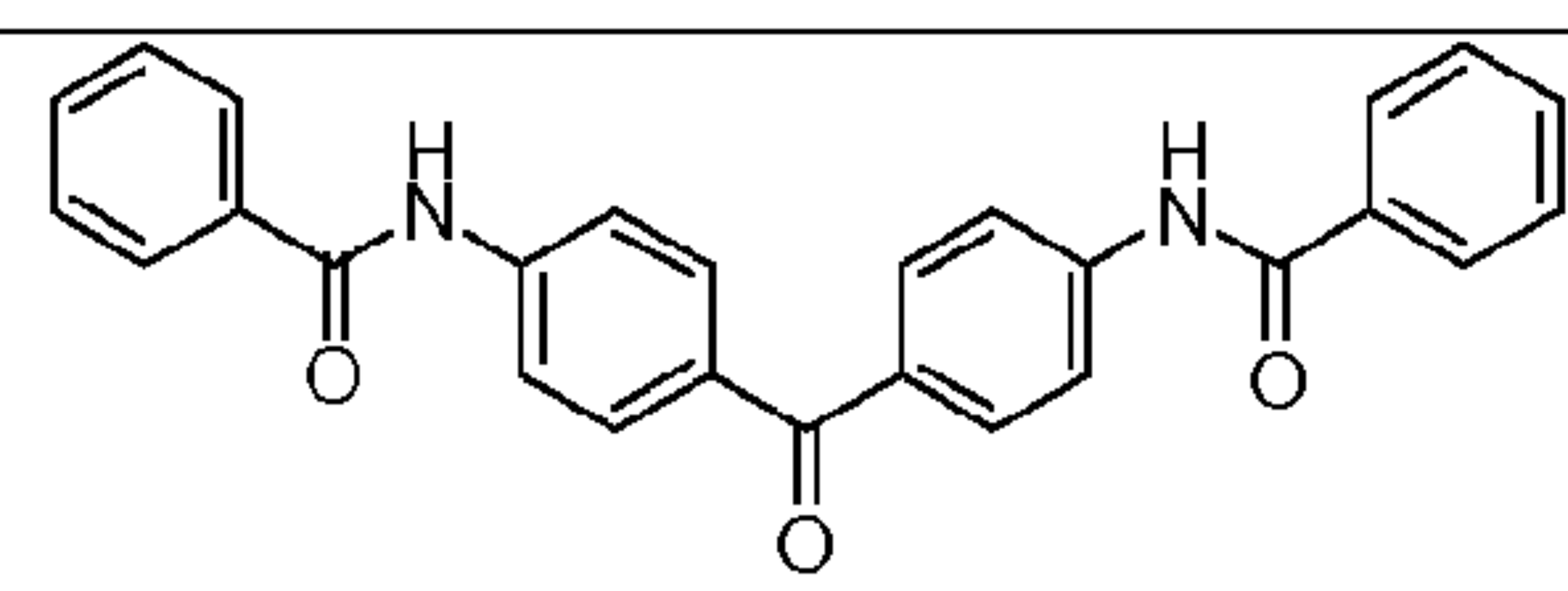
[0299] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVh:**  (**IVh**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{R^{80}}$ can be selected from the group consisting of hydrogen, $\mathbf{R^{31}}$, $\mathbf{R^{32}}$, and $\mathbf{R^{33}}$.

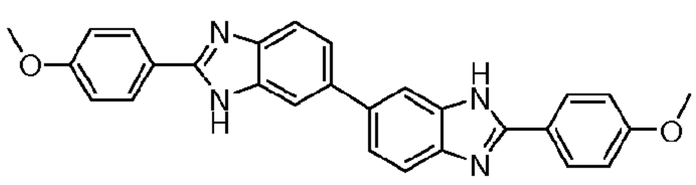
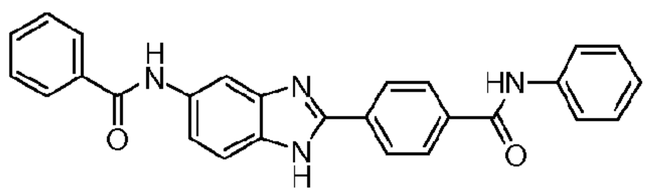
[0300] Some embodiments disclosed herein provide a compound of Formula **IV** having the structure of Formula **IVi:**  (**IVi**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{R^{80}}$ can be selected from the group consisting of hydrogen, $\mathbf{R^{31}}$, $\mathbf{R^{32}}$, and $\mathbf{R^{33}}$. Some embodiments disclosed herein provide a compound of Formula **IVi**, wherein $\mathbf{G^8}$ can be phenyl optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{34}}$, $\mathbf{R^{35}}$, and $\mathbf{R^{36}}$.

[0301] Some embodiments disclosed herein provide a compound of Formula **IV** having the proviso that a compound of Formula **IV** is not selected from the group consisting of:

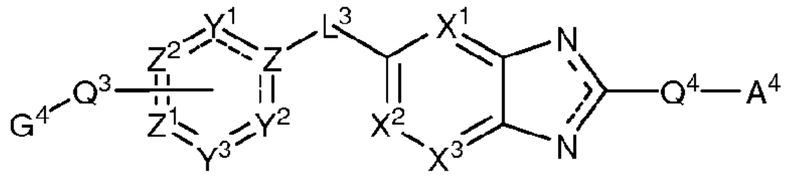
 ,	 ,

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,

 ,	and
 .	

[0302] Some embodiments disclosed herein provide a compound of Formula **V**:

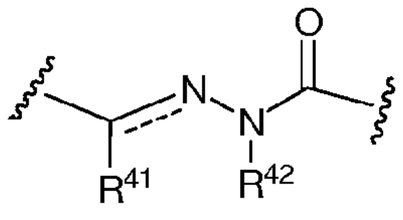

(**V**)

and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof;

wherein:

[0303] $\mathbf{G^4}$ is selected from the group consisting of is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{43}}$ and $\mathbf{R^{44}}$, said aryl and heteroaryl in the definition of $\mathbf{G^4}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0304] $\mathbf{Q^3}$ is selected from the group consisting of an ester, an amide, a urea, a carbamide, a thioamide, a sulfonamide; or $\mathbf{Q^3}$ is selected from the group consisting of -C(=O)O–, -C(=O)N$\mathbf{R^{45}}$–, -C(=O)NHN=CH–, -N$\mathbf{R^{45}}$C(=O)N$\mathbf{R^{45}}$–, -N$\mathbf{R^{45}}$C(=O)$(CH_2)_m$O–, -OC(=O)N$\mathbf{R^{45}}$–, -C(=S)N$\mathbf{R^{45}}$–, –N$\mathbf{R^{45}}$S(O)$_{1\text{-}2}$–, C_1-C_6 alkylideneamino, and


; or when $\mathbf{Y^3}$ is C (carbon) substituted with –$\mathbf{Q^3}$– $\mathbf{G^4}$ then $\mathbf{Q^3}$ is optionally fused with $\mathbf{Z^1}$ to form a five-member ring heterocycle;

[0305] $\mathbf{L^3}$ is selected from the group consiting of -C(=O)N$\mathbf{R^{45}}$–, -O-C_1-C_8-alkyl, -C(=N$\mathbf{R^{45}}$)–, -N$\mathbf{R^{45}}$C(=O)-$(CH_2)_m$C(=O)N$\mathbf{R^{45}}$–, and -N$\mathbf{R^{45}}$C(=O)-$(CH_2)_m$N$\mathbf{R^{45}}$C(=O)–;

[0306] $\mathbf{Q^4}$ is selected from the group consisting of of N$\mathbf{R^{48}}$, and O (oxygen); or $\mathbf{Q^4}$ is null;

[0307] $\mathbf{A^4}$ is selected from the group consisting of C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, a C_1-C_6 heteroalkyl, phenyl, pyridinyl, imidazolyl, and thienyl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{41}}$ and $\mathbf{R^{42}}$;

[0308] $\mathbf{X^1}$, $\mathbf{X^2}$, and $\mathbf{X^3}$ are each independently selected from N (nitrogen) and $\mathbf{CR^{46}}$;

[0309] $\mathbf{Y^1}$, $\mathbf{Y^2}$, and $\mathbf{Y^3}$ are each independently selected from N (nitrogen) and $\mathbf{CR^{47}}$;

[0310] $\mathbf{Z}$, $\mathbf{Z^1}$, and $\mathbf{Z^2}$ are each independently selected from C (carbon), CH, and N (nitrogen);

[0311] $\mathbf{R^{41}}$ is independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl;

[0312] each $\mathbf{R^{42}}$ is independently selected from the group consisting of $-(CH_2)_mOR^A$, $-O(CH_2)_mOR^A$, $-NR^BR^C$, $-C(=O)NR^BR^C$, $-C(=NNR^BR^C)H$, $-(CH_2)_mSR^A$, $-(CH_2)_mR^K$, $-O(CH_2)_mR^K$;

[0313] or $\mathbf{R^{41}}$ and $\mathbf{R^{42}}$ are linked to form an optionally substituted ring;

[0314] each $\mathbf{R^{43}}$ is independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl;

[0315] each $\mathbf{R^{44}}$ is independently selected from the group consisting of $-(CH_2)_mOR^A$, $-O(CH_2)_mOR^A$, $-NR^BR^C$, $-C(=O)NR^BR^C$, $-C(=NNR^BR^C)H$, $-(CH_2)_mSR^A$, $-(CH_2)_mR^K$, $-O(CH_2)_mR^K$;

[0316] each $\mathbf{R^{45}}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_4 alkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0317] each $\mathbf{R^{46}}$ and $\mathbf{R^{47}}$ is independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0318] $\mathbf{R^{48}}$ is selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0319] each $\mathbf{R^A}$ is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl;

[0320] each $-N\mathbf{R^B}\mathbf{R^C}$ is separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ are each independently selected from the group consisting of hydrogen, $-SO_2\mathbf{R^F}$, $-C(=O)\mathbf{R^F}$, $-(CH_2)_m\mathbf{R^F}$, $-SO_2N\mathbf{R^D}\mathbf{R^E}$, $-C(=O)N\mathbf{R^D}\mathbf{R^E}$, $-(CH_2)_mN\mathbf{R^D}\mathbf{R^E}$, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl where the alkyl and the heteroalkyl are optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B}\mathbf{R^C}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-N\mathbf{R^B}\mathbf{R^C}$ is an optionally substituted C_1-C_6 alkylideneamino;

[0321] each $-N\mathbf{R^D}\mathbf{R^E}$ is separately selected, wherein $\mathbf{R^D}$ and $\mathbf{R^E}$ are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_m\mathbf{R^G}$; or $-N\mathbf{R^D}\mathbf{R^E}$ is an optionally substituted C_1-C_6 alkylideneaminyl; or $-N\mathbf{R^D}\mathbf{R^E}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

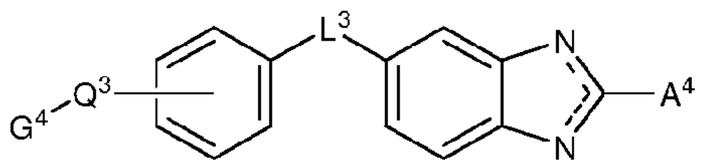
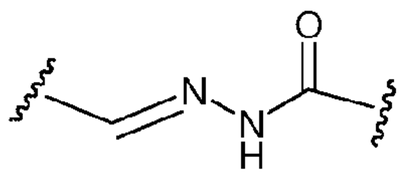
[0322] each $\mathbf{R^F}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_4 alkyl, an optionally substituted C_1-C_4 haloalkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, aryl and heteroaryl, where the aryl and heteroaryl in the definition of $\mathbf{R^F}$ are each optionally substituted with $-C(=O)N\mathbf{R^D}\mathbf{R^E}$ or $-N\mathbf{R^D}\mathbf{R^E}$;

[0323] each $\mathbf{R^G}$ is independently selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl;

[0324] each $\mathbf{R^K}$ is independently selected from the group consisting of $-C(=O)N\mathbf{R^D}\mathbf{R^E}$, $-N\mathbf{R^D}\mathbf{R^E}$, an optionally substituted aryl and an optionally substituted heteroaryl;

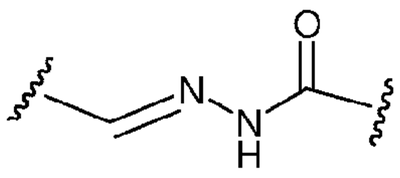
[0325] each **m** is independently 0, 1, or 2; and

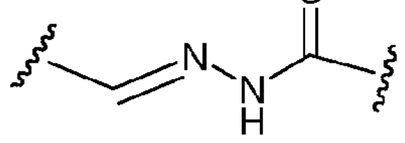
[0326] each dashed line represents an optional double bond.

[0327] Some embodiments disclosed herein provide a compound of Formula **V** having the structure of Formula **Va**:  (**Va**), and pharmaceutically acceptable salts, esters, or prodrugs thereof, wherein $\mathbf{G^4}$ can be selected from the group consisting of hydrogen, halogen, $-(CH_2)_m\mathbf{OR^A}$, $-O(CH_2)_m\mathbf{OR^A}$, $-N\mathbf{R^BR^C}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted phenyl, an optionally substituted pyridinyl, an optionally substituted tetrazolyl, and an optionally substituted imidazolyl; $\mathbf{Q^3}$ can be selected from the group consisting of -C(=O)O–, -C(=O)NH–, -C(=O)NHNH–, $-N\mathbf{R^{45}}C(=O)N\mathbf{R^{45}}–$, $-OC(=O)N\mathbf{R^{45}}–$, $-C(=S)N\mathbf{R^{45}}–$, $–N\mathbf{R^{45}}S(O)_{1\text{-}2}–$, C_1-C_6 alkylideneaminyl, and  ; or $\mathbf{Q^3}$ can be null; $\mathbf{A^4}$ can be selected from the group consisting of a aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{41}}$ and $\mathbf{R^{42}}$, said aryl and heteroaryl in the definition of $\mathbf{A^4}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{L^3}$ can be selected from –O– (oxygen), $–S(O)_{0\text{-}2}–$, $–N\mathbf{R^{45}}S(O)_{1\text{-}2}–$, $-N\mathbf{R^{45}}C(=O)\text{-}(CH_2)_mC(=O)N\mathbf{R^{45}}–$, $-N\mathbf{R^{45}}C(=O)\text{-}(CH_2)_mN\mathbf{R^{45}}C(=O)–$, $–N\mathbf{R^{45}}–$, –C(=O)–, –C(=S)–, $-C(=O)N\mathbf{R^{45}}–$, $-C(=N\mathbf{R^{45}})–$, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 heteroalkyl, an optionally substituted heterocycle, an optionally substituted aryl, and an optionally substituted heteroaryl; or $\mathbf{L^3}$ can be null; each $\mathbf{R^{41}}$ can be independently selected from the group consisting of hydrogen, halogen, and an optionally substituted C_1-C_3 alkyl; each $\mathbf{R^{42}}$ can be independently selected from the group consisting of hydrogen and an optionally substituted C_1-C_3 alkyl; each $\mathbf{R^{43}}$ can be independently selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl; each $\mathbf{R^{44}}$ can be independently selected from the group consisting of halogen, $-(CH_2)_m\mathbf{OR^A}$, $–O(CH_2)_m\mathbf{OR^A}$, $-N\mathbf{R^BR^C}$, $–C(=O)N\mathbf{R^BR^C}$, $-C(=NN\mathbf{R^BR^C})H$, $-(CH_2)_m\mathbf{R^K}$, $-O(CH_2)_m\mathbf{R^K}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl; each

$\mathbf{R^{45}}$ can be independently selected from the group consisting of hydrogen, and an optionally substituted C_1-C_4 alkyl; each $\mathbf{R^A}$ can be independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; each -$N\mathbf{R^B R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, $-SO_2\mathbf{R^F}$, $-C(=O)\mathbf{R^F}$, -$(CH_2)_m\mathbf{R^F}$, -$(CH_2)_m O\mathbf{R^F}$, -$SO_2N\mathbf{R^D R^E}$, -$C(=O)N\mathbf{R^D R^E}$, -$C(=NH)N\mathbf{R^D R^E}$, -$(CH_2)_m N\mathbf{R^D R^E}$, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl where the alkyl and the heteroalkyl are optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B R^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-N\mathbf{R^B R^C}$ can be an optionally substituted C_1-C_6 alkylideneamino; each $-N\mathbf{R^D R^E}$ can be separately selected, wherein $\mathbf{R^D}$ and $\mathbf{R^E}$ can each be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and -$(CH_2)_m\mathbf{R^G}$; or $-N\mathbf{R^D R^E}$ can be an optionally substituted C_1-C_6 alkylideneamino; or $-N\mathbf{R^D R^E}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each $\mathbf{R^F}$ can be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_3 alkyl, an optionally substituted C_1-C_3 haloalkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, aryl and heteroaryl, where the aryl and heteroaryl in the definition of $\mathbf{R^F}$ can each be optionally substituted with $-C(=O)N\mathbf{R^D R^E}$ or -$N\mathbf{R^D R^E}$; each $\mathbf{R^G}$ can be independently selected from an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^K}$ can be independently selected from the group consisting of -$C(=O)N\mathbf{R^D R^E}$, -$N\mathbf{R^D R^E}$, an optionally substituted aryl and an optionally substituted heteroaryl; each **m** can be independently 0, 1, or 2; and each dashed line represents an optionally double bond.

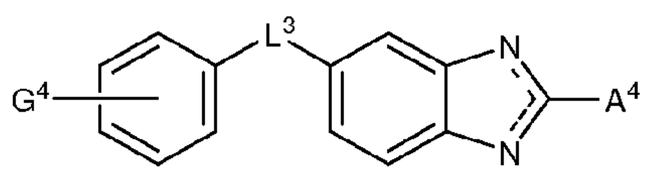
[0328] Some embodiments disclosed herein provide a compound of Formula **Va**, wherein $\mathbf{G^4}$ can be selected from the group consisting of hydrogen, halogen, -$(CH_2)_m O\mathbf{R^A}$, -$O(CH_2)_m O\mathbf{R^A}$, -$N\mathbf{R^B R^C}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted phenyl, an optionally substituted pyridinyl, an optionally substituted tetrazolyl, and an optionally substituted imidazolyl; $\mathbf{Q^3}$ can be selected from the group consisting of

-C(=O)NH–, and  ; or $\mathbf{Q^3}$ can be null: $\mathbf{A^4}$ can be selected from the group consisting of phenyl, naphthyl, dihydrobenzofuranyl, 1,4-benzodioxanyl, benzotriazolyl, benzimidazolyl, benzofuranyl, and 2,1,3-benzoxadiazolyl, each optionally substituted with one or more substituents selected from the group consisting of, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{41}}$ and $\mathbf{R^{42}}$; $\mathbf{L^3}$ can be a 1-6 atom long linker comprising one or more groups selected from–$N\mathbf{R^{45}}$–, –C(=O)–, –C(=S)–, and -C(=O)$N\mathbf{R^{45}}$—; or $\mathbf{L^3}$ can be null; each $\mathbf{R^{41}}$ can be independently selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy; each $\mathbf{R^{42}}$ can be independently selected from the group consisting of -$(CH_2)_m$O$\mathbf{R^A}$, -O$(CH_2)_m$O$\mathbf{R^A}$, -$N\mathbf{R^B}\mathbf{R^C}$, –C(=O)$N\mathbf{R^B}\mathbf{R^C}$, -C(=NN$\mathbf{R^B}\mathbf{R^C}$)H, –$(CH_2)_m\mathbf{R^K}$ and -O$(CH_2)_m\mathbf{R^K}$; each $\mathbf{R^{45}}$ can be independently selected from the group consisting of hydrogen, and methyl; each $\mathbf{R^A}$ can be independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; each –$N\mathbf{R^B}\mathbf{R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, –C(=O)$\mathbf{R^F}$, -$(CH_2)_m\mathbf{R^F}$, -$SO_2N\mathbf{R^D}\mathbf{R^E}$, -C(=O)$N\mathbf{R^D}\mathbf{R^E}$, -C(=NH)$N\mathbf{R^D}\mathbf{R^E}$, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, and C_1-C_6 haloalkyl; or –$N\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or –$N\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted C_1-C_6 alkylideneamino; each –$N\mathbf{R^D}\mathbf{R^E}$ can be separately selected, wherein $\mathbf{R^D}$ and $\mathbf{R^E}$ can each be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, and -$(CH_2)_m\mathbf{R^G}$; or –$N\mathbf{R^D}\mathbf{R^E}$ can be an optionally substituted C_1-C_6 alkylideneaminyl; or –$N\mathbf{R^D}\mathbf{R^E}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each $\mathbf{R^F}$ can be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_3 alkyl, an optionally substituted C_3-C_6 cycloalkyl, an optionally substituted C_3-C_6 cycloalkenyl, an optionally substituted C_1-C_3 haloalkyl, aryl and heteroaryl, where the aryl and heteroaryl in the definition of $\mathbf{R^F}$ can each be optionally substituted with –C(=O)$N\mathbf{R^D}\mathbf{R^E}$ or -$N\mathbf{R^D}\mathbf{R^E}$; each $\mathbf{R^G}$ can be independently selected from an optionally substituted aryl and an optionally substituted heteroaryl; each **m** can be independently 0, 1, or 2; and each dashed line represents an optional double bond.

[0329] Some embodiments disclosed herein provide a compound of Formula **V**, wherein $\mathbf{G^4}$ can be selected from the group consisting of hydrogen, halogen, $-(CH_2)_mO\mathbf{R^A}$, $-O(CH_2)_mO\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted phenyl, an optionally substituted pyridinyl, an optionally substituted tetrazolyl, and an optionally substituted imidazolyl; $\mathbf{Q^3}$ can be selected from the group consisting of an ester, an amide, a urea, a carbamide, a thioamide, an imidamide, a sulfonamide, and a hydrazide derivative; or $\mathbf{Q^3}$ is selected from the group consisting of $-C(=O)O-$, $-C(=O)NH-$, $-N\mathbf{R^{45}}C(=O)N\mathbf{R^{45}}-$, $-OC(=O)N\mathbf{R^{45}}-$, $-C(=S)N\mathbf{R^{45}}-$, $-N\mathbf{R^{45}}S(O)_{1-2}-$, C_1-C_6 alkylidenecaminyl, and  ; or $\mathbf{Q^3}$ can be null; $\mathbf{A^4}$ can be selected from the group consisting of a aryl and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^{41}}$ and $\mathbf{R^{42}}$, said aryl and heteroaryl in the definition of $\mathbf{A^4}$ can each be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{L^3}$ can be selected from –O– (oxygen), $-S(O)_{0-2}-$, $-N\mathbf{R^{45}}S(O)_{1-2}-$, $-N\mathbf{R^{45}}-$, $-C(=O)-$, $-C(=S)-$, $-C(=O)N\mathbf{R^{45}}-$, $-C(=N\mathbf{R^{45}})-$, $-N\mathbf{R^{45}}C(=O)-(CH_2)_mC(=O)N\mathbf{R^{45}}-$, $-N\mathbf{R^{45}}C(=O)-(CH_2)_mN\mathbf{R^{45}}C(=O)-$, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 heteroalkyl, an optionally substituted heterocycle, an optionally substituted aryl, and an optionally substituted heteroaryl; or $\mathbf{L^3}$ can be null; each $\mathbf{R^{41}}$ can be independently selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and null; each $\mathbf{R^{42}}$ can be independently selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-C(=NN\mathbf{R^B}\mathbf{R^C})H$, $-(CH_2)_m\mathbf{R^K}$, $-O(CH_2)_m\mathbf{R^K}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl; each $\mathbf{R^{45}}$ can be independently selected from the group consisting of hydrogen, and an optionally substituted C_1-C_4 alkyl; each $\mathbf{R^A}$ can be independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; each $-N\mathbf{R^B}\mathbf{R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, $-SO_2\mathbf{R^F}$, $-C(=O)\mathbf{R^F}$, $-(CH_2)_m\mathbf{R^F}$, $-(CH_2)_mO\mathbf{R^F}$, $-SO_2N\mathbf{R^D}\mathbf{R^E}$, $-C(=O)N\mathbf{R^D}\mathbf{R^E}$, $-C(=NH)N\mathbf{R^D}\mathbf{R^E}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl where the alkyl and the heteroalkyl

are optionally fused with an aryl or heteroaryl; or $-NR^BR^C$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-NR^BR^C$ can be an optionally substituted C_1-C_6 alkylideneamino; each $-NR^DR^E$ can be separately selected, wherein R^D and R^E can each be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_mR^G$; or $-NR^DR^E$ can be an optionally substituted C_1-C_6 alkylideneaminyl; or $-NR^DR^E$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each R^F can be independently selected from the group consisting of hydrogen, C_1-C_3 alkyl, C_1-C_3 haloalkyl, aryl and heteroaryl, where the aryl and heteroaryl in the definition of R^F can each be optionally substituted with $-C(=O)NR^DR^E$ or $-NR^DR^E$; each R^G can be independently selected from an optionally substituted aryl and an optionally substituted heteroaryl; each **m** can be independently 0, 1, or 2; and one dashed line represents a double bond.

[0330] Some embodiments disclosed herein provide a compound of Formula **Va** having the structure of Formula **Vb**:



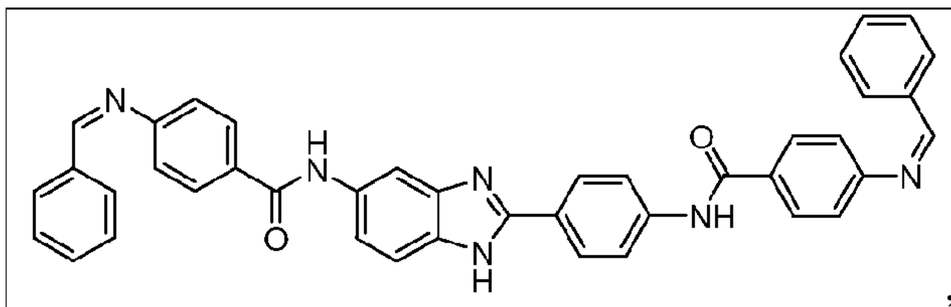
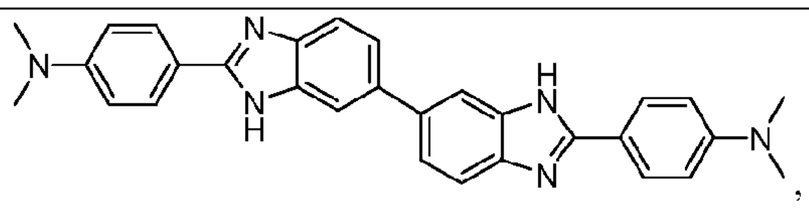
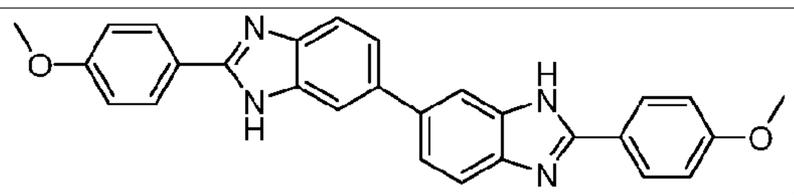
(**Vb**), and pharmaceutically acceptable salts, wherein G^4 can be selected from the group consisting of hydrogen, halogen, fluoro, chloro, bromo, $-OR^A$, $-O(CH_2)_mOR^A$, $-NR^BR^C$, an optionally substituted C_1-C_6 alkyl, an optionally substituted phenyl, an optionally substituted pyridinyl, an optionally substituted tetrazolyl, and an optionally substituted imidazolyl; A^4 can be phenyl optionally substituted with one or more substituents selected from the group consisting of R^{41} and R^{42}, where the phenyl in the definition of A^4 can be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; L^3 can be selected from $-C(=O)NR^{45}$–, $-NR^{45}C(=O)-(CH_2)_mC(=O)NR^{45}$–, $-NR^{45}C(=O)-(CH_2)_mNR^{45}C(=O)$–, and an optionally substituted heteroaryl; or L^3 can be null; each R^{41} can be independently selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy; each R^{42} can be independently selected from the group consisting of $-(CH_2)_mOR^A$, $-O(CH_2)_mOR^A$, $-NR^BR^C$, $-C(=O)NR^BR^C$, $-C(=NNR^BR^C)H$, $-(CH_2)_mR^K$, $-O(CH_2)_mR^K$; each R^{45} can be independently selected from the group consisting of hydrogen, and an optionally substituted C_1-C_4 alkyl; each R^A is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; each $-NR^BR^C$ can be separately selected,

wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, $-SO_2\mathbf{R^F}$, $-C(=O)\mathbf{R^F}$, $-(CH_2)_m\mathbf{R^F}$, $-(CH_2)_mO\mathbf{R^F}$, $-SO_2N\mathbf{R^D}\mathbf{R^E}$, $-C(=O)N\mathbf{R^D}\mathbf{R^E}$, $-C(=NH)N\mathbf{R^D}\mathbf{R^E}$, $-(CH_2)_mN\mathbf{R^D}\mathbf{R^E}$, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl where the alkyl and the heteroalkyl are optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B}\mathbf{R^C}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each $-N\mathbf{R^D}\mathbf{R^E}$ can be separately selected, wherein $\mathbf{R^D}$ and $\mathbf{R^E}$ can each be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, and $-(CH_2)_m\mathbf{R^G}$; or $-N\mathbf{R^D}\mathbf{R^E}$ can be an optionally substituted C_1-C_6 alkylideneaminyl; or $-N\mathbf{R^D}\mathbf{R^E}$ can be an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; each $\mathbf{R^F}$ can be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_3 alkyl, an optionally substituted C_3-C_7 cycloalkyl, aryl and heteroaryl, where the aryl and heteroaryl in the definition of $\mathbf{R^F}$ can each be optionally substituted with $-C(=O)N\mathbf{R^D}\mathbf{R^E}$ or $-N\mathbf{R^D}\mathbf{R^E}$; each $\mathbf{R^G}$ can be independently selected from an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^K}$ can be independently selected from the group consisting of $-C(=O)N\mathbf{R^D}\mathbf{R^E}$, $-N\mathbf{R^D}\mathbf{R^E}$, an optionally substituted aryl and an optionally substituted heteroaryl; each **m** can be independently 0, 1, or 2; and, each dashed line represents an optionally double bond.

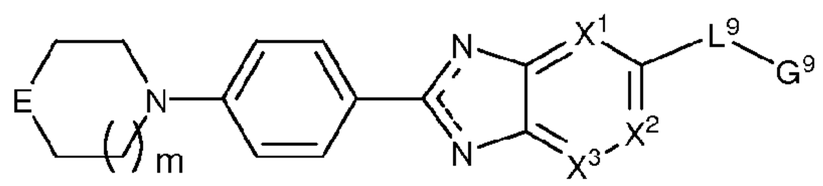
[0331] Some embodiments disclosed herein provide a compound of Formula **Vb**, wherein $\mathbf{G^4}$ can be selected from the group consisting of hydrogen, fluoro, chloro, bromo, imidazolyl, tetrazolyl, N-methyl-N-(2-hydroxyethyl)aminyl, methylaminosulfonamido, 2-hydroxyethyloxy, $-(CH_2)_mO\mathbf{R^A}$, $-O(CH_2)_mO\mathbf{R^A}$, and $-N\mathbf{R^B}\mathbf{R^C}$; $\mathbf{A^4}$ can be phenyl optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{41}}$ and $\mathbf{R^{42}}$, where the phenyl in the definition of $\mathbf{G^4}$ can be further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle; $\mathbf{L^3}$ can be selected from the group consisting of $-C(=O)NH-$, $-NHC(=O)-C(=O)NH-$ and an optionally substituted heteroaryl; or $\mathbf{L^3}$ can be null; each $\mathbf{R^{41}}$ can be an optionally substituted C_1-C_6 alkoxy; each $\mathbf{R^{42}}$ can be independently selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-O(CH_2)_mO\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-C(=NN\mathbf{R^B}\mathbf{R^C})H$, $-(CH_2)_m\mathbf{R^K}$, and $-O(CH_2)_m\mathbf{R^K}$; each $\mathbf{R^A}$ can be independently selected from the group consisting of hydrogen,

and C_1-C_6 alkyl; each -N$\mathbf{R^B R^C}$ can be separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ can each be independently selected from the group consisting of hydrogen, –$SO_2\mathbf{R^F}$, –C(=O)$\mathbf{R^F}$, -$(CH_2)_m\mathbf{R^F}$, -O$\mathbf{R^F}$, -SO_2N$\mathbf{R^D R^E}$, -$(CH_2)_m$N$\mathbf{R^D R^E}$, C_1-C_6 alkyl, and C_3-C_7 cycloalkyl; or –N$\mathbf{R^B R^C}$ can be selected from the group consisting of pyrrolidinyl, morpholinyl, 4-methylpiperazinyl, piperazinyl, piperidinyl, 3-hydroxypyrrolidinyl, and 4-hydroxypiperidinyl, each optionally substituted with oxo; each –N$\mathbf{R^D R^E}$ can be separately selected, wherein $\mathbf{R^D}$ and $\mathbf{R^E}$ can each be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_3-C_6 cycloalkyl, and -$(CH_2)_m\mathbf{R^G}$; or –N$\mathbf{R^D R^E}$ can be selected from the group consisting of pyrrolidinyl, morpholinyl, 4-methylpiperazinyl, piperazinyl, piperidinyl, 3-hydroxypyrrolidinyl, and 4-hydroxypiperidinyl, each optionally substituted with oxo; each $\mathbf{R^F}$ can be independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_3 alkyl, an optionally substituted C_3-C_6 cycloalkyl, aryl and heteroaryl, where the aryl and heteroaryl in the definition of $\mathbf{R^F}$ can each be optionally substituted with -N$\mathbf{R^D R^E}$; each $\mathbf{R^G}$ can be independently selected from an optionally substituted aryl and an optionally substituted heteroaryl; each $\mathbf{R^K}$ can be independently selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl; each **m** can be independently 0, 1, or 2; and each dashed line represents an optionally double bond.

[0332] Some embodiments disclosed herein provide a compound of Formula **V**, having the proviso that a compound of Formula **V** is not selected from the group consisting of:

 ,	 ,
and	 .

[0333] Some embodiments disclosed herein provide a compound of Formula **VI**:



(VI)

and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof;

wherein:

[0334] **E** is selected from the group consisting of O (oxygen), S (sulfur), N$\mathbf{R^{41}}$ and C$\mathbf{R^{42}R^{43}}$;

[0335] $\mathbf{R^{41}}$ is selected from the group consisting of hydrogen, halogen, cyano, -C(=O)$\mathbf{R^{C}}$, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and an optionally substituted C_1-C_6 alkyl;

[0336] $\mathbf{R^{42}}$ and $\mathbf{R^{43}}$ are each independently selected from the group consisting of hydrogen, halogen, -O$\mathbf{R^{AA}}$, -O$\mathbf{R^{CC}}$, -N$\mathbf{R^{A}R^{B}}$, -N$\mathbf{R^{C}R^{D}}$, -S$\mathbf{R^{AA}}$, -$(CH_2)_m\mathbf{R^{E}}$, -CON$\mathbf{R^{C}R^{D}}$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl; or C$\mathbf{R^{42}R^{43}}$ is an optionally substituted C_3-C_7 cycloalkyl;

[0337] $\mathbf{X^{1}}$, $\mathbf{X^{2}}$, and $\mathbf{X^{3}}$ are each independently selected from the group consisting of N (nitrogen) and C$\mathbf{R^{41}}$;

[0338] $\mathbf{G^{9}}$ is selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{44}}$ and $\mathbf{R^{45}}$, said aryl and heteroaryl in the definition of $\mathbf{G^{9}}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0339] each $\mathbf{R^{44}}$ is separately selected from the group consisting of halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0340] each $\mathbf{R^{45}}$ is separately selected from the group consisting of hydrogen, halogen, -O$\mathbf{R^{AA}}$, –O$\mathbf{R^{CC}}$, -N$\mathbf{R^{A}R^{B}}$, –N$\mathbf{R^{C}R^{D}}$, –S$\mathbf{R^{AA}}$, –$(CH_2)_m\mathbf{R^{E}}$, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and an optionally substituted C_1-C_6 alkyl;

[0341] each $\mathbf{R^{AA}}$ is independently selected from the group consisting of hydrogen, -$(CH_2)_m$$SO_2\mathbf{R^{F}}$, –$(CH_2)_m$C(=O)$\mathbf{R^{F}}$, -$(CH_2)_m$C(=O)N$\mathbf{R^{C}R^{D}}$, an optionally substituted C_1-C_8

alkyl, an optionally substituted C_1-C_8 alkoxy, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, and an optionally substituted C_3-C_7 cycloalkyl, where said C_3-C_7 cycloalkyl is optionally fused with an aryl or heteroaryl;

[0342] each $\mathbf{R^{BB}}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 alkoxy, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, and $(CH_2)_m\mathbf{R^E}$;

[0343] each $-N\mathbf{R^A}\mathbf{R^B}$ is separately selected, wherein $\mathbf{R^A}$ and $\mathbf{R^B}$ are each independently selected from the group consisting of hydrogen, $-(CH_2)_mSO_2\mathbf{R^F}$, $-(CH_2)_mC(=O)\mathbf{R^F}$, $-(CH_2)_mC(=O)N\mathbf{R^C}\mathbf{R^D}$, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 alkoxy, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, and an optionally substituted C_3-C_7 cycloalkyl, where said C_3-C_7 cycloalkyl is optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^A}\mathbf{R^B}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^A}\mathbf{R^B}$ is an optionally substituted C_1-C_6 alkylideneamino;

[0344] each $-N\mathbf{R^C}\mathbf{R^D}$ is separately selected, wherein $\mathbf{R^C}$ and $\mathbf{R^D}$ are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 alkoxy, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, and $(CH_2)_m\mathbf{R^E}$; or $-N\mathbf{R^C}\mathbf{R^D}$ is an optionally substituted C_1-C_8 alkylideneamino; or $-N\mathbf{R^C}\mathbf{R^D}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0345] each $\mathbf{R^E}$ is separately selected from the group consisting of an optionally substituted aryl and an optionally substituted heteroaryl;

[0346] each $\mathbf{R^F}$ is separately selected from the group consisting of hydrogen, a an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted aryl and an optionally substituted heteroaryl;

[0347] $\mathbf{L^9}$ is selected from the group consisting of $-(CH_2)_mC(=O)N\mathbf{R^{46}}(CH_2)_q-$, $-(CH_2)_mC(=O)N\mathbf{R^{46}}(CH_2)_qC(=O)N\mathbf{R^{46}}-$, $-S(O)_2NH-$, O (oxygen), $-N\mathbf{R^{46}}-$, $-OC(=O)O-$, $-OC(=O)NH-$, $-NHC(=O)NH-$, $-NHC=SNH-$, $-C(=N\mathbf{R^{46}})-$, $-C(=O)N\mathbf{R^{46}}-$, $-C(=S)N\mathbf{R^{46}}-$; or $\mathbf{L^9}$ is null;

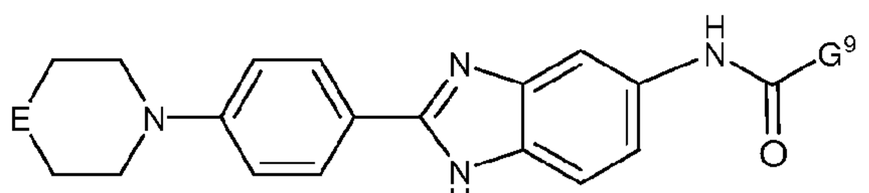
[0348] each $\mathbf{R^{46}}$ is independently selected from the group consisting of hydrogen, C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 alkyl;

[0349] each **m** is independently 0, 1, or 2;

[0350] each **q** is independently 1, 2, 3, 4, 5, or 6; and

[0351] any bond represented by a dashed and solid line represents a bond selected from the group consisting of a single bond and a double bond.

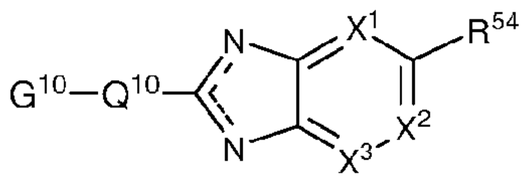
[0352] Some embodiments disclosed herein provide a compound of Formula **VI** having the structure of Formula **VIa**:



(VIa),

and pharmaceutically acceptable salts.

[0353] Some embodiments disclosed herein provide a compound of Formula **VII**:



(VII)

[0354] and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof;

wherein:

[0355] $\mathbf{G^{10}}$ is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^{51}}$, $\mathbf{R^{52}}$, and $\mathbf{R^{53}}$, said aryl and heteroaryl in the definition of $\mathbf{G^{10}}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0356] $\mathbf{Q^{10}}$ is selected from the group consisting of $\mathbf{Q^{11}}$, $\mathbf{Q^{11}}$–$\mathbf{Q^{12}}$, and $\mathbf{Q^{11}}$–$\mathbf{Q^{12}}$–$\mathbf{Q^{13}}$;

[0357] $\mathbf{Q^{11}}$ and $\mathbf{Q^{13}}$ are each independently selected from the group consisting of piperazinyl, -C(=O)O–, -C(=O)N$\mathbf{R^{51}}$–, -N$\mathbf{R^{51}}$C(=O)N$\mathbf{R^{51}}$–, -OC(=O)N$\mathbf{R^{51}}$–, -C(=S)N$\mathbf{R^{51}}$–, -N$\mathbf{R^{51}}$S(O)$_{1\text{-}2}$–, -$(CH_2)_m$C(=O)N$\mathbf{R^{51}}$$(CH_2)_q$-, and -$(CH_2)_m$C(=O)N$\mathbf{R^{51}}$$(CH_2)_q$C(=O)N$\mathbf{R^{51}}$-;

[0358] $\mathbf{Q^{12}}$ is selected from the group consisting of an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocycle;

[0359] each $\mathbf{R^{51}}$ is separately selected from the group consisting of hydrogen, halogen, cyano, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0360] each $\mathbf{R^{52}}$ is separately selected from the group consisting of $-(CH_2)_mO\mathbf{R^A}$, $-(CH_2)_mN\mathbf{R^B}\mathbf{R^C}$, $-(CH_2)_mSO_2N\mathbf{R^B}\mathbf{R^C}$, and $-(CH_2)_mS\mathbf{R^A}$;

[0361] each $\mathbf{R^{53}}$ is separately selected from the group consisting of $-(CH_2)_mO\mathbf{R^D}$, $-(CH_2)_mN\mathbf{R^E}\mathbf{R^F}$, $-(CH_2)_mS(O)_{0-2}\mathbf{R^D}$, $-(CH_2)_mNO_2$, $-(CH_2)_mCN$, and $-(CH_2)_m\mathbf{R^G}$;

[0362] each $\mathbf{R^{54}}$ is separately selected from the group consisting of hydrogen, $-(CH_2)_mO\mathbf{R^A}$, $-(CH_2)_mN\mathbf{R^B}\mathbf{R^C}$, $-O(CH_2)_mN\mathbf{R^B}\mathbf{R^C}$, $-C(=O)N\mathbf{R^B}\mathbf{R^C}$, $-(CH_2)_mS\mathbf{R^A}$, $-(CH_2)_m\mathbf{R^G}$, $-O(CH_2)_m\mathbf{R^G}$, $-(CH_2)_mSO_2N\mathbf{R^B}\mathbf{R^C}$, $-(CH_2)_mCN$, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0363] each $\mathbf{R^A}$ is separately selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_3-C_7 cycloalkenyl, an optionally substituted C_1-C_6 haloalkyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0364] each $-N\mathbf{R^B}\mathbf{R^C}$ is separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ are each independently selected from the group consisting of hydrogen, $-(CH_2)_mSO_2\mathbf{R^H}$, $-(CH_2)_mCO\mathbf{R^H}$, $-(CH_2)_mCON\mathbf{R^E}\mathbf{R^F}$, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 alkoxy, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, and $-(CH_2)_m\mathbf{R^G}$, where said C_3-C_7 cycloalkyl is optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B}\mathbf{R^C}$ or is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B}\mathbf{R^C}$ is an optionally substituted C_1-C_8 alkylideneamino;

[0365] each $\mathbf{R^D}$ is separately selected from the group consisting of hydrogen, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, an optionally substituted C_3-C_8 cycloalkyl, an optionally

substituted C_3-C_8 cycloalkenyl, an optionally substituted C_1-C_8 haloalkyl, and an optionally substituted C_1-C_8 heteroalkyl;

[0366] each $-N\mathbf{R}^{E}\mathbf{R}^{F}$ is separately selected, wherein $\mathbf{R}^{E}$ and $\mathbf{R}^{F}$ are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_8 alkyl, an optionally substituted C_1-C_8 alkoxy, an optionally substituted C_2-C_8 alkenyl, an optionally substituted C_2-C_8 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, and $(CH_2)_m\mathbf{R}^{G}$; or $-N\mathbf{R}^{E}\mathbf{R}^{F}$ or is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-N\mathbf{R}^{C}\mathbf{R}^{D}$ is an optionally substituted C_1-C_8 alkylideneamino;

[0367] each $\mathbf{R}^{G}$ is separately selected from a substituted or unsubstituted aryl and a substituted or unsubstituted heteroaryl;

[0368] each $\mathbf{R}^{H}$ is separately selected from the group consisting of hydrogen, a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, an optionally substituted heterocycle, an optionally substituted aryl, and an optionally substituted heteroaryl;

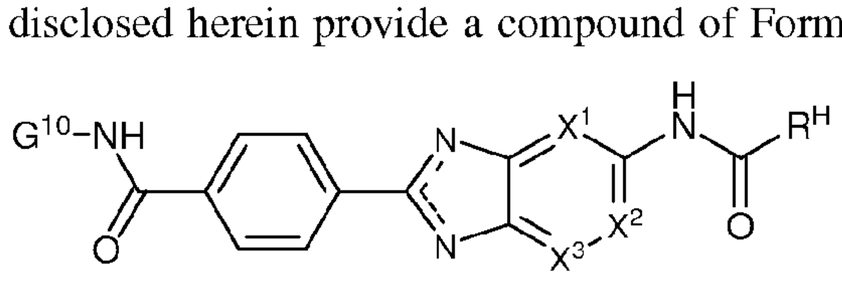
[0369] $\mathbf{X}^{1}$, $\mathbf{X}^{2}$, and $\mathbf{X}^{3}$ are each independently selected from the group consisting of N (nitrogen) and $C\mathbf{R}^{47}$;

[0370] each $\mathbf{R}^{47}$ is separately selected from the group consisting of hydrogen, halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 heteroalkyl

[0371] each **m** is independently 0, 1, 2, or 3; and

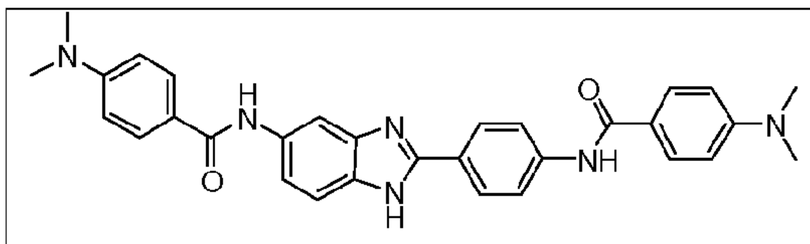
[0372] any bond represented by a dashed and solid line represents a bond selected from the group consisting of a single bond and a double bond.

[0373] Some embodiments disclosed herein provide a compound of Formula **VII** having the structure of Formula **VIIa**:



(**VIIa**), and pharmaceutically acceptable salts.

[0374] Some embodiments disclosed herein provide a compound of Formula **VII**, having the proviso that a compound of Formula **VII** is not selected from the group consisting of:



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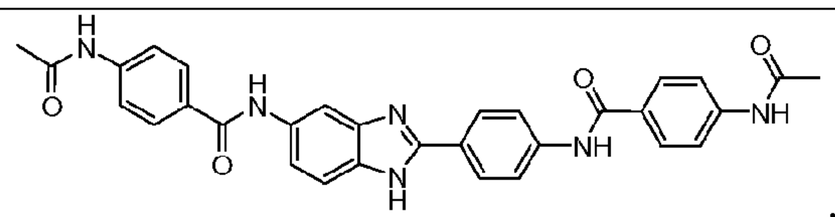

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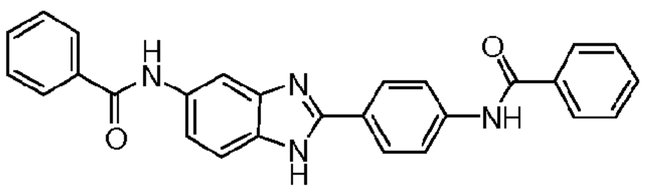

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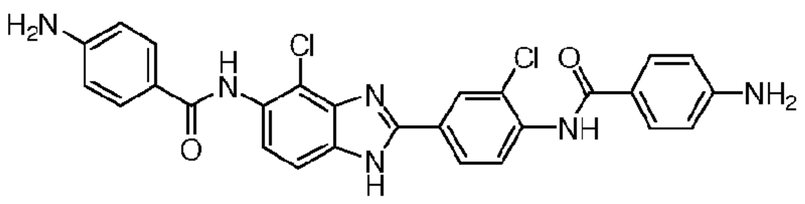

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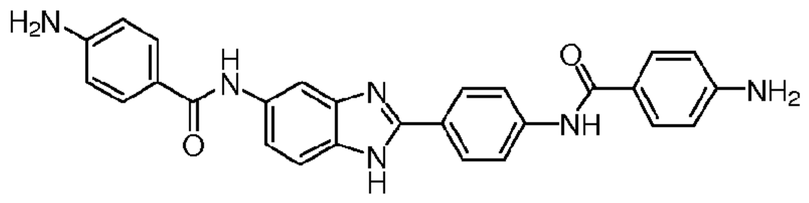

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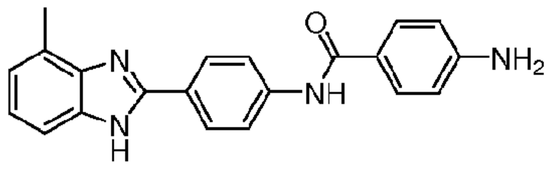

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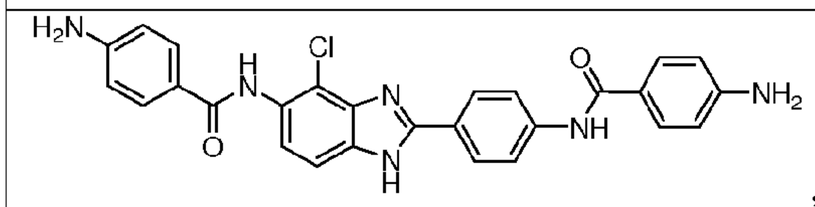

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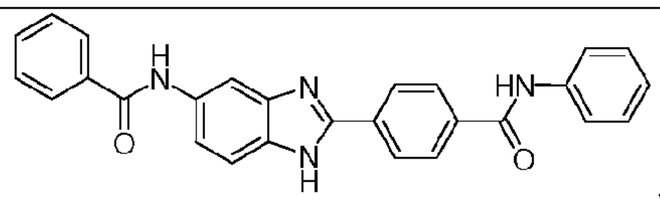
and 

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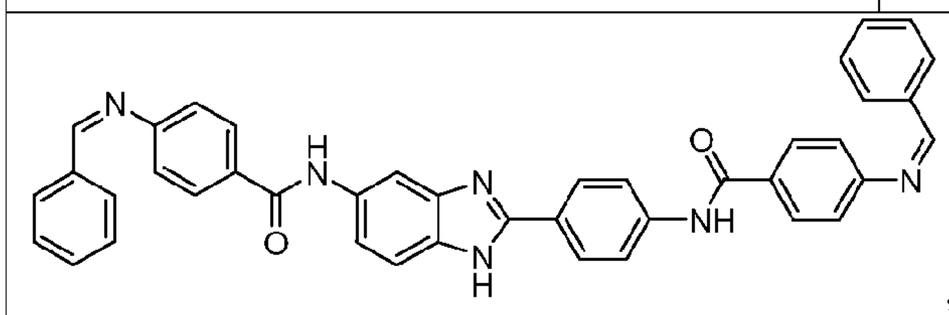

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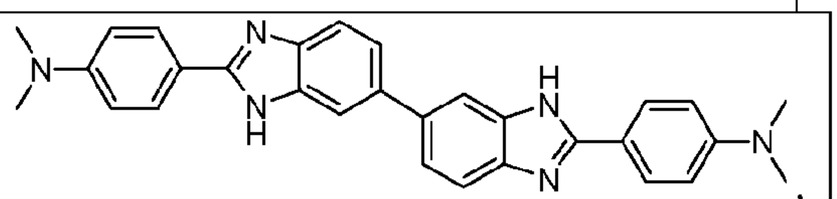

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[0375] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is a HGF mimetic, an HGF receptor agonist or an HGF receptor antagonist.

[0376] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is a hematopoietic growth factor mimetic, a hematopoietic growth factor receptor agonist or a a hematopoietic growth factor receptor antagonist.

[0377] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is an EPO mimic.

[0378] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is a selective EPO receptor agonist.

[0379] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is a selective EPO receptor partial agonist.

[0380] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is a selective EPO receptor antagonist.

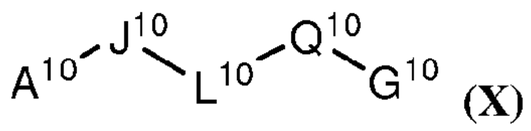
[0381] Some embodiments disclosed herein provide a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein, that is a selective EPO receptor binding compound.

[0382] Some embodiments disclosed herein provide a method for modulating an EPO activity in a cell comprising contacting a cell with a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein.

[0383] Some embodiments disclosed herein provide a method for identifying a compound that modulates an EPO activity, comprising contacting a cell that expresses an EPO receptor with a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein; and monitoring an effect of the compound on the cell.

[0384] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein.

[0385] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a compound having Formula **X**:



(X)

[0386] and pharmaceutically acceptable salts, esters, stereoisomers, tautomers or prodrugs thereof;

wherein:

[0387] $\mathbf{A^{10}}$ is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in

the definition of $\mathbf{A^{10}}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0388] $\mathbf{G^{10}}$ is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^{10}}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0389] $\mathbf{J^{10}}$ is a 1-8 atom long spacer containing at least 2 heteroatoms separated by 2 bonds and comprising one or more groups selected from -$S(O)_2N\mathbf{R^A}$–, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted heterocycle, and an optionally substituted heteroalkylheterocycle; including the proviso that $\mathbf{J^{10}}$ is not a 1-8 atom spacer containing at least 2 heteroatoms separated by 3 or 4 bonds and comprising one or more groups selected from an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted heterocycle, and an optionally substituted heteroalkylheterocycle;

[0390] $\mathbf{Q^{10}}$ is a 1-8 atom long spacer containing at least 2 heteroatoms separated by 2 bonds and comprising one or more groups selected from -$S(O)_2N\mathbf{R^A}$–, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted heterocycle, and an optionally substituted heteroalkylheterocycle;

[0391] $\mathbf{L^{10}}$ is a 2-14 atom long linker comprising one or more groups selected from -O– (oxygen), -C(=O)–, -C(=S)–, –$N\mathbf{R^A}$–, –$S(O)_{0\text{-}2}$–, –$N\mathbf{R^A}S(O)_{1\text{-}2}N\mathbf{R^A}$–, and –$N\mathbf{R^A}S(O)_{1\text{-}2}$O–, and one or more groups selected from –O– (oxygen), -C(=O)–, -C(=S)–, –$N\mathbf{R^A}$–, –$S(O)_{0\text{-}2}$–, -$N\mathbf{R^A}S(O)_{1\text{-}2}N\mathbf{R^A}$–, and –$N\mathbf{R^A}S(O)_{1\text{-}2}$O–, an optionally substituted C_1-C_{10} alkyl, an optionally substituted aryl, and an optionally substituted heteroaryl; where the an optionally substituted aryl and an optionally substituted heteroaryl in the definition of $\mathbf{L^{10}}$ are each further optionally fused with an optionally substituted nonaromatic heterocycle or an optionally substituted nonaromatic carbocycle;

[0392] $\mathbf{R^1}$ is selected from the group consisting of halogen, optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, optionally substituted C_3-C_7 cycloalkenyl, and an optionally substituted C_1-C_6 heteroalkyl;

[0393] $\mathbf{R^2}$ is selected from the group consisting of halogen, $-O\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, $-S\mathbf{R^A}$;

[0394] $\mathbf{R^3}$ is selected from the group consisting of $-O\mathbf{R^D}$, $-N\mathbf{R^E}\mathbf{R^F}$, $-S(O)_{0-2}\mathbf{R^D}$, $-NO_2$, –CN, and $-(CH_2)_m\mathbf{R^G}$, ;

[0395] $\mathbf{R^4}$ is selected from the group consisting of halogen, optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy, an optionally substituted C_2-C_6 alkenyl, an optionally substituted C_2-C_6 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, optionally substituted C_3-C_7 cycloalkenyl, , an optionally substituted C_1-C_6 heteroalkyl;

[0396] $\mathbf{R^5}$ is selected from the group consisting of $-O\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, $-S\mathbf{R^A}$;

[0397] $\mathbf{R^6}$ is selected from the group consisting of $-O\mathbf{R^D}$, $-N\mathbf{R^E}\mathbf{R^F}$, $-S(O)_{0-2}\mathbf{R^D}$, $-NO_2$, –CN, and $-(CH_2)_m\mathbf{R^G}$;

[0398] each $\mathbf{R^A}$ is separately selected from the group consisting of hydrogen, $-SO_2\mathbf{R^F}$, $-C(=O)\mathbf{R^F}$, $-C(=O)N\mathbf{R^C}\mathbf{R^D}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl, where the C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 heteroalkyl, and C_1-C_6 heterohaloalkyl in the definition of $\mathbf{R^A}$ are optionally substituted;

[0399] each $-N\mathbf{R^B}\mathbf{R^C}$ is separately selected, wherein $\mathbf{R^B}$ and $\mathbf{R^C}$ are each independently selected from the group consisting of hydrogen, $-SO_2\mathbf{R^H}$, $-C(=O)\mathbf{R^H}$, $-C(=O)N\mathbf{R^E}\mathbf{R^F}$, C_1-C_6 alkyl, C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, heterocycle, and C_1-C_6 heterohaloalkyl where the cycloalkyl and the heterocycle are optionally fused with an aryl or heteroaryl; or $-N\mathbf{R^B}\mathbf{R^C}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom; or $-N\mathbf{R^B}\mathbf{R^C}$ is an optionally substituted C_1-C_6 alkylideneamino;

[0400] each $\mathbf{R^D}$ is independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an optionally substituted C_1-C_6 heteroalkyl, an optionally substituted heterocyle, and $-(CH_2)_m\mathbf{R^G}$;

[0401] each $-N\mathbf{R^E}\mathbf{R^F}$ is separately selected, wherein $\mathbf{R^E}$ and $\mathbf{R^F}$ are each independently selected from the group consisting of hydrogen, an optionally substituted C_1-C_6 alkyl, an optionally substituted C_2-C_4 alkenyl, an optionally substituted C_2-C_4 alkynyl, an optionally substituted C_3-C_7 cycloalkyl, an optionally substituted C_1-C_6 haloalkyl, an

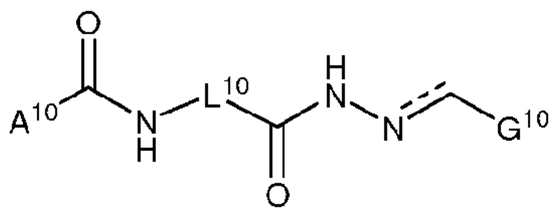
optionally substituted C_1-C_6 heteroalkyl, an optionally substituted heterocycle, and $-(CH_2)_m\mathbf{R^G}$; or $-N\mathbf{R^E}\mathbf{R^F}$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

[0402] each $\mathbf{R^G}$ is separately selected from an optionally substituted aryl and an optionally substituted heteroaryl;

[0403] each $\mathbf{R^H}$ is separately selected from the group consisting of hydrogen, a C_1-C_6 alkyl, a C_1-C_6 haloalkyl, a C_1-C_6 heteroalkyl, a C_3-C_6 cycloalkyl, an optionally substituted heterocycle, and an optionally substituted aryl or an optionally substituted heteroaryl; and

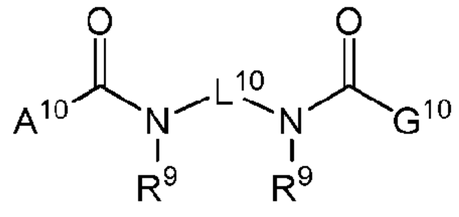
[0404] each **m** is independently 0, 1, or 2.

[0405] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a compound having Formula **X** having the structure of Formula **Xa**:



(**Xa**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{A^{10}}$ can be selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; and $\mathbf{G^{10}}$ can be selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle.

[0406] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a compound having Formula **X** having the structure of Formula **Xb**:



(**Xb**), and pharmaceutically acceptable salts thereof, wherein $\mathbf{A^{10}}$ can be selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in

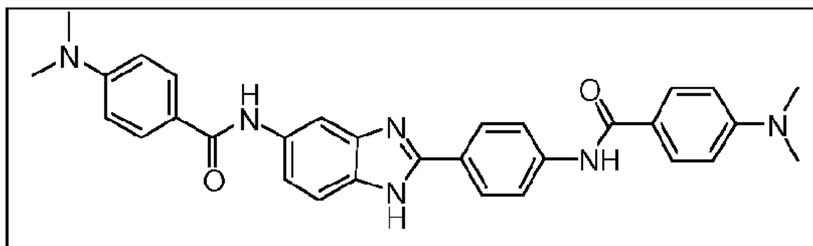
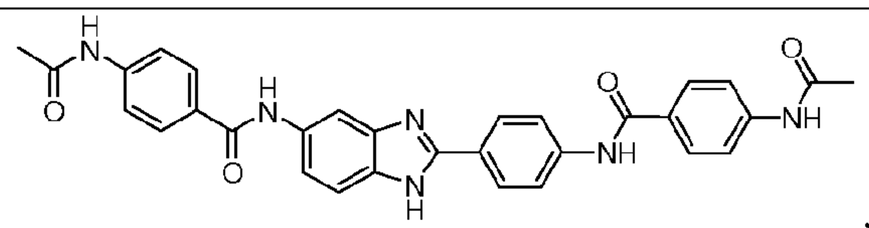
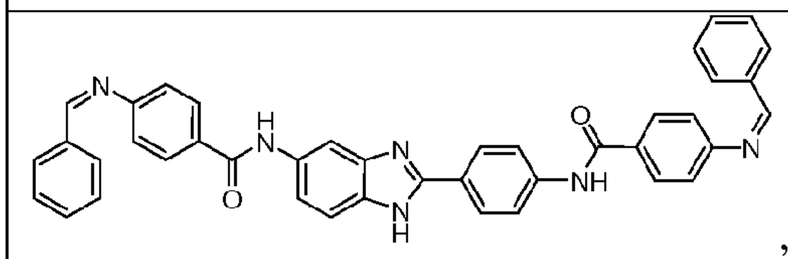
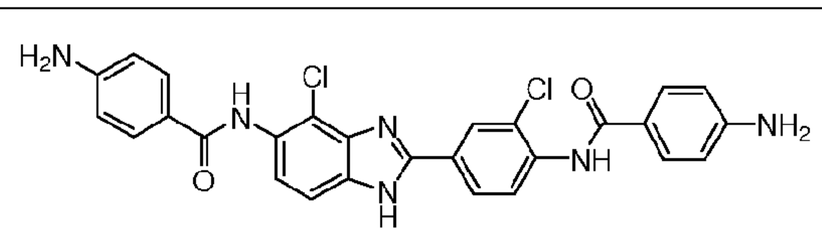
the definition of $\mathbf{A^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; and $\mathbf{G^{10}}$ can be selected from the group consisting of aryl and heteroaryl, each optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle.

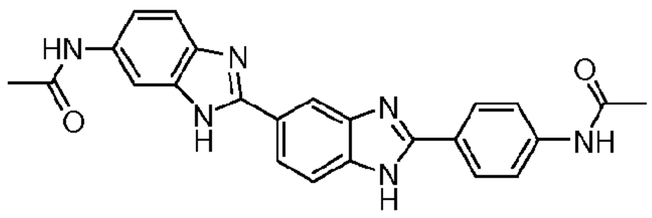
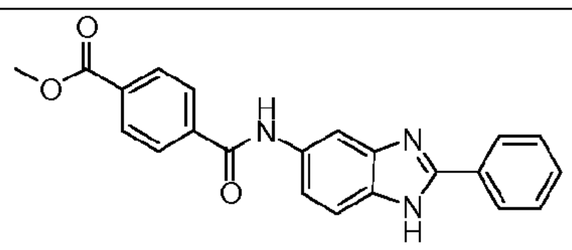
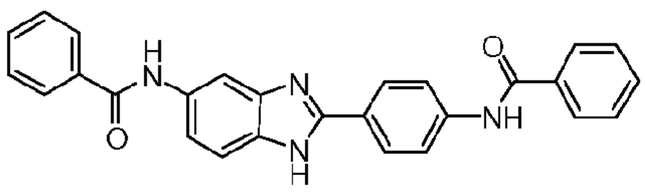
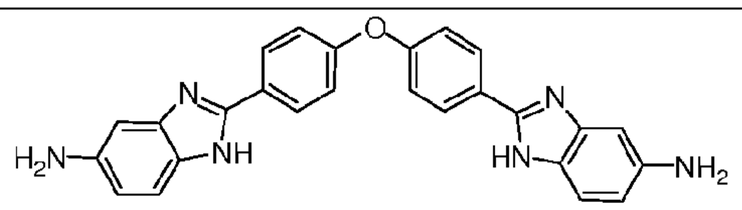
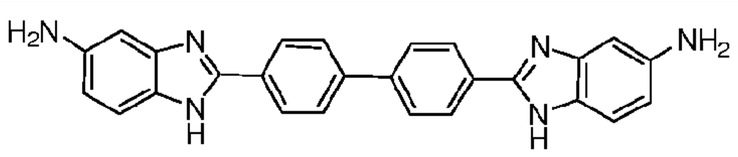
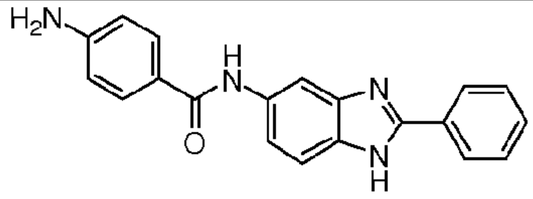
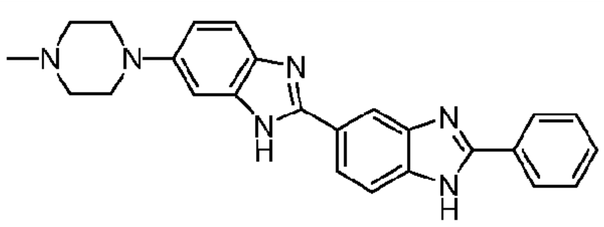
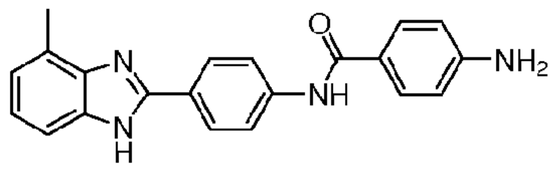
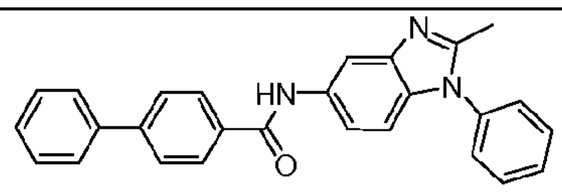
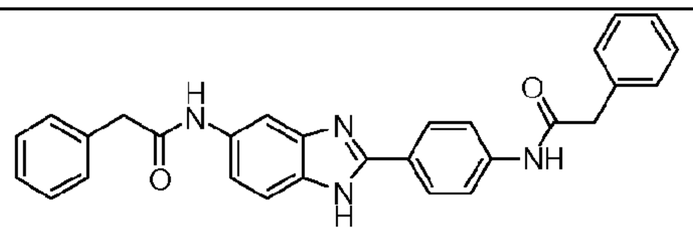
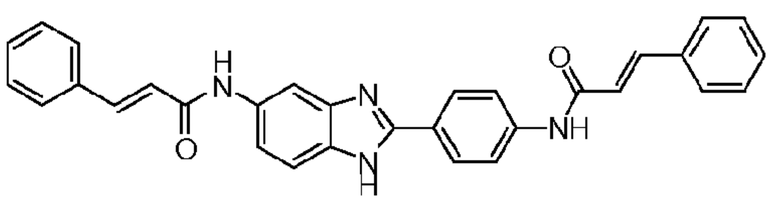
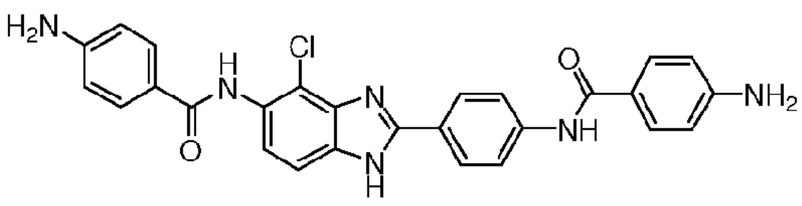
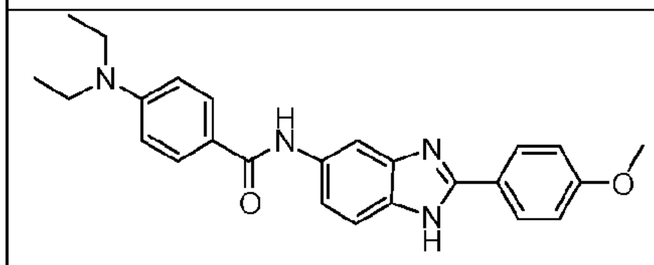
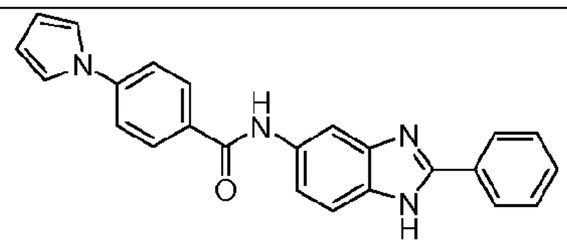
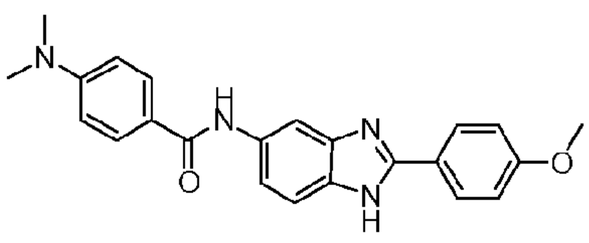
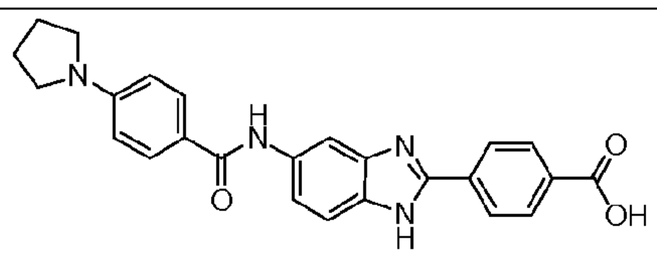
[0407] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a compound having Formula **X**, wherein $\mathbf{A^{10}}$ can be selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$, said aryl and heteroaryl in the definition of $\mathbf{A^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{G^{10}}$ can be selected from the group consisting of C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 heteroalkyl, heterocycle, aryl, and heteroaryl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, said aryl and heteroaryl in the definition of $\mathbf{G^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or nonaromatic carbocycle; $\mathbf{R^1}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^2}$ can be selected from the group consisting of $-O\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, and $-S\mathbf{R^A}$; $\mathbf{R^3}$ can be selected from the group consisting of $-(CH_2)_m\mathbf{R^G}$, $-O\mathbf{R^D}$, and $-N\mathbf{R^E}\mathbf{R^F}$; $\mathbf{R^4}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^5}$ can be selected from the group consisting of $-O\mathbf{R^A}$, $-N\mathbf{R^B}\mathbf{R^C}$, and $-S\mathbf{R^A}$; $\mathbf{R^6}$ can be selected from the group consisting of $-(CH_2)_m\mathbf{R^G}$, $-O\mathbf{R^D}$, and $-N\mathbf{R^E}\mathbf{R^F}$; $\mathbf{J^{10}}$ and $\mathbf{Q^{10}}$ can each be independently selected from the group consisting of an ester, an amide, a urea, a carbamide, $-S(O)_2N\mathbf{R^A}-$, a thioamide, a thioester, and an imidamide; $\mathbf{L^{10}}$ can be a 3-13 atom long linker comprising comprising one or more groups selected from –O– (oxygen), $-N\mathbf{R^A}-$, $-S(O)_{0\text{-}2}-$, and $-N\mathbf{R^A}S(O)_{1\text{-}2}O-$, and one or more groups selected from –O– (oxygen), $-N\mathbf{R^A}-$, $-S(O)_{0\text{-}2}-$, and $-N\mathbf{R^A}S(O)_{1\text{-}2}O-$, an optionally substituted C_1-C_8 alkyl, an optionally substituted aryl, and an optionally substituted heteroaryl; where the an optionally substituted aryl and an optionally substituted heteroaryl in the definition of $\mathbf{L^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or a nonaromatic carbocycle; and each m can be independently 0, 1, or 2.

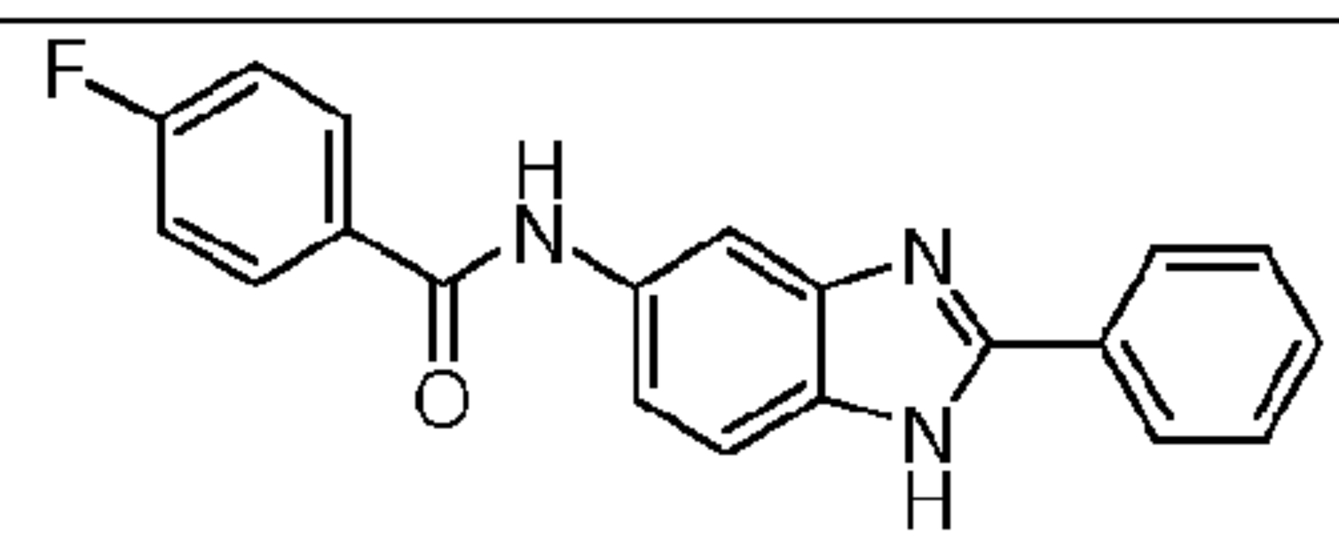
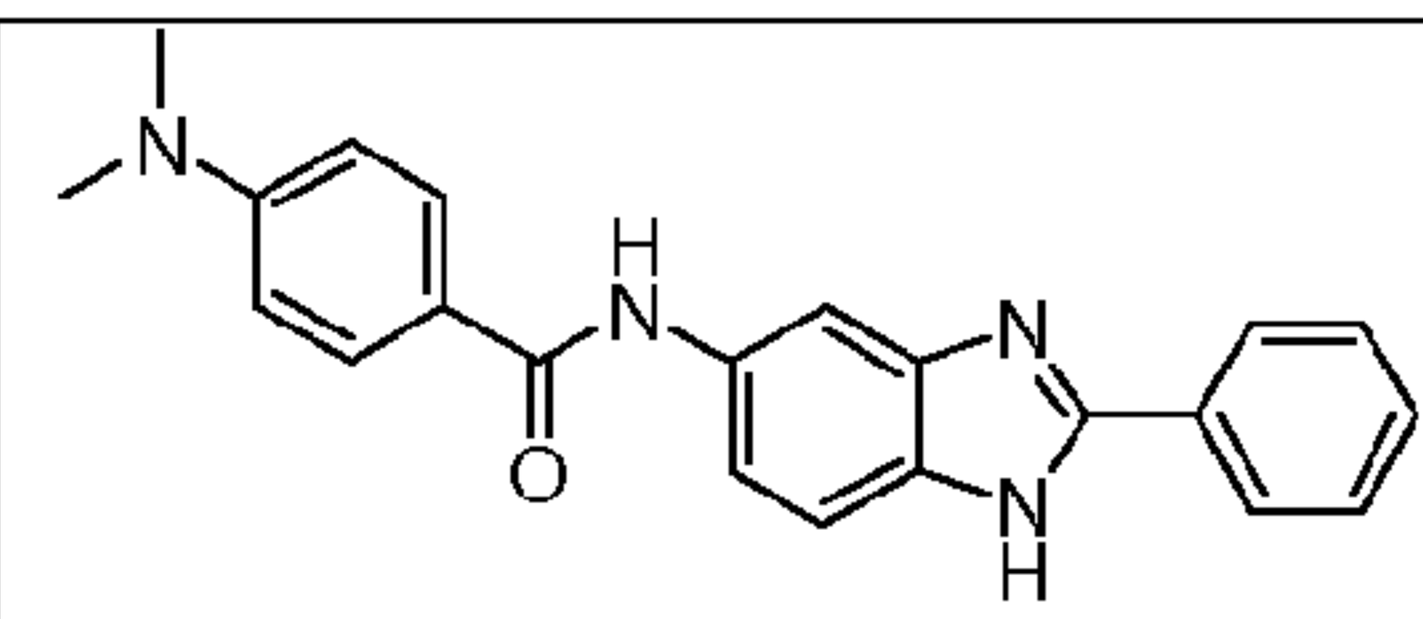
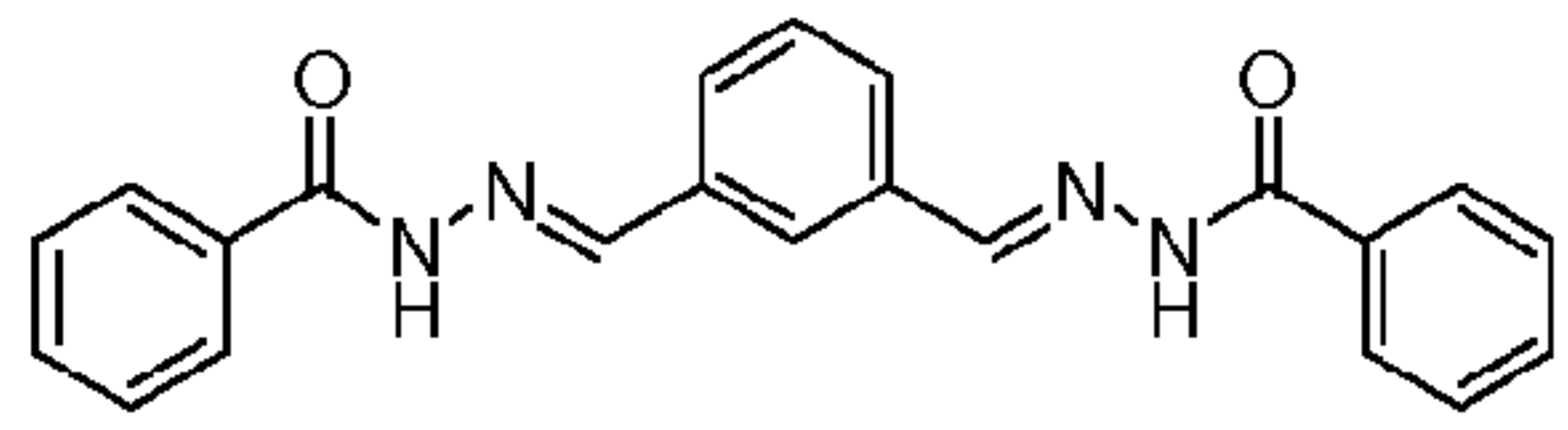
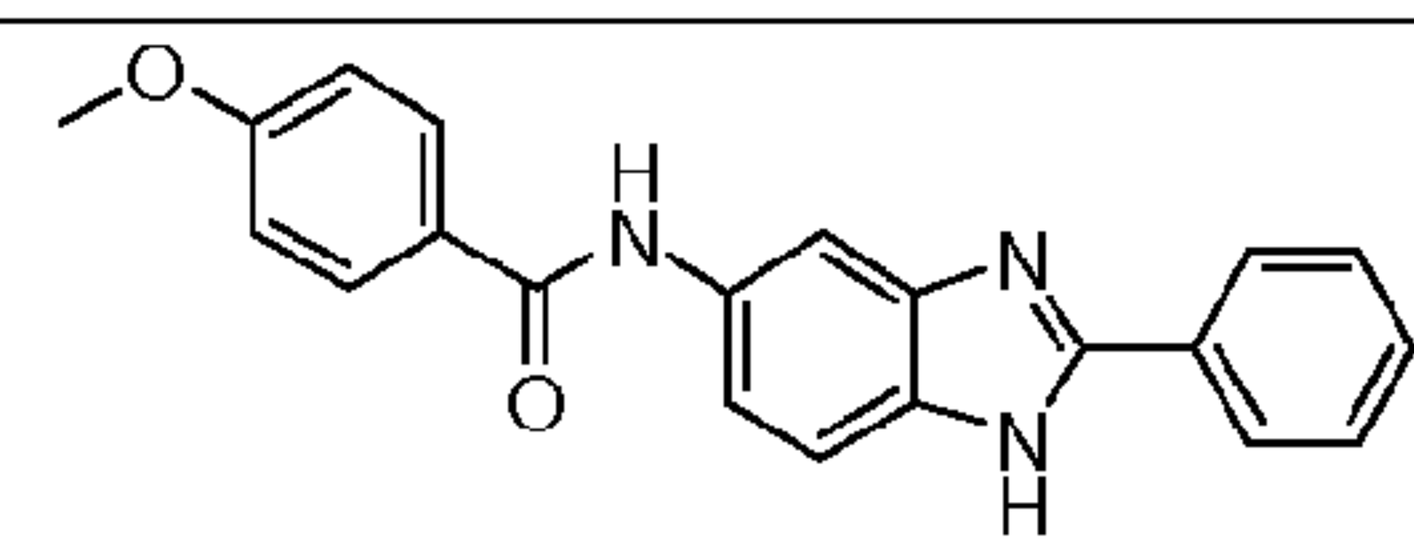
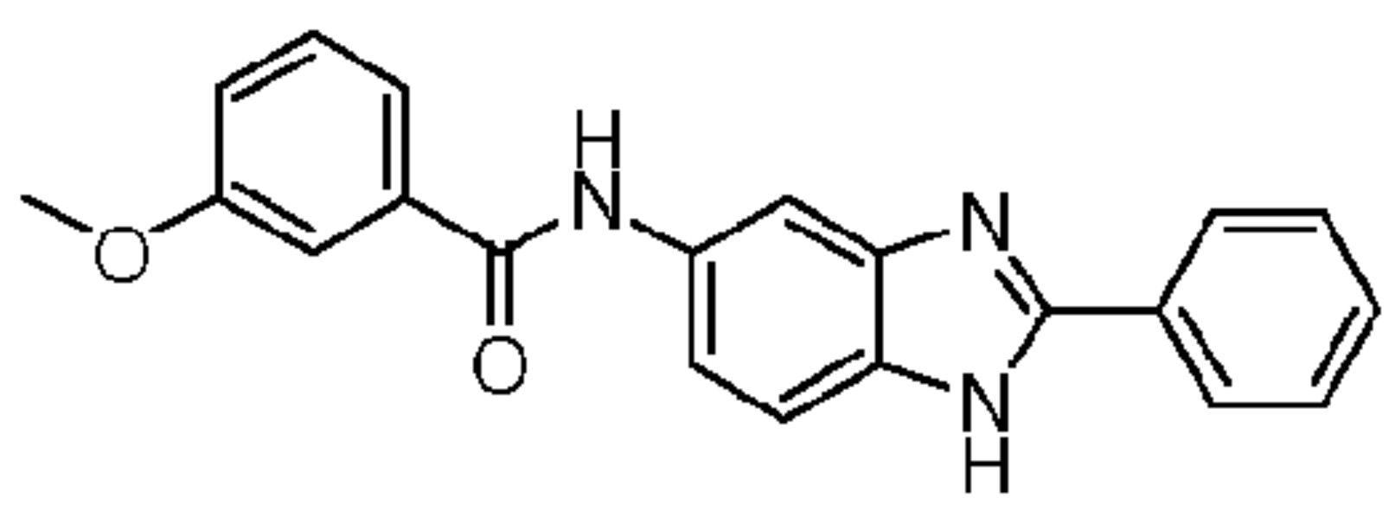
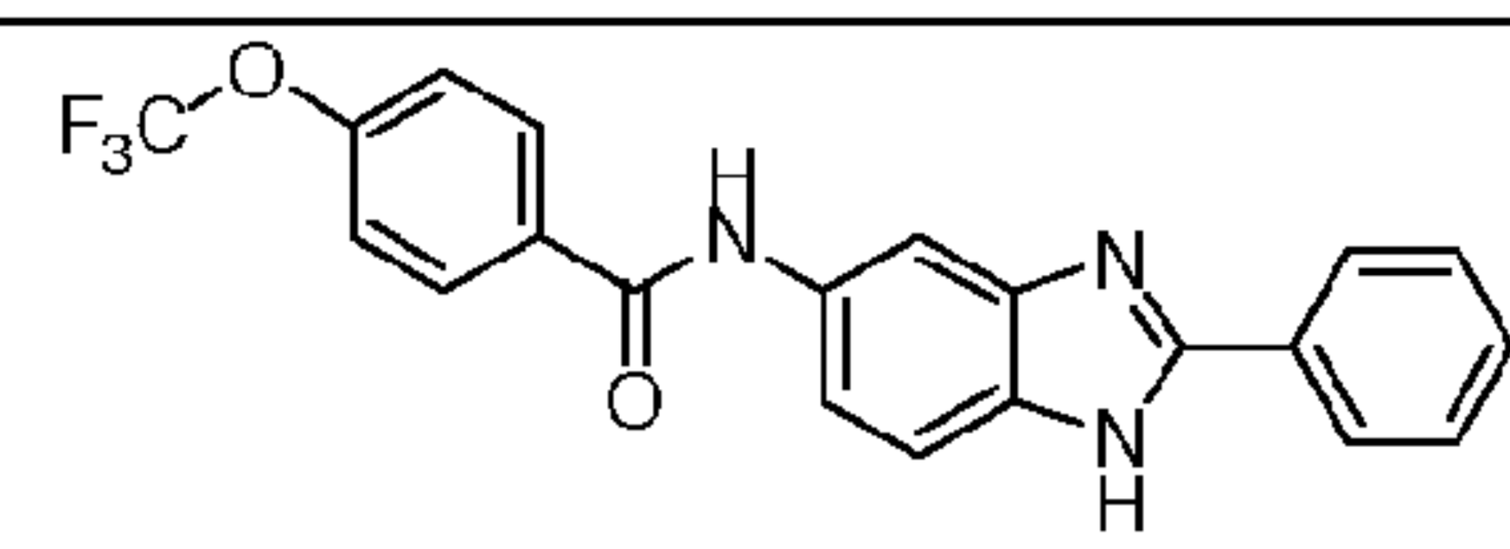
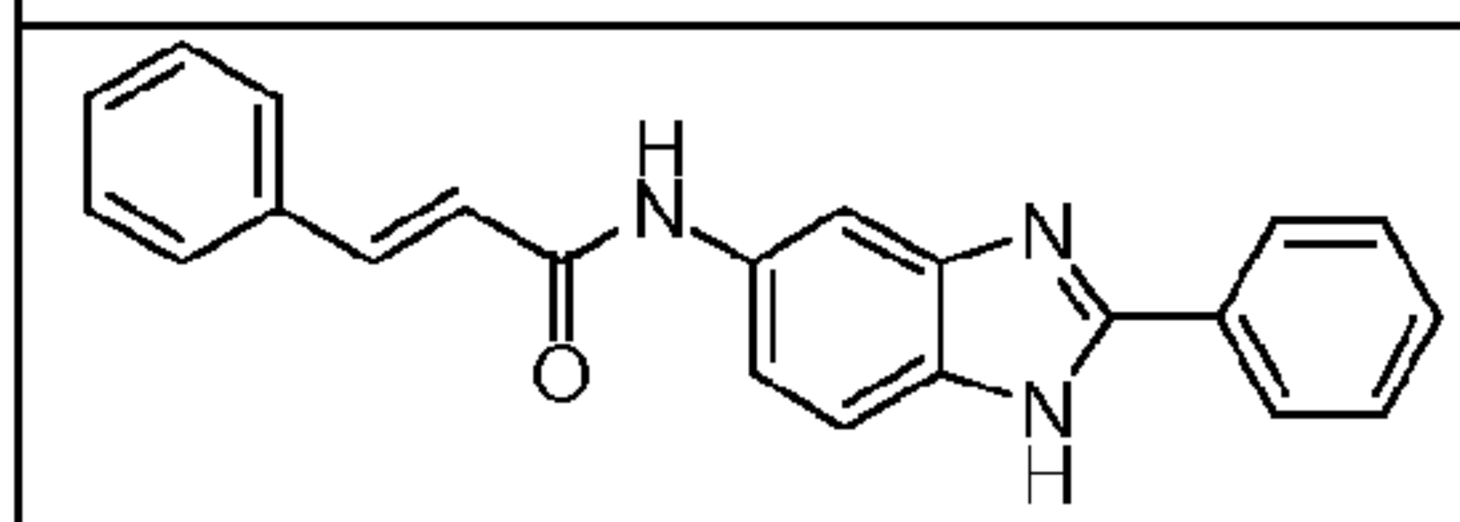
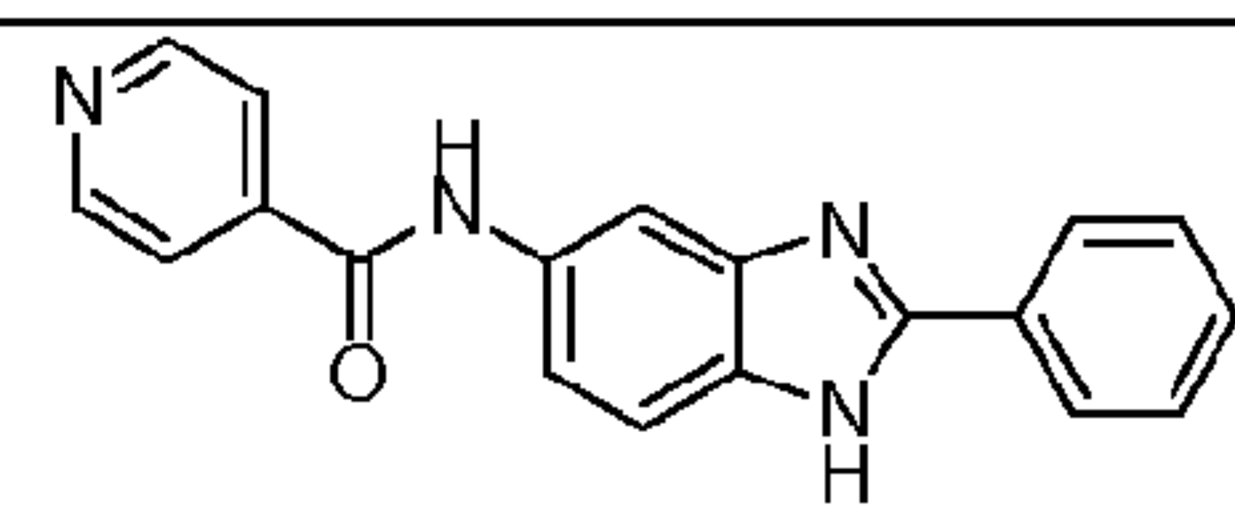
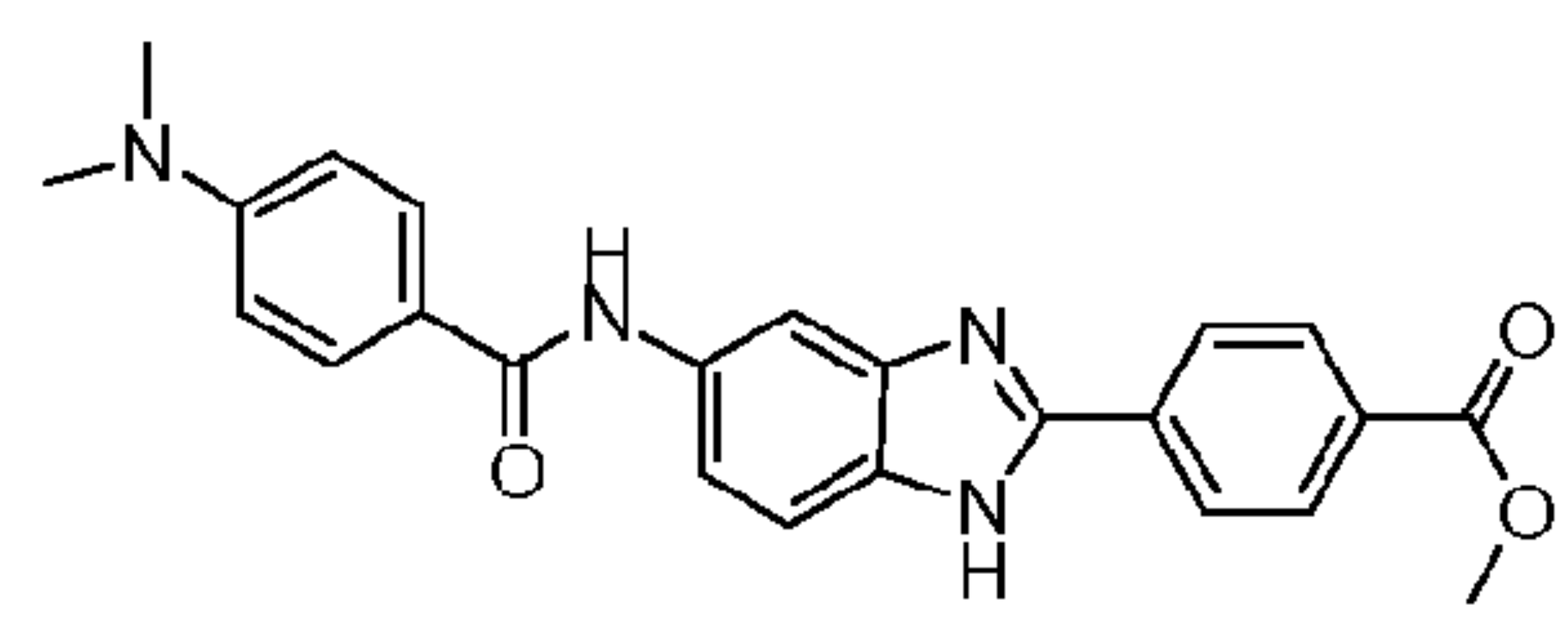
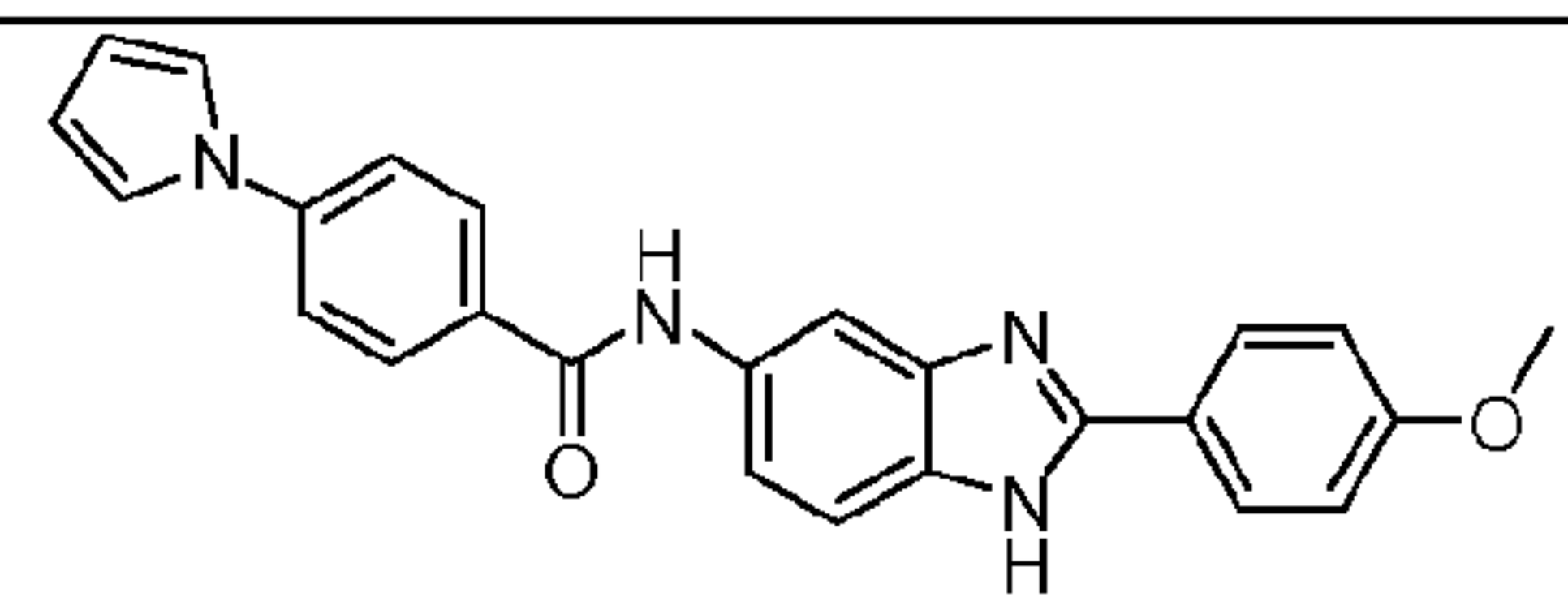
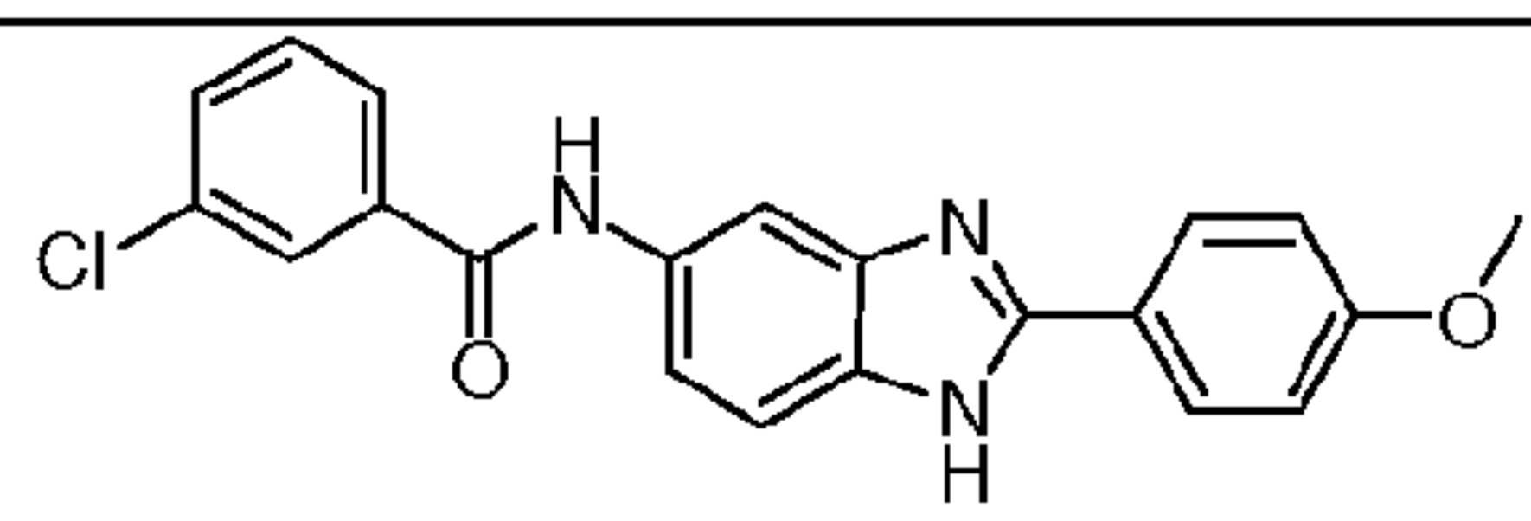
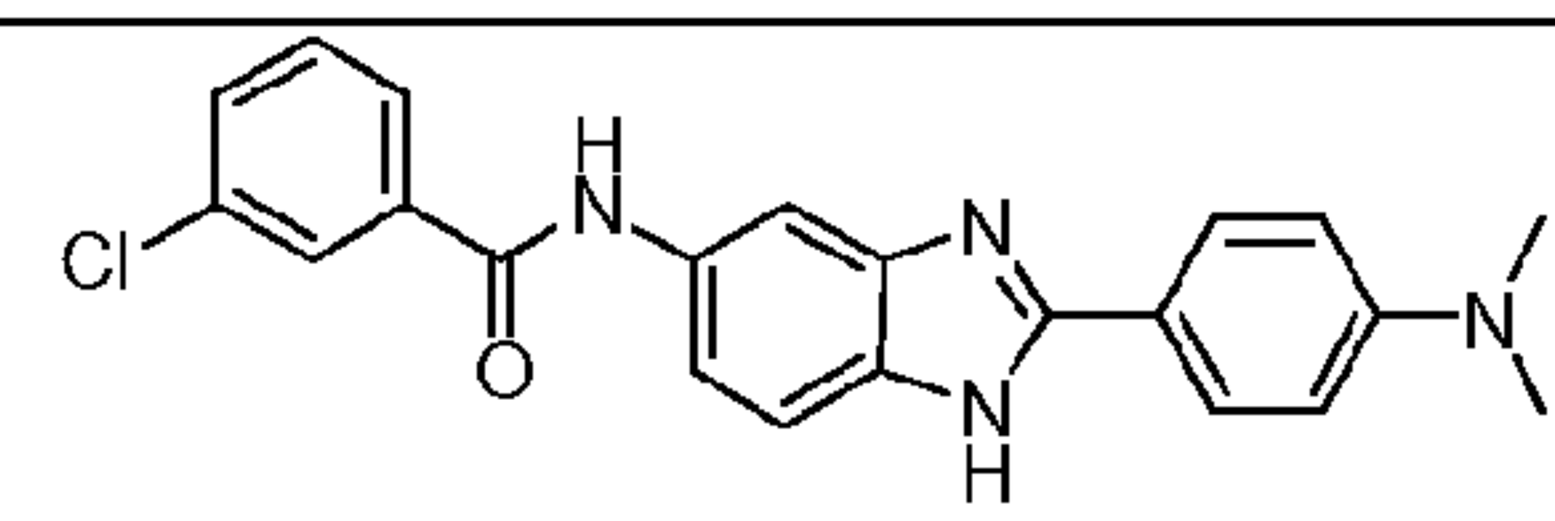
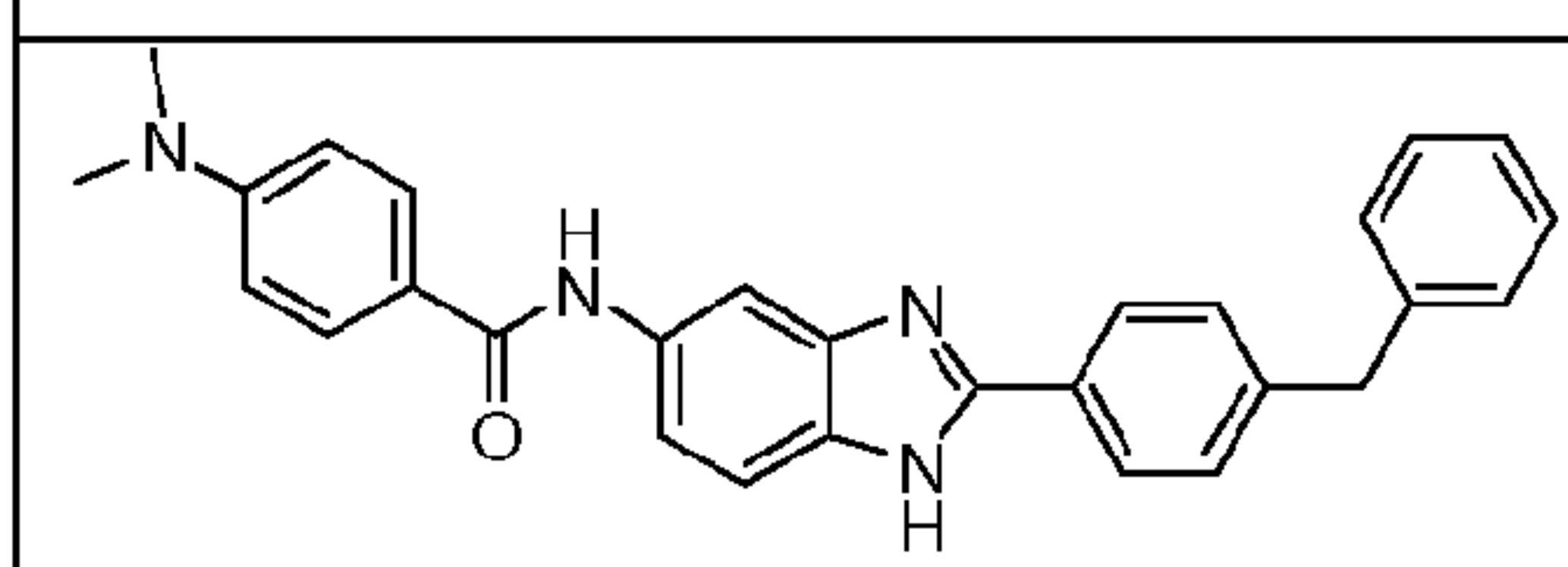
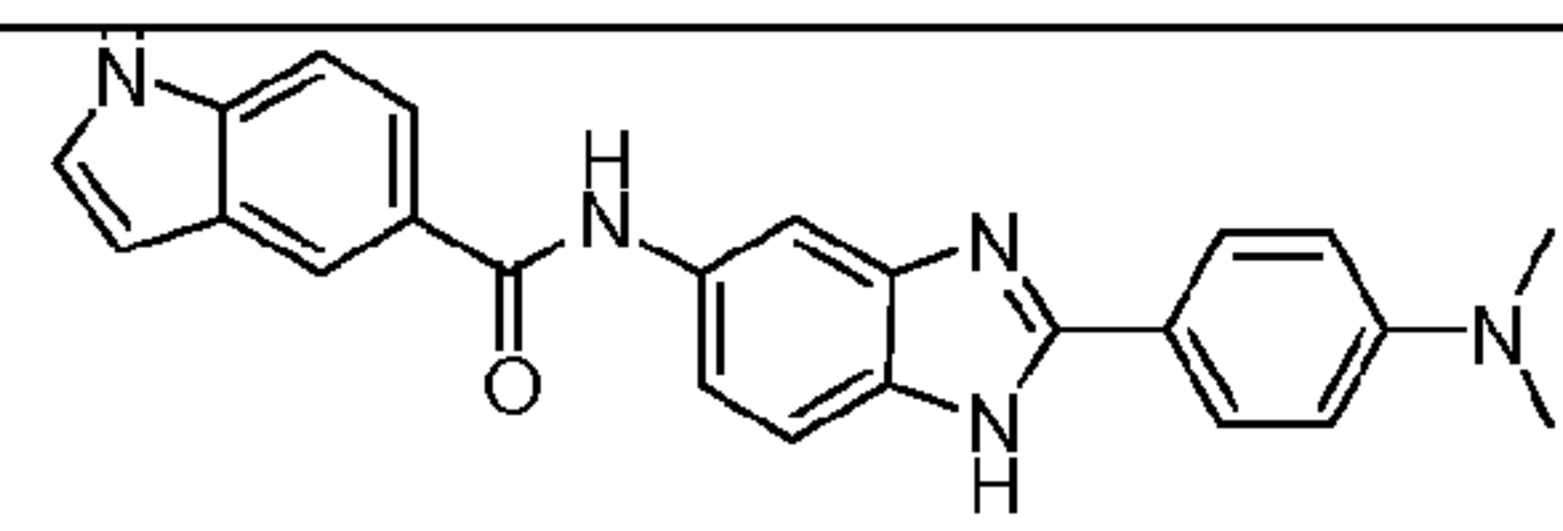
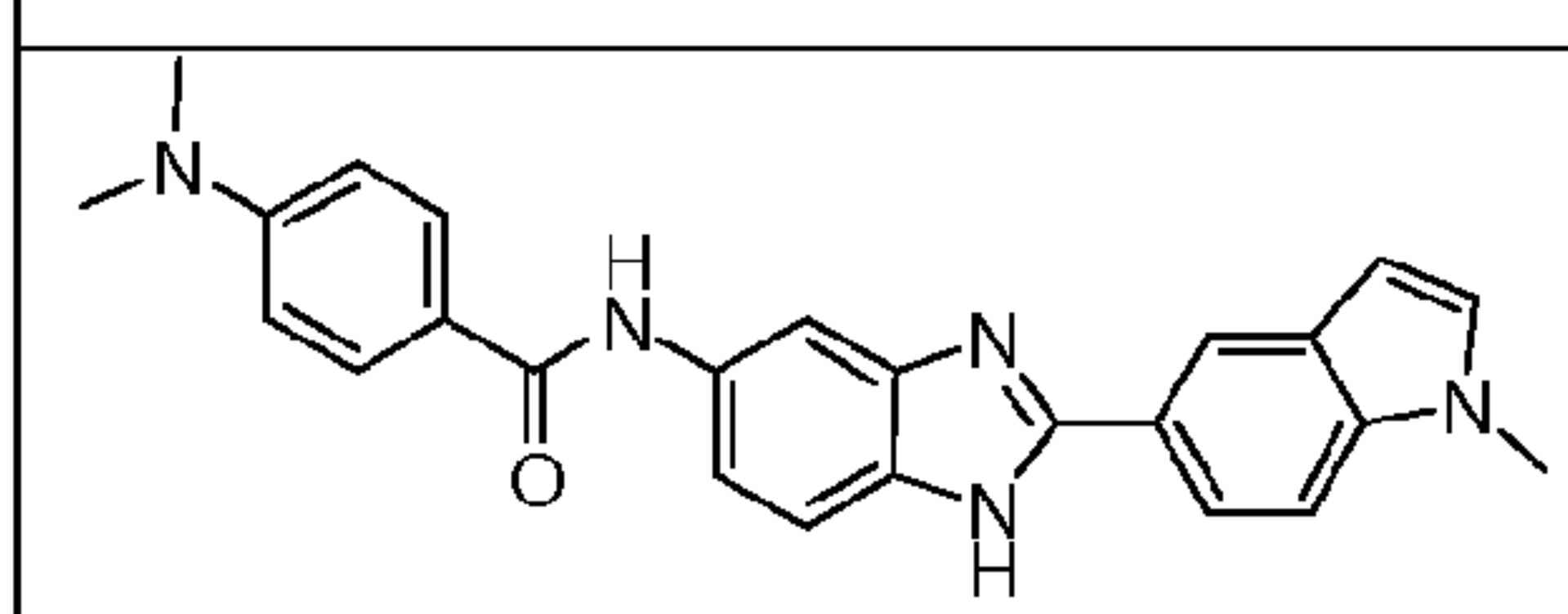
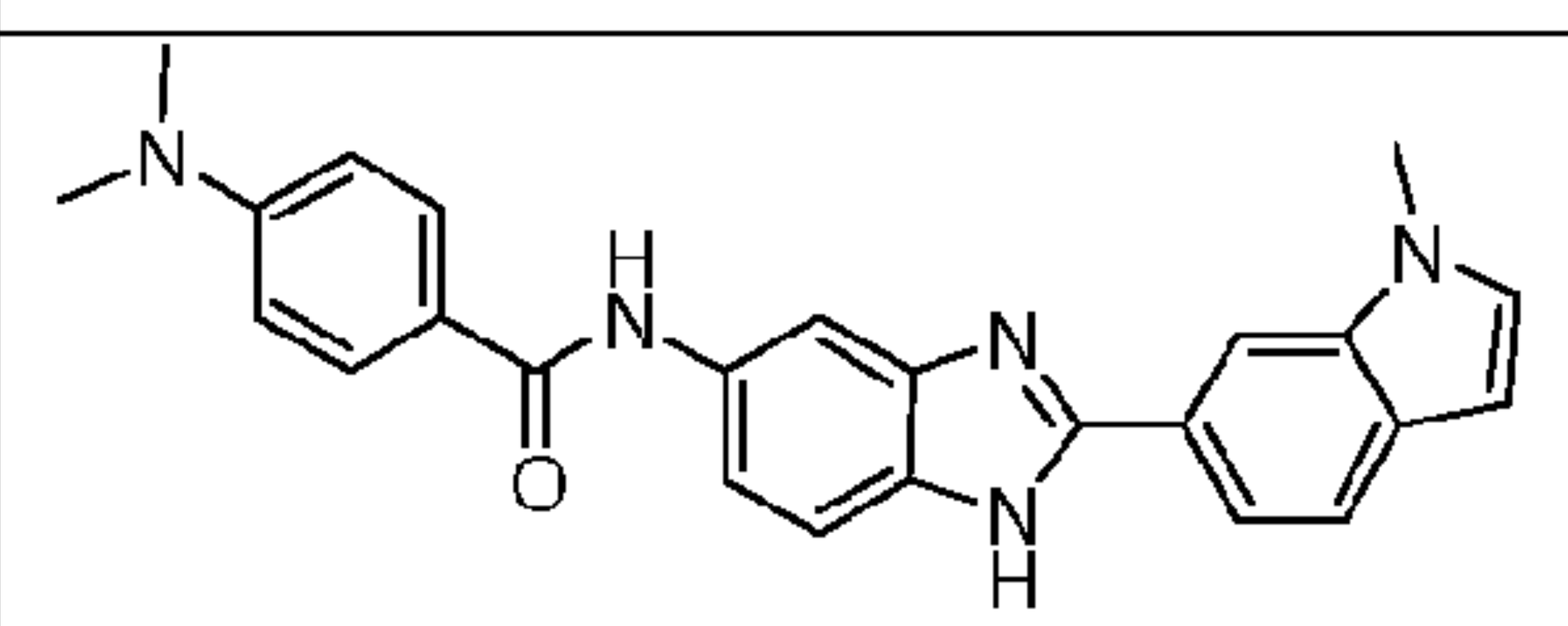
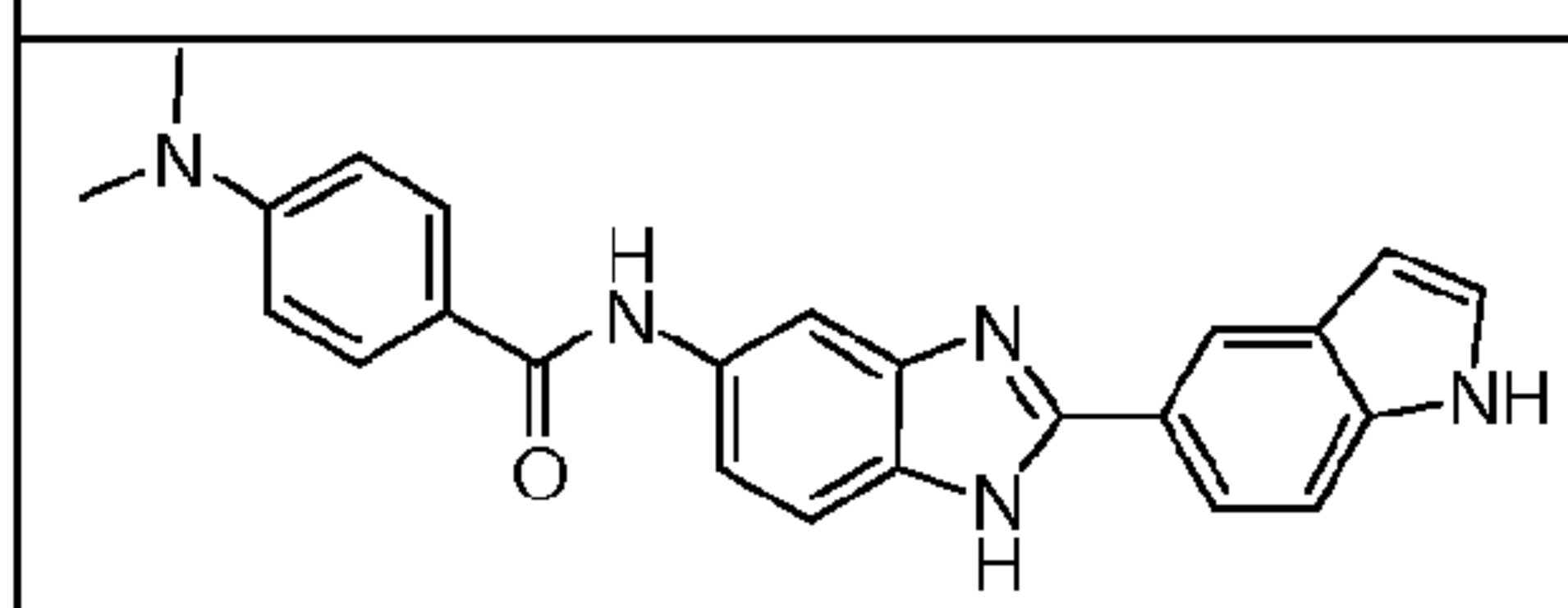
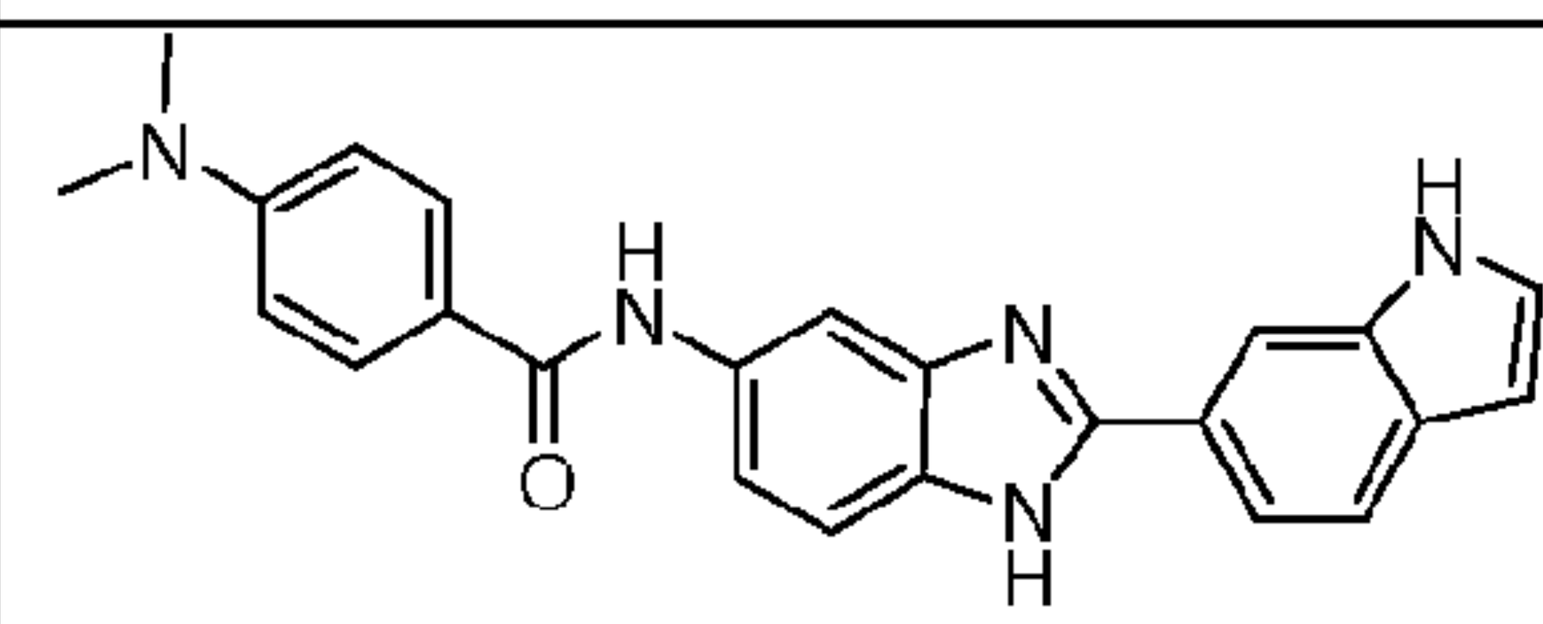
[0408] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a

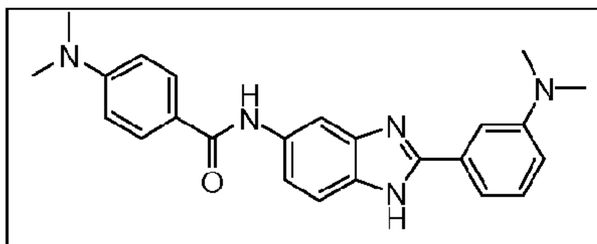
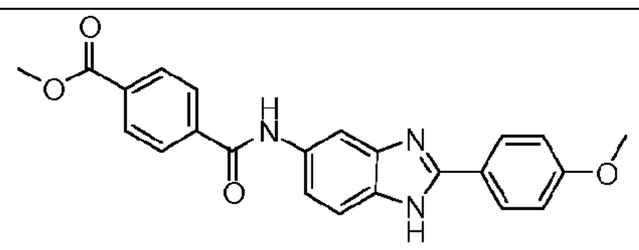
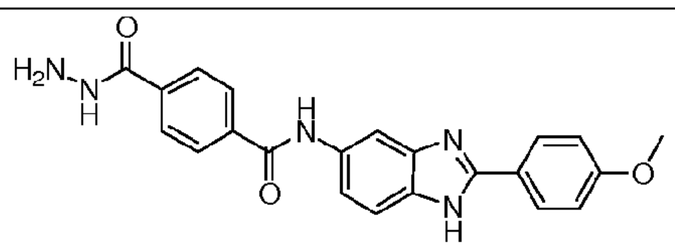
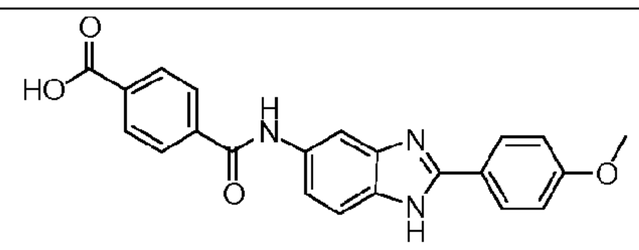
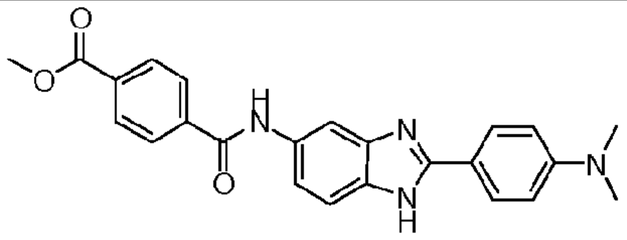
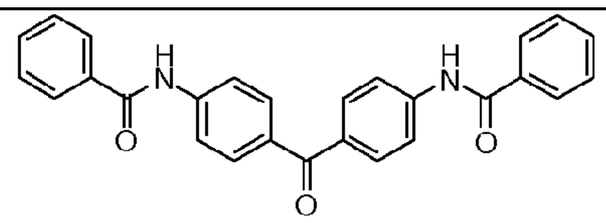
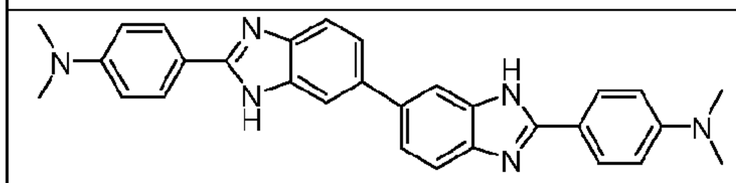
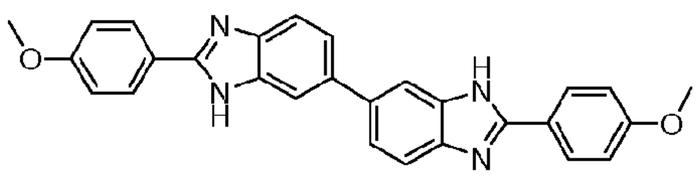
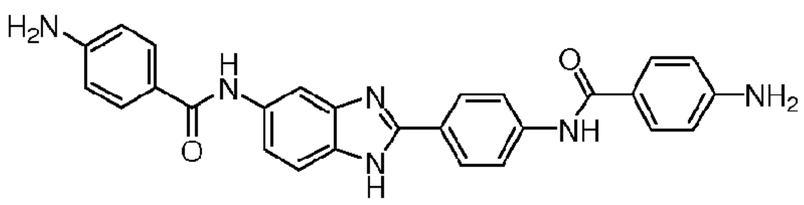
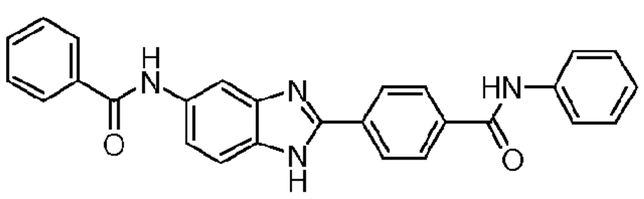
compound having Formula **X**, wherein $\mathbf{A^{10}}$ can be selected from the group consisting of a C_2-C_6 alkyl, a C_2-C_7 cycloalkyl, a C_1-C_6 heteroalkyl, a heterocycle, phenyl, pyridinyl, pyrrolyl, pyrimidinyl, imidazolyl, isoxazolyl, thiazolyl, thienyl, indolyl, benzoxazolyl, benzthiazolyl, benzimidazolyl, and purinyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$; $\mathbf{G^{10}}$ can be selected from the group consisting of a C_2-C_6 alkyl, a C_2-C_7 cycloalkyl, a C_1-C_6 heteroalkyl, a heterocycle, phenyl, pyridinyl, pyrrolyl, pyrimidinyl, imidazolyl, isoxazolyl, thiazolyl, thienyl, indolyl, benzoxazolyl, benzthiazolyl, benzimidazolyl, and purinyl, each substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$; $\mathbf{R^1}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^2}$ can be selected from the group consisting of $-O\mathbf{R^A}$ and $-N\mathbf{R^B}\mathbf{R^C}$; $\mathbf{R^3}$ can be $\mathbf{R^G}$; $\mathbf{R^4}$ can be selected from the group consisting of fluorine, chlorine, and methyl; $\mathbf{R^5}$ can be selected from the group consisting of $-O\mathbf{R^A}$ and $-N\mathbf{R^A}\mathbf{R^B}$; $\mathbf{R^6}$ can be $\mathbf{R^G}$; $\mathbf{J^{10}}$ and $\mathbf{Q^{10}}$ can each be independently selected from the group consisting of an amide, a urea, a carbamide, $-S(O)_2N\mathbf{R^A}-$, a thioamide, and an imidamide; $\mathbf{L^{10}}$ can be a 3-13 atom long linker comprising one or more groups selected from –O– (oxygen), -C(=O)–, $-N\mathbf{R^A}-$, $-S(O)_{0\text{-}2}-$, $-N\mathbf{R^A}S(O)_{1\text{-}2}N\mathbf{R^A}-$, and one or more groups selected from an optionally substituted aryl, and an optionally substituted heteroaryl; where the an optionally substituted aryl and an optionally substituted heteroaryl in the definition of $\mathbf{L^{10}}$ can each be further optionally fused with a nonaromatic heterocycle or a nonaromatic carbocycle.

[0409] Some embodiments disclosed herein provide a method of treating a patient, comprising administering to the patient a therapeutically effective amount of a compound having the structure:

 ,	 ,
 ,	 ,

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,

 ,	 ,
 ,	 ,
 ,	 ,
 ,	 ,
 ,	and
 .	

[0410] Some embodiments disclosed herein provide a pharmaceutical composition comprising a physiologically acceptable carrier, diluent, or excipient; and a compound of any of Formulae **I** to **IX**, or any compound specifically disclosed herein.

[0411] A pharmaceutical composition comprising a physiologically acceptable carrier, diluent, or excipient; and a compound of any of Formulae **I** to **IX,** or any compound specifically disclosed herein.

[0412] In certain embodiments, a compound of Formula **I**, **II**, **III**, **IV**, **V**, **VI**, **VII**, **VIII**, or **IX**, is a hematopoietic growth factor mimetic.

[0413] In certain embodiments, provided are methods for modulating activity of HGF receptors. Such methods comprise contacting a cell with one or more compounds of the present embodiments. Such methods include, but are not limited to, contacting HGF and/or HGF receptors with one or more compounds of the present embodiments.

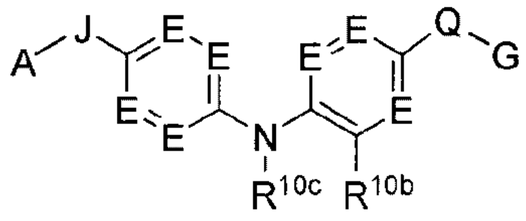
[0414] In certain embodiments, the embodiments provide a method for identifying a compound that is capable of modulating HGF activity comprising: a) contacting a cell capable of a HGF activity with a compound of the present embodiments; and b) monitoring an effect on the cell. In certain such embodiments, the cell expresses a HGF receptor.

[0415] In certain embodiments, provided are methods of treating a patient comprising administering to the patient a compound of the present embodiments. In certain embodiments, such a patient suffers from thrombocytopenia. In certain embodiments, one or more compounds of the present embodiments are administered to a patient before, during or after chemotherapy, bone marrow transplantation, and/or radiation therapy. In certain embodiments, one or more compounds of the embodiments are administered to a patient suffering from aplastic anemia, bone marrow failure, and/or idiopathic thrombocytopenia. In certain embodiments, one or more compounds of the present embodiments are administered to a patient suffering from a disease of the nervous system. In certain embodiments, one or more compounds of the present embodiments are administered to a patient suffering from amyotrophic lateral sclerosis, multiple sclerosis, or muscular dystrophy. In certain embodiments, one or more compounds of the present embodiments are administered to a patient with a nerve injury, including, but not limited to, a spinal cord injury.

[0416] In certain embodiments, provided are pharmaceutical compositions comprising: i) a physiologically acceptable carrier, diluent, or excipient, or a combination thereof; and ii) one or more compounds of the present embodiments.

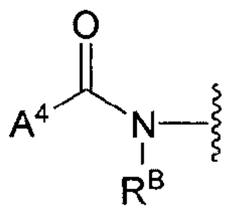
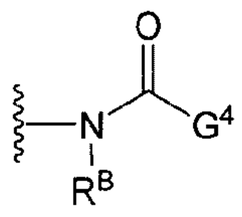
[0417] Certain embodiments provide a selective HGF modulator. Certain embodiments provide a selective HGF receptor agonist. Certain embodiments provide a selective HGF receptor antagonist. Certain embodiments provide a selective HGF partial agonist. Certain embodiments provide a selective HGF receptor binding compound. Certain embodiments provide a HGF mimic.

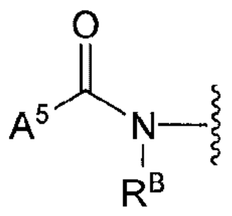
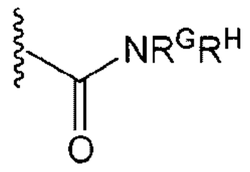
[0417A] Also provided is a compound or a pharmaceutically acceptable salt thereof of Formula **VIII**:

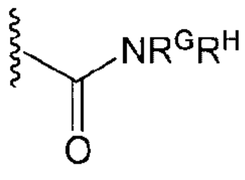
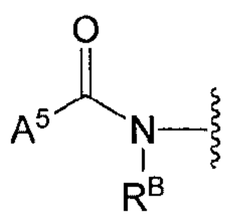


(**VIII**)

wherein:

or **A–J** is  and **Q–G** is  ;

or **A–J** is  and **Q–G** is  ;

or **A–J** is  and **Q–G** is  ;

each **E** is separately selected from the group consisting of -C**R**^{10a}- and N (nitrogen);

each **R**^{10a} is separately selected from the group consisting of H (hydrogen), halogen, and C_1-C_6 alkyl optionally substituted with up to five fluoro;

R^{10b} is selected from the group consisting of H (hydrogen), halogen, and C_1-C_6 alkyl optionally substituted with up to five fluoro;

R^{10c} is H (hydrogen);

A^4 is selected from the group consisting of phenyl and heteroaryl, wherein at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), and wherein each phenyl and heteroaryl is optionally substituted with one or more substituents selected from the group consisting of **R**^{1}, **R**^{2}, and **R**^{3};

G^4 is selected from the group consisting of phenyl and heteroaryl, wherein at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), and wherein each phenyl and heteroaryl is optionally substituted with one or more substituents selected from the group consisting of **R**^{4}, **R**^{5}, and **R**^{6};

A^5 is phenyl optionally substituted with one or more substituents selected from the group consisting of **R**^{1}, **R**^{2}, and **R**^{3};

R^B is hydrogen;

R^G is heteroaryl wherein at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), optionally substituted with one or more substituents selected from the group consisting of **R**^{4}, **R**^{5}, and **R**^{6}, and wherein said heteroaryl in the definition of **R**^{G} is further optionally fused with an optionally substituted nonaromatic carbocycle;

R^H is hydrogen;

each **R**^{1} is separately selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^2}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^3}$ is separately selected from the group consisting of halogen, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each $\mathbf{R^4}$ is separately selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^5}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^6}$ is separately selected from the group consisting of halogen, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each $\mathbf{R^I}$ is separately selected from the group consisting of hydrogen and C_1-C_6 alkyl;

each $-NR^JR^K$ is separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, or $-(CH_2)_mOR^{JA}$; or $-NR^JR^K$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

each $\mathbf{R^{JA}}$ is independently selected from the group consisting of hydrogen or C_1-C_6 alkyl; and

each **m** is independently 0, 1, or 2;

and wherein unless otherwise indicated, optionally substituted refers to a group in which none, one, or more than one of the hydrogen atoms has been replaced with one or more group(s) individually and independently selected from: alkyl, heteroalkyl, $HO(CH_2)_{1\text{-}3}O$-, $HO(CH_2)_{1\text{-}3}$-, hydroxy, and halo. Also provided is a pharmaceutical composition comprising a physiologically acceptable carrier, diluent, or excipient; and such a compound or pharmaceutically acceptable salt. Also provided is use of such a compound or pharmaceutically acceptable salt thereof for modulating an EPO activity in a cell, for identifying a compound that modulates an EPO activity and for treatment of a disease or condition resulting from radiation or chemotherapy in a patient. Also provided is use of such a compound or pharmaceutically acceptable salt thereof for the preparation of a medicament for such modulating and treatment. Also provided is an *in vitro* method for identifying a compound that modulates an EPO activity, comprising contacting a cell that expresses an EPO receptor with such a compound or pharmaceutically acceptable salt thereof and monitoring an effect of the compound or pharmaceutically acceptable salt thereof on the cell.

DETAILED DESCRIPTION

[0418] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the embodiments claimed. In this application, the use of the singular includes the plural unless specifically stated otherwise. In this application, the use of "or" means "and/or" unless stated otherwise. Furthermore, use of the term "including" as well as other forms, such as "includes," and "included," is not limiting.

[0419] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described.

Definitions

[0420] Unless specific definitions are provided, the nomenclatures utilized in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those known in the art. Standard chemical symbols are used interchangeably with the full names represented by such symbols. Thus, for example, the terms "hydrogen" and "H" are understood to have identical meaning. Standard techniques may be used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients. Standard techniques may be used for recombinant DNA, oligonucleotide synthesis, and tissue culture and transformation (*e.g.* , electroporation, lipofection). Reactions and purification techniques may be performed e.g., using kits according to manufacturer's specifications or as commonly accomplished in the art or as described herein. The foregoing techniques and procedures may be generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification. *See e.g.* , Sambrook et al. Molecular Cloning: A Laboratory Manual (2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)).

[0421] As used herein, the following terms are defined with the following meanings, unless expressly stated otherwise.

[0422] The term "selective binding compound" refers to a compound that selectively binds to any portion of one or more target.

[0423] The term "selective HGF receptor binding compound" refers to a compound that selectively binds to any portion of a HGF receptor.

[0424] The term "selectively binds" refers to the ability of a selective binding compound to bind to a target receptor with greater affinity than it binds to a non-target receptor. In certain embodiments, selective binding refers to binding to a target with an affinity that is at least 10, 50, 100, 250, 500, or 1000 times greater than the affinity for a non-target.

[0425] The term "target receptor" refers to a receptor or a portion of a receptor capable of being bound by a selective binding compound. In certain embodiments, a target receptor is a HGF receptor.

[0426] The term "modulator" refers to a compound that alters an activity. For example, a modulator may cause an increase or decrease in the magnitude of a certain activity compared to the magnitude of the activity in the absence of the modulator. In certain embodiments, a modulator is an inhibitor, which decreases the magnitude of one or more activities. In certain embodiments, an inhibitor completely prevents one or more biological activities. In certain embodiments, a modulator is an activator, which increases the magnitude of at least one activity. In certain embodiments the presence of a modulator results in a activity that does not occur in the absence of the modulator.

[0427] The term "selective modulator" refers to a compound that selectively modulates a target activity.

[0428] The term "selective HGF modulator" refers to a compound that selectively modulates at least one HGF activity. The term selective HGF modulator includes, but is not limited to "HGF mimic" which refers to a compound, the presence of which results in at least one HGF activity.

[0429] The term "selectively modulates" refers to the ability of a selective modulator to modulate a target activity to a greater extent than it modulates a non-target activity.

[0430] The term "target activity" refers to a biological activity capable of being modulated by a selective modulator. Certain exemplary target activities include, but are not limited to, binding affinity, signal transduction, enzymatic activity, the proliferation and/or

differentiation of progenitor cells, generation of platelets, and alleviation of symptoms of a disease or condition.

[0431] The term "HGF activity" refers to a biological activity that results, either directly or indirectly from the presence of HGF. Exemplary HGF activities include, but are not limited to, proliferation and or differentiation of progenitor cells to produce platelets; hematopoiesis; growth and/or development of glial cells; repair of nerve cells; and alleviation of thrombocytopenia.

[0432] The term "receptor mediated activity" refers to any biological activity that results, either directly or indirectly, from binding of a ligand to a receptor.

[0433] The term "agonist" refers to a compound, the presence of which results in a biological activity of a receptor that is the same as the biological activity resulting from the presence of a naturally occurring ligand for the receptor.

[0434] The term "partial agonist" refers to a compound, the presence of which results in a biological activity of a receptor that is of the same type as that resulting from the presence of a naturally occurring ligand for the receptor, but of a lower magnitude.

[0435] The term "antagonist" refers to a compound, the presence of which results in a decrease in the magnitude of a biological activity of a receptor. In certain embodiments, the presence of an antagonist results in complete inhibition of a biological activity of a receptor.

[0436] The term "alkyl" refers to a branched or unbranched fully saturated acyclic aliphatic hydrocarbon group. An alkyl may be branched or straight chain. Alkyls may be substituted or unsubstituted. Alkyls include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tertiary butyl, pentyl, hexyl, and the like, each of which may be optionally substituted.

[0437] In certain embodiments, an alkyl comprises 1 to 20 carbon atoms (whenever it appears herein, a numerical range such as "1 to 20" refers to each integer in the given range; *e.g.*, "1 to 20 carbon atoms" means that an alkyl group may comprise only 1 carbon atom, 2 carbon atoms, 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the term "alkyl" also includes instances where no numerical range of carbon atoms is designated). An alkyl may be designated as "C_1-C_6 alkyl" or similar designations. By way of example only, "C_1-C_4 alkyl" indicates an alkyl having one, two, three, or four carbon

atoms, e.g., the alkyl is selected from methyl, ethyl, propyl, *iso*-propyl, butyl, *iso*-butyl, *sec*-butyl, and *tert*-butyl.

[0438] The term "alkenyl" used herein refers to a monovalent straight or branched chain aliphatic hydrocarbon radical of from two to twenty carbon atoms containing at least one carbon-carbon double bond including, but not limited to, 1-propenyl, 2-propenyl, 2-methyl-1-propenyl, 1-butenyl, 2-butenyl, and the like. In certain embodiments, an alkenyl comprises 2 to 20 carbon atoms (whenever it appears herein, a numerical range such as "2 to 20" refers to each integer in the given range; *e.g.*, "2 to 20 carbon atoms" means that an alkenyl group may comprise only 2 carbon atoms, 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the term "alkenyl" also includes instances where no numerical range of carbon atoms is designated). An alkenyl may be designated as "C_2-C_6 alkenyl" or similar designations. By way of example only, "C_2-C_4 alkenyl" indicates an alkenyl having two, three, or four carbon atoms, e.g., the alkenyl is selected from ethenyl, propenyl, and butenyl.

[0439] The term "alkynyl" used herein refers to a monovalent straight or branched chain aliphatic hydrocarbon radical of from two to twenty carbon atoms containing at least one carbon-carbon triple bond including, but not limited to, 1-propynyl, 1-butynyl, 2-butynyl, and the like. In certain embodiments, an alkynyl comprises 2 to 20 carbon atoms (whenever it appears herein, a numerical range such as "2 to 20" refers to each integer in the given range; *e.g.*, "2 to 20 carbon atoms" means that an alkynyl group may comprise only 2 carbon atoms, 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the term "alkynyl" also includes instances where no numerical range of carbon atoms is designated). An alkynyl may be designated as "C_2-C_6 alkynyl" or similar designations. By way of example only, "C_2-C_4 alkynyl" indicates an alkenyl having two, three, or four carbon atoms, e.g., the alkenyl is selected from ethynyl, propynyl, and butynyl.

[0440] The term "cycloalkyl" used herein refers to saturated aliphatic ring system radical having three to twenty carbon atoms. A cycloalkyl refers to monocyclic and polycyclic saturated aliphatic ring system including, but not limited to, cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, bicyclo[4.4.0]decanyl, bicyclo[2.2.1]heptanyl, adamantyl, norbornyl, and the like. In certain embodiments, a cycloalkyl comprises 3 to 20 carbon atoms (whenever it appears herein, a numerical range such as "3 to 20" refers to each integer in the given range; *e.g.*, "3 to 20 carbon atoms" means that a cycloalkyl group may

comprise only 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the term "cycloalkyl" also includes instances where no numerical range of carbon atoms is designated). A cycloalkyl may be designated as "C_3-C_7 cycloalkyl" or similar designations. By way of example only, "C_3-C_6 cycloalkyl" indicates an alkenyl having two, three, four, five or six carbon atoms, e.g., the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0441] The term "cycloalkenyl" used herein refers to aliphatic ring system radical having three to twenty carbon atoms having at least one carbon-carbon double bond in the ring. A cycloalkenyl refers to monocyclic and polycyclic unsaturated aliphatic ring system including, but are not limited to, cyclopropenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, bicyclo[3.1.0]hexyl, norbornylenyl, 1,1'-bicyclopentenyl, and the like. In certain embodiments, a cycloalkenyl comprises 3 to 20 carbon atoms (whenever it appears herein, a numerical range such as "3 to 20" refers to each integer in the given range; *e.g.*, "3 to 20 carbon atoms" means that a cycloalkenyl group may comprise only 3 carbon atoms, *etc.*, up to and including 20 carbon atoms, although the term "cycloalkenyl" also includes instances where no numerical range of carbon atoms is designated). A cycloalkenyl may be designated as "C_3-C_7 cycloalkenyl" or similar designations. By way of example only, "C_3-C_6 cycloalkenyl" indicates an alkenyl having two, three, four, five or six carbon atoms, e.g., the cycloalkyl is selected from cyclopropenyl, cyclobutenyl, cyclopentenyl, and cyclohexenyl.

[0442] The term "haloalkyl" refers to an alkyl in which at least one hydrogen atom is replaced with a halogen atom. In certain of the embodiments in which two or more hydrogen atom are replaced with halogen atoms, the halogen atoms are all the same as one another. In certain of such embodiments, the halogen atoms are not all the same as one another.

[0443] The term "heteroalkyl" refers to a group comprising an alkyl and one or more heteroatoms. Certain heteroalkyls are acylalkyls, in which the one or more heteroatoms are within an alkyl chain. Examples of heteroalkyls include, but are not limited to, $CH_3C(=O)CH_2$-, $CH_3C(=O)CH_2CH_2$-, $CH_3CH_2C(=O)CH_2CH_2$-, $CH_3C(=O)CH_2CH_2CH_2$-, $CH_3OCH_2CH_2$-, CH_3NHCH_2-, $CH_3NHC(=O)CH_2$-, and the like.

[0444] The term "alkoxy" used herein refers to straight or branched chain alkyl radical covalently bonded to the parent molecule through an --O-- linkage. Examples of alkoxy groups include, but are not limited to, methoxy, ethoxy, propoxy, isopropoxy, butoxy,

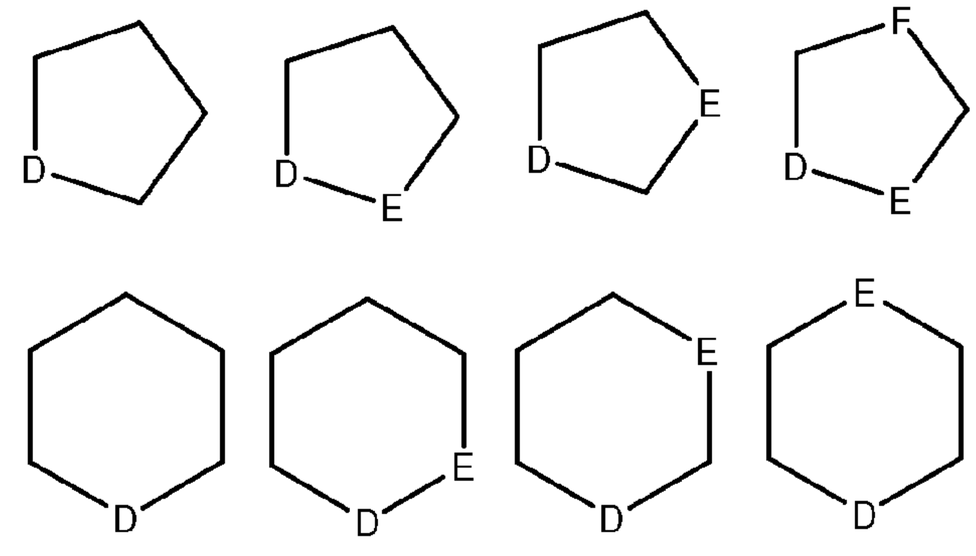
n-butoxy, sec-butoxy, t-butoxy and the like. An alkoxy may be designated as "C_1-C_6 alkoxy" or similar designations. By way of example only, "C_1-C_4 alkoxy" indicates an alkyl having one, two, three, or four carbon atoms, e.g., the alkoxy is selected from methoxy, ethoxy, propoxy, *iso*-propoxy, butoxy, *iso*-butoxy, *sec*-butoxy, and *tert*-butoxy.

[0445] The term "olefin" refers to a C=C bond.

[0446] The term "alkylideneamino" used herein refers to a moiety of from one to twenty carbon atoms containing at least one carbon-nitrogen double bond where the moiety is connected to the main group through the nitrogen, including, but not limited to, methylideneamino, ethylideneamino, methylethylideneamino, propylideneamino, 1-methylpropylideneaminyl, 2-methylpropylideneamino, butylideneamino, 1-methylbutylideneamino, 2-methylbutylideneamino, cyclopropylideneamino, cyclobutylideneamino, cyclopentylideneamino, cyclohexylideneamino and the like.

[0447] The term "carbocycle" refers to a group comprising a covalently closed ring, wherein each of the atoms forming the ring is a carbon atom. Carbocylic rings may be formed by three, four, five, six, seven, eight, nine, or more than nine carbon atoms. Carbocycles may be optionally substituted.

[0448] The term "heterocycle" refers to a group comprising a covalently closed ring wherein at least one atom forming the ring is a heteroatom. Heterocyclic rings may be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Any number of those atoms may be heteroatoms (*i.e.*, a heterocyclic ring may comprise one, two, three, four, five, six, seven, eight, nine, or more than nine heteroatoms). In heterocyclic rings comprising two or more heteroatoms, those two or more heteroatoms may be the same or different from one another. Heterocycles may be optionally substituted. Binding to a heterocycle can be at a heteroatom or via a carbon atom. For example, binding for benzo-fused derivatives, may be via a carbon of the benzenoid ring. Examples of heterocycles include, but are not limited to the following: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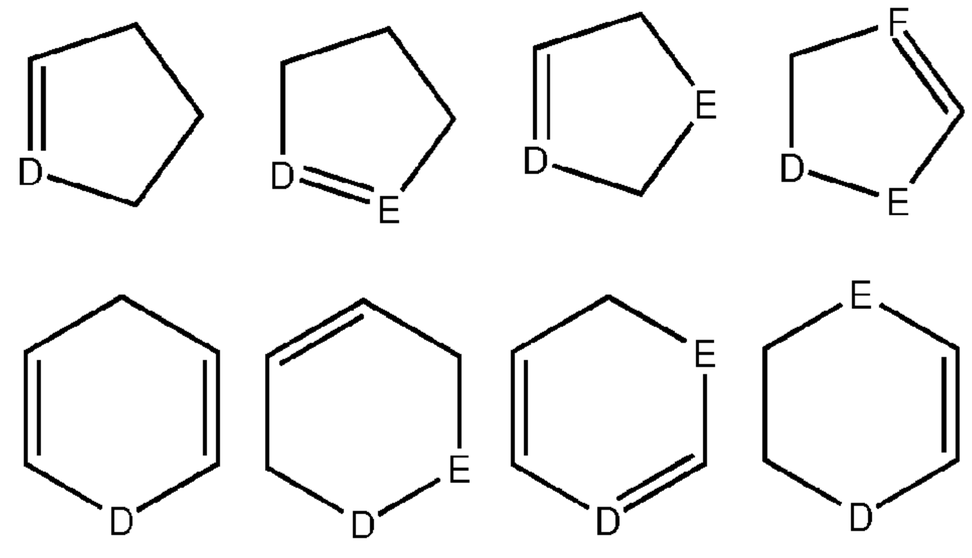


wherein **D**, **E**, **F**, and **G** independently represent a heteroatom. Each of **D**, **E**, **F**, and **G** may be the same or different from one another. Heterocycles may be aromatic heterocycles (i.e., heteroaryls) or non-aromatic heterocycles. In some embodiments, a non-aromatic heterocycle is a fully statured covalently closed ring (for example, piperidine, pyrrolidine, morpholine, piperazine, and the like).

[0449] The term "heteroatom" refers to an atom other than carbon or hydrogen. Heteroatoms are typically independently selected from oxygen, sulfur, nitrogen, and phosphorus, but are not limited to those atoms. In embodiments in which two or more heteroatoms are present, the two or more heteroatoms may all be the same as one another, or some or all of the two or more heteroatoms may each be different from the others.

[0450] The term "aromatic" refers to a group comprising a covalently closed ring having a delocalized π-electron system. Aromatic rings may be formed by five, six, seven, eight, nine, or more than nine atoms. Aromatics may be optionally substituted. Examples of aromatic groups include, but are not limited to phenyl, naphthalenyl, phenanthrenyl, anthracenyl, tetralinyl, fluorenyl, indenyl, and indanyl. The term aromatic includes, for example, benzenoid groups, connected via one of the ring-forming carbon atoms, and optionally carrying one or more substituents selected from an aryl, a heteroaryl, a cycloalkyl, a non-aromatic heterocycle, a halo, a hydroxy, an amino, a cyano, a nitro, an alkylamido, an acyl, a C_{1-6} alkoxy, a C_{1-6} alkyl, a C_{1-6} hydroxyalkyl, a C_{1-6} aminoalkyl, a C_{1-6} alkylamino, an alkylsulfenyl, an alkylsulfinyl, an alkylsulfonyl, an sulfamoyl, or a trifluoromethyl. In certain

embodiments, an aromatic group is substituted at one or more of the para, meta, and/or ortho positions. Examples of aromatic groups comprising substitutions include, but are not limited to, phenyl, 3-halophenyl, 4-halophenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 3-aminophenyl, 4-aminophenyl, 3-methylphenyl, 4-methylphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-trifluoromethoxyphenyl, 3-cyanophenyl, 4-cyanophenyl, dimethylphenyl, naphthyl, hydroxynaphthyl, hydroxymethylphenyl, (trifluoromethyl)phenyl, alkoxyphenyl, 4-morpholin-4-ylphenyl, 4-pyrrolidin-1-ylphenyl, 4-pyrazolylphenyl, 4-triazolylphenyl, and 4-(2-oxopyrrolidin-1-yl)phenyl.

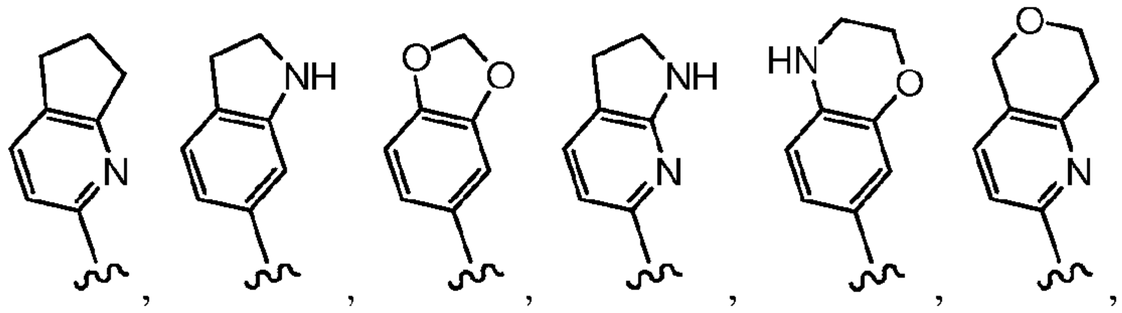
[0451] The term "aryl" refers to an aromatic group wherein each of the atoms forming the ring is a carbon atom. Aryl rings may be formed by five, six, seven, eight, nine, or more than nine carbon atoms. Aryl groups may be optionally substituted.

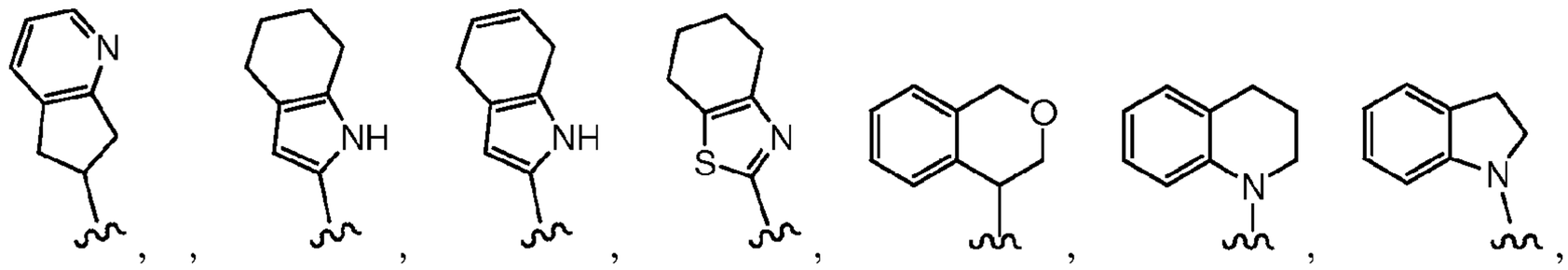
[0452] The term "heteroaryl" refers to an aromatic mono-, bi- or tricyclic ring system wherein at least one atom forming the aromatic ring system is a heteroatom. Heteroaryl rings may be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Heteroaryl groups may be optionally substituted. Examples of heteroaryl groups include, but are not limited to, aromatic C_{3-8} heterocyclic groups comprising one oxygen or sulfur atom or up to four nitrogen atoms, or a combination of one oxygen or sulfur atom and up to two nitrogen atoms, and their substituted as well as benzo- and pyrido-fused derivatives, for example, connected via one of the ring-forming carbon atoms. In certain embodiments, heteroaryl groups are optionally substituted with one or more substituents, independently selected from halo, hydroxy, amino, cyano, nitro, alkylamido, acyl, C_{1-6}-alkoxy, C_{1-6}-alkyl, C_{1-6}-hydroxyalkyl, C_{1-6}-aminoalkyl, C_{1-6}-alkylamino, alkylsulfenyl, alkylsulfinyl, alkylsulfonyl, sulfamoyl, or trifluoromethyl. In some embodiments, the substituents are halo, hydroxy, cyano, O-C_{1-6}-alkyl, C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, and amino-C_{1-6}-alkyl. Examples of heteroaryl groups include, but are not limited to, unsubstituted and mono- or di-substituted derivatives of furan, benzofuran, thiophene, benzothiophene, pyrrole, pyridine, indole, oxazole, benzoxazole, isoxazole, benzisoxazole, thiazole, benzothiazole, isothiazole, imidazole, benzimidazole, pyrazole, indazole, tetrazole, quinoline, isoquinoline, pyridazine, pyrimidine, purine and pyrazine, furazan, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, triazole, benzotriazole, pteridine, phenoxazole, oxadiazole, benzopyrazole, quinolizine, cinnoline, phthalazine, quinazoline, and quinoxaline.

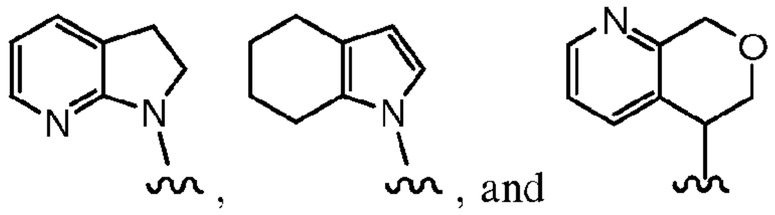
[0453] The term "non-aromatic ring" refers to a group comprising a covalently closed ring that does not have a delocalized π-electron system.

[0454] The term "non-aromatic heterocycle" refers to a group comprising a non-aromatic ring wherein one or more atoms forming the ring is a heteroatom. Non-aromatic heterocyclic rings may be formed by three, four, five, six, seven, eight, nine, or more than nine atoms. Non-aromatic heterocycles may be optionally substituted. In certain embodiments, non-aromatic heterocycles comprise one or more carbonyl or thiocarbonyl groups such as, for example, oxo- and thio-containing groups. Examples of non-aromatic heterocycles include, but are not limited to, lactams, lactones, cyclic imides, cyclic thioimides, cyclic carbamates, tetrahydrothiopyran, 4*H*-pyran, tetrahydropyran, piperidine, 1,3-dioxin, 1,3-dioxane, 1,4-dioxin, 1,4-dioxane, piperazine, 1,3-oxathiane, 1,4-oxathiin, 1,4-oxathiane, tetrahydro-1,4-thiazine, 2*H*-1,2-oxazine, maleimide, succinimide, barbituric acid, thiobarbituric acid, dioxopiperazine, hydantoin, dihydrouracil, morpholine, trioxane, hexahydro-1,3,5-triazine, tetrahydrothiophene, tetrahydrofuran, pyrroline, pyrrolidine, pyrrolidone, pyrrolidione, pyrazoline, pyrazolidine, imidazoline, imidazolidine, 1,3-dioxole, 1,3-dioxolane, 1,3-dithiole, 1,3-dithiolane, isoxazoline, isoxazolidine, oxazoline, oxazolidine, oxazolidinone, thiazoline, thiazolidine, and 1,3-oxathiolane.

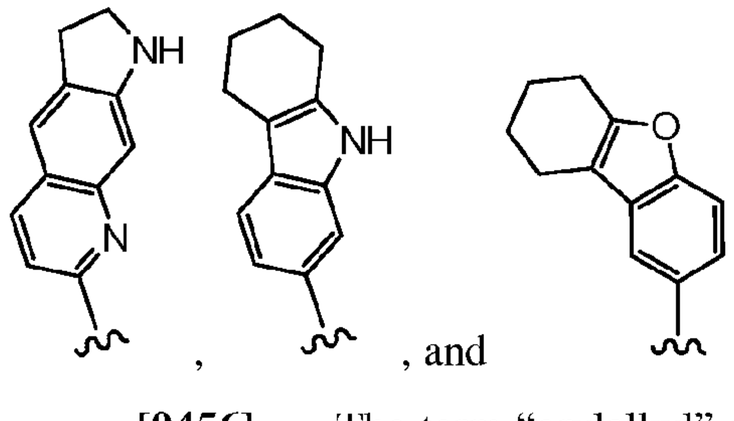
[0455] The term "polycyclic heterocyclyl" used herein refers a bicyclic moiety or tricyclic moiety optionally containing one or more heteroatoms wherein at least one of the rings is an aryl or heteroaryl ring and at least one of the rings is non-aromatic. The bicyclic moiety contains two rings wherein the rings are fused. The bicyclic moiety can be appended at any position of the two rings. For example, bicyclic moiety may refer to a radical

including but not limited to: 





. The tricyclic moiety contains a bicyclic moiety with an additional fused ring. The tricyclic moiety can be appended at any position of the three rings. For example, tricyclic moiety may refer to a radical including but not limited to:



[0456] The term "arylalkyl" refers to a group comprising an aryl group bound to an alkyl group.

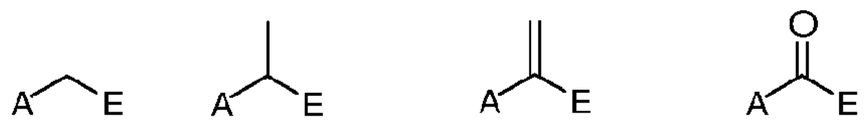
[0457] The term "carbocycloalkyl" refers to a group comprising a carbocyclic cycloalkyl ring. Carbocycloalkyl rings may be formed by three, four, five, six, seven, eight, nine, or more than nine carbon atoms. Carbocycloalkyl groups may be optionally substituted.

[0458] The term "ring" refers to any covalently closed structure. Rings include, for example, carbocycles (*e.g.*, aryls and cycloalkyls), heterocycles (*e.g.*, heteroaryls and non-aromatic heterocycles), aromatics (*e.g.*, aryls and heteroaryls), and non-aromatics (*e.g.*, cycloalkyls and non-aromatic heterocycles). Rings may be optionally substituted. Rings may form part of a ring system.

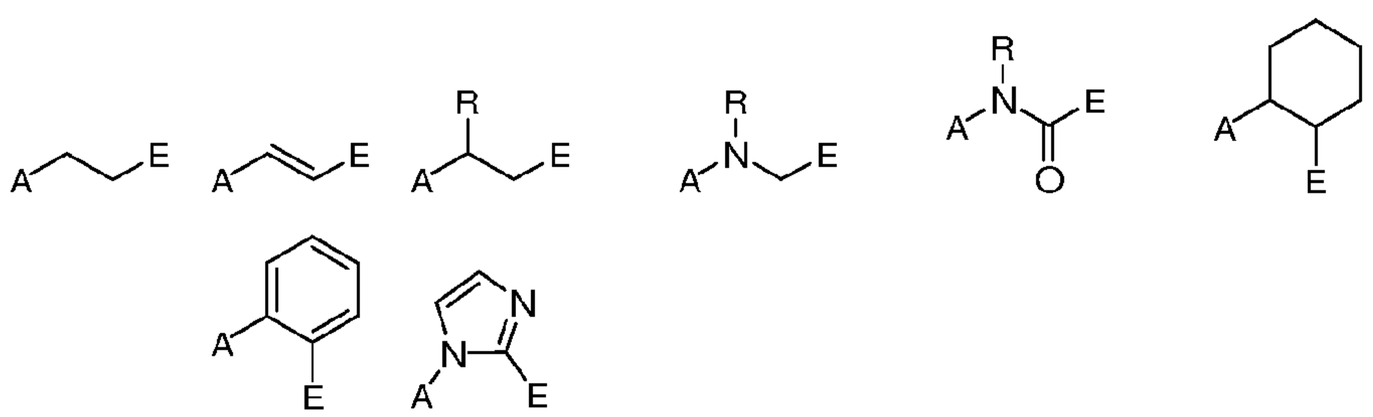
[0459] The term "ring system" refers to a either a single ring or two or more rings, wherein, if two or more rings are present, the two or more of the rings are fused. The term "fused" refers to structures in which two or more rings share one or more bonds.

[0460] The term "spacer" refers to an atom or group of atoms that separate two or more groups from one another by a desired number of atoms. For example, in certain embodiments, it may be desirable to separate two or more groups by one, two, three, four, five, six, or more than six atoms. In such embodiments, any atom or group of atoms may be used to separate those groups by the desired number of atoms. Spacers are optionally substituted. In certain embodiments, a spacer comprises saturated or unsaturated alkyls, heteroalkyls and/or haloalkyls. In certain embodiments, a spacer comprises atoms that are part of a ring.

[0461] Solely for the purposes of illustration, and without limiting the above definition, some examples of spacers are provided. Examples of 1 atom spacers include, but are not limited to, the following:

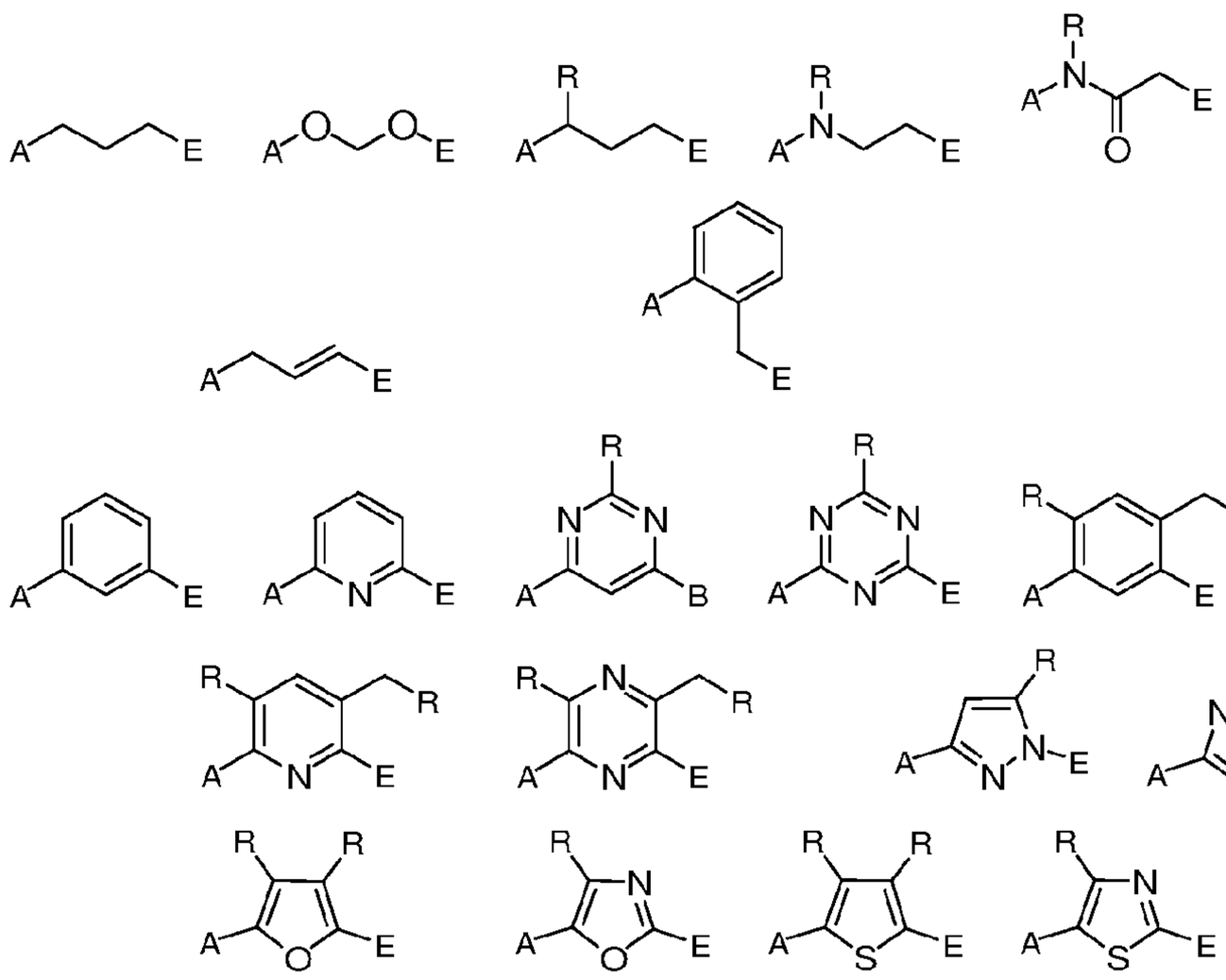


where **A** and **E** represent groups which are separated by the desired number of atoms. Examples of 2 atom spacers include, but are not limited to, the following:

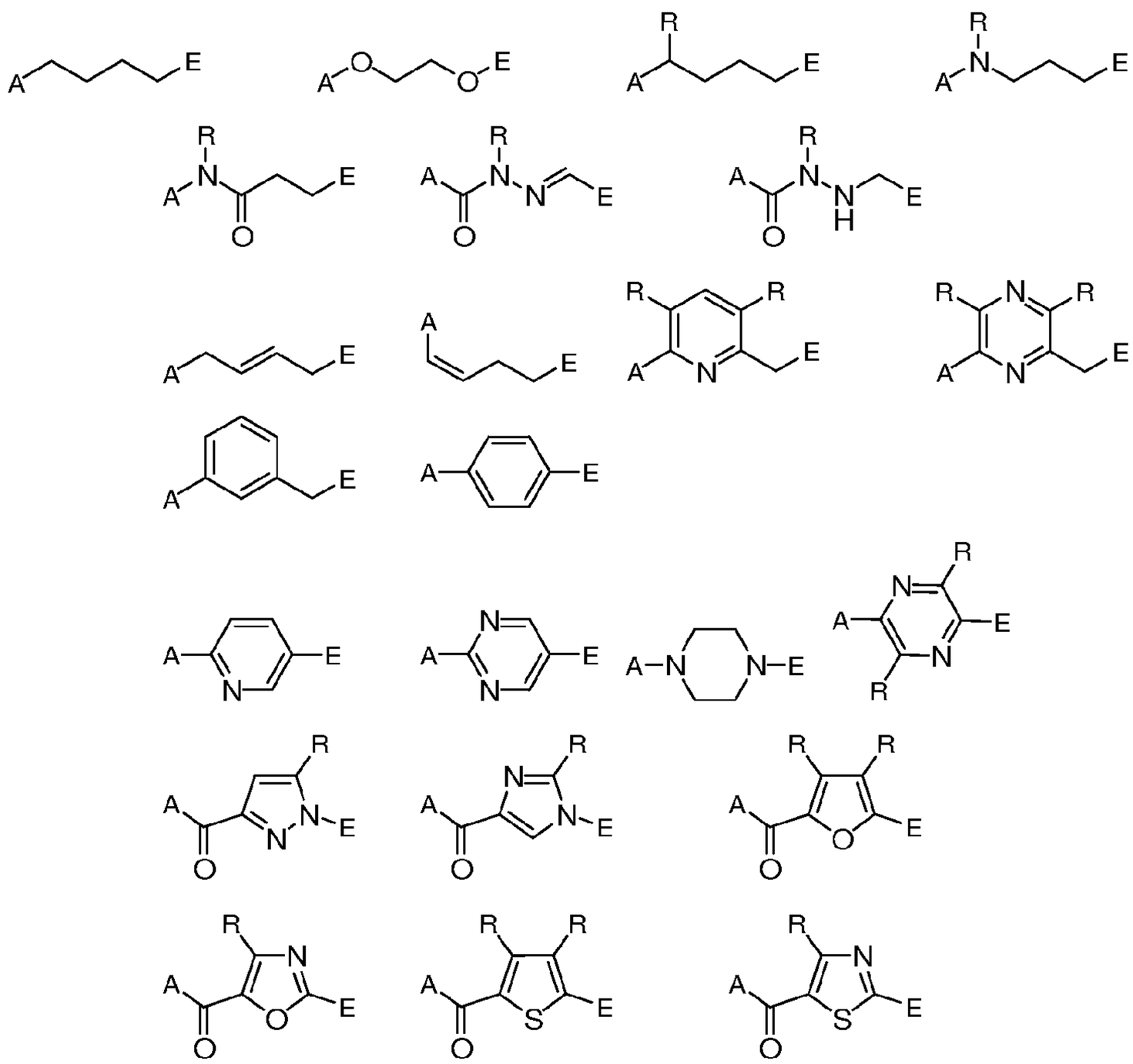


where **A** and **E** represent groups which are separated by the desired number of atoms.

[0462] Examples of 3 atom spacers include, but are not limited to, the following:

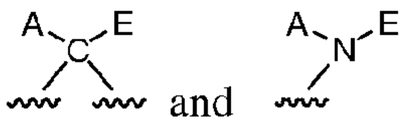


where **A** and **E** represent groups which are separated by the desired number of atoms. Examples of 4 atom spacers include, but are not limited to, the following:

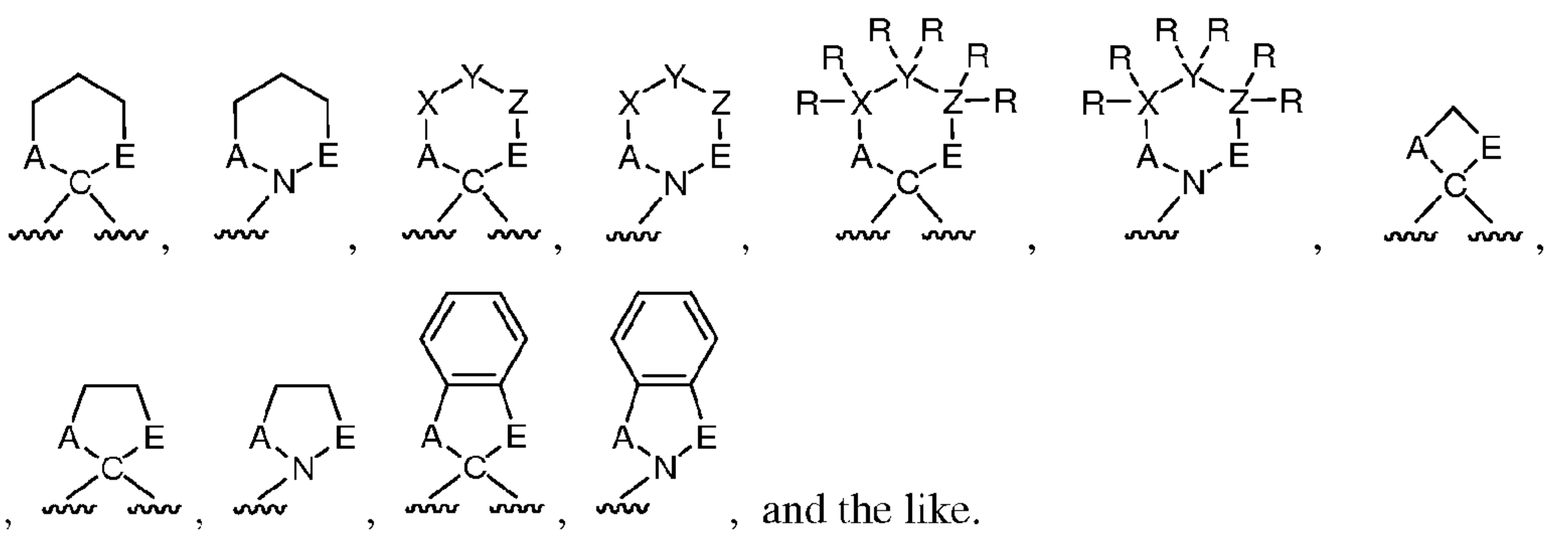


where **A** and **E** represent groups which are separated by the desired number of atoms. As is evident from the above examples, the atoms that create the desired separation may themselves be part of a group. That group may be, for example, an alkyl, heteroalkyl, haloalkyl, heterohaloalkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, non-aromatic heterocycle, or substituted alkyl all of which are optionally substituted. Thus the term "1-5 atom spacer" refers to a spacer that separates two groups by 1, 2, 3, 4, or 5 atoms and does not indicate the total size of the group that constitutes the spacer.

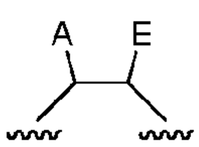
[0463] As used herein, the term "linked to form a ring" refers to instances where two atoms that are bound either to a single atom or to atoms that are themselves ultimately bound, are each bound to a linking group, such that the resulting structure forms a ring. That resulting ring comprises the two atoms that are linked to form a ring, the atom (or atoms) that previously linked those atoms, and the linker. For example, if **A** and **E** below are "linked to form a ring"

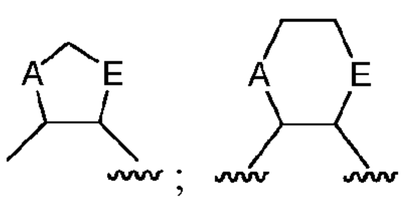
 and

the resulting ring includes **A**, **E**, the C (carbon) or N (nitrogen) to which they are attached, and a linking group. Unless otherwise indicated, that linking group may be of any length and may be optionally substituted. Referring to the above example, resulting structures include, but are not limited to:

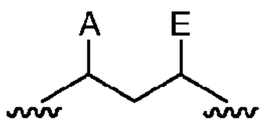


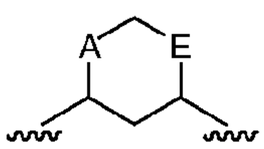
[0464] In certain embodiments, the two substituents that together form a ring are not immediately bound to the same atom. For example, if **A** and **E**, below, are linked to form a ring:

 , the resulting ring comprises **A**, **E**, the two atoms that already link **A** and **E** and a linking group. Examples of resulting structures include, but are not limited to:

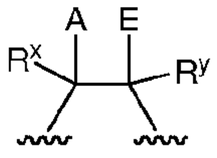
 ; ; and the like.

[0465] In certain embodiments, the atoms that together form a ring are separated by three or more atoms. For example, if **A** and **E**, below, are linked to form a ring:

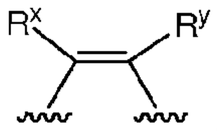
 , the resulting ring comprises **A**, **E**, the 3 atoms that already link **A** and **E**, and a linking group. Examples of resulting structures include, but are not limited to:

 , and the like.

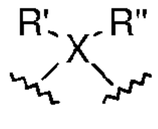
[0466] As used herein, the term "together form a bond" refers to the instance in which two substituents to neighboring atoms are null the bond between the neighboring atoms becomes a double bond. For example, if **A** and **E** below "together form a bond"



the resulting structure is:



.

[0467] The term "null" refers to a group being absent from a structure. For example, in the structure 

, where in certain instances **X** is N (nitrogen), if **X** is N (nitrogen), one of **R'** or **R"** is null, meaning that only three groups are bound to the N (nitrogen).

[0468] The substituent "**R**" appearing by itself and without a number designation refers to a substituent selected from alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and non-aromatic heterocycle (bonded through a ring carbon).

[0469] The term "O-carboxy" refers to the group consisting of formula **R**C(=O)O-

.

[0470] The term "C-carboxy" refers to the group consisting of formula -C(=O)O**R**.

[0471] The term "acetyl" refers to the group consisting of formula -C(=O)CH_3.

[0472] The term "trihalomethanesulfonyl" refers to the group consisting of formula $\mathbf{X}_3$CS(=O)$_2$- where **X** is a halogen.

[0473] The term "cyano" refers to the group consisting of formula -CN.

[0474] The term "isocyanato" refers to the group consisting of formula -NCO.

[0475] The term "thiocyanato" refers to the group consisting of formula -CNS.

[0476] The term "isothiocyanato" refers to the group consisting of formula -NCS.

[0477] The term "sulfonyl" refers to the group consisting of formula -S(=O)-**R**.

[0478] The term "S-sulfonamido" refers to the group consisting of formula -S(=O)$_2$N**R**.

[0479] The term "N-sulfonamido" refers to the group consisting of formula **R**S(=O)$_2$NH-.

[0480] The term "trihalomethanesulfonamido" refers to the group consisting of formula $X_3CS(=O)_2N\mathbf{R}$-.

[0481] The term "O-carbamyl" refers to the group consisting of formula -OC(=O)-N**R**.

[0482] The term "N-carbamyl" refers to the group consisting of formula **R**OC(=O)NH-.

[0483] The term "O-thiocarbamyl" refers to the group consisting of formula -OC(=S)-N**R**.

[0484] The term "N-thiocarbamyl" refers to the group consisting of formula **R**OC(=S)NH-.

[0485] The term "C-amido" refers to the group consisting of formula $-C(=O)-N\mathbf{R}_2$.

[0486] The term "N-amido" refers to the group consisting of formula **R**C(=O)NH-.

[0487] The term "oxo" refers to the group consisting of formula =O.

[0488] The term "keto" and "carbonyl" used herein refers to C=O.

[0489] The term "thiocarbonyl" used herein refers to C=S.

[0490] The term "ester" refers to a chemical moiety with formula $-(\mathbf{R})_n$-C(=O)O**R'**, where **R** and **R'** are independently selected from alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and non-aromatic heterocycle (bonded through a ring carbon), where **n** is 0 or 1.

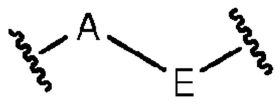
[0491] The term "amide" refers to a chemical moiety with formula $-(\mathbf{R})_n$-C(=O)NHR' or $-(\mathbf{R})_n$-NHC(=O)**R'**, where **R** is selected from alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and heteroalicyclic (bonded through a ring carbon), where **n** is 0 or 1 and **R'** is selected from hydrogen, alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and heteroalicyclic (bonded through a ring carbon), where **n** is 0 or 1. In certain embodiments, an amide may be an amino acid or a peptide.

[0492] The term "amino" refers to a chemical moiety with formula –NH**R'R''**, where **R'** and **R''** are each independently selected from hydrogen, alkyl, cycloalkyl, aryl, heteroaryl (bonded through a ring carbon) and heteroalicyclic (bonded through a ring carbon).

[0493] The terms "amine," "hydroxy," and "carboxyl" include such groups that have been esterified or amidified. Procedures and specific groups used to achieve esterification and amidification are known to those of skill in the art and can readily be found in reference sources such as Greene and Wuts, Protective Groups in Organic Synthesis, 3rd Ed., John Wiley & Sons, New York, NY, 1999, which is incorporated herein in its entirety.

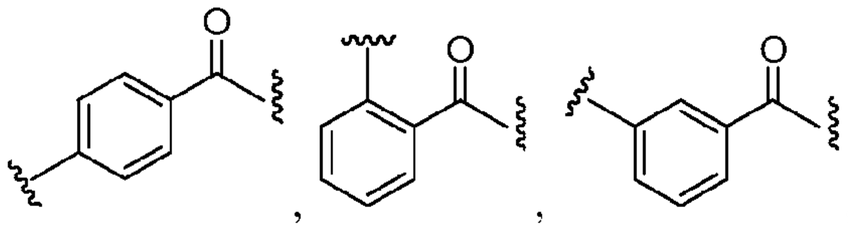
[0494] Unless otherwise indicated, the term "optionally substituted," refers to a group in which none, one, or more than one of the hydrogen atoms has been replaced with one or more group(s) individually and independently selected from: alkyl, alkenyl, cycloalkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, aryl, arylalkyl, alkenylO–, arylalkylO–, arylalkylNH–, alkenylO–, cycloalkylC(=O)–, arylC(=O)–, arylC(=O)NH–, arylNHC(=O)–, aryl$(CH_2)_{0-3}O(CH_2)_{0-3}$–, HO$(CH_2)_{1-3}$NH–, HO$(CH_2)_{1-3}$O–, HO$(CH_2)_{1-3}$–, HO$(CH_2)_{1-3}O(CH_2)_{1-3}$–, –C(=O)$NHNH_2$, heteroaryl, heterocycle, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, cyano, halo, carbonyl, oxo, thiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, C-carboxy, O-carboxy, isocyanato, thiocyanato, isothiocyanato, nitro, silyl, trihalomethanesulfonyl, and amino, including mono- and di-substituted amino groups, and the protected derivatives of amino groups. Such protective derivatives (and protecting groups that may form such protective derivatives) are known to those of skill in the art and may be found in references such as Greene and Wuts, above. When the group contains a nitrogen, or a sulfur, an oxo as a substituent also includes oxides, for example pyridine-N-oxide, thiopyran sulfoxide and thiopyran-S,S-dioxide. In embodiments in which two or more hydrogen atoms have been substituted, the substituent groups may together form a ring.

[0495] The term "stereoisomers" as used herein means isomers that possess identical constitution, but which differ in the arrangement of their atoms in space. Including, for example, all enantiomers, diastereomers, geometric isomers, and atropisomers.

[0496] Whereever a substituent as depicted as a di-radical (i.e., has two points of attachment to the rest of the molecule), it is to be understood that the substituent can be attached in any directional configuration unless otherwise indicated. Thus, for example, a substituent depicted as –AE– or 

includes the substituent being oriented such that the A is attached at the leftmost attachment point of the molecule as well as attached at the rightmost attachment point of the molecule.

[0497] It is to be understood that certain radical naming conventions can include either a mono-radical or a di-radical, depending on the context. For example, where a substituent requires two points of attachment to the rest of the molecule, it is understood that the substituent is a di-radical. A substituent identified as alkyl, that requires two points of attachment, includes di-radicals such as $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH(CH_3)CH_2-$, and the like; a substituent depicted as alkoxy that requires two points of attachment, includes di-radicals such as $-OCH_2-$, $-OCH_2CH_2-$, $-OCH_2CH(CH_3)CH_2-$, and the like: and a substituent depicted as arylC(=O)– that requires two points of attachment, includes di-radicals such as



, and the like.

[0498] Throughout the specification, groups and substituents thereof can be chosen by one skilled in the field to provide stable moieties and compounds.

[0499] The term "carrier" refers to a compound that facilitates the incorporation of another compound into cells or tissues. For example, dimethyl sulfoxide (DMSO) is a commonly used carrier for improving incorporation of certain organic compounds into cells or tissues.

[0500] The term "pharmaceutical agent" refers to a chemical compound or composition capable of inducing a desired therapeutic effect in a patient. In certain embodiments, a pharmaceutical agent comprises an active agent, which is the agent that induces the desired therapeutic effect. In certain embodiments, a pharmaceutical agent comprises a prodrug. In certain embodiments, a pharmaceutical agent comprises inactive ingredients such as carriers, excipients, and the like.

[0501] The term "therapeutically effective amount" refers to an amount of a pharmaceutical agent sufficient to achieve a desired therapeutic effect.

[0502] The term "prodrug" refers to an pharmaceutical agent that is converted from a less active form into a corresponding more active form *in vivo*.

[0503] The term "pharmaceutically acceptable" refers to a formulation of a compound that does not significantly abrogate the biological activity, a pharmacological activity and/or other properties of the compound when the formulated compound is administered to a patient. In certain embodiments, a pharmaceutically acceptable formulation does not cause significant irritation to a patient.

[0504] The term "co-administer" refers to administering more than one pharmaceutical agent to a patient. In certain embodiments, co-administered pharmaceutical agents are administered together in a single dosage unit. In certain embodiments, co-administered pharmaceutical agents are administered separately. In certain embodiments, co-administered pharmaceutical agents are administered at the same time. In certain embodiments, co-administered pharmaceutical agents are administered at different times.

[0505] The term "patient" includes human and animal subjects.

[0506] The term "substantially pure" means an object species (*e.g.*, compound) is the predominant species present (i.e., on a molar basis it is more abundant than any other individual species in the composition). In certain embodiments, a substantially purified fraction is a composition wherein the object species comprises at least about 50 percent (on a molar basis) of all species present. In certain embodiments, a substantially pure composition will comprise more than about 80%, 85%, 90%, 95%, or 99% of all species present in the composition. In certain embodiments, the object species is purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of a single species.

[0507] The term "tissue-selective" refers to the ability of a compound to modulate a biological activity in one tissue to a greater or lesser degree than it modulates a biological activity in another tissue. The biological activities in the different tissues may be the same or they may be different. The biological activities in the different tissues may be mediated by the same type of target receptor. For example, in certain embodiments, a tissue-selective compound may modulate receptor mediated biological activity in one tissue and fail to modulate, or modulate to a lesser degree, receptor mediated biological activity in another tissue type.

[0508] The term "monitoring" refers to observing an effect or absence of any effect. In certain embodiments, one monitors cells after contacting those cells with a compound of the present embodiments. Examples of effects that may be monitored include, but are not limited to, changes in cell phenotype, cell proliferation, receptor activity, or the interaction between a receptor and a compound known to bind to the receptor.

[0509] The term "cell phenotype" refers to physical or biological characteristics. Examples of characteristics that constitute phenotype included, but are not limited to, cell size, cell proliferation, cell differentiation, cell survival, apoptosis (cell death), or the

utilization of a metabolic nutrient (*e.g.*, glucose uptake). Certain changes or the absence of changes in cell phenotype are readily monitored using techniques known in the art.

[0510] The term "cell proliferation" refers to the rate at which cells divide. In certain embodiments, cells are *in situ* in an organism. In certain embodiments, cell are grown *in vitro* in a vessel. The number of cells growing in a vessel can be quantified by a person skilled in the art (*e.g.*, by counting cells in a defined area using a microscope or by using laboratory apparatus that measure the density of cells in an appropriate medium). One skilled in that art can calculate cell proliferation by determining the number of cells at two or more times.

[0511] The term "contacting" refers to bringing two or more materials into close enough proximity that they may interact. In certain embodiments, contacting can be accomplished in a vessel such as a test tube, a petri dish, or the like. In certain embodiments, contacting may be performed in the presence of additional materials. In certain embodiments, contacting may be performed in the presence of cells. In certain of such embodiments, one or more of the materials that are being contacted may be inside a cell. Cells may be alive or may dead. Cells may or may not be intact.

Certain compounds

[0512] Certain compounds that modulate one or more HGF activity and/or bind to HGF receptors play a role in health. In certain embodiments, compounds are useful for treating any of a variety of diseases or conditions.

[0513] Certain embodiments provide selective HGF modulators. Certain embodiments provide selective HGF receptor binding agents. Certain embodiments provide methods of making and methods of using selective HGF modulators and/or selective HGF receptor binding agents. In certain embodiments, selective HGF modulators are agonists, partial agonists, and/or antagonists for the HGF receptor.

[0514] The compounds disclosed herein can be used alone or in combination with other agents, for example, to modulate hematopoiesis, erythropoiesis, granulopoiesis, thrombopoiesis, and myelopoiesis. The instant compounds can also be used alone or in combination with other agents in treatment or prevention of a disease or condition caused by abnormal function of hematopoiesis, erythropoiesis, granulopoiesis, thrombopoiesis, and myelopoiesis. Some non-limiting examples of diseases include anemia, neutropenia,

thrombocytopenia, cardiovascular disorders, immune/autoimmune disorders, cancers, infectious disorders or diseases, and neurologic disorders.

[0515] One of skill in the art will recognize that analogous synthesis schemes may be used to synthesize similar compounds. One of skill will recognize that compounds of the present embodiments may be synthesized using other synthesis schemes. In certain embodiments, a salt corresponding to any of the compounds provided herein is provided.

[0516] In certain embodiments, a salt corresponding to a selective HGF modulator is provided. In certain embodiments, a salt corresponding to a selective HGF receptor binding agent is provided. In certain embodiments, a salt is obtained by reacting a compound with an acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. In certain embodiments, a salt is obtained by reacting a compound with a base to form a salt such as an ammonium salt, an alkali metal salt, such as a sodium or a potassium salt, an alkaline earth metal salt, such as a calcium or a magnesium salt, a salt of organic bases such as choline, dicyclohexylamine, N-methyl-D-glucamine, tris(hydroxymethyl)methylamine, 4-(2-hydroxyethyl)-morpholine, 1-(2-hydroxyethyl)-pyrrolidine, ethanolamine and salts with amino acids such as arginine, lysine, and the like. In certain embodiments, a salt is obtained by reacting a free acid form of a selective HGF modulator or selective HGF binding agent with multiple molar equivalents of a base, such as bis-sodium, bis-ethanolamine, and the like.

[0517] In certain embodiments, a salt corresponding to a compound of the present embodiments is selected from acetate, ammonium, benzenesulfonate, benzoate, bicarbonate, bisulfate, bitartrate, borate, bromide, calcium edetate, camsylate, carbonate, chloride, cholinate, clavulanate, citrate, dihydrochloride, diphosphate, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycollylarsanilate, hexylresorcinate, hydrabanine, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isethionate, lactate, lactobionate, laurate, magnesium, malate, maleate, mandelate, mucate, napsylate, nitrate, N-methylglucamine, oxalate, pamoate (embonate), palmitate, pantothenate, phosphate, polygalacturonate, potassium, salicylate, sodium, stearate, subaceatate, succinate, sulfate, tannate, tartrate, teoclate, tosylate, triethiodide, tromethamine, trimethylammonium, and valerate salts.

[0518] In certain embodiments, one or more carbon atoms of a compound of the present embodiments are replaced with silicon. *See e.g.,* WO 03/037905 Al ; Tacke and Zilch, Endeavour, New Series, 10, 191-197 (1986); Bains and Tacke, Curr. Opin. Drug Discov Devel. Jul:6(4):526-43(2003). In certain embodiments, compounds comprising one or more silicon atoms possess certain desired properties, including, but not limited to, greater stability and/or longer half-life in a patient, when compared to the same compound in which none of the carbon atoms have been replaced with a silicon atom.

Certain Assays

[0519] In certain embodiments, assays may be used to determine the level of HGF modulating activity of the compounds of the present embodiments.

Proliferation Assay

[0520] In some embodiments, compounds are tested in an in vitro proliferation assay using the cell lines that express EPO, GCSF or other cytokine receptors that may be dependent upon these cytokines for their growth.

Luciferase Assay

[0521] In some embodiments, compounds are tested in a reporter assay using the cell lines that express EPO, GCSF or other cytokine receptors. These cells are transfected with the STAT responsive reporter (such as luciferase) and the activity of the compounds is determined by a reporter assay.

Differentiation Assay

[0522] In some embodiments, compounds are tested in purified human CD34+ progenitor cells. After addition of the compounds to the cells, the number of cells expressing markers of hematopoiesis, erythropoiesis, granulopoiesis, thrombopoiesis, or myelopoiesis is measured by flow cytometry or by analyzing expression of genes associated with these pathways.

Certain Pharmaceutical Agents

[0523] In certain embodiments, at least one selective HGF modulator, or pharmaceutically acceptable salt, ester, amide, and/or prodrug thereof, either alone or combined with one or more pharmaceutically acceptable carriers, forms a pharmaceutical agent. Techniques for formulation and administration of compounds of the present embodiments may be found for example, in "Remington's Pharmaceutical Sciences," Mack

Publishing Co., Easton, PA, 18th edition, 1990.

[0524] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is prepared using known techniques, including, but not limited to mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or tabletting processes.

[0525] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is a liquid (*e.g.*, a suspension, elixir and/or solution). In certain of such embodiments, a liquid pharmaceutical agent comprising one or more compounds of the present embodiments is prepared using ingredients known in the art, including, but not limited to, water, glycols, oils, alcohols, flavoring agents, preservatives, and coloring agents.

[0526] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is a solid (*e.g.* , a powder, tablet, and/or capsule). In certain of such embodiments, a solid pharmaceutical agent comprising one or more compounds of the present embodiments is prepared using ingredients known in the art, including, but not limited to, starches, sugars, diluents, granulating agents, lubricants, binders, and disintegrating agents.

[0527] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is formulated as a depot preparation. Certain such depot preparations are typically longer acting than non-depot preparations. In certain embodiments, such preparations are administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. In certain embodiments, depot preparations are prepared using suitable polymeric or hydrophobic materials (for example an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[0528] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments comprises a delivery system. Examples of delivery systems include, but are not limited to, liposomes and emulsions. Certain delivery systems are useful for preparing certain pharmaceutical agents including those comprising hydrophobic compounds. In certain embodiments, certain organic solvents such as dimethylsulfoxide are used.

[0529] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments comprises one or more tissue-specific delivery molecules designed to deliver the pharmaceutical agent to specific tissues or cell types. For example, in certain embodiments, pharmaceutical agents include liposomes coated with a tissue-specific antibody.

[0530] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments comprises a co-solvent system. Certain of such co-solvent systems comprise, for example, benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. In certain embodiments, such co-solvent systems are used for hydrophobic compounds. A non-limiting example of such a co-solvent system is the VPD co-solvent system, which is a solution of absolute ethanol comprising 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant Polysorbate 80™ , and 65% w/v polyethylene glycol 300. The proportions of such co-solvent systems may be varied considerably without significantly altering their solubility and toxicity characteristics. Furthermore, the identity of co-solvent components may be varied: for example, other surfactants may be used instead of Polysorbate 80™; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.*, polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose.

[0531] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments comprises a sustained-release system. A non-limiting example of such a sustained-release system is a semi-permeable matrix of solid hydrophobic polymers. In certain embodiments, sustained-release systems may, depending on their chemical nature, release compounds over a period of hours, days, weeks or months.

[0532] Certain compounds used in pharmaceutical agent of the present embodiments may be provided as pharmaceutically acceptable salts with pharmaceutically compatible counterions. Pharmaceutically compatible salts may be formed with many acids, including but not limited to hydrochloric, sulfuric, acetic, lactic, tartaric, malic, succinic, *etc.*

[0533] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments comprises an active ingredient in a therapeutically effective amount. In certain embodiments, the therapeutically effective amount is sufficient to prevent, alleviate or ameliorate symptoms of a disease or to prolong the survival of the

subject being treated. Determination of a therapeutically effective amount is well within the capability of those skilled in the art.

[0534] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is formulated as a prodrug. In certain embodiments, prodrugs are useful because they are easier to administer than the corresponding active form. For example, in certain instances, a prodrug may be more bioavailable (*e.g.*, through oral administration) than is the corresponding active form. In certain instances, a prodrug may have improved solubility compared to the corresponding active form. In certain embodiments, a prodrug is an ester. In certain embodiments, such prodrugs are less water soluble than the corresponding active form. In certain instances, such prodrugs possess superior transmittal across cell membranes, where water solubility is detrimental to mobility. In certain embodiments, the ester in such prodrugs is metabolically hydrolyzed to carboxylic acid. In certain instances the carboxylic acid containing compound is the corresponding active form. In certain embodiments, a prodrug comprises a short peptide (polyaminoacid) bound to an acid group. In certain of such embodiments, the peptide is metabolized to form the corresponding active form.

[0535] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is useful for treating a conditions or disorder in a mammalian, and particularly in a human patient. Suitable administration routes include, but are not limited to, oral, rectal, transmucosal, intestinal, enteral, topical, suppository, through inhalation, intrathecal, intraventricular, intraperitoneal, intranasal, intraocular and parenteral (*e.g.*, intravenous, intramuscular, intramedullary, and subcutaneous). In certain embodiments, pharmaceutical intrathecals are administered to achieve local rather than systemic exposures. For example, pharmaceutical agents may be injected directly in the area of desired effect (*e.g.*, in the renal or cardiac area).

[0536] In certain embodiments, a pharmaceutical agent comprising one or more compounds of the present embodiments is administered in the form of a dosage unit (*e.g.*, tablet, capsule, bolus, etc.). In certain embodiments, such dosage units comprise a selective HGF modulator in a dose from about 1 μg/kg of body weight to about 50 mg/kg of body weight. In certain embodiments, such dosage units comprise a selective HGF modulator in a dose from about 2 μg/kg of body weight to about 25 mg/kg of body weight. In certain embodiments, such dosage units comprise a selective HGF modulator in a dose from about

10 μg/kg of body weight to about 5 mg/kg of body weight. In certain embodiments, pharmaceutical agents are administered as needed, once per day, twice per day, three times per day, or four or more times per day. It is recognized by those skilled in the art that the particular dose, frequency, and duration of administration depends on a number of factors, including, without limitation, the biological activity desired, the condition of the patient, and tolerance for the pharmaceutical agent.

[0537] In certain embodiments, a pharmaceutical agent comprising a compound of the present embodiments is prepared for oral administration. In certain of such embodiments, a pharmaceutical agent is formulated by combining one or more compounds of the present embodiments with one or more pharmaceutically acceptable carriers. Certain of such carriers enable compounds of the present embodiments to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient. In certain embodiments, pharmaceutical agents for oral use are obtained by mixing one or more compounds of the present embodiments and one or more solid excipient. Suitable excipients include, but are not limited to, fillers, such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). In certain embodiments, such a mixture is optionally ground and auxiliaries are optionally added. In certain embodiments, pharmaceutical agents are formed to obtain tablets or dragee cores. In certain embodiments, disintegrating agents (*e.g.*, cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof, such as sodium alginate) are added.

[0538] In certain embodiments, dragee cores are provided with coatings. In certain of such embodiments, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to tablets or dragee coatings.

[0539] In certain embodiments, pharmaceutical agents for oral administration are push-fit capsules made of gelatin. Certain of such push-fit capsules comprise one or more compounds of the present embodiments in admixture with one or more filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally,

stabilizers. In certain embodiments, pharmaceutical agents for oral administration are soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. In certain soft capsules, one or more compounds of the present embodiments are be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

[0540] In certain embodiments, pharmaceutical agents are prepared for buccal administration. Certain of such pharmaceutical agents are tablets or lozenges formulated in conventional manner.

[0541] In certain embodiments, a pharmaceutical agent is prepared for administration by injection (*e.g.*, intravenous, subcutaneous, intramuscular, etc.). In certain of such embodiments, a pharmaceutical agent comprises a carrier and is formulated in aqueous solution, such as water or physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. In certain embodiments, other ingredients are included (*e.g.*, ingredients that aid in solubility or serve as preservatives). In certain embodiments, injectable suspensions are prepared using appropriate liquid carriers, suspending agents and the like. Certain pharmaceutical agents for injection are presented in unit dosage form, *e.g.*, in ampoules or in multi-dose containers. Certain pharmaceutical agents for injection are suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Certain solvents suitable for use in pharmaceutical agents for injection include, but are not limited to, lipophilic solvents and fatty oils, such as sesame oil, synthetic fatty acid esters, such as ethyl oleate or triglycerides, and liposomes. Aqueous injection suspensions may contain substances that increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, such suspensions may also contain suitable stabilizers or agents that increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

[0542] In certain embodiments, a pharmaceutical agent is prepared for transmucosal administration. In certain of such embodiments penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

[0543] In certain embodiments, a pharmaceutical agent is prepared for administration by inhalation. Certain of such pharmaceutical agents for inhalation are

prepared in the form of an aerosol spray in a pressurized pack or a nebulizer. Certain of such pharmaceutical agents comprise a propellant, *e.g.* , dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In certain embodiments using a pressurized aerosol, the dosage unit may be determined with a valve that delivers a metered amount. In certain embodiments, capsules and cartridges for use in an inhaler or insufflator may be formulated. Certain of such formulations comprise a powder mixture of a compound of the present embodiments and a suitable powder base such as lactose or starch.

[0544] In certain embodiments, a pharmaceutical agent is prepared for rectal administration, such as a suppositories or retention enema. Certain of such pharmaceutical agents comprise known ingredients, such as cocoa butter and/or other glycerides.

[0545] In certain embodiments, a pharmaceutical agent is prepared for topical administration. Certain of such pharmaceutical agents comprise bland moisturizing bases, such as ointments or creams. Exemplary suitable ointment bases include, but are not limited to, petrolatum, petrolatum plus volatile silicones, lanolin and water in oil emulsions such as Eucerin™, available from Beiersdorf (Cincinnati, Ohio). Exemplary suitable cream bases include, but are not limited to, Nivea™ Cream, available from Beiersdorf (Cincinnati, Ohio), cold cream (USP), Purpose Cream™, available from Johnson & Johnson (New Brunswick, New Jersey), hydrophilic ointment (USP) and Lubriderm™, available from Pfizer (Morris Plains, New Jersey).

[0546] In certain embodiments, the formulation, route of administration and dosage for a pharmaceutical agent of the present embodiments can be chosen in view of a particular patient's condition. (*See e.g.* , Fingl et al. 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p. 1). In certain embodiments, a pharmaceutical agent is administered as a single dose. In certain embodiments, a pharmaceutical agent is administered as a series of two or more doses administered over one or more days.

[0547] In certain embodiments, a pharmaceutical agent of the present embodiments is administered to a patient between about 0.1% and 500%, 5% and 200%, 10% and 100%, 15% and 85%, 25% and 75%, or 40% and 60% of an established human dosage. Where no human dosage is established, a suitable human dosage may be inferred from ED_{50} or ID_{50} values, or other appropriate values derived from *in vitro* or *in vivo* studies.

[0548] In certain embodiments, a daily dosage regimen for a patient comprises an oral dose of between 0.1 mg and 2000 mg, 5 mg and 1500 mg, 10 mg and 1000 mg, 20 mg and 500 mg, 30 mg and 200 mg, or 40 mg and 100 mg of a compound of the present embodiments. In certain embodiments, a daily dosage regimen is administered as a single daily dose. In certain embodiments, a daily dosage regimen is administered as two, three, four, or more than four doses.

[0549] In certain embodiments, a pharmaceutical agent of the present embodiments is administered by continuous intravenous infusion. In certain of such embodiments, from 0.1 mg to 500 mg of a composition of the present embodiments is administered per day.

[0550] In certain embodiments, a pharmaceutical agent of the present embodiments is administered for a period of continuous therapy. For example, a pharmaceutical agent of the present embodiments may be administered over a period of days, weeks, months, or years.

[0551] Dosage amount, interval between doses, and duration of treatment may be adjusted to achieve a desired effect. In certain embodiments, dosage amount and interval between doses are adjusted to maintain a desired concentration on compound in a patient. For example, in certain embodiments, dosage amount and interval between doses are adjusted to provide plasma concentration of a compound of the present embodiments at an amount sufficient to achieve a desired effect. In certain of such embodiments the plasma concentration is maintained above the minimal effective concentration (MEC). In certain embodiments, pharmaceutical agents of the present embodiments are administered with a dosage regimen designed to maintain a concentration above the MEC for 10-90% of the time, between 30-90% of the time, or between 50-90% of the time.

[0552] In certain embodiments in which a pharmaceutical agent is administered locally, the dosage regimen is adjusted to achieve a desired local concentration of a compound of the present embodiments.

[0553] In certain embodiments, a pharmaceutical agent may be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may for example comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. The pack or dispenser may also be accompanied with a notice associated with the container

in form prescribed by a governmental agency regulating the manufacture, use, or sale of pharmaceuticals, which notice is reflective of approval by the agency of the form of the drug for human or veterinary administration. Such notice, for example, may be the labeling approved by the U.S. Food and Drug Administration for prescription drugs, or the approved product insert. Compositions comprising a compound of the present embodiments formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

[0554] In certain embodiments, a pharmaceutical agent is in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

Certain Combination Therapies

[0555] In certain embodiments, one or more pharmaceutical agents of the present embodiments are co-administered with one or more other pharmaceutical agents. In certain embodiments, such one or more other pharmaceutical agents are designed to treat the same disease or condition as the one or more pharmaceutical agents of the present embodiments. In certain embodiments, such one or more other pharmaceutical agents are designed to treat a different disease or condition as the one or more pharmaceutical agents of the present embodiments. In certain embodiments, such one or more other pharmaceutical agents are designed to treat an undesired effect of one or more pharmaceutical agents of the present embodiments. In certain embodiments, one or more pharmaceutical agents of the present embodiments are co-administered with another pharmaceutical agent to treat an undesired effect of that other pharmaceutical agent. In certain embodiments, one or more pharmaceutical agents of the present embodiments and one or more other pharmaceutical agents are administered at the same time. In certain embodiments, one or more pharmaceutical agents of the present embodiments and one or more other pharmaceutical agents are administered at the different times. In certain embodiments, one or more pharmaceutical agents of the present embodiments and one or more other pharmaceutical agents are prepared together in a single formulation. In certain embodiments, one or more pharmaceutical agents of the present embodiments and one or more other pharmaceutical agents are prepared separately.

[0556] Examples of pharmaceutical agents that may be co-administered with a pharmaceutical agent of the present embodiments include, but are not limited to, anti-cancer treatments, including, but not limited to, chemotherapy and radiation treatment;

corticosteroids, including but not limited to prednisone; immunoglobulins, including, but not limited to intravenous immunoglobulin (IVIg); analgesics (*e.g.*, acetaminophen); antiinflammatory agents, including, but not limited to non-steroidal anti-inflammatory drugs (*e.g.* , ibuprofen, COX-1 inhibitors, and COX-2, inhibitors); salicylates; antibiotics; antivirals; antifungal agents; antidiabetic agents (*e.g.*, biguanides, glucosidase inhibitors, insulins, sulfonylureas, and thiazolidenediones); adrenergic modifiers; diuretics; hormones (*e.g.* , anabolic steroids, androgen, estrogen, calcitonin, progestin, somatostan, and thyroid hormones); immunomodulators; muscle relaxants; antihistamines; osteoporosis agents (*e.g.*, biphosphonates, calcitonin, and estrogens); prostaglandins, antineoplastic agents; psychotherapeutic agents; sedatives; poison oak or poison sumac products; antibodies; and vaccines.

Certain Indications

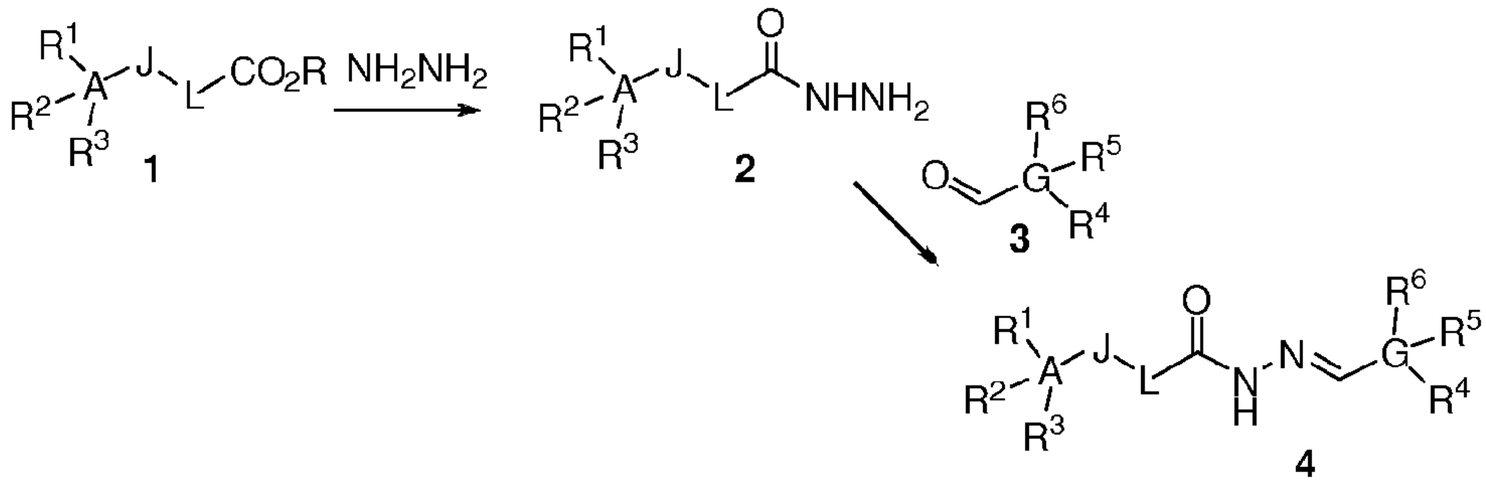
[0557] In certain embodiments, provided are methods of treating a patient comprising administering one or more compounds of the present embodiments. In certain embodiments, such patient suffers from thrombocytopenia. In certain such embodiments, thrombocytopenia results from chemotherapy and/or radiation treatment. In certain embodiments, thrombocytopenia results bone marrow failure resulting from bone marrow transplantation and/or aplastic anemia. In certain embodiments thrombocytopenia is idiopathic. In certain embodiments, one or more compounds of the present embodiments are administered to a patient to in conjunction with harvesting peripheral blood progenitor cells and/or in conjunction with platelet apheresis. Such administration may be done before, during, and/or after such harvesting.

[0558] In certain embodiments, one or more compounds of the present embodiments are administered to a patient who suffers from a condition affecting the nervous system, including, but are not limited to, diseases affecting the nervous system and injuries to the nervous system. Such diseases, include, but not limited to, amyotrophic lateral sclerosis, multiple sclerosis, and muscular dystrophy. Injury to the nervous system include, but are not limited to spinal cord injury or peripheral nerve damage, including, but not limited to, injury resulting from trauma or from stroke. In certain embodiments, one or more compounds of the present embodiments are used to promote growth and/or development of glial cells. Such glial cells may repair nerve cells. In certain embodiments, compounds of the present

embodiments are used to treat psychological disorders, including, but not limited to, cognitive disorders.

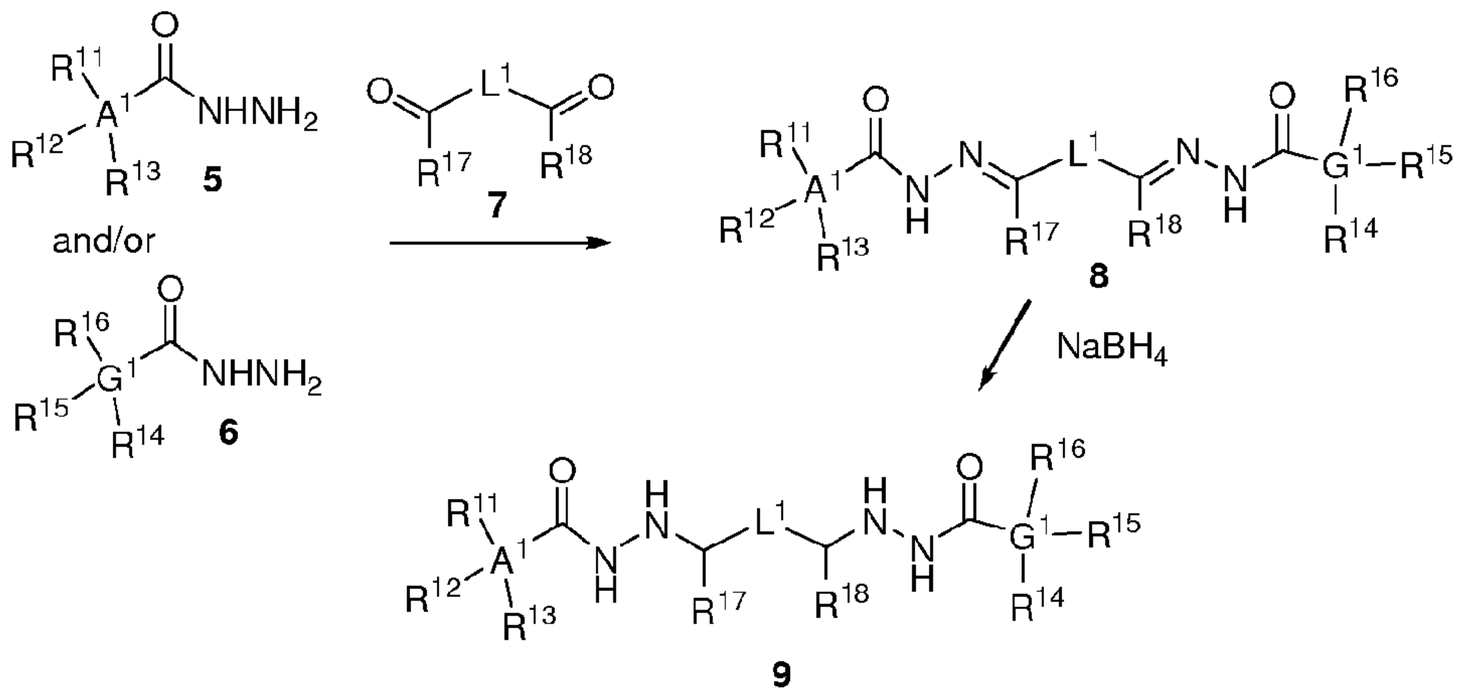
Certain Synthesis Methods

Scheme I



[0559] The process of Scheme **I** describes the general synthesis of compounds of general structure **4** described in Formula **I**, wherein **R** can be C_{1-6} alkyl, aryl and the like. Treatment of the ester derivatives of general structure **1** with hydrazine affords hydrazide derivatives of general structure **2**. The intermediates of general structure **2** are condensed with an aldehyde of general structure **3** to generate the compounds of general structure **4**.

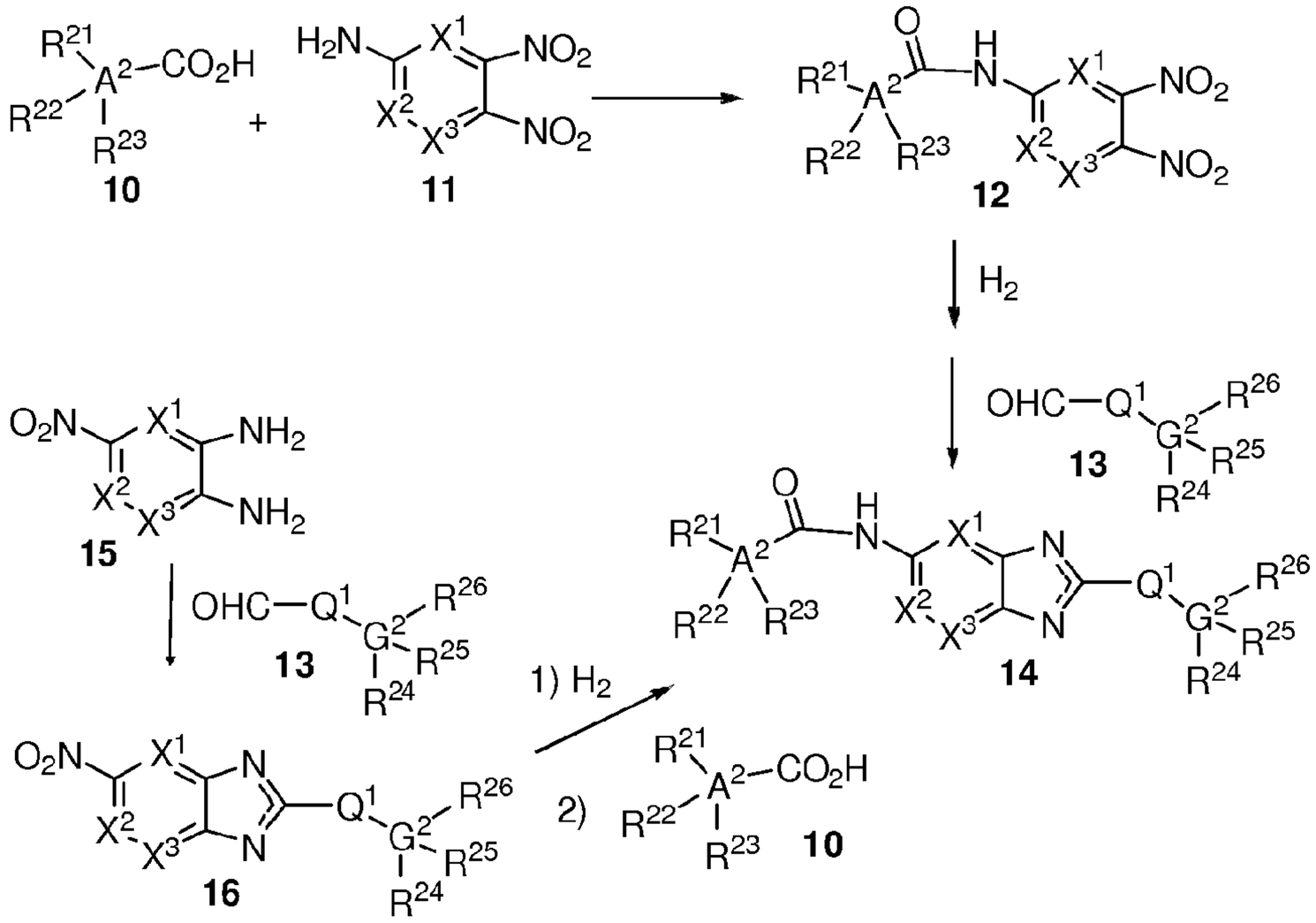
Scheme II



[0560] The process of Scheme **II** describes general synthesis of the compounds of Formula **II**. Condensation reactions of the biscarbonyl compounds of general structure **7** and substituted hydrazides of general structures **5** or **6** under standard conditions provide the pseudo-symmetric compounds of structure **8**. Alternatively, when the hydrazides of general structures **5** and **6** are different, the condensation reactions can be run sequentially to provide

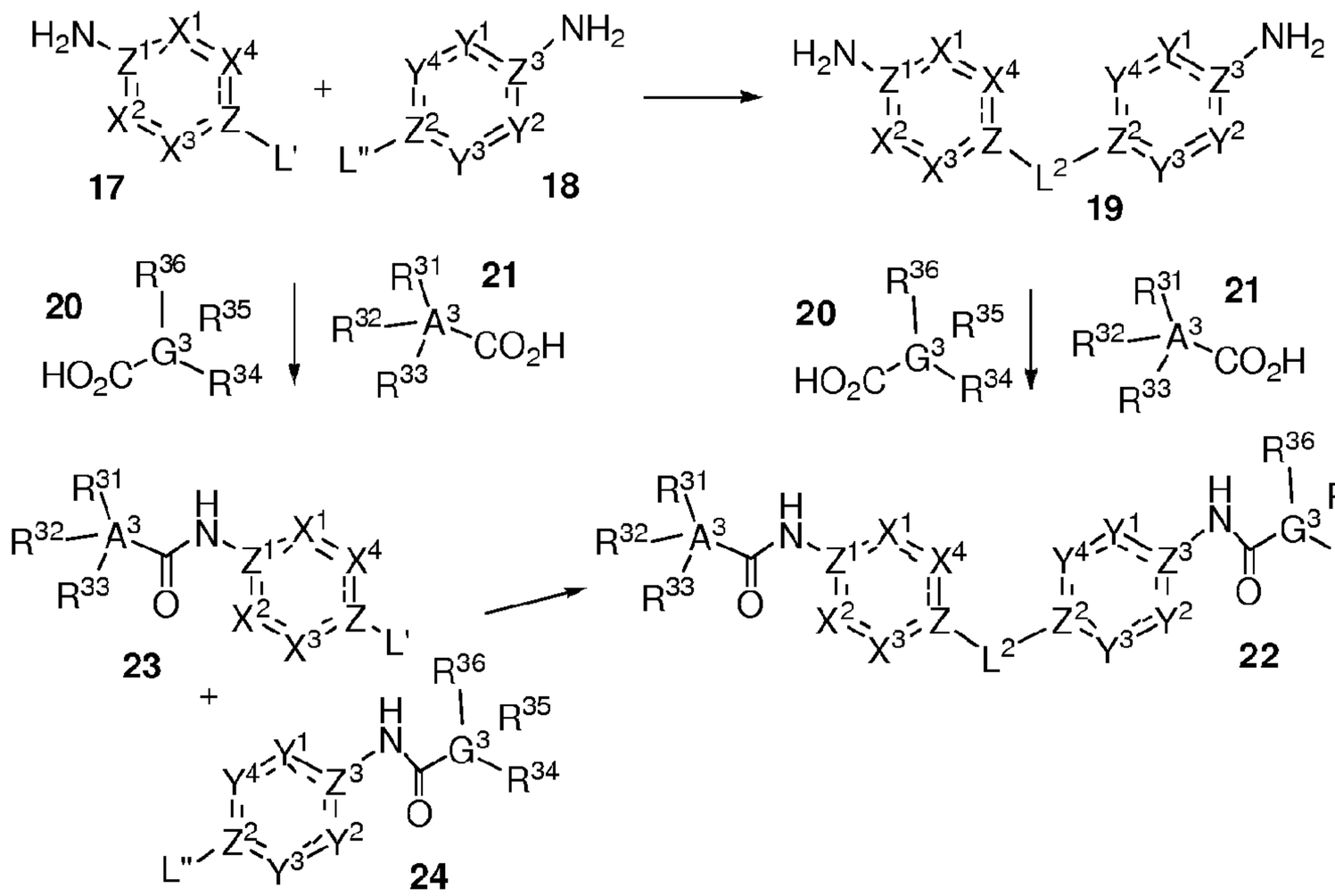
compounds of general structure **8**. Compounds of general structure **9** can be obtained by a standard reduction of compounds of general structure **8**. For example, reducing agents such sodium borohydride, lithium borohydride, sodium cyanoborohydride, potassium trisiamylborohydride, potassium tri-sec-butylborohydride, lithium trisiamylborohydride, lithium tri-sec-butylborohydride, diisobutylaluminum hydride, lithium triethoxyaluminum hydride and the like can be used in the reduction.

Scheme III



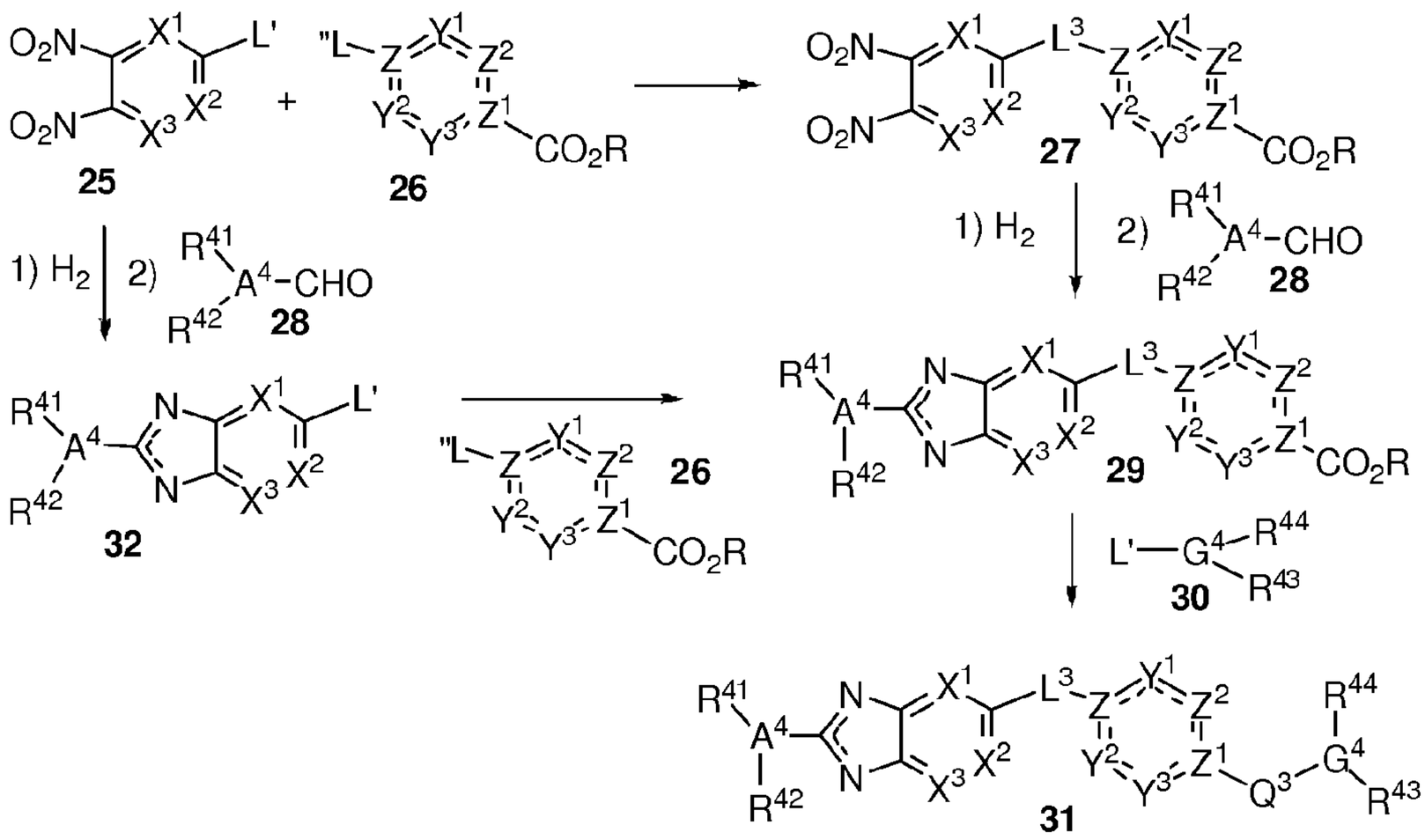
[0561] The process of Scheme **III** describes general synthesis of the compounds of Formula **III**. Coupling of an acid derivative of structure **10** with an amino derivative of structure **11** under standard conditions provides the amide intermediate of structure **12**. The two nitro groups of structure **12** are reduced under a typical reduction condition such as a metal catalyzed hydrogenation to give the diamino intermediate and then the intermediate is condensed with an aldehyde of structure **13** under an oxidative condition to afford desired compounds of structure **14**. Alternatively, compounds of structure **10** can be prepared from diamino derivatives of structure **15**. Condensation reaction of compounds of structure **15** with compounds of structure **13** under an oxidative condition provides the intermediate of structure **16**. A nitro reduction of intermediates **16** followed by an amide formation reaction under similar conditions described previously generate the compounds of structure **14**.

Scheme IV



[0562] The process of Scheme **IV** describes general synthesis of the compounds of Formula **IV**. Coupling reaction of compounds of structure **17** and compounds of structure 18 under the standard condition based on the nature of substituents **L′** and **L″** provides intermediates of structure **19**. Amide formation reaction of compounds of structures **20** and **21** and intermediates of structure **19** affords the products of structure **22**. Alternatively, especially for compounds of structure **22** that have different rings or side chains, compounds of structure **22** can be prepared with different coupling strategy. Amide coupling reactions between compounds of structures **17** and **21** and between compounds of structures **18** and **20** generate separate intermediates of structures **23** and **24**. The intermediates of structures **23** and **24** are then coupled to form final compounds of structure **22**.

Scheme V



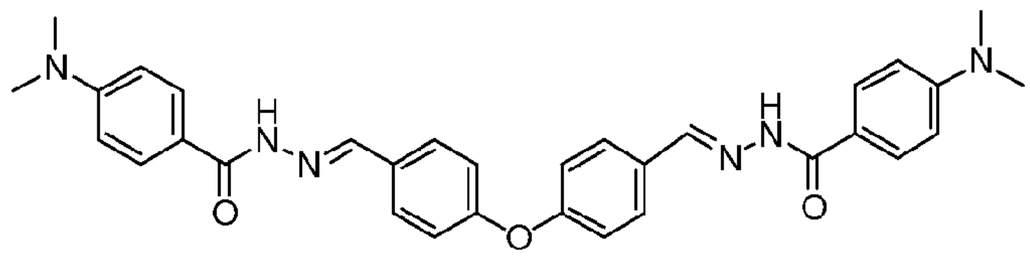
[0563] The process of Scheme **V** describes general synthesis of the compounds of Formula **V**. General coupling reaction of compounds of structures **25** and **26** affords the intermediates of structure **27**. A reduction of intermediate of structure **27** by a reducing agent such as metal catalyzed hydrogenation followed by an oxidative condensation with compounds of structure **28** give intermediates of structure **29**. The acid derivatives of structure **29** are coupled with compounds of structure **30** to provide the final products of structure **31**. Alternatively, compounds of structure **25** can be reduced and coupled with aldehydes **28** to provide bicyclic imidazole derivatives of structure **32**. Coupling reaction between compounds of structures **32** and **26** affords the same intermediates of structure **29**.

Examples

[0564] The following examples are set forth merely to assist in understanding the embodiments and should not be construed as limiting the embodiments described and claimed herein in any way. Variations of the invention, including the substitution of all equivalents now known or later developed, which would be within the purview of those skilled in the art, and changes in formulation or minor changes in experimental design, are to be considered to fall within the scope of the invention incorporated herein.

EXAMPLE 1

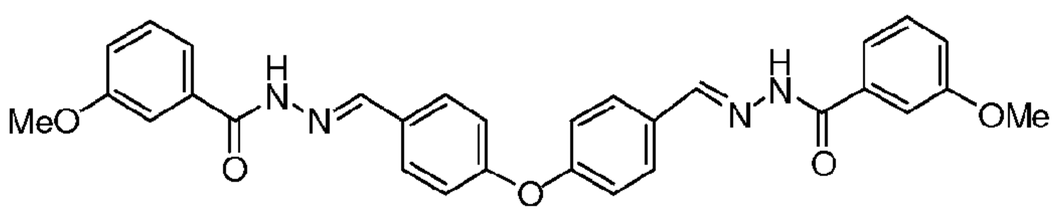
(*N',N'''E,N',N'''E*)-*N',N'''*-((Oxybis(4,1-phenylene))bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **101**)



[0565] Compound **101** was prepared according to the procedure described in Scheme **II**. To a solution of 4,4'-oxybisbenzaldehyde (Aldrich, 42 mg, 0.186 mmol) and 4-dimethylaminobenzyhydrazide (Alfa Aesar, 73 mg, 0.408 mmol) in 3 mL of ethanol was added 3 drops of acetic acid. The reaction was heated to 60 °C for 12 h, cooled to room temperature and filtered. The white precipitate was washed with water (5 mL) followed by methanol (5 mL) and dried under vacuum to yield 55 mg of compound **101** as a white powder. $[M+H]^+$ calcd for $C_{32}H_{33}N_6O_3$: 549.26; found: 549.05.

EXAMPLE 2

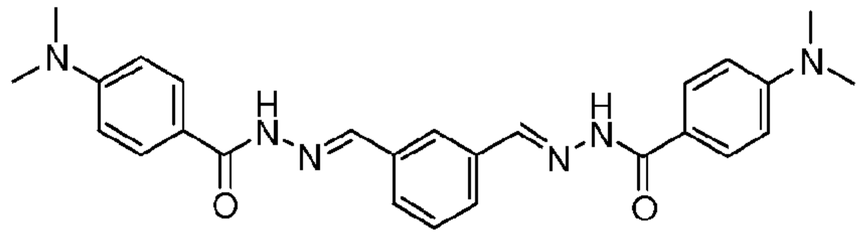
(N',N'''E,N',N'''E)-N',N'''-((oxybis(4,1-phenylene))bis(methanylylidene))bis(3-methoxybenzohydrazide) (Compound **102**)



[0566] Compound **102** was prepared according to the procedure described in Scheme **II** from 4,4'-oxybisbenzaldehyde and 3-methoxybenzoate. $[M+H]^+$ calcd for $C_{30}H_{26}N_4O_5$: 523.20; found: 513.15.

EXAMPLE 3

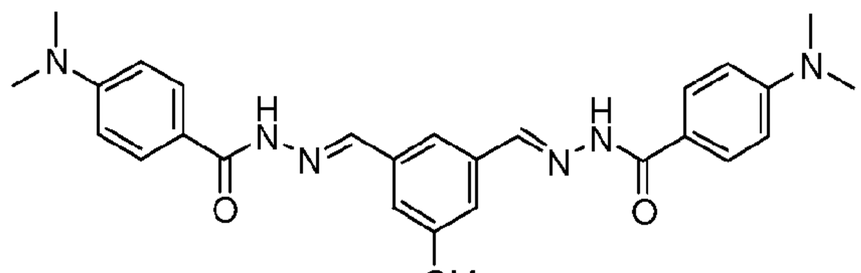
(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **103**)



[0567] Compound **103** was prepared according to the procedure described in Scheme **II** from benzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{26}H_{28}N_6O_2$: 457.23; found: 457.01.

EXAMPLE 4

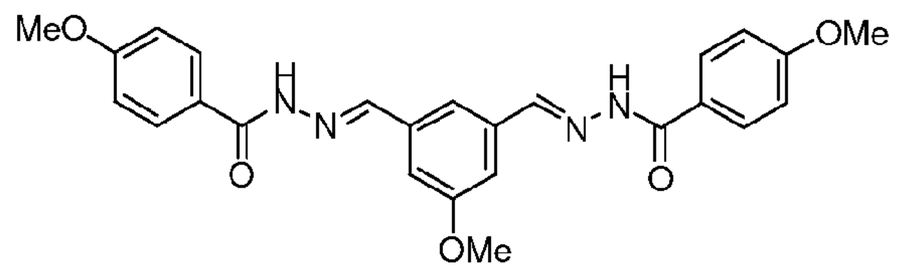
(*N',N'''E,N',N'''E*)-*N',N'''*-((5-methoxy-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **104**)



[0568] Compound **104** was prepared according to the procedure described in Scheme **II** from 5-5-methoxybenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. ^1H NMR (300MHz, DMSO-d_6) δ 11.62 (s, 2H), 8.41 (s, 2H), 7.81 (d, J = 7.5 Hz, 4H), 7.60 (s, 1H), 7.26 (d, J = 3 Hz, 2H), 6.76 (d, J = 7.5 Hz, 4H), 3.84 (s, 3H), 2.99 (s, 12H).

EXAMPLE 5

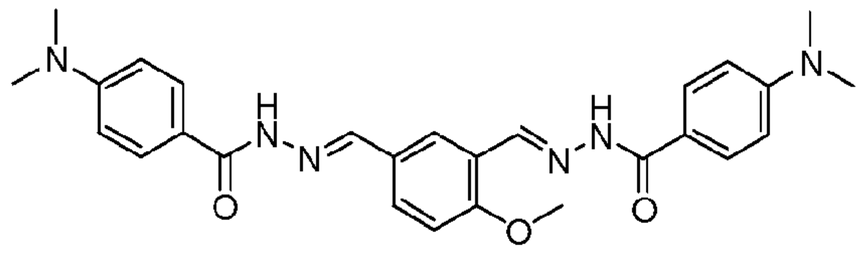
(*N',N'''E,N',N'''E*)-*N',N'''*-((5-methoxy-1,3-phenylene)bis(methanylylidene))bis(4-methoxybenzohydrazide) (Compound **105**)



[0569] Compound **105** was prepared according to the procedure described in Scheme II from 5-5-methoxybenzene-1,3-dicarboxaldehyde and 4-methoxybenzoate. $[M+II]^+$ calcd for $C_{25}II_{24}N_4O_5$: 461.18; found: 461.00.

EXAMPLE 6

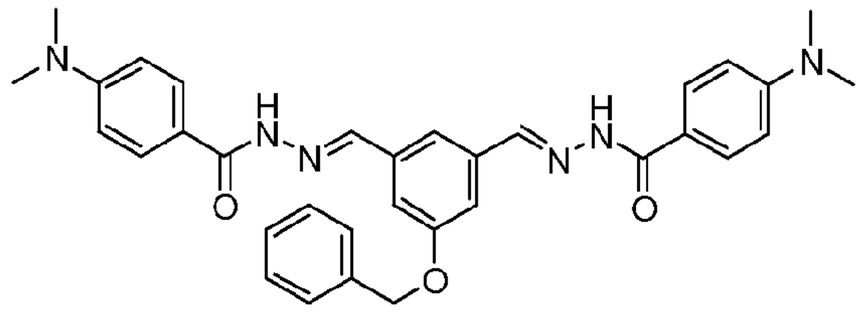
(*N',N'''E,N',N'''E*)-*N',N'''*-((4-methoxy-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **106**)



[0570] Compound **106** was prepared according to the procedure described in Scheme II from 4-4-methoxybenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 11.72 (s, 1H), 11.58 (s, 1H), 8.88 (s, 1H), 8.51 (s, 1H), 8.33 (s, 1H), 7.94 (dd, J = 7.5, 15 Hz, 4H), 7.80 (d, J =7.5 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 6.86 (d, J = 7.5 Hz, 4H), 4.10 (s, 3H), 3.10 (s, 12H).

EXAMPLE 7

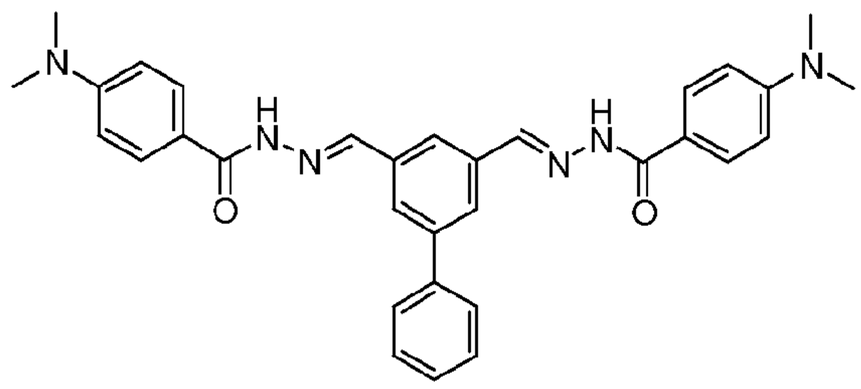
(*N',N'''E,N',N'''E*)-*N',N'''*-((5-(benzyloxy)-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **107**)



[0571] Compound **107** was prepared according to the procedure described in Scheme II from 5-5-benzyloxybenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{33}H_{35}N_6O_3$: 563.28; found: 563.08.

EXAMPLE 8

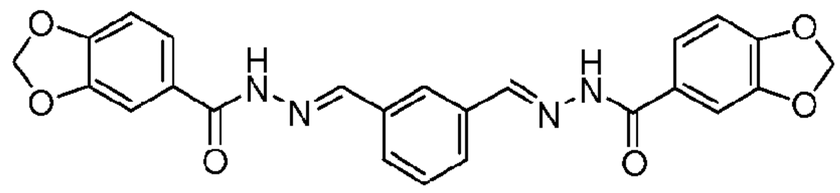
2(*N',N'''E,N',N'''E*)-*N',N'''*-([1,1'-biphenyl]-3,5-diylbis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **108**)



[0572] Compound **108** was prepared according to the procedure described in Scheme II from 5-phenylbenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{32}H_{32}N_6O_2$: 533.26; found: 533.08.

EXAMPLE 9

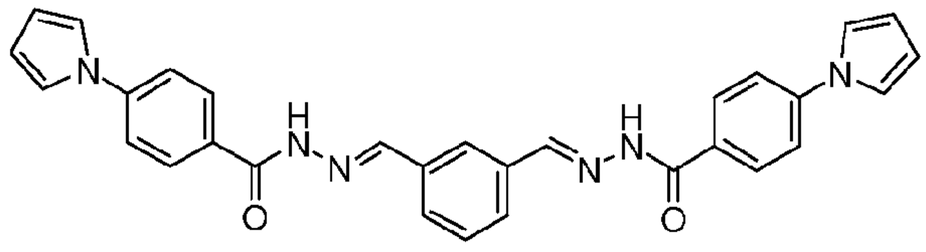
(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(benzo[*d*][1,3]dioxole-5-carbohydrazide) (Compound **109**)



[0573] Compound **109** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 5-(1,3-dioxolano)benzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 11.88 (s, 2H), 8.58 (s, 2H), 8.19 (s, 1H), 7.85 (d, J = 6.3 Hz, 2H), 7.64 (m, 3H), 7.56 (s, 2H), 7.17 (d, J = 6 Hz, 2H), 6.22 (s, 4H).

EXAMPLE 10

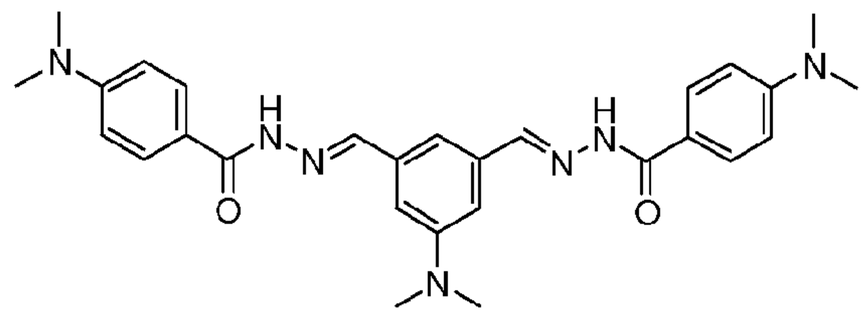
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(1*H*-pyrrol-1-yl)benzohydrazide) (Compound **110**)



[0574] Compound **110** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-pyrrolebenzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 12.15 (s, 2H), 8.63 (s, 2H), 8.24 (s, 1H), 8.13 (d, J = 7.5 Hz, 4H), 7.89 (d, J = 7.5 Hz, 6H), 7.64 (m, 5H), 6.43 (s, 4H).

EXAMPLE 11

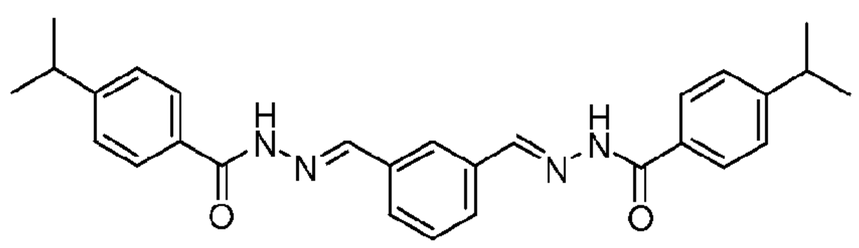
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-((5-(dimethylamino)-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **111**)



[0575] Compound **111** was prepared according to the procedure described in Scheme II from 5-dimethylaminobenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{28}H_{33}N_7O_2$: 500.27; found: 500.07.

EXAMPLE 12

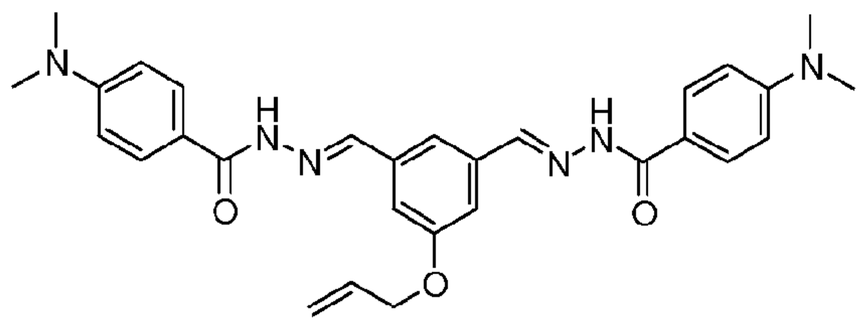
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-isopropylbenzohydrazide) (Compound **112**)



[0576] Compound **112** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-isopropylbenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.9 (s, 2H), 8.51 (s, 2H), 8.12 (s, 1H), 7.87 (d, J = 8.1 Hz, 4H), 7.77 (d, J = 7.3 Hz, 2H), 7.56 (dd, J = 7.3, 7.3 Hz, 1H), 7.42 (d, J = 8.1 Hz, 4H), 3.01-2.96 (m, 2H), 1.25 (d, J = 6.8 IIz, 12II).

EXAMPLE 13

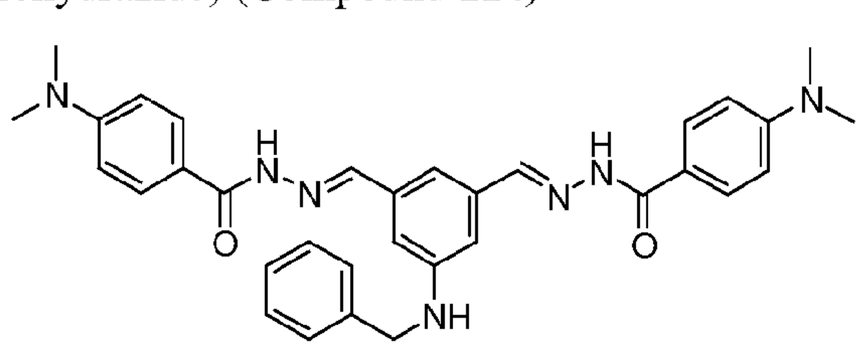
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-((5-(allyloxy)-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **113**)



[0577] Compound **113** was prepared according to the procedure described in Scheme II from 5-allyloxybenzene-1,3-dicarboxaldehydeand 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{29}H_{32}N_6O_3$: 513.26; found: 513.10.

EXAMPLE 14

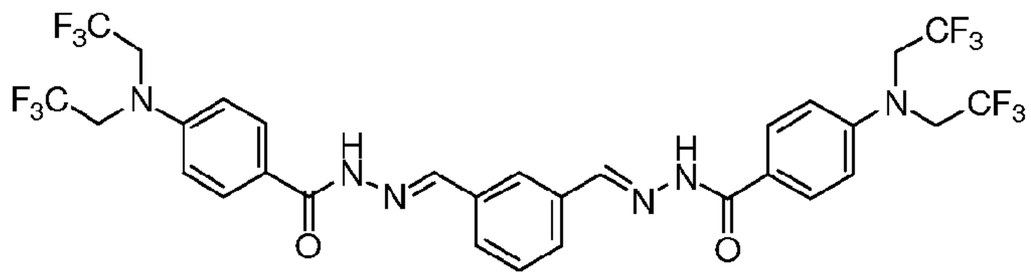
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-((5-(benzylamino)-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **114**)



[0578] Compound **114** was prepared according to the procedure described in Scheme II from 5-benzylaminobenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{33}H_{35}N_7O_2$: 562.29; found: 562.17.

EXAMPLE 15

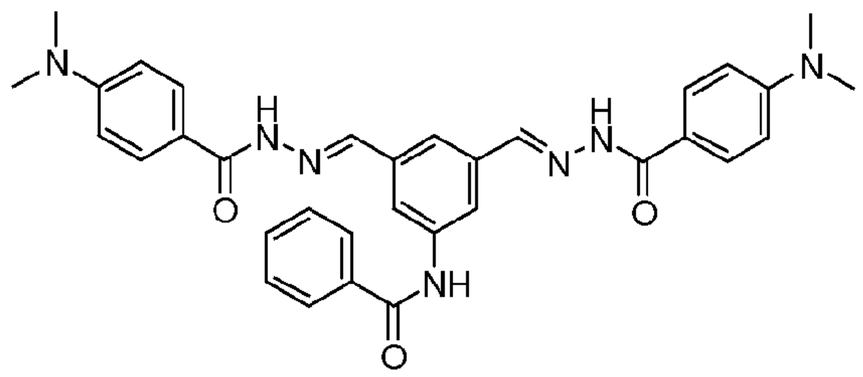
(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(bis(2,2,2-trifluoroethyl)amino)benzohydrazide) (Compound **115**)



[0579] Compound **115** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-di(2,2,2-trifluoroethyl)aminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.7 (s, 2H), 8.47 (s, 2H), 8.08 (s, 1H), 7.83 (d, J = 8.3 Hz, 4H), 7.72 (m, 2H), 7.53 (t, J = 7.8 Hz, 1H), 7.19 (d, J = 7.8 Hz, 4H), 4.49 (q, J_{H-F} = 8.3 Hz, 8H).

EXAMPLE 16

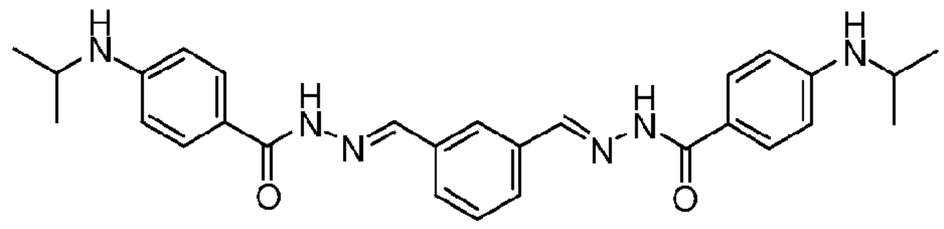
N-(3,5-bis((*E*)-(2-(4-(dimethylamino)benzoyl)hydrazono)methyl)phenyl)benzamide (Compound **116**)



[0580] Compound **116** was prepared according to the procedure described in Scheme II from 5-benzoylaminobenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{35}H_{38}N_8O_3$: 619.31; found: 619.16.

EXAMPLE 17

(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(isopropylamino)benzohydrazide) (Compound **117**)

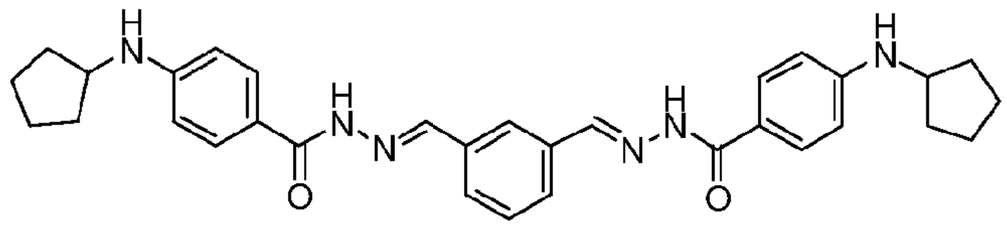


[0581] Compound **117** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-isopropylaminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.52 (s, 2H), 8.45 (s, 2H), 8.04 (s, 1H), 7.74-7.69 (m, 6H), 7.52 (t,

J = 7.8 Hz, 1H), 6.61 (d, *J* = 8.8 Hz, 4H), 6.16 (d, *J* = 7.8 Hz, 2H), 3.68-3.61 (m, 2H), 1.16 (d, *J* = 6.3 Hz, 12H).

EXAMPLE 18

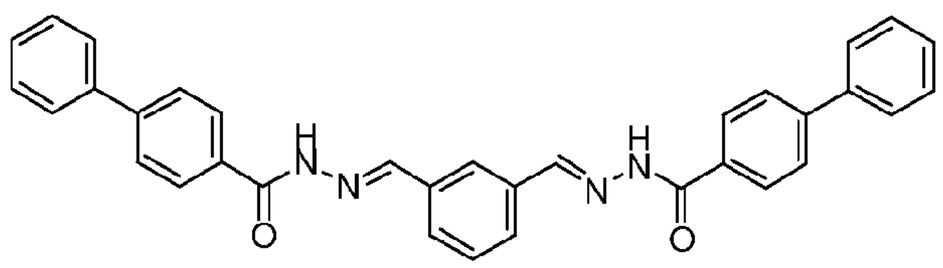
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(cyclopentylamino) benzohydrazide) (Compound **118**)



[0582] Compound **118** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-cyclopentylaminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, *J* = 8.9 Hz, 1H), 7.17 (d, *J* = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, *J* = 9.2 Hz, 2H), 3.04 (q, *J* = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, *J* = 7.3 Hz, 3H).

EXAMPLE 19

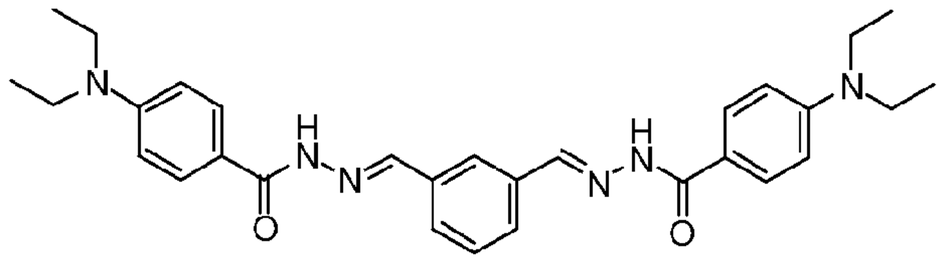
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(([1,1'-biphenyl]-4-carbohydrazide)) (Compound **119**)



[0583] Compound **119** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-phenylbenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, *J* = 8.9 Hz, 1H), 7.17 (d, *J* = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, *J* = 9.2 Hz, 2H), 3.04 (q, *J* = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, *J* = 7.3 Hz, 3H).

EXAMPLE 20

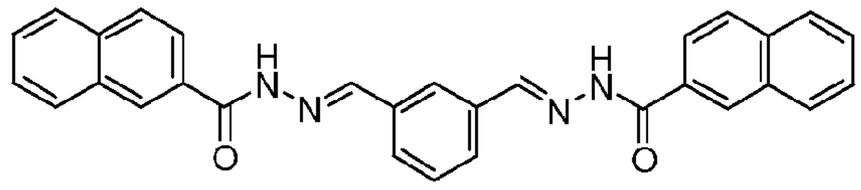
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(diethylamino) benzohydrazide) (Compound **120**)



[0584] Compound **120** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-diethylaminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 21

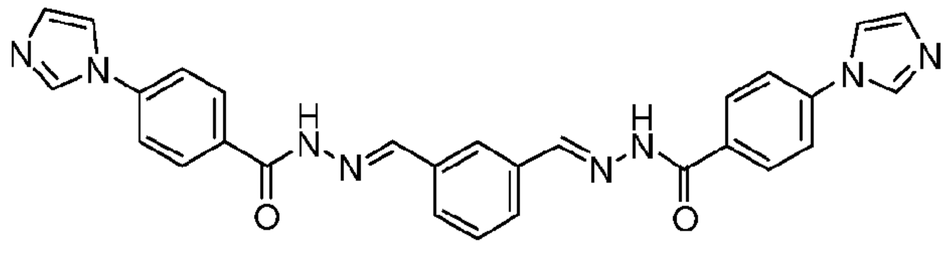
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(2-naphthohydrazide) (Compound **121**)



[0585] Compound **121** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 22

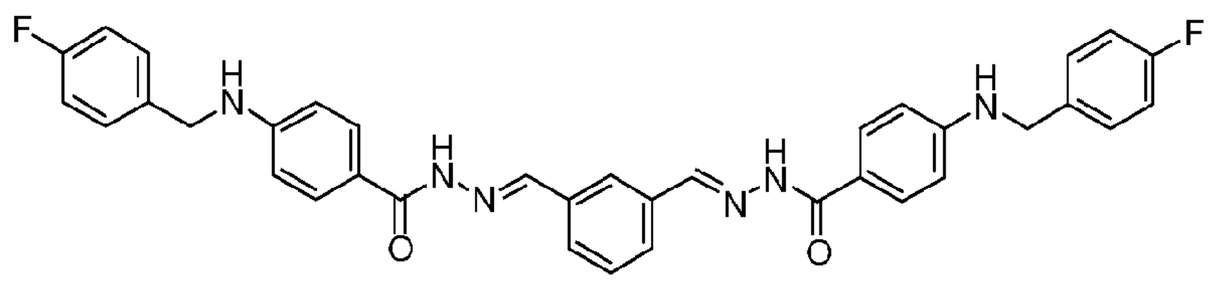
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(1*H*-imidazol-1-yl) benzohydrazide) (Compound **122**)



[0586] Compound **122** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-imidazolebenzoate. ^{1}II NMR (500 MIIz, DMSO-d_6) δ 12.0 (s, 2II), 8.55 (s, 2II), 8.49 (s, 2II), 8.16 (s, 1II), 8.09 (d, J = 8.3 IIz, 4H), 7.93 (s, 2H), 7.89 (d, J = 7.5 Hz, 4H), 7.81 (d, J = 7.5 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.21 (bs, 2H).

EXAMPLE 23

(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-((4-fluorobenzyl)amino) benzohydrazide) (Compound **123**)

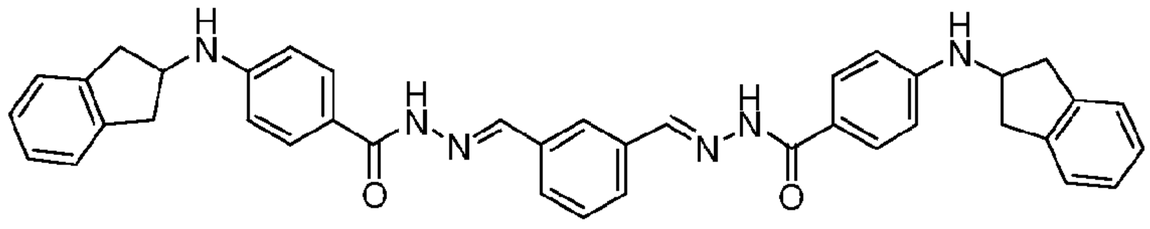


[0587] Compound **123** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-(4-fluorobenzylamino)benzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 24

(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(4-((2,3-dihydro-1*H*-inden-2-yl)

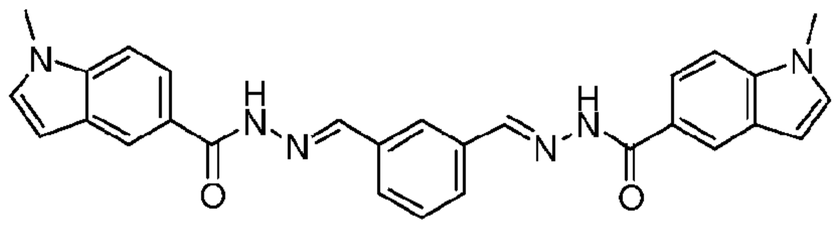
amino)benzohydrazide) (Compound **124**)



[0588] Compound **124** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-(2-indanylamino)benzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 25

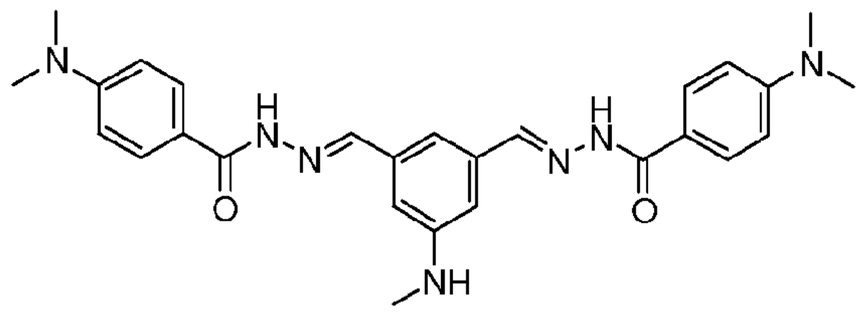
(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(1-methyl-1*H*-indole-5-carbohydrazide) (Compound **125**)



[0589] Compound **125** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 1-methyl-5-indolecarboxylate. $[M+H]^+$ calcd for $C_{28}H_{24}N_6O_2$: 477.20; found: 477.06.

EXAMPLE 26

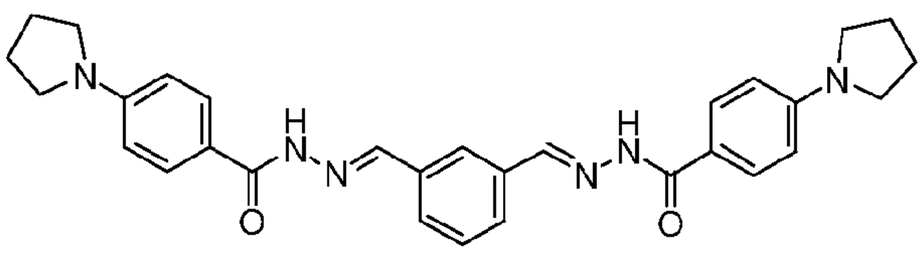
(*N',N'''E,N',N'''E*)-*N',N'''*-((5-(methylamino)-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **126**)



[0590] Compound **126** was prepared according to the procedure described in Scheme II from 5-methylaminobenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{27}H_{31}N_7O_2$: 486.26; found: 486.03.

EXAMPLE 27

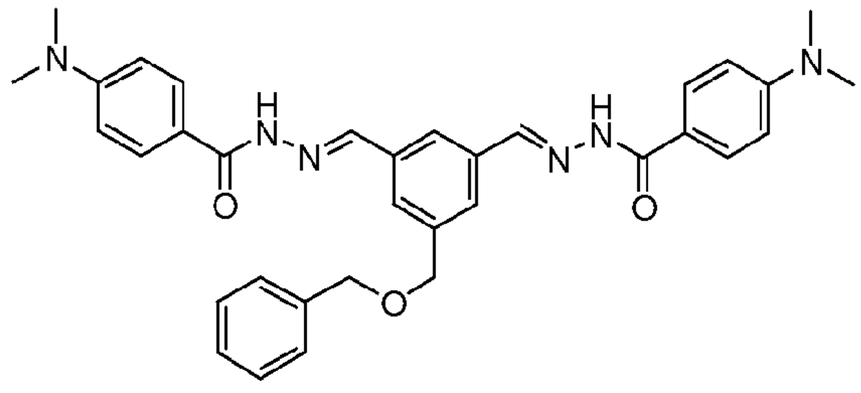
(*N',N'''E,N',N'''E*)-*N',N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(pyrrolidin-1-yl) benzohydrazide) (Compound **127**)



[0591] Compound **127** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-pyrrolidinebenzoate. ^1H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 28

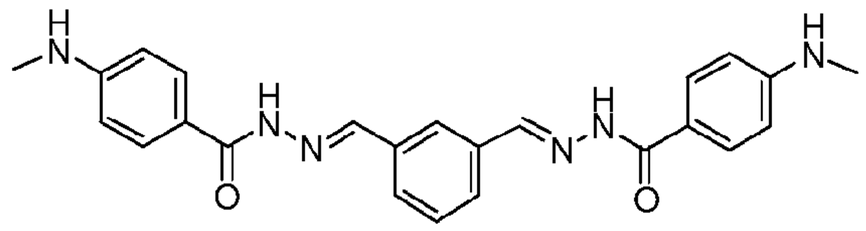
(*N',N'''E,N',N'''E*)-*N',N'''*-((5-((benzyloxy)methyl)-1,3-phenylene)bis(methanylylidene))bis(4-(dimethylamino)benzohydrazide) (Compound **128**)



[0592] Compound **128** was prepared according to the procedure described in Scheme II from 5-benzyloxymethylbenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{34}H_{36}N_6O_3$: 577.26; found: 577.10.

EXAMPLE 29

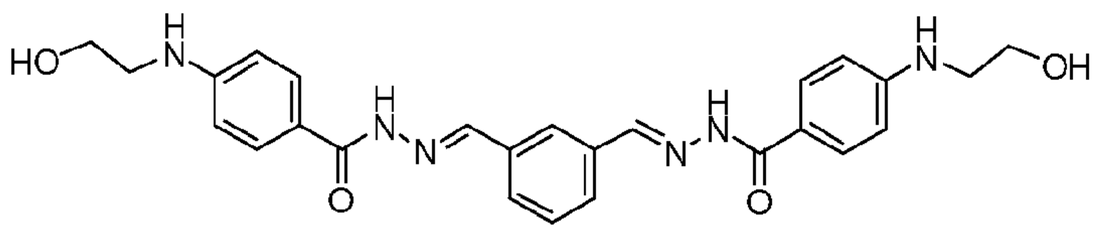
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(methylamino) benzohydrazide) (Compound **129**)



[0593] Compound **129** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-methylaminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 30

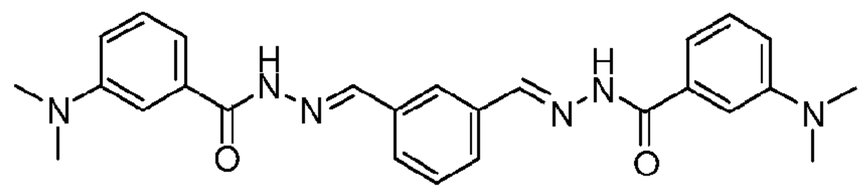
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-((2-hydroxyethyl) amino)benzohydrazide) (Compound **130**)



[0594] Compound **130** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-(2-hydroxyethylamino)benzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 6.70 (s, 1H), 5.28 (q, J = 9.2 Hz, 2H), 3.04 (q, J = 7.3 Hz, 2H), 2.44 (s, 3H), 1.09 (t, J = 7.3 Hz, 3H).

EXAMPLE 31

(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(3-(dimethylamino) benzohydrazide) (Compound **131**)

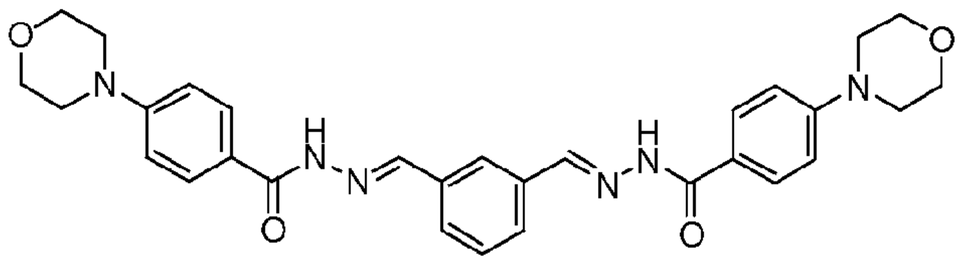


[0595] Compound **131** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 3-dimethylaminobenzoate. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.82 (s, 2H), 8.52 (s, 2H), 8.11 (s, 1H), 7.76 (d, J = 7.5 Hz, 2H),

7.56 (t, *J* = 7.5 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 7.0 Hz, 4H), 6.94 (d, *J* = 2.2 Hz, 2H), 2.97 (s, 12H).

EXAMPLE 32

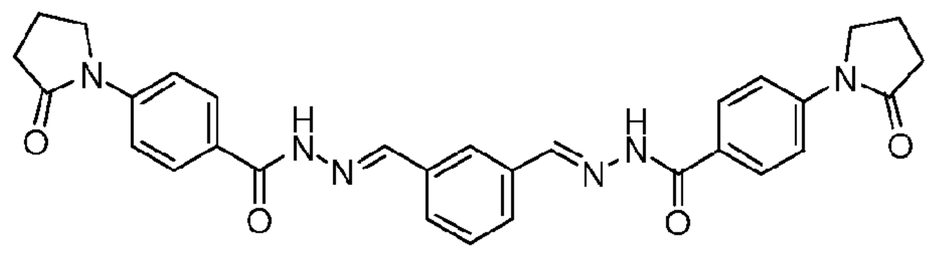
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-morpholinobenzohydrazide) (Compound **132**)



[0596] Compound **132** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{30}H_{33}N_6O_4$: 541.26; found: 541.05

EXAMPLE 33

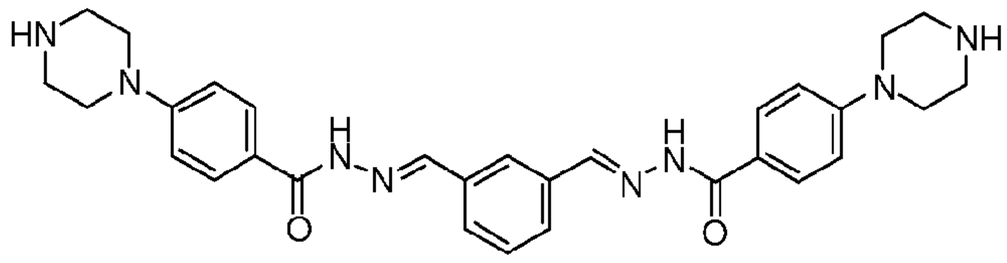
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(2-oxopyrrolidin-1-yl) benzohydrazide) (Compound **133**)



[0597] Compound **133** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-pyrrolidonobenzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 11.93 (s, 2H), 8.47 (s, 2H), 8.17 (s, 1H), 7.95 (d, *J* = 13.7 Hz, 4H), 7.81 (d, *J* = 10 Hz, 4H), 7.77 (d, *J* = 10 Hz, 2H), 7.55 (t, *J* = 10, 12.5 Hz, 1H), 4.28 (m, 4H), 2.53 (m, 4H), 2.07 (m, 4H).

EXAMPLE 34

(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(1,3-phenylenebis(methanylylidene))bis(4-(piperazin-1-yl) benzohydrazide) (Compound **134**)

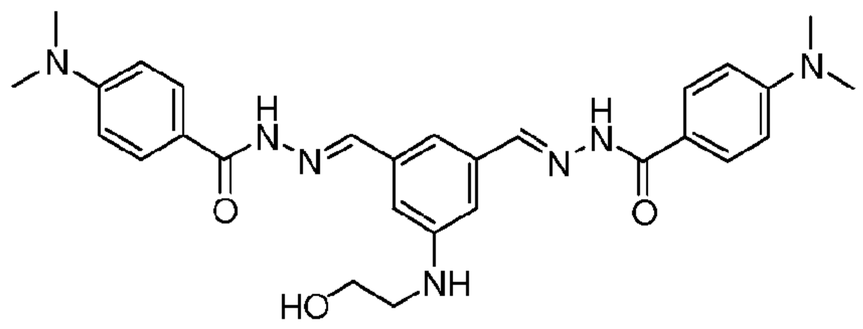


[0598] Compound **134** was prepared according to the procedure described in Scheme II from benzene-1,3-dicarboxaldehyde and 4-piperizinylbenzoate. ^{1}H NMR

(500MHz, DMSO-d_6) δ 11.54 (s, 2H), 10.15 (s, 2H), 8.47 (s, 2H), 8.25 (s, 1H), 7.86 (d, J = 12 Hz, 4H), 7.71 (m, 3H), 7.02 (d, J = 12 Hz, 4H), 3.17 (m, 8H), 2.86 (m, 8H).

EXAMPLE 35

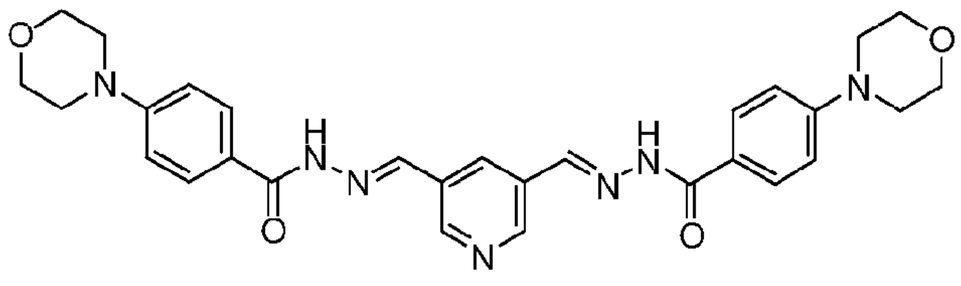
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-((5-((2-hydroxyethyl)amino)-1,3-phenylene)bis(methanylylidene)) bis(4-(dimethylamino)benzohydrazide) (Compound **135**)



[0599] Compound **135** was prepared according to the procedure described in Scheme II from 5-(2-hydroxyethyl)aminobenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{28}H_{33}N_7O_3$: 516.27; found: 516.00.

EXAMPLE 36

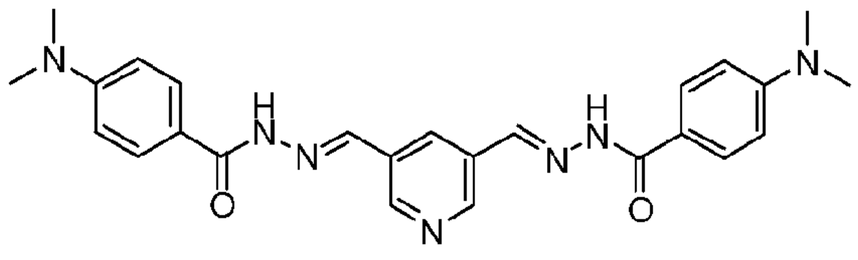
(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(pyridine-3,5-diylbis(methanylylidene))bis(4-morpholinobenzohydrazide) (Compound **136**)



[0600] Compound **136** was prepared according to the procedure described in Scheme II from pyridine-3,5-dicarboxaldehyde and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{31}N_7O_4$: 542.25; found: 541.99.

EXAMPLE 37

(*N',N'''E,N',N'''E*)-*N'*,*N'''*-(pyridine-3,5-diylbis(methanylylidene))bis(4-(dimethylamino) benzohydrazide) (Compound **137**)

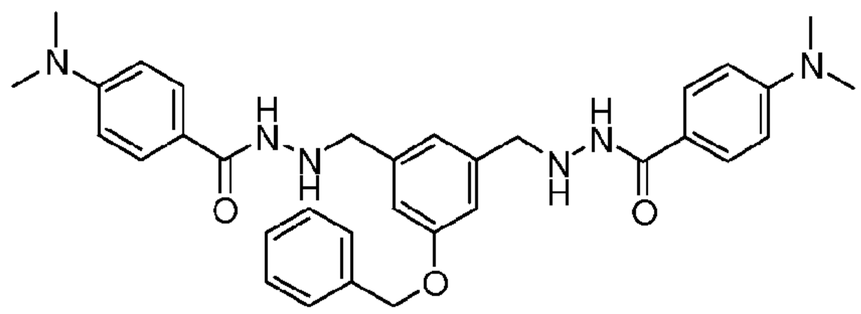


[0601] Compound **137** was prepared according to the procedure described in Scheme II from pyridine-3,5-dicarboxaldehyde and 4-dimethylaminobenzoate. ^{1}H NMR

(500MHz, DMSO-d_6) δ 11.79 (s, 2H), 8.81 (d, J = 3.75 Hz, 2H), 8.51 (s, 2H), 8.45 (s, 1H), 7.83 (d, J = 15 Hz, 4H), 6.77 (d, J = 11.2 Hz, 4H), 3.01 (s, 12H).

EXAMPLE 38

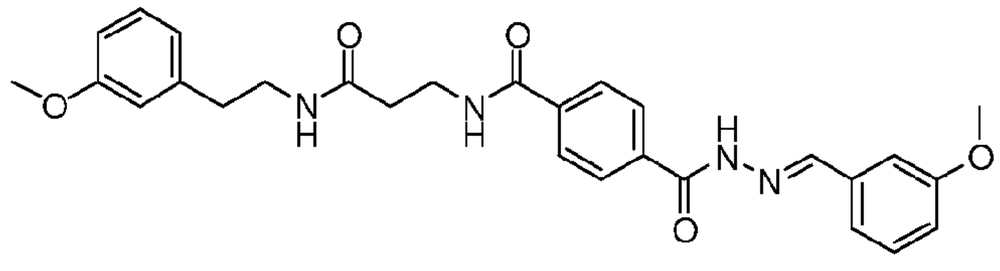
N',*N*'''-((5-(benzyloxy)-1,3-phenylene)bis(methylene))bis(4-(dimethylamino)benzohydrazide) (Compound **138**)



[0602] Compound **138** was prepared according to the procedure described in Scheme II from 5-5-benzyloxybenzene-1,3-dicarboxaldehyde and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{33}H_{28}N_6O_3$: 567.30; found: 567.17.

EXAMPLE 39

(*E*)-4-(2-(3-Methoxybenzylidene)hydrazinecarbonyl)-*N*-(3-((3-methoxyphenethyl)amino)-3-oxopropyl)benzamide (Compound **139**)



[0603] Compound **139** was prepared according to the general procedure described in Scheme I. Preparation of 3-((tert-butoxycarbonyl)amino)propanoic acid: β-Alanine (Sigma-Aldrich, 1.0 g, 11.2 mmol) and K_2CO_3 (3.1 g, 22.4 mmol) were dissolved in a mixture of dioxane (25 mL) and water (12.5 mL) then the solution was cooled to 0 °C in an ice bath. Di-*tert*-butyl dicarbonate (2.7 g, 12.3 mmol) was added then the solution was warmed slowly to room temperature and allowed to stir overnight. Upon completion, the solution was acidified with $KHSO_4$ until pH 3 then extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 then the solvent was removed under reduced pressure to give crude product which was taken forward without further purification.

[0604] Preparation of *tert*-butyl (3-((3-methoxyphenethyl)amino)-3-oxopropyl)carbamate: 3-methoxyphenethylamine (Aldrich, 100 mg, 0.66 mmol), 3-((*tert*-butoxycarbonyl)amino)-propanoic acid (125 mg, 0.66 mmol), hydroxybenzotriazole (8.9 mg, 0.066 mmol), triethylamine (102 μL, 0.73 mmol) and dimethyformamide (6.6 mL) were

combined, then 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (139 mg, 0.73 mmol) was added. The solution was allowed to stir at room temperature overnight. Upon completion, ethyl acetate and water were added and the layers were separated. The aqueous phase was extracted with ethyl acetate then the combined organic layers were washed with brine and dried over Na_2SO_4. Solvent was removed under reduced pressure to give crude product which was purified by flash chromatography using 0 – 80% ethyl acetate/hexane as the eluent to give the product as a pure white solid (140 mg, 66 %).

[0605] Preparation of 3-amino-*N*-(3-methoxyphenethyl)propanamide: *tert*-butyl (3-((3-methoxyphenethyl)amino)-3-oxopropyl)carbamate was dissolved in dichloromethane (0.5 mL) then the solution was cooled to 0 °C in an ice bath. Trifluoroacetic acid (300 µL) was added then the solution was allowed to warm slowly to room temperature with stirring. Upon completion of the reaction the solvent is removed under reduced pressure to give crude product which is used without further purification.

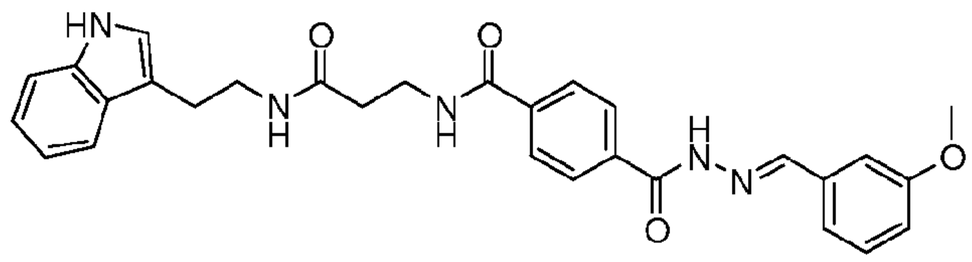
[0606] Preparation of methyl 4-((3-((3-methoxyphenethyl)amino)-3-oxopropyl)carbamoyl)benzoate: To 3-amino-*N*-(3-methoxyphenethyl)propanamide (60 mg, 0.27 mmol) was added 4-(methoxycarbonyl)benzoic acid (49 mg, 0.27 mmol), hydroxybenzotriazole (3.7 mg, 0.027 mmol), triethylamine (42 µL, 0.30 mmol) and dimethyformamide (2.7 mL). Lastly, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (57 mg, 0.30 mmol) was added and the solution was allowed to stir overnight at room temperature in a capped vial. Upon completion of the reaction an aqueous workup is performed to give the crude product which was purified using flash chromatography.

[0607] Preparation of 4-(hydrazinecarbonyl)-*N*-(3-((3-methoxyphenethyl)amino)-3-oxopropyl)benzamide: Methyl 4-((3-((3-methoxyphenethyl)amino)-3-oxopropyl)carbamoyl)benzoate was treated with methanol (3 mL) and hydrazine hydrate (300 µL), heated to 65 °C, then allowed to stir overnight. The reaction is monitored by TLC and upon completion the solvent is removed under reduced pressure to give crude product which is used without purification.

[0608] Preparation of Compound **139**: To the above crude product (15.0 mg, 0.039 mmol) was added 3-anisaldehyde (9.5 µL, 0.078 mmol), acetic acid (several drops) and ethanol (1 mL). The reaction was allowed to stir overnight at room temperature. The solid product that has formed is isolated by centrifugation then analyzed by LCMS. MS $[M+H]^+$ calcd for $C_{28}H_{30}N_4O_5$: 503.22; found: 503.04.

EXAMPLE 40

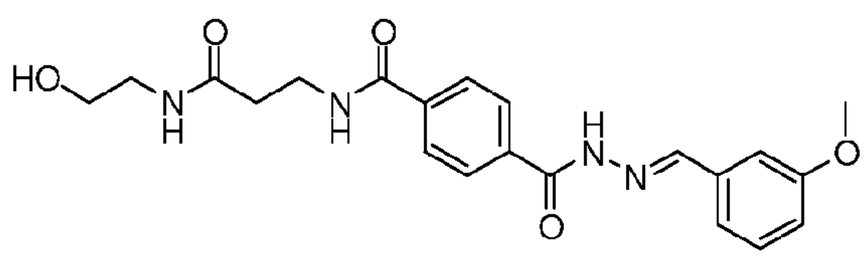
(*E*)-N-(3-((2-(1H-indol-3-yl)ethyl)amino)-3-oxopropyl)-4-(2-(3-methoxybenzylidene) hydrazinecarbonyl)benzamide (Compound **140**)



[0609] Compound **140** was prepared according to the procedure described in Scheme I from 4-(2-(3-indolylethyl)aminocarbonyl)ethylaminocarbonyl)benzoate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{29}N_5O_4$: 512.22; found: 512.03.

EXAMPLE 41

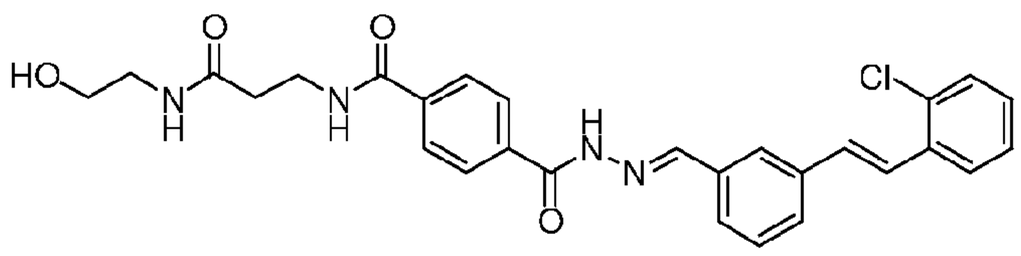
(*E*)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)-4-(2-(3-methoxybenzylidene) hydrazinecarbonyl)benzamide (Compound **141**)



[0610] Compound **141** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{21}H_{24}N_4O_5$: 413.17; found: 413.00.

EXAMPLE 42

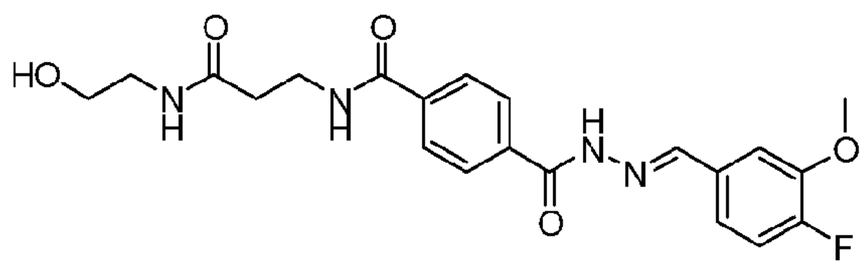
4-((*E*)-2-(3-((*E*)-2-chlorostyryl)benzylidene)hydrazinecarbonyl)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)benzamide (Compound **142**)



[0611] Compound **142** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 3-(2*E*-(2-chlorophenyl)ethenyl)benzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{27}ClN_4O_4$: 519.17; found: 519.00.

EXAMPLE 43

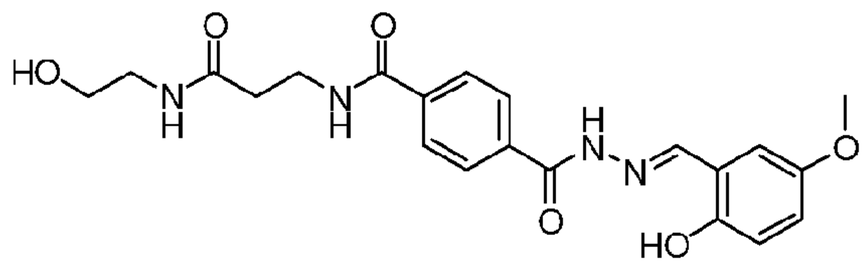
(*E*)-4-(2-(4-fluoro-3-methoxybenzylidene)hydrazinecarbonyl)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)benzamide (Compound **143**)



[0612] Compound **143** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 4-fluoro-3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{21}H_{23}FN_4O_5$: 431.17; found: 431.00.

EXAMPLE 44

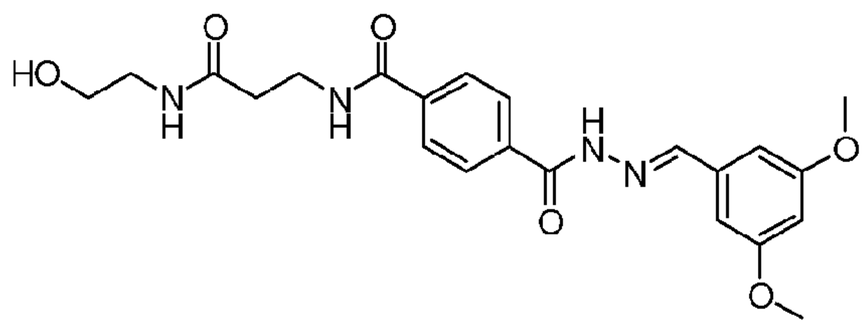
(*E*)-4-(2-(2-hydroxy-5-methoxybenzylidene)hydrazinecarbonyl)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)benzamide (Compound **144**)



[0613] Compound **144** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 2-hydroxy-5-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{21}H_{24}N_4O_6$: 429.17; found: 429.00

EXAMPLE 45

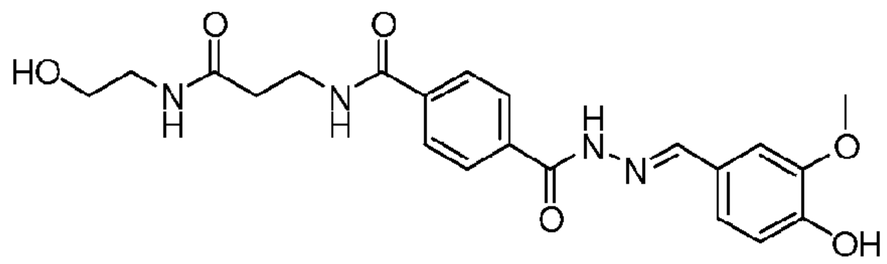
(*E*)-4-(2-(3,5-dimethoxybenzylidene)hydrazinecarbonyl)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)benzamide (Compound **145**)



[0614] Compound **145** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 3,5-dimethoxybenzaldehyde. $[M+H]^+$ calcd for $C_{22}H_{26}N_4O_6$: 443.19; found: 442.91.

EXAMPLE 46

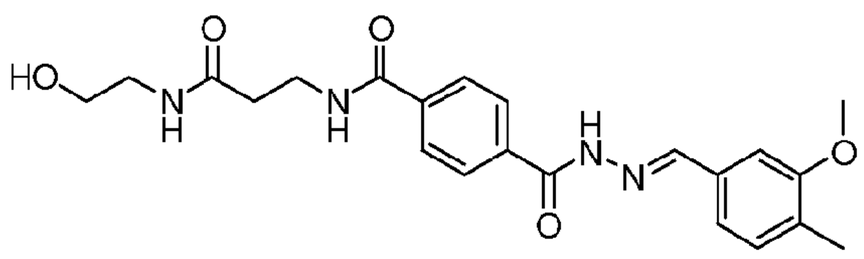
(*E*)-4-(2-(4-hydroxy-3-methoxybenzylidene)hydrazinecarbonyl)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)benzamide (Compound **146**)



[0615] Compound **146** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 4-hydroxy-5-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{21}H_{24}N_4O_6$: 429.17; found: 428.88.

EXAMPLE 47

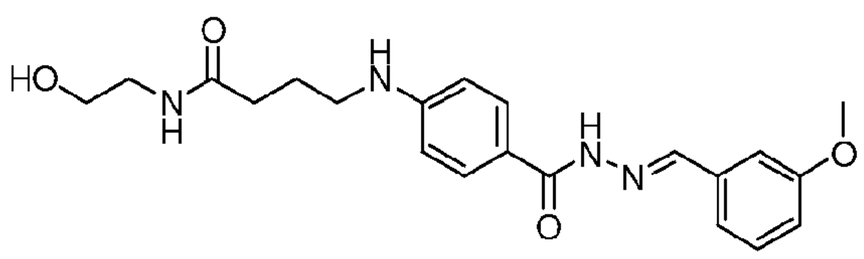
(E)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)-4-(2-(3-methoxy-4-methylbenzylidene) hydrazinecarbonyl)benzamide (Compound **147**)



[0616] Compound **147** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 3-methoxy-4-methylbenzaldehyde. $[M+H]^+$ calcd for $C_{22}H_{26}N_4O_5$: 427.19; found: 426.92.

EXAMPLE 48

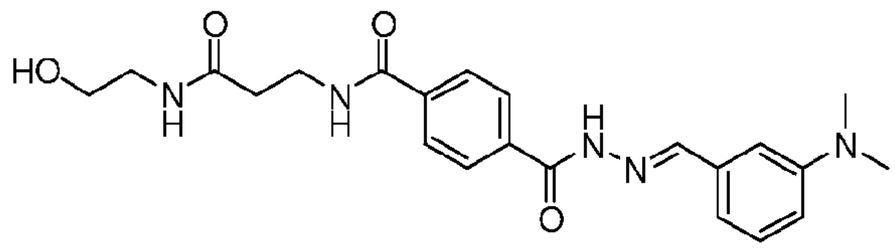
(*E*)-*N*-(2-hydroxyethyl)-4-((4-(2-(3-methoxybenzylidene)hydrazinecarbonyl)phenyl)amino) butanamide (Compound **148**)



[0617] Compound **148** was prepared according to the procedure described in Scheme I from 4-(3-(2-hydroxyethylaminocarbonyl)propylamino)benzoate and 3-methoxybenzaldehyde. $[M+II]^+$ calcd for $C_{21}II_{26}N_4O_4$: 399.20; found: 399.47.

EXAMPLE 49

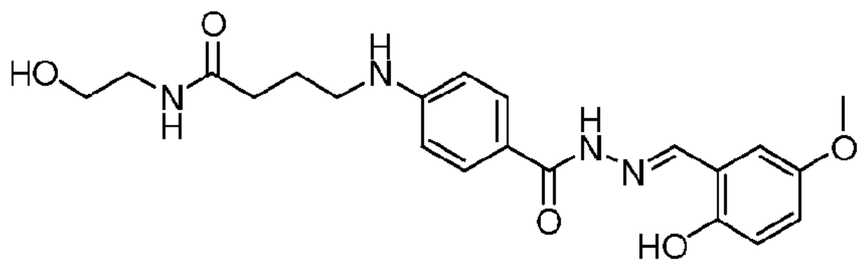
(*E*)-4-(2-(3-(dimethylamino)benzylidene)hydrazinecarbonyl)-*N*-(3-((2-hydroxyethyl)amino)-3-oxopropyl)benzamide (Compound **149**)



[0618] Compound **149** was prepared according to the procedure described in Scheme I from 4-(2-(2-hydroxyethylaminocarbonyl)ethylaminocarbonyl)benzoate and 3-dimethylaminobenzaldehyde. $[M+H]^+$ calcd for $C_{22}H_{27}N_5O_4$: 426.21; found: 426.53.

EXAMPLE 50

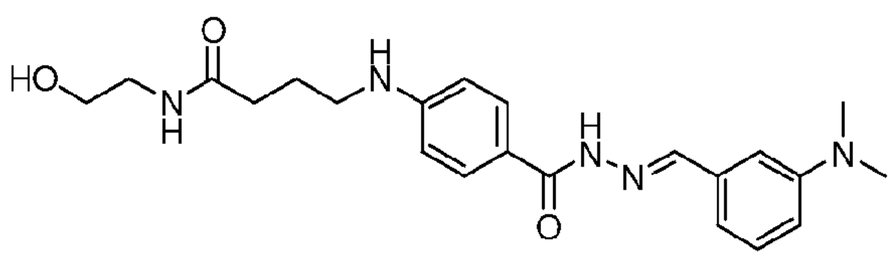
(*E*)-4-((4-(2-(2-hydroxy-5-methoxybenzylidene)hydrazinecarbonyl)phenyl)amino)-*N*-(2-hydroxyethyl)butanamide (Compound **150**)



[0619] Compound **150** was prepared according to the procedure described in Scheme I from 4-(3-(2-hydroxyethylaminocarbonyl)propylamino)benzoate and 2-hydroxy-5-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{21}H_{26}N_4O_5$: 415.19; found: 415.53.

EXAMPLE 51

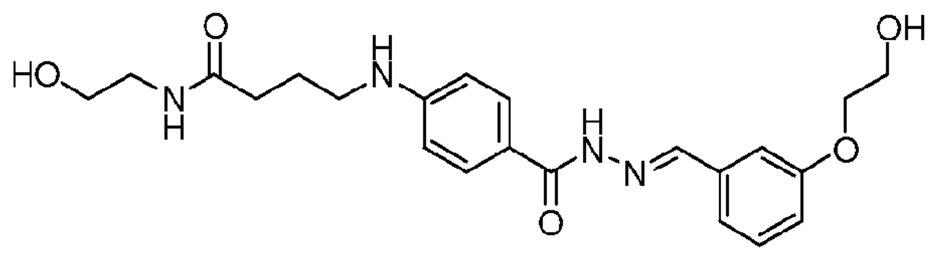
(*E*)-4-((4-(2-(3-(dimethylamino)benzylidene)hydrazinecarbonyl)phenyl)amino)-*N*-(2-hydroxyethyl)butanamide (Compound **151**)



[0620] Compound **151** was prepared according to the procedure described in Scheme I from 4-(3-(2-hydroxyethylaminocarbonyl)propylamino)benzoate and 3-dimethylaminobenzaldehyde. $[M+H]^+$ calcd for $C_{22}H_{29}N_5O_3$: 412.23; found: 412.56.

EXAMPLE 52

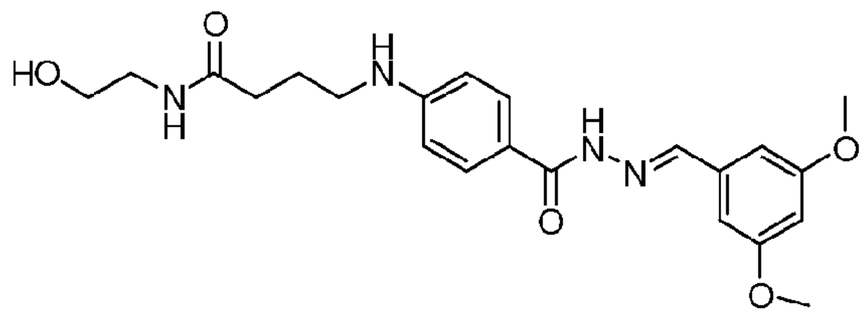
(*E*)-4-((4-(2-(3-(2-hydroxyethoxy)benzylidene)hydrazinecarbonyl)phenyl)amino)-*N*-(2-hydroxyethyl)butanamide (Compound **152**)



[0621] Compound **152** was prepared according to the procedure described in Scheme I from 4-(3-(2-hydroxyethylaminocarbonyl)propylamino)benzoate and 3-(2-hydroxyethoxy)benzaldehyde. $[M+H]^+$ calcd for $C_{22}H_{28}N_4O_5$: 429.21; found: 429.50.

EXAMPLE 53

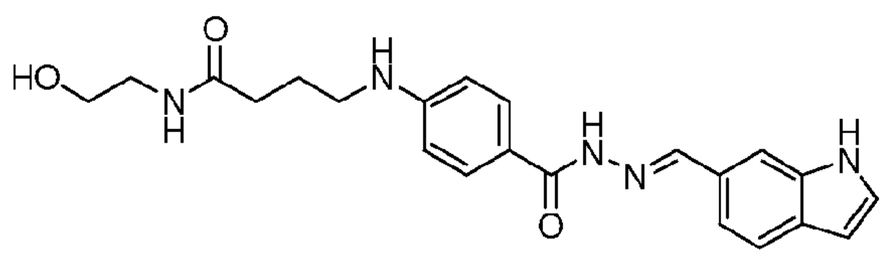
(*E*)-4-((4-(2-(3,5-dimethoxybenzylidene)hydrazinecarbonyl)phenyl)amino)-*N*-(2-hydroxyethyl)butanamide (Compound **153**)



[0622] Compound **153** was prepared according to the procedure described in Scheme I from 4-(3-(2-hydroxyethylaminocarbonyl)propylamino)benzoate and 3,5-dimethoxybenzaldehyde. $[M+H]^+$ calcd for $C_{22}H_{28}N_4O_5$: 429.21; found: 429.50.

EXAMPLE 54

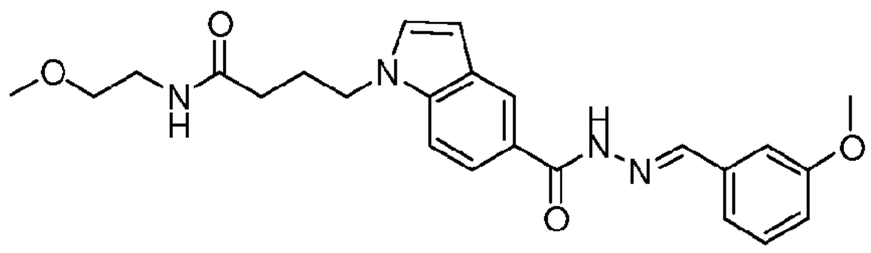
(*E*)-4-((4-(2-((1*H*-indol-6-yl)methylene)hydrazinecarbonyl)phenyl)amino)-*N*-(2-hydroxyethyl)butanamide (Compound **154**)



[0623] Compound **154** was prepared according to the procedure described in Scheme I from 4-(3-(2-hydroxyethylaminocarbonyl)propylamino)benzoate and 6-indolecarboxaldehyde. $[M+H]^+$ calcd for $C_{22}H_{25}N_5O_3$: 408.20; found: 408.51.

EXAMPLE 55

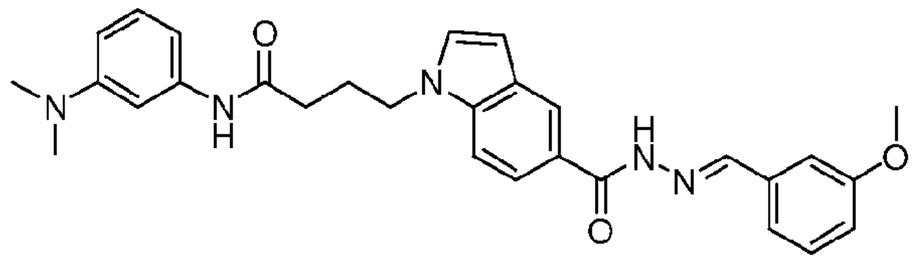
(*E*)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)-*N*-(2-methoxyethyl)butanamide (Compound **155**)



[0624] Compound **155** was prepared according to the procedure described in Scheme I from 1-(3-(2-methoxyethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. ^{1}H NMR (500MHz, DMSO-d_6) δ 11.77 (s, 1H), 8.43 (s, 1H), 8.20 (d, J = 1.5 Hz, 1H), 7.89 (t, J = 5.5 Hz, 1H), 7.72 (dd, J = 2, 9 Hz, 1H), 7.57 (d, J = 9 Hz, 1H), 7.46 (d, J = 3IIz, 1II), 7.36 (t, J = 8 IIz, 1II), 7.27 (s, 2II), 6.99 (d, J = 8IIz, 1II), 6.58 (d, J = 2.5 Hz, 1H), 4.20 (t, J = 6.5 Hz, 2H), 3.80 (s, 3H), 3.32-3.29 (m, 2H), 3.20-3.14 (m, 5H), 2.05 (t, J = 8 Hz, 2H), 1.96 (p, J = 7 Hz, 2H).

EXAMPLE 56

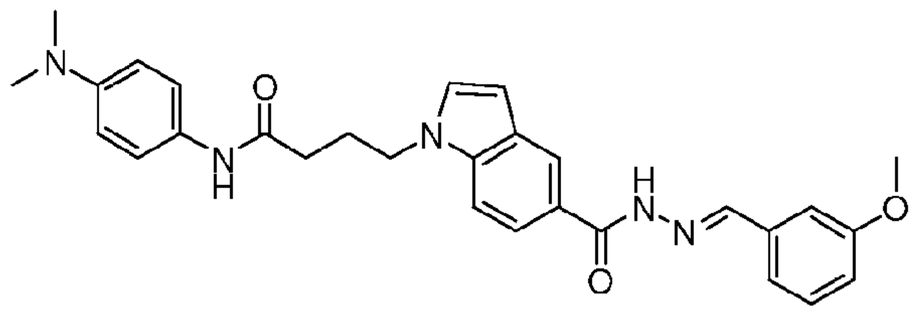
(*E*)-*N*-(3-(dimethylamino)phenyl)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)butanamide (Compound **156**)



[0625] Compound **156** was prepared according to the procedure described in Scheme I from 1-(3-(3-dimethylaminophenyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{31}N_5O_3$: 498.24; found: 497.98.

EXAMPLE 57

(*E*)-*N*-(4-(dimethylamino)phenyl)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)butanamide (Compound **157**)

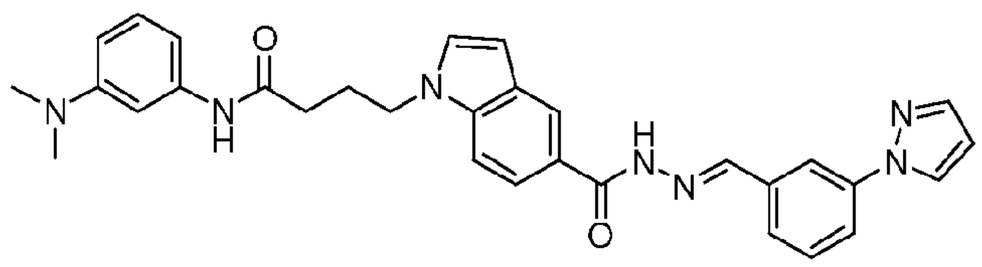


[0626] Compound **157** was prepared according to the procedure described in Scheme I from 1-(3-(4-dimethylaminophenyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. ^{1}H NMR (500MHz, DMSO-d_6) δ 11.77 (s, 1H), 9.58 (s, 1H), 8.43 (bs, 1H), 8.21 (d, J = 1.0 Hz, 1H), 7.73 (dd, J = 1.5, 8.5 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H),

7.50 (d, *J* = 2.5Hz, 1H), 7.44 (m, 1H), 7.36 (d, *J* = 9 Hz, 2H), 7.26 (m, 2H), 6.99 (d, *J* = 8 Hz, 1H), 6.75 (d, *J* = 9 Hz, 1H), 6.65 (d, *J* = 9 Hz, 2H), 6.60 (d, *J* = 2.5 Hz, 1H), 4.27 (t, *J* = 7 Hz, 2H), 3.80 (s, 3H), 2.81 (s, 6H), 2.23 (t, *J* = 7.5 Hz, 2H), 2.06 (p, *J* = 7.5 Hz, 2H).

EXAMPLE 58

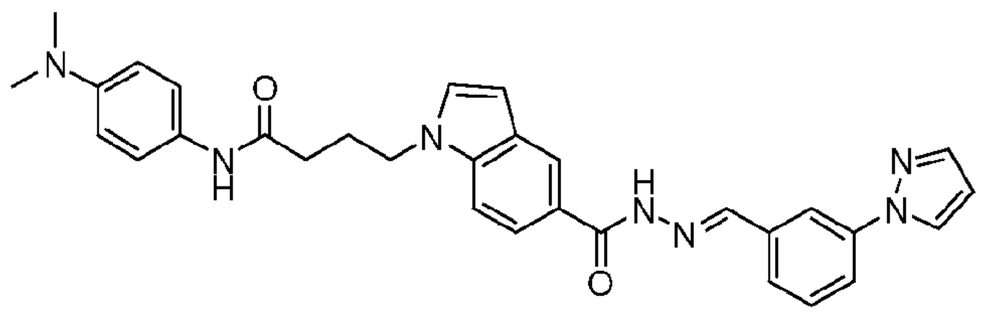
(*E*)-4-(5-(2-(3-(1*H*-pyrazol-1-yl)benzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)-*N*-(3-(dimethylamino)phenyl)butanamide (Compound **158**)



[0627] Compound **158** was prepared according to the procedure described in Scheme I from 1-(3-(3-dimethylaminophenyl)aminocarbonylpropyl)indole-5-carboxylate and 3-(pyrazol-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{31}N_7O_2$: 534.25; found: 534.00.

EXAMPLE 59

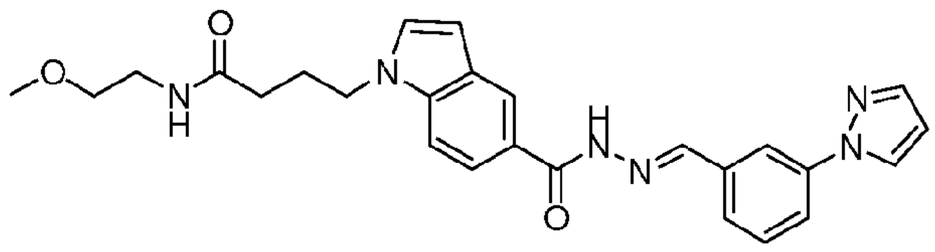
(*E*)-4-(5-(2-(3-(1*H*-pyrazol-1-yl)benzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)-*N*-(4-(dimethylamino)phenyl)butanamide (Compound **159**)



[0628] Compound **159** was prepared according to the procedure described in Scheme I from 1-(3-(4-dimethylaminophenyl)aminocarbonylpropyl)indole-5-carboxylate and 3-(pyrazol-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{31}N_7O_2$: 534.25; found: 533.97.

EXAMPLE 60

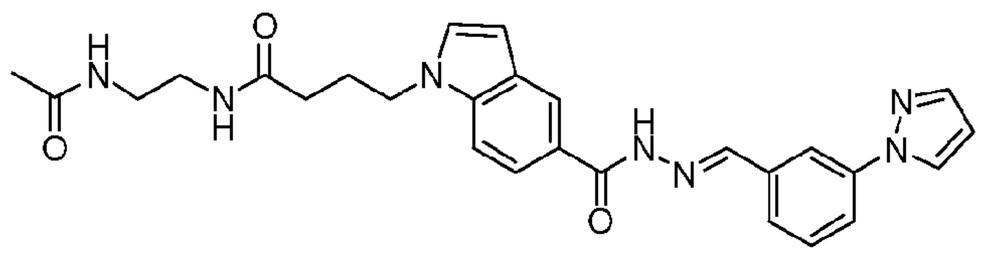
(*E*)-4-(5-(2-(3-(1*H*-pyrazol-1-yl)benzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)-*N*-(2-methoxyethyl)butanamide (Compound **160**)



[0629] Compound **160** was prepared according to the procedure described in Scheme I from 1-(3-(2-methoxyethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-(pyrazol-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{26}H_{28}N_6O_3$: 473.22; found: 472.94.

EXAMPLE 61

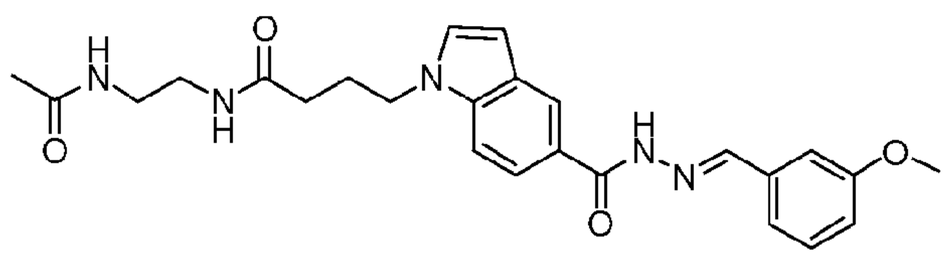
(*E*)-4-(5-(2-(3-(1*H*-pyrazol-1-yl)benzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)-*N*-(2-acetamidoethyl)butanamide (Compound **161**)



[0630] Compound **161** was prepared according to the procedure described in Scheme I from 1-(3-(2-acetylamidoethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-(pyrazol-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{27}H_{29}N_7O_3$: 500.23; found: 499.94.

EXAMPLE 62

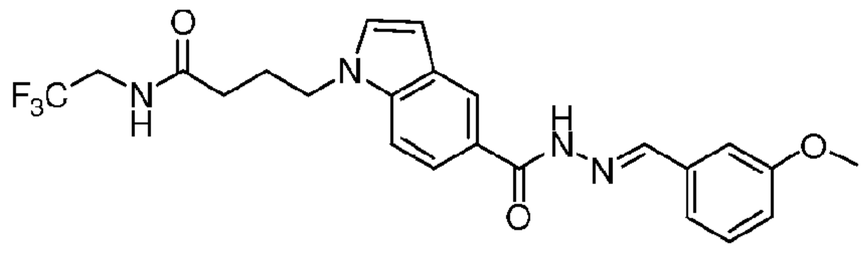
(*E*)-*N*-(2-acetamidoethyl)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)butanamide (Compound **162**)



[0631] Compound **162** was prepared according to the procedure described in Scheme I from 1-(3-(2-acetylamidoethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{29}N_5O_4$: 464.22; found: 463.93.

EXAMPLE 63

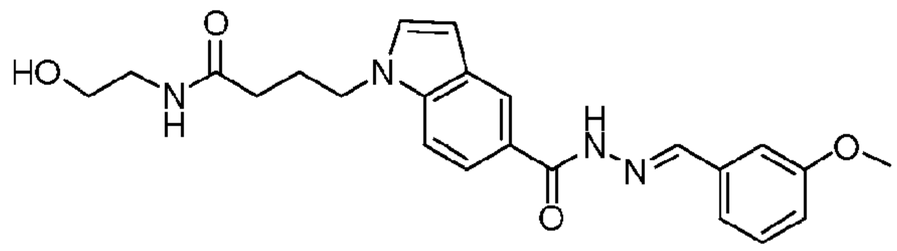
(*E*)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)-*N*-(2,2,2-trifluoroethyl)butanamide (Compound **163**)



[0632] Compound **163** was prepared according to the procedure described in Scheme I from 1-(3-(2,2,2-trifluoroethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{23}H_{23}F_3N_4O_3$: 461.17; found: 460.92.

EXAMPLE 64

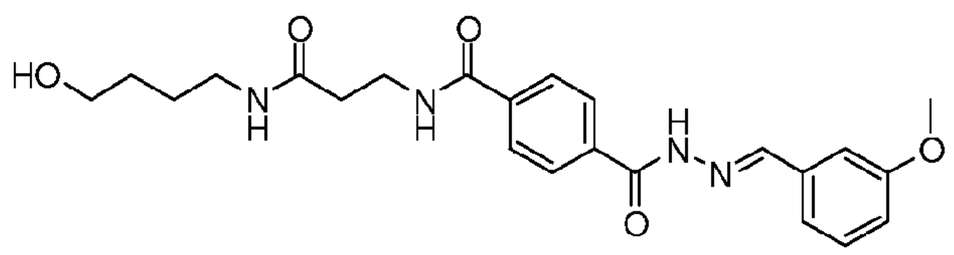
(*E*)-*N*-(2-hydroxyethyl)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)butanamide (Compound **164**)



[0633] Compound **164** was prepared according to the procedure described in Scheme I from 1-(3-(2-hydroxyethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{23}H_{26}N_4O_4$: 423.20; found: 422.88.

EXAMPLE 65

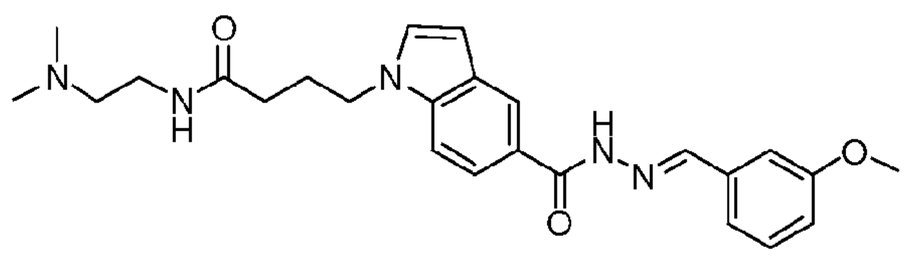
(*E*)-*N*-(3-((4-hydroxybutyl)amino)-3-oxopropyl)-4-(2-(3-methoxybenzylidene) hydrazinecarbonyl)benzamide (Compound **165**)



[0634] Compound **165** was prepared according to the procedure described in Scheme I from 4-(2-(4-hydroxybutylaminocarbonyl)ethylaminocarbonyl)benzoate and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{23}H_{28}N_4O_5$: 441.21; found: 441.01.

EXAMPLE 66

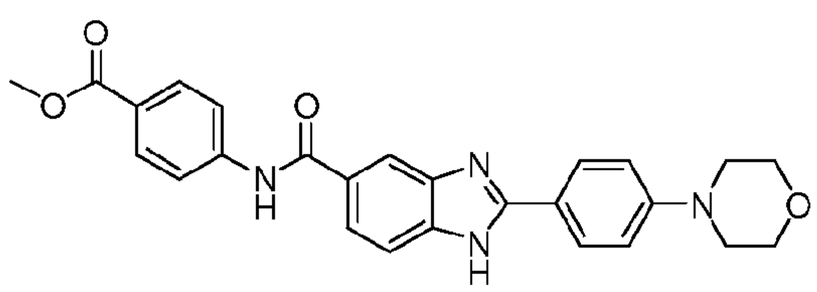
(*E*)-*N*-(2-(dimethylamino)ethyl)-4-(5-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-1*H*-indol-1-yl)butanamide (Compound **166**)



[0635] Compound **166** was prepared according to the procedure described in Scheme I from 1-(3-(2-dimethylaminoethyl)aminocarbonylpropyl)indole-5-carboxylate and 3-methoxybenzaldehyde. ^{1}H NMR (500MHz, Acetone-d_6) δ 11.09 (bs, 1H), 8.51 (bs, 1H), 8.26 (d, J = 19 Hz, 2H), 7.83 (dd, J = 1.5, 8.5 Hz, 1H), 7.39 (bs, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.30 (m, 1H), 7.08 (s, 1H), 6.99-6.97 (m, 1H), 6.58 (d, J = 3 Hz, 1H), 4.31 (t, J = 7 Hz, 2H), 3.85 (s, 3H), 3.39 (q, J = 6 Hz, 2H), 2.67 (t, J = 6 Hz, 2H), 2.41 (s, 6H), 2.18-2.11 (m, 4H).

EXAMPLE 67

Methyl 4-(2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-5-carboxamido)benzoate (Compound **167**)

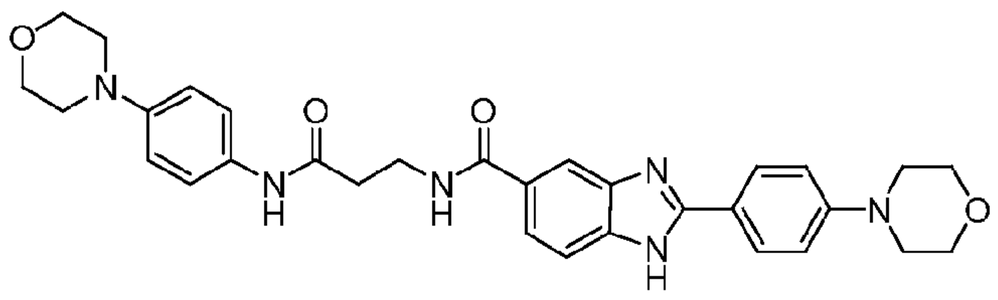


[0636] Compound **167** was prepared according to the general procedure similar to that described in Scheme III. Preparation of 2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid: 4-Morpholinobenzaldehyde (475 mg, 2.5 mmole), sodium metabisulfite (85 mg) and 3,4-diaminobenzoic acid (152 mg, 2.7 mmole) were placed in a 10-mL microwave tube and 5.0 mL HPLC grade 2-propanol added. The reaction mixture was microwaved at 170 °C for 55 minutes. The reaction mixture was added dropwise to 25 mL water and stirred at room temperature for 30 min. then it was filtered and washed with plenty of water, ethyl acetate and hexanes and dried to provide the pure intermediate acid (323 mg, 40% yield). This compound was used for next step without any further purification.

[0637] Preparation of Compound **167**: 2-(4-Morpholinophenyl)-1*H*-benzo[*d*]imidazole-5-carboxylic acid (32 mg, 0.1 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC) (40 mg, 0.2 mmole) were place in a 20 mL vial and pyridine (1.0 mL) added and capped tightly. The reaction mixture was stirred at room temperature for overnight. The reaction mixture was evaporated to dryness and the residue was washed thoroughly with plenty of water, hexanes and EtOAc then dried. Crystallization out of methanol/water provided compound **167** in 25% yield (11.4 mg). $[M+H]^+$ calcd for $C_{26}H_{24}N_4O_4$: 457.18; found: 456.94.

EXAMPLE 68

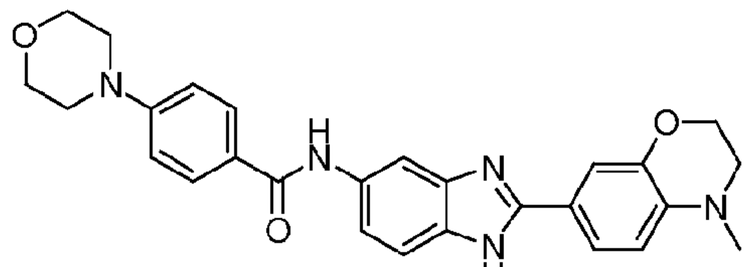
2-(4-Morpholinophenyl)-*N*-(3-((4-morpholinophenyl)amino)-3-oxopropyl)-1*H*-benzo[*d*]imidazole-5-carboxamide (Compound **168**)



[0638] Compound **168** was prepared according to the procedure similar to that described in Scheme III from the 3,4-dinitrobenzamide and 4-morpholinobenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{34}N_6O_4$: 555.26; found: 555.03.

EXAMPLE 69

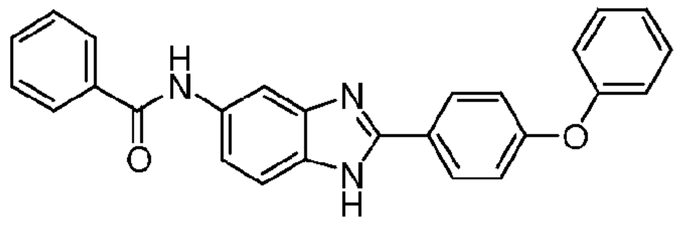
N-(2-(4-Methyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-7-yl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **169**)



[0639] Compound **169** was prepared according to the procedure similar to that described in Scheme III from 5-amino-2-(4-methyl-3,4-dihydrobenzoxazin-7-yl)benzimidazole and 4-morpholinobenzoic acid. $[M+H]^+$ calcd for $C_{27}H_{27}N_5O_3$: 470.21; found: 496.96.

EXAMPLE 70

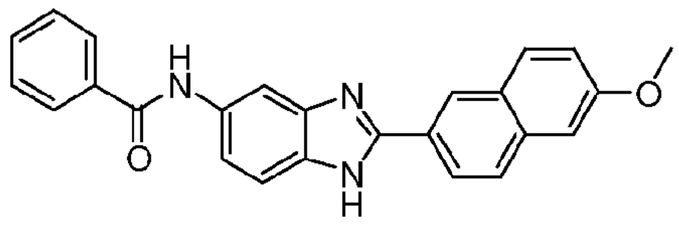
N-(2-(4-Phenoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **170**)



[0640] Compound **170** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-benzoaniline and 4-phenoxybenzaldehyde. $[M+H]^+$ calcd for $C_{26}H_{19}N_3O_2$: 406.16; found: 406.08.

EXAMPLE 71

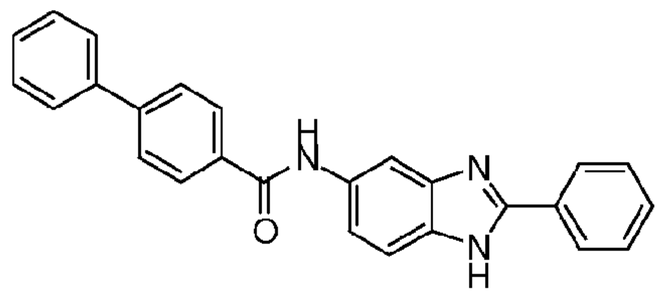
N-(2-(6-Methoxynaphthalen-2-yl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **171**)



[0641] Compound **171** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-benzoaniline and 6-methoxynaphthalene-2-carboxaldehyde. $[M+H]^+$ calcd for $C_{25}H_{19}N_3O_2$: 394.15; found: 394.10.

EXAMPLE 72

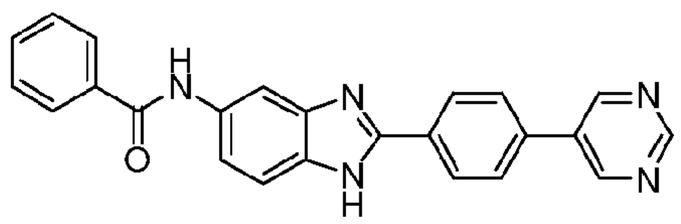
N-(2-Phenyl-1*H*-benzo[*d*]imidazol-5-yl)-[1,1'-biphenyl]-4-carboxamide (Compound **172**)



[0642] Compound **172** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-phenylbenzo)aniline and benzaldehyde. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.62 (s, 1H), 8.83 (m, 1H), 8.52 (d, *J* = 1.5 Hz, 1H), 8.23 (m, 2H), 8.13 (d, *J* = 8.5 Hz, 2H), 7.82 (d, *J* = 9 Hz, 3H), 7.79 (dd, *J* = 1.5, 9 Hz, 1H), 7.70 (dd, *J* = 1.5, 9 Hz, 2H), 7.73 (m, 3H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.44 (dt, *J* = 1, 7.5 Hz, 1H).

EXAMPLE 73

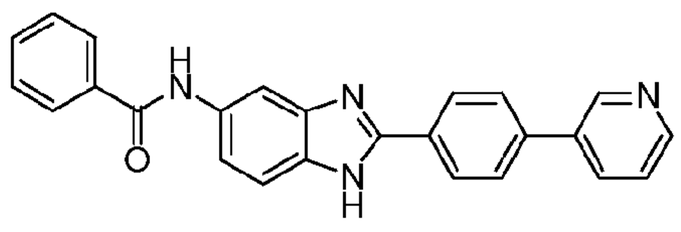
N-(2-(4-(pyrimidin-5-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **173**)



[0643] Compound **173** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-benzoaniline and 4-(pyrimidin-5-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{17}N_5O$: 392.15; found: 391.91.

EXAMPLE 74

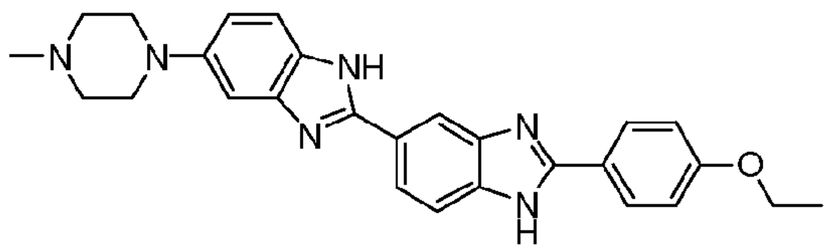
N-(2-(4-(pyridin-3-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **174**)



[0644] Compound **174** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-benzoaniline and 4-(pyridyl-3-)benzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{18}N_4O$: 391.16; found: 390.90.

EXAMPLE 75

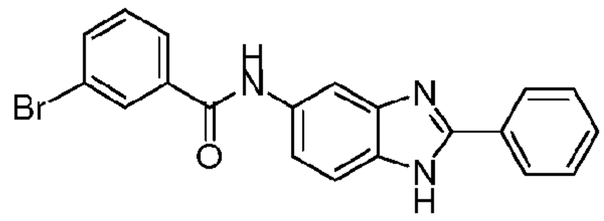
2'-(4-Ethoxyphenyl)-5-(4-methylpiperazin-1-yl)-1*H*,1'*H*-2,5'-bibenzo[*d*]imidazole (Compound **175**)



[0645] Compound **175** was prepared according to the procedure similar to that described in Scheme III from 5-(*N*-methylpiperizinyl)-2-(3,4-diaminophenyl)benzimidazole and 4-ethoxybenzaldehyde.

EXAMPLE 76

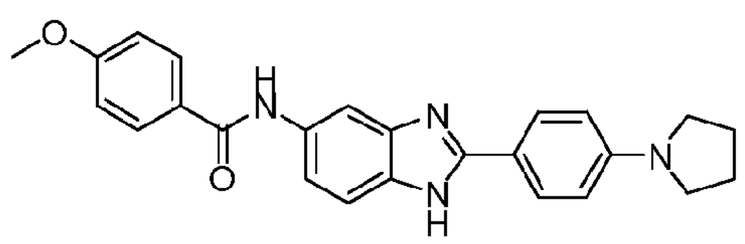
3-Bromo-*N*-(2-phenyl-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **176**)



[0646] Compound **176** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(3-bromobenzo)aniline and benzaldehyde. ^{1}H NMR (300MHz, Acetone-d_6) δ 9.77 (bs, 1H), 8.37 (s, 1H), 8.23 (d, J = 7 Hz, 2H), 8.18 (s, 1H), 8.04 (m, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.62-7.46 (m, 7H).

EXAMPLE 77

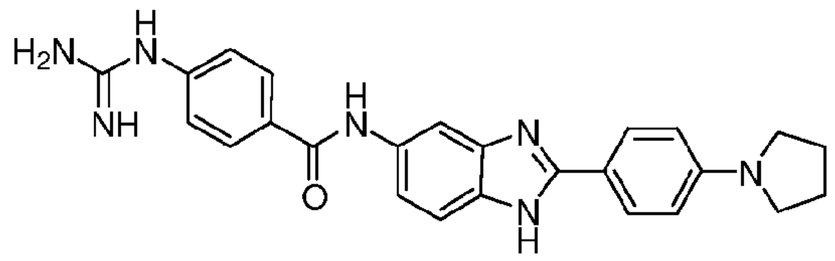
4-Methoxy-*N*-(2-(4-(pyrrolidin-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **177**)



[0647] Compound **177** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-methoxybenzo)aniline and 4-(pyrrolidin-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{24}N_4O_2$: 413.20; found: 413.51.

EXAMPLE 78

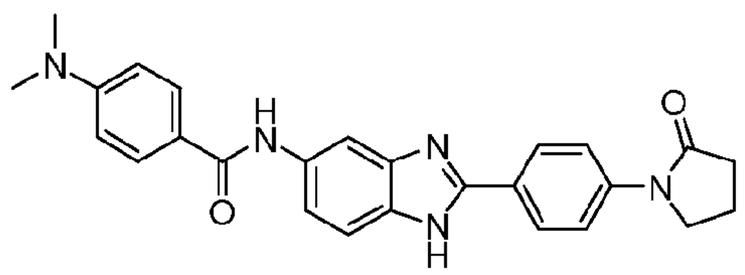
4-Guanidino-*N*-(2-(4-(pyrrolidin-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **178**)



[0648] Compound **178** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-amidinoaminobenzo)aniline and 4-(pyrrolidin-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{25}N_7O$: 440.22; found: 440.57.

EXAMPLE 79

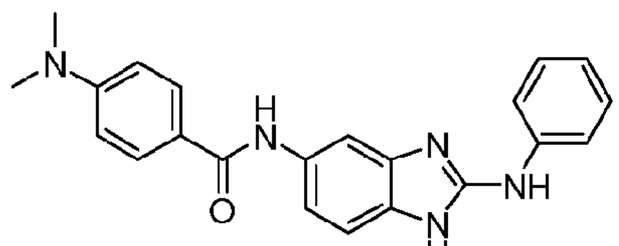
4-(Dimethylamino)-*N*-(2-(4-(2-oxopyrrolidin-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **179**)



[0649] Compound **179** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzo)aniline and 4-(pyrrolidon-1-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{26}H_{25}N_5O_2$: 440.20; found: 440.50.

EXAMPLE 80

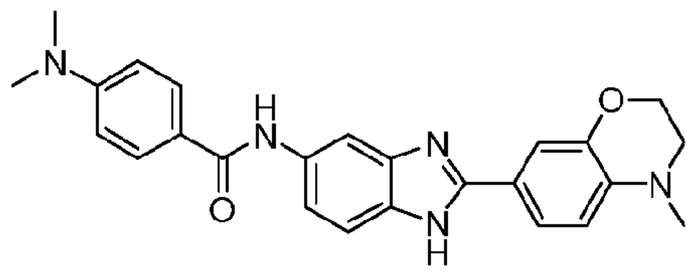
4-(Dimethylamino)-*N*-(2-(phenylamino)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **180**)



[0650] Compound **180** was prepared according to the procedure similar to that described in Scheme III from 4-dimethylaminobenzoic acid and 5-amino-2-phenylaminobenzimidazole. $[M+II]^+$ calcd for $C_{22}II_{22}N_5O$: 372.18; found: 371.95.

EXAMPLE 81

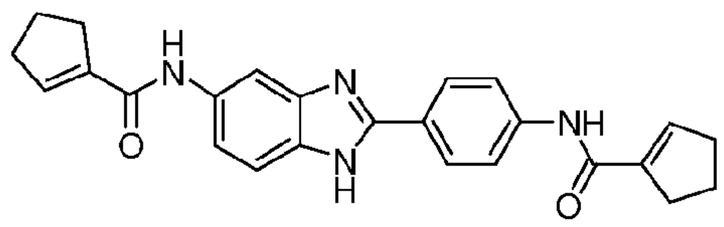
4-(Dimethylamino)-*N*-(2-(4-methyl-3,4-dihydro-2*H*-benzo[b][1,4]oxazin-7-yl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **181**)



[0651] Compound **181** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-dimethylaminobenzoyl)aniline and 1-methyl-2,3-dihydrobenzo[1,4]oxazine-6-carboxaldehyde. $[M+H]^+$ calcd for $C_{25}H_{25}N_5O_2$: 428.20; found: 428.49.

EXAMPLE 82

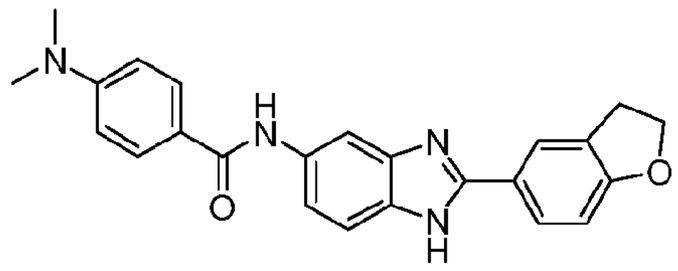
N-(4-(5-(cyclopent-1-enecarboxamido)-1*H*-benzo[*d*]imidazol-2-yl)phenyl)cyclopent-1-enecarboxamide (Compound **182**)



[0652] Compound **182** was prepared according to the procedure similar to that described in Scheme III from 5-amino-2-(4-aminophenyl)benzimidazole and 1-cyclohexenecarboxylic acid. $[M+H]^+$ calcd for $C_{25}H_{24}N_4O_2$: 413.20; found: 412.96.

EXAMPLE 83

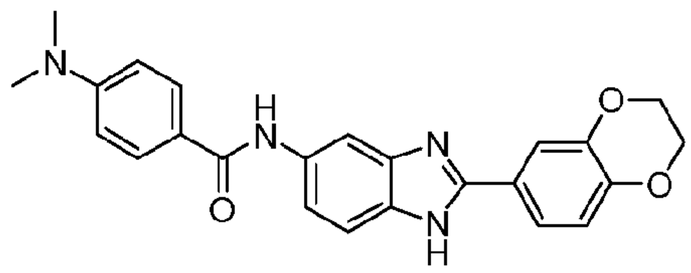
N-(2-(2,3-dihydrobenzofuran-5-yl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(dimethylamino)benzamide (Compound **183**)



[0653] Compound **183** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and 2,3-dihydrobenzofuran-5-carboxaldehyde. $[M+H]^+$ calcd for $C_{24}H_{24}N_4O_2$: 399.18; found: 399.47.

EXAMPLE 84

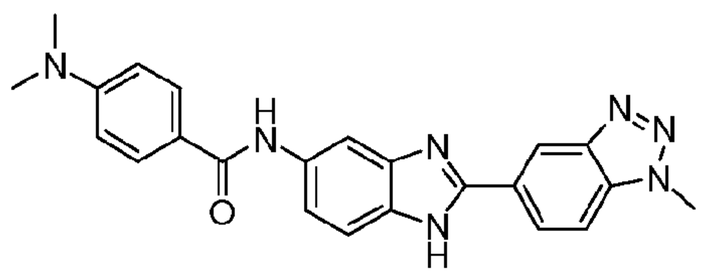
N-(2-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(dimethylamino)benzamide (Compound **184**)



[0654] Compound **184** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and benzo[1,4]dioxane-6-carboxaldehyde. $[M+H]^+$ calcd for $C_{24}H_{22}N_4O_3$: 415.17; found: 415.47.

EXAMPLE 85

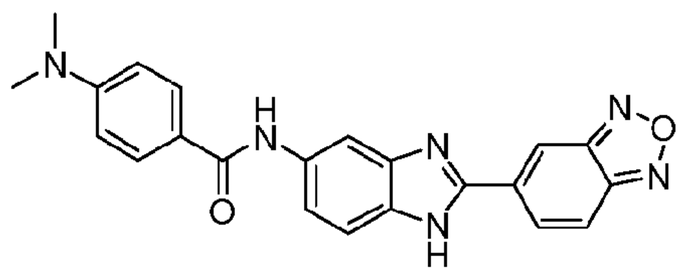
4-(dimethylamino)-*N*-(2-(1-methyl-1*H*-benzo[*d*][1,2,3]triazol-5-yl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **185**)



[0655] Compound **185** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-dimethylaminobenzoyl)aniline and 1-methylbenzotriazole-5-carboxaldehyde. $[M+H]^+$ calcd for $C_{23}H_{21}N_7O$: 412.18; found: 412.50.

EXAMPLE 86

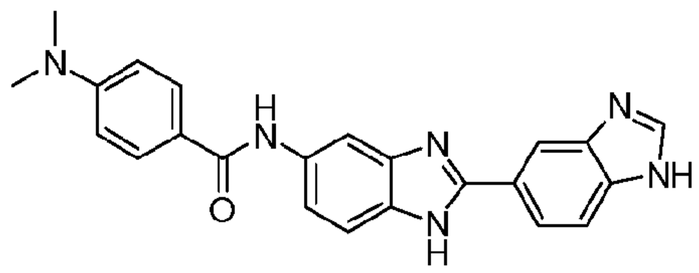
N-(2-(benzo[*c*][1,2,5]oxadiazol-5-yl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(dimethylamino)benzamide (Compound **186**)



[0656] Compound **186** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and benzofurazan-5-carboxaldehyde. $[M+H]^+$ calcd for $C_{22}H_{18}N_6O_2$: 399.15; found: 399.47.

EXAMPLE 87

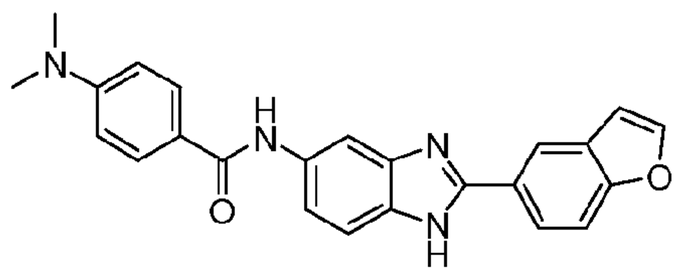
N-(1*H*,1'*H*-[2,5'-bibenzo[*d*]imidazol]-5-yl)-4-(dimethylamino)benzamide (Compound **187**)



[0657] Compound **187** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and benzimidazole-5-carboxaldehyde. $[M+H]^+$ calcd for $C_{23}H_{20}N_6O$: 397.17; found: 397.52.

EXAMPLE 88

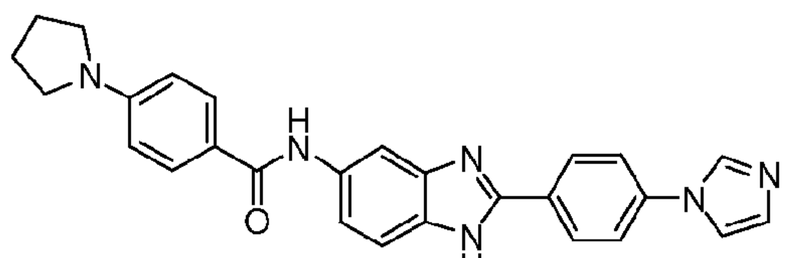
N-(2-(benzofuran-5-yl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(dimethylamino)benzamide (Compound **188**)



[0658] Compound **188** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and benzofuran-5-carboxaldehyde. $[M+H]^+$ calcd for $C_{24}H_{20}N_4O_2$: 397.16; found: 397.52.

EXAMPLE 89

2*N*-(2-(4-(1*H*-imidazol-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(pyrrolidin-1-yl)benzamide (Compound **189**)

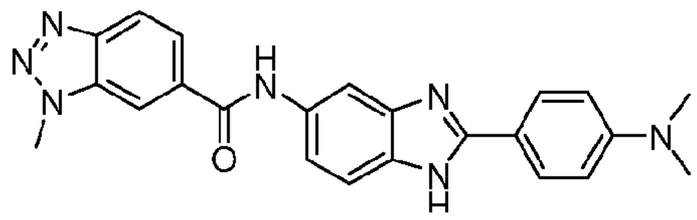


H

[0659] Compound **189** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-pyrrolidin-1-ylbenzoyl)aniline and 4-imidazolylbenzaldehyde. $[M+H]^+$ calcd for $C_{27}H_{24}N_6O$: 449.21; found: 449.48.

EXAMPLE 90

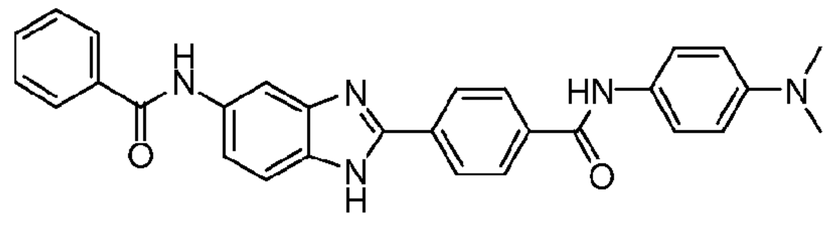
N-(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1-methyl-1*H*-benzo[*d*][1,2,3]triazole-6-carboxamide (Compound **190**)



[0660] Compound **190** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(1-methyl-6-benzotriazolylcarbonyl)aniline and 4-dimethylaminobenzaldehyde. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.74 (s, 1H), 8.78 (s, 1H), 8.43 (d, J = 1.5 Hz, 1H), 8.16 (dd, J = 1, 8.5 Hz, 1H), 8.10 (d, J = 9 Hz, 2H), 8.01 (d, J = 8.5 IIz, 2II), 7.84 (dd, J = 2, 9 IIz, 1II), 7.72 (d, J = 9 IIz, 1II), 6.96 (d, J = 9 IIz, 2II), 4.39 (s, 3H), 3.10 (s, 6H).

EXAMPLE 91

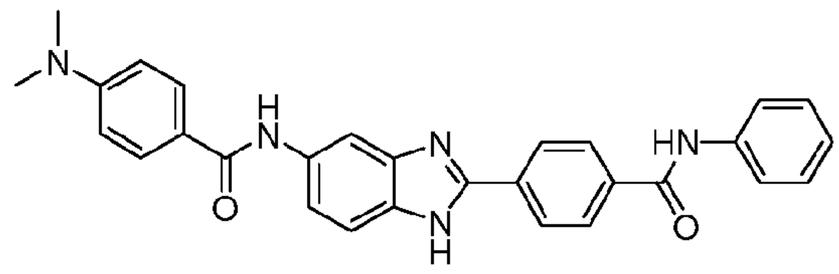
4-(5-benzamido-1*H*-benzo[*d*]imidazol-2-yl)-*N*-(4-(dimethylamino)phenyl)benzamide (Compound **191**)



[0661] Compound **191** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{25}N_5O_2$: 476.20; found: 475.98.

EXAMPLE 92

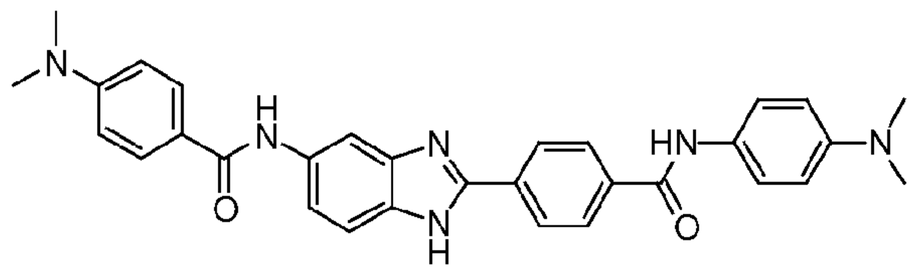
4-(dimethylamino)-*N*-(2-(4-(phenylcarbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **192**)



[0662] Compound **192** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-benzoylaniline and 4-(4-dimethylaminophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{25}N_5O_2$: 476.20; found: 475.91.

EXAMPLE 93

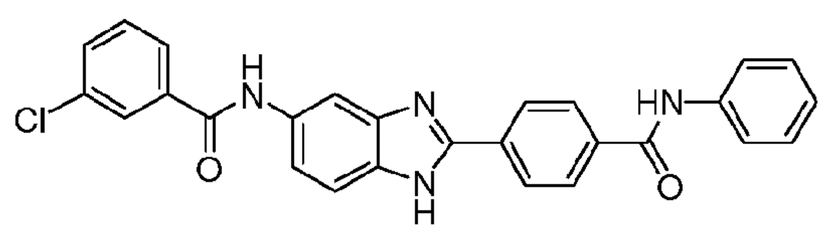
4-(dimethylamino)-*N*-(2-(4-((4-(dimethylamino)phenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **193**)



[0663] Compound **193** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and 4-(4-dimethylaminophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{30}N_6O_2$: 519.24; found: 519.04.

EXAMPLE 94

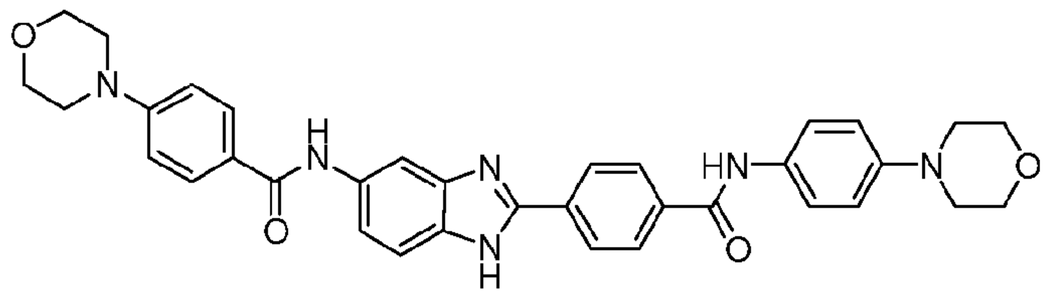
3-chloro-*N*-(2-(4-(phenylcarbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **194**)



[0664] Compound **194** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-chlorobenzoyl)aniline and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{27}H_{19}ClN_4O_2$: 467.12; found: 466.93.

EXAMPLE 95

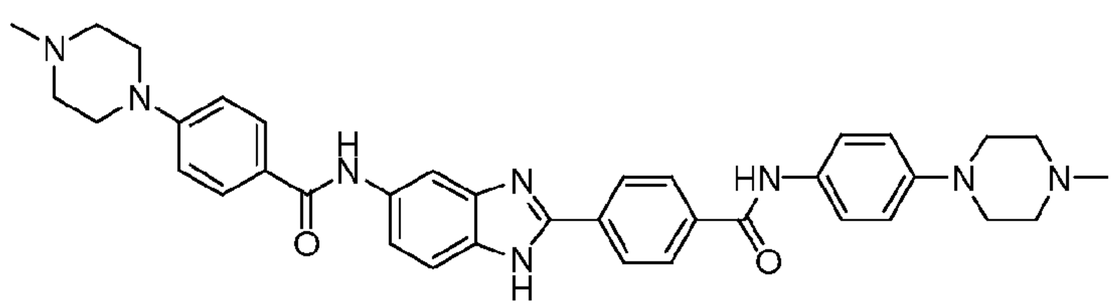
4-morpholino-*N*-(2-(4-((4-morpholinophenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **195**)



[0665] Compound **195** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholin-4-ylbenzoyl)aniline and 4-(4-morpholinylphenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{35}H_{34}N_6O_4$: 603.26; found: 603.36.

EXAMPLE 96

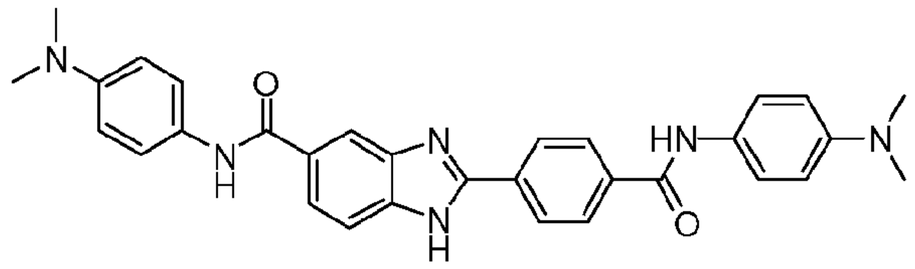
4-(4-methylpiperazin-1-yl)-*N*-(2-(4-((4-(4-methylpiperazin-1-yl)phenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **196**)



[0666] Compound **196** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-(4-methylpiperazin-1-yl)benzoyl)aniline and 4-(4-(4-methylpiperazin-1-yl)phenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{37}H_{40}N_8O_2$: 629.33; found: 629.16.

EXAMPLE 97

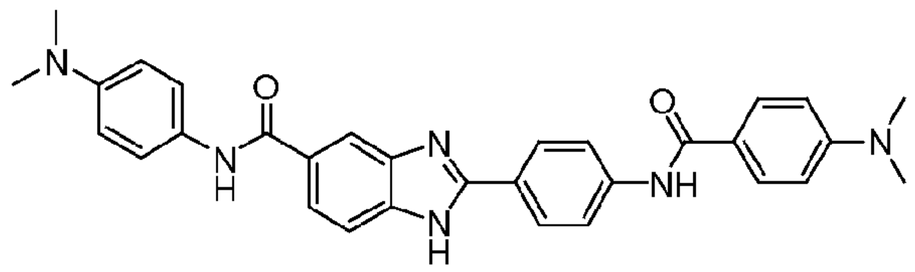
N-(4-(dimethylamino)phenyl)-2-(4-((4-(dimethylamino)phenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide (Compound **197**)



[0667] Compound **197** was prepared according to the procedure similar to that described in Scheme III from *N*-(4-dimethylaminophenyl)-3,4-dinitrobenzamide and 4-(4-dimethylaminophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{30}N_6O_2$: 519.24; found: 519.04.

EXAMPLE 98

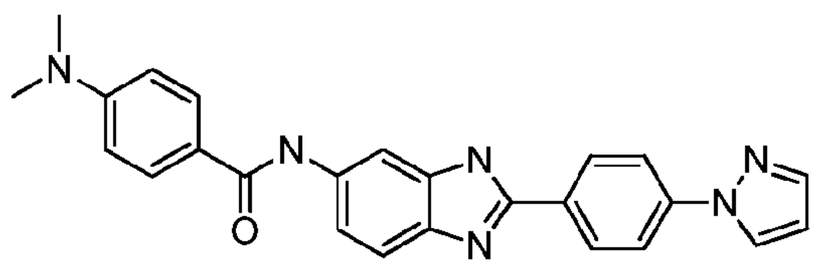
2-(4-(4-(dimethylamino)benzamido)phenyl)-*N*-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide (Compound **198**)



[0668] Compound **198** was prepared according to the procedure similar to that described in Scheme III from *N*-(4-dimethylaminophenyl)-3,4-dinitrobenzamide and 4-(4-dimethylaminobenz)amidobenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{30}N_6O_2$: 519.24; found: 518.97.

EXAMPLE 99

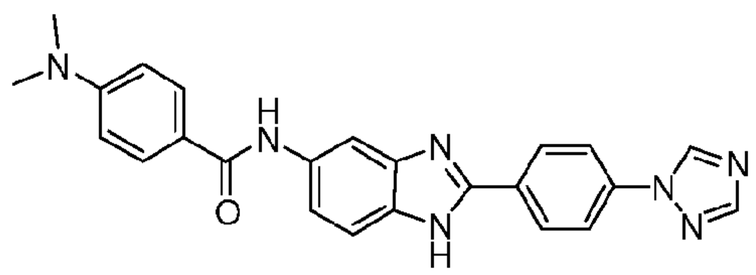
N-(2-(4-(1*H*-pyrazol-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-6-yl)-4-(dimethylamino)benzamide (Compound **199**)



[0669] Compound **199** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-dimethylaminobenzoyl)aniline and 4-imidazolylbenzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{22}N_6O$: 423.20; found: 423.01.

EXAMPLE 100

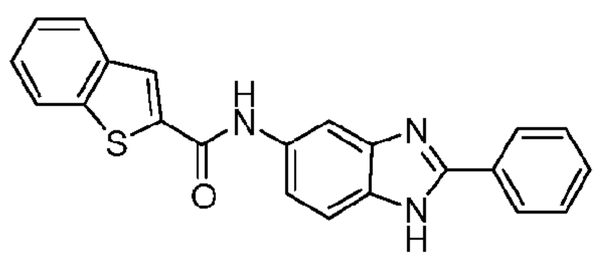
N-(2-(4-(1*H*-1,2,4-triazol-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(dimethylamino)benzamide (Compound **200**)



[0670] Compound **200** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and 4-(1,2,4-triazolyl-1-)benzaldehyde. $[M+II]^+$ calcd for $C_{24}II_{21}N_7O$: 424.19; found: 424.02.

EXΛMPLE 101

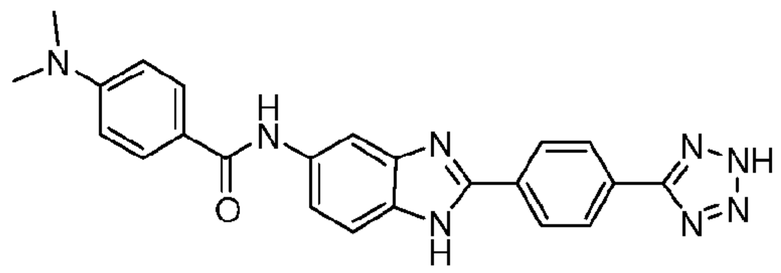
N-(2-phenyl-1*H*-benzo[*d*]imidazol-5-yl)benzo[*b*]thiophene-2-carboxamide (Compound **201**)



[0671] Compound **201** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)benzo[*b*]thiophene-2-carboxamide and benzaldehyde. ^{1}H NMR (500MHz, CD_3OD) δ 8.18 (d, *J* = 2 Hz, 1H), 8.14 (s, 1H), 8.06 (d, *J* = 8 Hz, 2H), 7.91 (m, 2H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.53 (m, 3H), 7.44 (m, 3H).

EXAMPLE 102

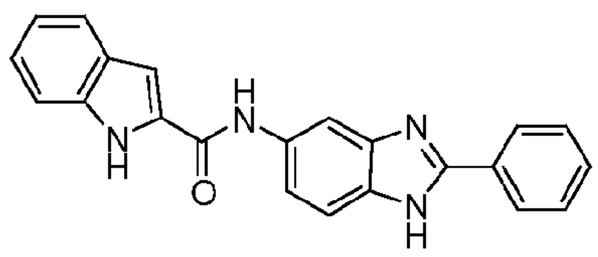
N-(2-(4-(2*H*-tetrazol-5-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(dimethylamino)benzamide (Compound **202**)



[0672] Compound **202** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and 4-(1,2,3,5-tetrazolyl-5-)benzaldehyde. $[M+H]^+$ calcd for $C_{23}H_{20}N_8O$: 415.19; found: 424.97.

EXAMPLE 103

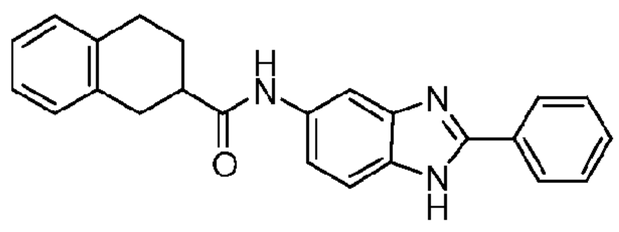
N-(2-phenyl-1*H*-benzo[*d*]imidazol-5-yl)-1*H*-indole-2-carboxamide (Compound **203**)



[0673] Compound **203** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(indol-2-oyl)aniline and benzaldehyde. ^1H NMR (500MHz, CD_3OD) δ 8.20 (d, *J* = 1.5 Hz, 1H), 8.09 (dd, *J* = 1.5, 8 Hz, 2H). 7.66 (d, *J* = 8 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.57 - 7.52 (m, 4H), 7.48 (dd, *J* = 0.5, 8 Hz, 1H), 7.34 (s, 1H), 7.25 (dt, *J* = 1, 7 Hz, 1H), 7.09 (dt, *J* = 0.5, 8 Hz, 1H).

EXAMPLE 104

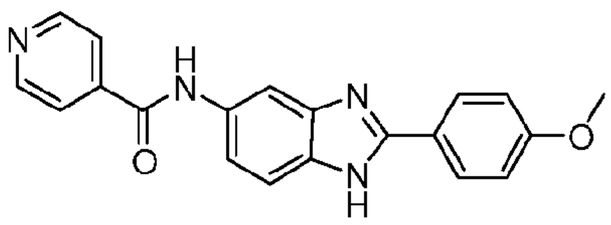
N-(2-phenyl-1*H*-benzo[*d*]imidazol-5-yl)-1,2,3,4-tetrahydronaphthalene-2-carboxamide (Compound **204**)



[0674] Compound **204** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(1,2,3,4-tetrahydronaphthalen-2-oyl)aniline and benzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{21}N_3O$: 368.17; found: 368.00.

EXAMPLE 105

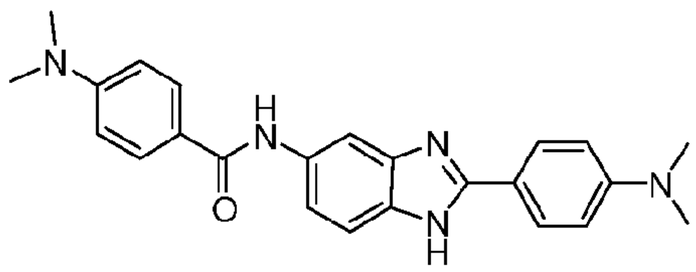
N-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)isonicotinamide (Compound **205**)



[0675] Compound **205** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(pyridin-4-oyl)aniline and 4-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{20}H_{16}N_4O_2$: 345.13; found: 345.00.

EXAMPLE 106

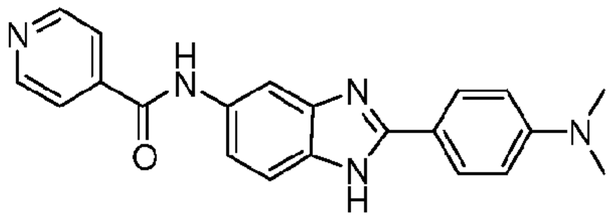
4-(dimethylamino)-*N*-(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **206**)



[0676] Compound **206** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzoyl)aniline and 4-dimethylaminobenzaldehyde. ^{1}H NMR (300MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.39 (s, 1H), 8.11 (d, J = 8 Hz, 2H), 7.90 (d, J = 9 Hz, 2H), 7.81 (d, J = 9 Hz, 2H), 7.68 (d, J = 9 Hz, 2H), 6.95 (d, J = 9 Hz, 2H), 6.78 (d, J = 9 Hz, 2H), 3.07 (s, 6H), 2.99 (s, 6H).

EXAMPLE 107

N-(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)isonicotinamide (Compound **207**)

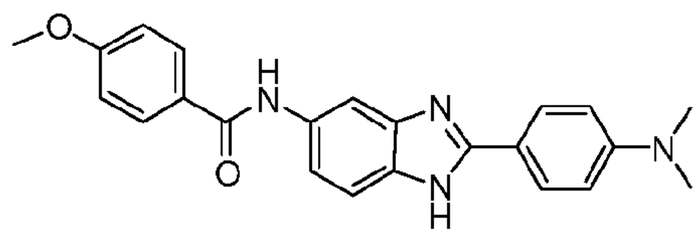


[0677] Compound **207** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(pyridin-4-oyl)aniline and 4-dimethylaminobenzaldehyde. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.90 (s, 1H), 8.83 (d, J = 6 Hz, 2H), 8.40 (s, 1H), 8.10 (d, J = 9 Hz, 2H), 7.98 (d, J = 6 Hz, 2H), 7.81 (dd, J = 2, 9 Hz, 1H), 7.75 (d, J = 9 Hz, 1H), 6.97 (d, J = 9 Hz, 2H), 3.09 (s, 6H).

EXAMPLE 108

N-(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-methoxybenzamide

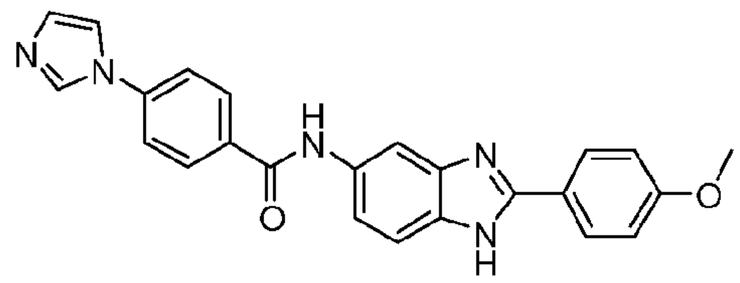
(Compound **208**)



[0678] Compound **208** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-methoxybenzoyl)aniline and 4-dimethylaminobenzaldehyde. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.41 (s, 1H), 8.39 (d, J = 1.5 IIz, 1II), 8.08 (d, J = 9.5 IIz, 2II), 8.01 (d, J = 7 IIz, 2II), 7.79 (dd, J = 2, 9 IIz, 1II), 7.67 (d, J = 9 Hz, 1H), 7.09 (d, J = 9 Hz, 2H), 6.96 (d, J = 9 Hz, 2H), 3.82 (s, 3H), 3.08 (s, 6H).

EXAMPLE 109

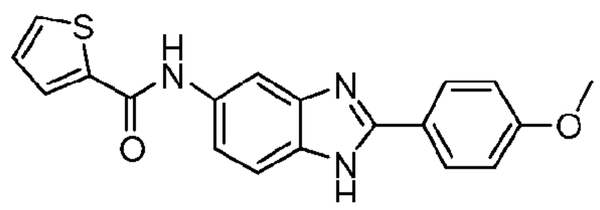
4-(1*H*-imidazol-1-yl)-*N*-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **209**)



[0679] Compound **209** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-imidazol-1-ylbenzoyl)aniline and 4-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{19}N_5O_2$: 410.05; found: 410.00.

EXAMPLE 110

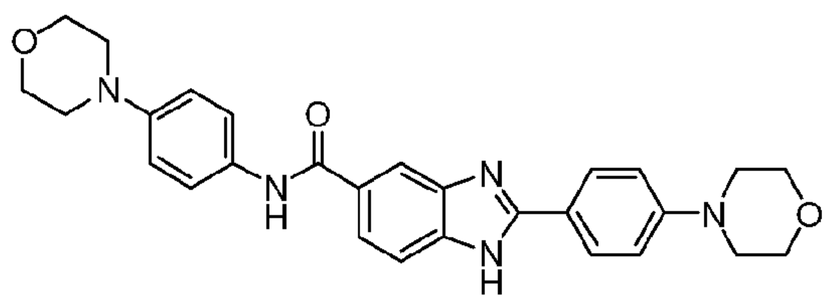
N-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)thiophene-2-carboxamide (Compound **210**)



[0680] Compound **210** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(thien-2-oyl)aniline and 4-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{19}H_{15}N_3O_2S$: 350.09; found: 349.89.

EXAMPLE 111

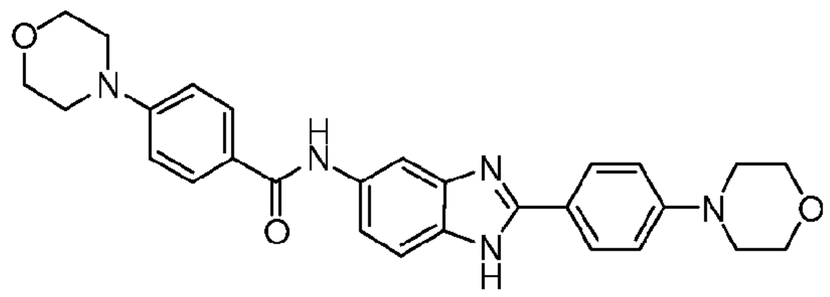
N,2-bis(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide (Compound **211**)



[0681] Compound **211** was prepared according to the procedure similar to that described in Scheme III from *N*-(4-morpholinylphenyl)-3,4-dinitrobenzamide and 4-morpholinylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O_3$: 484.23; found: 483.92.

EXAMPLE 112

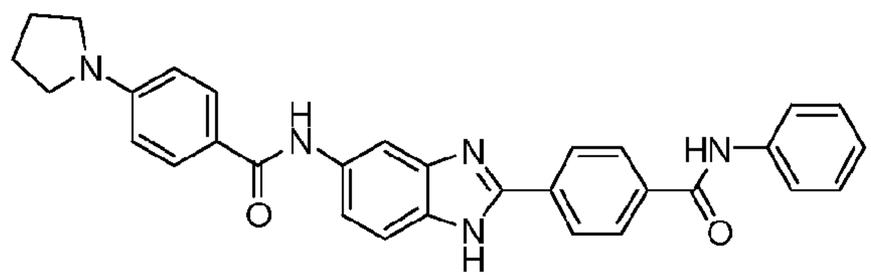
4-morpholino-*N*-(2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **212**)



[0682] Compound **212** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholin-4-ylbenzoyl)aniline and 4-morpholinylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O_3$: 484.23; found: 483.94.

EXAMPLE 113

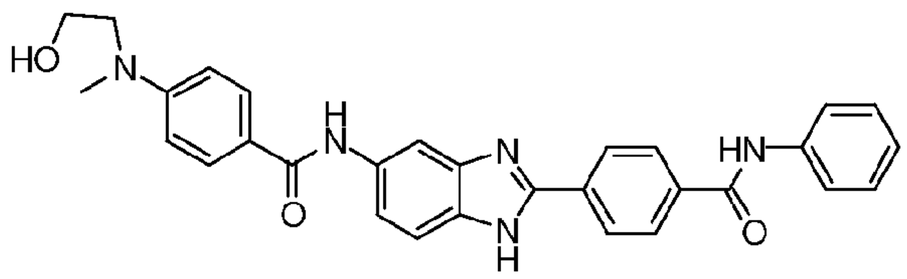
N-phenyl-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **213**)



[0683] Compound **213** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{27}N_5O_2$: 502.23; found: 502.03.

EXAMPLE 114

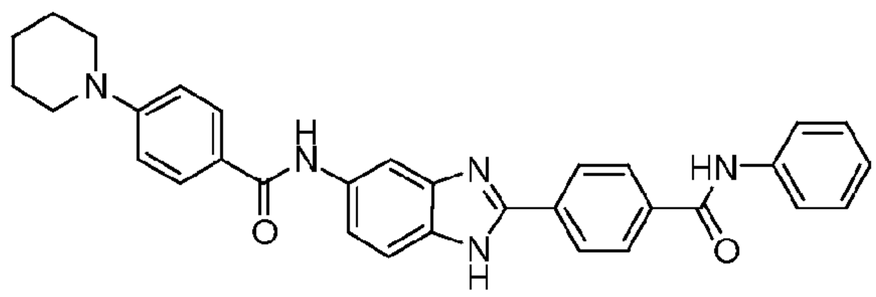
4-((2-hydroxyethyl)(methyl)amino)-*N*-(2-(4-(phenylcarbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **214**)



[0684] Compound **214** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(*N*-methyl-*N*-2-hydroxyethylamino)benzamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{30}H_{27}N_5O_3$: 506.22; found: 506.01

EXAMPLE 115

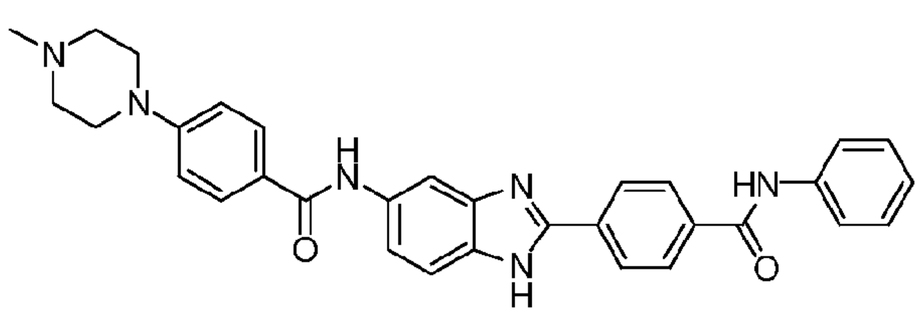
N-phenyl-4-(5-(4-(piperidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **215**)



[0685] Compound **215** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-piperidinylbenzamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{32}H_{29}N_5O_2$: 516.24; found: 516.07.

EXAMPLE 116

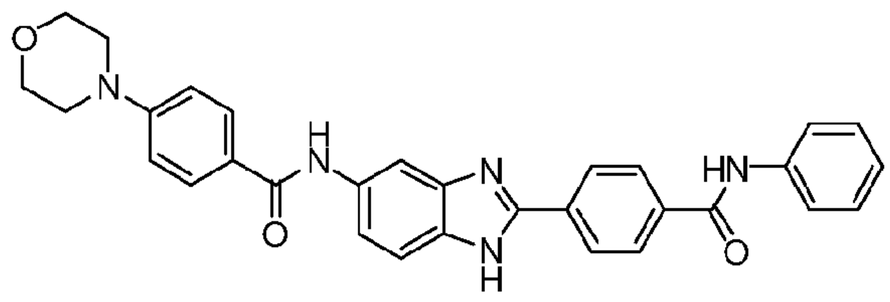
4-(4-methylpiperazin-1-yl)-*N*-(2-(4-(phenylcarbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **216**)



[0686] Compound **216** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(1-methyl-4-piperazinyl)benzamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{32}H_{30}N_6O_2$: 531.25; found: 531.05.

EXAMPLE 117

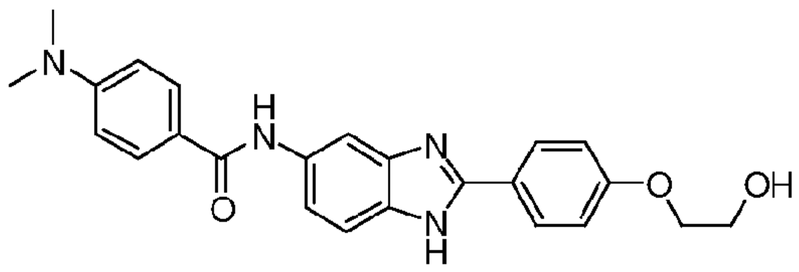
4-morpholino-*N*-(2-(4-(phenylcarbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **217**)



[0687] Compound **217** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-morpholinylbenzamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{27}N_5O_3$: 518.22; found: 518.03.

EXAMPLE 118

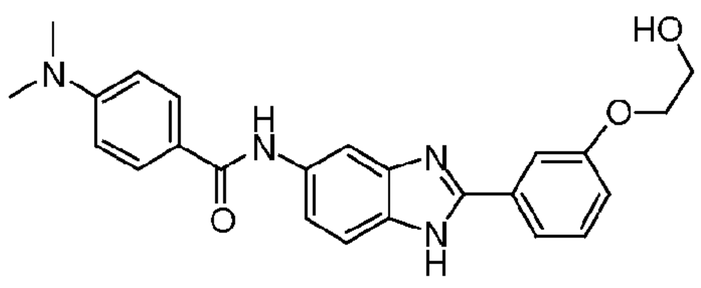
4-(dimethylamino)-*N*-(2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **218**)



[0688] Compound **218** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-dimethylaminobenzamide and 4-(2-hydroxyethyloxy)benzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{24}N_4O_3$: 417.19; found: 417.00.

EXAMPLE 119

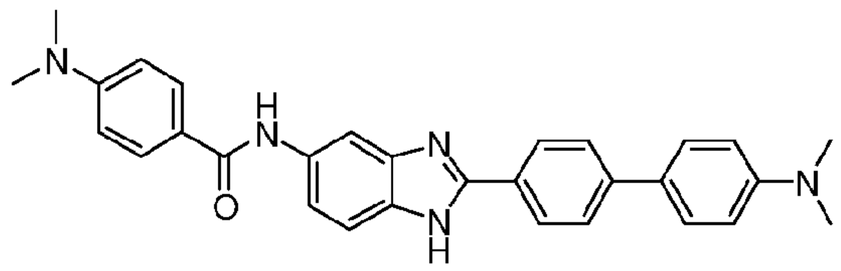
4-(dimethylamino)-*N*-(2-(3-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **219**)



[0689] Compound **219** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-dimethylaminobenzamide and 3-(2-hydroxyethyloxy)benzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{24}N_4O_3$: 417.19; found: 416.94.

EXAMPLE 120

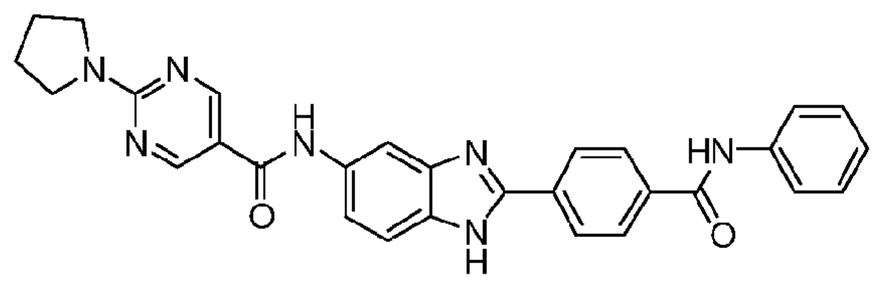
4-(dimethylamino)-*N*-(2-(4'-(dimethylamino)-[1,1'-biphenyl]-4-yl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **220**)



[0690] Compound **220** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-dimethylaminobenzamide and 4-(4-dimethylaminophenyl)benzaldehyde. $[M+H]^+$ calcd for $C_{30}H_{29}N_5O$: 476.24; found: 475.98.

EXAMPLE 121

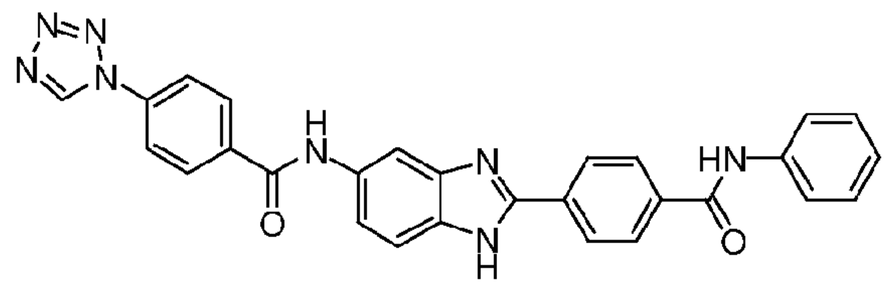
N-(2-(4-(phenylcarbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-2-(pyrrolidin-1-yl)pyrimidine-5-carboxamide (Compound **221**)



[0691] Compound **221** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-2-(pyrrolidin-1-yl)pyrimidine-5-carboxamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{25}N_7O_2$: 504.22; found: 503.92.

EXAMPLE 122

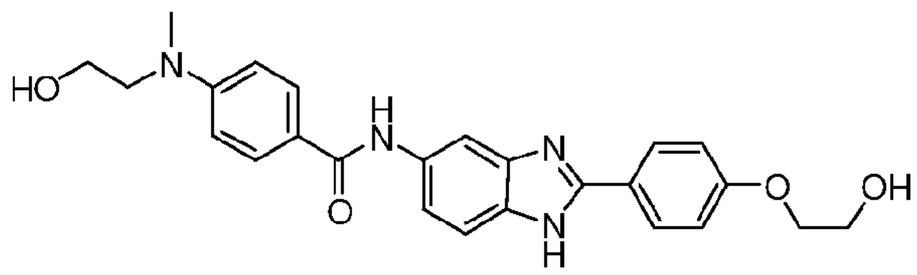
4-(5-(4-(1*H*-tetrazol-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)-*N*-phenylbenzamide (Compound **222**)



[0692] Compound **222** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-tetrazolylbenzamide and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{20}N_8O_2$: 501.18; found: 500.88.

EXAMPLE 123

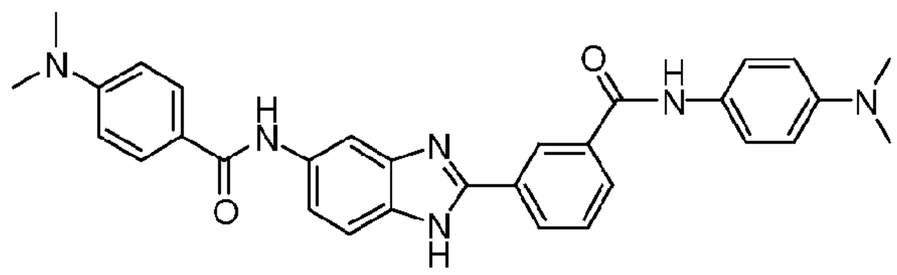
N-(2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-((2-hydroxyethyl)(methyl)amino)benzamide (Compound **223**)



[0693] Compound **223** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(*N*-methyl-*N*-2-hydroxyethylamino)benzamide and 4-(2-hydroxyethyloxy)benzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{26}N_4O_4$: 447.21; found: 446.89.

EXAMPLE 124

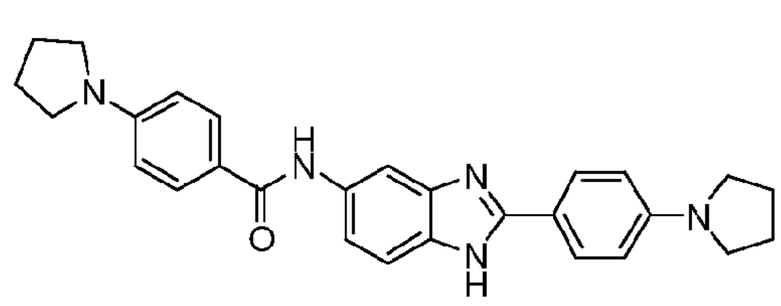
3-(5-(4-(dimethylamino)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)-*N*-(4-(dimethylamino)phenyl)benzamide (Compound **224**)



[0694] Compound **224** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-dimethylaminobenzo)aniline and 3-(4-dimethylaminophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{30}N_6O_2$: 519.25; found: 519.04.

EXAMPLE 125

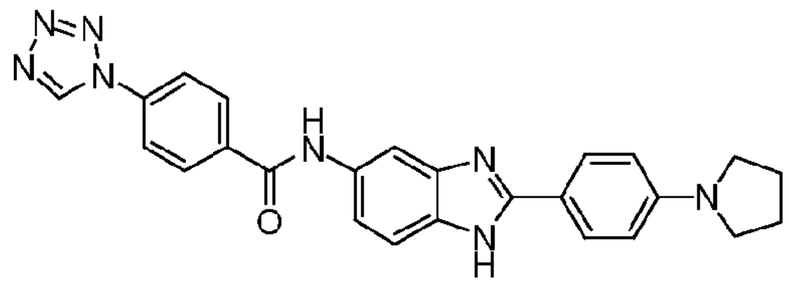
4-(pyrrolidin-1-yl)-*N*-(2-(4-(pyrrolidin-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **225**)



[0695] Compound **225** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-pyrrolidinylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O$: 452.25; found: 451.95.

EXAMPLE 126

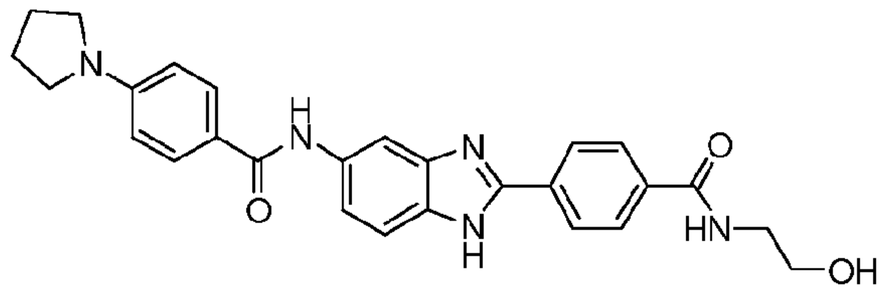
N-(2-(4-(pyrrolidin-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(1*H*-tetrazol-1-yl)benzamide (Compound **226**)



[0696] Compound **226** was prepared according to the procedure similar to that described in Scheme III from N-(3,4-dinitrophenyl)-4-tetrazolylbenzamide and 4-pyrrolidinylbenzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{22}N_8O$: 451.20; found: 451.50.

EXAMPLE 127

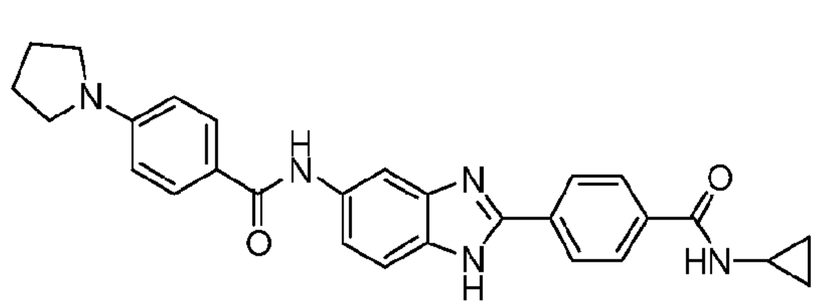
N-(2-hydroxyethyl)-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **227**)



[0697] Compound **227** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-(2-hydroxyethyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{27}H_{27}N_5O_3$: 470.22; found: 469.58.

EXAMPLE 128

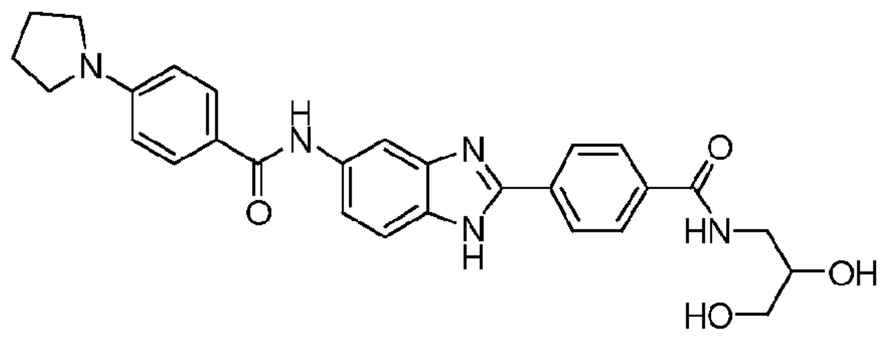
N-cyclopropyl-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **228**)



[0698] Compound **228** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-cyclopropylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{27}N_5O_2$: 466.23; found: 466.55.

EXAMPLE 129

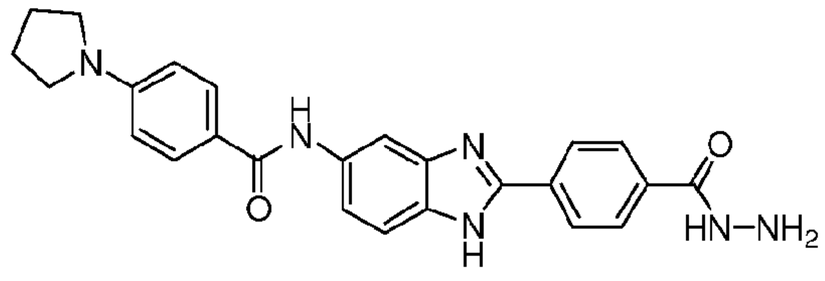
N-(2,3-dihydroxypropyl)-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **229**)



[0699] Compound **229** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-(2,3-dihydroxypropyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O_4$: 500.23; found: 500.56.

EXAMPLE 130

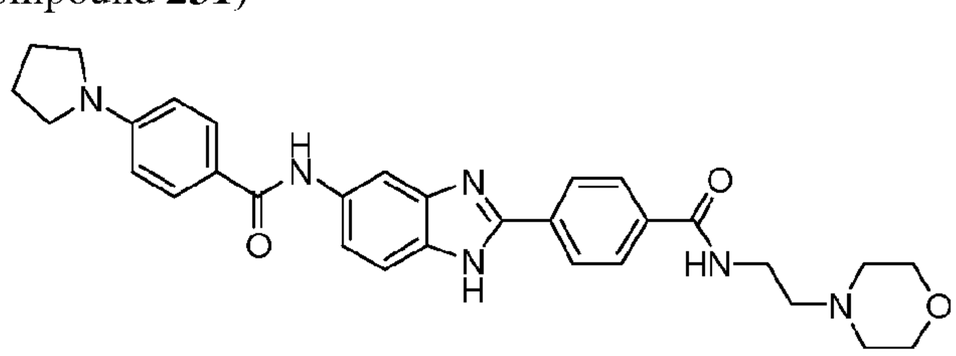
N-(2-(4-(hydrazinecarbonyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(pyrrolidin-1-yl)benzamide (Compound **230**)



[0700] Compound **230** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-hydrazinylcarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{24}N_6O_2$: 441.21; found: 441.51.

EXAMPLE 131

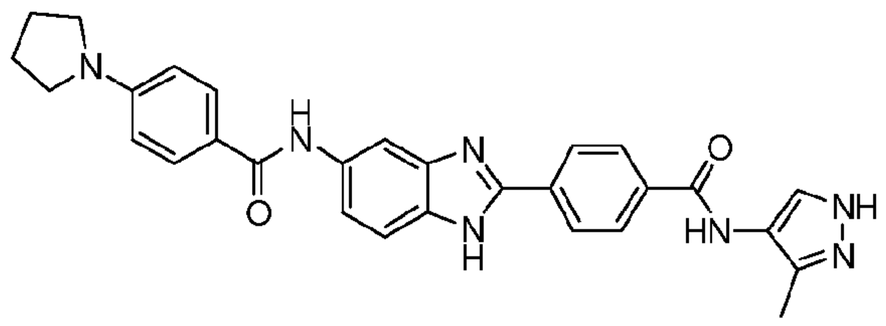
N-(2-morpholinoethyl)-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **231**)



[0701] Compound 231 was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-(2-morpholinylethyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{34}N_6O_3$: 539.28; found: 539.63.

EXAMPLE 132

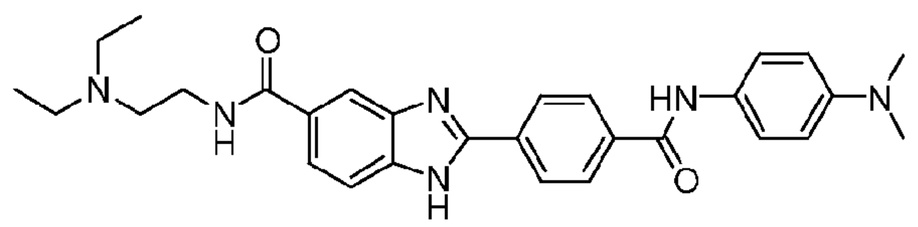
N-(3-methyl-1*H*-pyrazol-4-yl)-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **232**)



[0702] Compound **232** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-(3-methyl-4-pyrazolyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{27}N_7O_2$: 506.23; found: 506.25.

EXAMPLE 133

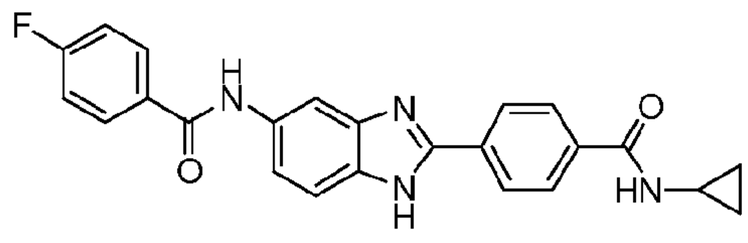
N-(2-(diethylamino)ethyl)-2-(4-((4-(dimethylamino)phenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide (Compound **233**)



[0703] Compound **233** was prepared according to the procedure similar to that described in Scheme III from *N*-(2-*N*,*N*-diethylaminoethyl)-dinitrophenyl)-3,4-dinitrobenzamide and 4-(4-dimethylaminophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{34}N_6O_2$: 499.27; found: 499.61.

EXAMPLE 134

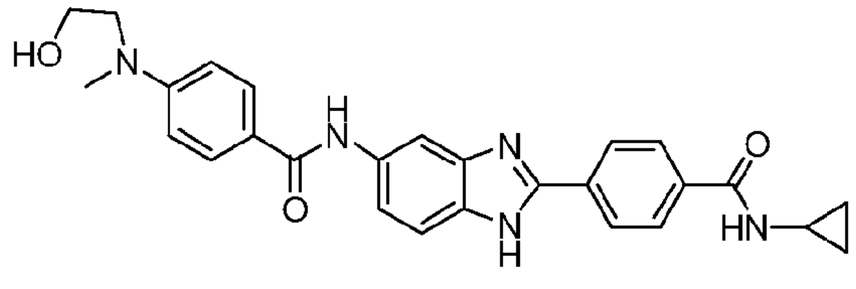
N-cyclopropyl-4-(5-(4-fluorobenzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **234**)



[0704] Compound **234** was prepared according to the procedure similar to that described in Scheme III from N-(3,4-dinitrophenyl)-4-fluorobenzamide and 4-cyclopropylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{19}FN_4O_2$: 415.16; found: 415.53.

EXAMPLE 135

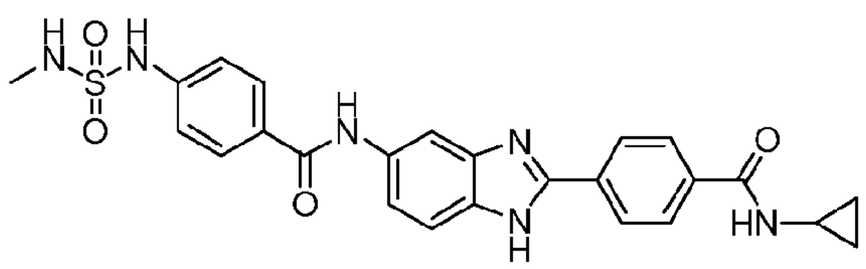
N-cyclopropyl-4-(5-(4-((2-hydroxyethyl)(methyl)amino)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **235**)



[0705] Compound **235** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(*N*-2-hydroxyethyl-*N*-methylamino)benzamide and 4-cyclopropylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{27}H_{27}N_5O_3$: 470.22; found: 470.60.

EXAMPLE 136

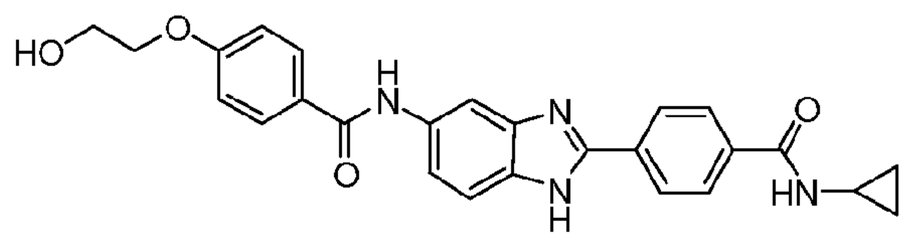
N-cyclopropyl-4-(5-(4-((*N*-methylsulfamoyl)amino)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **236**)



[0706] Compound **236** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-methylaminosulfonamido)benzamide and 4-cyclopropylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{25}H_{24}N_6O_4S$: 505.17; found: 504.47.

EXAMPLE 137

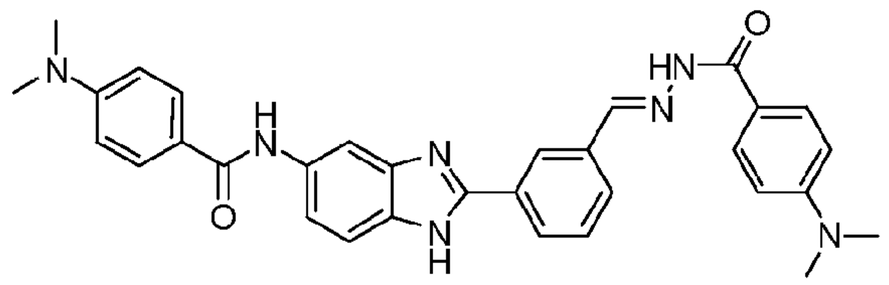
N-cyclopropyl-4-(5-(4-(2-hydroxyethoxy)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **237**)



[0707] Compound **237** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(2-hydroxyethoxy)benzamide and 4-cyclopropylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{26}H_{24}N_4O_4$: 457.19; found: 457.51.

EXAMPLE 138

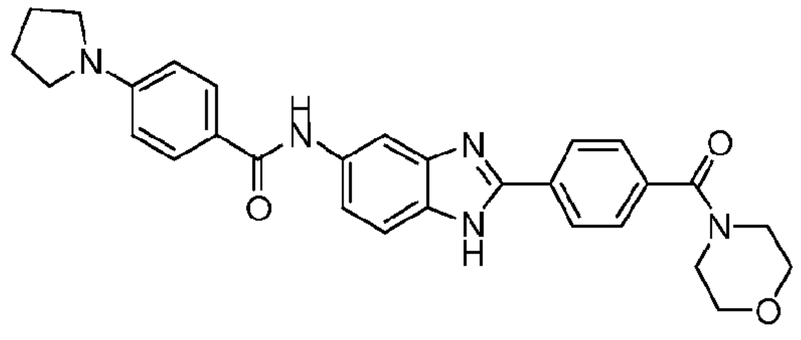
(*E*)-4-(dimethylamino)-*N*-(2-(3-((2-(4-(dimethylamino)benzoyl)hydrazono)methyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **238**)



[0708] Compound **238** was prepared according to the procedure described in Scheme I from 4-dimethylaminobenzohydrazide and 3-(5-(4-dimethylaminobenzamido)benzimidazolyl-2-)benzaldehyde. $[M+H]^+$ calcd for $C_{32}H_{31}N_7O_2$: 546.26; found: 546.65.

EXAMPLE 139

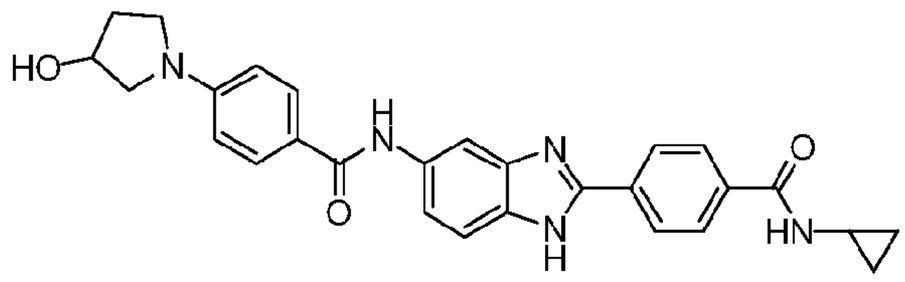
N-(2-(4-(morpholine-4-carbonyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(pyrrolidin-1-yl)benzamide (Compound **239**)



[0709] Compound **239** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-morpholinylcarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{29}N_5O_3$: 496.24; found: 496.25.

EXAMPLE 140

N-cyclopropyl-4-(5-(4-(3-hydroxypyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **240**)

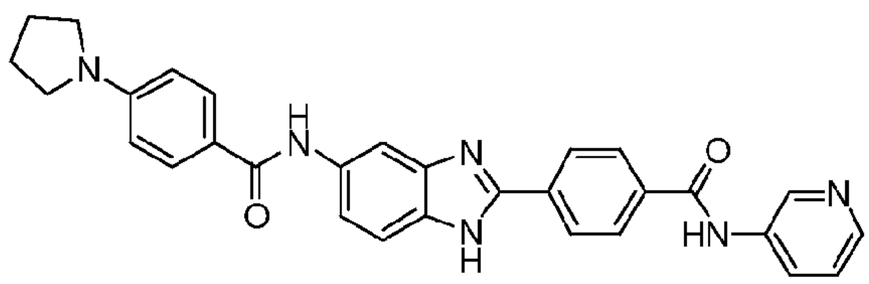


[0710] Compound **240** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(3-hydroxypyrrolidinyl)benzamide and

4-cyclopropyl aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{27}N_5O_3$: 482.22; found: 481.93.

EXAMPLE 141

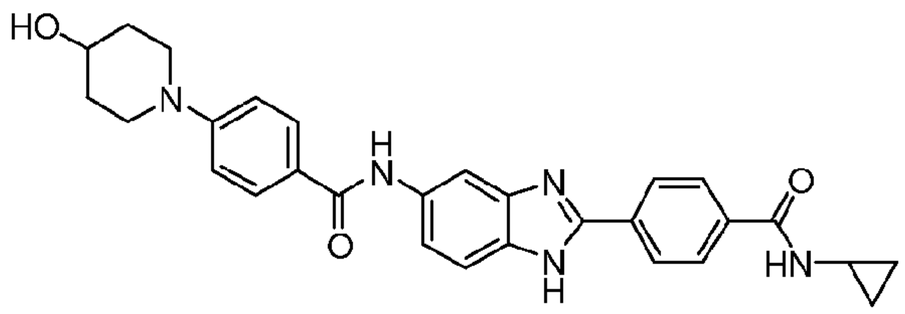
N-(pyridin-3-yl)-4-(5-(4-(pyrrolidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **241**)



[0711] Compound **241** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 4-(3-pyridinylaminocarbonyl)benzaldehyde. $[M+H]^+$ calcd for $C_{30}H_{26}N_6O_2$: 503.22; found: 502.97.

EXAMPLE 142

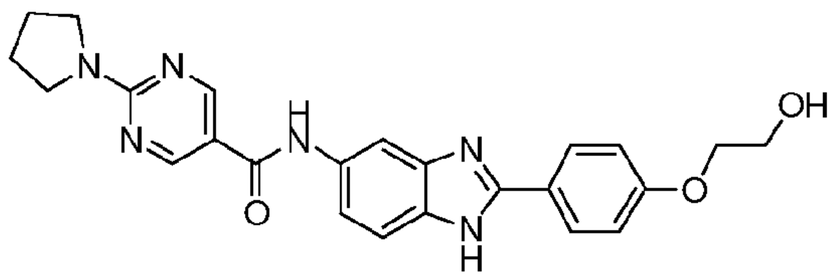
N-cyclopropyl-4-(5-(4-(4-hydroxypiperidin-1-yl)benzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **242**)



[0712] Compound **242** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(2-hydroxypiperidinyl)benzamide and 4-cyclopropyl aminocarbonylbenzaldehyde. $[M+II]^+$ calcd for $C_{29}II_{29}N_5O_3$: 496.24; found: 495.95.

EXAMPLE 143

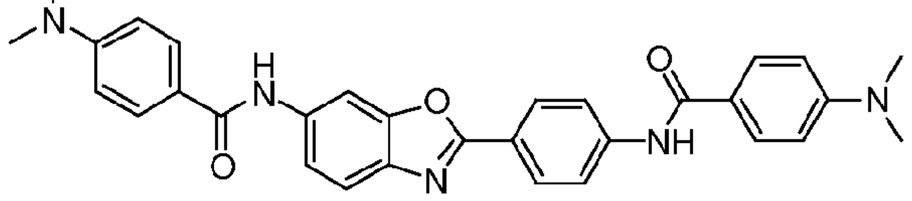
N-(2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-2-(pyrrolidin-1-yl)pyrimidine-5-carboxamide (Compound **243**)



[0713] Compound **243** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-2-(pyrrolidin-1-yl)pyrimidine-5-carboxamide and 4-(2-hydroxyethoxy)benzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{24}N_6O_3$: 445.20; found: 444.87.

EXAMPLE 144

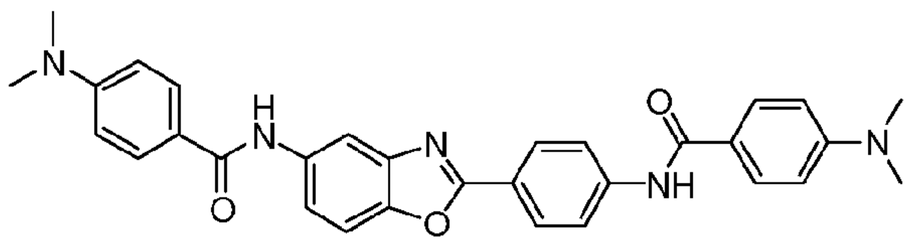
4-(dimethylamino)-*N*-(4-(6-(4-(dimethylamino)benzamido)benzo[*d*]oxazol-2-yl)phenyl)benzamide (Compound **244**)



[0714] Compound **244** was prepared according to the procedure similar to that described in Scheme III from *N*-(3-hydoxy-4-nitro)phenyl-4-dimethylaminobenzamide and 4-(4-dimethylaminobenz)amidobenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{29}N_5O_3$: 520.23; found: 520.60.

EXAMPLE 145

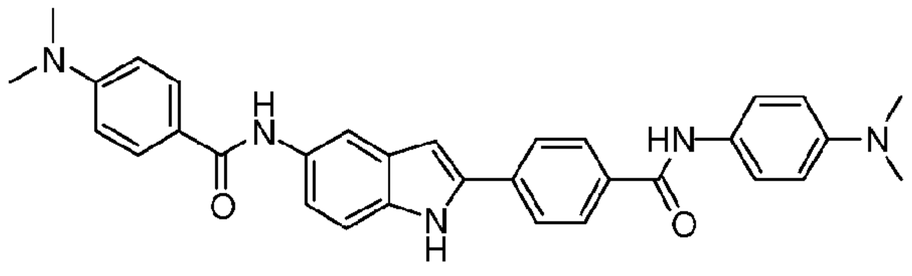
4-(dimethylamino)-*N*-(4-(5-(4-(dimethylamino)benzamido)benzo[*d*]oxazol-2-yl)phenyl)benzamide (Compound **245**)



[0715] Compound **245** was prepared according to the procedure similar to that described in Scheme III from *N*-(4-hydoxy-3-nitro)phenyl-4-dimethylaminobenzamide and 4-(4-dimethylaminobenz)amidobenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{29}N_5O_3$: 520.23; found: 520.60.

Example 146

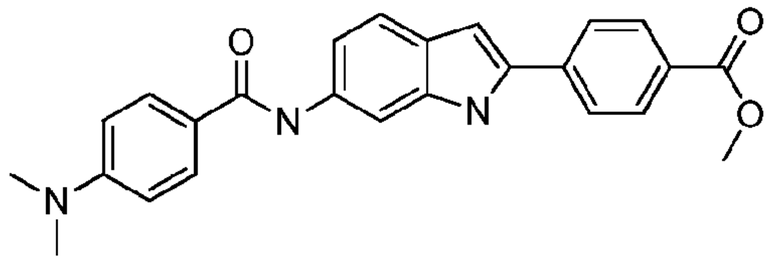
4-(dimethylamino)-*N*-(2-(4-((4-(dimethylamino)phenyl)carbamoyl)phenyl)-1*H*-indol-5-yl)benzamide (Compound **246**)



[0716] Compound **246** was prepared according to the procedure similar to that described in Scheme III from 5-nitro-2-(4-methoxycarbonylphenyl)indole, 4-dimethylaminoaniline, and 4-dimethylaminobenzoic acid. $[M+H]^+$ calcd for $C_{31}H_{30}N_6O_2$: 519.25; found: 519.59.

EXAMPLE 147

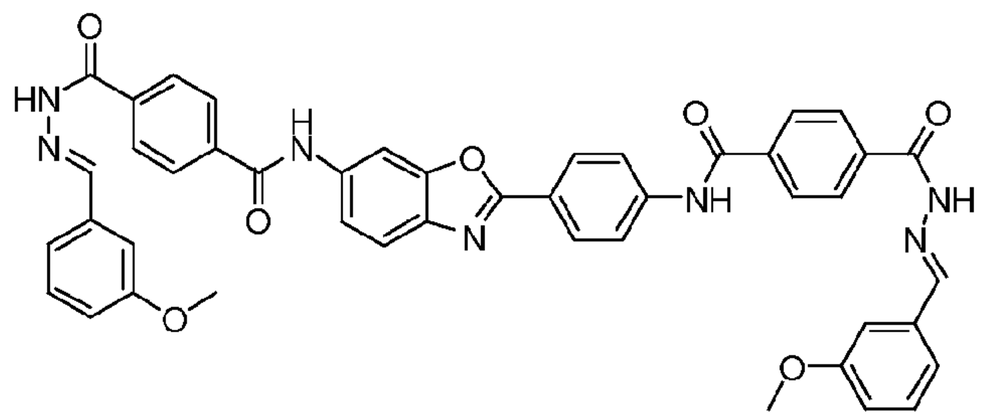
Methyl 4-(6-(4-(dimethylamino)benzamido)-1*H*-indol-2-yl)benzoate (Compound **247**)



[0717] Compound **247** was prepared according to the procedure similar to that described in Scheme III from 5-nitro-2-(4-methoxycarbonylphenyl)indole and 4-dimethylaminobenzoic acid. $[M+H]^+$ calcd for $C_{24}H_{22}N_4O_3$: 415.17; found: 415.60.

EXAMPLE 148

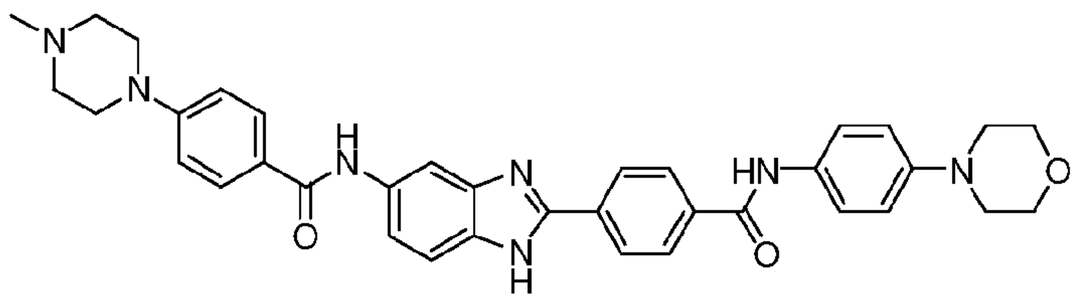
4-((*E*)-2-(3-methoxybenzylidene)hydrazinecarbonyl)-*N*-(4-(6-(4-((*E*)-2-(3-methoxybenzylidene)
hydrazinecarbonyl)benzamido)benzo[*d*]oxazol-2-yl)phenyl)benzamide (Compound **248**)



[0718] Compound **248** was prepared according to the procedure similar to that described in Scheme II from the 2-phenylbenzoxazole-bis-hydrazide and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{45}H_{35}N_7O_7$: 786.26; found: 786.23.

EXAMPLE 149

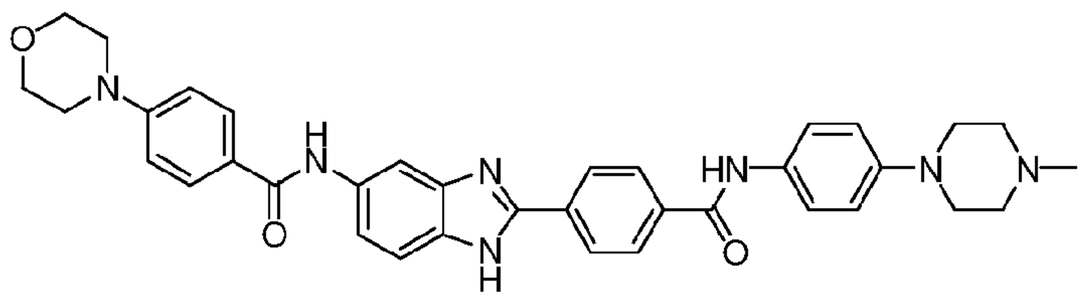
4-(4-methylpiperazin-1-yl)-*N*-(2-(4-((4-morpholinophenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **249**)



[0719] Compound **249** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(4-methylpiperazinyl)benzamide and 4-(4-morpholinophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{36}H_{37}N_7O_3$: 616.30; found: 616.09.

EXAMPLE 150

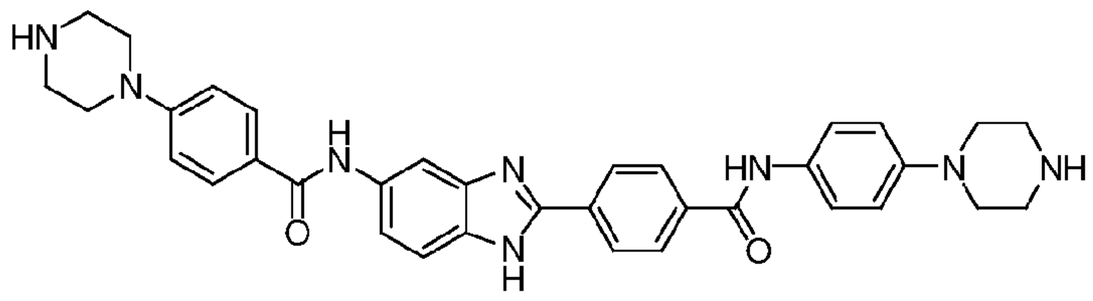
N-(4-(4-methylpiperazin-1-yl)phenyl)-4-(5-(4-morpholinobenzamido)-1*H*-benzo[*d*]imidazol-2-yl)benzamide (Compound **250**)



[0720] Compound **250** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-morpholinobenzamide and 4-(4-(4-methylpiperazinyl)phenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{36}H_{37}N_7O_3$: 616.30; found: 616.13.

EXAMPLE 151

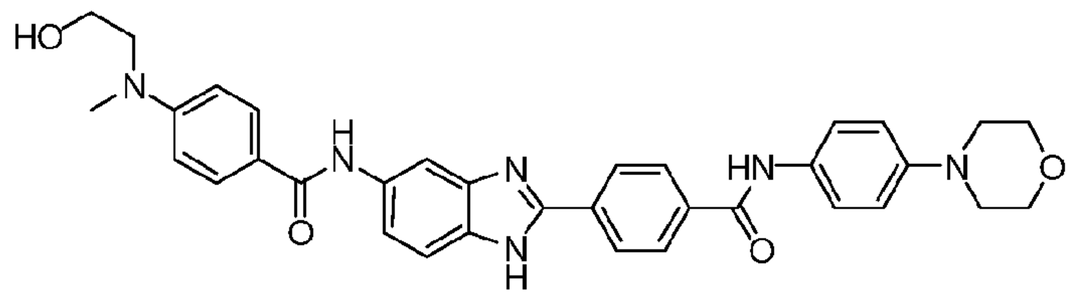
4-(piperazin-1-yl)-*N*-(2-(4-((4-(piperazin-1-yl)phenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **251**)



[0721] Compound **251** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-piperazinylbenzamide and 4-(4-(4-methylpiperazinyl)phenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{35}H_{36}N_8O_2$: 601.30; found: 601.19.

EXAMPLE 152

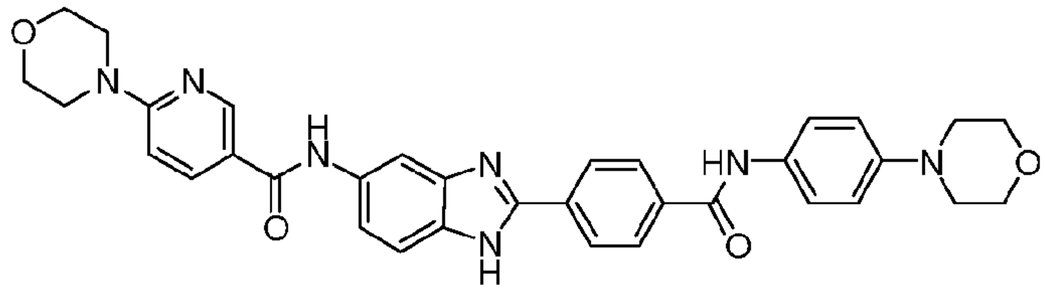
4-((2-hydroxyethyl)(methyl)amino)-*N*-(2-(4-((4-morpholinophenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **252**)



[0722] Compound **252** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-(*N*-methyl-*N*-2-hydroxyethylamino)-benzamide and 4-(4-morpholinophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{34}H_{34}N_6O_4$: 591.26; found: 591.06.

EXAMPLE 153

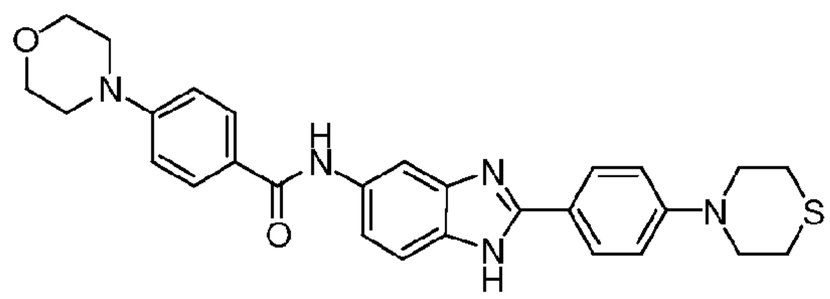
6-morpholino-*N*-(2-(4-((4-morpholinophenyl)carbamoyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)nicotinamide (Compound **253**)



[0723] Compound **253** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(2-morpholinyl-5-pyridinecarbonyl)aniline and 4-(4-morpholinylphenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{34}H_{33}N_7O_4$: 604.26; found: 604.10.

EXAMPLE 154

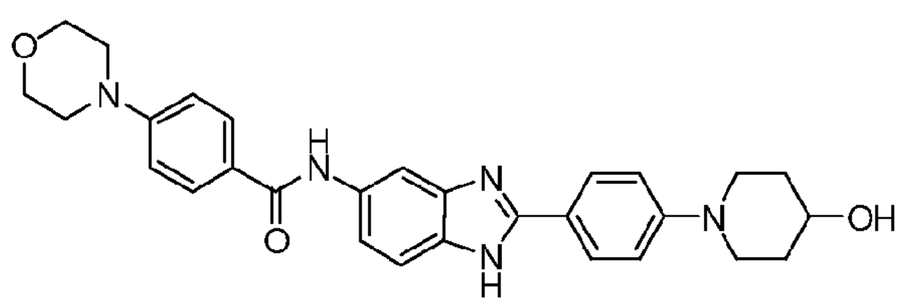
4-morpholino-*N*-(2-(4-thiomorpholinophenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **254**)



[0724] Compound **254** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-thiomorpholinylbenzoyl)aniline and 4-morpholinylbenzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O_2S$: 500.20; found: 500.00.

EXAMPLE 155

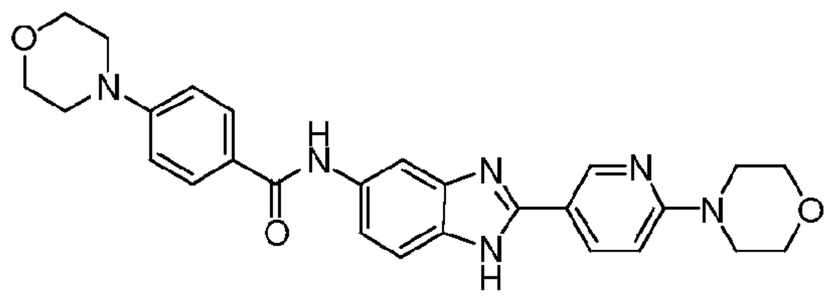
N-(2-(4-(4-hydroxypiperidin-1-yl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-morpholinobenzamide (Compound **255**)



[0725] Compound **255** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinylbenz)aniline and 4-(4-hydroxypiperidinyl)benzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{31}N_5O_3$: 498.24; found: 497.98.

EXAMPLE 156

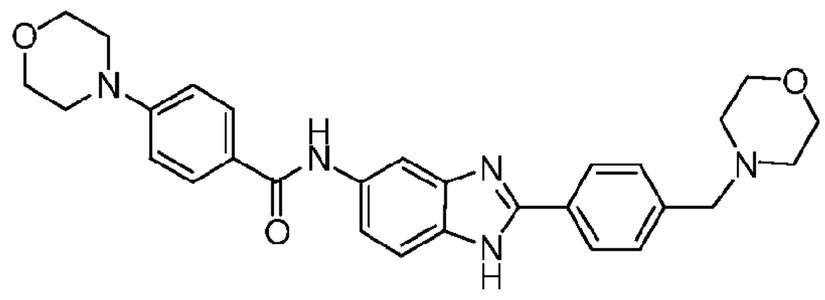
4-morpholino-*N*-(2-(6-morpholinopyridin-3-yl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **256**)



[0726] Compound **256** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinylbenz)aniline and 6-morpholinylpyridine-3-carboxaldehyde. $[M+H]^+$ calcd for $C_{27}H_{28}N_6O_3$: 485.22; found: 484.99.

EXAMPLE 157

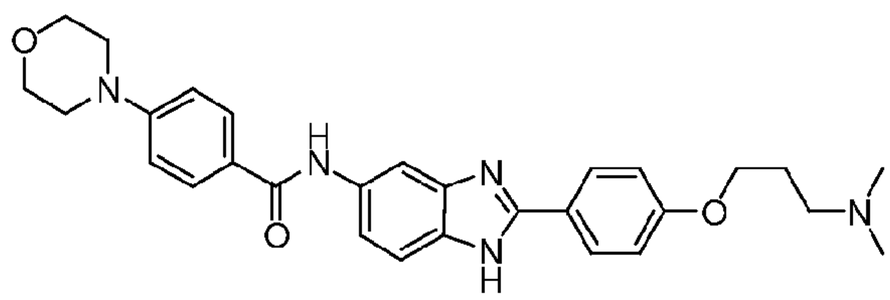
4-morpholino-*N*-(2-(4-(morpholinomethyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **257**)



[0727] Compound **257** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinylbenz)aniline and 4-morpholinomethylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{31}N_5O_3$: 498.24; found: 498.02.

EXAMPLE 158

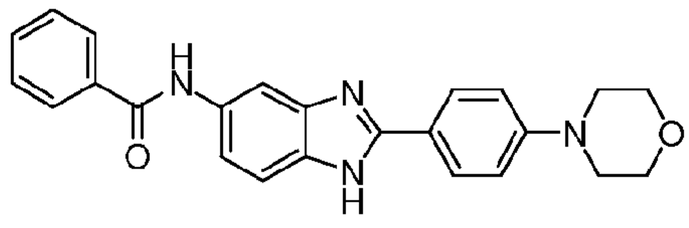
N-(2-(4-(3-(dimethylamino)propoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-morpholinobenzamide (Compound **258**)



[0728] Compound **258** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinylbenz)aniline and 4-(3-dimethylaminopropyloxy)benzaldehyde. $[M+II]^+$ calcd for $C_{29}II_{33}N_5O_3$: 500.26; found: 500.01.

EXAMPLE 159

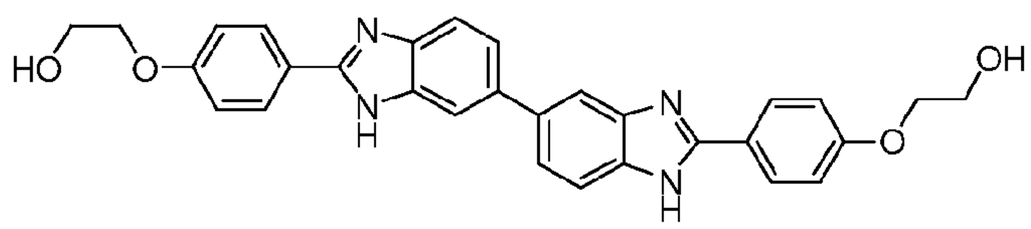
N-(2-(4-morpholinophenyl)-*1H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **259**)



[0729] Compound **259** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-benzoylaniline and 4-morpholinylbenzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{22}N_4O_2$: 399.18; found: 398.99.

EXAMPLE 160

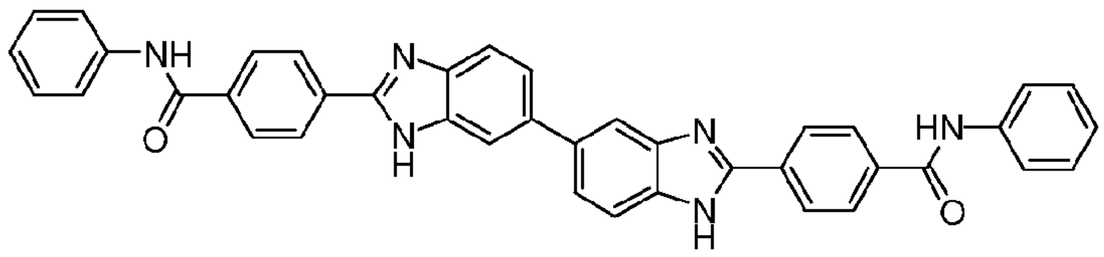
2,2'-((1*H*,3'*H*-[5,5'-bibenzo[*d*]imidazole]-2,2'-diylbis(4,1-phenylene))bis(oxy))diethanol (Compound **260**)



[0730] Compound **260** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 4-(2-hydroxyethoxy)benzaldehyde. $[M+H]^+$ calcd for $C_{30}H_{26}N_4O_4$: 507.20; found: 507.00.

EXAMPLE 161

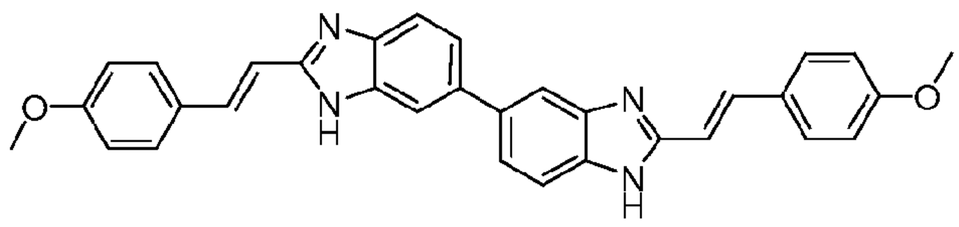
4,4'-(1*H*,3'*H*-[5,5'-bibenzo[*d*]imidazole]-2,2'-diyl)bis(*N*-phenylbenzamide) (Compound **261**)



[0731] Compound **261** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 4-phenylaminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{40}H_{28}N_6O_2$: 625.23; found: 625.53.

EXAMPLE 162

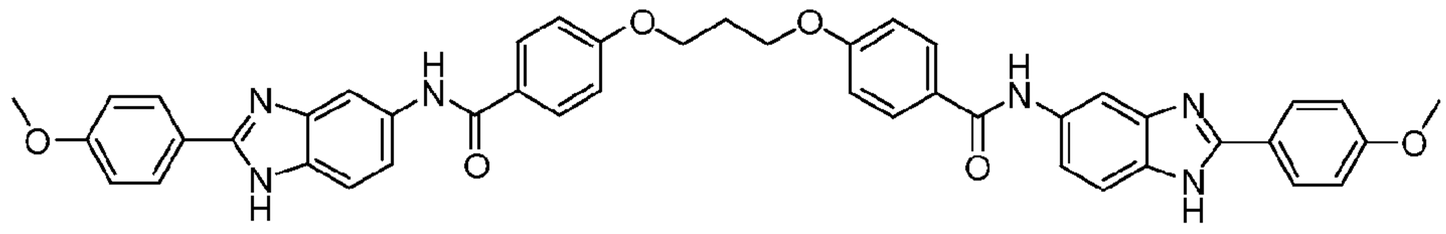
2,2'-bis((*E*)-4-methoxystyryl)-1*H*,3'*H*-5,5'-bibenzo[*d*]imidazole (Compound **262**)



[0732] Compound **262** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 3-(4-methoxyphenyl)acrylaldehyde. $[M+H]^+$ calcd for $C_{32}H_{26}N_4O_2$: 499.21; found: 499.00.

EXAMPLE 163

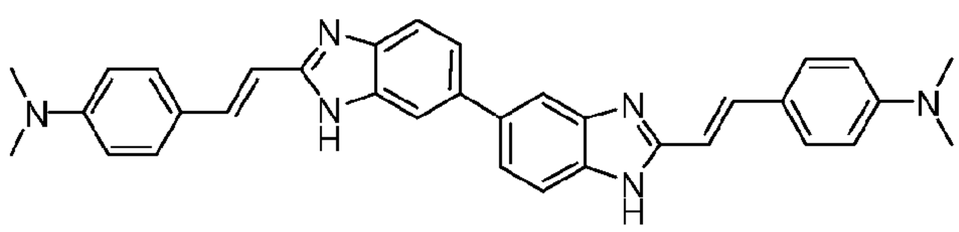
4,4'-(propane-1,3-diylbis(oxy))bis(*N*-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide) (Compound **263**)



[0733] Compound **263** was prepared according to the procedure similar to that described in Scheme III from 1,3-propanedioxybis-(4-benzoic acid) and 5-amino-2-(4-methoxyphenyl)benzimidazole. $[M+H]^+$ calcd for $C_{45}H_{38}N_6O_6$: 759.29; found: 759.54.

EXAMPLE 164

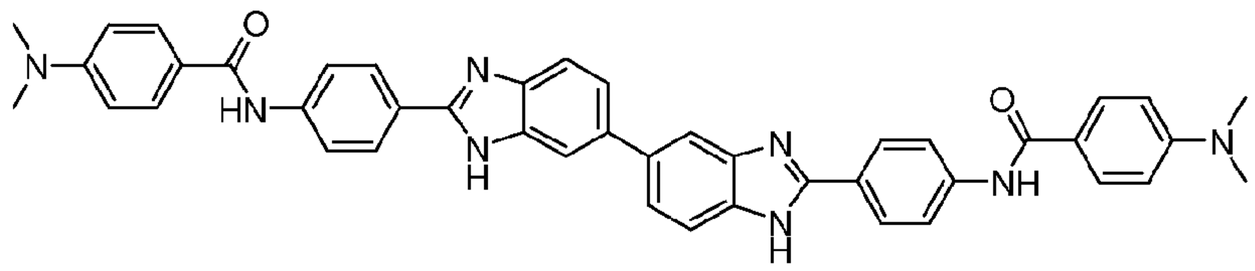
4,4'-((1*E*,1'*E*)-1*H*,3'*H*-[5,5'-bibenzo[*d*]imidazole]-2,2'-diylbis(ethene-2,1-diyl))bis(*N*,*N*-dimethylaniline) (Compound **264**)



[0734] Compound **264** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 3-(4-dimethylaminophenyl)acrylaldehyde. $[M+H]^+$ calcd for $C_{34}H_{32}N_6$: 525.27; found: 525.59.

EXAMPLE 165

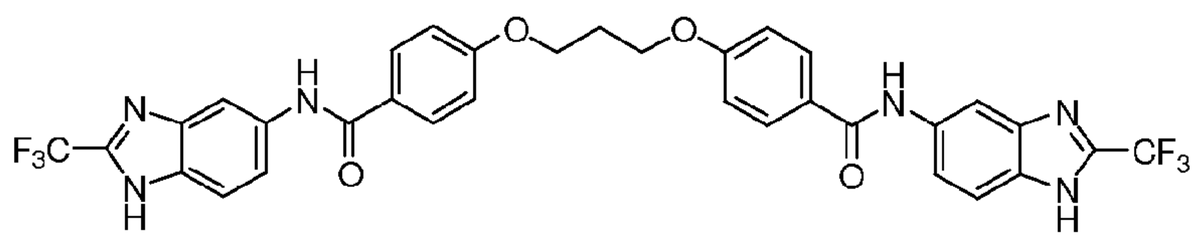
N,*N*'-(1*H*,3'*H*-[5,5'-bibenzo[*d*]imidazole]-2,2'-diylbis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **265**)



[0735] Compound **265** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 4-(4-dimethylaminobenzamido)benzaldehyde. $[M+H]^+$ calcd for $C_{44}H_{38}N_8O_2$: 711.31; found: 711.38.

EXAMPLE 166

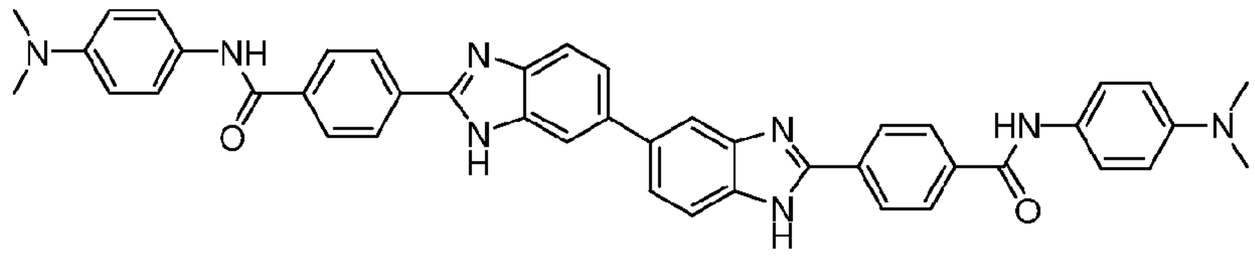
4,4'-(propane-1,3-diylbis(oxy))bis(*N*-(2-(trifluoromethyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide) (Compound **266**)



[0736] Compound **266** was prepared according to the procedure similar to that described in Scheme III from 1,3-propanedioxybis-(4-benzoic acid) and 5-amino-2-trifluoromethylbenzimidazole. $[M+H]^+$ calcd for $C_{33}H_{24}F_6N_6O_4$: 683.18; found: 683.04.

EXAMPLE 167

4,4'-(1*H*,3'*H*-[5,5'-bibenzo[*d*]imidazole]-2,2'-diyl)bis(*N*-(4-(dimethylamino)phenyl)benzamide) (Compound **267**)

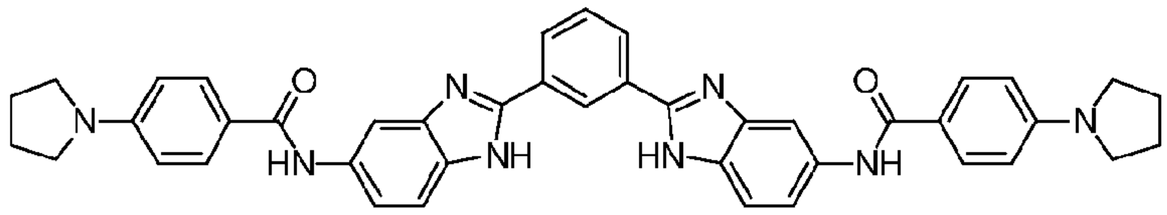


[0737] Compound **267** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 4-(4-

dimethylaminophenyl)aminocarbonylbenzaldehyde. $[M+H]^+$ calcd for $C_{44}H_{38}N_8O_2$: 711.31; found: 711.38.

EXAMPLE 168

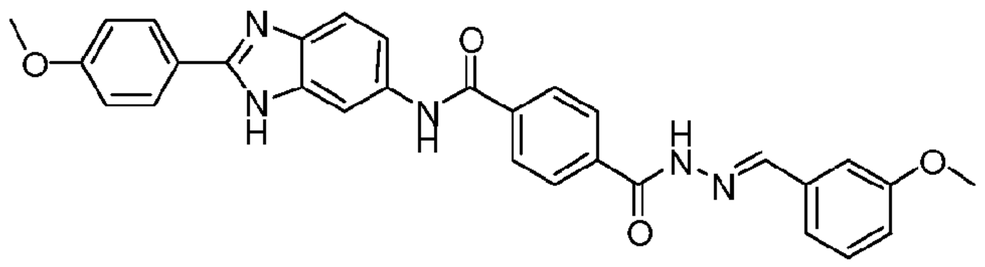
N,*N*'-(2,2'-(1,3-phenylene)bis(1*H*-benzo[*d*]imidazole-5,2-diyl))bis(4-(pyrrolidin-1-yl)benzamide) (Compound **268**)



[0738] Compound **268** was prepared according to the procedure similar to that described in Scheme III from *N*-(3,4-dinitrophenyl)-4-pyrrolidinylbenzamide and 1,3-benzbisaldehyde. $[M+H]^+$ calcd for $C_{42}H_{48}N_8O_2$: 687.32; found: 687.19.

EXAMPLE 169

(*E*)-4-(2-(3-Methoxybenzylidene)hydrazinecarbonyl)-*N*-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-6-yl)benzamide (Compound **269**)



[0739] Compound **269** was prepared according to the general procedure described in Scheme V. Preparation of methyl 4-((2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-6-yl)carbamoyl)benzoate: 2-(4-Methoxyphenyl)-1*H*-benzo[*d*]imidazol-6-amine (120 mg, 0.5 mmol) and methyl 4-(chlorocarbonyl)benzoate (80 mg, 0.4 mmole) were place in a 20 mL vial and pyridine (2.0 mL) added and capped tightly. The reaction mixture was stirred at room temperature for 2 h till a solid precipitated out. To this mixture, 10 mL EtOAC was added and stirred for further 15 minutes then filtered. The filter cake was washed with plenty of water and then with some EtOAc (10 mL) and dried to provide pure title compound (70 mg, 44% yield).

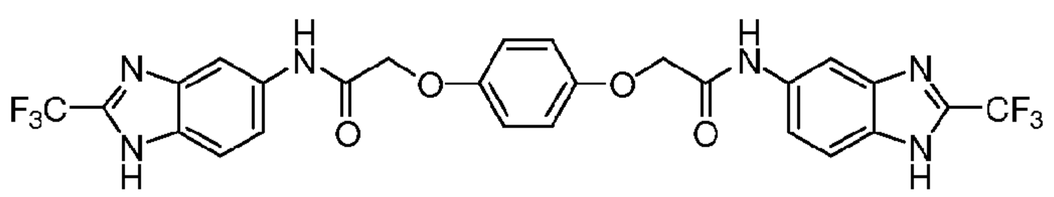
[0740] Preparation of 4-(hydrazinecarbonyl)-N-(2-(4-methoxyphenyl)-1H-benzo[d]imidazol-6-yl)benzamide: In a 15-mL sealed tube, methyl 4-((2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-6-yl)carbamoyl)benzoate (28 mg, 0.07 mmole) was dissolved in 2 mL absolute ethanol and hydrazine (1 mL) was added. The reaction mixture was heated in an oil bath at 70 °C for overnight. In the morning the reaction mixture was evaporated to dryness to

provide the title compound (28 mg, 99%, >95% pure by ^{1}H-NMR). This compound was used for next step without any further purification.

[0741] Preparation of Compound 269: In a 20-mL sealed tube, 4-(hydrazinecarbonyl)-*N*-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-6-yl)benzamide (28 mg, 0.07 mmole) was dissolved in 2 mL absolute ethanol then glacial acetic acid (1.0 mL) and sodium acetate (20 mg) was added. The reaction mixture was heated in an oil bath at 72 °C for overnight. In the morning, water (5.0 mL) added and stirred for 15 min. then it was filtered. The filter cake was washed with water, hexanes, ethyl acetate and dried to provide pure compound **269** (10 mg, 27% yield). $[M+H]^+$ calcd for $C_{30}H_{25}N_5O_4$: 520.19; found: 519.98.

EXAMPLE 170

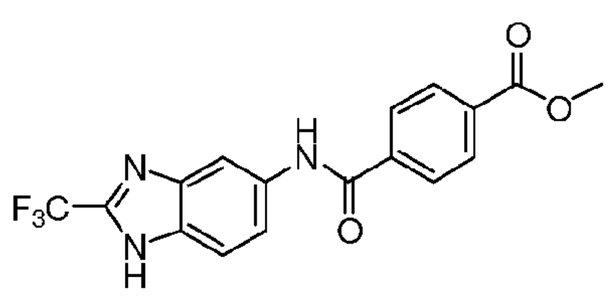
2,2'-(1,4-phenylenebis(oxy))bis(*N*-(2-(trifluoromethyl)-1*H*-benzo[*d*]imidazol-5-yl)acetamide) (Compound **270**)



[0742] Compound **270** was prepared according to the procedure similar to that described in Scheme V from 1,4-phenyldioxybisacetate and 5-amino-2-trifluoromethylbenzimidazole. $[M+H]^+$ calcd for $C_{26}H_{18}F_6N_6O_4$: 593.13; found: 592.86.

EXAMPLE 171

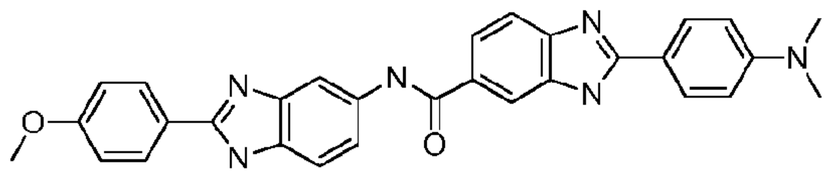
methyl 4-((2-(trifluoromethyl)-1*H*-benzo[*d*]imidazol-5-yl)carbamoyl)benzoate (Compound **271**)



[0743] Compound **271** was prepared according to the procedure similar to that described in Scheme V from terephthalic acid mono-ester and 5-amino-2-trifluoromethylbenzimidazole. $[M+H]^+$ calcd for $C_{17}H_{12}F_3N_3O_3$: 364.08; found: 363.86.

EXAMPLE 172

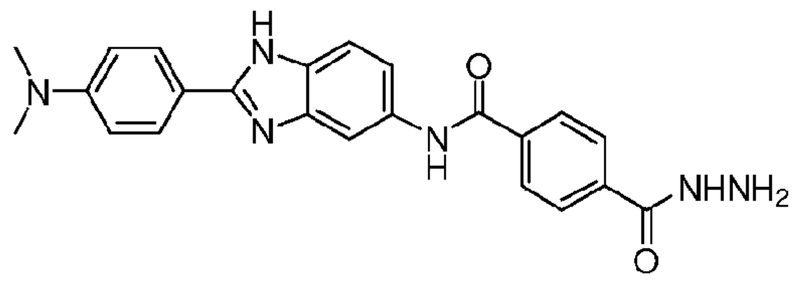
2-(4-(dimethylamino)phenyl)-*N*-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **272**)



[0744] Compound **272** was prepared according to the procedure similar to that described in Scheme V from 2-(4-dimethylaminophenyl)-5-aminobenzimidazole and 2-(4-dimethylaminophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{30}H_{26}N_6O_2$: 503.21; found: 503.25.

EXAMPLE 173

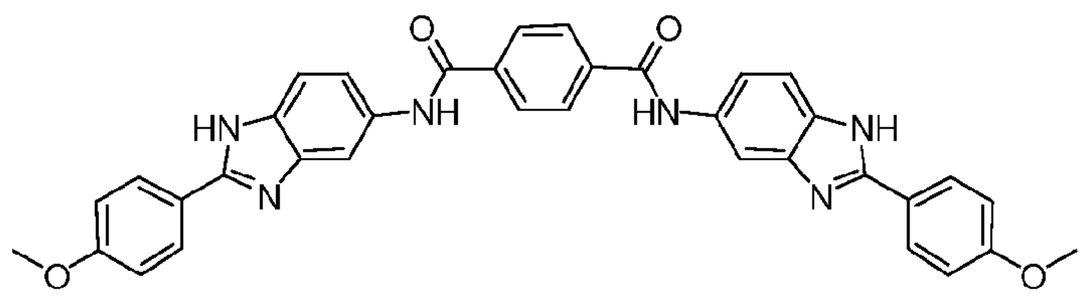
N-(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-(hydrazinecarbonyl)benzamide (Compound **273**)



[0745] Compound 273 was prepared according to the procedure similar to that described in Scheme V from 2-(4-dimethylaminophenyl)-5-aminobenzimidazole and terephthalic acid. $[M+H]^+$ calcd for $C_{23}H_{22}N_6O_2$: 415.18; found: 414.91.

EXAMPLE 174

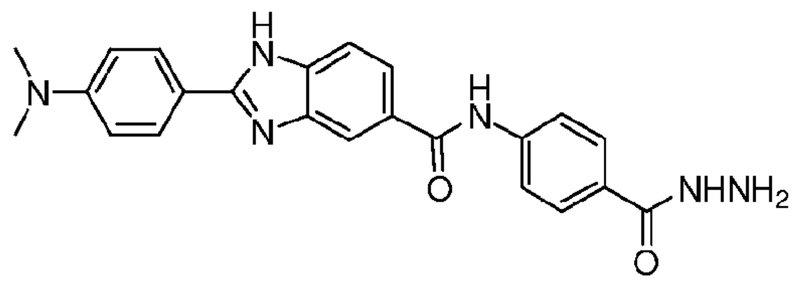
N^1,N^4-bis(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)terephthalamide (Compound **274**)



[0746] Compound **274** was prepared according to the procedure similar to that described in Scheme V from 2-(4-methoxyphenyl)-5-aminobenzimidazole and terephthalic acid. $[M+H]^+$ calcd for $C_{36}H_{28}N_6O_4$: 609.22; found: 608.99.

EXAMPLE 175

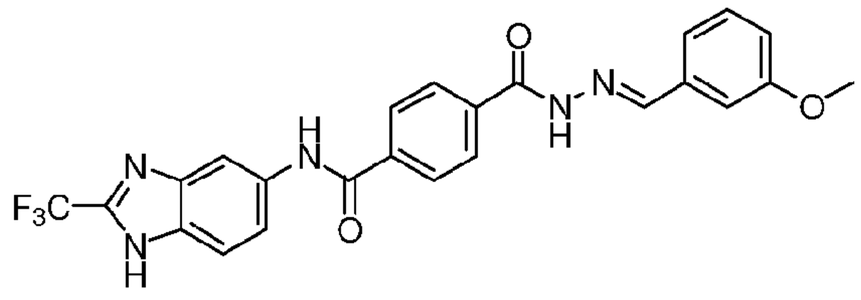
2-(4-(dimethylamino)phenyl)-*N*-(4-(hydrazinecarbonyl)phenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide (Compound **275**)



[0747] Compound **275** was prepared according to the procedure similar to that described in Scheme V from 2-(4-dimethylaminophenyl)benzimidazole-5-carboxylic acid and 4-aminobenzhydrazide. $[M+H]^+$ calcd for $C_{23}H_{22}N_6O_2$: 415.18; found: 414.91.

EXAMPLE 176

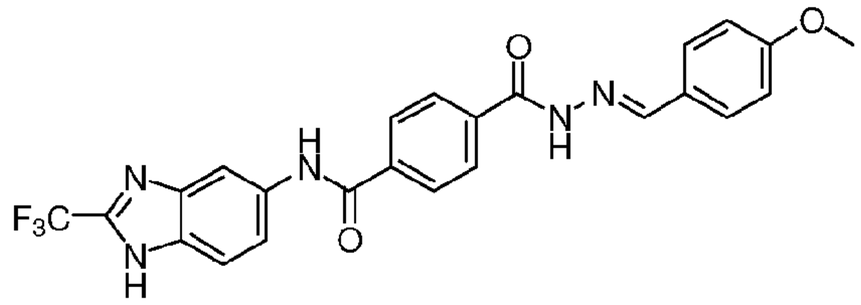
(*E*)-4-(2-(3-methoxybenzylidene)hydrazinecarbonyl)-*N*-(2-(trifluoromethyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **276**)



[0748] Compound **276** was prepared according to the procedure similar to that described in Scheme V from terephthalic acid mono-ester, 3-methoxybenzaldehyde and 5-amino-2-trifluoromethylbenzimidazole. $[M+H]^+$ calcd for $C_{24}H_{18}F_3N_5O_3$: 482.14; found: 481.45.

EXAMPLE 177

(*E*)-4-(2-(4-methoxybenzylidene)hydrazinecarbonyl)-*N*-(2-(trifluoromethyl)-1*H*-benzo[*d*]imidazol-5-yl)benzamide (Compound **277**)

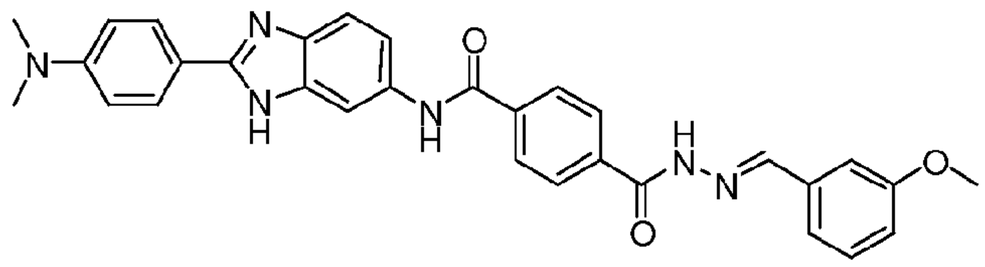


[0749] Compound **277** was prepared according to the procedure similar to that described in Scheme V from terephthalic acid mono-ester, 4-methoxybenzaldehyde and 5-

amino-2-trifluoromethylbenzimidazole. $[M+H]^+$ calcd for $C_{24}H_{18}F_3N_5O_3$: 482.14; found: 481.45.

EXAMPLE 178

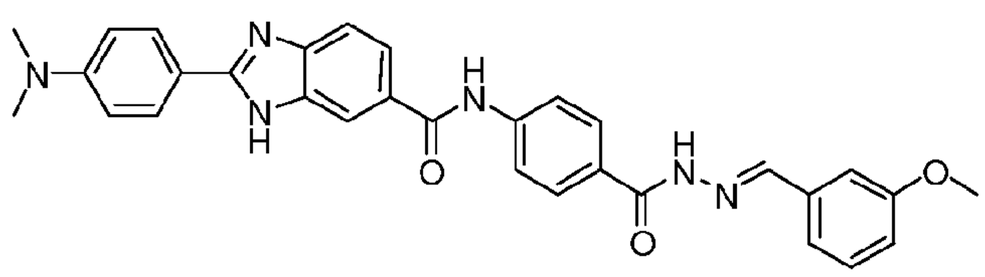
(*E*)-*N*-(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazol-6-yl)-4-(2-(3-methoxybenzylidene)hydrazinecarbonyl)benzamide (Compound **278**)



[0750] Compound **278** was prepared according to the procedure described in Scheme V from 5-amino-2-(4-dimethylaminophenyl)benzimidazole, terephthalic acid, and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{28}N_6O_3$: 533.22; found: 532.96.

EXAMPLE 179

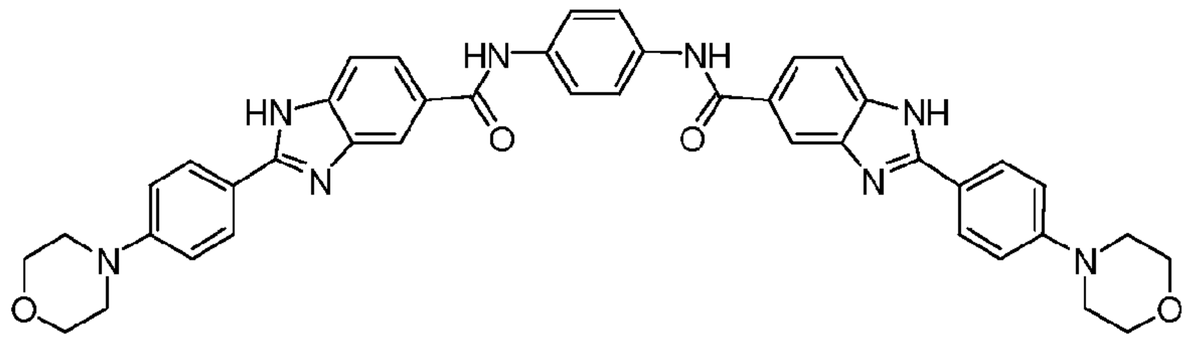
(*E*)-2-(4-(dimethylamino)phenyl)-*N*-(4-(2-(3-methoxybenzylidene)hydrazinecarbonyl)phenyl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **279**)



[0751] Compound **279** was prepared according to the procedure described in Scheme V from 2-(4-dimethylaminophenyl)benzimidazole-5-carboxylic acid, 4-aminobenzoic acid, and 3-methoxybenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{28}N_6O_3$: 533.22; found: 532.95.

EXAMPLE 180

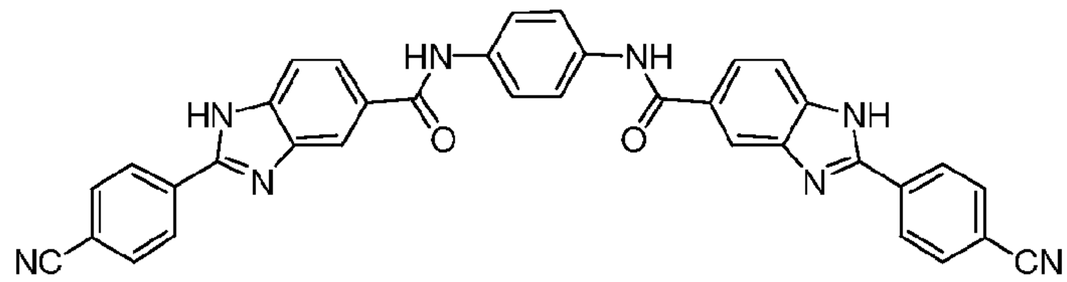
N,*N*'-(1,4-phenylene)bis(2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide) (Compound **280**)



[0752] Compound **280** was prepared according to the procedure similar to that described in Scheme V from 2-(4-morpholinylphenyl)benzimidazole-5-carboxylic acid and 1,4-phenylenediamine. $[M+H]^+$ calcd for $C_{42}H_{38}N_8O_4$: 719.30; found: 719.12.

EXAMPLE 181

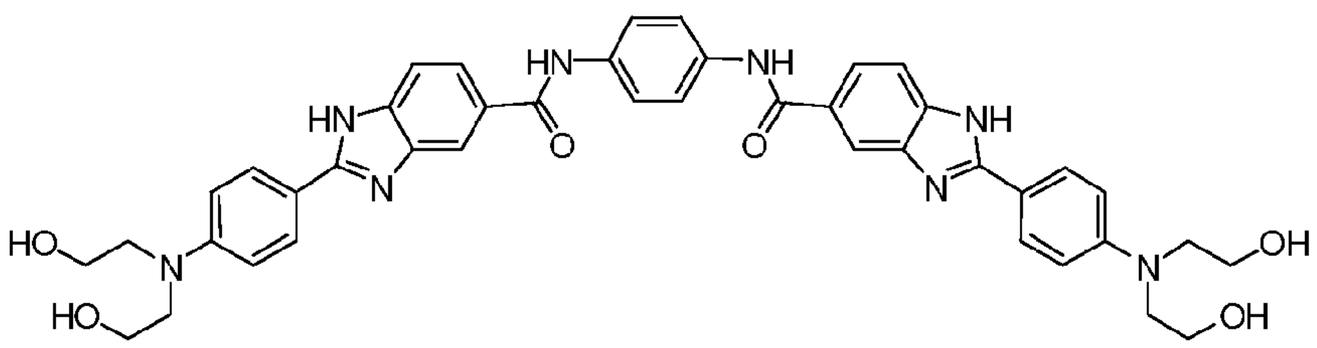
N,*N*'-(1,4-phenylene)bis(2-(4-cyanophenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide) (Compound **281**)



[0753] Compound **281** was prepared according to the procedure similar to that described in Scheme V from 2-(4-cyanophenyl)benzimidazole-5-carboxylic acid and 1,4-phenylenediamine. $[M+H]^+$ calcd for $C_{36}H_{22}N_8O_2$: 599.19; found: 598.97.

EXAMPLE 182

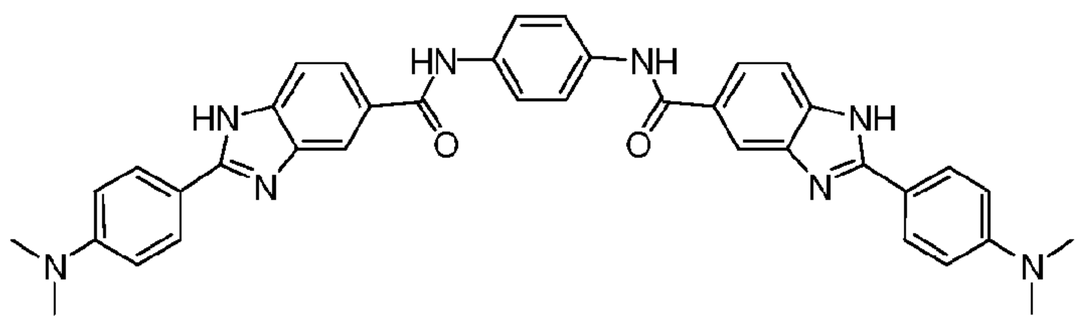
N,*N*'-(1,4-phenylene)bis(2-(4-(bis(2-hydroxyethyl)amino)phenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide) (Compound **282**)



[0754] Compound **282** was prepared according to the procedure similar to that described in Scheme V from 2-(4-di(2-hydroxyethyl)aminophenyl)benzimidazole-5-carboxylic acid and 1,4-phenylenediamine. $[M+H]^+$ calcd for $C_{42}H_{42}N_8O_6$: 755.32; found: 755.16.

EXAMPLE 183

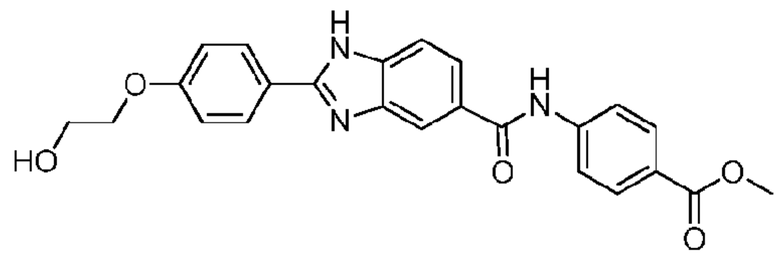
N,*N*'-(1,4-phenylene)bis(2-(4-(dimethylamino)phenyl)-1*H*-benzo[*d*]imidazole-5-carboxamide) (Compound **283**)



[0755] Compound **283** was prepared according to the procedure similar to that described in Scheme V from 2-(4-dimethylaminophenyl)benzimidazole-5-carboxylic acid and 1,4-phenylenediamine. $[M+H]^+$ calcd for $C_{38}H_{34}N_8O_2$: 635.28; found: 635.05.

EXAMPLE 184

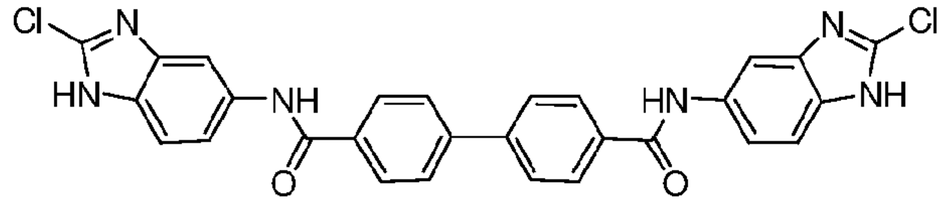
Methyl 4-((2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)carbamoyl)benzoate (Compound **284**)



[0756] Compound **284** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(2-hydroxyethoxy)phenyl)-5-aminobenzimidazole and terephthalic acid monoester. $[M+H]^+$ calcd for $C_{24}H_{21}N_3O_5$: 432.15; found: 431.86.

EXAMPLE 185

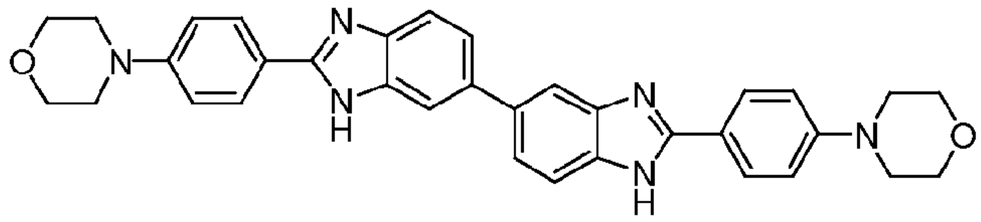
N^4,$N^{4'}$-bis(2-chloro-1*H*-benzo[*d*]imidazol-5-yl)-[1,1'-biphenyl]-4,4'-dicarboxamide (Compound **285**)



[0757] Compound **285** was prepared according to the procedure similar to that described in Scheme V from 4,4'-bisbenzoic acid and 5-amino-2-chlorobenzimidazole. $[M+H]^+$ calcd for $C_{28}H_{18}N_6O_2$: 541.09; found: 541.91.

EXAMPLE 186

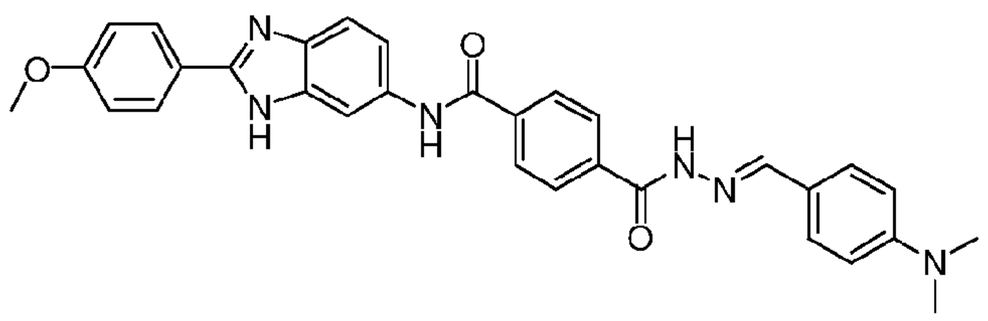
4,4'-(1*H*,3'*H*-[5,5'-bibenzo[*d*]imidazole]-2,2'-diylbis(4,1-phenylene))dimorpholine (Compound **286**)



[0758] Compound **286** was prepared according to the procedure similar to that described in Scheme III from 3,3'-diaminobenzidine and 4-morpholinylbenzaldehyde. $[M+H]^+$ calcd for $C_{34}H_{32}N_6O_2$: 557.26; found: 557.58.

EXAMPLE 187

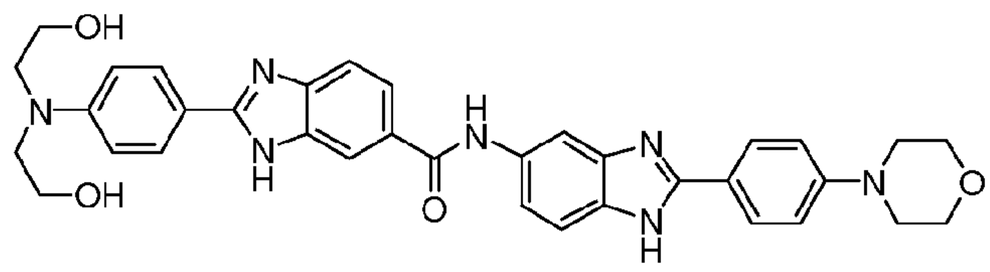
(*E*)-4-(2-(4-(dimethylamino)benzylidene)hydrazinecarbonyl)-*N*-(2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-6-yl)benzamide (Compound **287**)



[0759] Compound **287** was prepared according to the procedure described in Scheme V from 5-amino-2-(4-methoxyphenyl)benzimidazole, terephthalic acid, and 4-dimethylaminobenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{28}N_6O_3$: 533.22; found: 532.55.

EXAMPLE 188

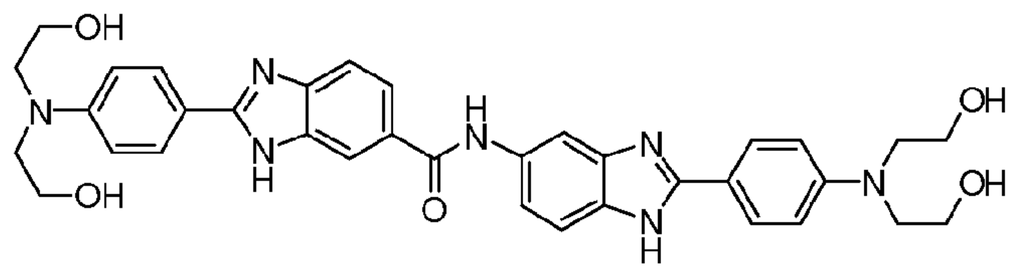
2-(4-(bis(2-hydroxyethyl)amino)phenyl)-*N*-(2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **288**)



[0760] Compound **288** was prepared according to the procedure similar to that described in Scheme V from 2-(4-morpholinophenyl)-5-aminobenzimidazole and 2-(4-*N*,*N*-(2-hydroxyethyl)aminophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{35}H_{35}N_7O_4$: 618.28; found: 618.03.

EXAMPLE 189

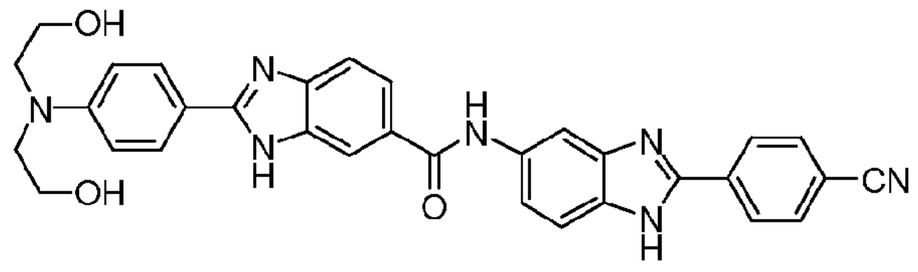
(2-(4-(bis(2-Hydroxyethyl)amino)phenyl)-*N*-(2-(4-(bis(2-hydroxyethyl)amino)phenyl)-1*H*-benzimidazol-5-yl)-1*H*-benzimidazole-6-carboxamide (Compound **289**)



[0761] Compound **289** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(bis(2-hydroxyethyl)amino)phenyl)-5-aminobenzimidazole and 2-(4-(bis(2-hydroxyethyl)amino)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{35}H_{37}N_7O_5$: 636.29; found: 636.06.

EXAMPLE 190

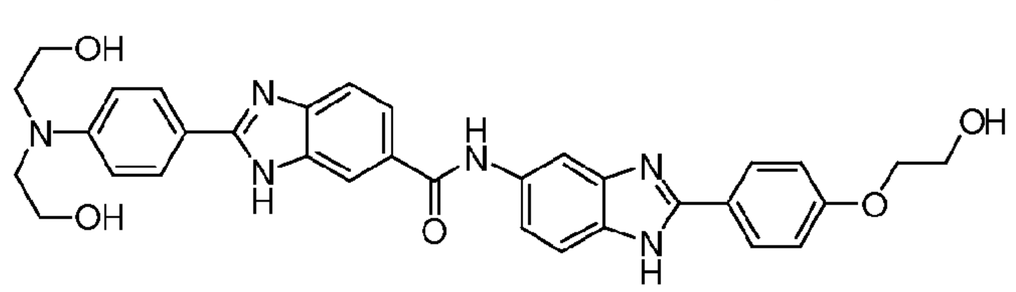
(2-(4-(bis(2-Hydroxyethyl)amino)phenyl)-*N*-(2-(4-cyano)phenyl)-1*H*-benzimidazol-5-yl)-1*H*-benzimidazole-6-carboxamide (Compound **290**)



[0762] Compound **290** was prepared according to the procedure similar to that described in Scheme V from 2-(4-cyanophenyl)-5-aminobenzimidazole and 2-(4-(bis(2-hydroxyethyl)amino)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{32}H_{27}N_7O_3$: 558.22; found: 557.95.

EXAMPLE 191

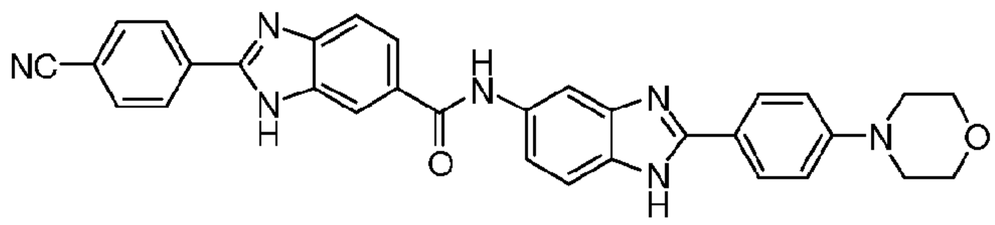
(2-(4-(bis(2-Hydroxyethyl)amino)phenyl)-*N*-(2-(4-(2-hydroxy)ethoxy)phenyl)-1*H*-benzimidazol-5-yl)-1*H*-benzimidazole-6-carboxamide (Compound **291**)



[0763] Compound **291** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(2-hydroxy)ethoxyphenyl)-5-aminobenzimidazole and 2-(4-(bis(2-hydroxyethyl)amino)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{33}H_{32}N_6O_5$: 593.24; found: 593.03.

EXAMPLE 192

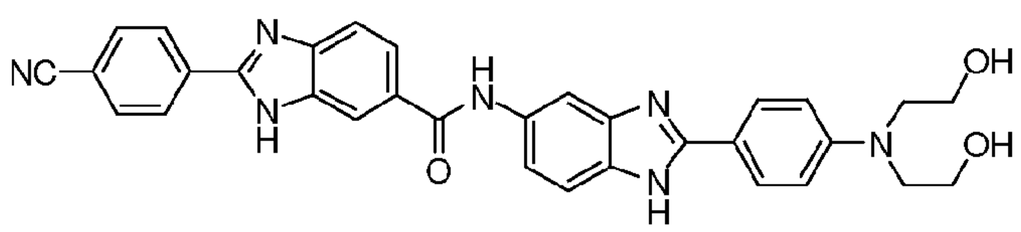
2-(4-cyanophenyl)-*N*-(2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1H-benzo[*d*]imidazole-6-carboxamide (Compound **292**)



[0764] Compound **292** was prepared according to the procedure similar to that described in Scheme V from 2-(4-morpholinophenyl)-5-aminobenzimidazole and 2-(4-cyanophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{32}H_{25}N_7O_2$: 540.21; found: 539.97.

EXAMPLE 193

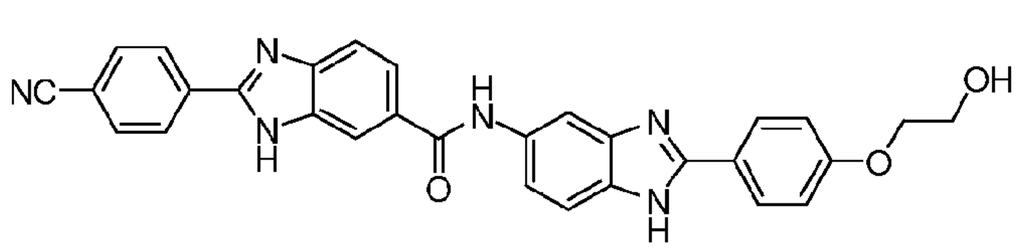
N-(2-(4-(bis(2-hydroxyethyl)amino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-2-(4-cyanophenyl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **293**)



[0765] Compound **293** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(bis(2-hydroxyethyl)amino)phenyl)-5-aminobenzimidazole and 2-(4-cyanophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{32}H_{25}N_7O_3$: 558.22; found: 557.99.

EXAMPLE 194

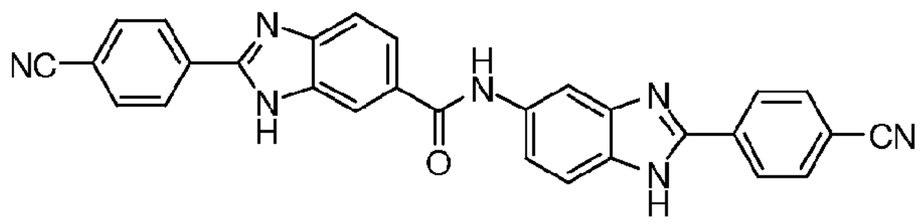
2-(4-cyanophenyl)-*N*-(2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **294**)



[0766] Compound **294** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(2-hydroxyethoxy)amino)phenyl)-5-aminobenzimidazole and 2-(4-cyanophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{30}H_{22}N_6O_3$: 515.18; found: 514.92.

EXAMPLE 195

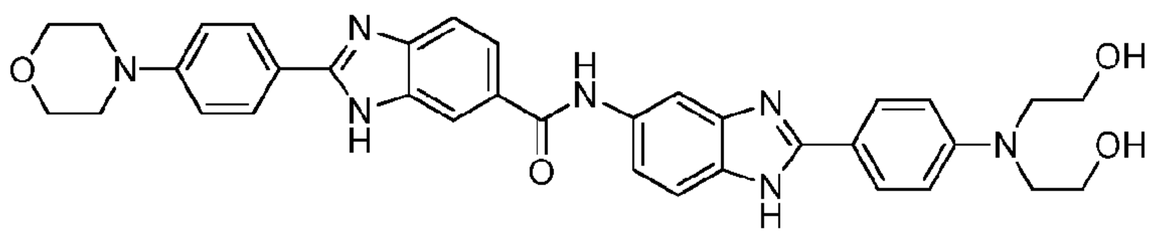
2-(4-cyanophenyl)-*N*-(2-(4-cyanophenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **295**)



[0767] Compound **295** was prepared according to the procedure similar to that described in Scheme V from 2-(4-cyano)phenyl)-5-aminobenzimidazole and 2-(4-cyanophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{29}H_{17}N_7O$: 480.15; found: 479.89.

EXAMPLE 196

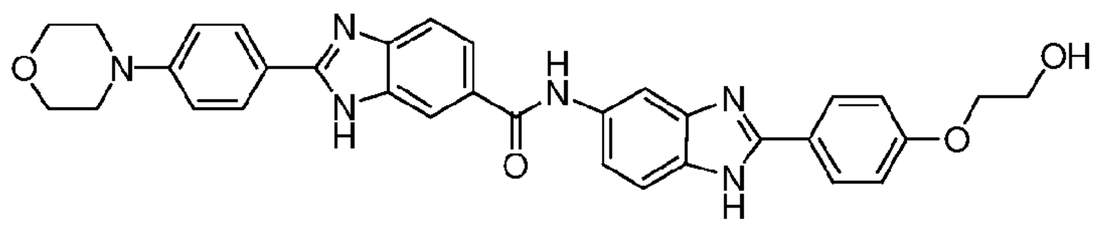
N-(2-(4-(bis(2-hydroxyethyl)amino)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **296**)



[0768] Compound **296** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(bis(2-hydroxyethyl)amino)phenyl)-5-aminobenzimidazole and 2-(4-morpholinophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{35}H_{35}N_7O_4$: 618.28; found: 618.03.

EXAMPLE 197

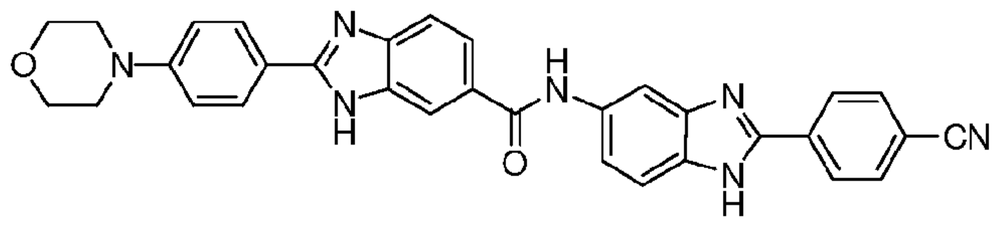
N-(2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **297**)



[0769] Compound **297** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(2-hydroxyethoxy)amino)phenyl)-5-aminobenzimidazole and 2-(4-morpholinophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{33}H_{30}N_6O_4$: 575.23; found: 575.00.

EXAMPLE 198

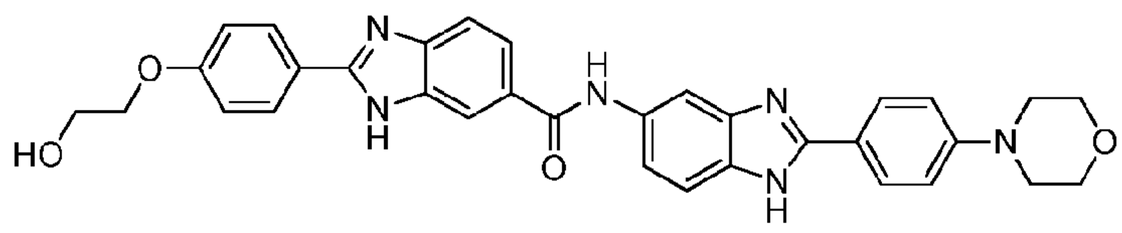
N-(2-(4-cyanophenyl)-1*H*-benzo[*d*]imidazol-5-yl)-2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **298**)



[0770] Compound **298** was prepared according to the procedure similar to that described in Scheme V from 2-(4-cyano)phenyl)-5-aminobenzimidazole and 2-(4-morpholinophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{32}H_{25}N_7O_2$: 540.21; found: 539.97.

EXAMPLE 199

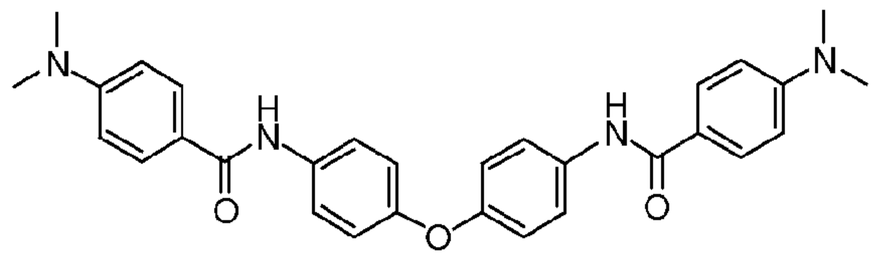
2-(4-(2-hydroxyethoxy)phenyl)-*N*-(2-(4-morpholinophenyl)-1*H*-benzo[*d*]imidazol-5-yl)-1*H*-benzo[*d*]imidazole-6-carboxamide (Compound **299**)



[0771] Compound **299** was prepared according to the procedure similar to that described in Scheme V from 2-(4-morpholinophenyl)-5-aminobenzimidazole and 2-(4-(2-hydroxyethoxy)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{33}H_{30}N_6O_4$: 575.23; found: 575.07.

EXAMPLE 200

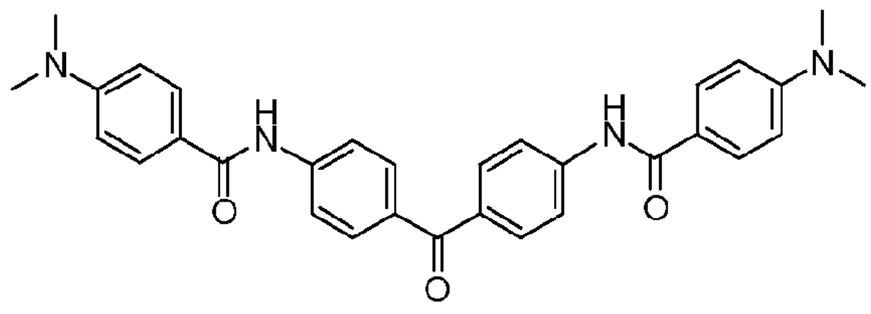
N,*N*'-(oxybis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **300**)



[0772] Compound **300** was prepared according to the procedure described in Scheme IV from 4,4'-oxybisphenylamine and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{30}H_{31}N_4O_3$: 495.24; found: 495.01

EXAMPLE 201

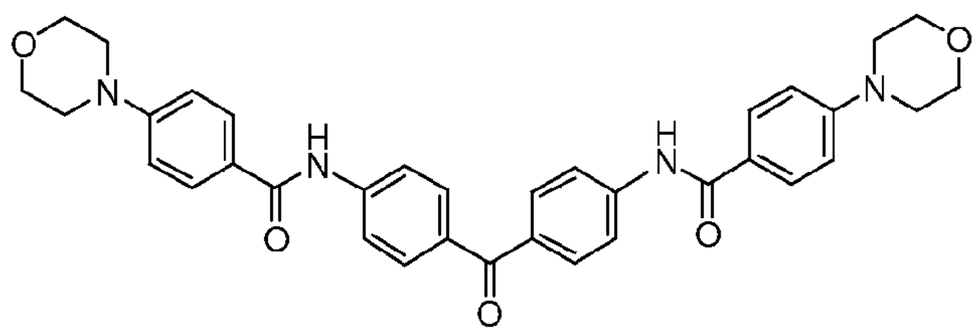
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **301**)



[0773] Compound **301** was prepared according to the procedure described in Scheme IV. 4-(Dimethylamino)benzoyl chloride (Aldrich, 151 mg, 0.825 mmol) in 1 mL of methylene chloride was slowly added over 5 min to 4,4'-diaminobenzophenone (Aldrich, 70 mg, 0.330 mmol) in 3 mL of methylene chloride containing 0.3 mL of pyridine. The reaction was allowed to stir at room temperature for 12 h and filtered. The white precipitate was washed with water (5 mL), ethanol (2 mL) and dried under vacuum to yield 165 mg of N,N'-(carbonylbis(4,1-phenylene))bis(4-(dimethylamino)benzamide) as a white powder. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.19 (s, 2H), 7.97 (d, J = 8.7 Hz, 4H), 7.89 (d, J = 8.5 Hz, 4H), 7.77 (d, J = 8.5 Hz, 4H), 6.77 (d, J = 8.7 Hz, 4H), 3.00 (s, 12H).

EXAMPLE 202

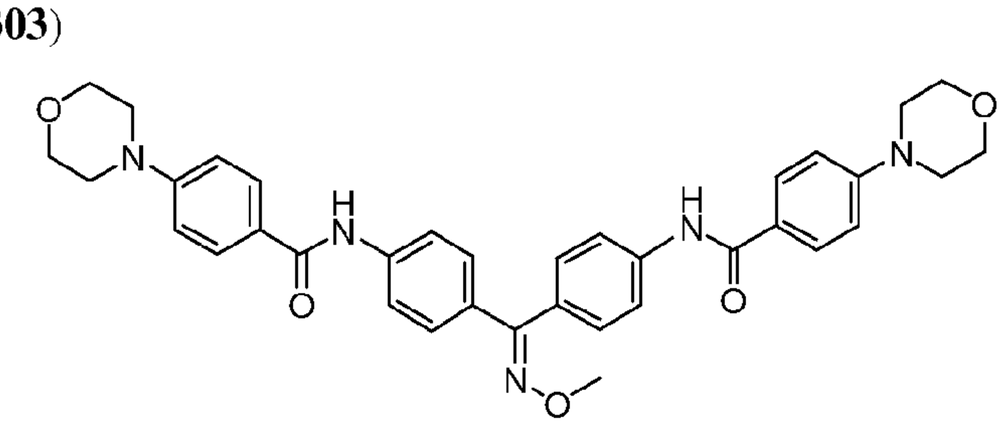
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-morpholinobenzamide) (Compound **302**)



[0774] Compound **302** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-morpholinylbenzoate. $[M+II]^+$ calcd for $C_{35}H_{35}N_4O_5$: 591.26; found: 591.20

EXAMPLE 203

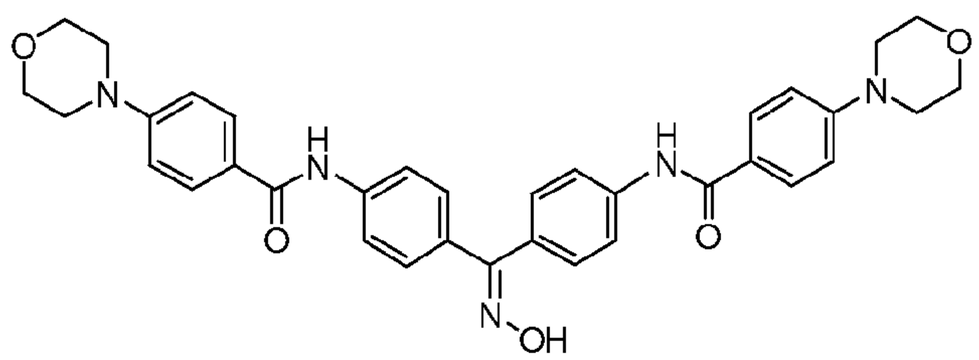
N,N'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-morpholinobenzamide) (Compound **303**)



[0775] Compound **303** was prepared from compound **302** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{36}H_{37}N_5O_5$: 620.24; found: 620.11.

EXAMPLE 204

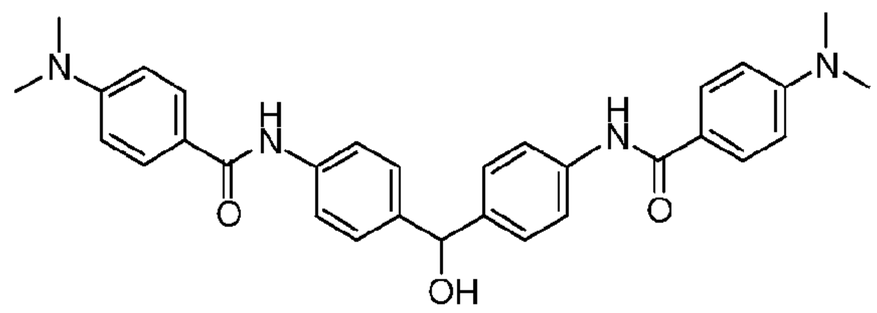
N,*N*'-(((hydroxyimino)methylene)bis(4,1-phenylene))bis(4-morpholinobenzamide) (Compound **304**)



[0776] Compound **304** was prepared from compound **302** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{35}H_{35}N_5O_5$: 606.27; found: 606.06.

EXAMPLE 205

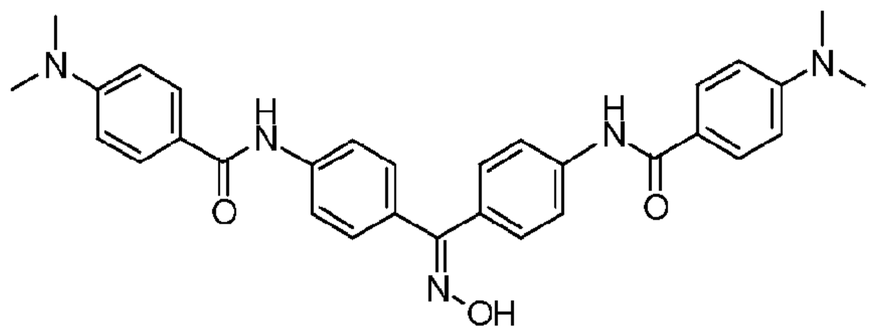
N,*N*'-((hydroxymethylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **305**)



[0777] Compound **305** was prepared from compound **301** by a standard reduction condition. $[M+H]^+$ calcd for $C_{31}H_{32}N_4O_3$: 509.14; found: 508.98.

EXAMPLE 206

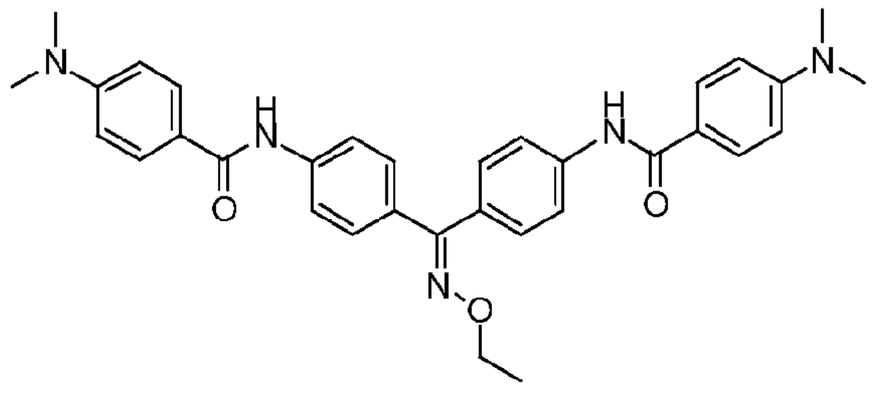
N,*N*'-(((hydroxyimino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **306**)



[0778] Compound **306** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{31}H_{31}N_5O_3$: 522.25; found: 522.01.

EXAMPLE 207

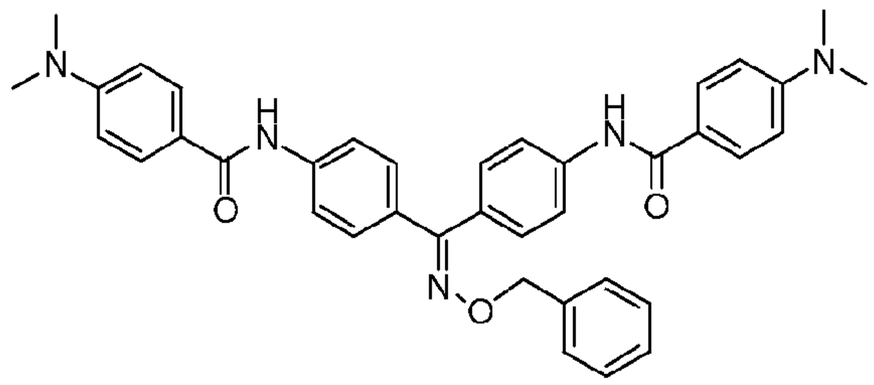
N,*N*'-(((ethoxyimino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **307**)



[0779] Compound **307** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{33}H_{35}N_5O_3$: 550.28; found: 550.02.

EXAMPLE 208

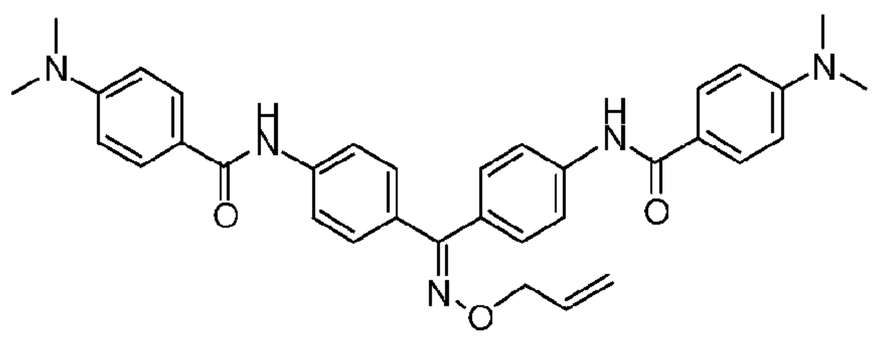
N,*N*'-((((benzyloxy)imino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **308**)



[0780] Compound **308** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{38}H_{37}N_5O_3$: 612.29; found: 612.07.

EXAMPLE 209

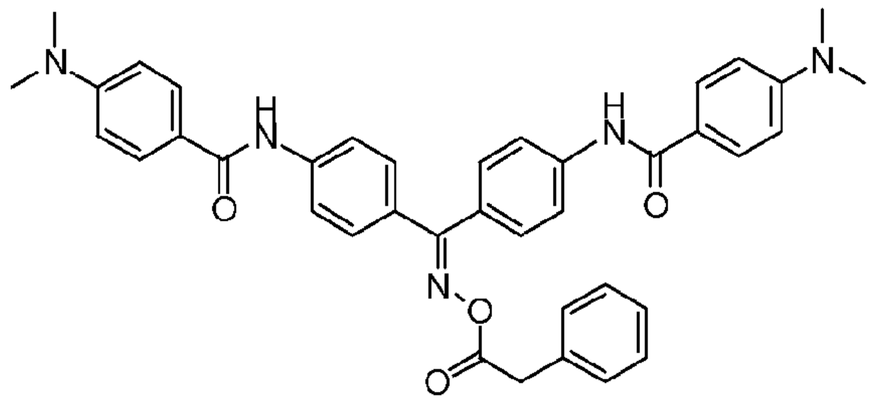
N,*N*'-((((allyloxy)imino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **309**)



[0781] Compound **309** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+II]^+$ calcd for $C_{34}II_{35}N_5O_3$: 562.28; found: 562.04.

EXAMPLE 210

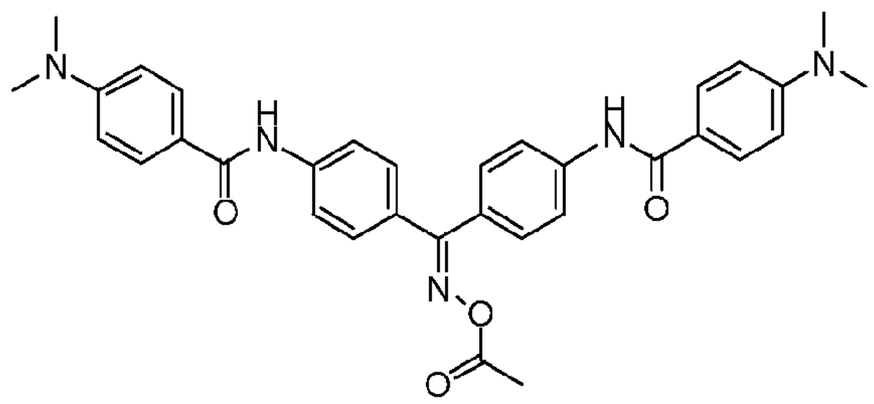
N,*N*'-((((2-phenylacetoxy)imino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **310**)



[0782] Compound **310** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{39}H_{37}N_5O_4$: 640.29; found: 640.23.

EXAMPLE 211

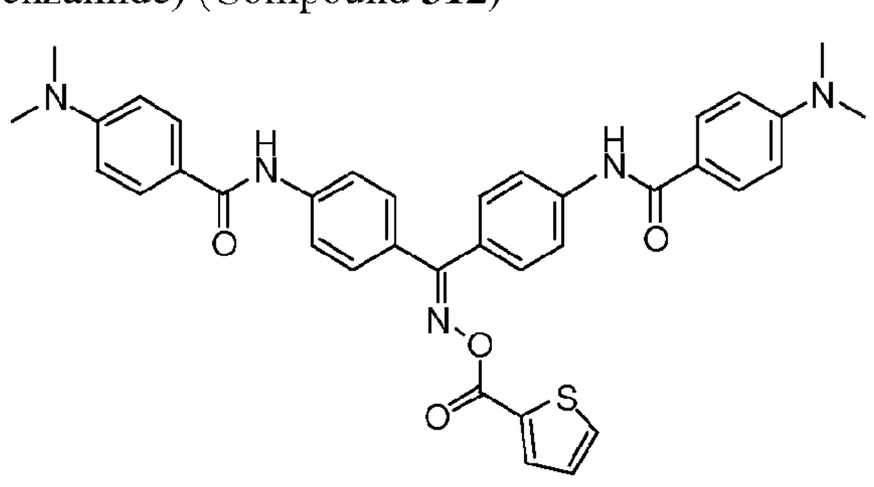
N,*N*'-(((acetoxyimino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **311**)



[0783] Compound **311** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{33}H_{33}N_5O_4$: 564.26; found: 564.00.

EXAMPLE 212

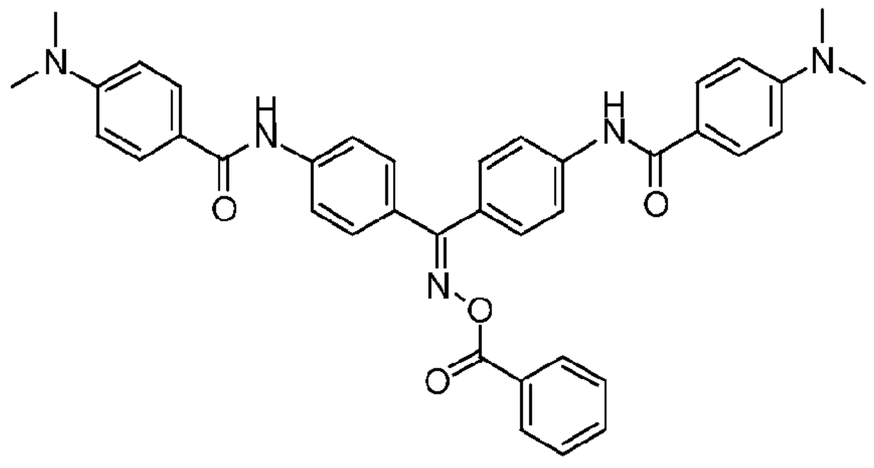
N,*N*'-(((((thiophene-2-carbonyl)oxy)imino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **312**)



[0784] Compound **312** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{36}H_{33}N_5O_4S$: 632.77; found: 631.99.

EXAMPLE 213

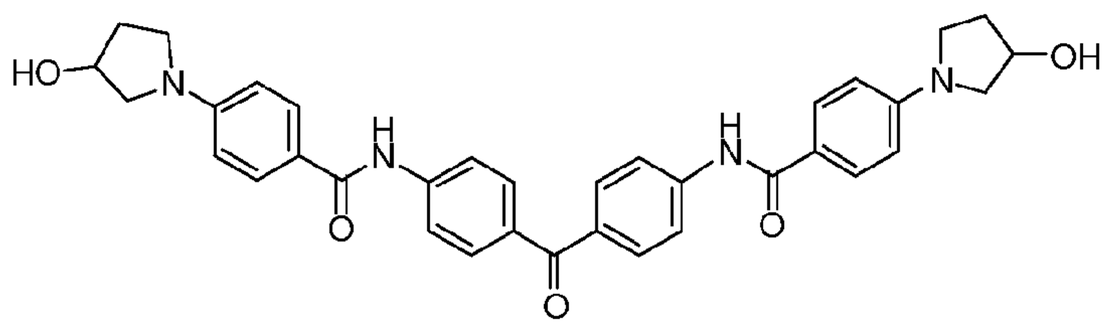
N,*N*'-((((benzoyloxy)imino)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **313**)



[0785] Compound **313** was prepared from compound **301** by a standard oxime synthesis procedure. $[M+Na]^+$ calcd for $C_{38}H_{35}N_5O_4$: 647.74; found: 647.86.

EXAMPLE 214

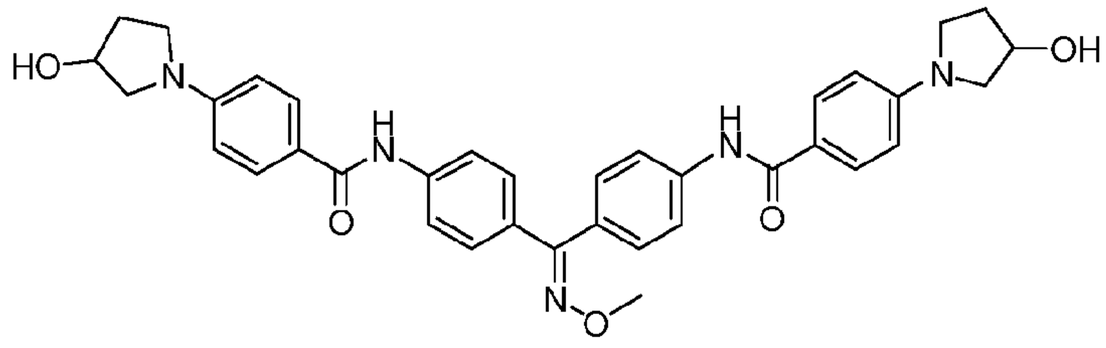
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(3-hydroxypyrrolidin-1-yl)benzamide) (Compound **314**)



[0786] Compound **314** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(2-hydroxypyrrolidino)benzoate. $[M+H]^+$ calcd for $C_{35}H_{35}N_4O_5$: 591.26; found: 591.03.

EXAMPLE 215

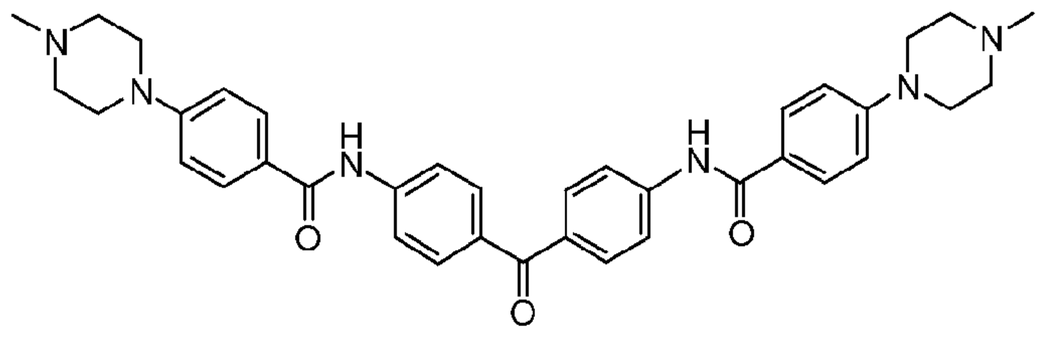
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-(3-hydroxypyrrolidin-1-yl)benzamide) (Compound **315**)



[0787] Compound **315** was prepared from compound **314** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{36}H_{37}N_5O_5$: 620.28; found: 620.11.

EXAMPLE 216

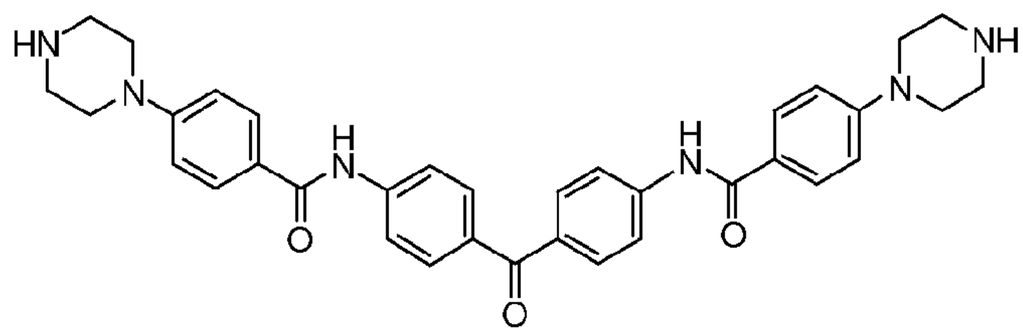
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(4-methylpiperazin-1-yl)benzamide) (Compound **316**)



[0788] Compound **316** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(4-methylpiperazino)benzoate. $[M+II]^+$ calcd for $C_{37}H_{41}N_6O_3$: 617.32; found: 617.12.

EXAMPLE 217

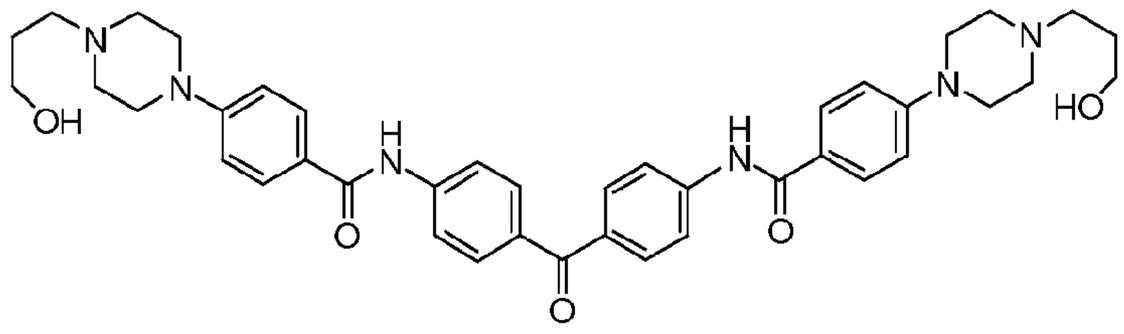
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(piperazin-1-yl)benzamide) (Compound **317**)



[0789] Compound **317** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-piperazinobenzoate. $[M+H]^+$ calcd for $C_{35}H_{37}N_6O_3$: 589.29; found: 589.07.

EXAMPLE 218

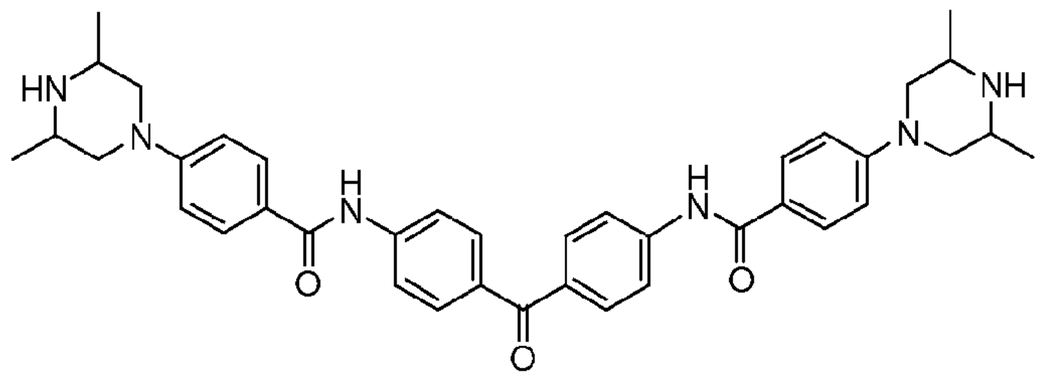
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(4-(3-hydroxypropyl)piperazin-1-yl)benzamide) (Compound **318**)



[0790] Compound **318** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(4-(3-hydroxypropyl)piperazino)benzoate. $[M+H]^+$ calcd for $C_{41}H_{48}N_6O_5$: 705.37; found: 705.19.

EXAMPLE 219

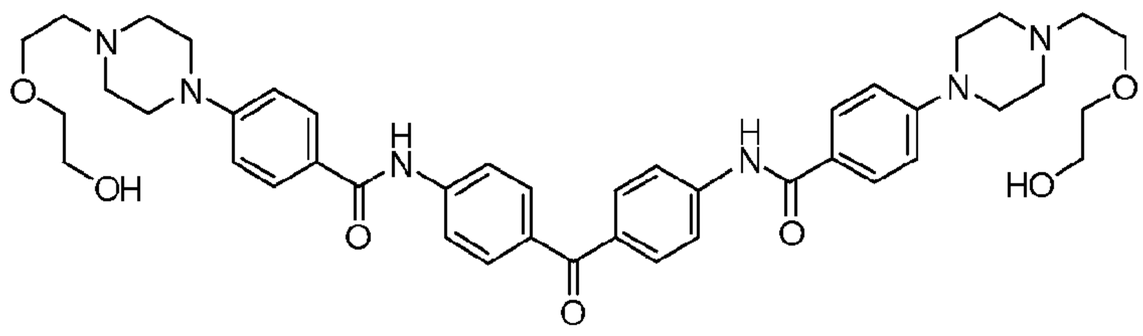
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(3,5-dimethylpiperazin-1-yl)benzamide) (Compound **319**)



[0791] Compound **319** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(3,5-dimethylpiperazino)benzoate. $[M+H]^+$ calcd for $C_{39}H_{44}N_6O_3$: 645.35; found: 645.16.

EXAMPLE 220

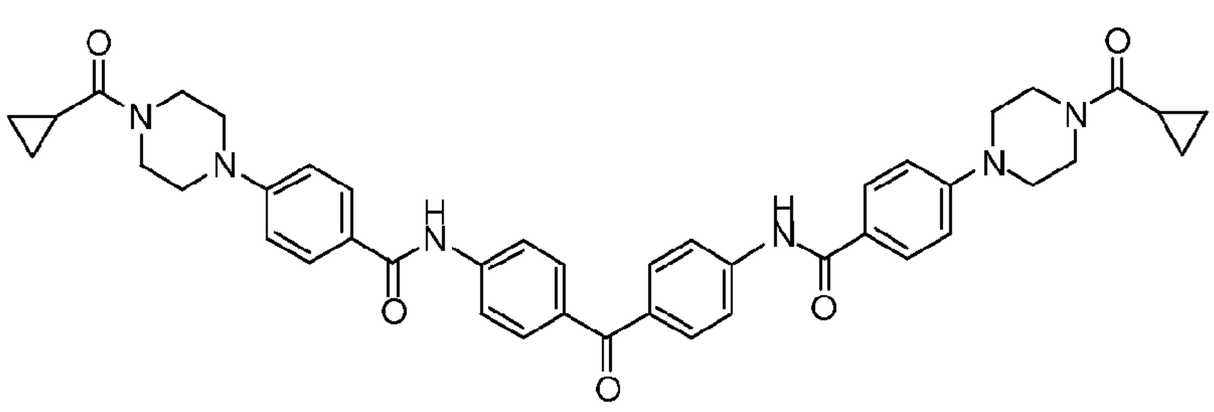
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(4-(2-(2-hydroxyethoxy)ethyl)piperazin-1-yl)benzamide) (Compound **320**)



[0792] Compound **320** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(4-(2-hydroxyethoxy)ethyl)piperazino)benzoate. $[M+H]^+$ calcd for $C_{43}H_{52}N_6O_7$: 765.39; found: 765.36.

EXAMPLE 221

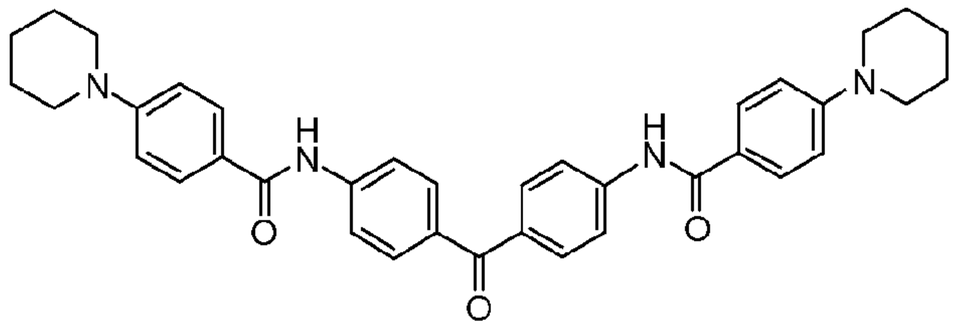
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(4-(cyclopropanecarbonyl)piperazin-1-yl)benzamide) (Compound **321**)



[0793] Compound **321** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(4-cyclopropylcarbonyl)piperazino)benzoate. $[M+H]^+$ calcd for $C_{43}H_{44}N_6O_5$: 725.34; found: 725.11.

EXAMPLE 222

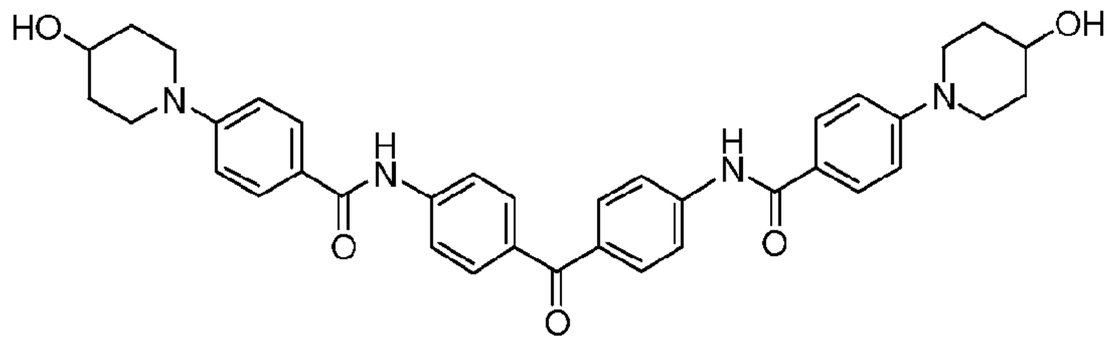
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(piperidin-1-yl)benzamide) (Compound **322**)



[0794] Compound **322** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-piperidinobenzoate. $[M+H]^+$ calcd for $C_{37}H_{38}N_4O_3$: 587.30; found: 587.02.

EXAMPLE 223

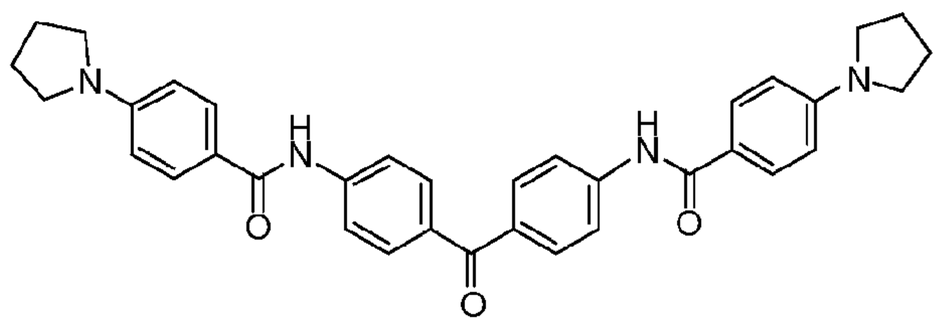
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(4-hydroxypiperidin-1-yl)benzamide) (Compound **323**)



[0795] Compound **323** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(4-hydroxypiperidino)benzoate. $[M+H]^+$ calcd for $C_{37}H_{39}N_4O_5$: 619.29; found: 619.10.

EXAMPLE 224

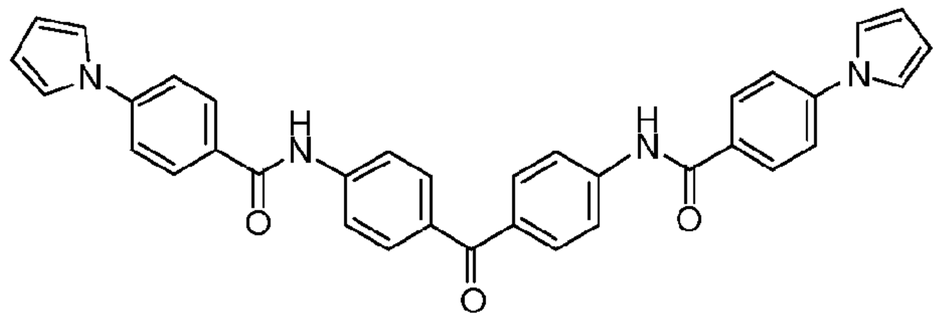
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(pyrrolidin-1-yl)benzamide) (Compound **324**)



[0796] Compound **324** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-pyrrolidinobenzoate. $[M+H]^+$ calcd for $C_{35}H_{34}N_4O_3$: 559.27; found: 559.00.

EXAMPLE 225

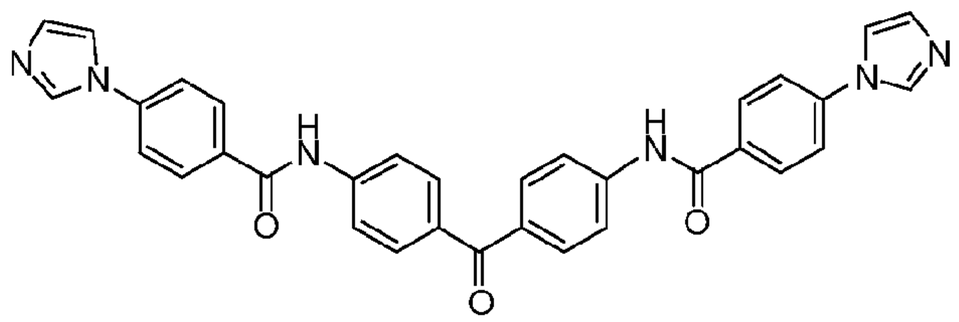
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(1*H*-pyrrol-1-yl)benzamide) (Compound **325**)



[0797] Compound **325** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-pyrrolylbenzoate. $[M+H]^+$ calcd for $C_{35}H_{26}N_4O_3$: 551.20; found: 551.04.

EXAMPLE 226

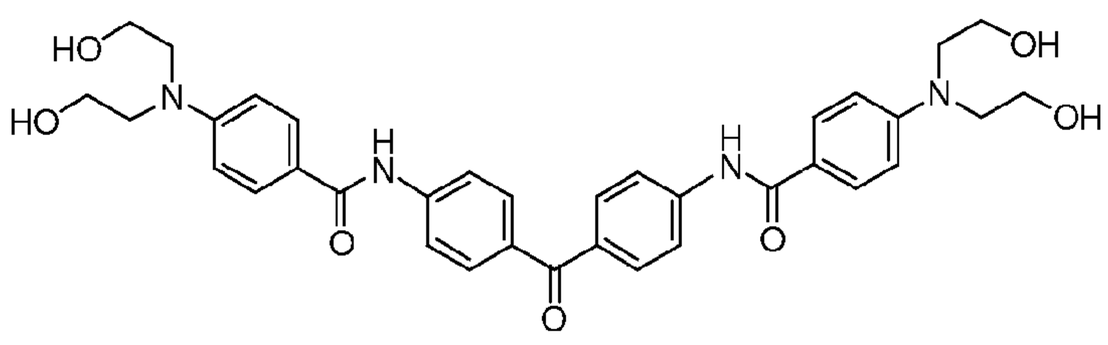
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(1*H*-imidazol-1-yl)benzamide) (Compound **326**)



[0798] Compound **326** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-imidazolylbenzoate. $[M+H]^+$ calcd for $C_{33}H_{24}N_6O_3$: 553.19; found: 552.98.

EXAMPLE 227

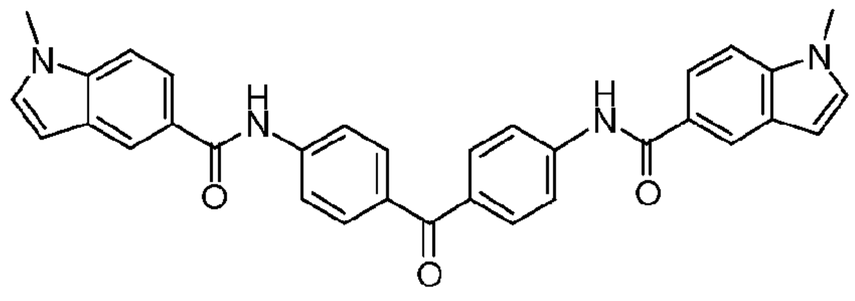
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-(bis(2-hydroxyethyl)amino)benzamide) (Compound **327**)



[0799] Compound **327** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-bis(2-hydroxylethyl)aminobenzoate. $[M+H]^+$ calcd for $C_{35}H_{38}N_4O_7$: 627.28; found: 627.06.

EXAMPLE 228

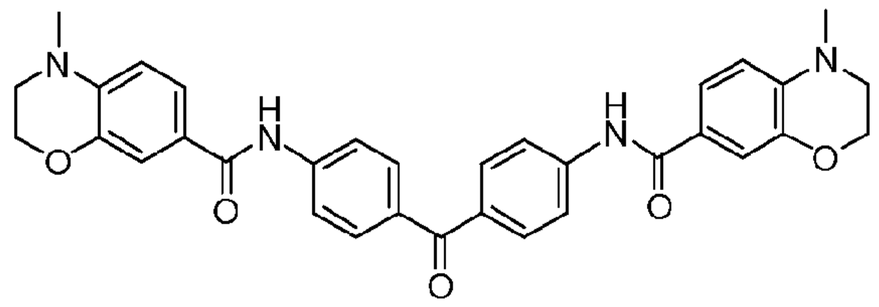
N,*N*'-(carbonylbis(4,1-phenylene))bis(1-methyl-1*H*-indole-5-carboxamide) (Compound **328**)



[0800] Compound **328** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 5-(1-methylindole)caboxylate. $[M+H]^+$ calcd for $C_{33}H_{26}N_4O_3$: 527.20; found: 527.00.

EXAMPLE 229

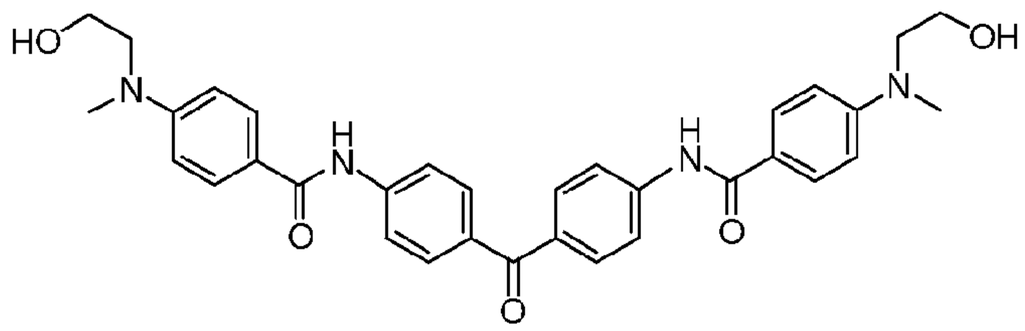
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-methyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine-7-carboxamide) (Compound **329**)



[0801] Compound **329** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 6-(1-methyl-1,4-benzoxazine)caboxylate. $[M+H]^+$ calcd for $C_{33}H_{30}N_4O_5$: 563.22; found: 562.92.

EXAMPLE 230

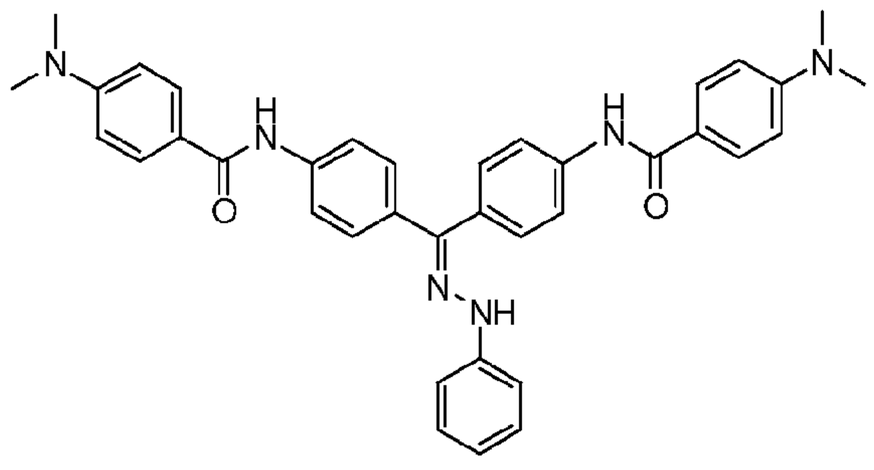
N,*N*'-(carbonylbis(4,1-phenylene))bis(4-((2-hydroxyethyl)(methyl)amino)benzamide) (Compound **330**)



[0802] Compound **330** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(N-2-hydroxylethyl-N-methylamino)benzoate. $[M+H]^+$ calcd for $C_{33}H_{35}N_4O_5$: 567.26; found: 567.04.

EXAMPLE 231

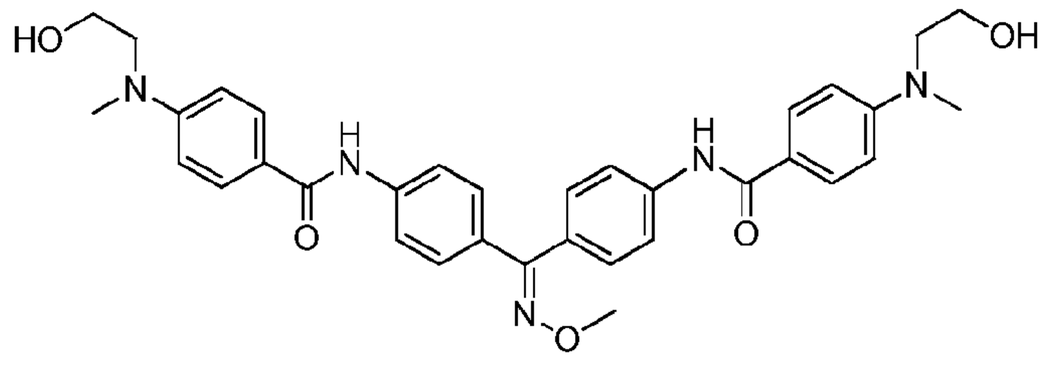
N,*N*'-(((2-phenylhydrazono)methylene)bis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **331**)



[0803] Compound **331** was prepared from compound **301** by a standard hydrazone synthesis procedure. $[M+H]^+$ calcd for $C_{37}H_{36}N_6O_2$: 597.29; found: 597.08.

EXAMPLE 232

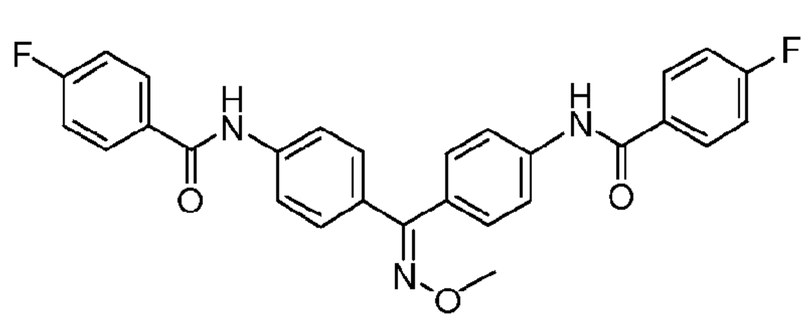
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-((2-hydroxyethyl)(methyl)amino)benzamide) (Compound **332**)



[0804] Compound **332** was prepared from compound **330** by a standard oxime synthesis procedure. $[M+H]^+$ calcd for $C_{34}H_{37}N_5O_5$: 596.28; found: 596.07.

EXAMPLE 233

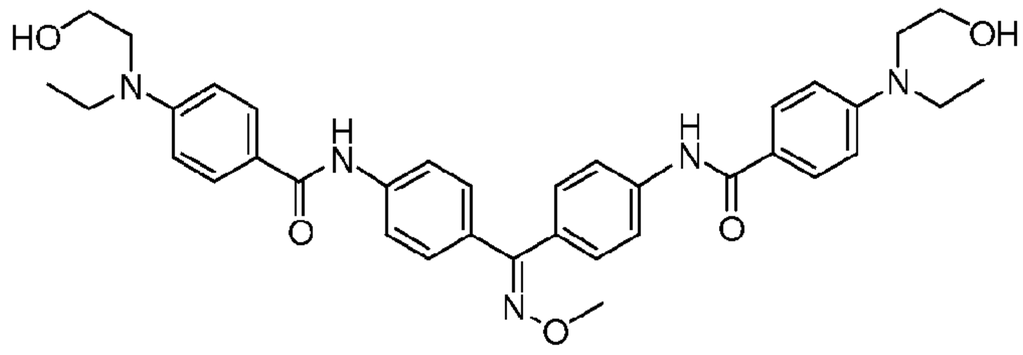
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-fluorobenzamide) (Compound **333**)



[0805] Compound **333** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-fluorobenzoate followed by a standard oxime synthesis procedure. ^{1}H NMR (500MHz, DMSO-d_6) δ 11.00 (d, J = 12.5 Hz, 1H), 10.41 (d, J = 12.5 Hz, 1H), 8.03 (m, 4H), 7.85 (d, J = 15 Hz, 2H), 7.79 (d, J = 15 Hz, 2H), 7.38 (m, 6H), 7.29 (d, J = 15 Hz, 2H), 3.79 (s, 3H).

EXAMPLE 234

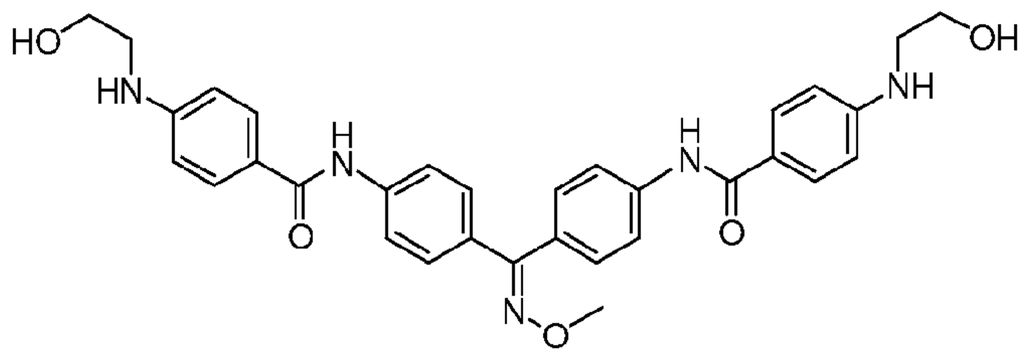
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-(ethyl(2-hydroxyethyl)amino) benzamide) (Compound **334**)



[0806] Compound **334** was prepared from compound **333** and *N*-2-hydroxyethyl-*N*-ethylamine by a standard procedure. $[M+H]^+$ calcd for $C_{36}H_{41}N_5O_5$: 624.31; found: 624.09.

EXAMPLE 235

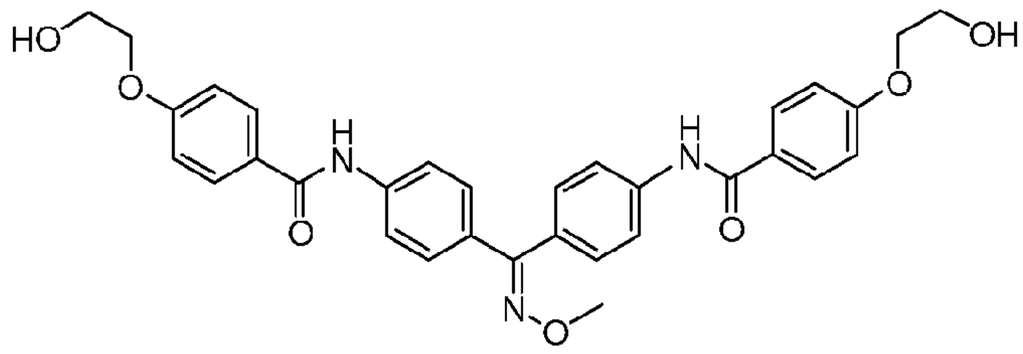
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-((2-hydroxyethyl)amino)benzamide) (Compound **335**)



[0807] Compound **335** was prepared from compound **333** and 2-hydroxyethylamine by a standard procedure. $[M+H]^+$ calcd for $C_{32}H_{33}N_5O_5$: 568.25; found: 567.98.

EXAMPLE 236

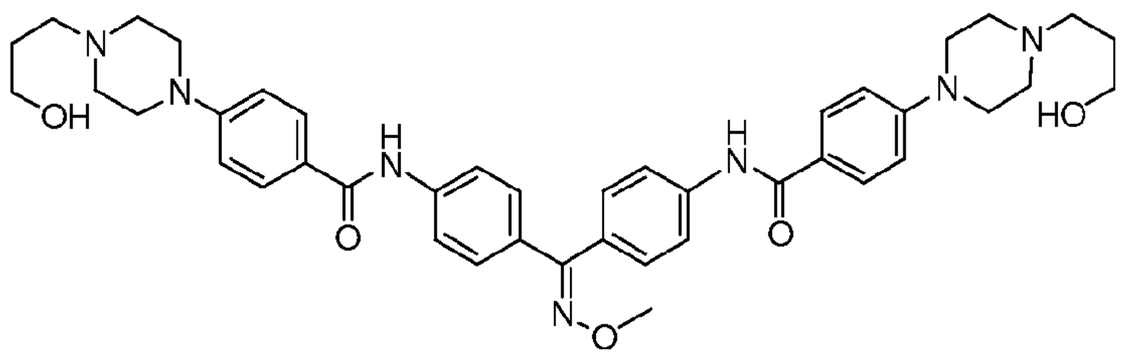
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-(2-hydroxyethoxy)benzamide) (Compound **336**)



[0808] Compound **336** was prepared from compound **333** and ethylenediol by a standard procedure. $[M+H]^+$ calcd for $C_{32}H_{31}N_3O_7$: 570.22; found: 570.01.

EXAMPLE 237

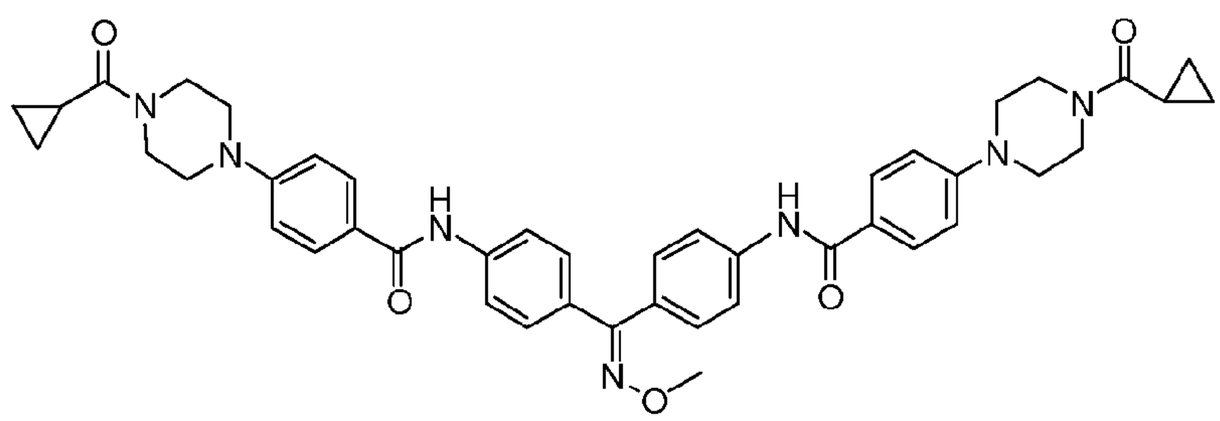
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-(4-(3-hydroxypropyl)piperazin-1-yl)benzamide) (Compound **337**)



[0809] Compound **337** was prepared from compound **333** and 3-hydroxypropylpiperazine by a standard procedure. $[M+H]^+$ calcd for $C_{42}H_{51}N_7O_5$: 734.93; found: 734.23.

EXAMPLE 238

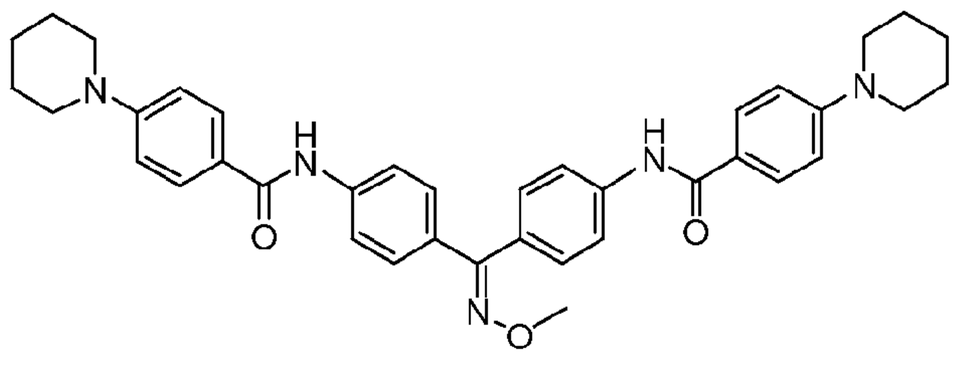
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-(4-(cyclopropanecarbonyl)piperazin-1-yl)benzamide) (Compound **338**)



[0810] Compound **338** was prepared from compound **333** and 4-cyclopropylcarbonylpiperazine by a standard procedure. $[M+H]^+$ calcd for $C_{44}H_{47}N_7O_5$: 754.92; found: 754.29.

EXAMPLE 239

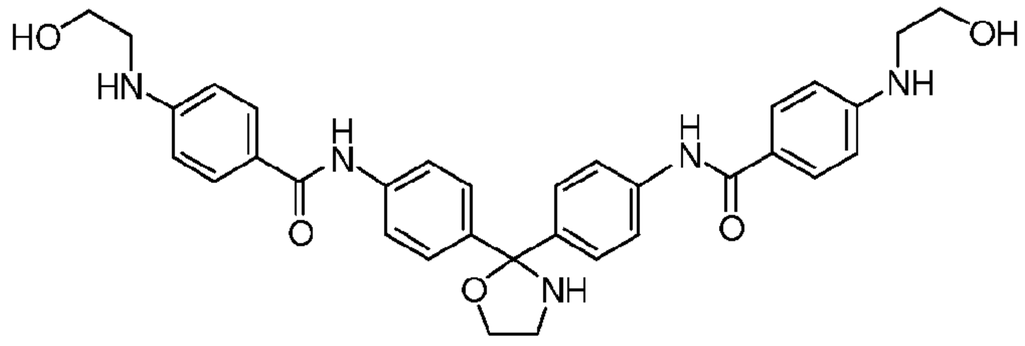
N,*N*'-(((methoxyimino)methylene)bis(4,1-phenylene))bis(4-(piperidin-1-yl)benzamide) (Compound **339**)



[0811] Compound **339** was prepared from compound **333** and piperidine by a standard procedure. $[M+H]^+$ calcd for $C_{38}H_{41}N_5O_3$: 616.79; found: 616.19.

EXAMPLE 240

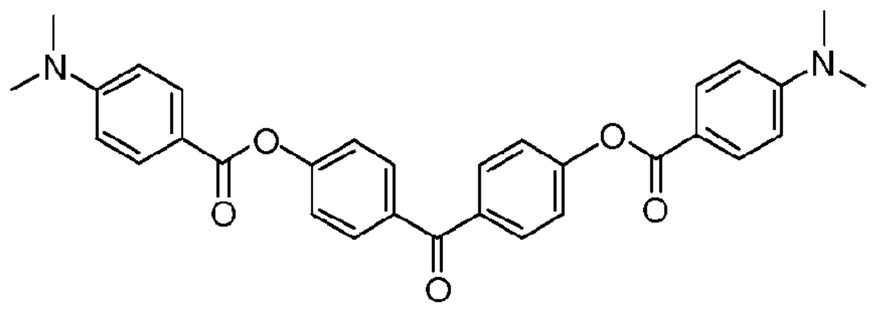
N,N'-(4,4'-(Oxazolidine-2,2-diyl)bis(4,1-phenylene))bis(4-(2-hydroxylethylamino)benzamide) (Compound **340**)



[0812] Compound **340** was prepared from N,N'-(4,4'-Benzophenone)bis(4-fluorobenzamide) and 2-hydroxyethylamine by a standard procedure. $[M+H]^+$ calcd for $C_{33}H_{36}N_5O_5$: 582.27; found: 582.07.

EXAMPLE 241

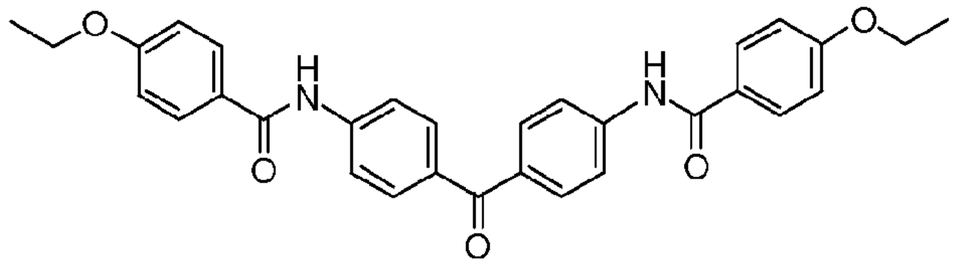
4,4'-Carbonylbis(4,1-phenylene)bis(4-(dimethylamino)benzoate (Compound **341**)



[0813] Compound **341** was prepared according to the procedure described in Scheme IV from 4,4'-dihydroxybenzophenone and 4-dimethylaminobenzoic acid. $[M+H]^+$ calcd for $C_{31}H_{28}N_2O_5$: 509.20; found: 509.05.

EXAMPLE 242

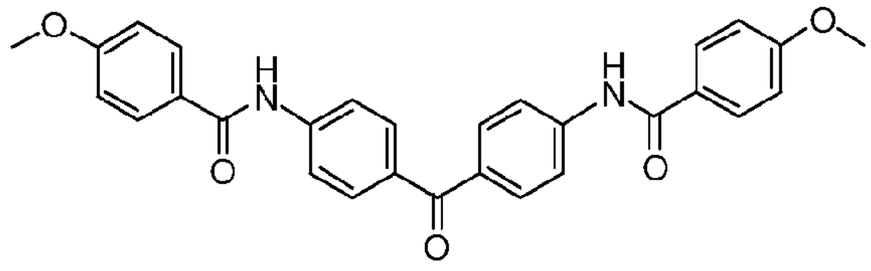
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(4-ethoxybenzamide) (Compound **342**)



[0814] Compound **342** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-ethoxybenzoate. $[M+H]^+$ calcd for $C_{31}H_{28}N_2O_5$: 509.20; found: 508.98.

EXAMPLE 243

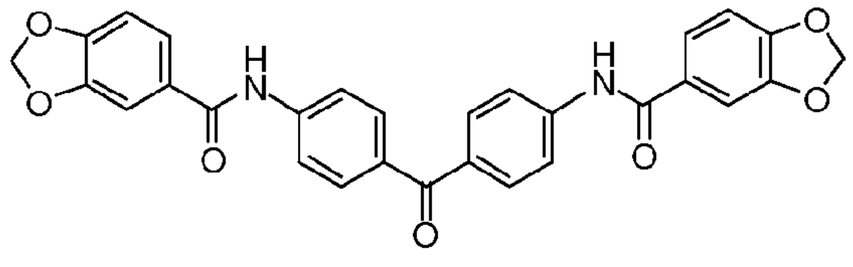
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(4-methoxybenzamide) (Compound **343**)



[0815] Compound **343** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-methoxybenzoate. $[M+H]^+$ calcd for $C_{29}H_{24}N_2O_5$: 481.17; found: 480.90.

EXAMPLE 244

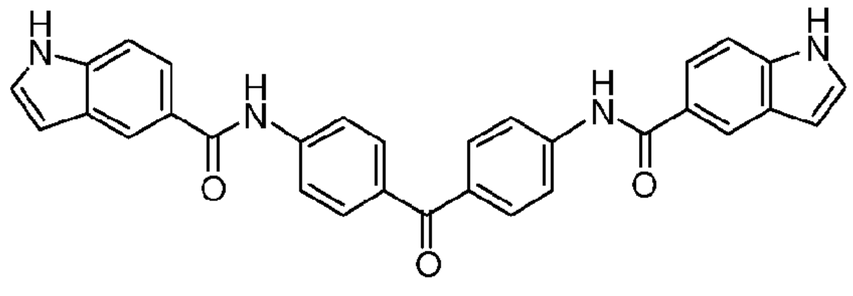
N,N'-(4,4'-Carbonylbis(4,1-phenylene))dibenzo[1,3]dioxole-5-carboxamide) (Compound **344**)



[0816] Compound **344** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and benzo[1,3]dioxole-5-carboxylate. $[M+H]^+$ calcd for $C_{29}H_{20}N_2O_7$: 509.13; found: 508.91.

EXAMPLE 245

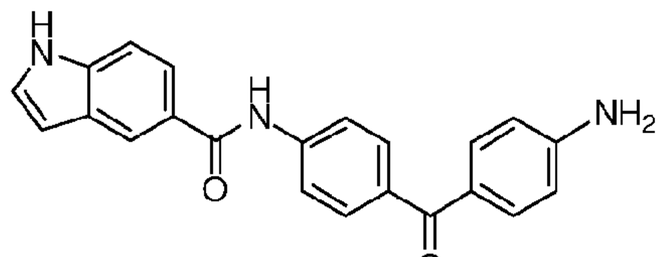
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(1*H*-indole-5-carboxamide) (Compound **345**)



[0817] Compound **345** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 1*H*-indole-5-carboxylate. $[M+H]^+$ calcd for $C_{31}H_{22}N_4O_3$: 499.17; found: 498.92.

EXAMPLE 246

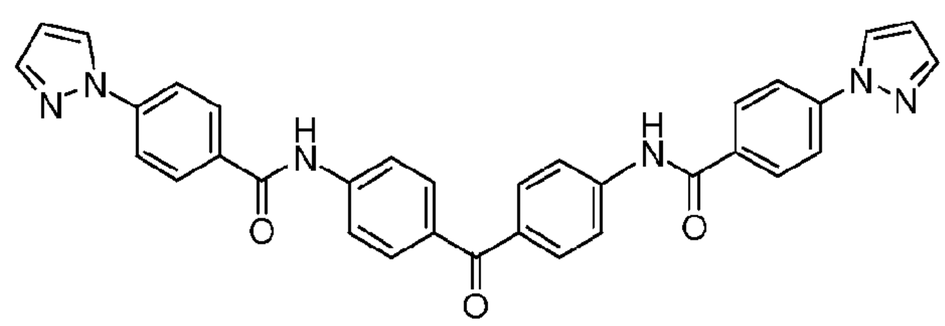
N-(4-(4-Aminobenzoyl)phenyl)-1*H*-indole-5-carboxamide (Compound **346**)



[0818] Compound **346** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 1*H*-indole-5-carboxylate. $[M+H]^+$ calcd for $C_{22}H_{17}N_3O_2$: 356.14; found: 355.90.

EXAMPLE 247

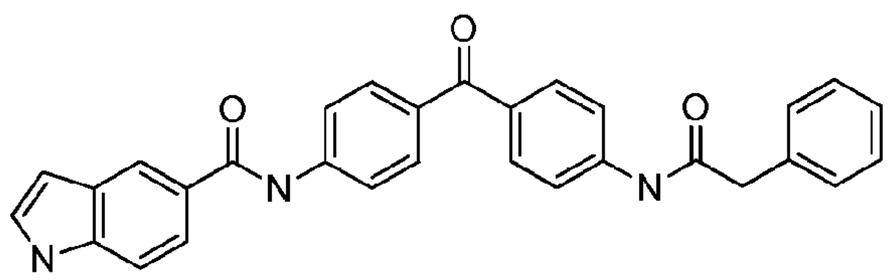
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(4-(1*H*-pyrazol-1-yl)benzamide) (Compound **347**)



[0819] Compound **347** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(pyrazol-1-yl)benzoate. $[M+H]^+$ calcd for $C_{33}H_{24}N_6O_3$: 553.19; found: 552.99.

EXAMPLE 248

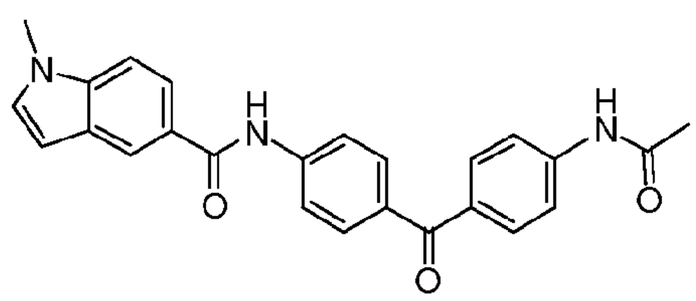
N-(4-(4-(2-phenylacetamido)benzoyl)phenyl)-1*H*-indole-5-carboxamide (Compound **348**)



[0820] Compound **348** was prepared from compound **346** and benzylbromide. $[M+H]^+$ calcd for $C_{30}H_{23}N_3O_3$: 474.05; found: 474.49.

EXAMPLE 249

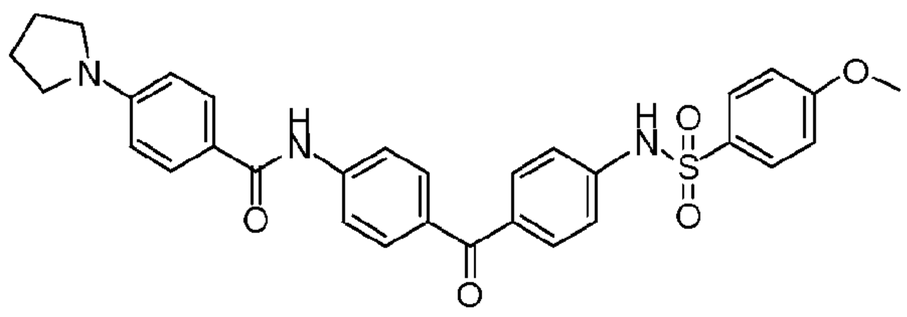
4-ethoxy-*N*-(4-(4-(2-(4-ethoxyphenyl)-2-oxoethyl)benzoyl)phenyl)benzamide (Compound **349**)



[0821] Compound **349** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 1-methylindole-5-carboxylate. $[M+H]^+$ calcd for $C_{25}H_{21}N_3O_3$: 412.07; found: 411.94.

EXAMPLE 250

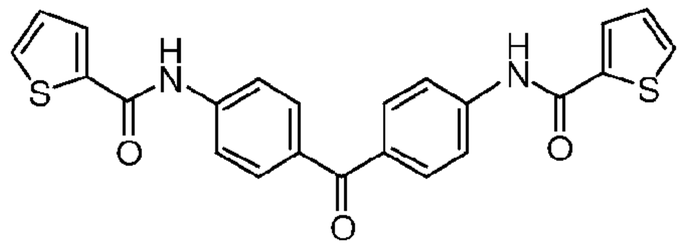
N-(4-(4-(4-Methoxyphenylsulfonamido)benzoyl)phenyl)-4-(pyrrolidin-1-yl)benzamide (Compound **350**)



[0822] Compound **350** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-pyrrolidinylbenzoate. $[M+H]^+$ calcd for $C_{31}H_{29}N_3O_5S$: 556.17; found: 555.99.

EXAMPLE 251

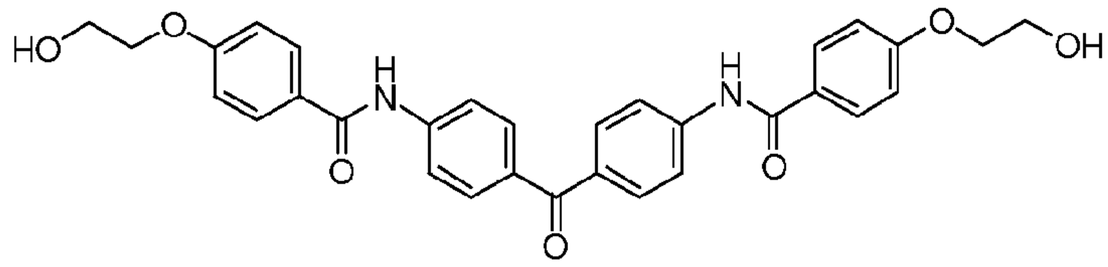
N,N'-(4,4'-Carbonylbis(4,1-phenylene))dithiophene-2-carboxamide (Compound **351**)



[0823] Compound **351** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 2-thiophenecarboxylate. ^1H NMR (500MHz, DMSO-d_6) δ 10.54 (s, 2H), 8.09 (d, J = 3.75 Hz, 2H), 7.94 (d, J = 12.5 Hz, 4H), 7.91 (d, J = 3.75 Hz, 2H), 7.88 (d, J = 12.5 Hz, 4H), 7.25 (t, J = 3.75 Hz, 2H).

EXAMPLE 252

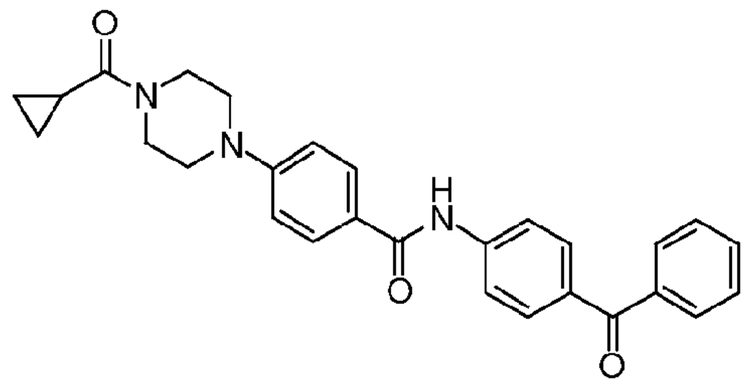
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(4-(2-hydroxyethoxy)benzamide (Compound **352**)



[0824] Compound **352** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-(2-hydroxyethoxy)benzoate. $[M+H]^+$ calcd for $C_{31}H_{28}N_2O_7$: 541.09; found: 541.05.

EXAMPLE 253

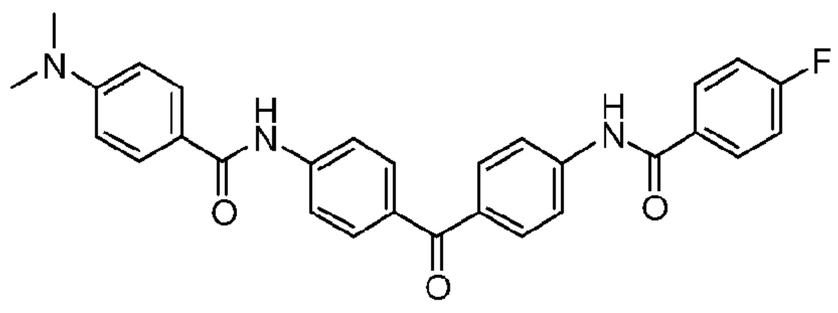
N-(4-Benzoylphenyl)-4-(4-cyclopropanecarbonylpiperazin-1-yl)benzamide (Compound **353**)



[0825] Compound **353** was prepared according to the procedure described in Scheme IV from 4-aminobenzophenone and 4-piperazinebenzoate. $[M+H]^+$ calcd for $C_{28}H_{28}N_3O_3$: 454.21; found: 454.01.

EXAMPLE 254

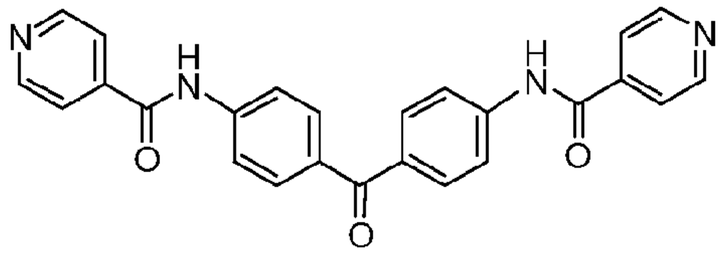
4-(Dimethylamino)-*N*-(4-(4-(4-fluorobenzamido)benzoyl)phenyl)benzamide (Compound **354**)



[0826] Compound **354** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and the substituted benzoates. $[M+H]^+$ calcd for $C_{29}H_{25}FN_3O_3$: 482.19; found: 482.22.

EXAMPLE 255

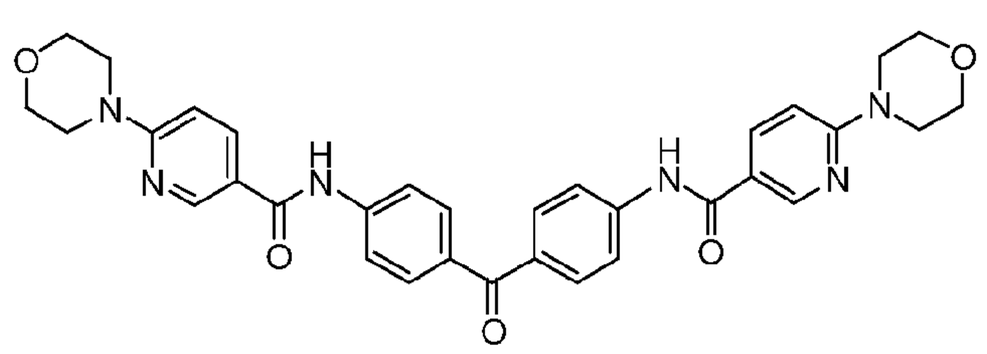
N,N'-(4,4'-Carbonylbis(4,1-phenylene))diisonicotinamide (Compound **355**)



[0827] Compound **355** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-picolinic acid. $[M+H]^+$ calcd for $C_{25}H_{19}N_4O_3$: 423.15; found: 422.87.

EXAMPLE 256

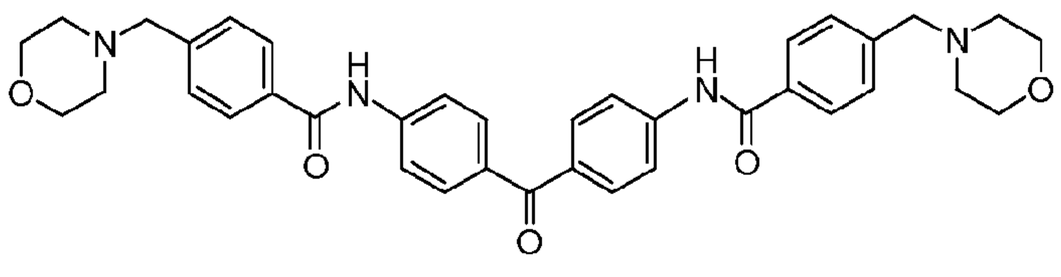
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(6-morpholinonicotinamide) (Compound **356**)



[0828] Compound **356** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 6-morpholinonicotinic acid. $[M+H]^+$ calcd for $C_{33}H_{33}N_6O_5$: 593.25; found: 593.03.

EXAMPLE 257

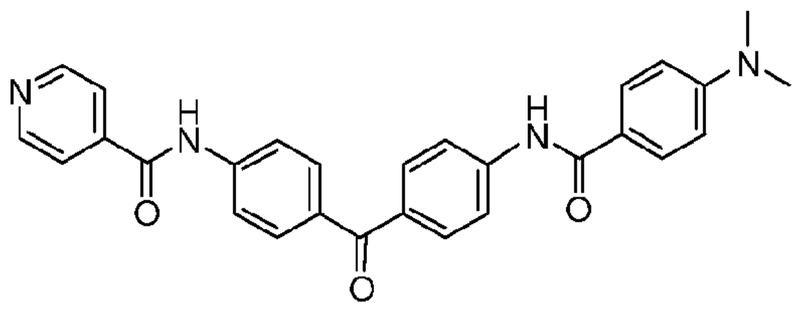
N,N'-(4,4'-Carbonylbis(4,1-phenylene))bis(4-(morpholinomethyl)benzamide) (Compound **357**)



[0829] Compound **357** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-morpholinomethylbenzoate. $[M+H]^+$ calcd for $C_{37}H_{39}N_4O_5$: 619.29; found: 619.10.

EXAMPLE 258

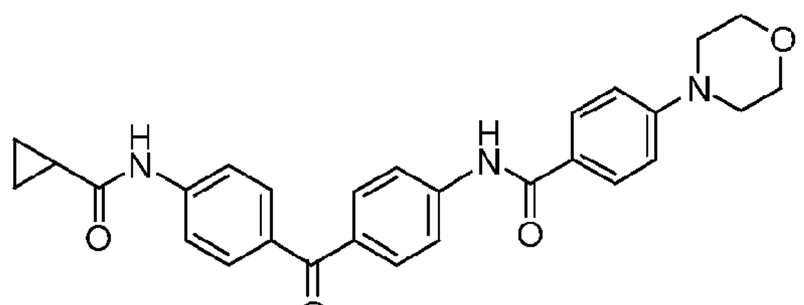
N-(4-(4-(4-Dimethylamino)benzoyl)phenyl)isonicotinamide (Compound **358**)



[0830] Compound **358** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-picolinic acid. $[M+H]^+$ calcd for $C_{28}H_{25}N_4O_3$: 465.19; found: 464.98.

EXAMPLE 259

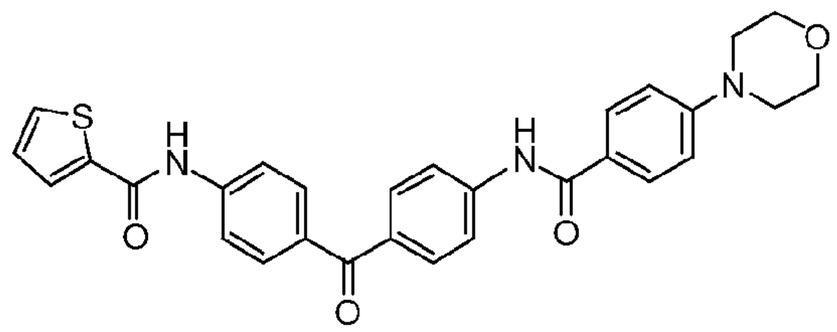
N-(4-(4-Cyclopropanecarboxamido)benzoyl)phenyl)-4-morpholinobenzamide (Compound **359**)



[0831] Compound **359** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{28}H_{28}N_3O_4$: 470.21; found: 469.97.

EXAMPLE 260

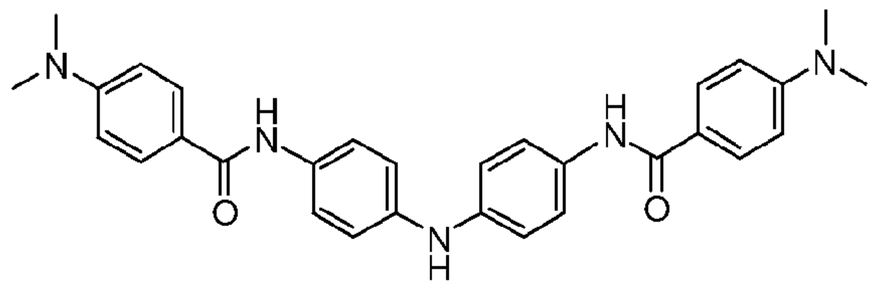
N-(4-(4-(2-Thienyl)carboxamido)benzoyl)phenyl)-4-morpholinobenzamide (Compound **360**)



[0832] Compound **360** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{26}N_3O_4S$: 512.16; found: 511.95.

EXAMPLE 261

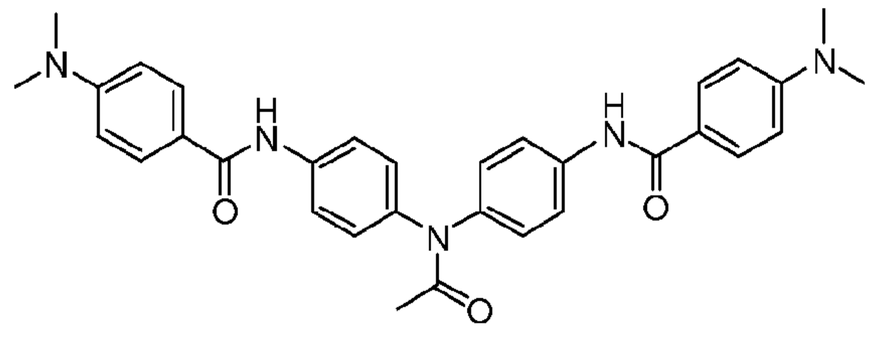
N,N'-(4,4'-Azanediylbis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **361**)



[0833] Compound **361** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{30}H_{31}N_5O_2$: 494.25; found: 494.04.

EXAMPLE 262

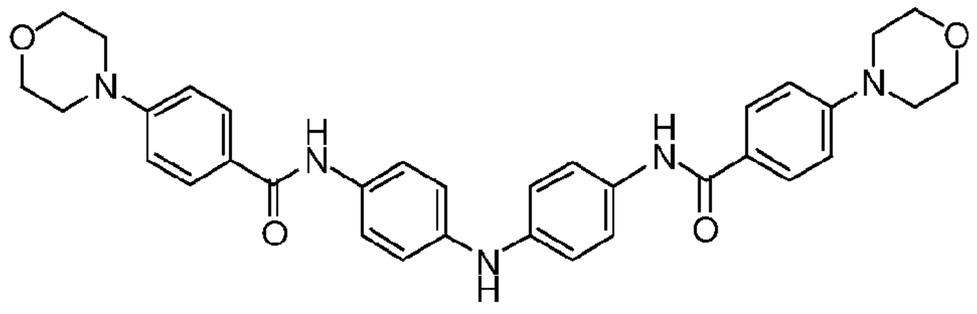
4-(dimethylamino)-*N*-(4-(*N*-(4-(4-(dimethylamino)benzamido)phenyl)acetamido) phenyl)benzamide (Compound **362**)



[0834] Compound **362** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-dimethylaminobenzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 9.99 (bs, 1H), 9.89 (bs, 1H), 7.84 (d, J = 9 Hz, 6H), 7.70 (bs, 2H), 7.36 (bs, 2H), 7.20 (bs, 2H), 6.73 (d, J = 9 Hz, 4H), 2.98 (s, 12H), 1.93 (s, 3H).

EXAMPLE 263

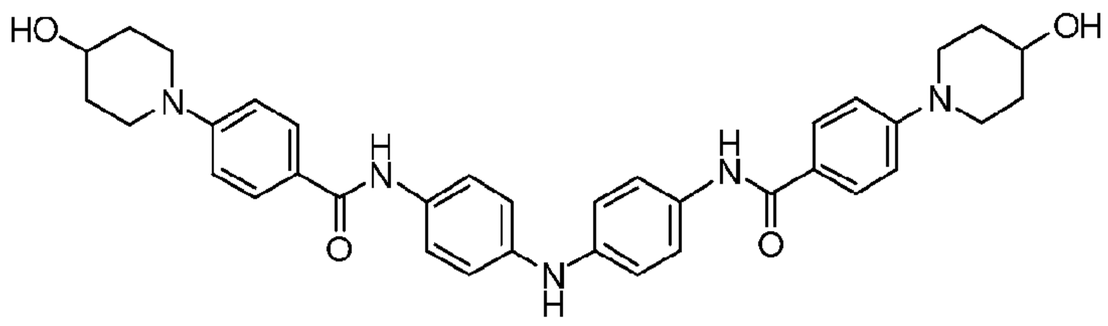
N,N'-(4,4'-Azanediylbis(4,1-phenylene))bis(4-morpholinobenzamide) (Compound **363**)



[0835] Compound **363** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{34}H_{35}N_5O_4$: 578.27; found: 578.11.

EXAMPLE 264

N,N'-(4,4'-Azanediylbis(4,1-phenylene))bis(4-(4-hydroxypiperidino)benzamide) (Compound **364**)

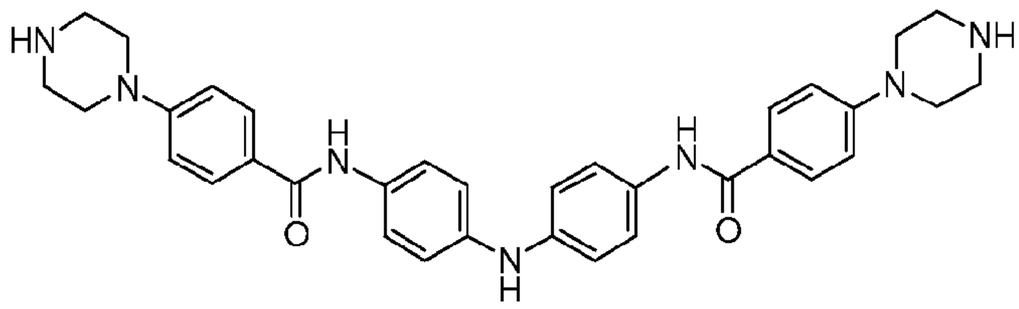


[0836] Compound **364** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-(4-hydroxypiperidinobenzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 9.75 (s, 2H), 7.94 (s, 1H), 7.82 (d, J = 9 Hz, 4H), 7.57 (d, J = 9 Hz,

4H), 6.98 (t, J = 9 Hz, 8H), 4.71 (d, J = 4.5 Hz, 2H), 3.67 (m, 8H), 2.98 (dt, J = 3, 10 Hz, 2H), 1.80 (m, 4H), 1.43 (m, 4H).

EXAMPLE 265

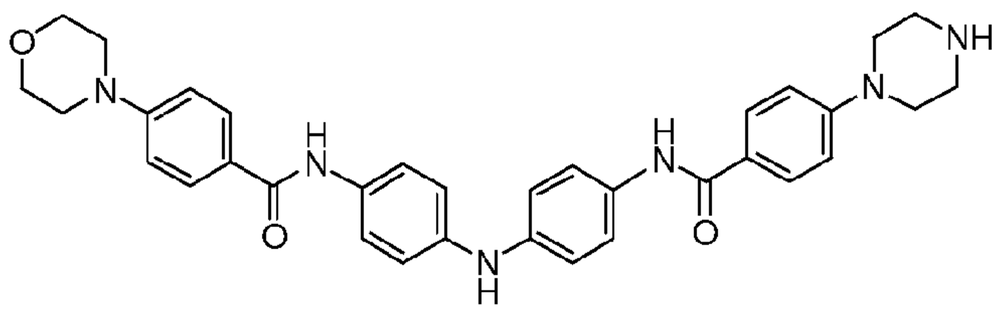
N,N'-(4,4'-Azanediylbis(4,1-phenylene))bis(4-piperazinobenzamide) (Compound **365**)



[0837] Compound **365** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-piperazinobenzoate. $[M+H]^+$ calcd for $C_{34}H_{38}N_7O_2$: 576.31; found: 576.17.

EXAMPLE 266

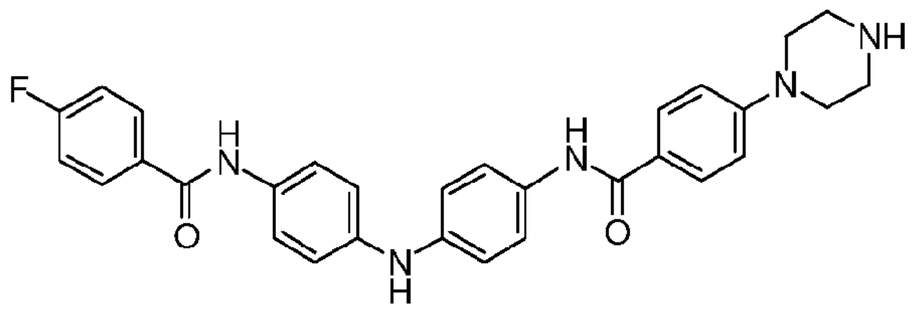
4-morpholino-*N*-(4-((4-(4-(piperazin-1-yl)benzamido)phenyl)amino)phenyl)benzamide (Compound **366**)



[0838] Compound **366** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{34}H_{36}N_6O_3$: 577.21; found: 577.16.

EXAMPLE 267

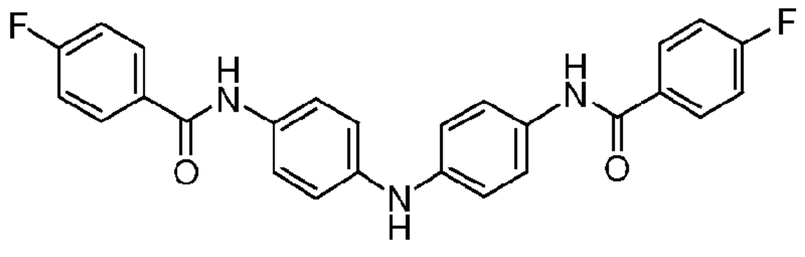
4-Fluoro-*N*-(4-(4-(4-piperazinobenzamido)phenylamino)phenyl)benzamide (Compound **367**)



[0839] Compound **367** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-piperazinobenzoate. $[M+H]^+$ calcd for $C_{30}H_{29}FN_5O_2$: 510.23; found: 510.06.

EXAMPLE 268

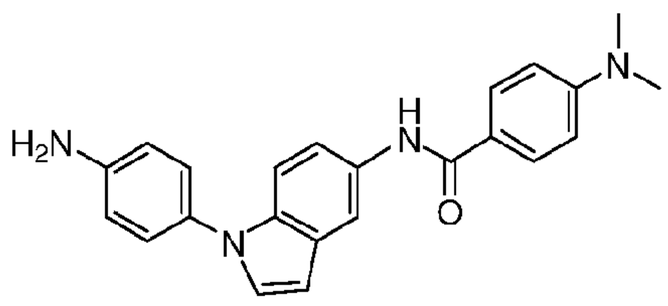
N,N'-(4,4'-Azanediylbis(4,1-phenylene))bis(4-fluorobenzamide) (Compound **368**)



[0840] Compound **368** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-fluorobenzoate. $[M+H]^+$ calcd for $C_{26}H_{19}F_2N_3O_2$: 444.14; found: 443.86.

EXAMPLE 269

N-(1-(4-Aminophenyl)-1*H*-indol-5-yl)-4-dimethylaminobenzamide (Compound **369**)



[0841] Compound **369** was prepared according to the general procedure described in Scheme IV. Preparation of 4-(dimethylamino)-*N*-(1*H*-indol-5-yl)benzamide: 1*H*-indol-5-amine (200 mg, 1.51 mmol), hydroxybenzotriazole (204 mg, 1.51 mmol), triethylamine (0.23 mL, 1.66 mmol), and 4-(dimethylamino)benzoic acid (275 mg, 1.66 mmol) were taken up in DMF (7.5 mL) and stirred. EDC (319 mg, 1.66 mmol) was added to the solution last. After the addition, the solution was stirred at room temperature for 4 h. Water was then added to the solution and stirred for 10 min. The formed precipitate was filtered and washed well with water, followed by hexanes. The grayish solid was dried under vacuum to give 393 mg (93%) of the product.

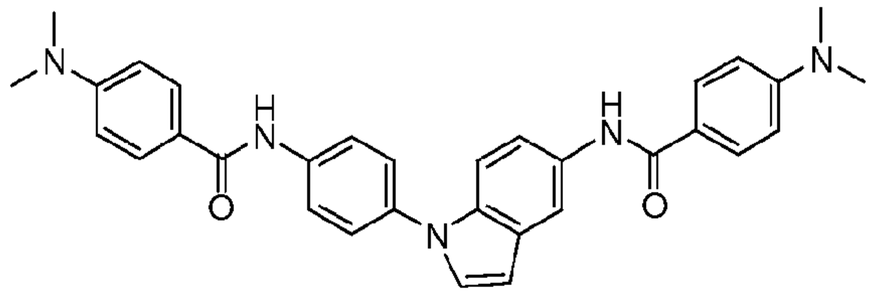
[0842] Preparation of 4-(dimethylamino)-*N*-(1-(4-nitrophenyl)-1*H*-indol-5-yl)benzamide: 4-(Dimethylamino)-*N*-(1*H*-indol-5-yl)benzamide (200 mg, 0.71 mmol), 4-fluoronitrobenze (101 mg, 0.71 mmol) and potassium carbonate (99 mg, 0.72 mmol) were taken up in DMSO (7.2 mL). The solution was heated to 100 °C and stirred for 24 h. After the solution was cooled it was diluted with water until a precipitate formed and stirred well for 5 min. Filtration gave a yellow solid, which was then washed well with water, followed by hexanes. The solid was dried under vacuum to give 258 mg (90%) product as a yellow solid.

[0843] Preparation of Compound **369**: 4-(Dimethylamino)-*N*-(1-(4-nitrophenyl)-1*H*-indol-5-yl)benzamide (330 mg, 0.82 mmol) was taken up in ethanol (28 mL) under

nitrogen. The solution was treated with $Pd(OH)_2$ (35 mg, 0.24 mmol) and placed under a balloon of H_2 gas. After stirring at RT for 2 h, the catalyst was removed via filtration through celite. Concentration of the filtrate yielded 260 mg (85%) of compound **369**. MS $[M+H]^+$ calcd for $C_{23}H_{22}N_4O$: 371.18; found: 370.94.

EXAMPLE 270

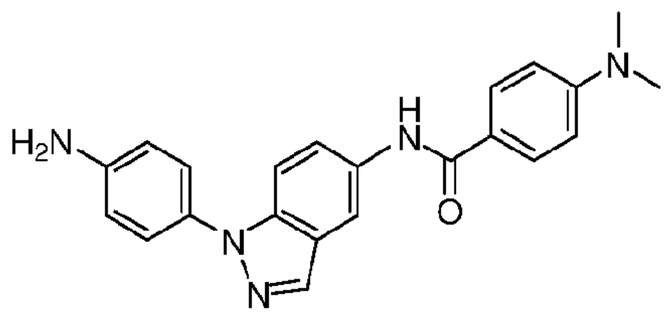
N-(1-(4-(4-Dimethylaminobenzamido)phenyl)-1*H*-indol-5-yl)-4-dimethylaminobenzamide (Compound **370**)



[0844] Compound **370** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{32}H_{31}N_5O_2$: 518.25; found: 517.95.

EXAMPLE 271

N-(1-(4-Aminophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **371**)



[0845] Compound **371** was prepared according to the general procedure described in Scheme IV. Preparation of 4-(dimethylamino)-*N*-(1*H*-indazol-5-yl)benzamide: 1*H*-Indazol-5-amine (200 mg, 1.50 mmol), hydroxybenzotriazole (20 mg, 0.15 mmol), triethylamine (0.23 mL, 1.65 mmol), and 4-(dimethylamino)benzoic acid (273 mg, 1.65 mmol) were taken up in DMF (7.5 mL) and stirred. EDC (317 mg, 1.65 mmol) was added to the solution last. After the addition, the solution was stirred at room temperature for 4 h. Water was then added to the solution and stirred for 10 min. The formed precipitate was filtered and washed well with water, followed by hexanes. The solid was dried under vacuum to give 410 mg (97%) of the product as a brown solid.

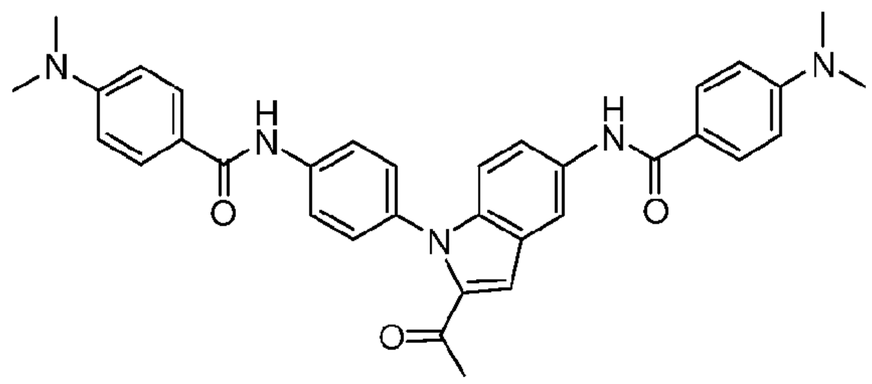
[0846] Preparation of 4-(dimethylamino)-*N*-(1-(4-nitrophenyl)-1*H*-indazol-5-yl)benzamide: 4-(dimethylamino)-*N*-(1*H*-indazol-5-yl)benzamide (100 mg, 0.35 mmol), 4-fluoronitrobenze (50 mg, 0.35 mmol) and potassium carbonate (49 mg, 0.35 mmol) were

taken up in DMSO (3.6 mL). The solution was heated to 100 °C and stirred for 24 h. After the solution was cooled it was diluted with water until a precipitate formed and stirred well for 5 min. Filtration gave a yellow solid, which was then washed well with water, followed by hexanes. The solid was dried under vacuum to give 133 mg (93%) of the product as a yellow solid.

[0847] Preparation of Compound **371**: 4-(Dimethylamino)-*N*-(1-(4-nitrophenyl)-1*H*-indazol-5-yl)benzamide (400 mg, 0.99 mmol) was taken up in ethanol (33 mL) under nitrogen. The solution was treated with $Pd(OH)_2$ (35 mg, 0.25 mmol) and placed under a balloon of H_2 gas. After stirring at RT for 2 h, the catalyst was removed via filtration through celite. The filtrate was concentrated onto silica under reduced pressure. Purification via flash chromatography (0-5% MeOH/ CH_2Cl_2) gave 180 mg (48%) of final compound **371** as a light brown solid. ^{1}H NMR (500 MHz, DMSO-d_6) 9.95 (s, 1H), 8.29 (s, 1H), 8.18 (s, 1H), 7.89 (d, J = 9 Hz, 2H), 7.69 (dd, J = 2, 9 Hz, 1H), 7.58 (d, J = 9 Hz, 1H), 7.32 (d, J = 9 Hz, 2H), 6.76 (d, J = 9 Hz, 2H), 6.71 (d, J = 9 Hz, 2H), 5.32 (s, 2H), 2.99 (s, 6H).

EXAMPLE 272

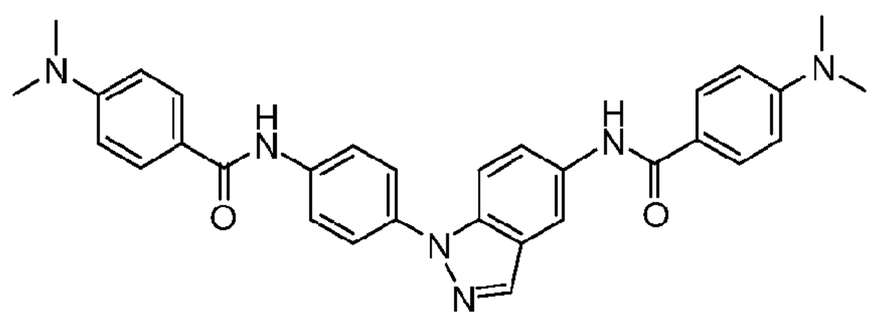
N-(2-Acetyl-1-(4-(4-dimethylaminobenzamido)phenyl)-1*H*-indol-5-yl)-4-dimethylaminobenzamide (Compound **372**)



[0848] Compound **372** was prepared according to the procedure described in Scheme IV from 2-acetyl-5-amino-1-(4-aminophenyl)indole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{34}H_{33}N_5O_3$: 560.26; found: 560.02.

EXAMPLE 273

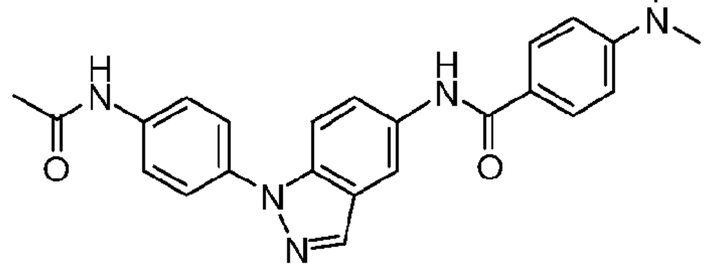
N-(1-(4-(4-Dimethylaminobenzamido)phenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **373**)



[0849] Compound **373** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. ^{1}H NMR (500MHz, Acetone-d_6) δ 9.44 (s, 1H), 9.38 (s, 1H), 8.49 (s, 1H), 8.23 (s, 1H), 8.08 (d, J = 9 Hz, 2H), 7.95 (d, J = 9 Hz, 4H), 7.81 (m, 2H), 7.76 (d, J = 9 Hz, 2H), 6.79 (d, J = 9 Hz, 4H), 3.06 (s, 6 H), 3.05 (s, 6H).

EXAMPLE 274

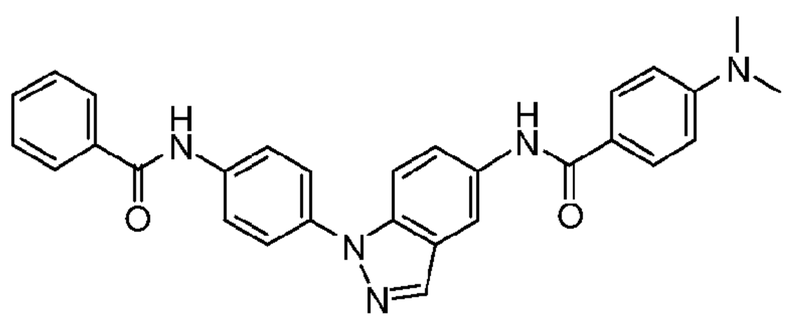
N-(1-(4-Acetamidophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **374**)



[0850] Compound **374** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{24}H_{23}N_5O_2$: 414.19; found: 413.97.

EXAMPLE 275

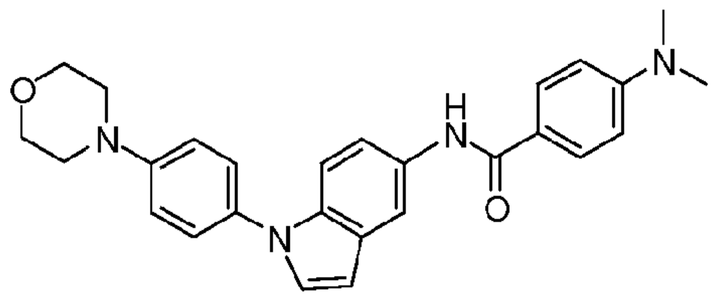
N-(1-(4-Benzamidophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **375**)



[0851] Compound **375** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. ^{1}H NMR (500MHz, DMSO-d_6) δ 10.45 (s, 1H), 10.01 (s, 1H), 8.37 (d, J = 1.5 Hz, 1H), 8.33 (d, J = 1 Hz, 1H), 8.01 - 7.78 (m, 11H), 7.55 (t, J = 8 Hz, 2H), 6.77 (d, J = 9 Hz, 2H), 3.00 (s, 6H).

EXAMPLE 276

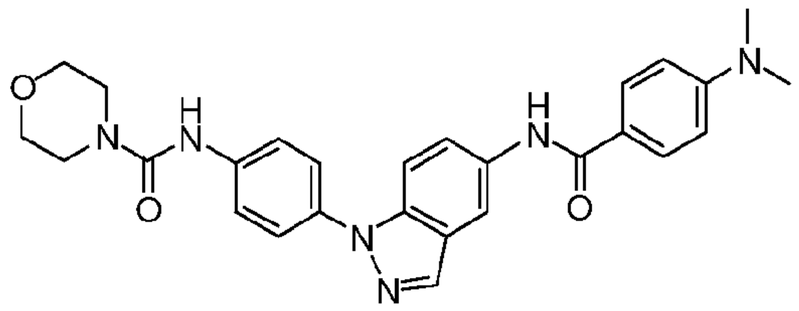
4-(dimethylamino)-*N*-(1-(4-morpholinophenyl)-1*H*-indol-5-yl)benzamide (Compound **376**)



[0852] Compound **376** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-morpholinophenyl)indole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{27}H_{28}N_4O_2$: 441.22; found: 441.02.

EXAMPLE 277

N-(1-(4-Morpholinocarboxamidophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **377**)

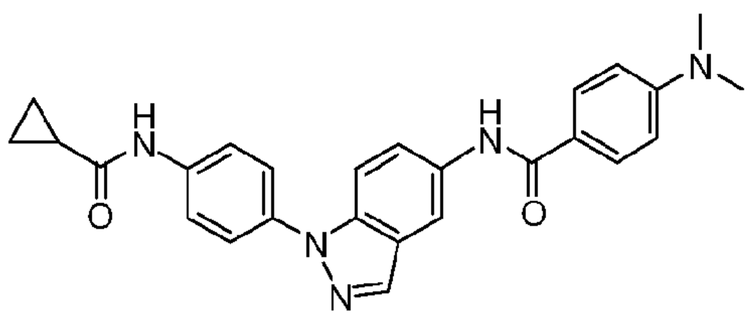


[0853] Compound **377** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-morpholinocarboxamidophenyl)indazole and 4-dimethylaminobenzoate.

$[M+H]^+$ calcd for $C_{27}H_{28}N_6O_3$: 485.22; found: 485.02.

EXAMPLE 278

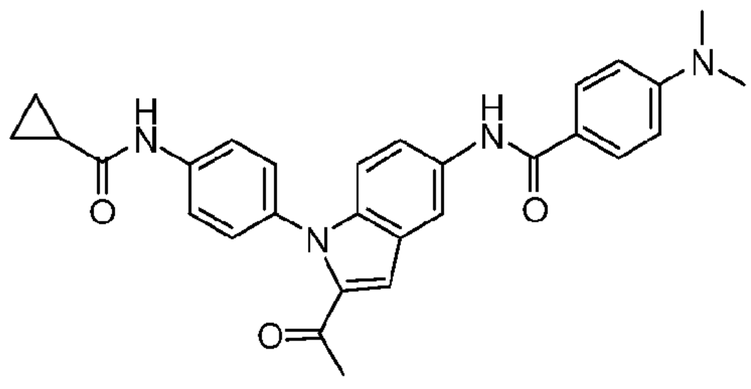
N-(1-(4-Cyclopropanecarboxamidophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **378**)



[0854] Compound **378** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. ^1H NMR (500MHz, DMSO- d_6) δ 10.38 (s, 1H), 10.00 (s, 1H), 8.35 (t, J = 1 Hz, 1H), 8.30 (d, J = 1 Hz, 1H), 7.89 (d, J = 7 Hz, 2H), 7.80 - 7.76 (m, 4H), 7.68 (d, J = 9 Hz, 2H), 6.76 (d, J = 9 Hz, 2H), 3.00 (s, 6H), 1.80 (m, 1H), 0.82 (m, 4H).

EXAMPLE 279

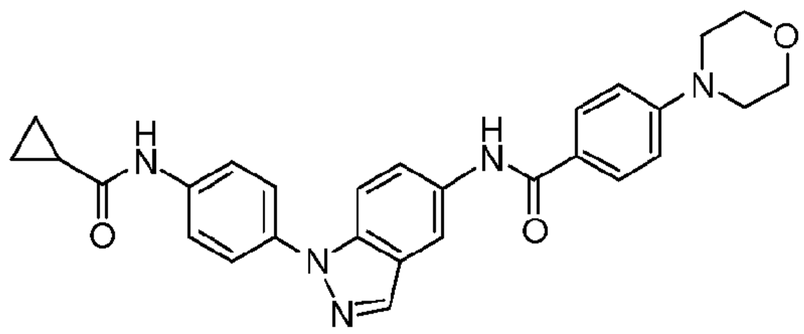
N-(2-Acetyl-1-(4-cyclopropanecarboxamidophenyl)-1*H*-indol-5-yl)-4-dimethylaminobenzamide (Compound **379**)



[0855] Compound **379** was prepared according to the procedure described in Scheme IV from 2-acetyl-5-amino-1-(4-aminophenyl)indole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{29}H_{28}N_4O_3$: 481.22; found: 480.97.

EXAMPLE 280

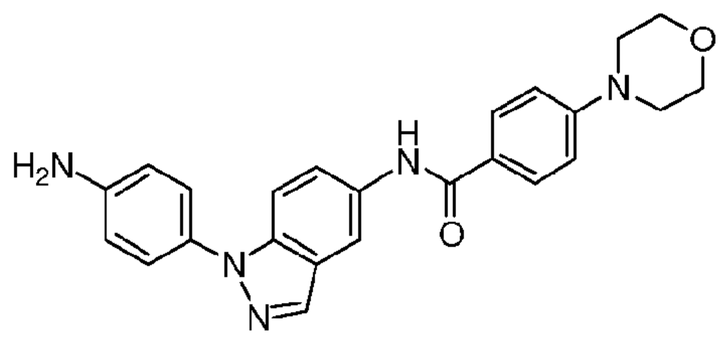
N-(1-(4-Cyclopropanecarboxamidophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **380**)



[0856] Compound **380** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{28}H_{27}N_5O_3$: 482.21; found: 481.98.

EXAMPLE 281

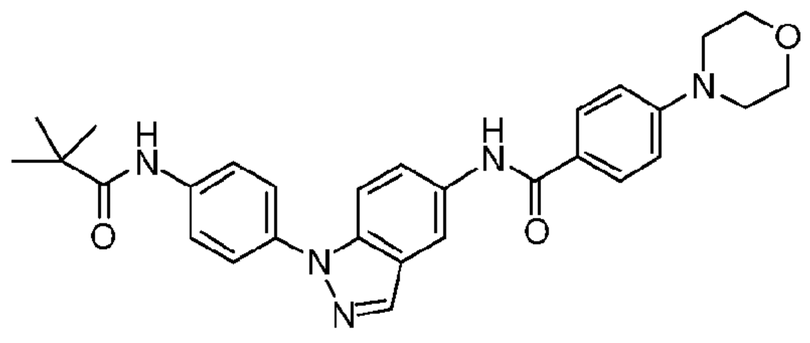
N-(1-(4-Aminophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **381**)



[0857] Compound **381** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{24}H_{23}N_5O_2$: 414.19; found: 414.01.

EXAMPLE 282

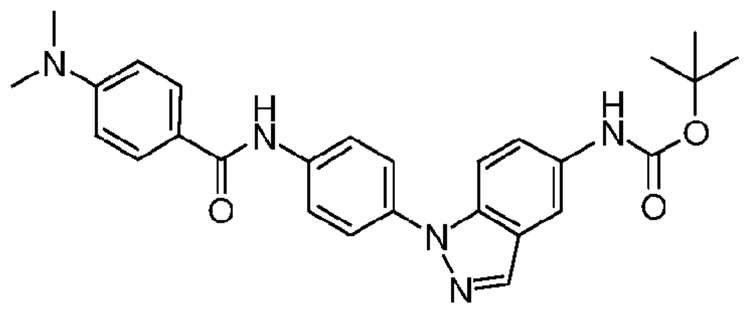
N-(1-(4-Pivaloylaminophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **382**)



[0858] Compound **382** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{31}N_5O_3$: 498.24; found: 498.05.

EXAMPLE 283

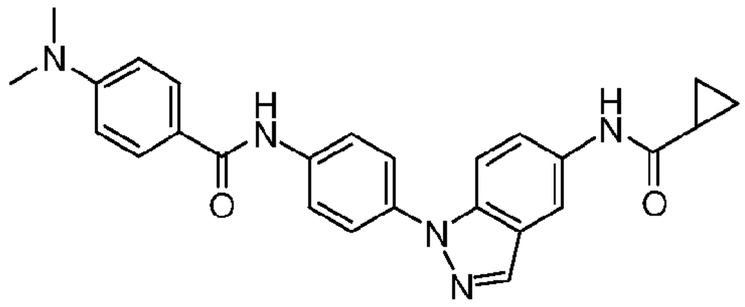
tert-Butyl 1-(4-(4-dimethylaminobenzamido)phenyl)-1*H*-indazol-5-ylcarbamate (Compound **383**)



[0859] Compound **383** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{27}H_{29}N_5O_3$: 472.23; found: 472.06.

EXAMPLE 284

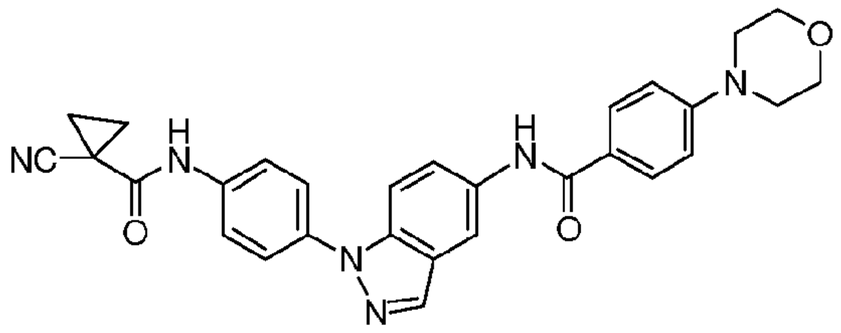
N-(4-(5-(cyclopropanecarboxamido)-1*H*-indazol-1-yl)phenyl)-4-(dimethylamino)benzamide (Compound **384**)



[0860] Compound **384** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. ^1H NMR (500MHz, DMSO- d_6) δ 10.30 (s, 1H), 10.05 (s, 1H), 8.27 (d, J = 1 Hz, 1H), 8.23 (s, 1H), 7.97 (d, J = 9 Hz, 2H), 7.89 (d, J = 9 Hz, 2H), 7.78 (d, J = 9 Hz, 1H), 7.70 (d, J = 9 Hz, 1H), 7.55 (dd, J = 2, 12 Hz, 1H), 6.77 (d, J = 9 Hz, 2H), 3.00 (s, 6H), 1.79 (m, 1H), 0.81 (m, 4H).

EXAMPLE 285

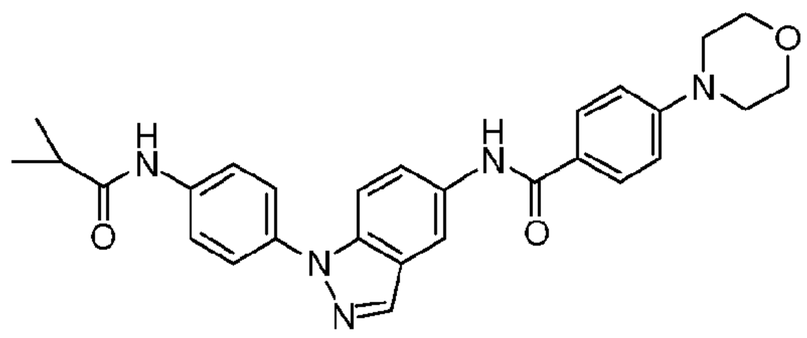
N-(1-(4-(1-Cyanocyclopropanecarboxamido)phenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **385**)



[0861] Compound **385** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{26}N_6O_3$: 507.21; found: 507.01.

EXAMPLE 286

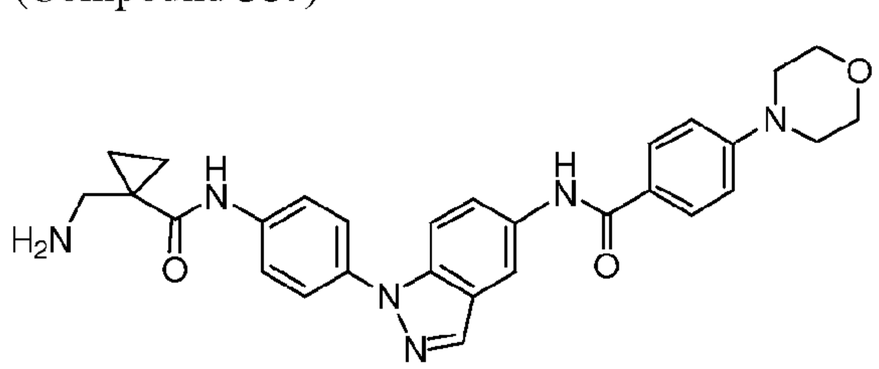
N-(1-(4-Isobutyramidophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **386**)



[0862] Compound **386** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O_3$: 484.23; found: 484.01.

EXAMPLE 287

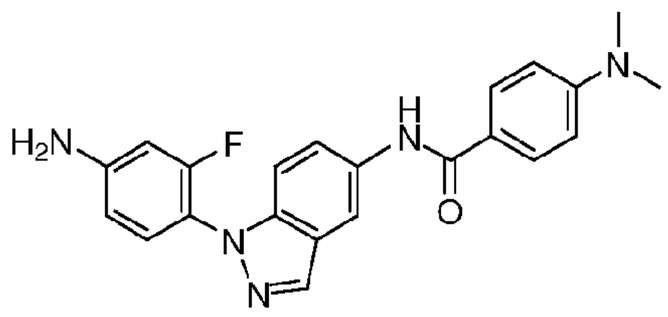
N-(1-(4-(1-Aminomethylcyclopropanecarboxamido)phenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **387**)



[0863] Compound **387** was prepared by reduction of compound **385**. $[M+H]^+$ calcd for $C_{29}H_{30}N_6O_3$: 511.24; found: 511.01.

EXAMPLE 288

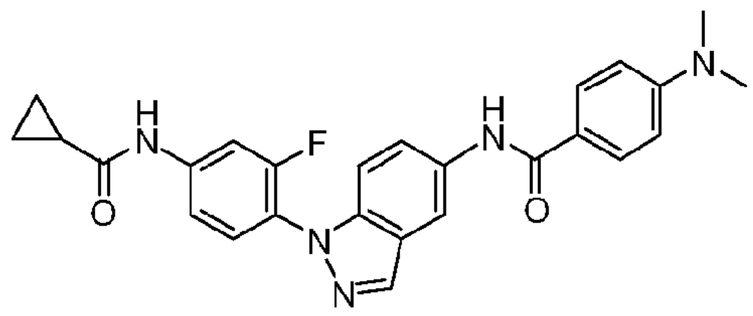
N-(1-(4-Amino-2-fluorophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **388**)



[0864] Compound **388** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-amino-2-fluorophenyl)indazole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{22}H_{20}FN_5O$: 390.17; found: 389.96.

EXAMPLE 289

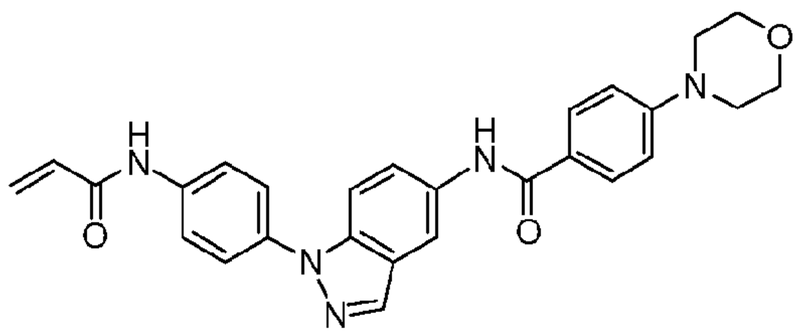
N-(1-(4-Cyclopropanecarboxamido-2-fluorophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **389**)



[0865] Compound **389** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-amino-2-fluorophenyl)indazole and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{26}H_{24}FN_5O_2$: 458.19; found: 457.98.

EXAMPLE 290

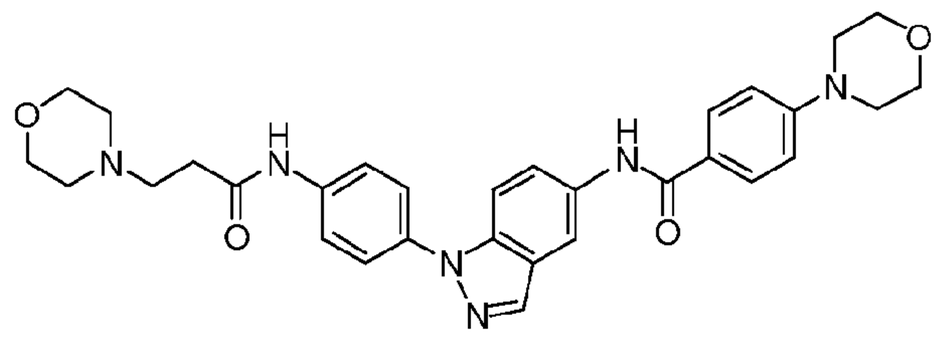
N-(1-(4-Acrylamidophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **390**)



[0866] Compound **390** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. ^{1}H NMR (500MHz, Acetone- d_6) δ 9.59 (s, 1H), 9.47 (s, 1H), 8.49 (s, 1H), 8.24 (s, 1H), 7.98 (dd, J = 2, 9 Hz, 4 H), 7.81 (m, 2H), 7.77 (d, J = 9 Hz, 1H), 7.05 (d, J = 9 Hz, 2H), 6.52 - 6.38 (m, 2H), 5.75 (dd, J = 2, 10 Hz, 1H), 3.80 (m, 4H), 3.29 (m, 4H).

EXAMPLE 291

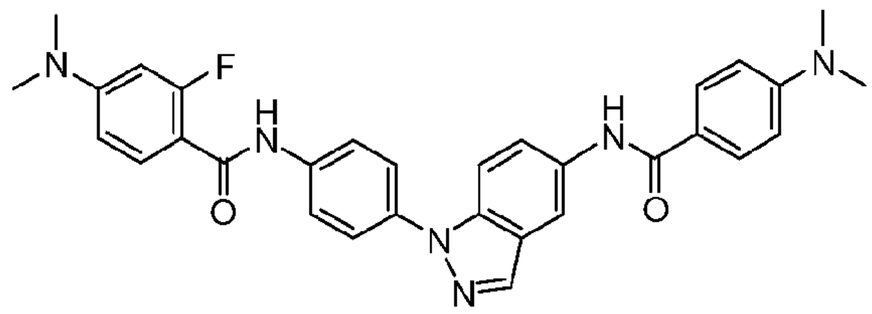
N-(1-(4-(3-Morpholinopropanamido)phenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **391**)



[0867] Compound **391** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{31}H_{34}N_6O_4$: 555.26; found: 555.09.

EXAMPLE 292

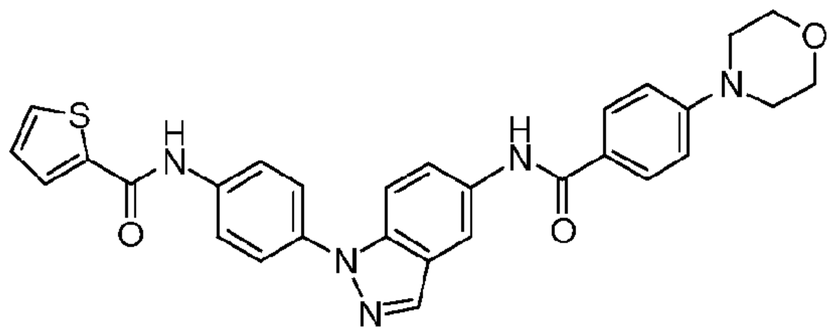
N-(1-(4-(4-Dimethylaminobenzamido)-2-fluorophenyl)-1*H*-indazol-5-yl)-4-dimethylaminobenzamide (Compound **392**)



[0868] Compound **392** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-dimethylaminobenzoate. ^1H NMR (500MHz, DMSO- d_6) δ 9.64 (s, 1H), 9.37 (s, 1H), 8.49 (m, 1H), 8.26 (s, 1H), 8.21 (m, 1H), 7.95 (d, J = 9 Hz, 4H), 7.79 (dt, J = 2, 9Hz, 1H), 7.76 (m, 1H), 7.61 (t, J = 9 Hz, 1H), 7.41 (dd, J = 3, 9 Hz, 1H), 6.80 (m, 4H), 3.07 (s, 6H), 3.05 (s, 6H).

EXAMPLE 293

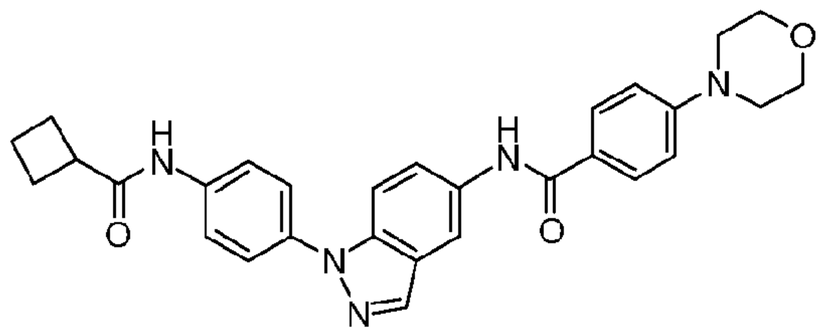
N-(1-(4-(2-Thienyl)carboxaminophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **393**)



[0869] Compound **393** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{25}N_5O_3S$: 524.17; found: 523.97.

EXAMPLE 294

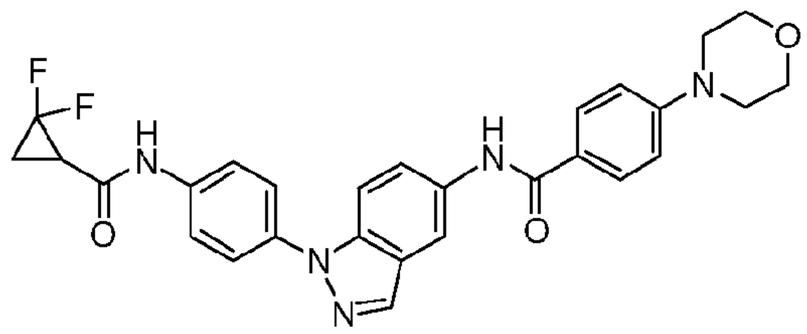
N-(1-(4-Cyclobutanecarboxaminophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **394**)



[0870] Compound **394** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{29}N_5O_3$: 496.23; found: 496.03.

EXAMPLE 295

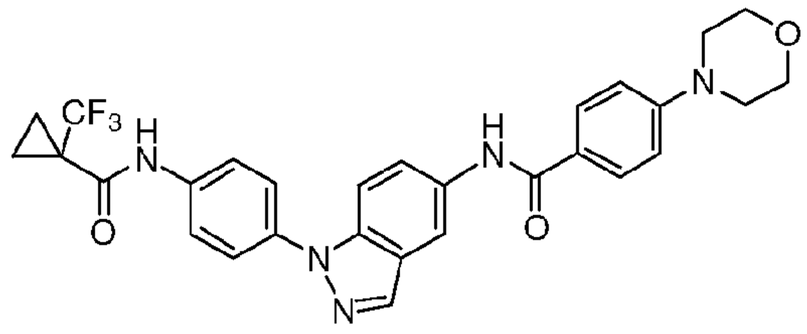
(±)-*N*-(1-(4-(2,2-Difluorocyclopropane)carboxamidophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **395**)



[0871] Compound **395** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{28}H_{25}F_2N_5O_3$: 518.19; found: 518.03.

EXAMPLE 296

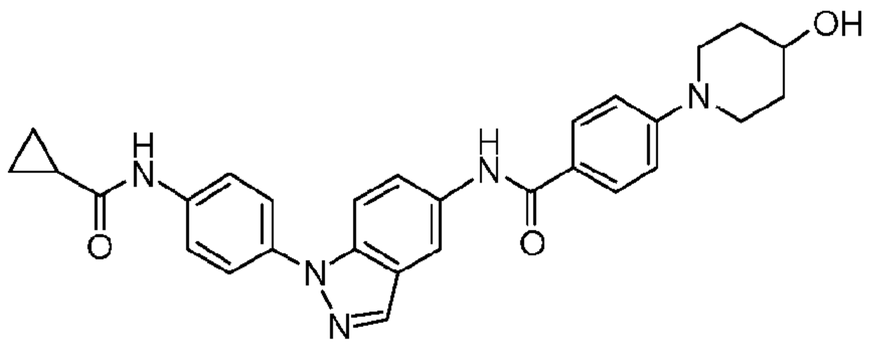
N-(1-(4-(1-Trifluoromethylcyclopropane)carboxaminophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **396**)



[0872] Compound **396** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{29}H_{26}F_3N_5O_3$: 550.21; found: 550.16.

EXAMPLE 297

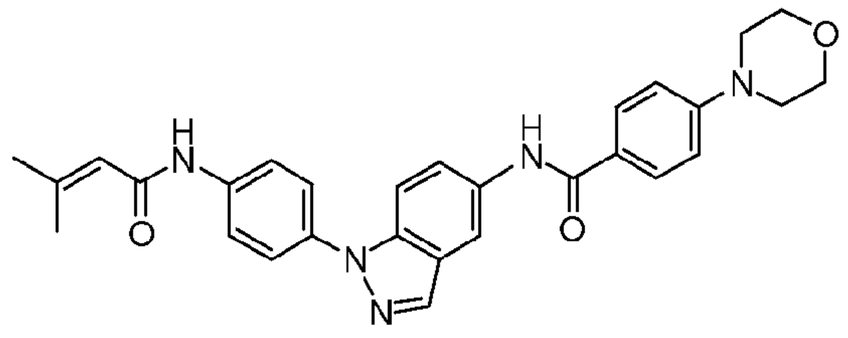
N-(1-(4-Cyclopropanecarboxamidophenyl)-1*H*-indazol-5-yl)-4-(4-hydroxypiperidino)benzamide (Compound **397**)



[0873] Compound **397** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-(4-hydroxypiperidino)benzoate. $[M+H]^+$ calcd for $C_{29}H_{29}N_5O_3$: 496.23; found: 496.10.

EXAMPLE 298

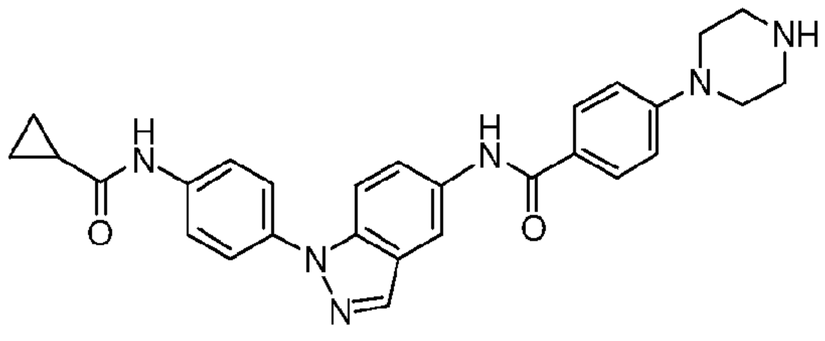
N-(1-(4-(3-Methylbut-2-enamido)phenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **398**)



[0874] Compound **398** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-morpholinobenzoate. ^{1}H NMR (500MHz, Acetone-d_6) δ 9.47 (s, 1H), 9.27 (s, 1H), 8.48 (s, 1H), 8.23 (s, 1H), 7.98 (d, J = 8.5 Hz, 2H), 7.94 (d, J = 8.5 Hz, 2H), 7.80 (s, 2H), 7.73 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.5 Hz, 2H), 5.92 (s, 1H), 3.80 (t, J = 5 Hz, 4H), 3.29 (t, J = 5 Hz, 4H), 2.24 (s, 3H), 1.90 (s, 3H).

EXAMPLE 299

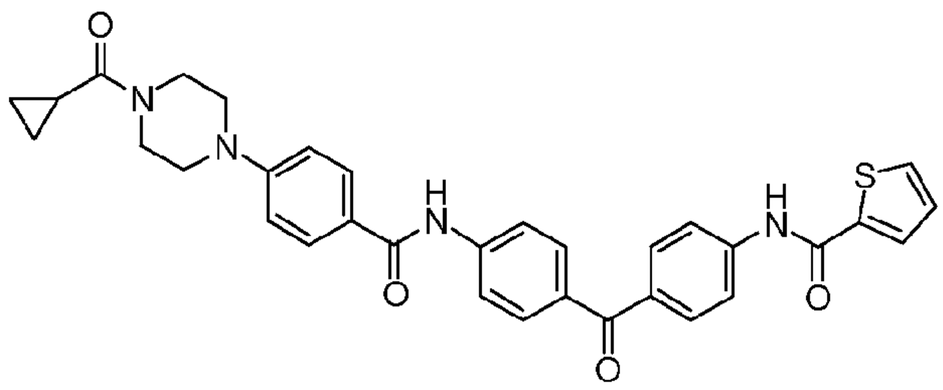
N-(1-(4-Cyclopropanecarboxamidophenyl)-1*H*-indazol-5-yl)-4-piperazinobenzamide (Compound **399**)



[0875] Compound **399** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-aminophenyl)indazole and 4-piperazinobenzoate. $[M+H]^+$ calcd for $C_{28}H_{28}N_6O_2$: 481.23; found: 481.04.

EXAMPLE 300

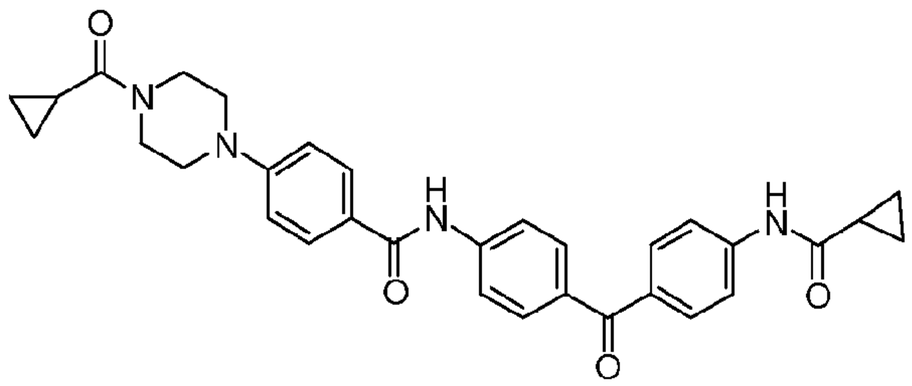
N-(4-(4-(4-(4-Cyclopropanecarbonyl)piperazin-1-yl)benzamido)benzoyl)phenyl)thiophene-2-carboxamide (Compound **400**)



[0876] Compound **400** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-piperazinebenzoate. $[M+H]^+$ calcd for $C_{33}H_{30}N_4O_4S$: 579.51; found: 579.06.

EXAMPLE 301

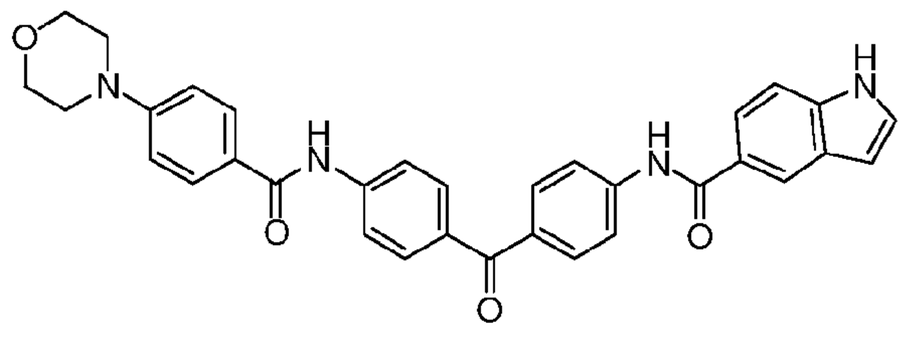
N-(4-(4-(4-(4-Cyclopropanecarbonyl)piperazin-1-yl)benzamido)benzoyl)phenyl) cyclopropanecarboxamide (Compound **401**)



[0877] Compound **401** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-piperazinebenzoate. $[M+H]^+$ calcd for $C_{32}H_{32}N_4O_4$: 537.15; found: 537.06.

EXAMPLE 302

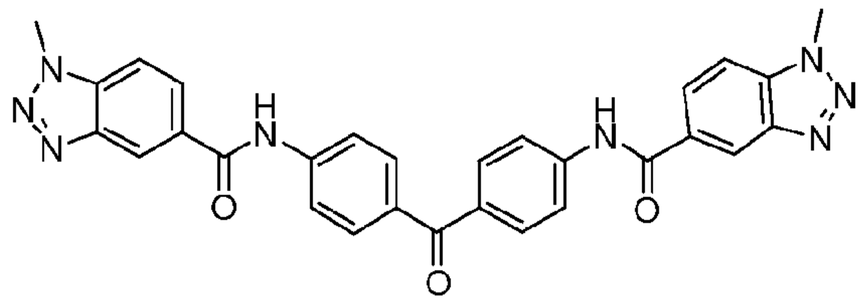
N-(4-(4-(4-Morpholinobenzamido)benzoyl)phenyl)-1*H*-indole-5-carboxamide (Compound **402**)



[0878] Compound **402** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 4-piperazinebenzoate. $[M+H]^+$ calcd for $C_{33}H_{28}N_4O_4$: 545.13; found: 545.03.

EXAMPLE 303

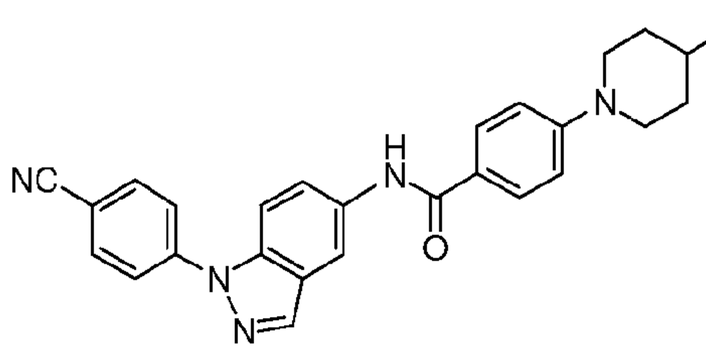
N,*N*'-(carbonylbis(4,1-phenylene))bis(1-methyl-1*H*-benzo[*d*][1,2,3]triazole-5-carboxamide) (Compound **403**)



[0879] Compound **403** was prepared according to the procedure described in Scheme IV from 4,4'-diaminobenzophenone and 1-methyl-1*H*-benzotriazole-5-carboxylate. $[M+H]^+$ calcd for $C_{29}H_{22}N_8O_3$: 531.06; found: 531.05.

EXAMPLE 304

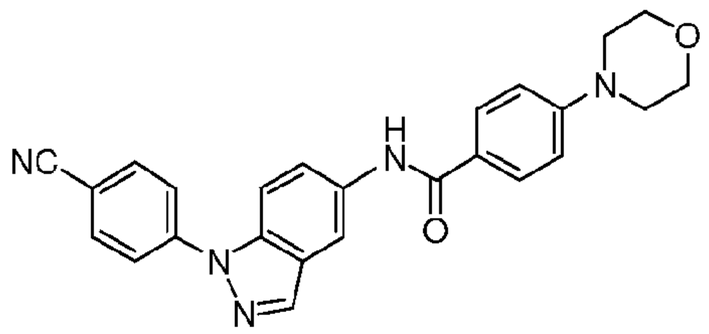
N-(1-(4-Cyanophenyl)-1*H*-indazol-5-yl)-4-(4-hydroxypiperidino)benzamide (Compound **404**)



[0880] Compound **404** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-cyanophenyl)indazole and 4-(4-hydroxypiperidino)benzoate. $[M+H]^+$ calcd for $C_{26}H_{23}N_5O_2$: 438.19; found: 437.99.

EXAMPLE 305

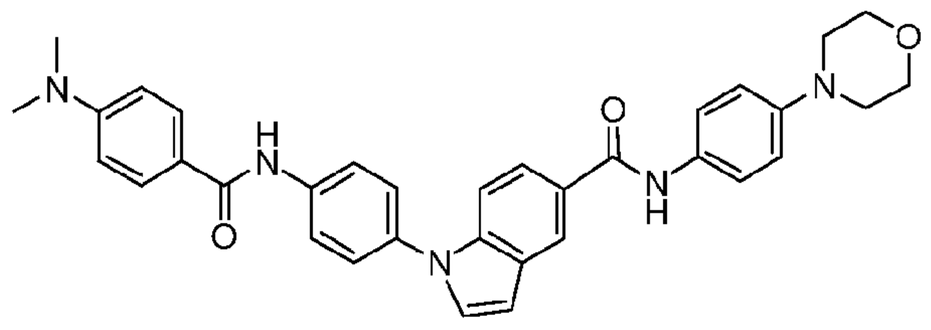
N-(1-(4-Cyanophenyl)-1*H*-indazol-5-yl)-4-morpholinobenzamide (Compound **405**)



[0881] Compound **405** was prepared according to the procedure described in Scheme IV from 5-amino-1-(4-cyanophenyl)indazole and 4-morpholinobenzoate. $[M+H]^+$ calcd for $C_{25}H_{21}N_5O_2$: 424.17; found: 424.09.

EXAMPLE 306

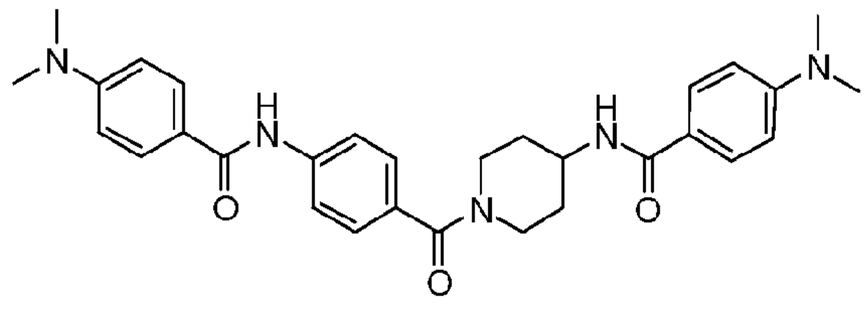
1-(4-(4-Dimethylaminobenzamido)phenyl)-*N*-(4-morpholinophenyl)-1*H*-indole-5-carboxamide (Compound **406**)



[0882] Compound **406** was prepared according to the procedure described in Scheme IV from 1-(4-dimethylaminophenylbenzamido)indole and 4-morpholinoaniline. ^1H NMR (500MHz, DMSO- d_6) δ10.08 (s, 1H), 10.02 (2, 1H), 8.33 (d, J = 2 Hz, 1H), 7.99 (d, J = 9 Hz, 2H), 7.89 (d, J = 9 Hz, 2H), 7.82 (dd, J = 2, 9 Hz, 1H), 7.74 (d, J = 3 Hz, 1H), 7.66 (d, J = 9 Hz, 2H), 7.60 (d, J = 9 Hz, 1H), 7.57 (d, J = 5 Hz, 2H), 6.93 (d, J = 9 Hz, 2H), 6.83 (d, J = 3 Hz, 1H), 6.78 (d, J = 9 Hz, 2H), 3.73 (m, 4H), 3.06 (m, 4H), 3.01 (s, 6H).

EXAMPLE 307

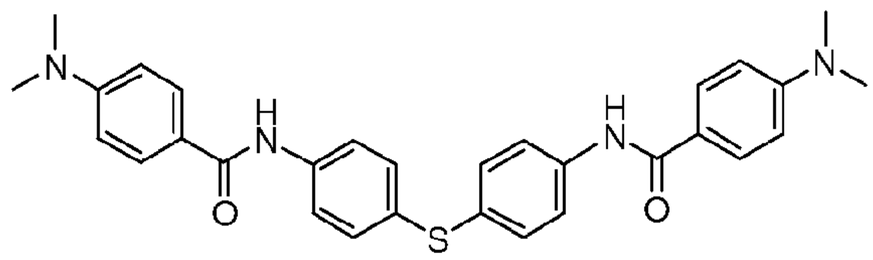
4-Dimethylamino-*N*-(1-(4-(4-dimethylaminobenzamido)benzoyl)piperidin-4-yl)benzamide (Compound **407**)



[0883] Compound **407** was prepared according to the procedure described in Scheme IV from 4-(4-dimethylaminobenzamido)benzoate and 4-(4-dimethylaminophenyl)piperidine. $[M+H]^+$ calcd for $C_{30}H_{35}N_5O_3$: 514.27; found: 513.98.

EXAMPLE 308

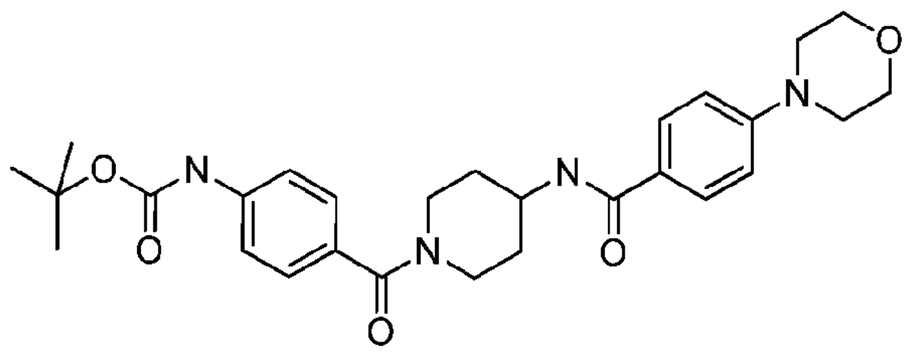
N,N'-(4,4'-Thiobis(4,1-phenylene))bis(4-(dimethylamino)benzamide) (Compound **408**)



[0884] Compound **408** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{30}H_{30}N_4O_2S$: 511.21; found: 510.94.

EXAMPLE 309

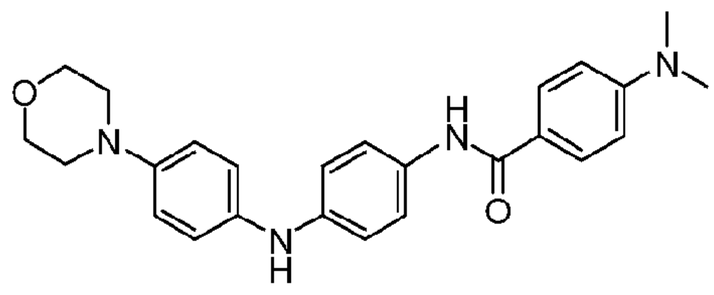
tert-butyl (4-(4-(4-morpholinobenzamido)piperidine-1-carbonyl)phenyl)carbamate (Compound **409**)



[0885] Compound **409** was prepared according to the procedure described in Scheme IV from 4-aminobenzoate and 4-(4-dimethylaminophenyl)piperidine. $[M+H]^+$ calcd for $C_{28}H_{36}N_4O_5$: 509.27; found: 508.99.

EXAMPLE 310

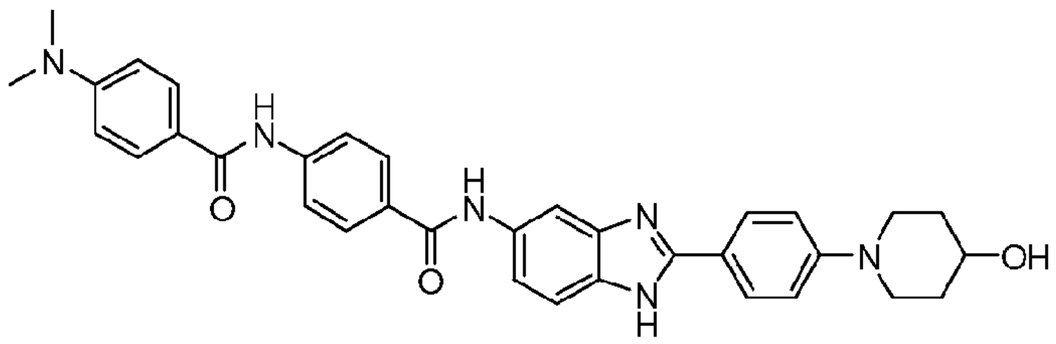
N-(4-(4-Morpholinophenylamino)phenyl)-4-dimethylaminobenzamide (Compound **410**)



[0886] Compound **410** was prepared according to the procedure described in Scheme IV from 4,4'-diaminodiphenylamine and 4-dimethylaminobenzoate. $[M+H]^+$ calcd for $C_{25}H_{29}N_4O_2$: 417.23; found: 417.01.

EXAMPLE 311

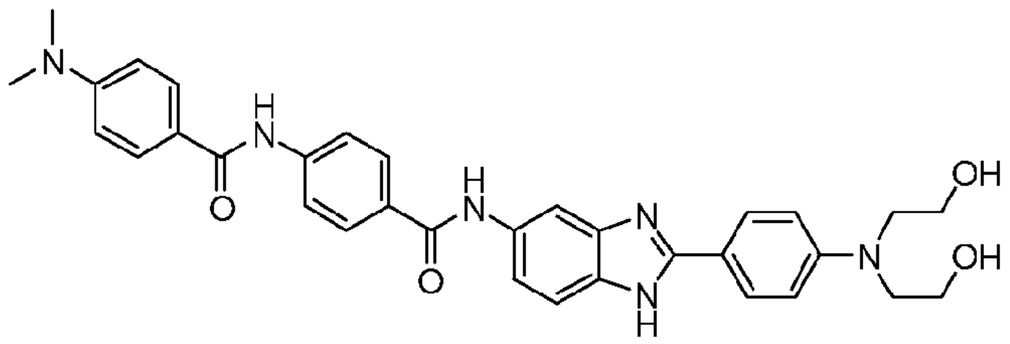
4-Dimethylamino-*N*-(4-(2-(4-(4-hydroxypiperidinyl)phenyl)-1*H*-benzimidazol-5-ylcarbamoyl)phenyl)benzamide (Compound **411**)



[0887] Compound **411** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-aminobenzoyl)aniline and 4-(4-hydroxypiperidinyl)benzaldehyde. $[M+H]^+$ calcd for $C_{34}H_{34}N_6O_3$: 575.27; found: 575.07.

EXAMPLE 312

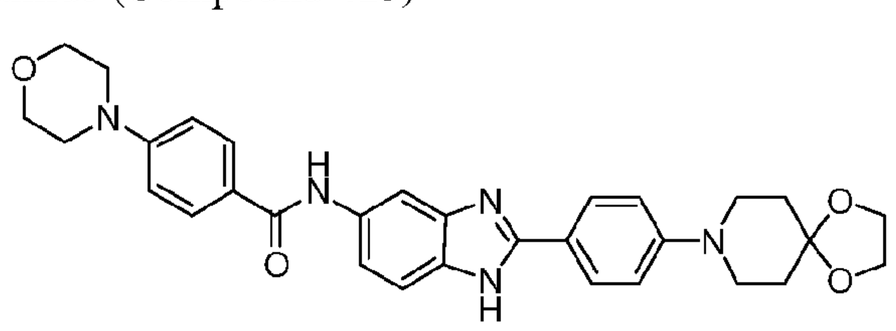
4-Dimethylamino-*N*-(4-(2-(4-(bis(2-hydroxyethyl)amino)phenyl)-1*H*-benzimidazol-5-ylcarbamoyl)phenyl)benzamide (Compound **412**)



[0888] Compound **412** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-aminobenzoyl)aniline and 4-bis(2-hydroxyethyl)aminobenzaldehyde. $[M+H]^+$ calcd for $C_{33}H_{34}N_6O_4$: 579.26; found: 579.06.

EXAMPLE 313

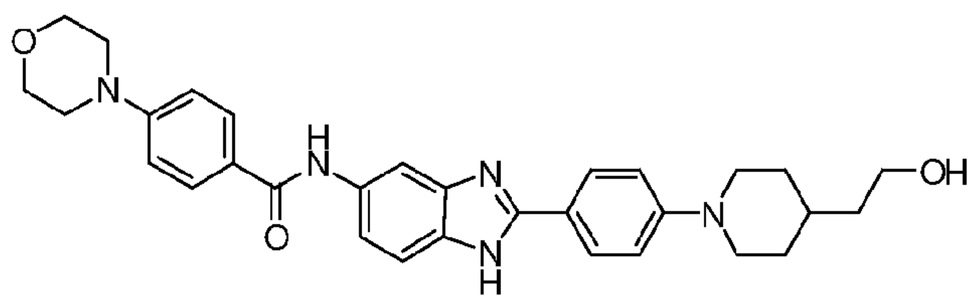
N-(2-(4-(1,4-Dioxa-8-azaspiro[4,5]decan-8-yl)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **413**)



[0889] Compound **413** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinobenzoyl)aniline and 4-(1,4-dioxa-8-azaspiro[4,5]decan-8-yl)benzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{33}N_5O_4$: 540.25; found: 540.05.

EXAMPLE 314

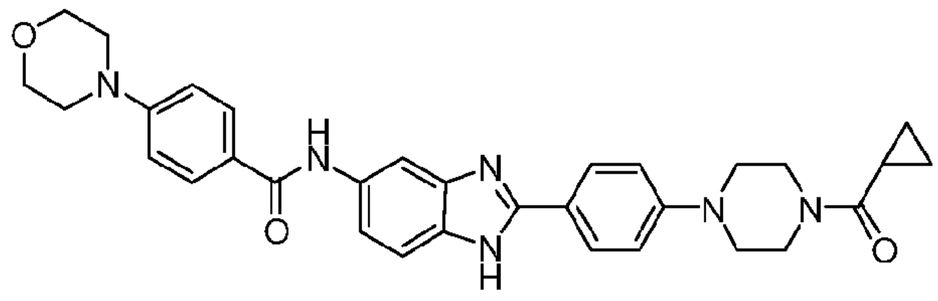
N-(2-(4-(4-(2-Hydroxyethyl)piperidinyl)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **414**)



[0890] Compound **414** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinobenzoyl)aniline and 4-(2-hydroxyethyl)piperidinylbenzaldehyde. $[M+H]^+$ calcd for $C_{31}H_{35}N_5O_3$: 526.27; found: 526.11.

EXAMPLE 315

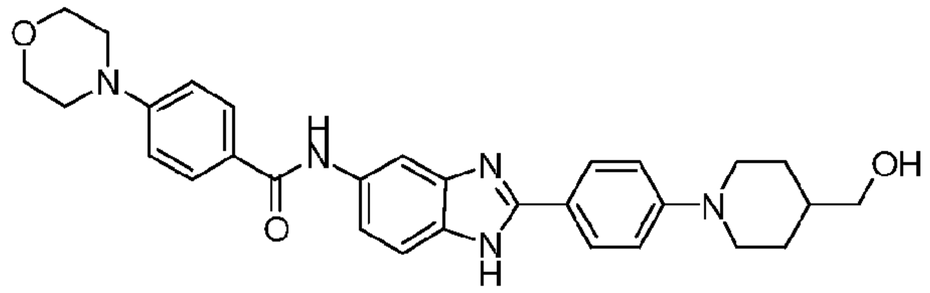
N-(2-(4-(4-Cyclopropanecarbonylpiperazinyl)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **415**)



[0891] Compound **415** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinobenzoyl)aniline and 4-(4-cyclopropanecarbonylpiperazinyl)benzaldehyde. $[M+H]^+$ calcd for $C_{32}H_{34}N_6O_3$: 551.27; found: 551.10.

EXAMPLE 316

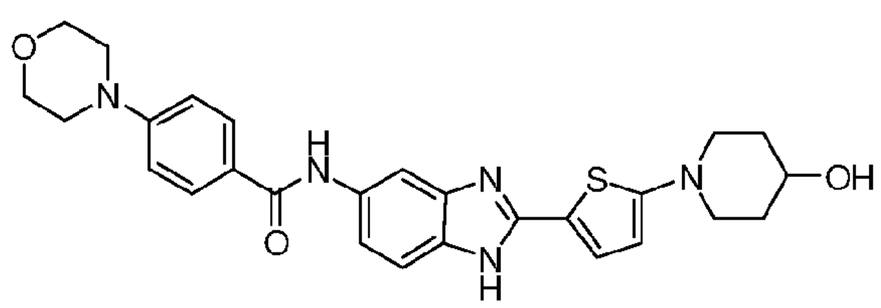
N-(2-(4-(4-(2-Hydroxymethyl)piperidinyl)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **416**)



[0892] Compound **416** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 4-(2-hydroxymethyl)piperidinylbenzaldehyde. $[M+H]^+$ calcd for $C_{30}H_{33}N_5O_3$: 512.26; found: 512.09.

EXAMPLE 317

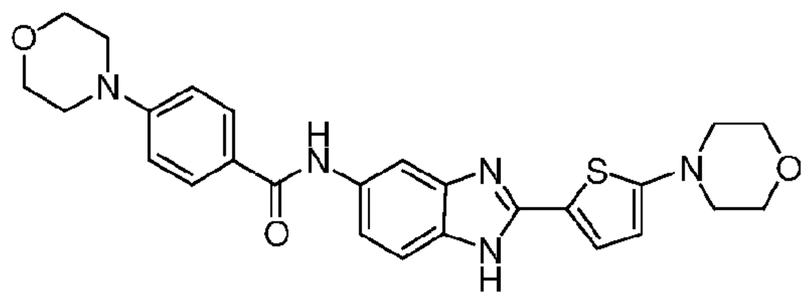
N-(2-(2-(4-Hydroxypiperidinyl)thien-5-yl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **417**)



[0893] Compound **417** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 5-(4-hydroxypiperidinyl)thiophene-2-carboxaldehyde. $[M+H]^+$ calcd for $C_{27}H_{29}N_5O_3S$: 504.20; found: 503.99.

EXAMPLE 318

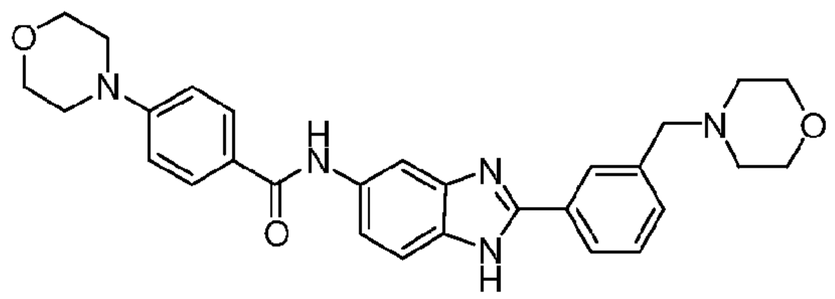
N-(2-(2-Morpholinothien-5-yl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **418**)



[0894] Compound **418** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 5-morpholinothiophene-2-carboxaldehyde. $[M+H]^+$ calcd for $C_{26}H_{27}N_5O_3S$: 490.18; found: 489.95.

EXAMPLE 319

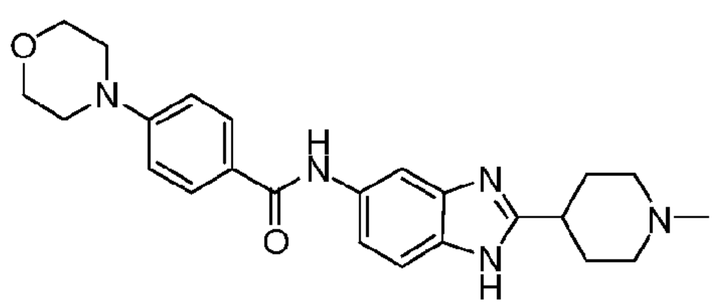
N-(2-(3-Morpholinomethylphenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **419**)



[0895] Compound **419** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 3-morpholinomethylbenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{31}N_5O_3$: 498.24; found: 497.98.

EXAMPLE 320

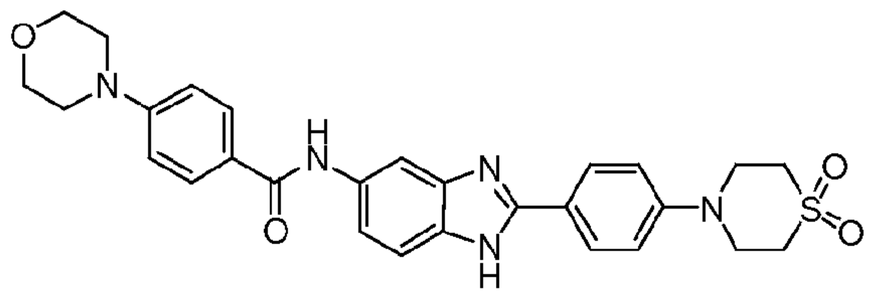
N-(2-(1-Methylpiperidin-4-yl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **420**)



[0896] Compound **420** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 4-(1-methylpiperidinyl)caboxaldehyde. $[M+H]^+$ calcd for $C_{24}H_{29}N_5O_2$: 420.23; found: 420.04.

EXAMPLE 321

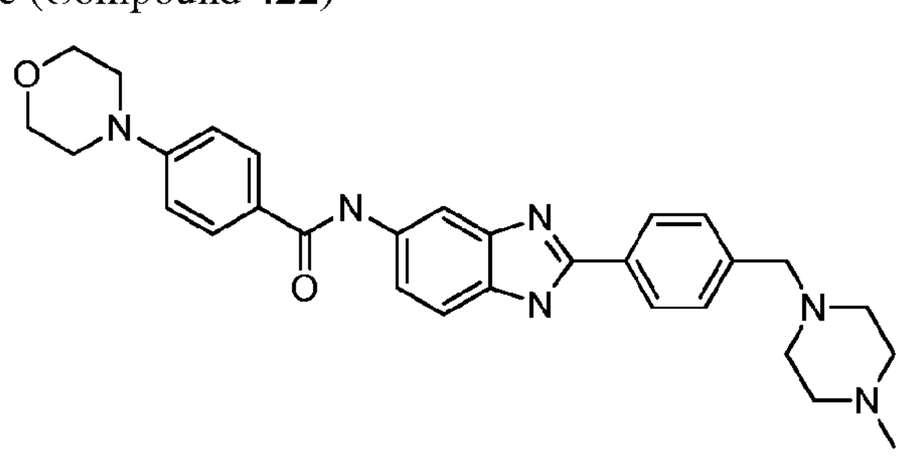
N-(2-(4-(1,1-Dioxo-4-thiomorpholino)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **421**)



[0897] Compound **421** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 4-(1,1-dioxo-4-thiomorpholino)benzaldehyde. $[M+H]^+$ calcd for $C_{28}H_{29}N_5O_4S$: 532.19; found: 532.02.

EXAMPLE 322

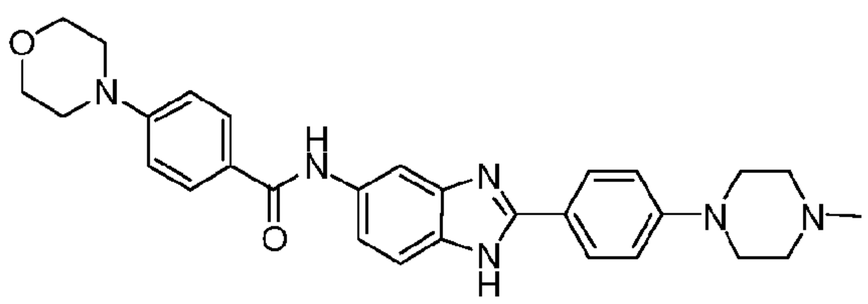
N-(2-(4-((4-methylpiperazin-1-yl)methyl)phenyl)-1*H*-benzo[*d*]imidazol-5-yl)-4-morpholinobenzamide (Compound **422**)



[0898] Compound **422** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-*N*-(4-morpholinobenzoyl)aniline and 4-piperazinomethylbenzaldehyde. $[M+H]^+$ calcd for $C_{30}H_{34}N_6O_2$: 511.27; found: 511.07.

EXAMPLE 323

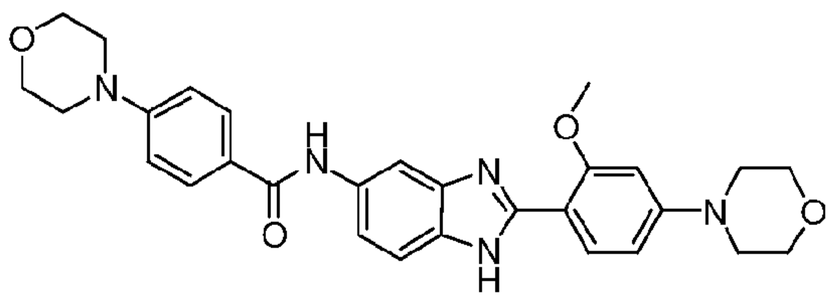
N-(2-(4-(4-Methylpiperazino)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **423**)



[0899] Compound **423** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 4-(4-methylpiperazino)benzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{32}N_6O_2$: 497.26; found: 496.98.

EXAMPLE 324

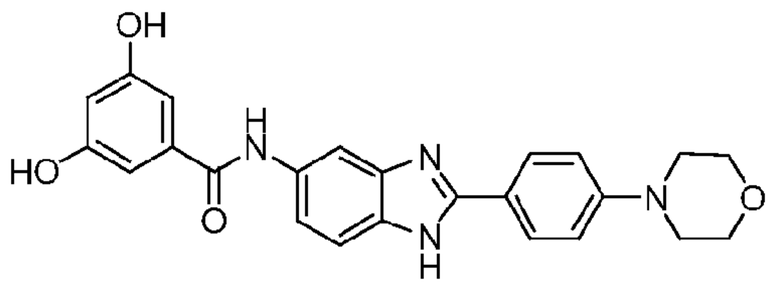
N-(2-(2-Methoxy-4-morpholinophenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **424**)



[0900] Compound **424** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-morpholinobenzoyl)aniline and 2-methoxy-4-morpholinobenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{31}N_5O_4$: 514.25; found: 514.05.

EXAMPLE 325

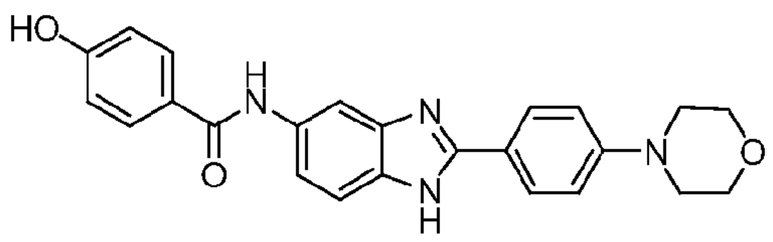
N-(2-(4-Morpholinophenyl)-1*H*-benzimidazol-5-yl)-3,5-dihydroxybenzamide (Compound **425**)



[0901] Compound **425** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(3,5-dihydroxybenzoyl)aniline and 4-morpholinobenzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{22}N_4O_4$: 431.17; found: 431.18.

EXAMPLE 326

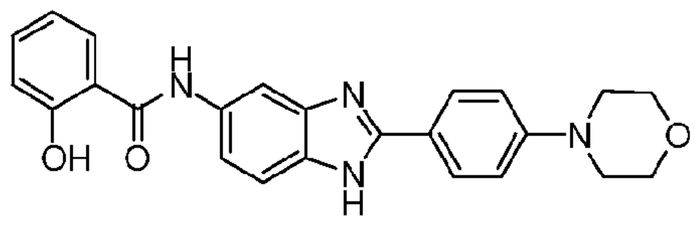
N-(2-(4-Morpholinophenyl)-1*H*-benzimidazol-5-yl)-4-hydroxybenzamide (Compound **426**)



[0902] Compound **426** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(4-hydroxybenzoyl)aniline and 4-morpholinobenzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{22}N_4O_3$: 415.18; found: 415.17.

EXAMPLE 327

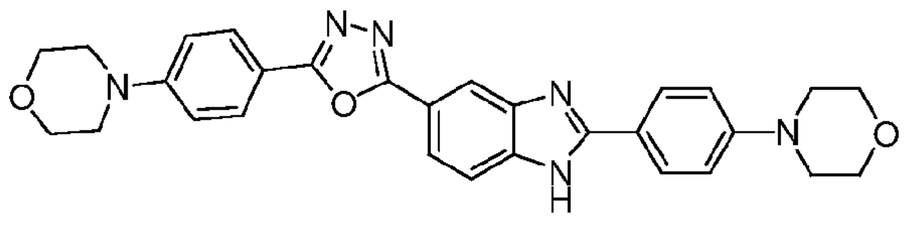
N-(2-(4-Morpholinophenyl)-1*H*-benzimidazol-5-yl)-2-hydroxybenzamide (Compound **427**)



[0903] Compound **427** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-N-(2-hydroxybenzoyl)aniline and 4-morpholinobenzaldehyde. $[M+H]^+$ calcd for $C_{24}H_{22}N_4O_3$: 415.18; found: 414.98.

EXAMPLE 328

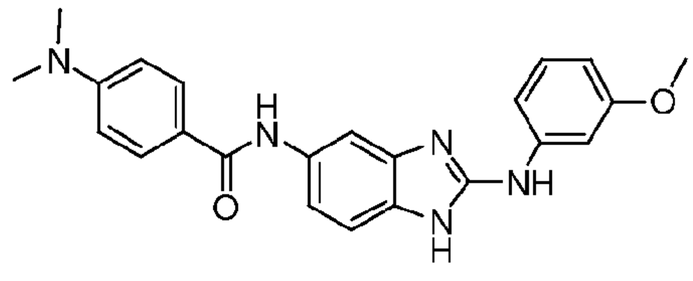
4-(4-(5-(5-(4-Morpholinophenyl)-1,3,4-oxadiazol-2-yl)-1*H*-benzimidazol-2-yl)phenyl) morpholine (Compound **428**)



[0904] Compound **428** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitro-1-(5-(4-morpholinophenyl)-1,3,4-oxadiazol-2-yl)benzene and 4-morpholinobenzaldehyde. $[M+H]^+$ calcd for $C_{29}H_{28}N_6O_3$: 590.23; found: 508.98.

EXAMPLE 329

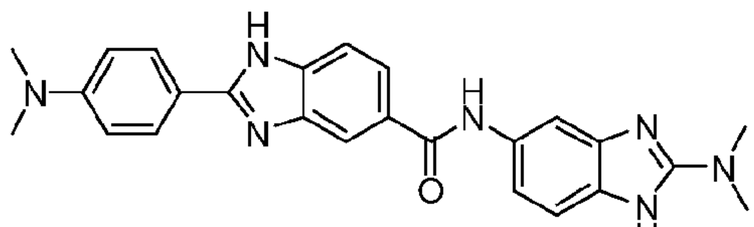
4-Dimethylamino-*N*-(2-(3-methoxyphenylamino)-1*H*-benzimidazol-5-yl)benzamide (Compound **429**)



[0905] Compound **429** was prepared from 4-dimethylaminobenzoate and 5-amino-2-(3-methoxyphenylamino)benzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{23}H_{23}N_5O_2$: 402.19; found: 401.96.

EXAMPLE 330

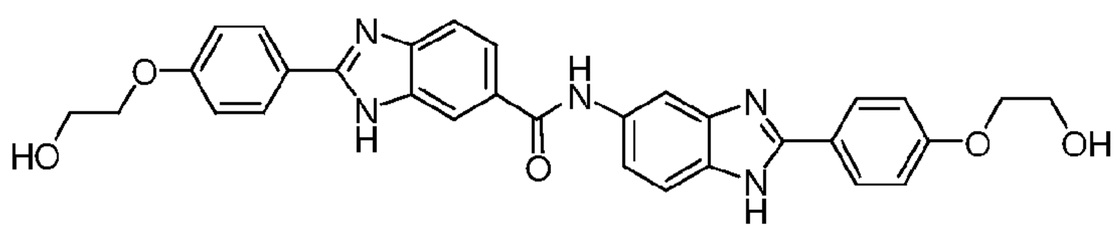
N-(2-Dimethylamino)-1*H*-benzimidazol-5-yl)-2-(4-dimethylaminophenyl)-1*H*-benzimidazole-5-carbamide (Compound **430**)



[0906] Compound **430** was prepared from 2-(4-dimethylaminophenyl)benzimidazole-5-caboxylate and 5-amino-2-(dimethylamino)benzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{25}H_{25}N_7O$: 440.21; found: 440.01.

EXAMPLE 331

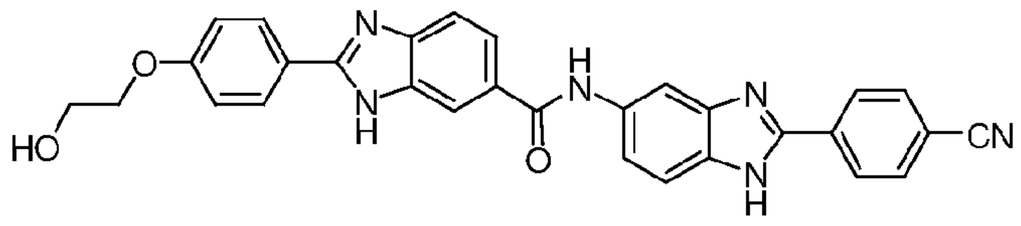
2-(4-(2-Hydroxyethoxy)phenyl)-*N*-2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzimidazol-5-yl)-1*H*-benzimidazole-6-carboxamide (Compound **431**)



[0907] Compound **431** was prepared according to the procedure similar to that described in Scheme V from 2-(4-(2-hydroxyethoxy)phenyl)-5-aminobenzimidazole and 2-(4-(2-hydroxyethoxy)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{31}H_{27}N_5O_5$: 550.20; found: 549.96.

EXAMPLE 332

2-(4-Cyanophenyl)-*N*-2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzimidazol-5-yl)-1*H*-benzimidazole-6-carboxamide (Compound **432**)

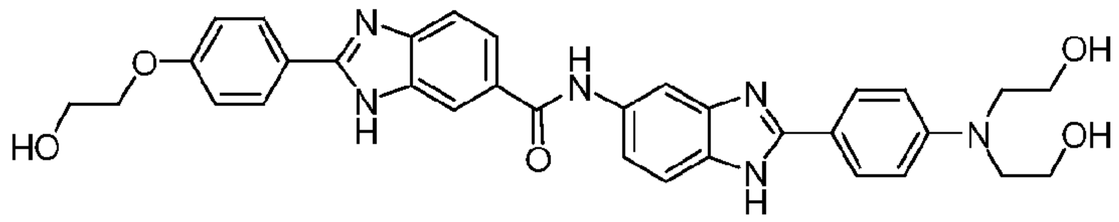


[0908] Compound **432** was prepared according to the procedure similar to that described in Scheme V from 2-(4-cyanophenyl)-5-aminobenzimidazole and 2-(4-(2-

hydroxyethoxy)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{30}H_{22}N_6O_3$: 515.18; found: 514.92.

EXAMPLE 333

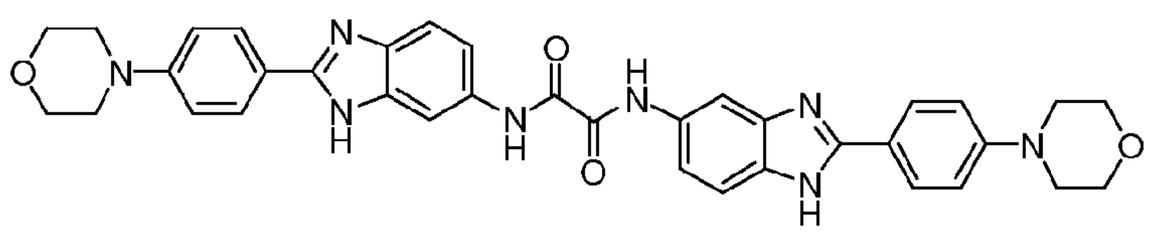
2-(4-bis(2-Hydroxyethyl)aminophenyl)-*N*-2-(4-(2-hydroxyethoxy)phenyl)-1*H*-benzimidazol-5-yl)-1*H*-benzimidazole-6-carboxamide (Compound **433**)



[0909] Compound **433** was prepared according to the procedure similar to that described in Scheme V from 2-(4-bis(2-hydroxyethyl)aminophenyl)-5-aminobenzimidazole and 2-(4-(2-hydroxyethoxy)phenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{33}H_{32}N_6O_5$: 593.24; found: 593.03.

EXAMPLE 334

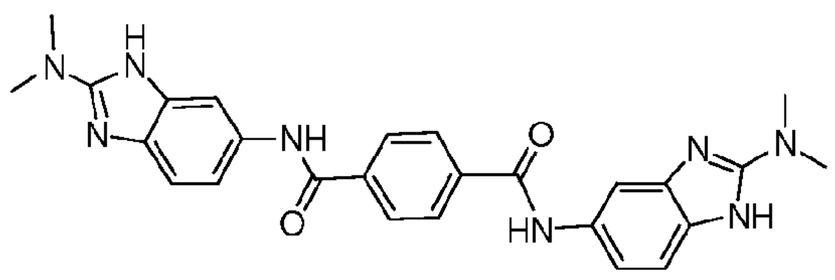
N,N'-bis-(2-(4-Morpholinophenyl)-1*H*-benzimidazol-5-yl)oxalamide (Compound **434**)



[0910] Compound **434** was prepared according to the procedure similar to that described in Scheme V from 2-(4-morpholinophenyl)-5-aminobenzimidazole and oxalic acid. $[M+H]^+$ calcd for $C_{36}H_{34}N_8O_4$: 643.27; found: 643.09.

EXAMPLE 335

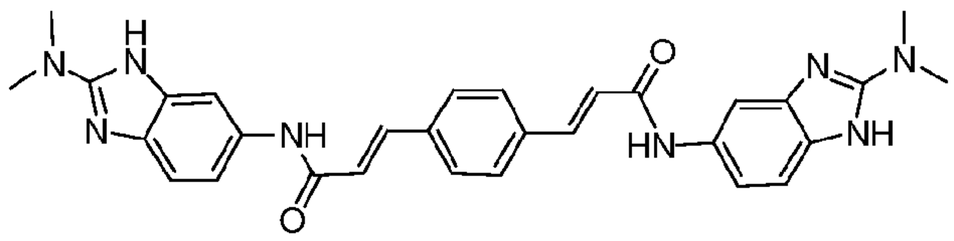
N,N'-bis(2-Dimethylamino-1*H*-benzimidazol-5-yl)terephthalamide (Compound **435**)



[0911] Compound **435** was prepared according to the procedure similar to that described in Scheme V from 2-dimethylamino-5-aminobenzimidazole and terephthalic acid. $[M+H]^+$ calcd for $C_{26}H_{26}N_8O_2$: 483.22; found: 483.02.

EXAMPLE 336

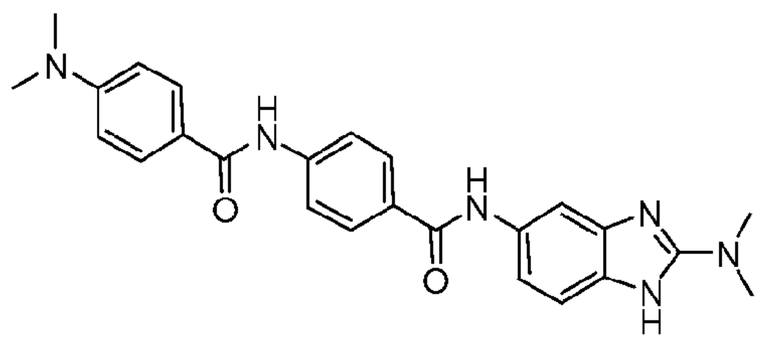
N,N'-bis(2-Dimethylamino-1*H*-benzimidazol-5-yl)-3(*E*),3'(*E*)-(1,4-phenylene)bis(acrylamide) (Compound **436**)



[0912] Compound **436** was prepared according to the procedure similar to that described in Scheme V from 2-dimethylamino-5-aminobenzimidazole and 3(*E*),3'(*E*)-(1,4-phenylene)bisacrylic acid. $[M+H]^+$ calcd for $C_{30}H_{30}N_8O_2$: 535.25; found: 535.09.

EXAMPLE 337

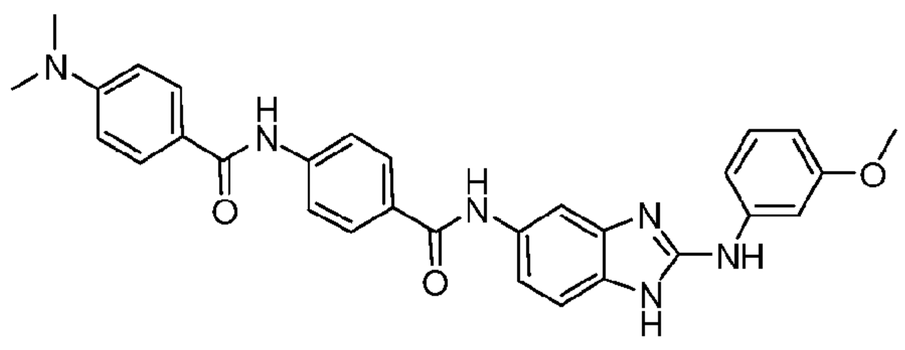
N-(2-Dimethylamino)-1*H*-benzimidazol-5-yl)-4-(4-dimethylaminobenzamido)benzamide (Compound **437**)



[0913] Compound **437** was prepared from 4-(4-dimethylaminobenzamido)benzoate and 5-amino-2-(dimethylamino)benzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{25}H_{26}N_6O_2$: 443.21; found: 443.05.

EXAMPLE 338

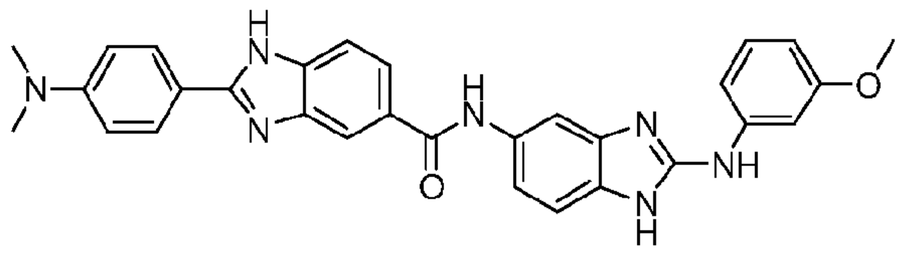
N-(2-(3-Methoxyphenyl)amino)-1*H*-benzimidazol-5-yl)-4-(4- dimethylaminobenzamido) benzamide (Compound **438**)



[0914] Compound **438** was prepared from 4-(4-dimethylaminobenzamido)benzoate and 5-amino-2-(3-methoxyphenyl)aminobenzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{30}H_{28}N_6O_3$: 521.22; found: 521.06.

EXAMPLE 339

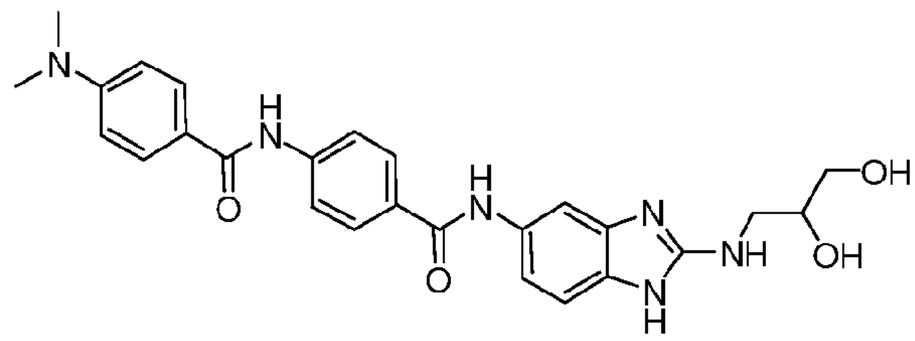
N-(2-(3-Methoxyphenyl)amino-1*H*-benzimidazol-5-yl)-2-(4-dimethylaminophenyl)-1*H*-benzimidazole-5-carbamide (Compound **439**)



[0915] Compound **439** was prepared from 2-(4-dimethylaminophenyl)benzimidazole-5-caboxylate and 5-amino-2-(3-methoxyphenyl)aminobenzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{30}H_{27}N_7O_2$: 518.22; found: 518.03.

EXAMPLE 340

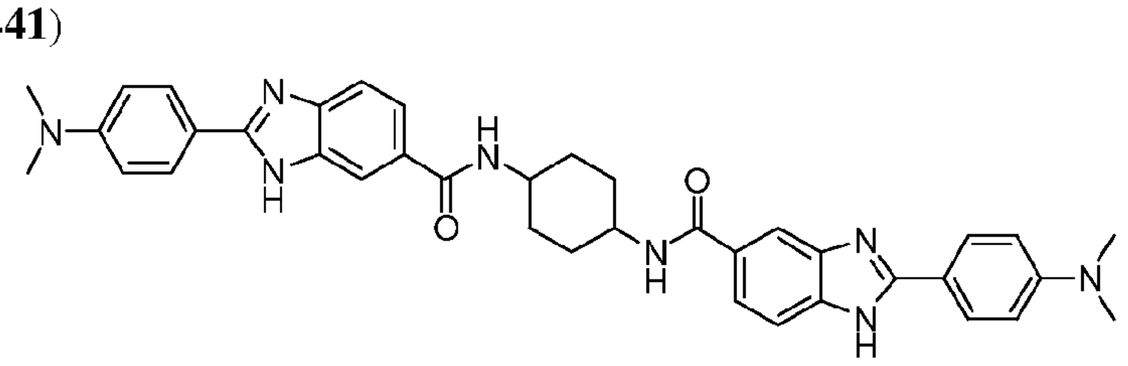
N-(2-(2,3-Dihydroxypropyl)amino-1*H*-benzimidazol-5-yl)-4-(4-dimethylaminobenzamido)benzamide (Compound **440**)



[0916] Compound **440** was prepared from 4-(4-dimethylaminobenzamido)benzoate and 5-amino-2-(2,3-dihydroxypropylamino)benzimidazole by standard conditions.
$[M+H]^+$ calcd for $C_{26}H_{28}N_6O_4$: 489.22; found: 489.01.

EXAMPLE 341

N,N'-(1,4-Cyclohexane)bis(2-(4-dimethylaminophenyl)-1*H*-benzimidazole-5-carboxamide) (Compound **441**)

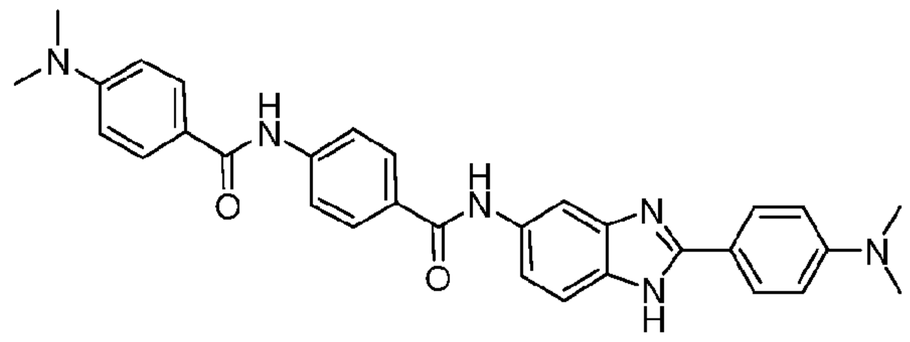


[0917] Compound **441** was prepared according to the procedure similar to that described in Scheme V from 1,4-cyclohexanediamine and 2-(4-dimethylaminophenyl)benzimidazole-5-carboxylate. $[M+H]^+$ calcd for $C_{38}H_{40}N_8O_2$: 641.33; found: 641.24.

EXAMPLE 342

N-(2-(4-Dimethylaminophenyl)-1*H*-benzimidazol-5-yl)-4-(4-dimethylaminobenzamido)

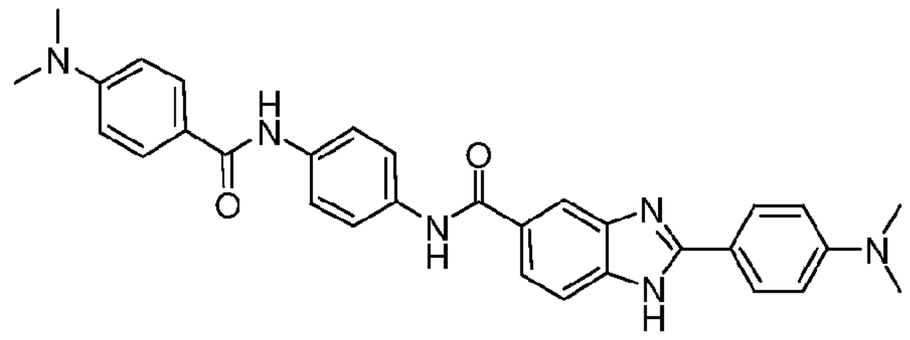
benzamide (Compound **442**)



[0918] Compound **442** was prepared from 4-(4-dimethylaminobenzamido)benzoate and 5-amino-2-(4-dimethylaminophenyl)benzimidazole by standard conditions. $[M+II]^+$ calcd for $C_{31}II_{30}N_6O_2$: 519.24; found: 518.99.

EXAMPLE 343

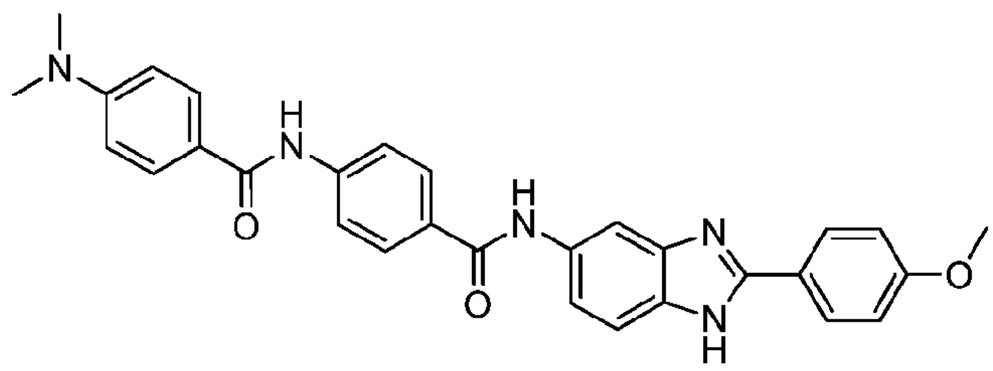
N-(4-(4-Dimethylaminobenzamido)phenyl)-2-(4-dimethylaminophenyl)-1*H*-benzimidazole-5-carboxamide (Compound **443**)



[0919] Compound **443** was prepared from 4-(4-dimethylaminobenzamido)aniline and 2-(4-dimethylaminophenyl)benzimidazole-5-carboxylate by standard conditions. $[M+H]^+$ calcd for $C_{31}H_{30}N_6O_2$: 519.24; found: 519.04.

EXAMPLE 344

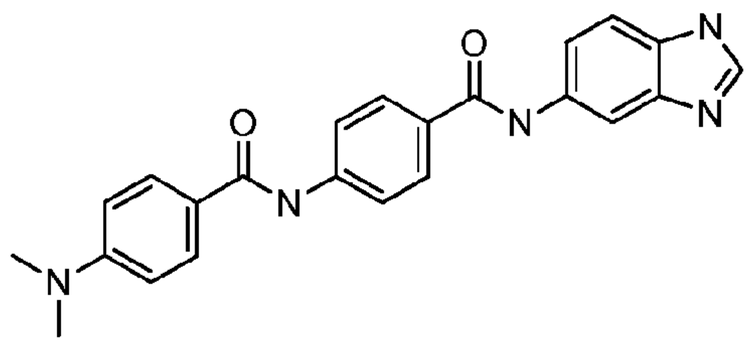
4-(dimethylamino)-*N*-(4-((2-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazol-5-yl)carbamoyl) phenyl)benzamide (Compound **444**)



[0920] Compound **444** was prepared from 4-(4-dimethylaminobenzamido)aniline and 2-(4-methoxyphenyl)benzimidazole-5-carboxylate by standard conditions. $[M+H]^+$ calcd for $C_{30}II_{27}N_5O_3$: 506.21; found: 507.02.

EXAMPLE 345

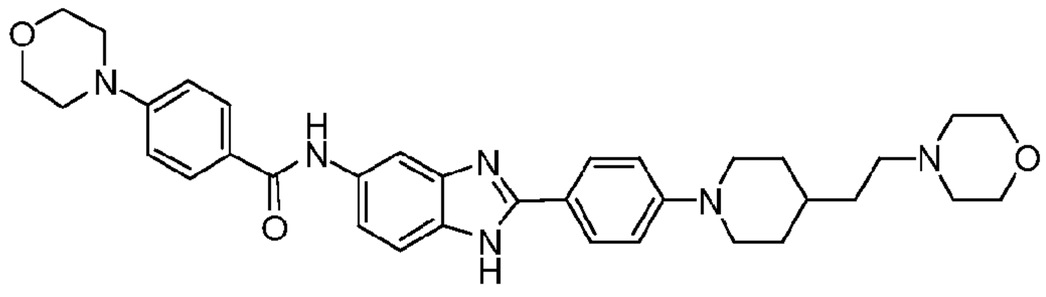
N-(4-(4-Dimethylaminobenzamido)phenyl)-1*H*-benzimidazole-5-carboxamide (Compound **445**)



[0921] Compound **445** was prepared from 4-(4-dimethylaminobenzamido)aniline and benzimidazole-5-carboxylate by standard conditions. $[M+II]^+$ calcd for $C_{23}II_{21}N_5O_2$: 400.17; found: 400.01.

EXAMPLE 346

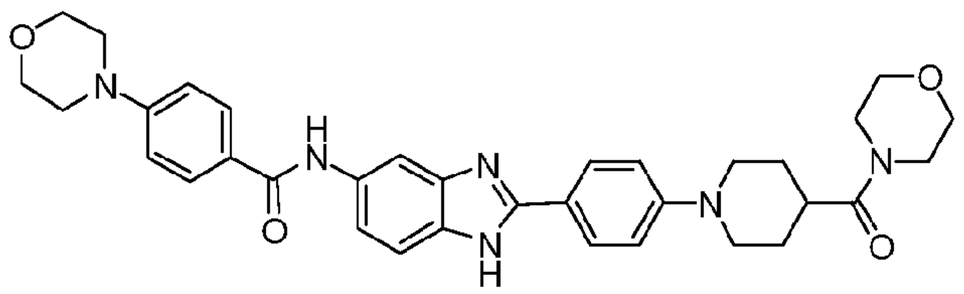
N-(2-(4-(4-(2-Morpholinoethyl)piperidino)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **446**)



[0922] Compound **446** was prepared from 4-morpholinobenzoate and 5-amino-2-(4-(4-(2-morpholinoethyl)piperidino)phenyl)benzimidazole by standard conditions. $[M+H]^+$ calcd for : $C_{35}H_{42}N_6O_3$; 595.33 found: 595.12.

EXAMPLE 347

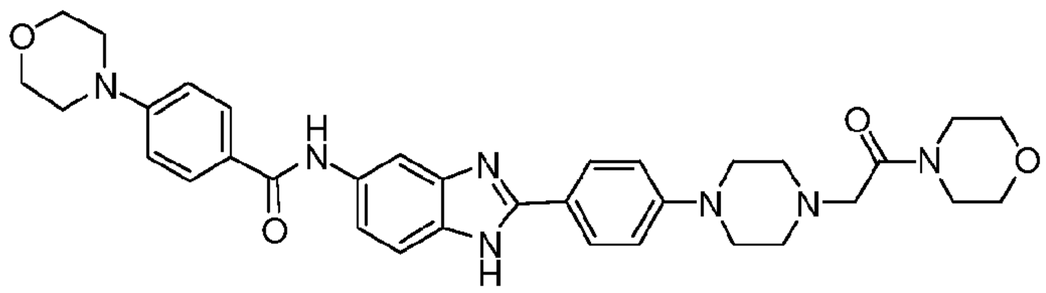
N-(2-(4-(4-Morpholinocarbonyl)piperidino)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **447**)



[0923] Compound **447** was prepared from 4-morpholinobenzoate and 5-amino-2-(4-(4-morpholinocarbonyl)piperidino)phenylbenzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{34}H_{38}N_6O_4$: 595.30; found: 595.13.

EXAMPLE 348

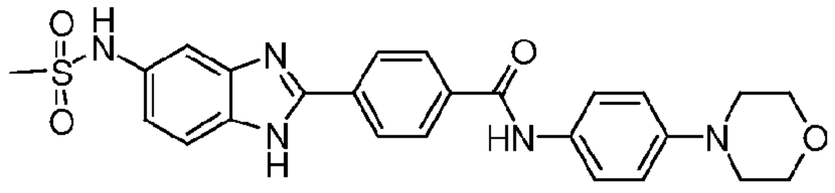
N-(2-(4-(4-Morpholinocarbonylmethyl)piperazino)phenyl)-1*H*-benzimidazol-5-yl)-4-morpholinobenzamide (Compound **448**)



[0924] Compound **448** was prepared from 4-morpholinobenzoate and 5-amino-2-(4-(4-morpholinocarbonylmethyl)piperazino)phenylbenzimidazole by standard conditions. $[M+H]^+$ calcd for $C_{34}H_{39}N_7O_4$: 610.31; found: 610.11.

EXAMPLE 349

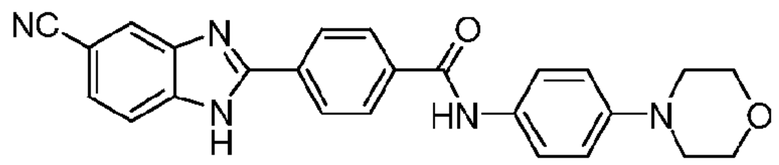
4-(5-Methylsulfonylamido)-1*H*-benzimidazol-2-yl)-*N*-(4-morpholinophenyl)benzamide (Compound **449**)



[0925] Compound **449** was prepared from 4-morpholinoaniline and 4-(5-methylsulfonylamino-1*H*-benzimidazol-2-yl)benzoate by standard conditions. $[M+H]^+$ calcd for $C_{25}H_{25}N_5O_4S$: 492.17; found: 491.97.

EXAMPLE 350

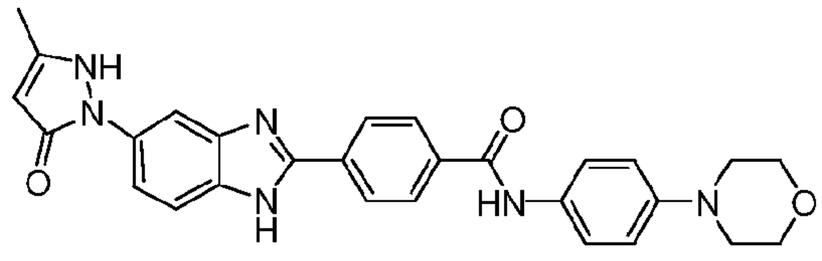
4-(5-Cyano-1*H*-benzimidazol-2-yl)-*N*-(4-morpholinophenyl)benzamide (Compound **450**)



[0926] Compound **450** was prepared from 4-morpholinoaniline and 4-(5-cyano-1*H*-benzimidazol-2-yl)benzoate by standard conditions. $[M+H]^+$ calcd for $C_{25}H_{21}N_5O_2$: 424.18; found: 423.95.

EXAMPLE 351

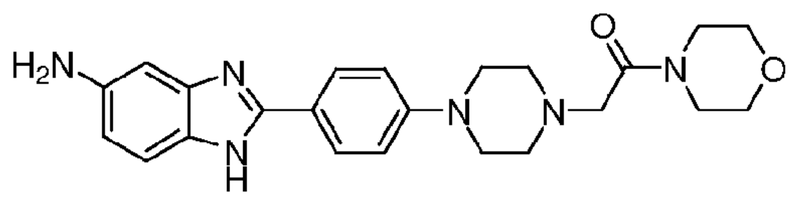
4-(5-(3-Methyl-5-oxo-2,5-dihydro-1*H*-pyrazol-1-yl)-1*H*-benzimidazol-2-yl)-*N*-(4-morpholinophenyl)benzamide (Compound **451**)



[0927] Compound **451** was prepared from 4-morpholinoaniline and 4-(5-(3-methyl-5-oxo-2,5-dihydro-1*H*-pyrazol-1-yl)-1*H*-benzimidazol-2-yl)benzoate by standard conditions. $[M+H]^+$ calcd for $C_{28}H_{26}N_6O_3$: 495.22; found: 495.01.

EXAMPLE 352

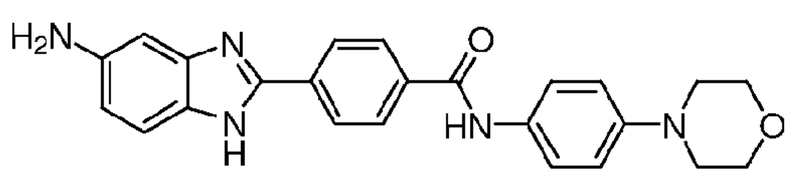
5-Amino-(2-(4-(4-morpholinocarbonylmethyl)piperazino)phenyl)-1*H*-benzimidazole (Compound **452**)



[0928] Compound **452** was prepared according to the procedure similar to that described in Scheme III from 3,4-dinitroaniline and 2-(4-(4-morpholinocarbonylmethyl)piperazino)benzaldehyde. $[M+H]^+$ calcd for $C_{23}H_{28}N_6O_2$: 421.23; found: 420.98.

EXAMPLE 353

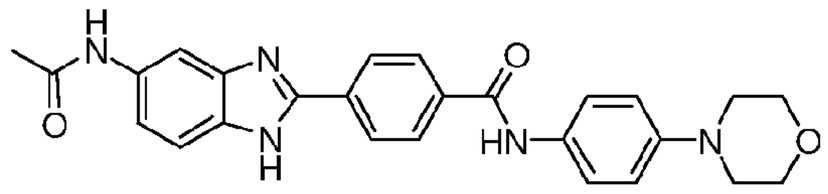
4-(5-Amino-1*H*-benzimidazol-2-yl)-*N*-(4-morpholinophenyl)benzamide (Compound **453**)



[0929] Compound **453** was prepared from 4-morpholinoaniline and 4-(5-amino-1*H*-benzimidazol-2-yl)benzoate by standard conditions. $[M+H]^+$ calcd for $C_{24}H_{23}N_5O_2$: 414.19; found: 413.97.

EXAMPLE 354

4-(5-Acetamino-1*H*-benzimidazol-2-yl)-*N*-(4-morpholinophenyl)benzamide (Compound **454**)



[0930] Compound **454** was prepared from 4-morpholinoaniline and 4-(5-acetamino-1*H*-benzimidazol-2-yl)benzoate by standard conditions. $[M+H]^+$ calcd for $C_{26}H_{25}N_5O_3$: 456.20; found: 455.95.

DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME __1___ DE __2___

NOTE: Pour les tomes additionels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

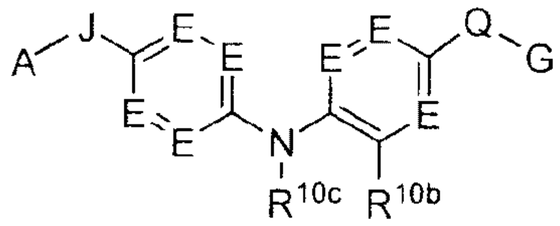
THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __2___

NOTE: For additional volumes please contact the Canadian Patent Office.

WHAT IS CLAIMED IS:

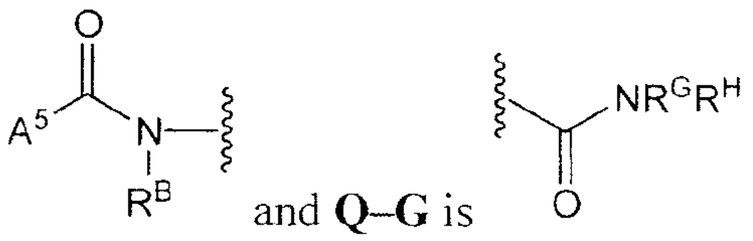
1. A compound or a pharmaceutically acceptable salt thereof of Formula **VIII**:



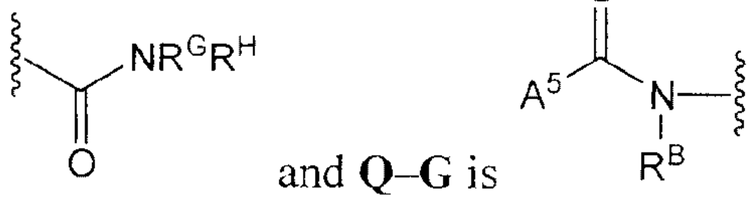
(VIII)

wherein:

or **A–J** is and **Q–G** is ;



or **A–J** is and **Q–G** is ;



or **A–J** is and **Q–G** is ;

each **E** is separately selected from the group consisting of -C**R**^{10a}- and N (nitrogen);

each **R**^{10a} is separately selected from the group consisting of H (hydrogen), halogen, and C_1-C_6 alkyl optionally substituted with up to five fluoro;

R^{10b} is selected from the group consisting of H (hydrogen), halogen, and C_1-C_6 alkyl optionally substituted with up to five fluoro;

R^{10c} is H (hydrogen);

A^4 is selected from the group consisting of phenyl and heteroaryl, wherein at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), and wherein each phenyl and heteroaryl is optionally substituted with one or more substituents selected from the group consisting of **R**^{1}, **R**^{2}, and **R**^{3};

G^4 is selected from the group consisting of phenyl and heteroaryl, wherein at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), and wherein each phenyl and

heteroaryl is optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$;

$\mathbf{A^5}$ is phenyl optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^1}$, $\mathbf{R^2}$, and $\mathbf{R^3}$;

$\mathbf{R^B}$ is hydrogen;

$\mathbf{R^G}$ is heteroaryl wherein at least one atom forming the heteroaryl aromatic ring is a N (nitrogen), optionally substituted with one or more substituents selected from the group consisting of $\mathbf{R^4}$, $\mathbf{R^5}$, and $\mathbf{R^6}$, and wherein said heteroaryl in the definition of $\mathbf{R^G}$ is further optionally fused with an optionally substituted nonaromatic carbocycle;

$\mathbf{R^H}$ is hydrogen;

each $\mathbf{R^I}$ is separately selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^2}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^3}$ is separately selected from the group consisting of halogen, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each $\mathbf{R^4}$ is separately selected from the group consisting of halogen, an optionally substituted C_1-C_6 alkyl, and an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^5}$ is separately selected from the group consisting of halogen, $-O(CH_2)_mOR^I$, $-(CH_2)_mOR^I$, $-NR^JR^K$an optionally substituted C_1-C_6 alkyl, an optionally substituted C_1-C_6 alkoxy;

each $\mathbf{R^6}$ is separately selected from the group consisting of halogen, C_1-C_6 alkyl, and C_1-C_6 alkoxy;

each $\mathbf{R^I}$ is separately selected from the group consisting of hydrogen and C_1-C_6 alkyl;

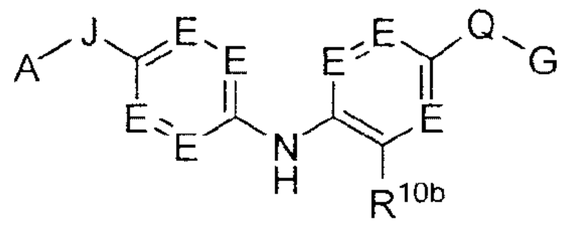
each $-NR^JR^K$ is separately selected, wherein $\mathbf{R^J}$ and $\mathbf{R^K}$ are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl optionally substituted with up to 5 fluoro, or $-(CH_2)_mOR^{JA}$; or $-NR^JR^K$ is an optionally substituted non-aromatic heterocycle linked through a ring nitrogen atom;

each $\mathbf{R^{JA}}$ is independently selected from the group consisting of hydrogen or C_1-C_6 alkyl; and

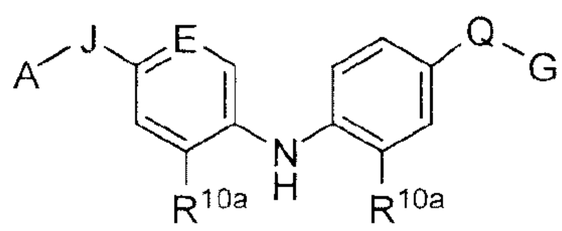
each **m** is independently 0, 1, or 2;

and wherein unless otherwise indicated, optionally substituted refers to a group in which none, one, or more than one of the hydrogen atoms has been replaced with one or more group(s) individually and independently selected from: alkyl, heteroalkyl, $HO(CH_2)_{1\text{-}3}O$-, $HO(CH_2)_{1\text{-}3}$-, hydroxy, and halo.

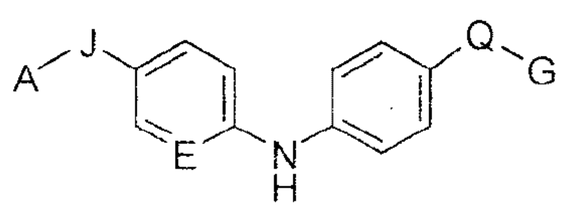
2. The compound or pharmaceutically acceptable salt thereof of claim 1, having the formula **VIIIa:**



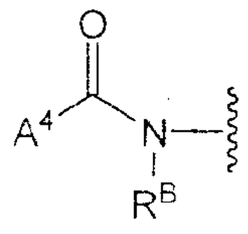
3. The compound or pharmaceutically acceptable salt thereof of claim 2, having the formula **VIIIaa:**

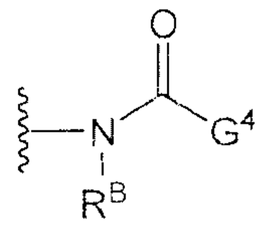


4. The compound or pharmaceutically acceptable salt thereof of claim 3, having the formula **VIIIab:**



5. The compound or pharmaceutically acceptable salt thereof of claim 3, wherein:

A–J is 

and **Q–G** is 

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6. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5 for modulating an EPO activity in a cell.

7. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5 for the preparation of a medicament for modulating an EPO activity in a cell.

8. An *in vitro* method for identifying a compound that modulates an EPO activity, comprising contacting a cell that expresses an EPO receptor with a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5; and monitoring an effect of the compound or pharmaceutically acceptable salt thereof on the cell.

9. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5 for identifying a compound that modulates an EPO activity.

10. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5 for treatment of a disease or condition resulting from radiation or chemotherapy in a patient.

11. Use of a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5 in preparation of a medicament for treatment of a disease or condition resulting from radiation or chemotherapy in a patient.

12. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 for use in treatment of a disease or condition resulting from radiation or chemotherapy in a patient.

13. The use according to claim 10 or 11, wherein said treatment is on cells harvested from the patient.

14. The use according to claim 10, 11 or 13, wherein the treatment is prophylactic.

15. The use according to claim 10, 11, 13, or 14, wherein the patient suffers from a condition affecting the nervous system.

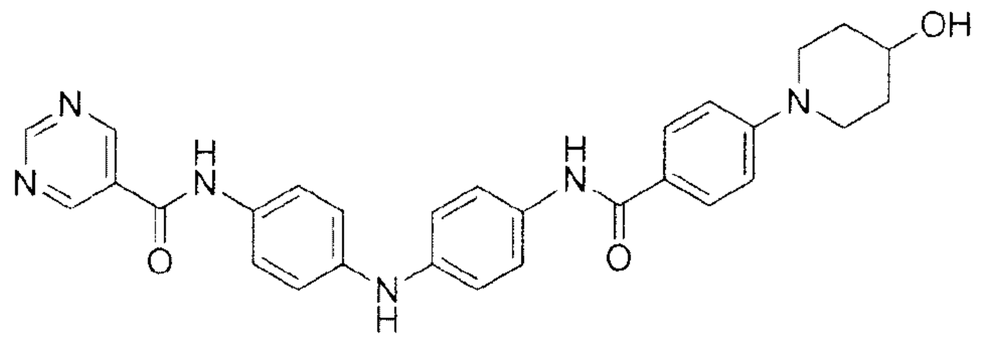
16. The use of claim 15, wherein the condition affecting the nervous system is amyotrophic lateral sclerosis, multiple sclerosis, or muscular dystrophy.

17. The use of claim 15, wherein the condition affecting the nervous system is an injury to the nervous system.

18. The use of claim 15, wherein the condition affecting the nervous system is an injury to the spinal cord.

19. A pharmaceutical composition comprising a physiologically acceptable carrier, diluent, or excipient; and a compound or a pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 5.

20. A compound or a pharmaceutically acceptable salt thereof having the structure:



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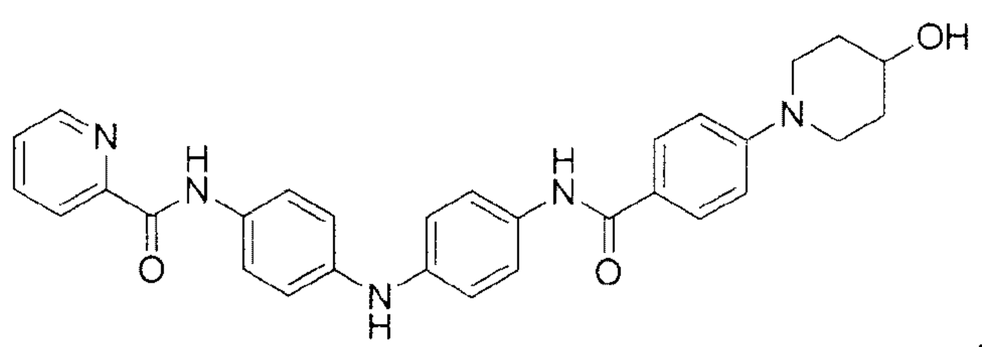

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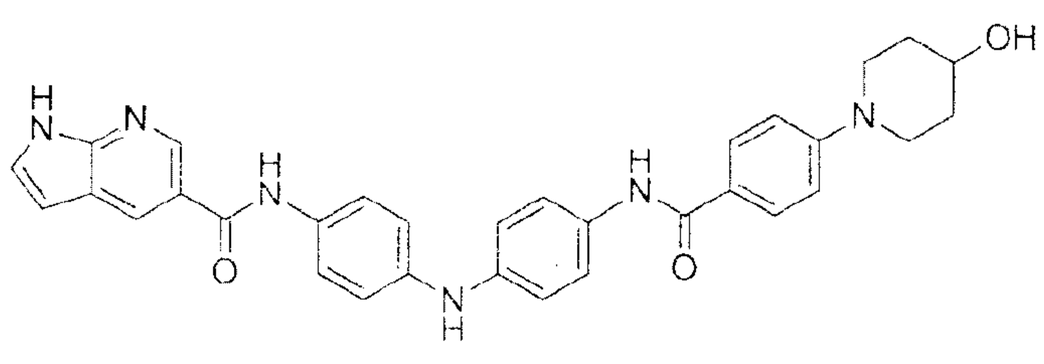

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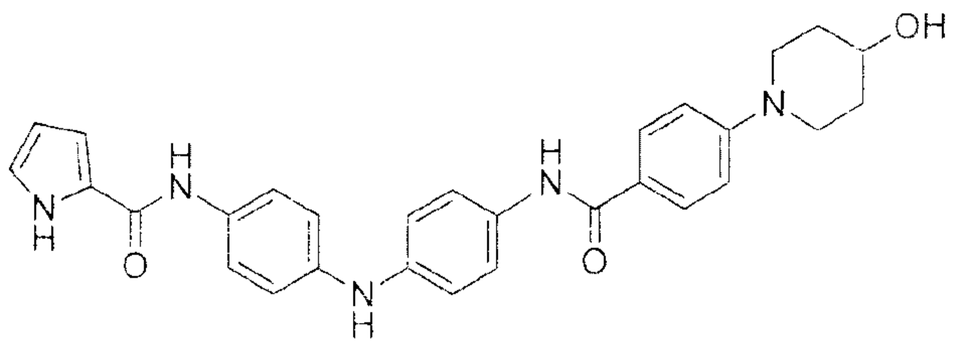

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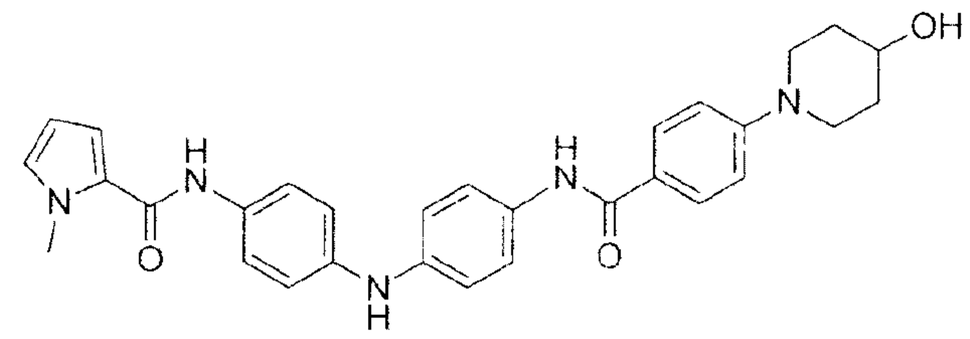

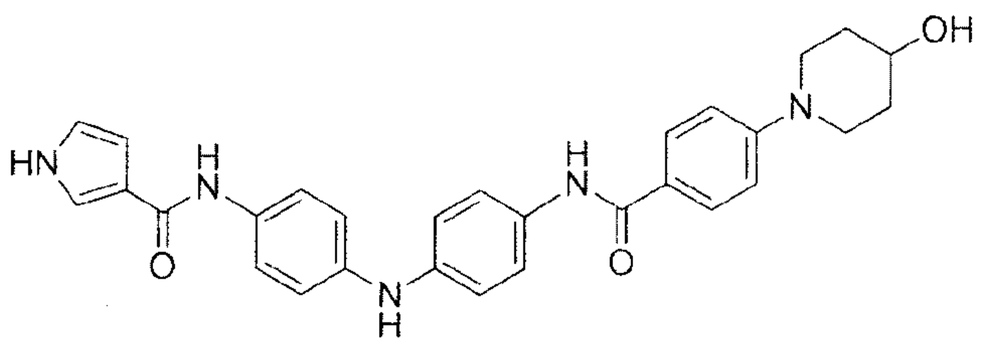

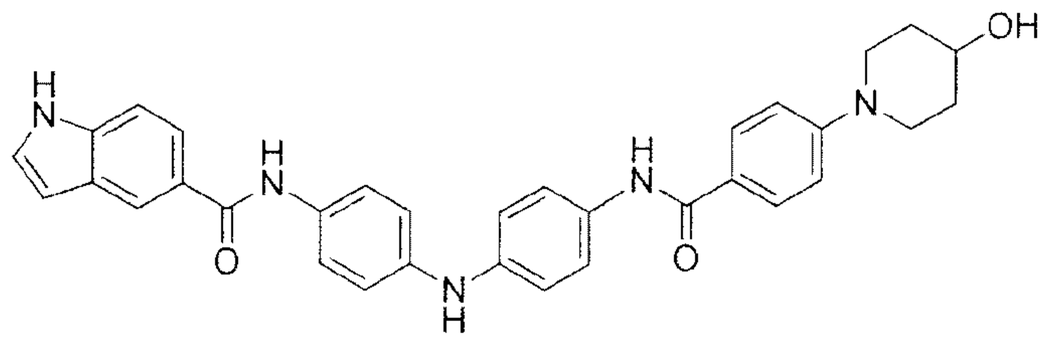

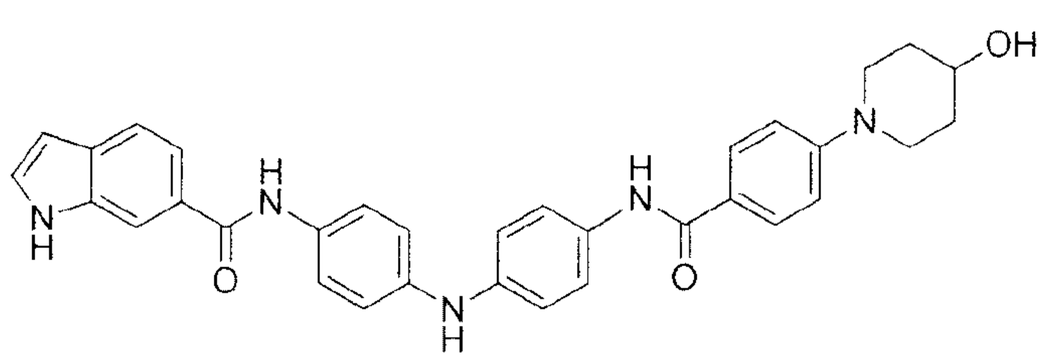

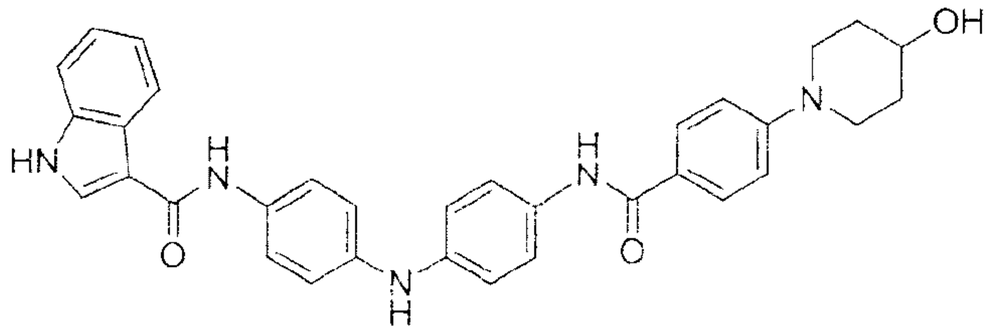

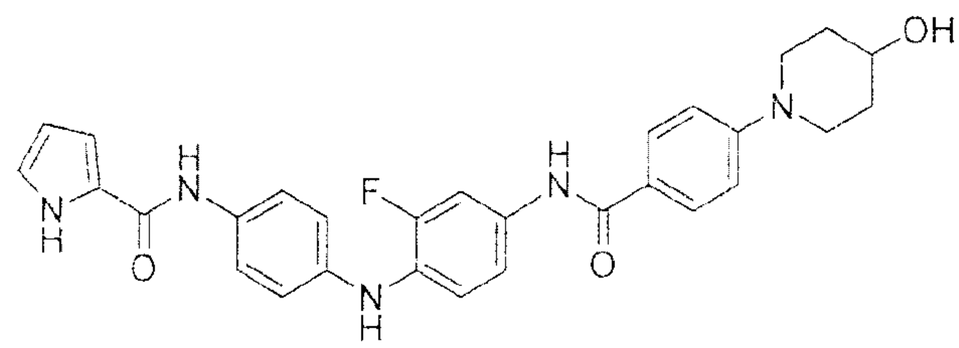

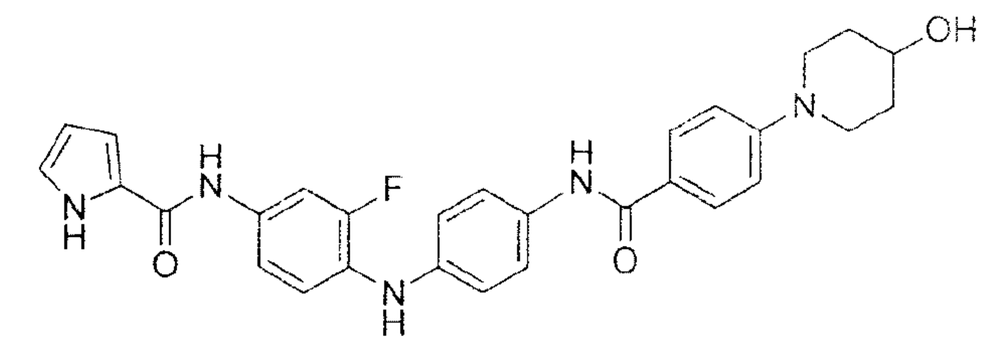

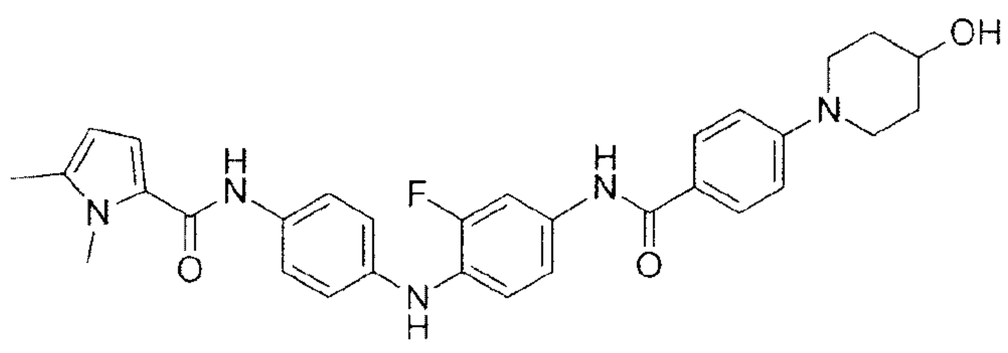

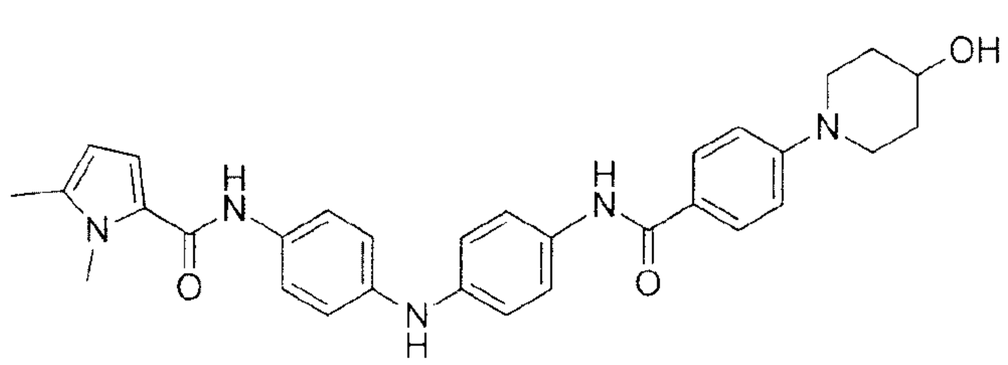

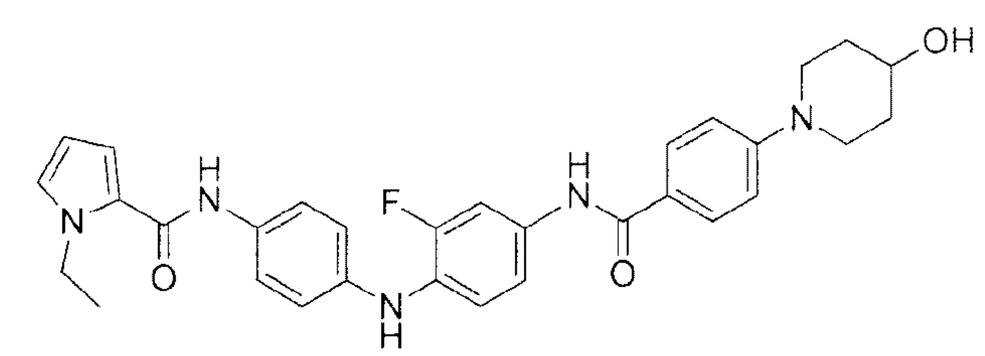

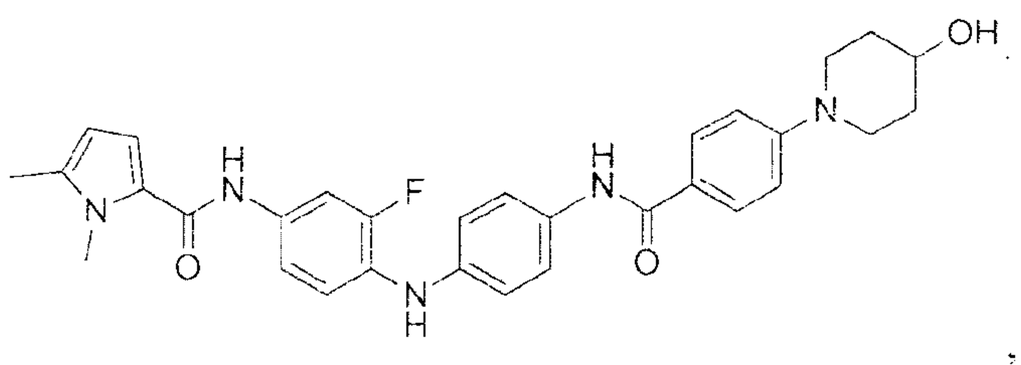

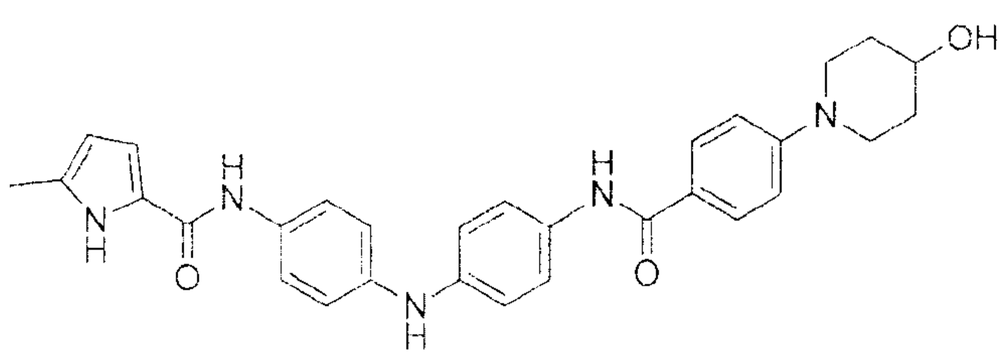

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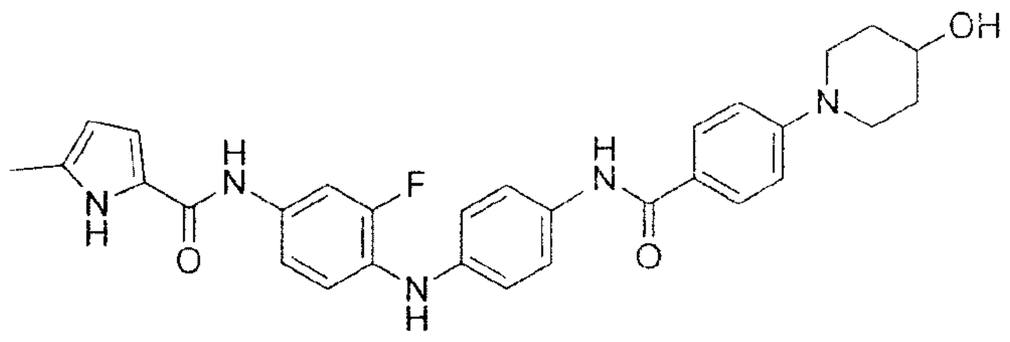

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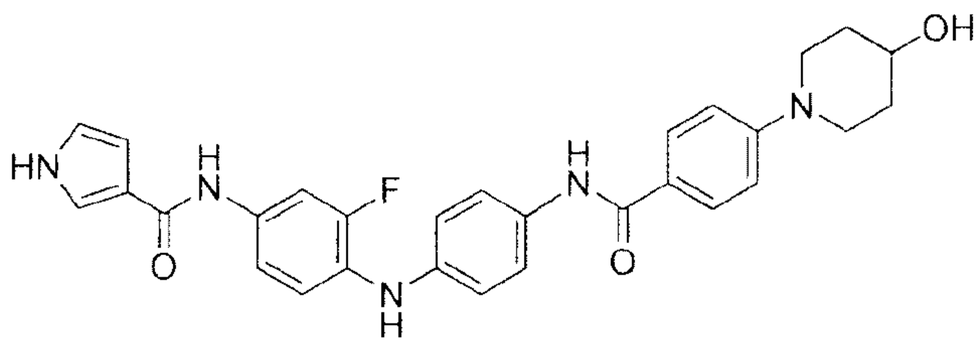

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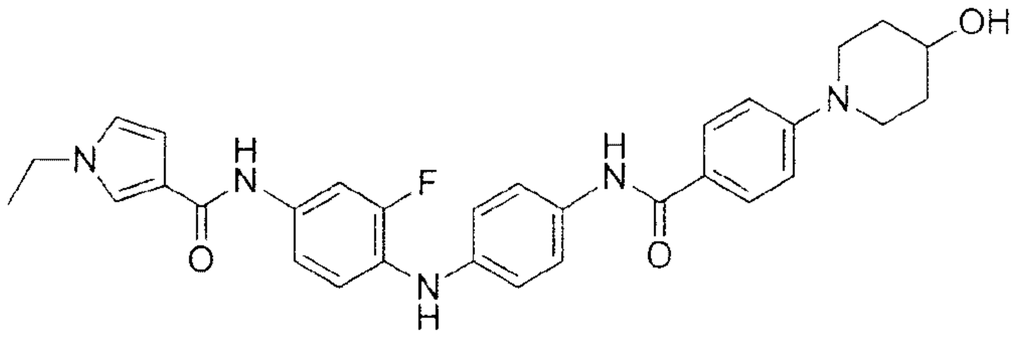

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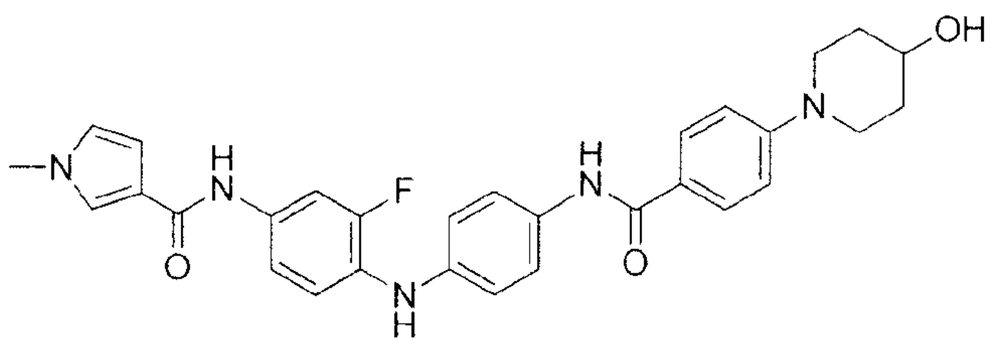

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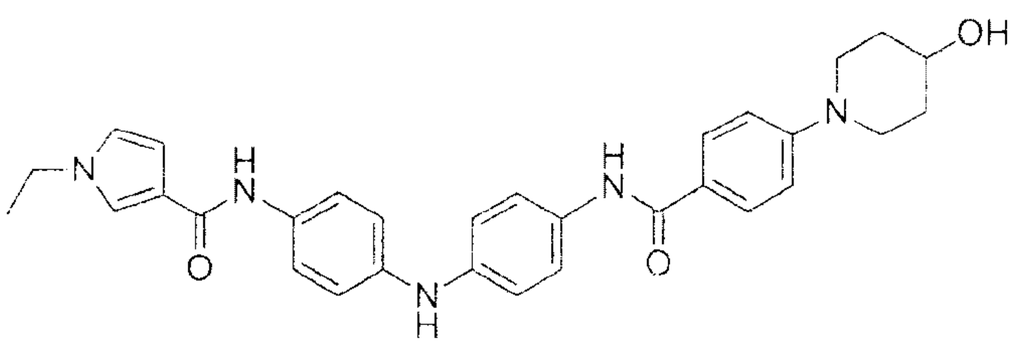

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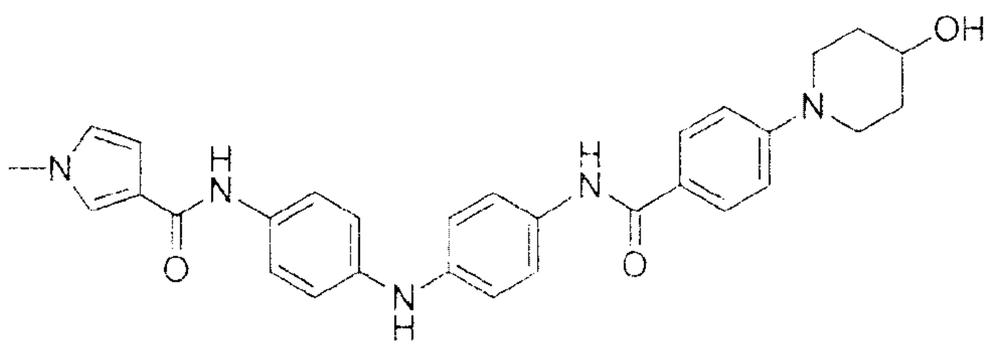

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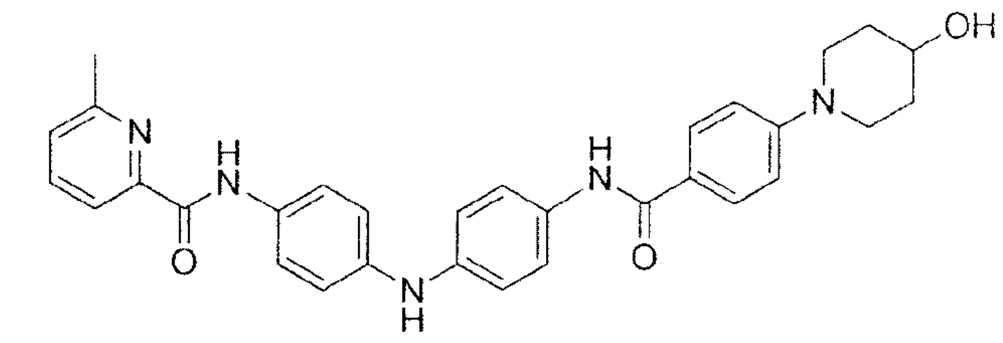

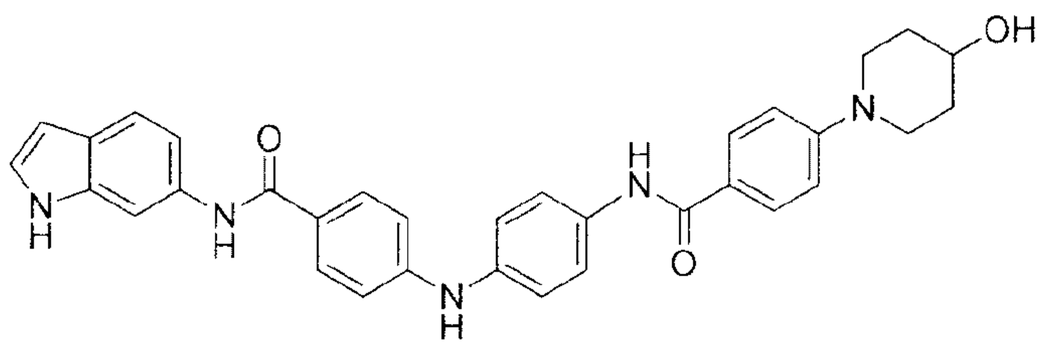

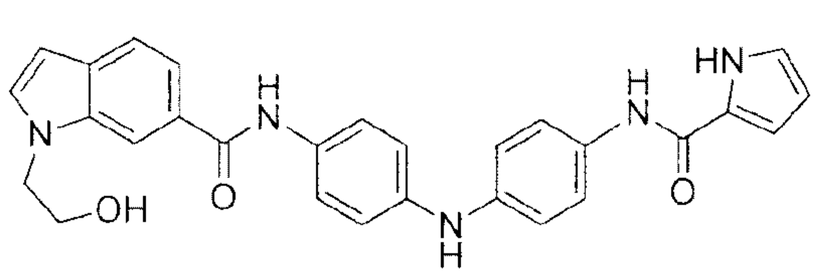

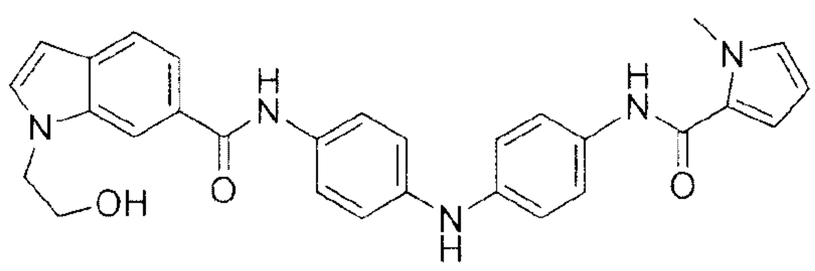

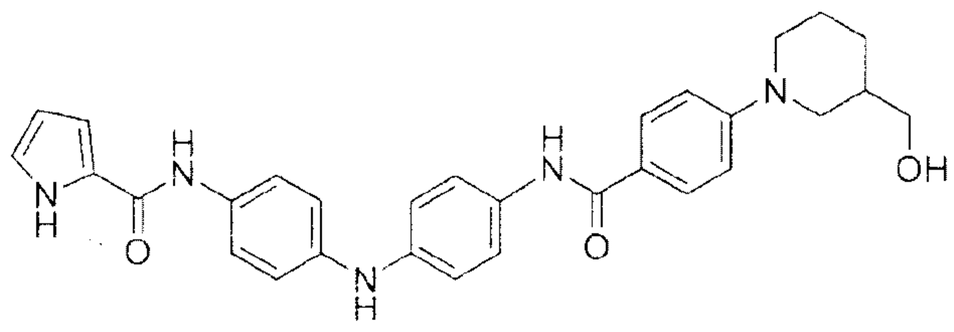

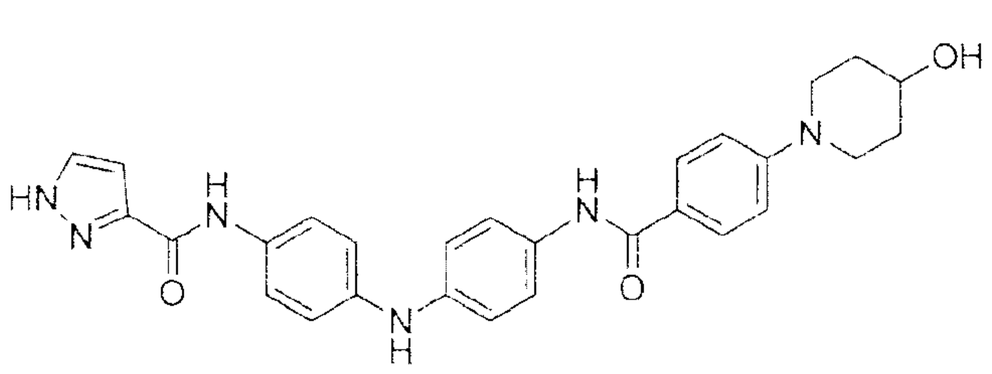

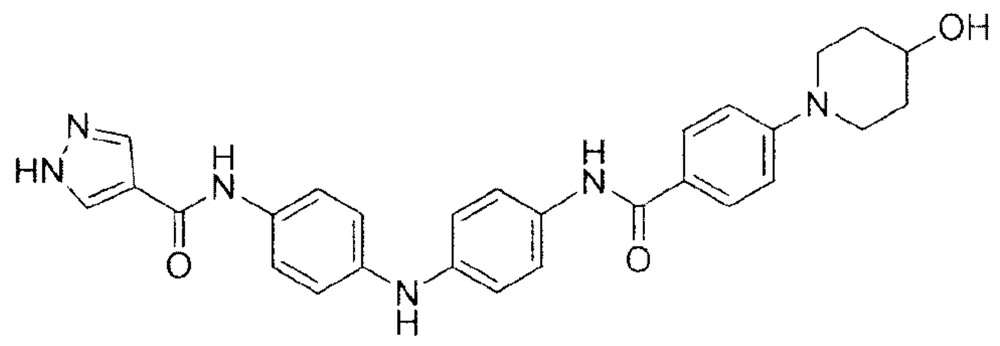

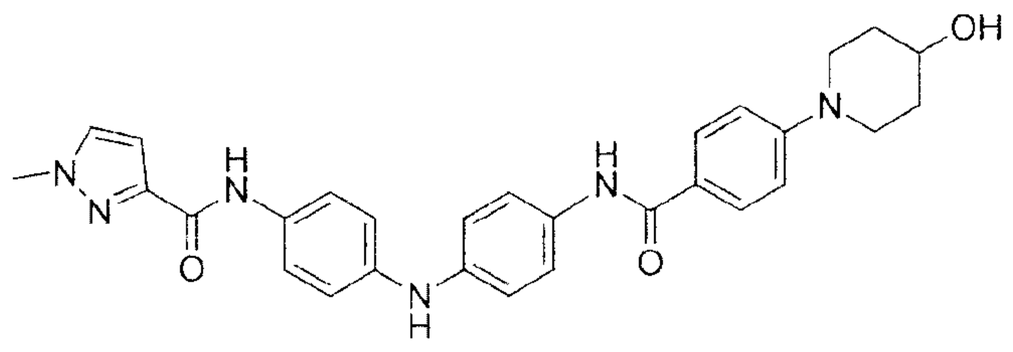

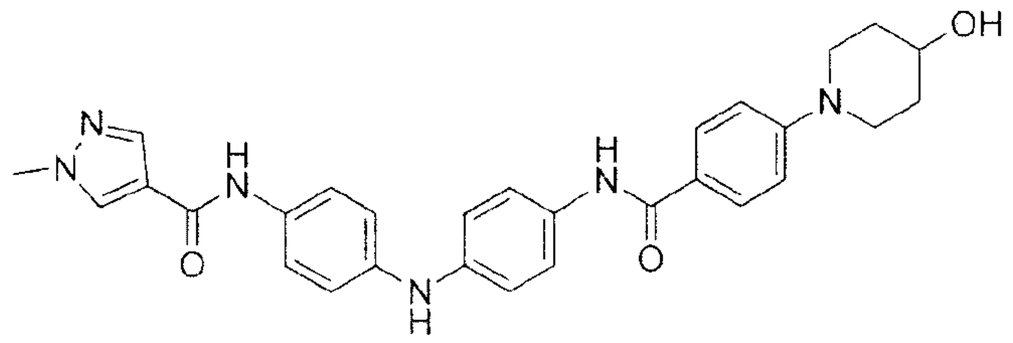

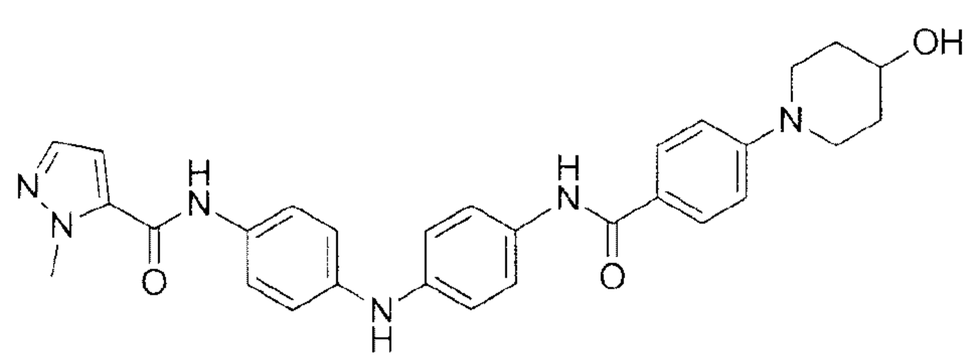

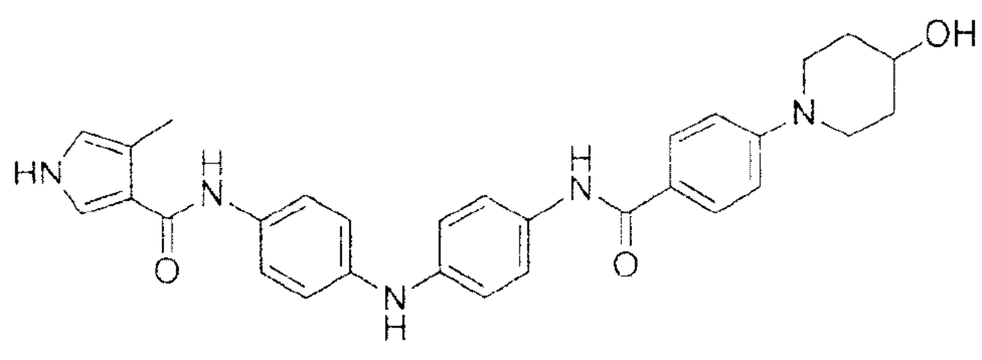

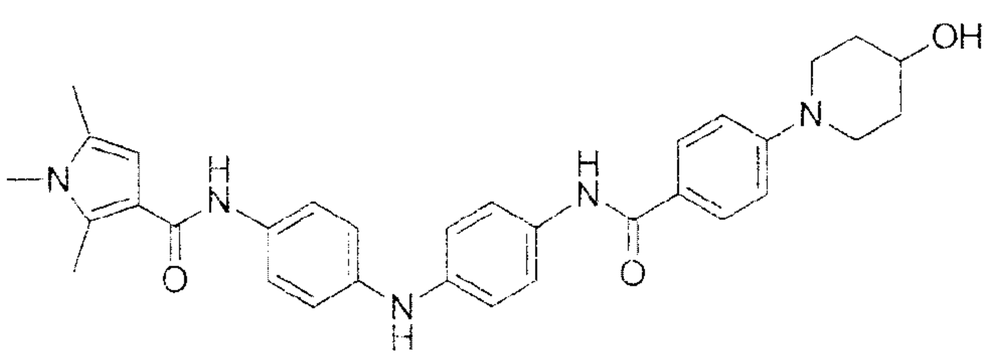

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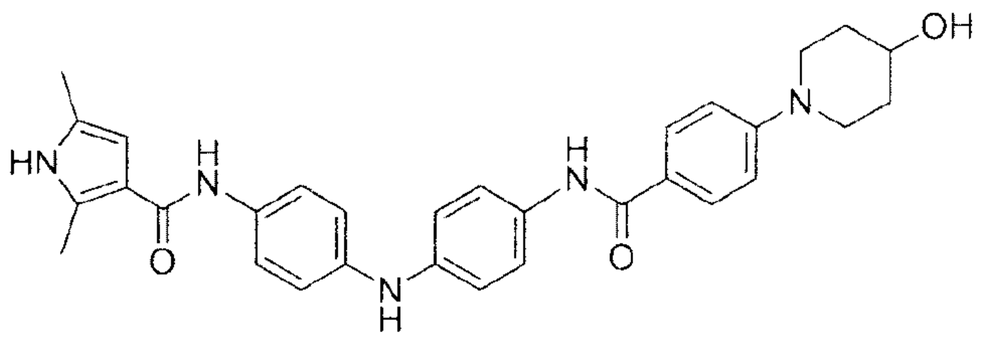

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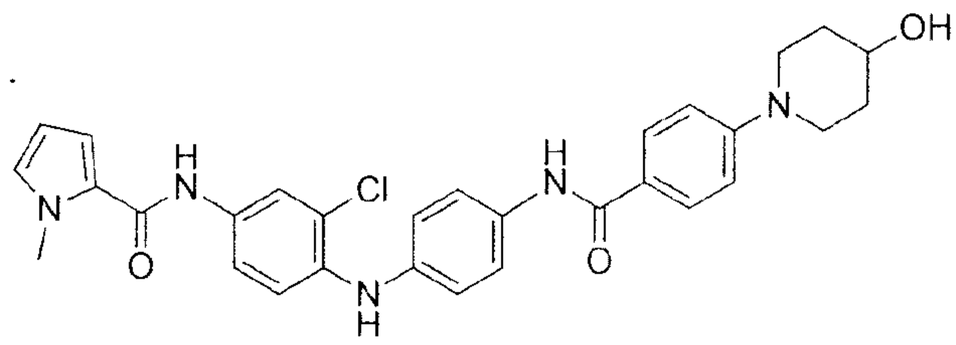

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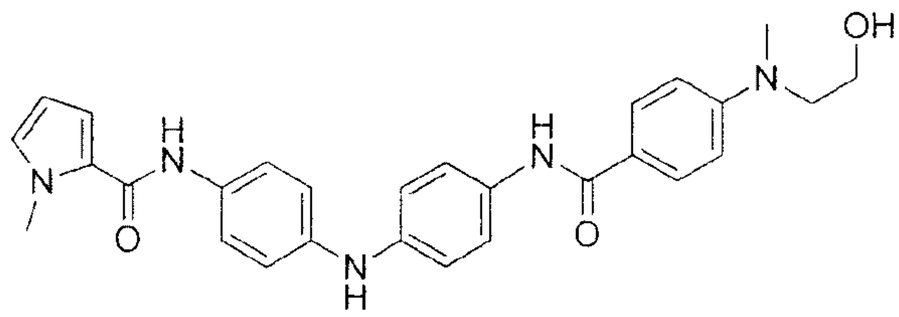

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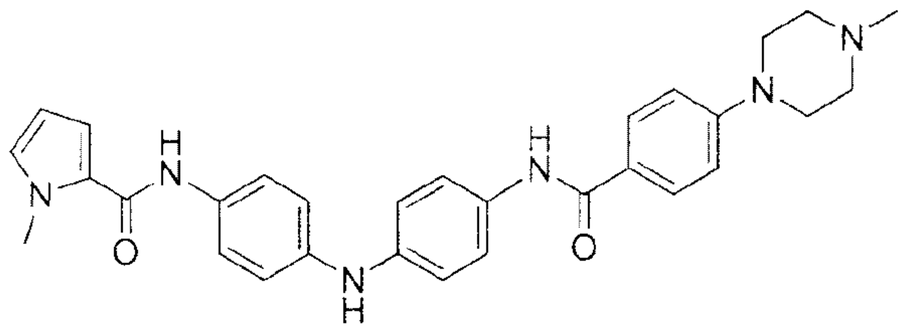

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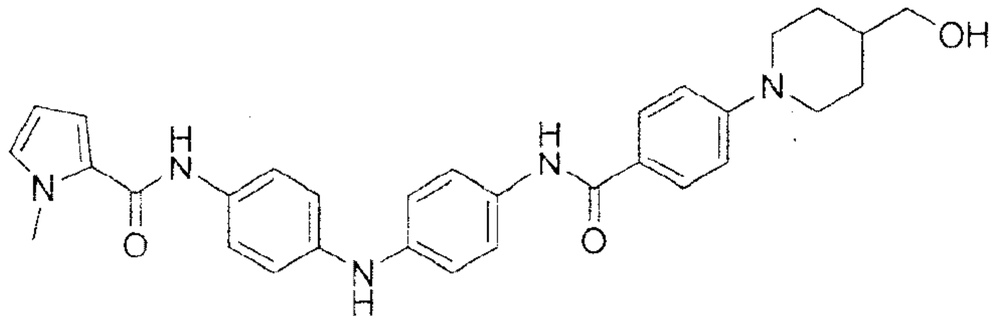

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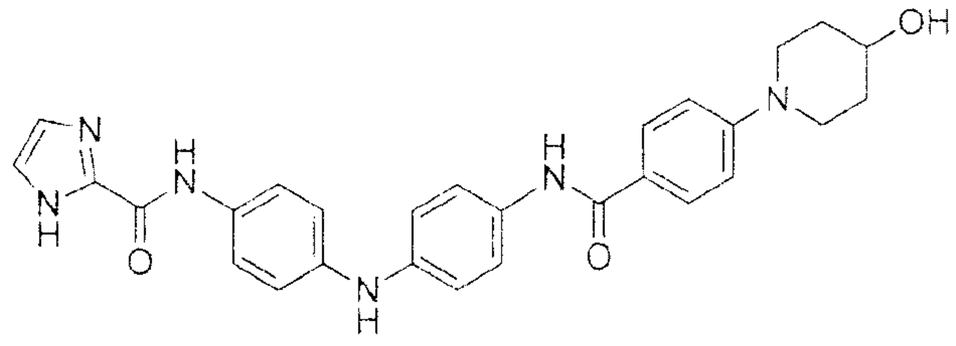

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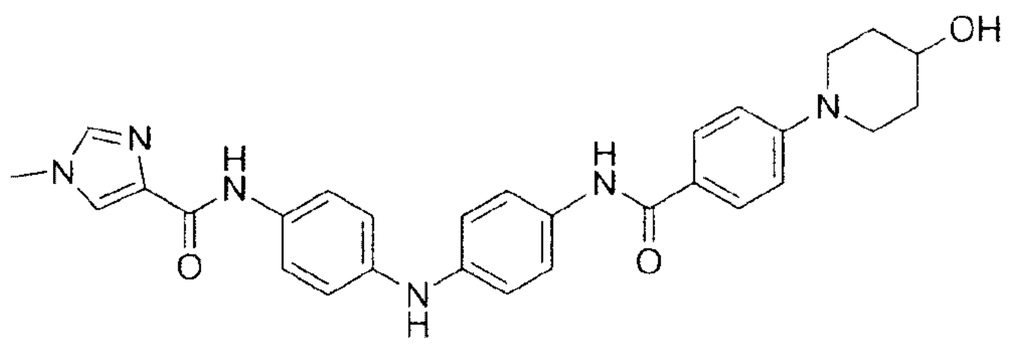

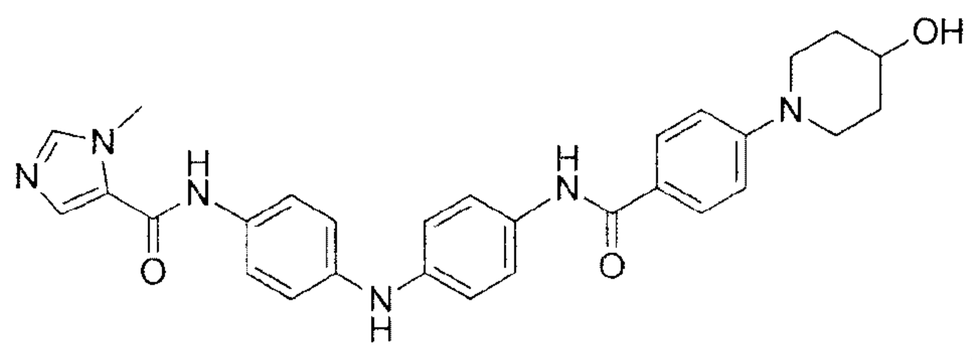

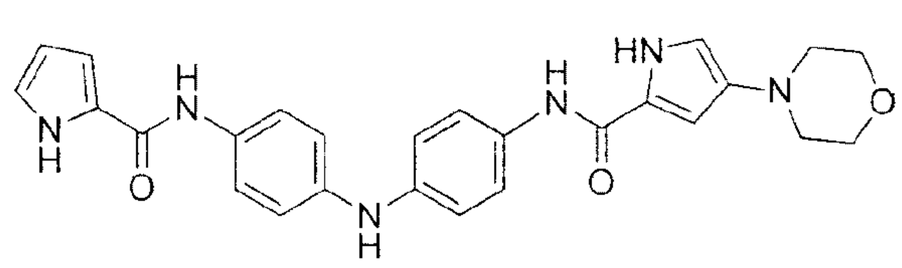

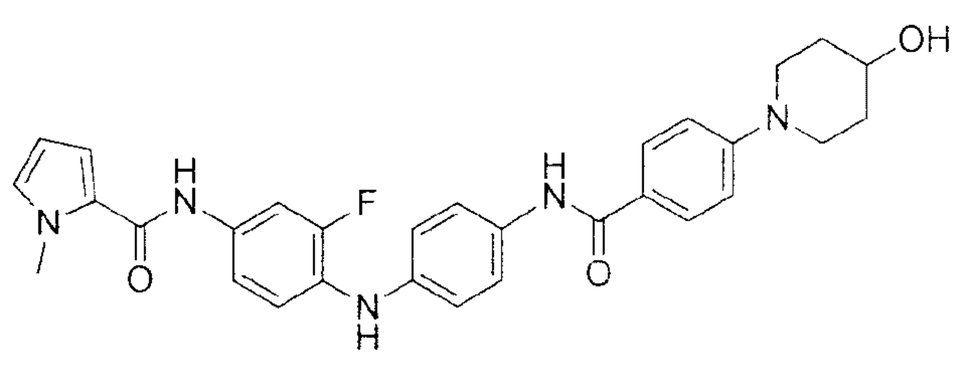

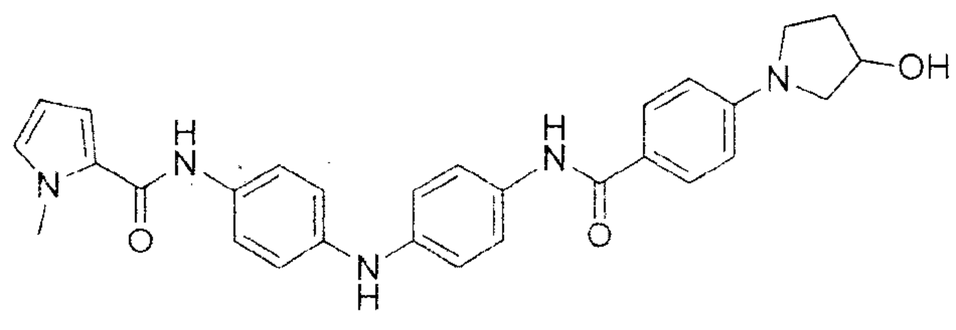

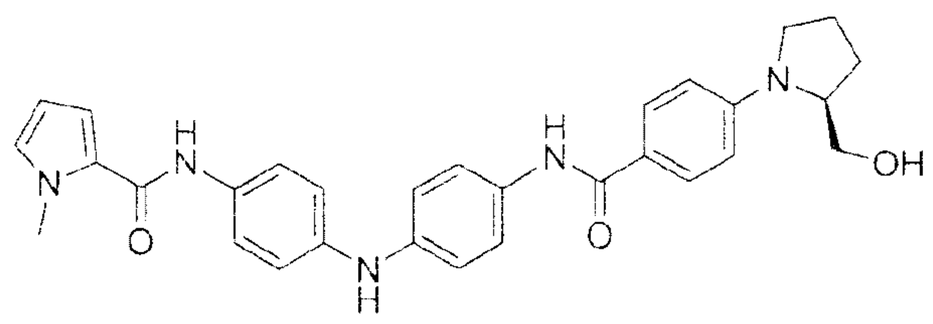

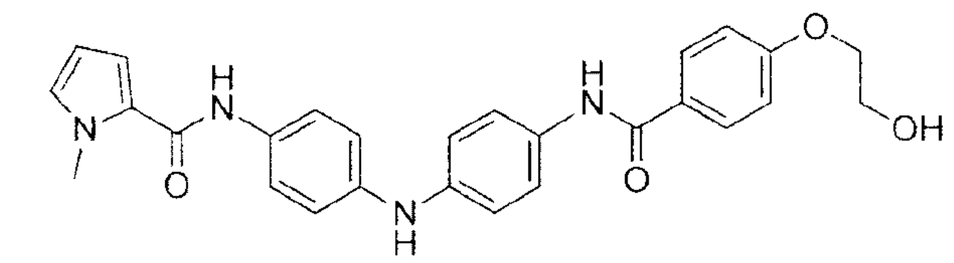

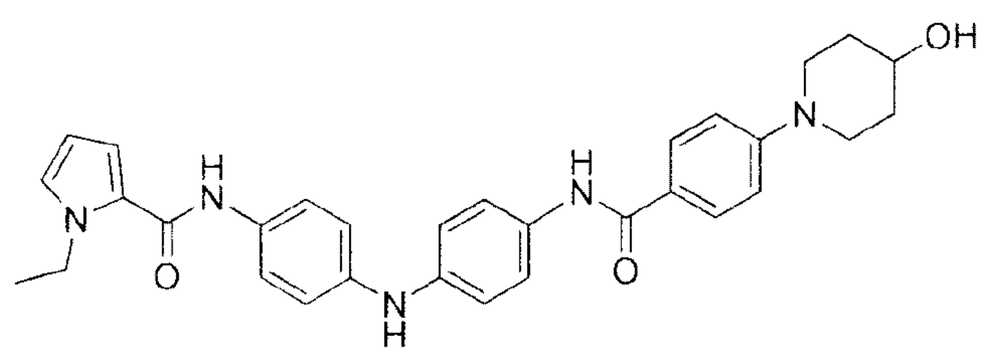

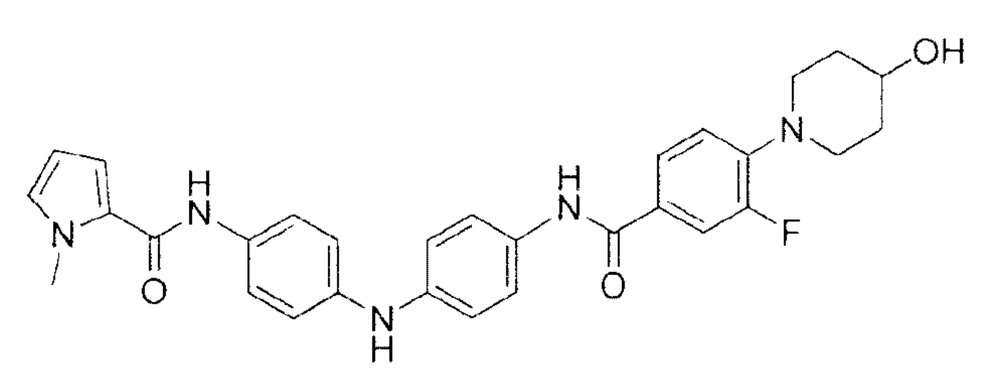

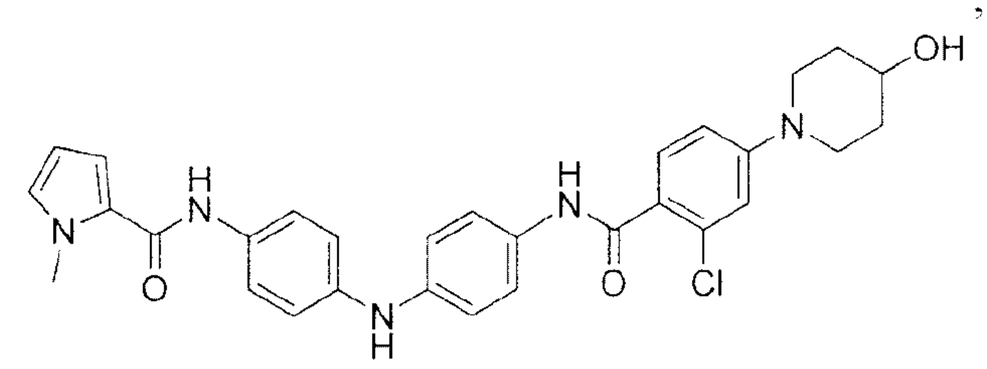

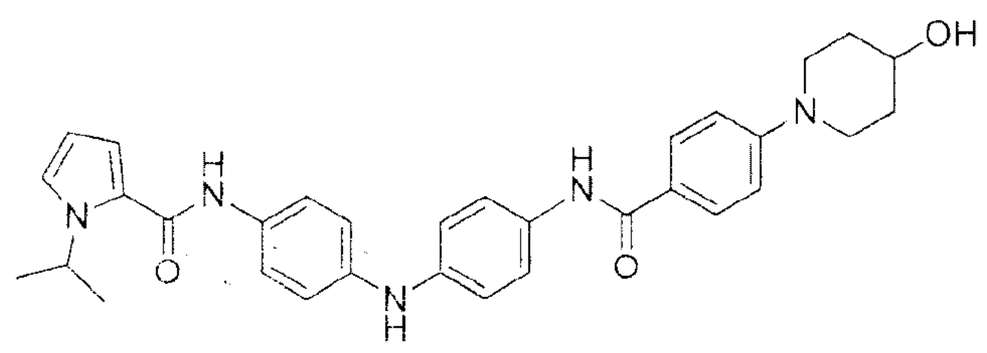

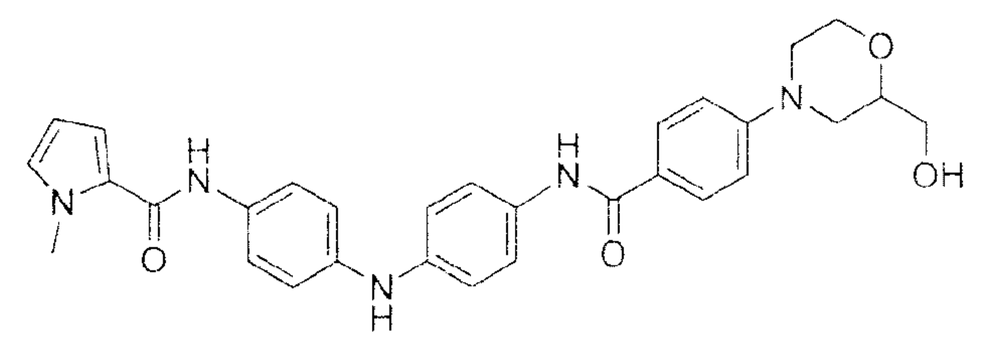

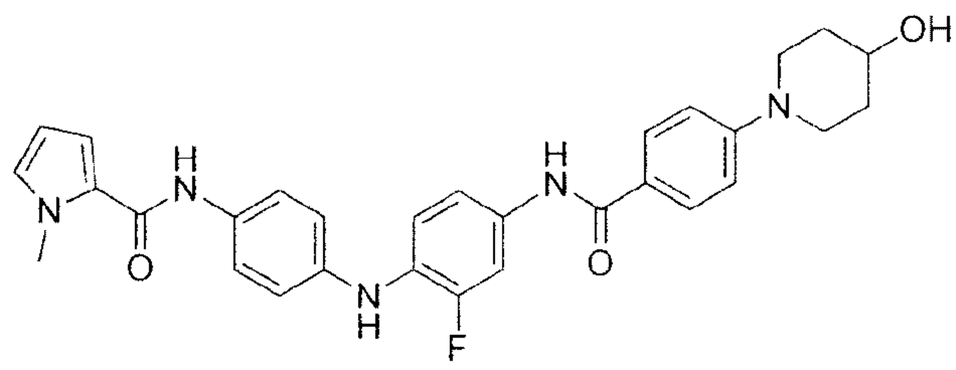

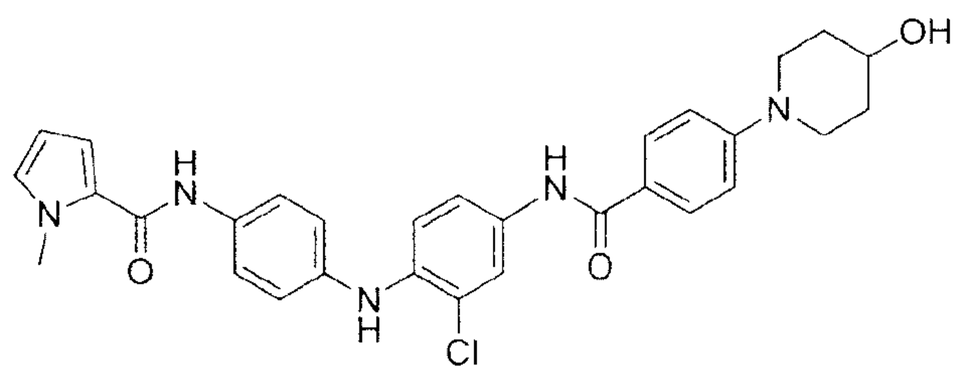

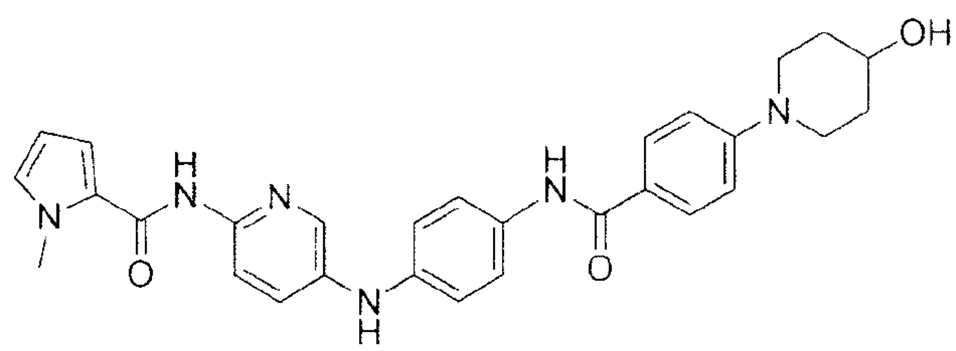

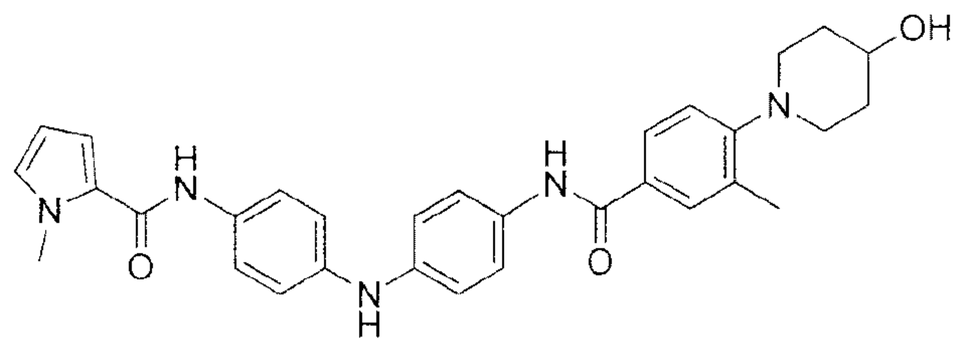

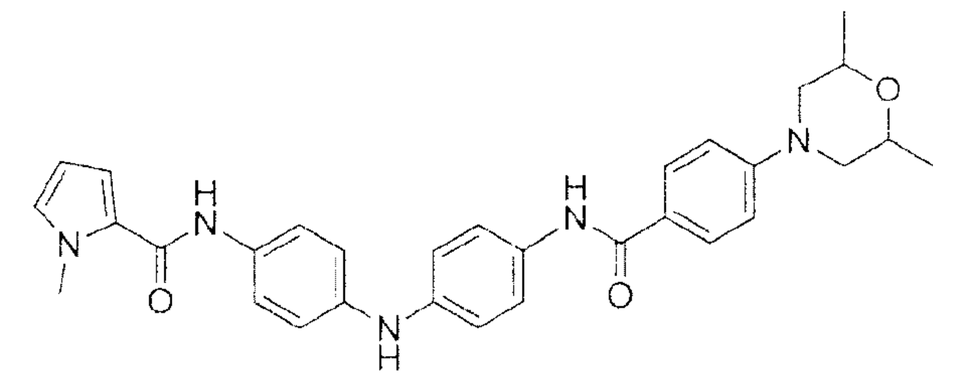

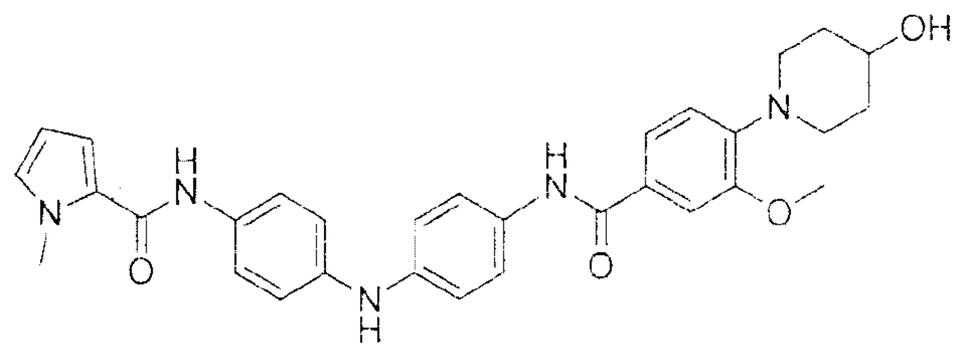

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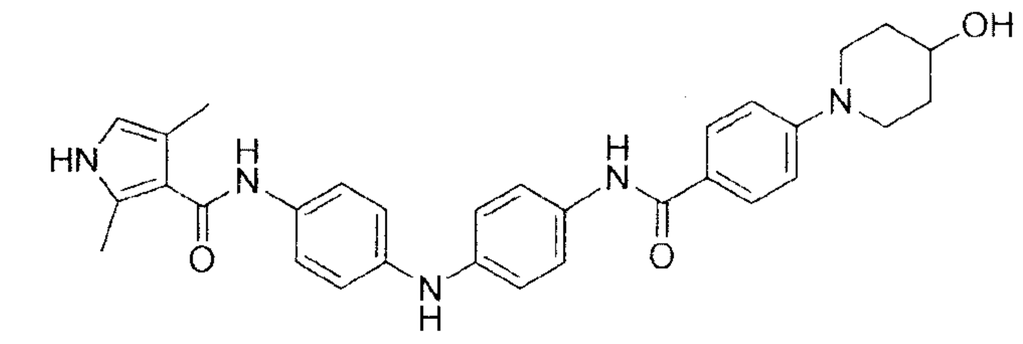

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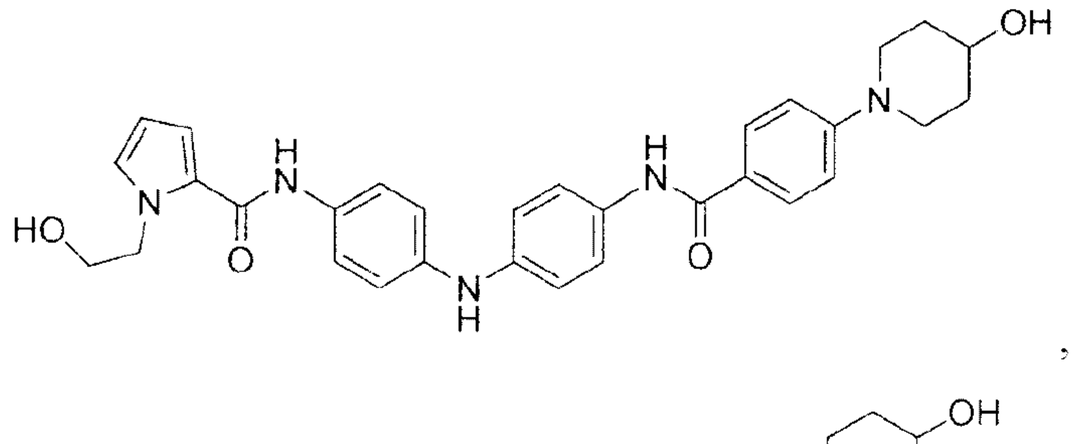

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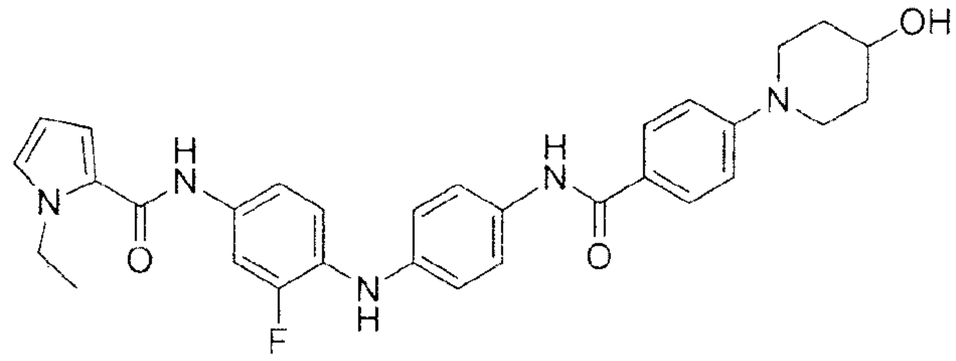

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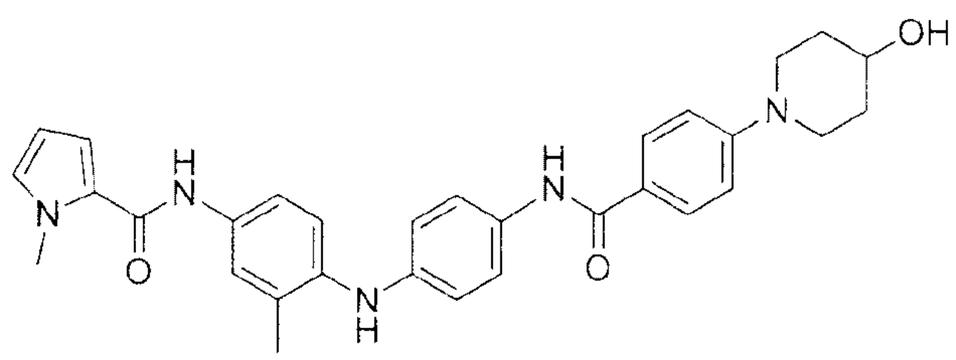

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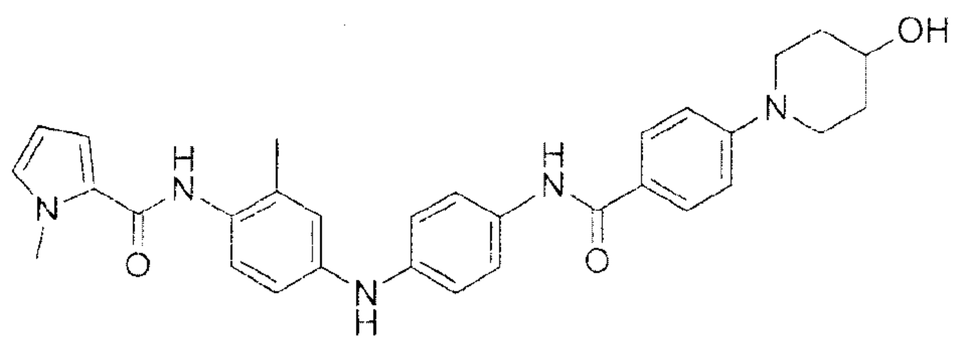

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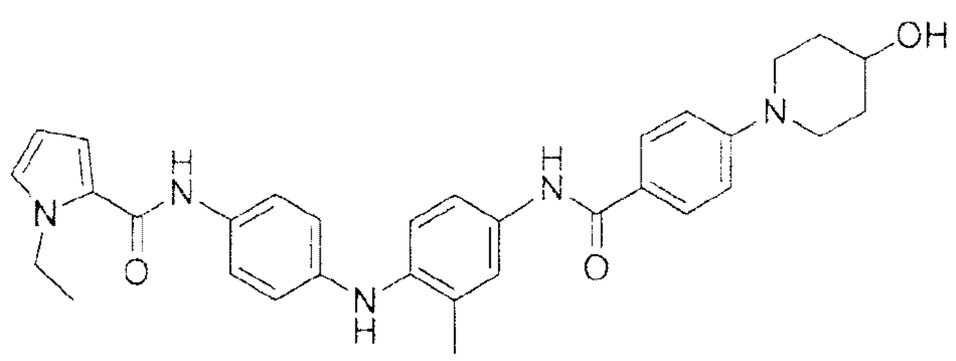

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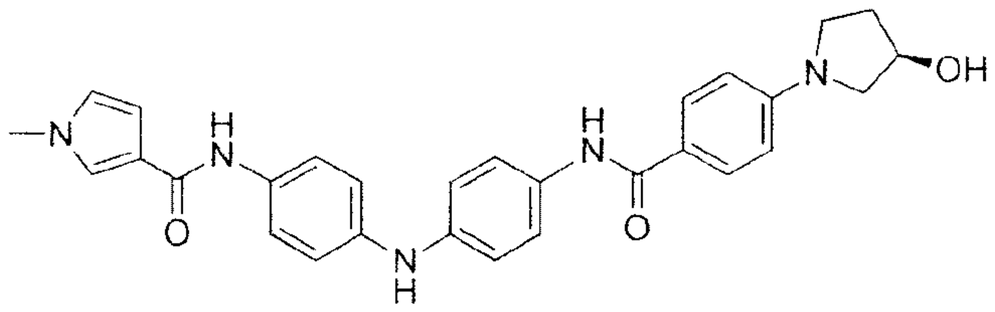

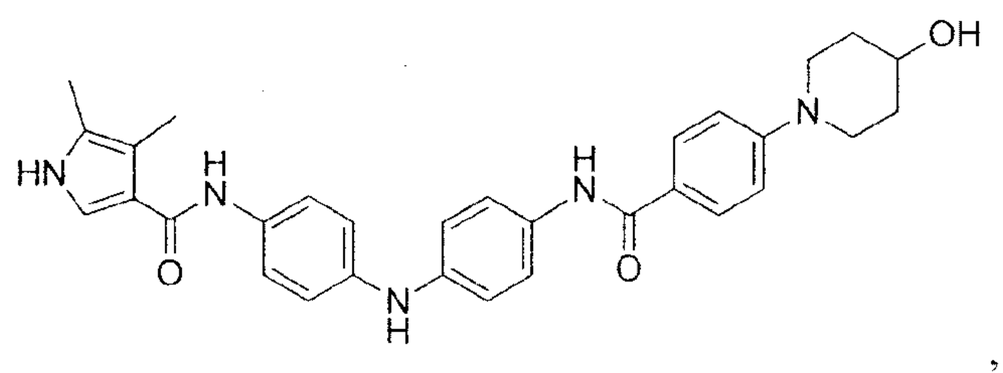

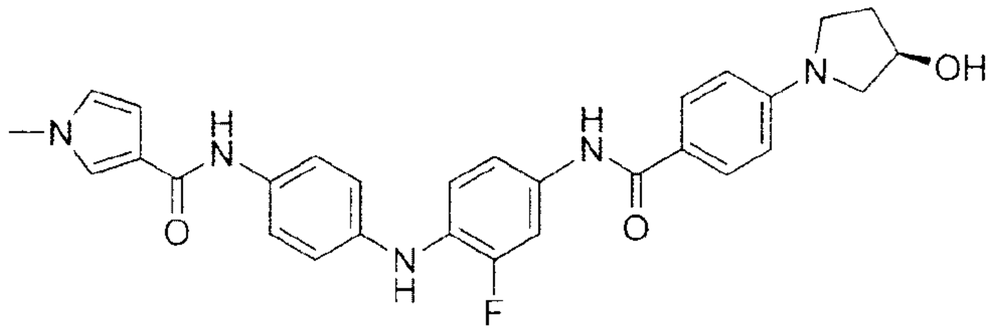

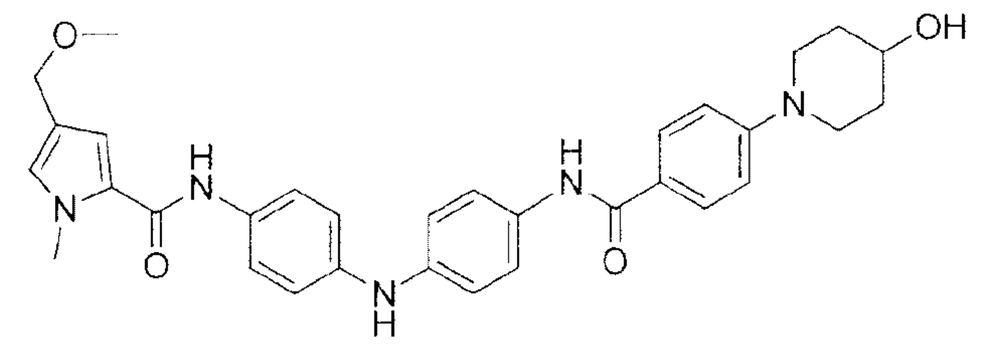

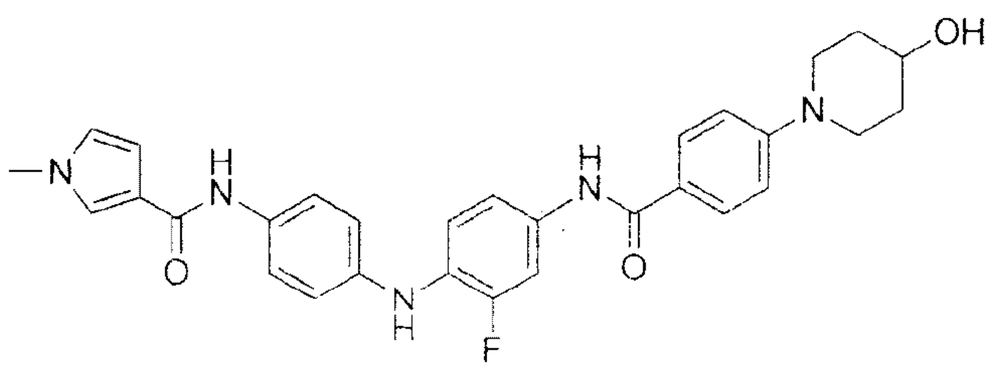

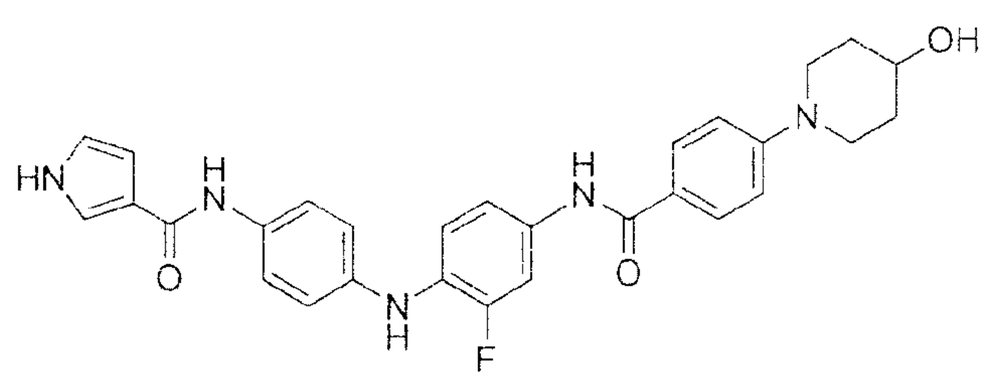

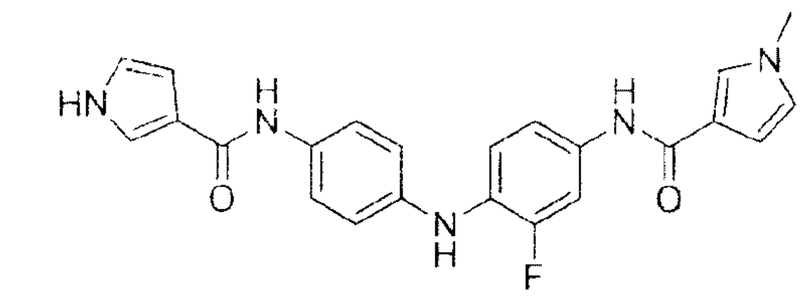

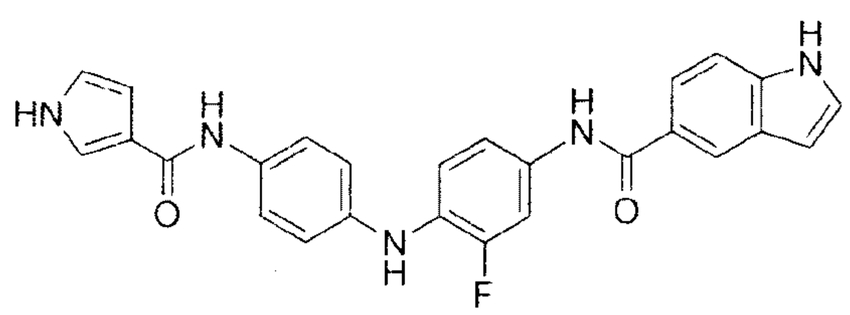

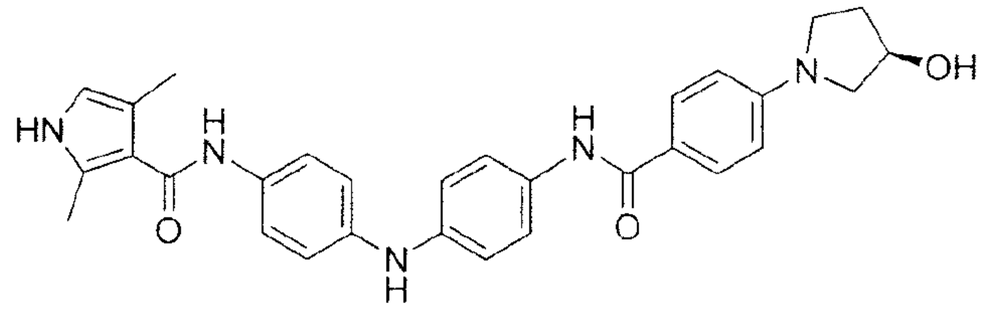

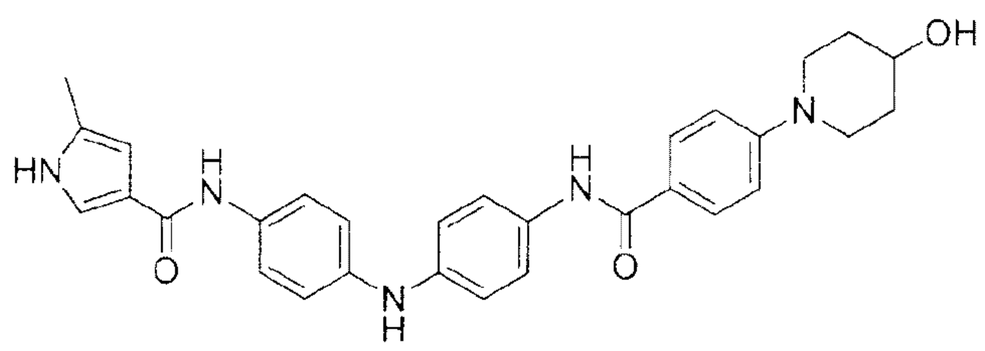

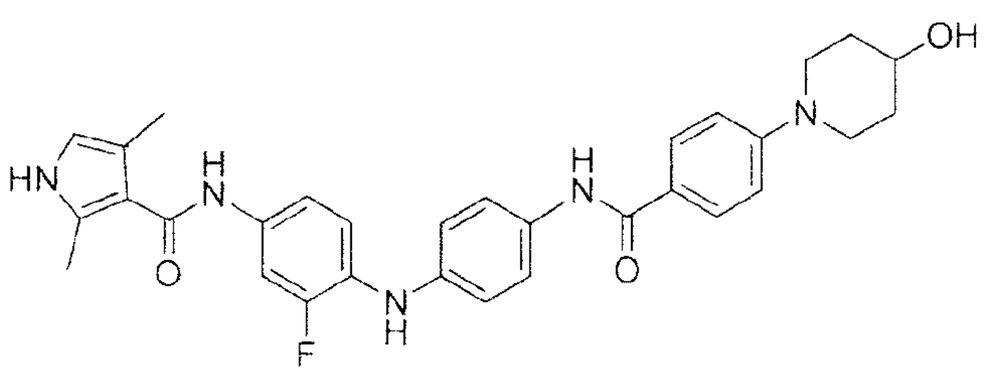

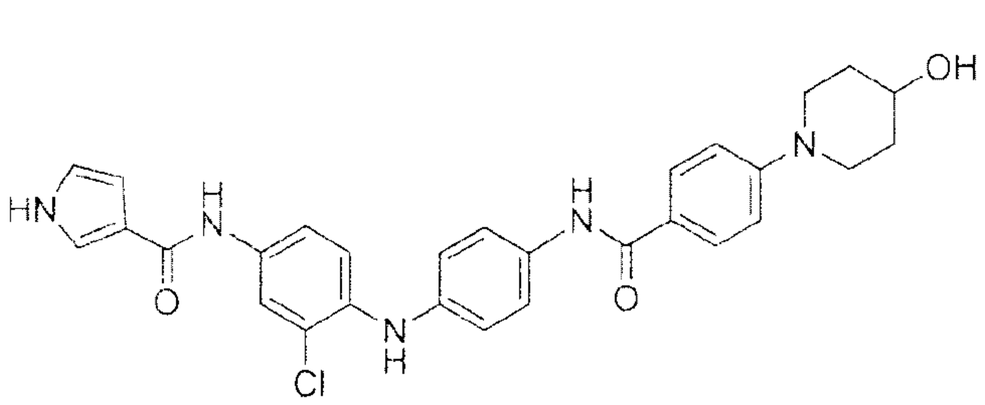

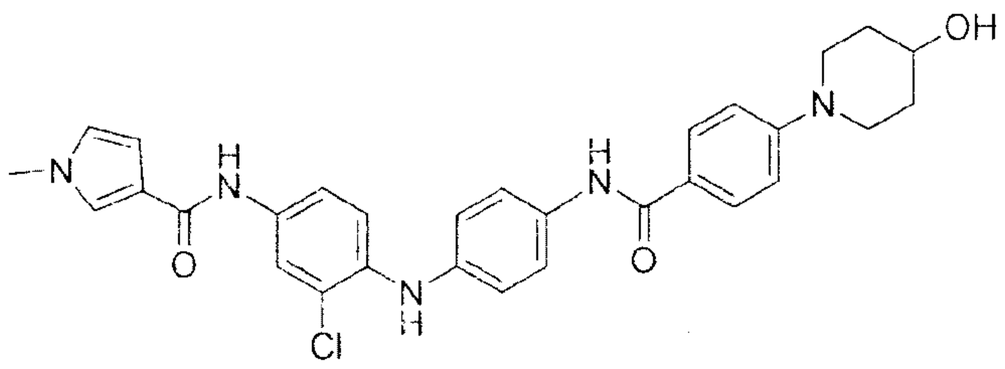

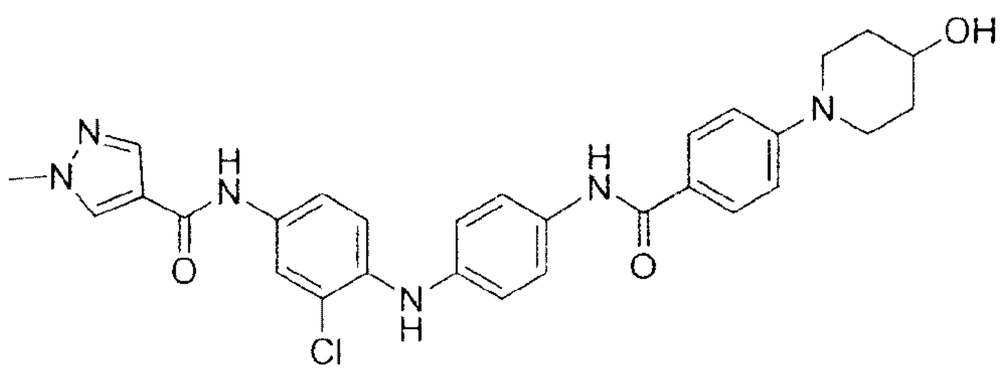

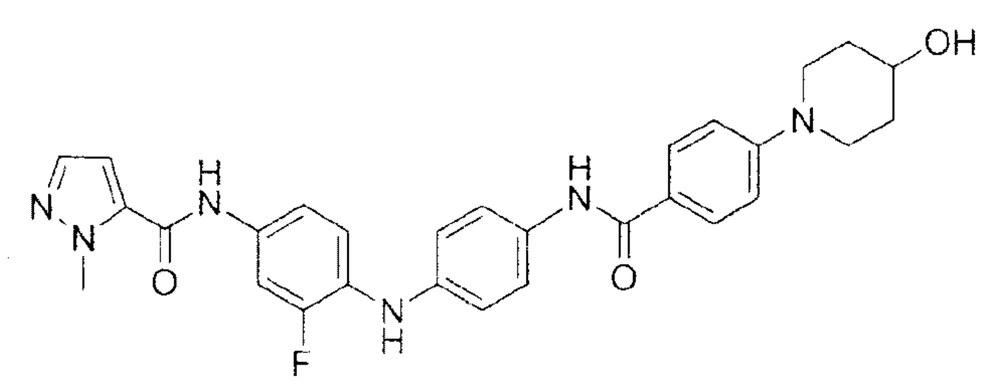

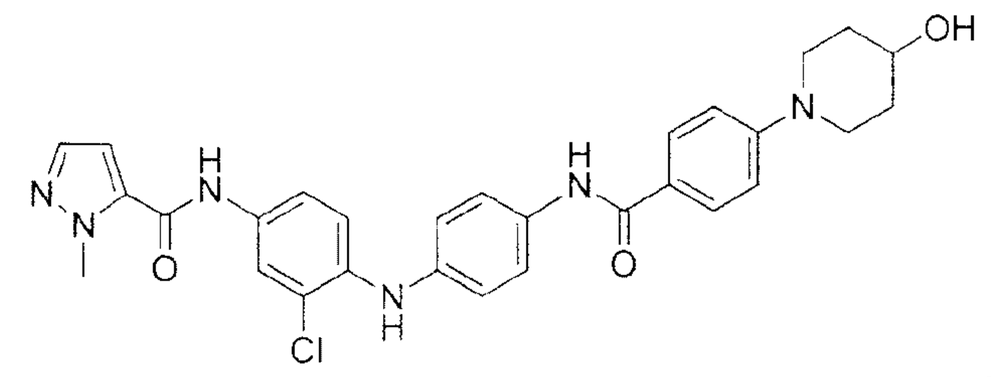

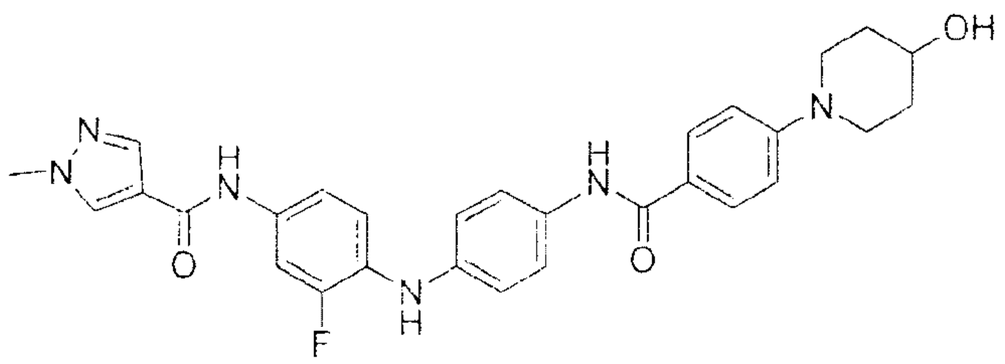

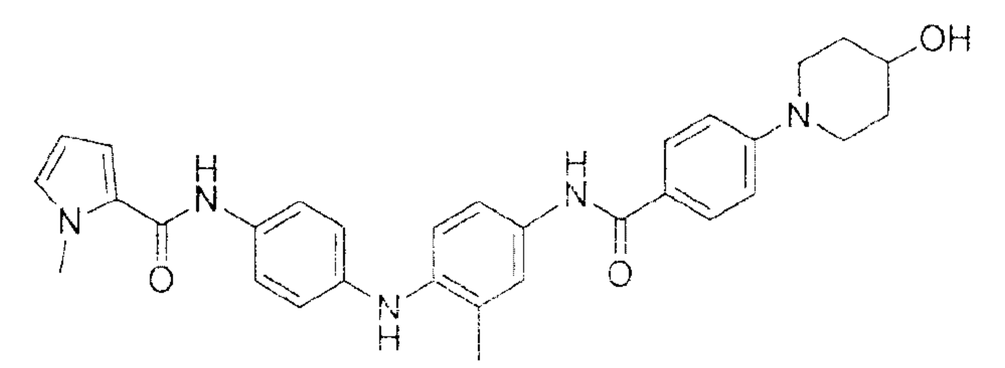

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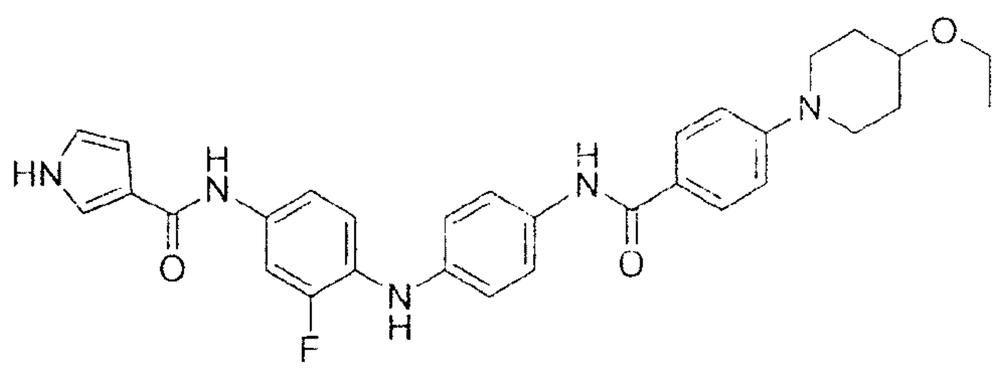

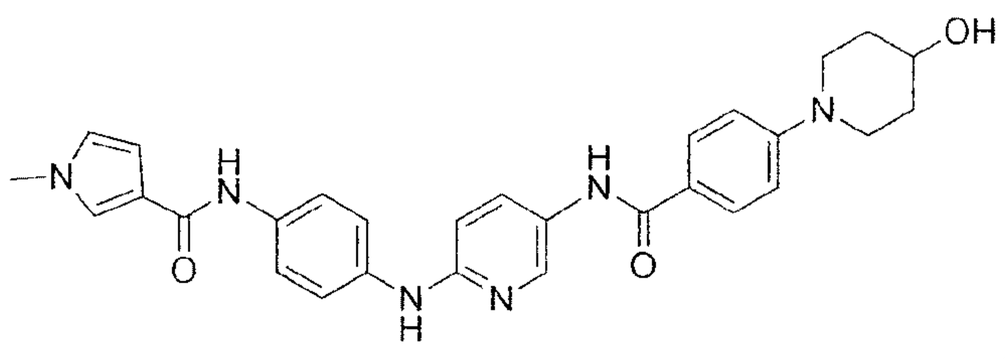

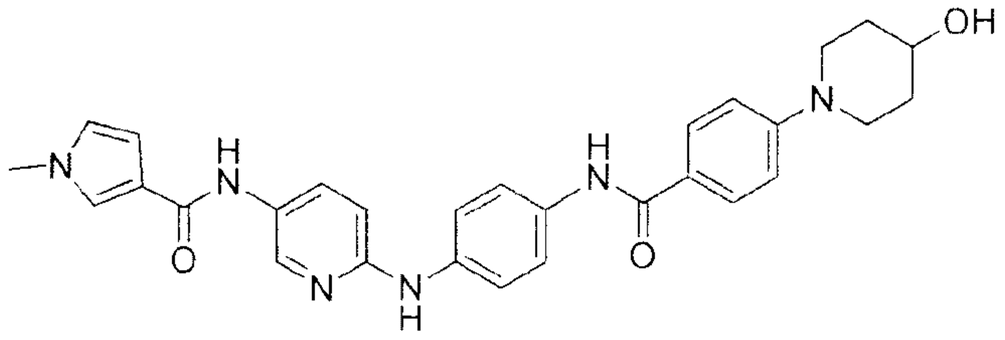

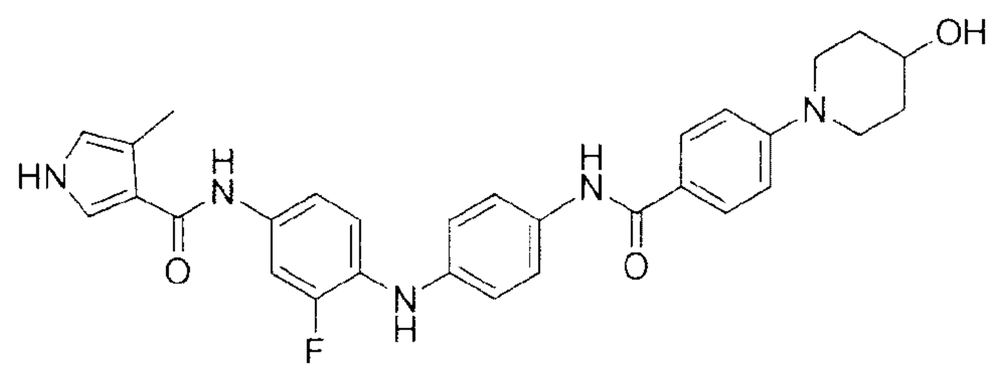

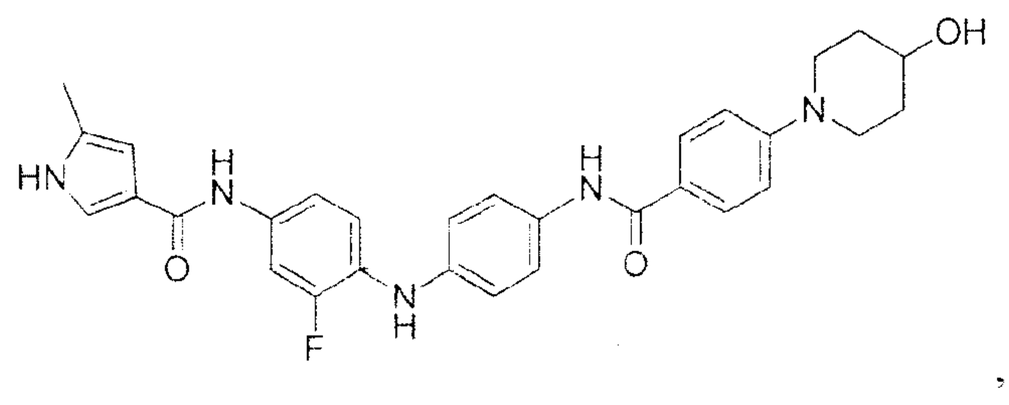

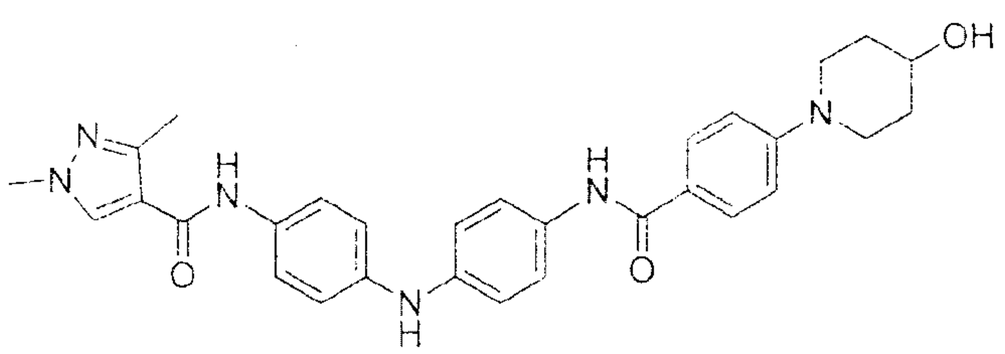

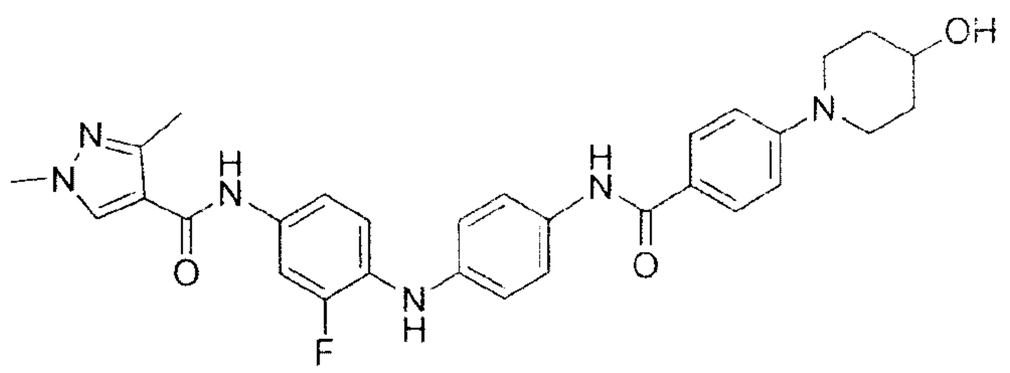

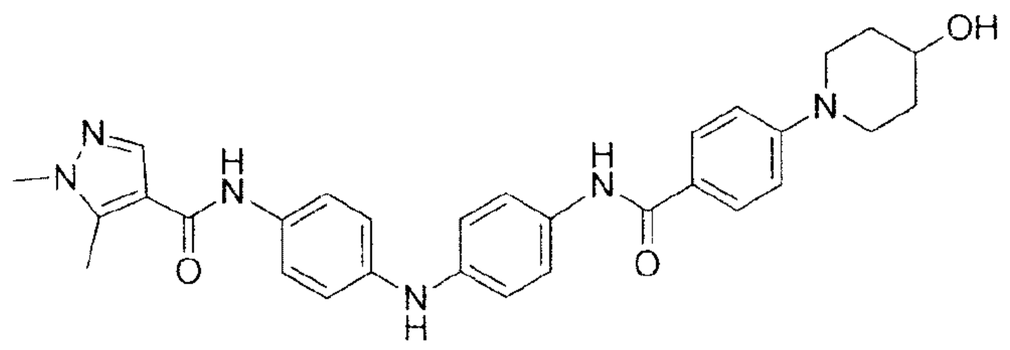

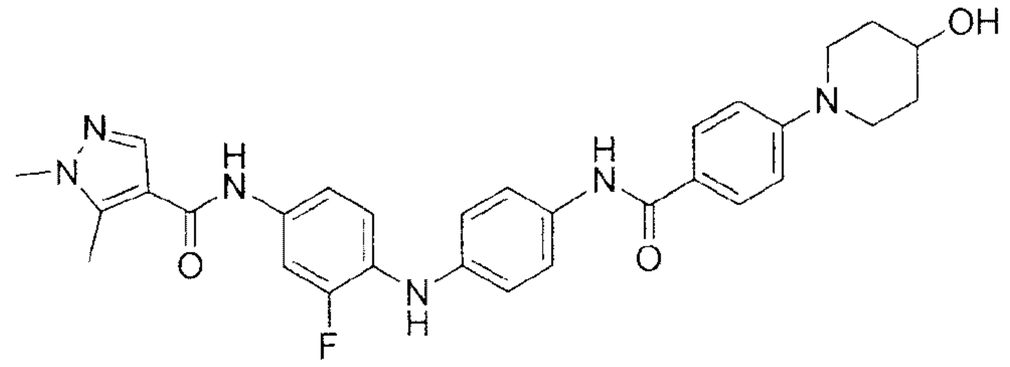

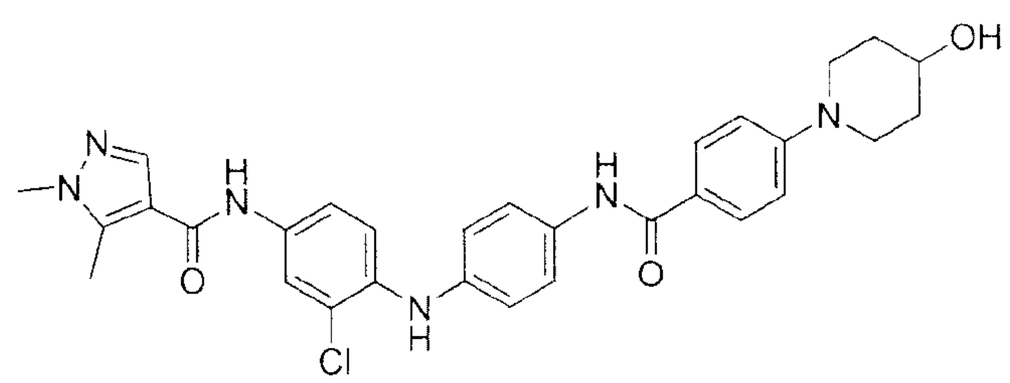

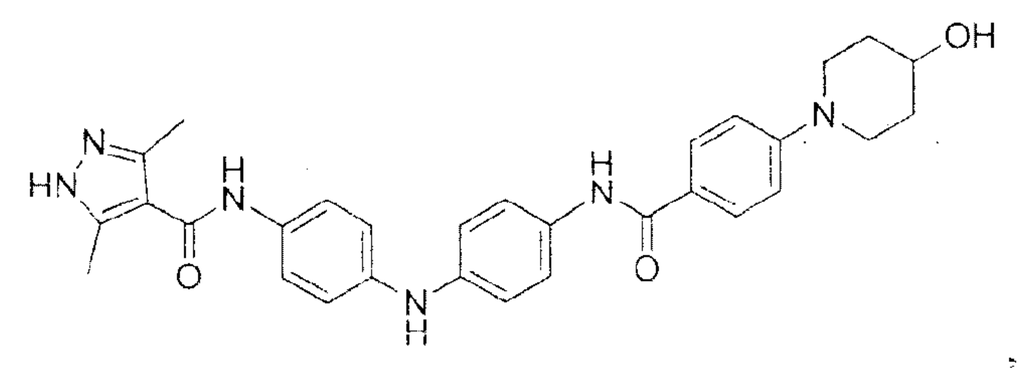

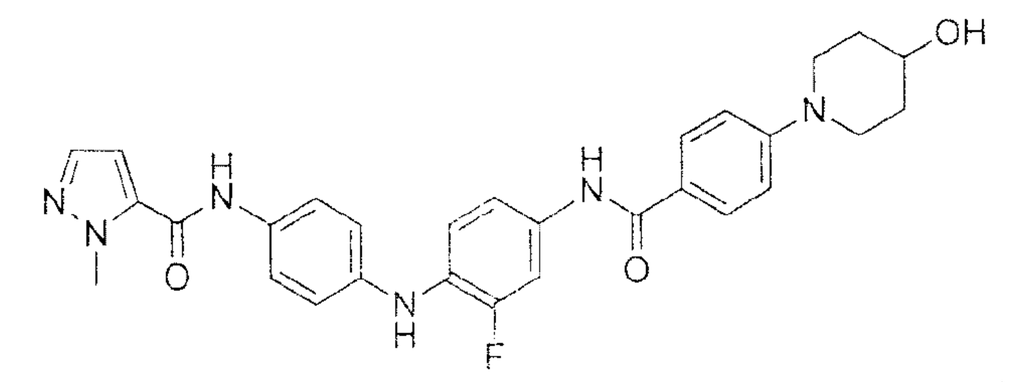

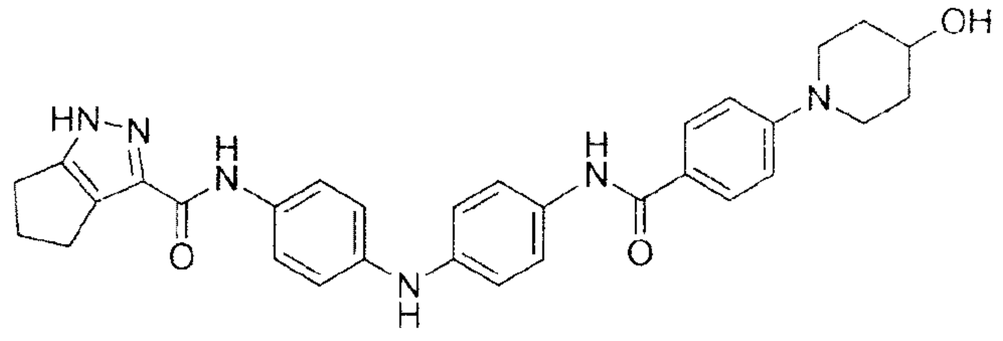

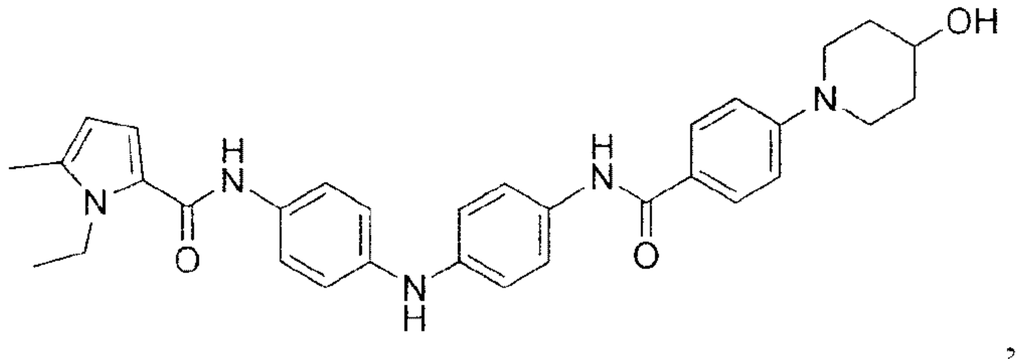

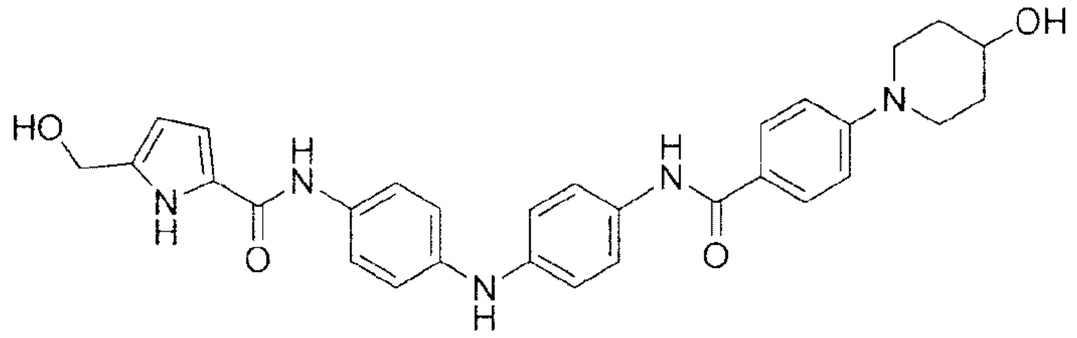

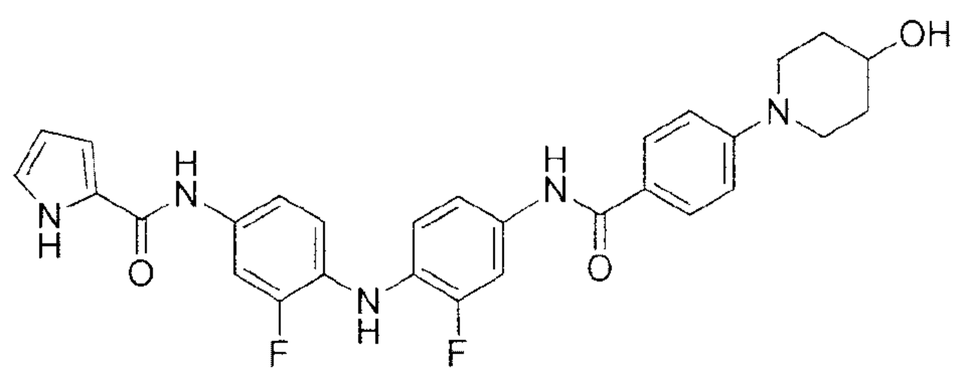

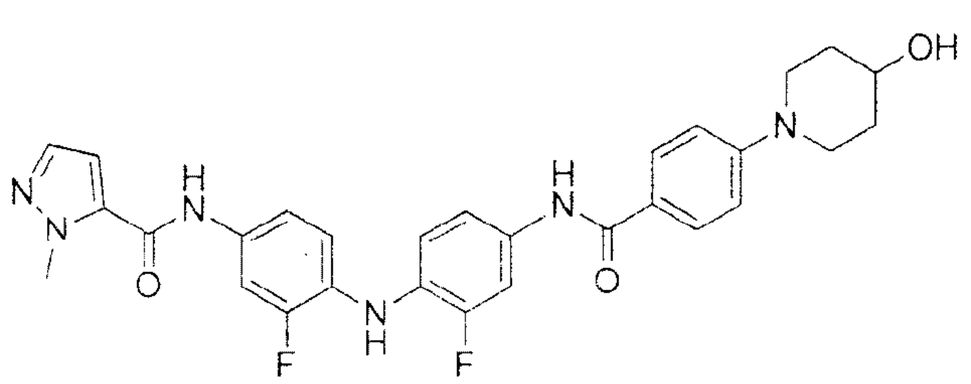

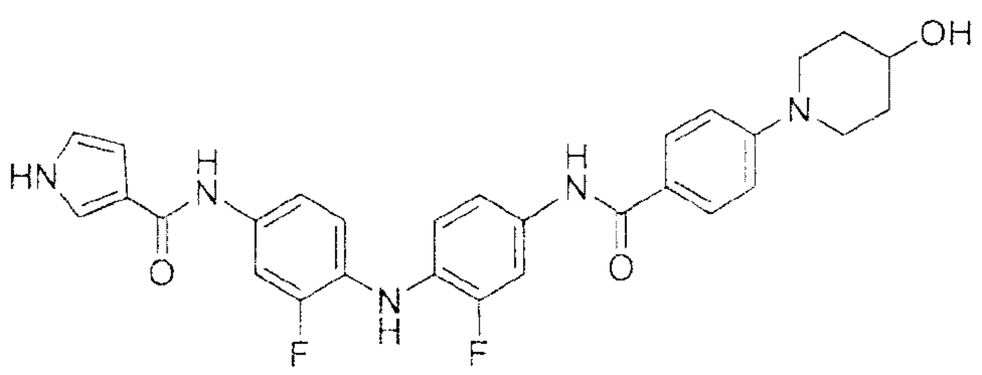

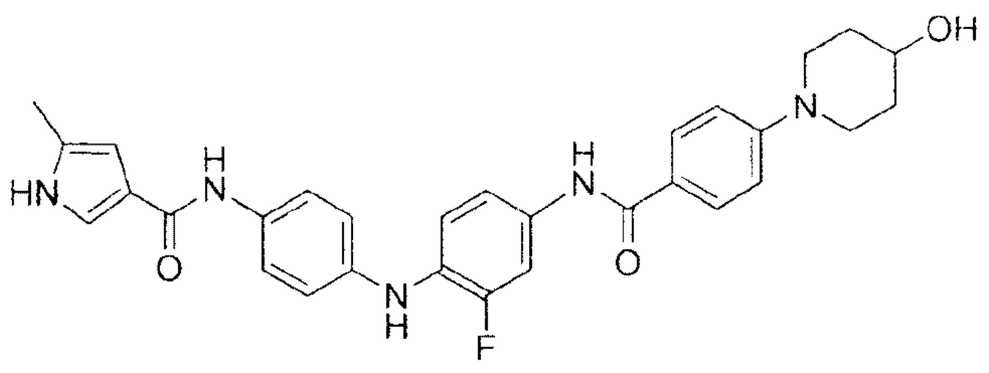

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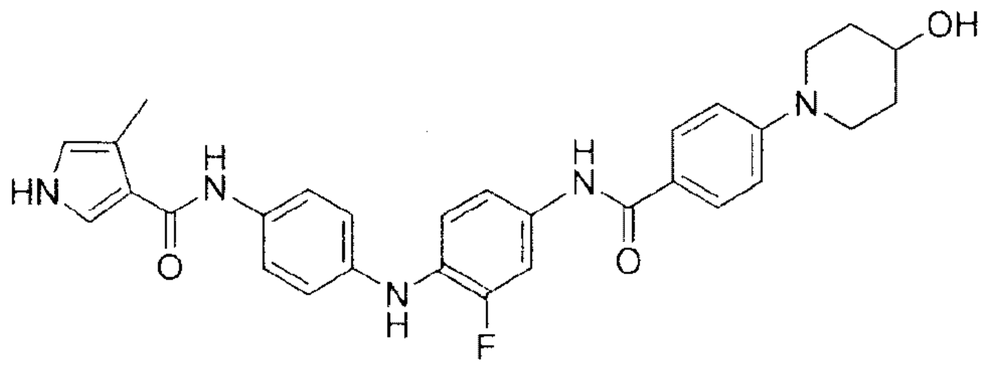

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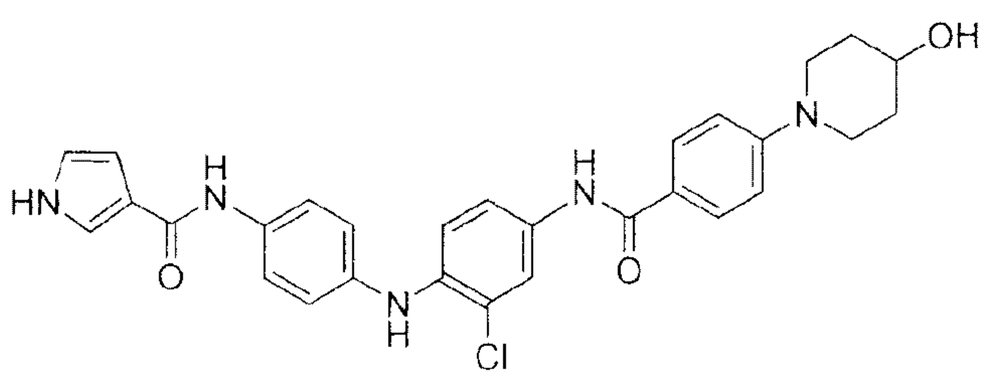

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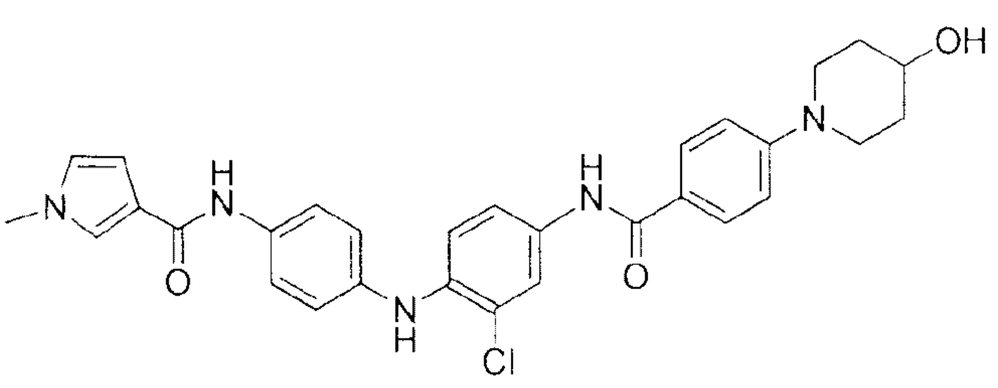

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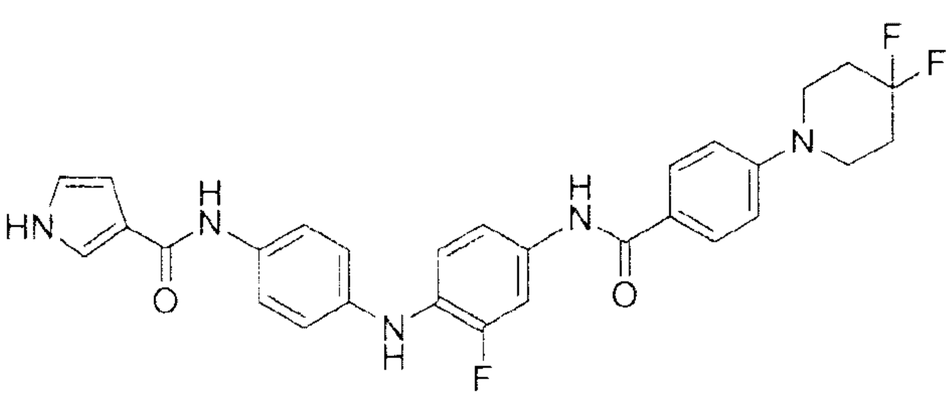

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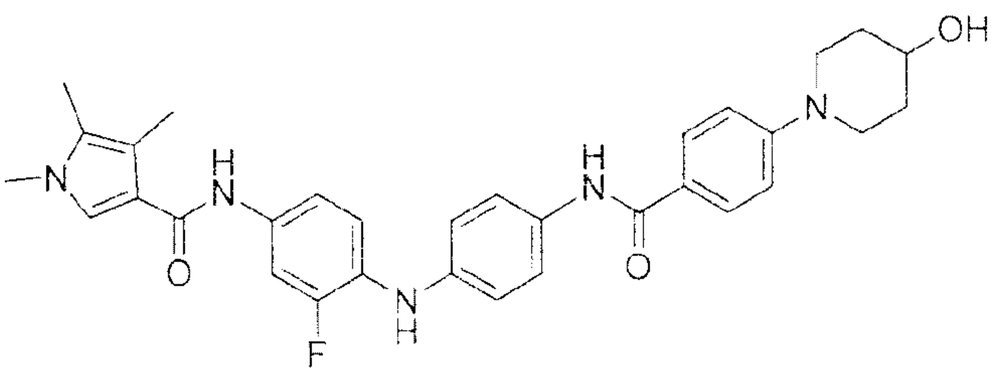

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