QUINOLINE AND QUINOXALINE AMIDES AS MODULATORS OF SODIUM CHANNELS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Patent Application No. 61/759,300, filed January 31, 2013, the entire contents of which are incorporated herein by reference.

TECHNICAL FIELD OF THE INVENTION

[001] The invention relates to compounds useful as inhibitors of sodium channels. The invention also provides pharmaceutically acceptable compositions comprising the compounds of the invention and methods of using the compositions in the treatment of various disorders including pain.

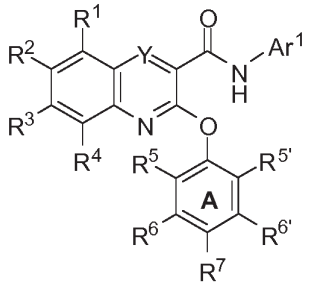
BACKGROUND OF THE INVENTION

[002] Pain is a protective mechanism that allows healthy animals to avoid tissue damage and to prevent further damage to injured tissue. Nonetheless there are many conditions where pain persists beyond its usefulness, or where patients would benefit from inhibition of pain. Neuropathic pain is a form of chronic pain caused by an injury to the sensory nerves (Dieleman, J.P., et al., Incidence rates and treatment of neuropathic pain conditions in the general population. *Pain*, 2008. **137**(3): p. 681-8). Neuropathic pain can be divided into two categories, pain caused by generalized metabolic damage to the nerve and pain caused by a discrete nerve injury. The metabolic neuropathies include post herpetic neuropathy, diabetic neuropathy, and drug-induced neuropathy. Discrete nerve injuries indications include post amputation pain, post-surgical nerve injury pain, and nerve entrapment injuries like neuropathic back pain.

[003] Voltage-gated sodium channels (Na_V's) play a critical role in pain signaling. Na_V's are key biological mediators of electrical signaling as they are the primary mediators of the rapid upstroke of the action potential of many excitable cell types (e.g. neurons, skeletal myocytes, cardiac myocytes). The evidence for the role of these channels in normal physiology, the pathological states arising from mutations in sodium channel genes, preclinical work in animal models, and the clinical pharmacology of known sodium channel modulating agents all point to the central role of Na_V's in pain sensation (Rush, A.M. and T.R. Cummins, *Painful Research: Identification of a Small-Molecule Inhibitor that Selectively Targets $Na_V1.8$ Sodium Channels.* Mol Interv, 2007. 7(4): p. 192-5); England, S., Voltage-gated sodium channels: the search for subtype-selective analgesics. *Expert Opin Investig Drugs* **17** (12), p. 1849-64 (2008); Krafte, D. S. and Bannon, A. W., Sodium channels and nociception: recent concepts and therapeutic opportunities. *Curr Opin Pharmacol* **8** (1), p. 50-56 (2008)). Na_V's are the primary mediators of the rapid

Claims

1. A compound of formula **I**



I;

or a pharmaceutically acceptable salt thereof,

wherein, independently for each occurrence:

Y is CH or N;

Ar^1 is a 5-6 membered aromatic monocyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein said ring is optionally fused to a 5-membered monocyclic aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein Ar^1 has m substituents, each independently selected from $-WR^W$;

m is an integer from 0 to 5 inclusive;

W is a bond or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-, -CO-, -S-, -SO-, or $-SO_2$-;

R^W is absent, H, halogen, OH, NH_2, NHR′, NO_2, CN, CF_3, OCF_3, or a 3-6 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R′ is C_1-C_6 alkyl;

R^1 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen and wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^2 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^3 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^4 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^5 is H, halogen, CN, or $-X-R^X$;

$R^{5'}$ is H, halogen, CN, or $-X-R^X$;

R^6 is H, halogen, CN, or $-X-R^X$;

$R^{6'}$ is H, halogen, CN, or $-X-R^X$;

R^7 is H, halogen, CN, or $-X-R^X$;

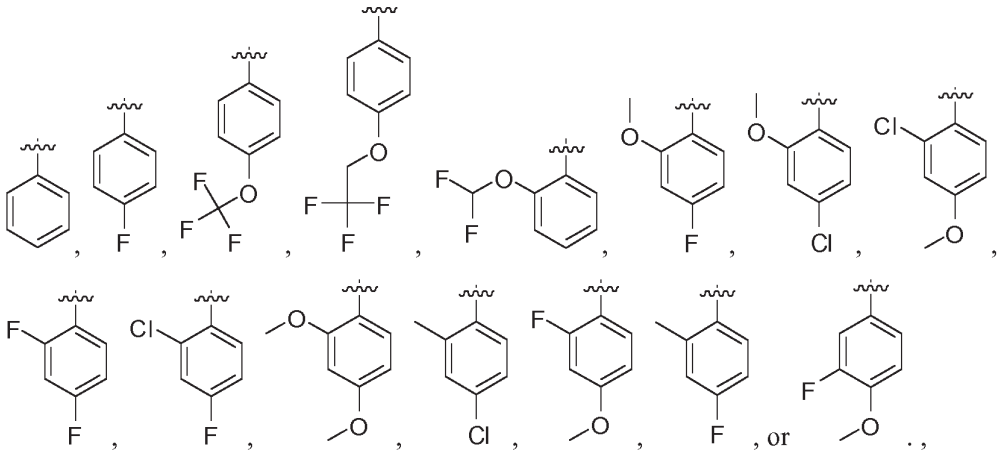
X is a bond or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-; and

R^X is absent, H, or C_3-C_8 cycloaliphatic, wherein up to two non-adjacent CH_2 units of said C_3-C_8 cycloaliphatic may be replaced with -O- and said C_3-C_8 cycloaliphatic is substituted with 0-3 substituents selected from halogen and C_1-C_4 alkyl.

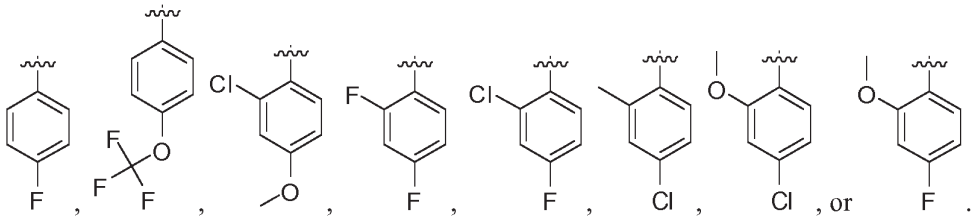
2. The compound or pharmaceutically acceptable salt according to claim 1, wherein R^1 is H or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, preferably wherein R^1 is CF_3;
or wherein R^2 is H, halogen, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen and wherein one CH_2 unit of said C_1-C_6 alkyl is replaced with –O-, preferably wherein R^2 is F, Cl, CF_3 or OCF_3;
or wherein R^3 is H, halogen or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, preferably wherein R^3 is *t*-butyl, Cl, CF_3 or CF_2CF_3;
or wherein R^4 is H, halogen or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, preferably wherein R^4 is CF_3; or wherein R^1, R^2, R^3 and R^4 are H.

3. The compound or pharmaceutically acceptable salt according to any one of claims 1 to 2, wherein R^5 and R^7 are each independently halogen, or $-X-R^X$ and $R^{5'}$, R^6, and $R^{6'}$ are each hydrogen, preferably wherein R^5 and R^7 are each independently F, Cl, CH_3, OCF_3, or OCH_3.

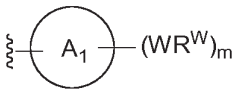
4. The compound or pharmaceutically acceptable salt according to claim 1, wherein ring A is selected from:



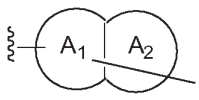
preferably wherein ring A is selected from:



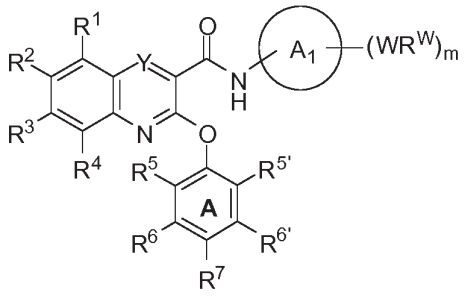
5. The compound or pharmaceutically acceptable salt according to claim 1, wherein Ar^1 is



, A_1 is a 6 membered aromatic ring having 0-4 heteroatoms, independently selected from nitrogen, oxygen, or sulfur, m is 1, W is a bond or C_1-C_6 alkyl wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -CO-, or -SO_2-, and R^W is selected from H, OH, NH_2, or CN, preferably wherein A_1 is phenyl or pyridyl, m is 1 and WR^W is selected from H, SO_2NH_2, CO_2H, SO_2CH_3, $CONH_2$ or CN;

or wherein Ar^1 is , A_1 is phenyl, A_2 is a 5-membered aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, m is 1, W is a bond or C_1-C_6 alkyl wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -CO-, or -SO_2-, and R^W is selected from H, OH, NH_2, or CN, preferably wherein A_1 is phenyl, A_2 is pyrrolyl, pyrazolyl, thiazolyl, thiadiazolyl, imidazolyl, oxazolyl, or triazolyl, m is 1 and WR^W is selected from H or CO_2H.

6. The compound according to claim 1, wherein the compound has formula **I-A**:



I-A

or a pharmaceutically acceptable salt thereof,

wherein, independently for each occurrence:

Y is CH or N;

A_1 is a 5-6 membered aromatic ring having 0-4 heteroatoms, independently selected from nitrogen, oxygen, or sulfur;

m is an integer from 0 to 5 inclusive;

W is a bond or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-, -CO-, -S-, -SO-, or -SO_2-;

R^W is absent, H, halogen, OH, NH_2, NHR′, NO_2, CN, CF_3, OCF_3, or a 3-6 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R′ is C_1-C_6 alkyl;

R^1 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen and wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^2 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^3 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^4 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^5 is H, halogen, CN, or –X-R^X;

$R^{5'}$ is H, halogen, CN, or –X-R^X;

R^6 is H, halogen, CN, or –X-R^X;

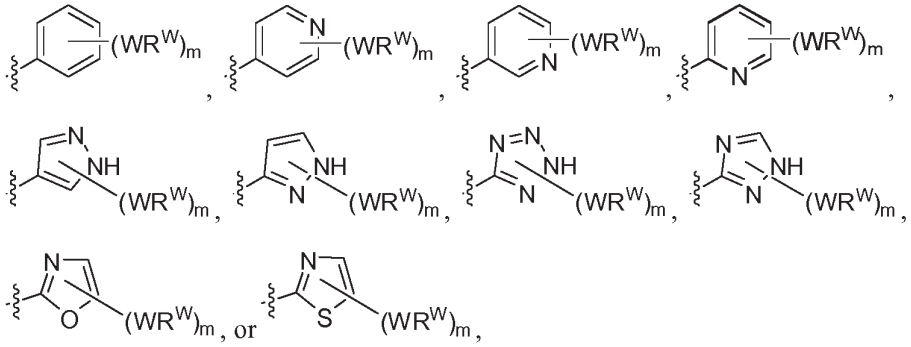
$R^{6'}$ is H, halogen, CN, or –X-R^X;

R^7 is H, halogen, CN, or –X-R^X;

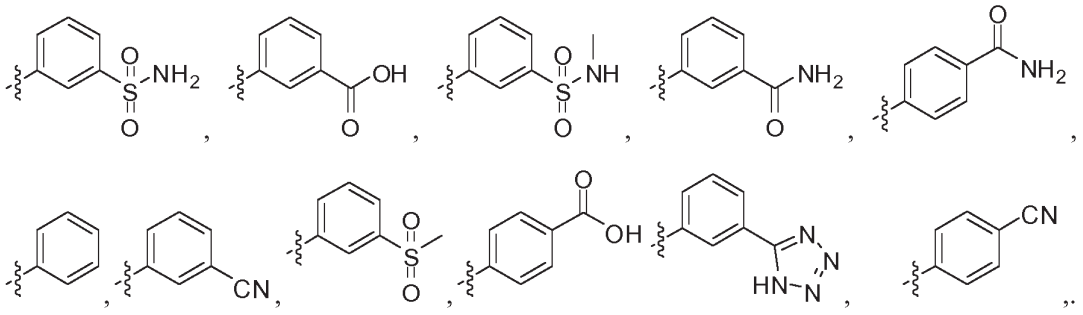
X is a bond or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-; and

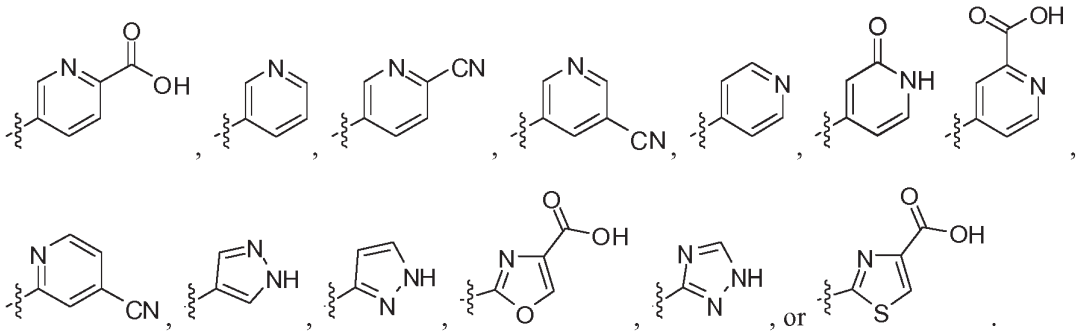
R^X is absent, H, or C_3-C_8 cycloaliphatic, wherein up to two non-adjacent CH_2 units of said C_3-C_8 cycloaliphatic may be replaced with -O- and said C_3-C_8 cycloaliphatic is substituted with 0-3 substituents selected from halogen and C_1-C_4 alkyl.

7. The compound or pharmaceutically acceptable salt according to claim 6, wherein ring A_1 is selected from:

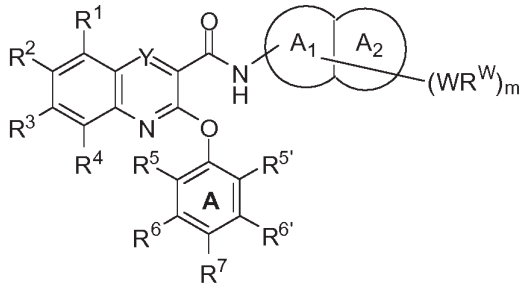


preferably wherein ring A_1 is selected from:





8. The compound according to claim 1, wherein the compound has formula **I-E**:



I-E

or a pharmaceutically acceptable salt thereof,

wherein, independently for each occurrence:

Y is CH or N;

A_1 and A_2, together, form an 8-9 membered aromatic, bicyclic ring, wherein each ring contains 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

m is an integer from 0 to 5 inclusive;

W is a bond or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-, -CO-, -S-, -SO-, or -SO_2-;

R^W is absent, H, halogen, OH, NH_2, NHR′, NO_2, CN, CF_3, OCF_3, or a 3-6 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

R′ is C_1-C_6 alkyl;

R^1 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen and wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^2 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^3 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^4 is H, halogen, CN, or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-;

R^5 is H, halogen, CN, or $-X-R^X$;

$R^{5'}$ is H, halogen, CN, or $-X-R^X$;

R^6 is H, halogen, CN, or $-X-R^X$;

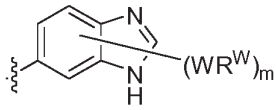
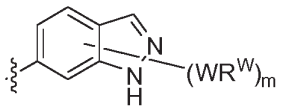
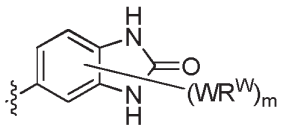
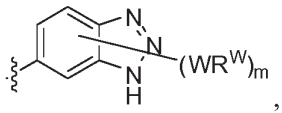
$R^{6'}$ is H, halogen, CN, or $-X-R^X$;

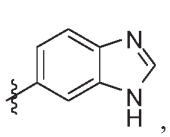
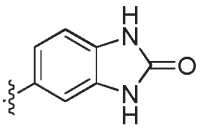
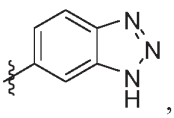
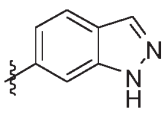
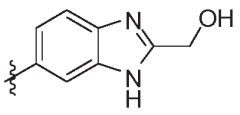
R^7 is H, halogen, CN, or $-X-R^X$;

X is a bond or C_1-C_6 alkyl wherein said C_1-C_6 alkyl is substituted with 0-6 halogen, wherein up to two non-adjacent CH_2 units of said C_1-C_6 alkyl may be replaced with -O-; and

R^X is absent, H, or C_3-C_8 cycloaliphatic, wherein up to two non-adjacent CH_2 units of said C_3-C_8 cycloaliphatic may be replaced with -O- and said C_3-C_8 cycloaliphatic is substituted with 0-3 substituents selected from halogen and C_1-C_4 alkyl.

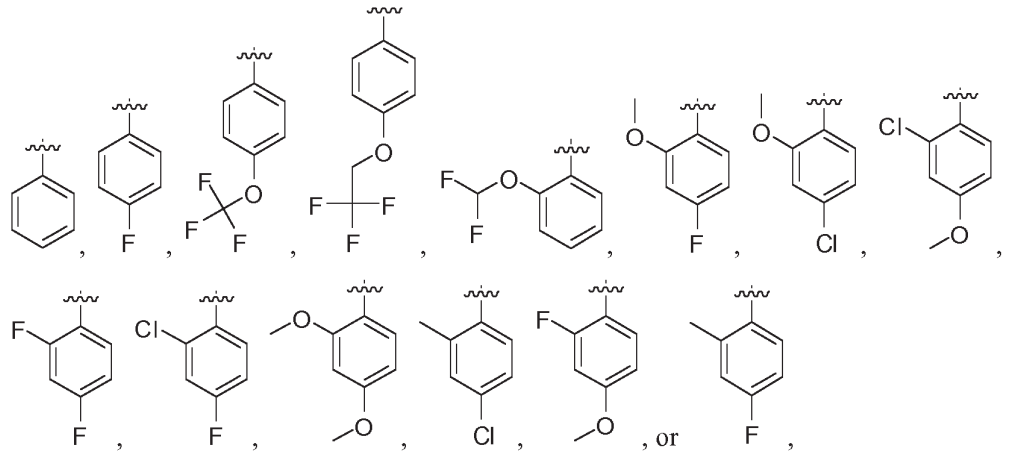
9. The compound or pharmaceutically acceptable salt according to claim 8, wherein A_1 and A_2, together, are selected from:




or

, preferably wherein A_1 and A_2, together with WR^W, are selected from:

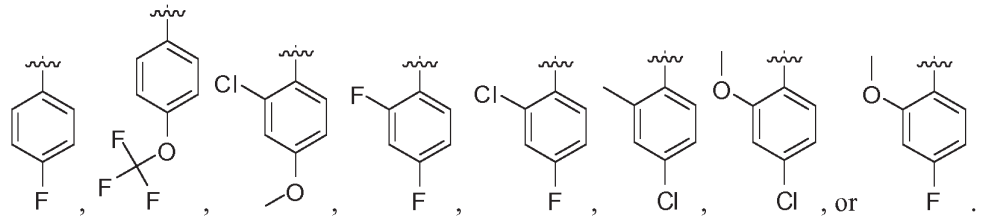

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, or

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10. The compound or pharmaceutically acceptable salt according to any one of claims 6 to 9, wherein R^1, R^2, R^3 and R^4 are H.

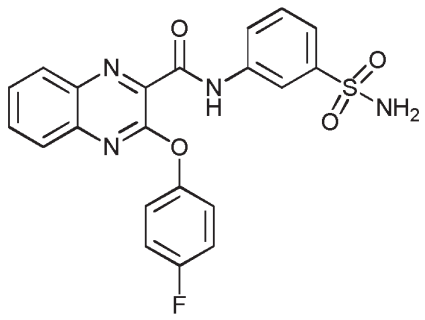
11. The compound or pharmaceutically acceptable salt according to any one of claims 6 to 10, wherein R^5 and R^7 are each independently halogen, or $-X-R^X$ and $R^{5'}$, R^6, and $R^{6'}$ are each hydrogen, preferably wherein R^5 and R^7 are each independently F, Cl, CH_3, OCF_3, or OCH_3; or wherein ring A is selected from:



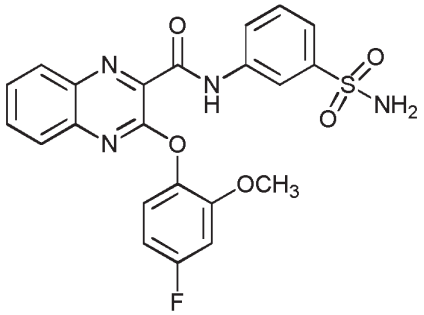
preferably wherein ring A is selected from:



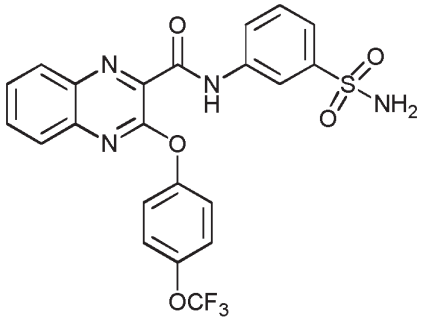
12. The compound or pharmaceutically acceptable salt of claim 1, wherein the compound or a pharmaceutically acceptable salt is selected from the group consisting of:



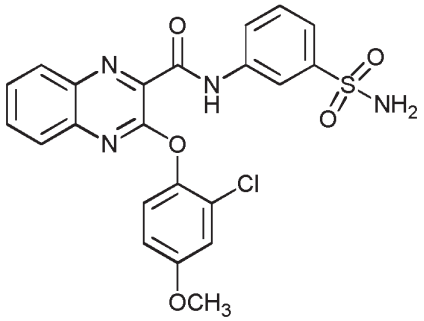
3-(4-fluorophenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



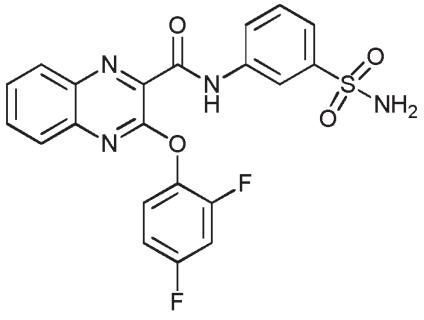
3-(4-fluoro-2-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



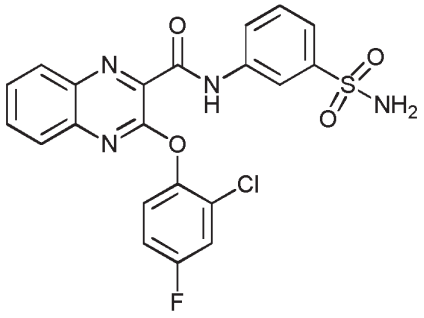
N-(3-sulfamoylphenyl)-3-(4-(trifluoromethoxy)phenoxy)quinoxaline-2-carboxamide;



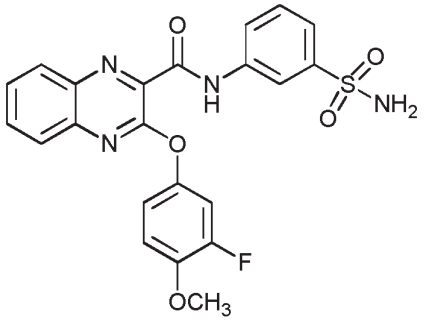
3-(2-chloro-4-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



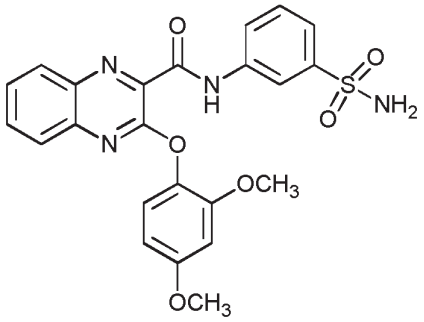
3-(2,4-difluorophenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



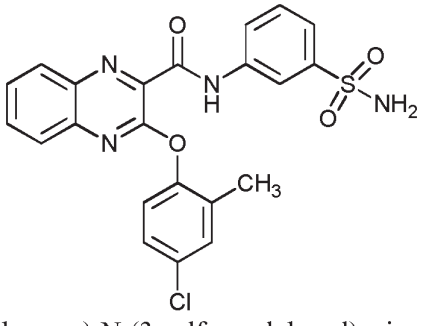
3-(2-chloro-4-fluorophenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



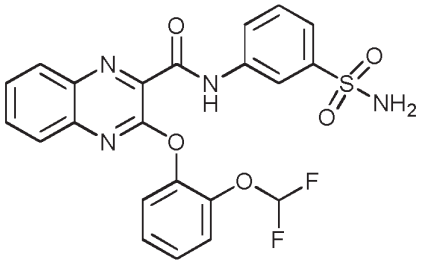
3-(3-fluoro-4-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



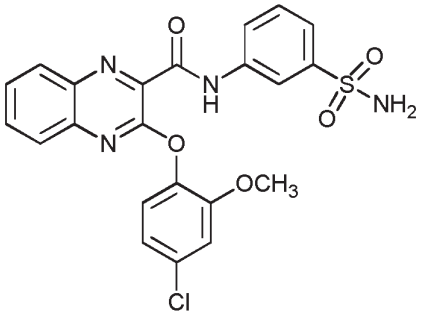
3-(2,4-dimethoxyphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



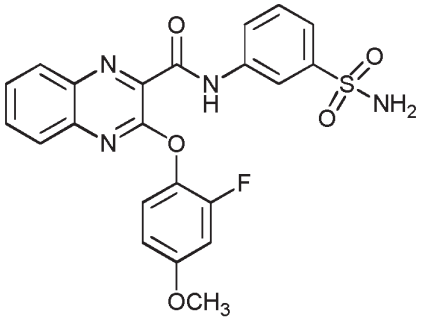
3-(4-chloro-2-methylphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



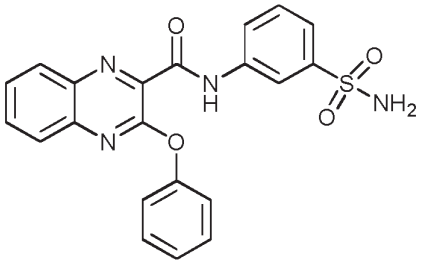
3-(2-(difluoromethoxy)phenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



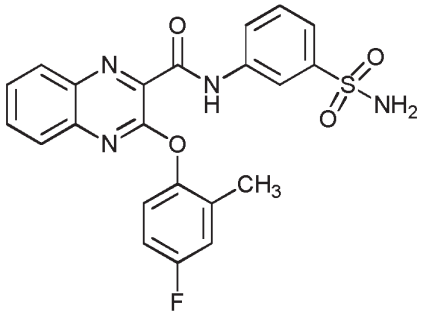
3-(4-chloro-2-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



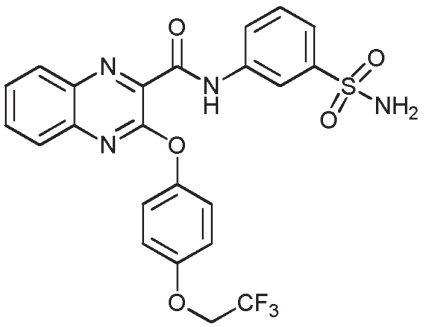
3-(2-fluoro-4-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



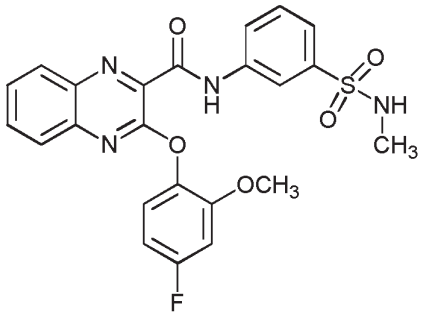
3-phenoxy-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



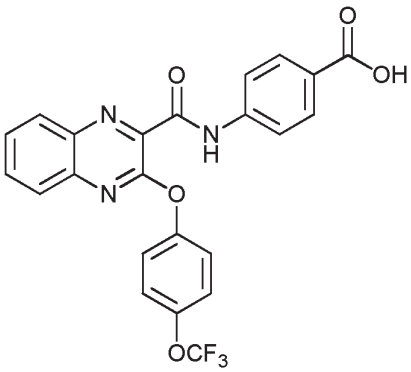
3-(4-fluoro-2-methylphenoxy)-N-(3-sulfamoylphenyl)quinoxaline-2-carboxamide;



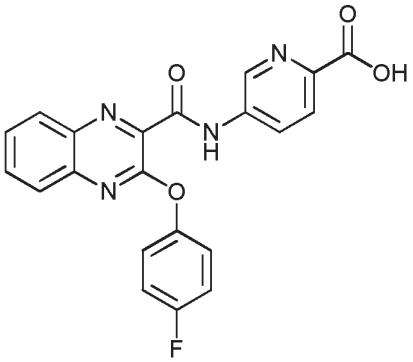
N-(3-sulfamoylphenyl)-3-(4-(2,2,2-trifluoroethoxy)phenoxy)quinoxaline-2-carboxamide;



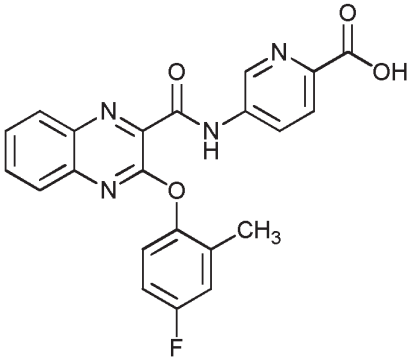
3-(4-fluoro-2-methoxyphenoxy)-N-(3-(N-methylsulfamoyl)phenyl)quinoxaline-2-carboxamide;



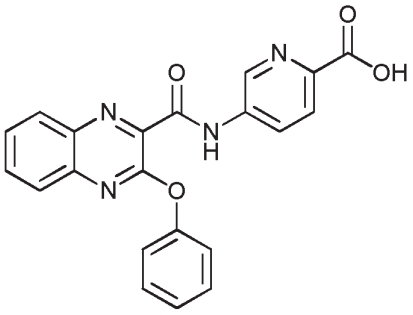
4-(3-(4-(trifluoromethoxy)phenoxy)quinoxaline-2-carboxamido)benzoic acid;



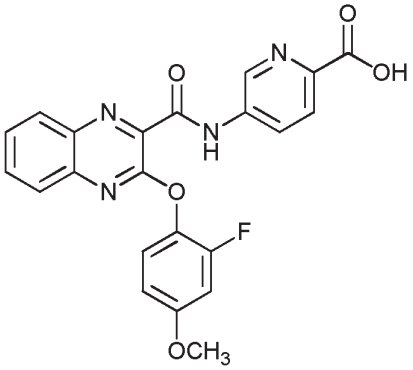
5-(3-(4-fluorophenoxy)quinoxaline-2-carboxamido)picolinic acid;



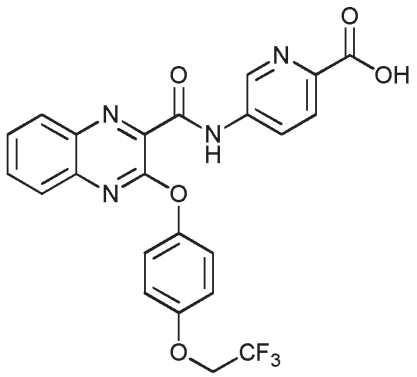
5-(3-(4-fluoro-2-methylphenoxy)quinoxaline-2-carboxamido)picolinic acid;



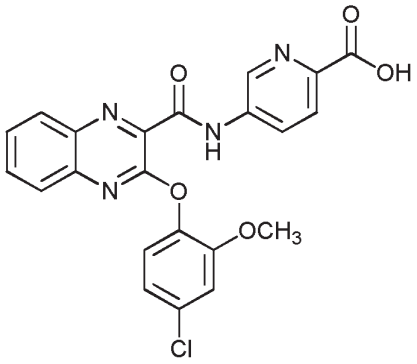
5-(3-phenoxyquinoxaline-2-carboxamido)picolinic acid;



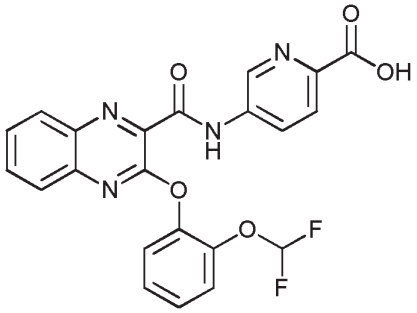
5-(3-(2-fluoro-4-methoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



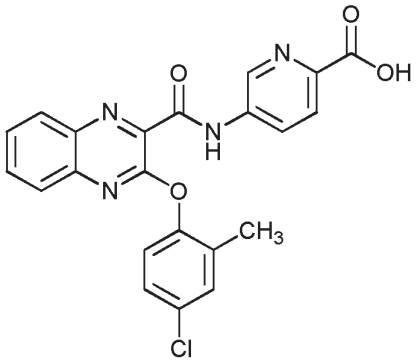
5-(3-(4-(2,2,2-trifluoroethoxy)phenoxy)quinoxaline-2-carboxamido)picolinic acid;



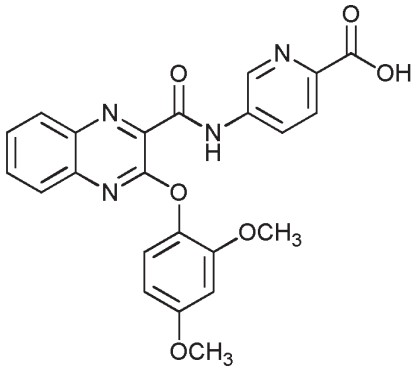
5-(3-(4-chloro-2-methoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



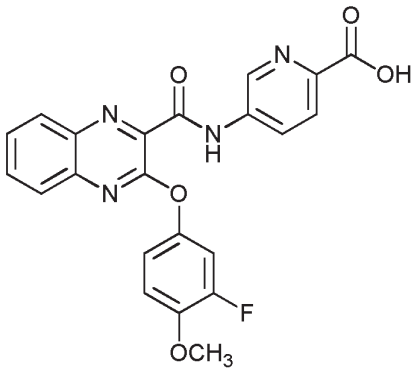
5-(3-(2-(difluoromethoxy)phenoxy)quinoxaline-2-carboxamido)picolinic acid;



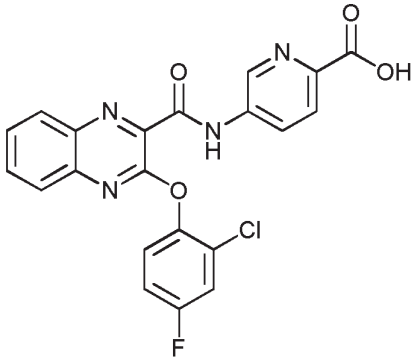
5-(3-(4-chloro-2-methylphenoxy)quinoxaline-2-carboxamido)picolinic acid;



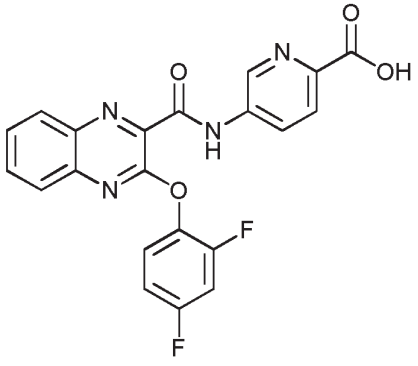
5-(3-(2,4-dimethoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



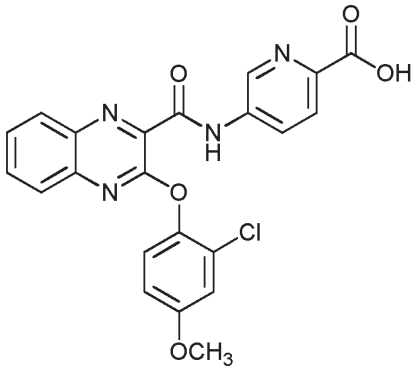
5-(3-(3-fluoro-4-methoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



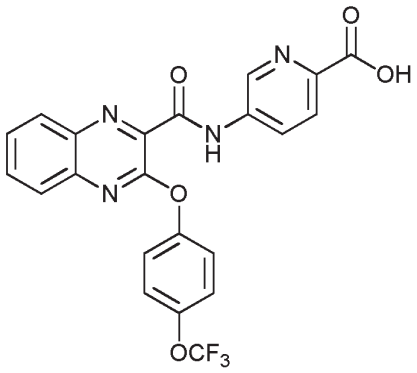
5-(3-(2-chloro-4-fluorophenoxy)quinoxaline-2-carboxamido)picolinic acid;



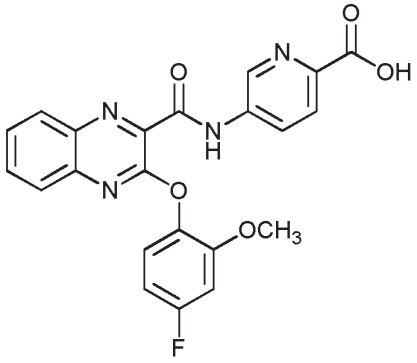
5-(3-(2,4-difluorophenoxy)quinoxaline-2-carboxamido)picolinic acid;



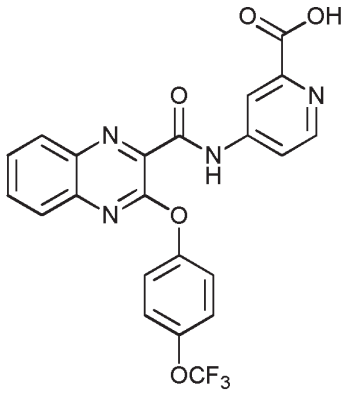
5-(3-(2-chloro-4-methoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



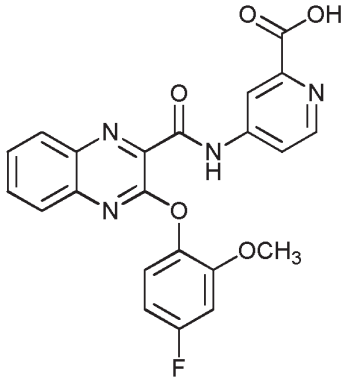
5-(3-(4-(trifluoromethoxy)phenoxy)quinoxaline-2-carboxamido)picolinic acid;



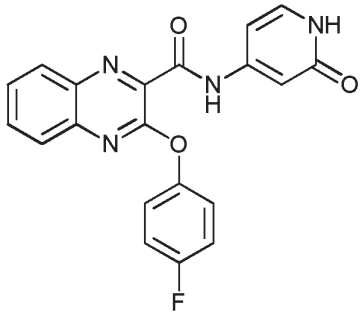
5-(3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



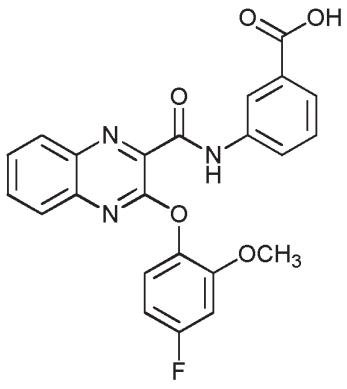
4-(3-(4-(trifluoromethoxy)phenoxy)quinoxaline-2-carboxamido)picolinic acid;



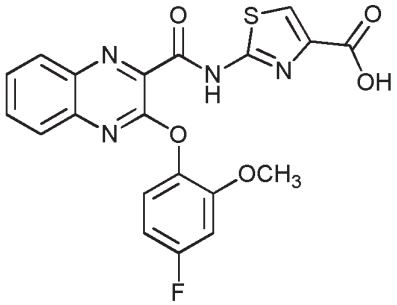
4-(3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamido)picolinic acid;



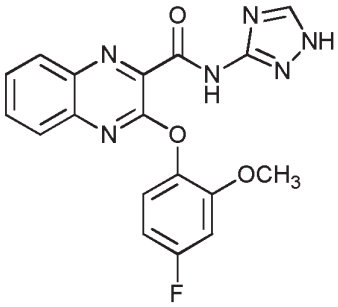
3-(4-fluorophenoxy)-N-(2-oxo-1,2-dihydropyridin-4-yl)quinoxaline-2-carboxamide;



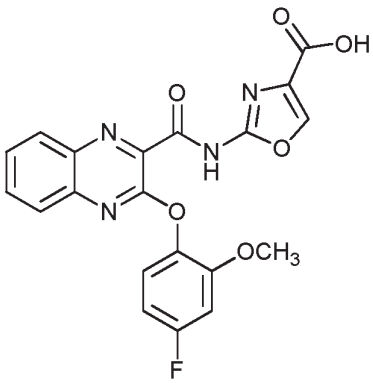
3-(3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamido)benzoic acid;



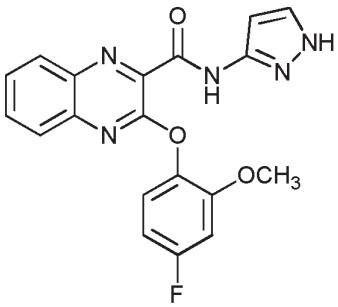
2-(3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamido)thiazole-4-carboxylic acid;



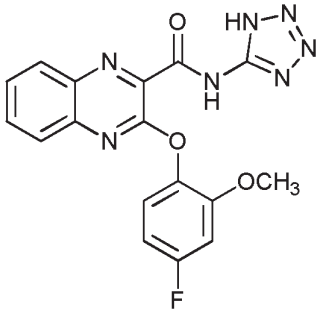
3-(4-fluoro-2-methoxyphenoxy)-N-(1H-1,2,4-triazol-3-yl)quinoxaline-2-carboxamide;



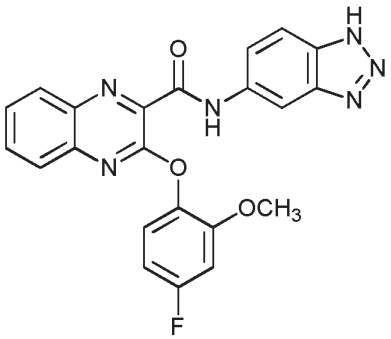
2-(3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamido)oxazole-4-carboxylic acid;



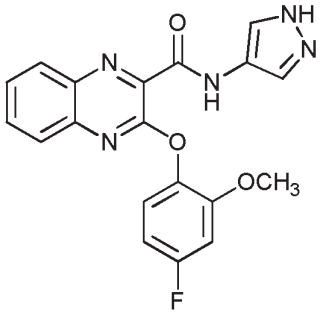
3-(4-fluoro-2-methoxyphenoxy)-N-(1H-pyrazol-3-yl)quinoxaline-2-carboxamide;



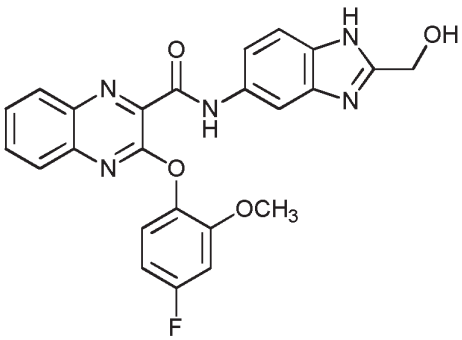
3-(4-fluoro-2-methoxyphenoxy)-N-(1H-tetrazol-5-yl)quinoxaline-2-carboxamide;



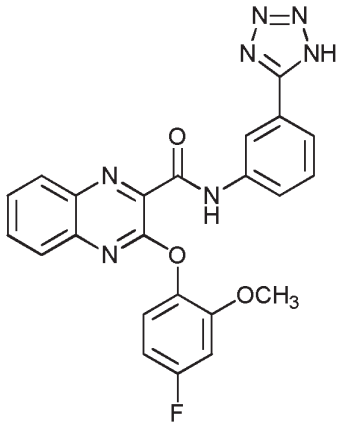
N-(1H-benzo[d][1,2,3]triazol-5-yl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



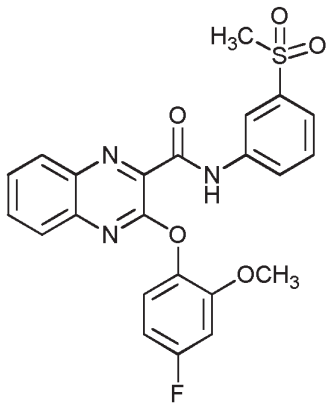
3-(4-fluoro-2-methoxyphenoxy)-N-(1H-pyrazol-4-yl)quinoxaline-2-carboxamide;



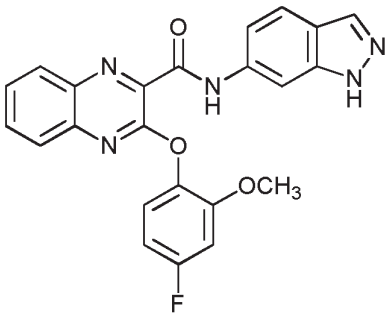
3-(4-fluoro-2-methoxyphenoxy)-N-(2-(hydroxymethyl)-1H-benzo[d]imidazol-5-yl)quinoxaline-2-carboxamide;



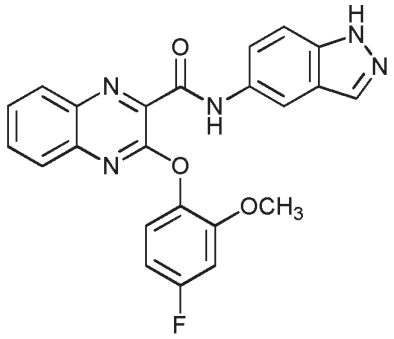
N-(3-(1H-tetrazol-5-yl)phenyl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



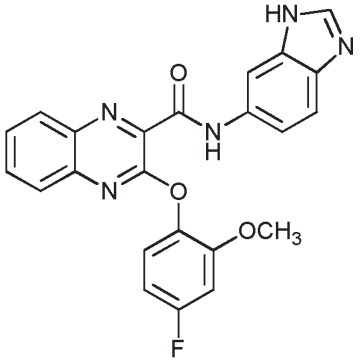
3-(4-fluoro-2-methoxyphenoxy)-N-(3-(methylsulfonyl)phenyl)quinoxaline-2-carboxamide;



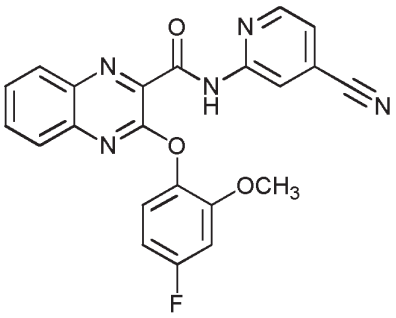
3-(4-fluoro-2-methoxyphenoxy)-N-(1H-indazol-6-yl)quinoxaline-2-carboxamide;



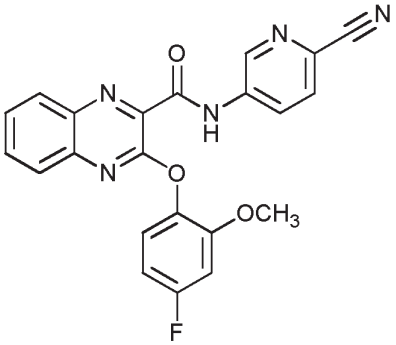
3-(4-fluoro-2-methoxyphenoxy)-N-(1H-indazol-5-yl)quinoxaline-2-carboxamide;



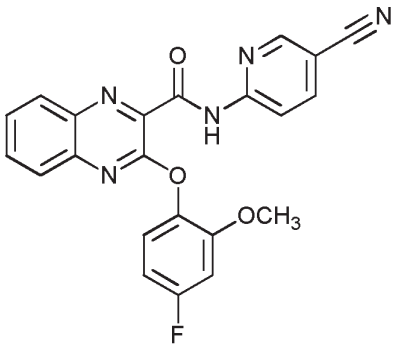
N-(1H-benzo[d]imidazol-6-yl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



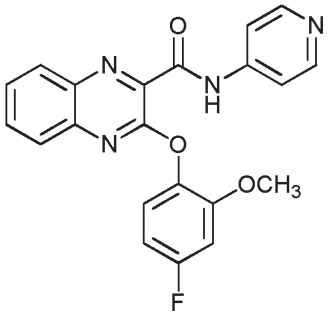
N-(4-cyanopyridin-2-yl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



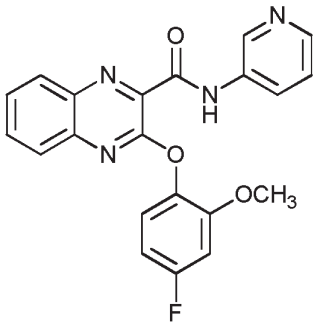
N-(6-cyanopyridin-3-yl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



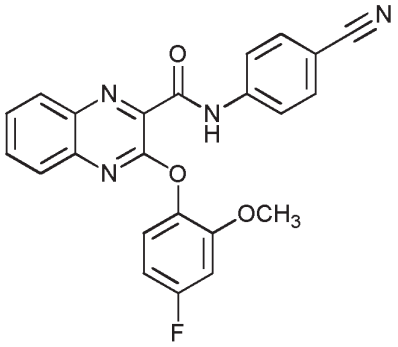
N-(5-cyanopyridin-2-yl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



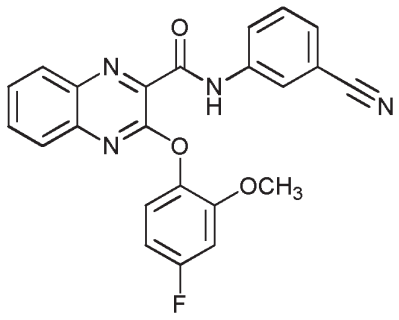
3-(4-fluoro-2-methoxyphenoxy)-N-(pyridin-4-yl)quinoxaline-2-carboxamide;



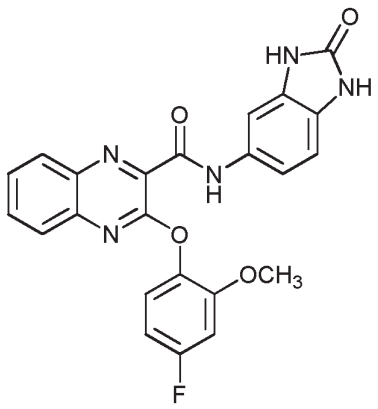
3-(4-fluoro-2-methoxyphenoxy)-N-(pyridin-3-yl)quinoxaline-2-carboxamide;



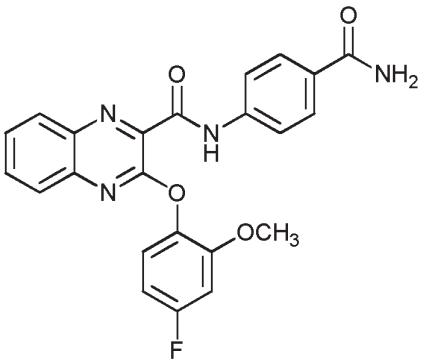
N-(4-cyanophenyl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



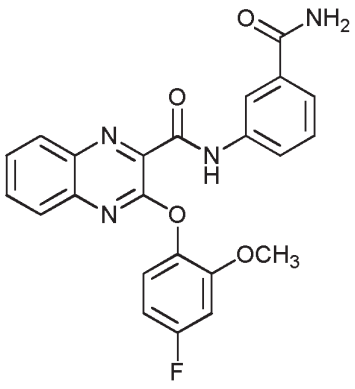
N-(3-cyanophenyl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



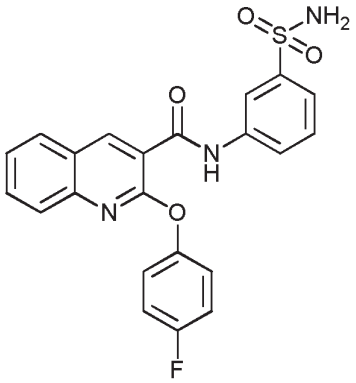
3-(4-fluoro-2-methoxyphenoxy)-N-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)quinoxaline-2-carboxamide;



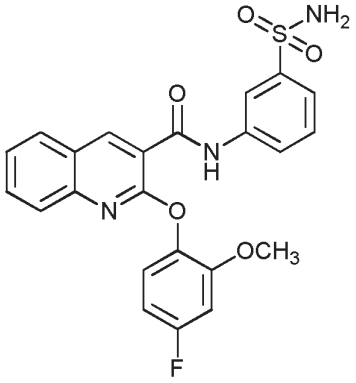
N-(4-carbamoylphenyl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



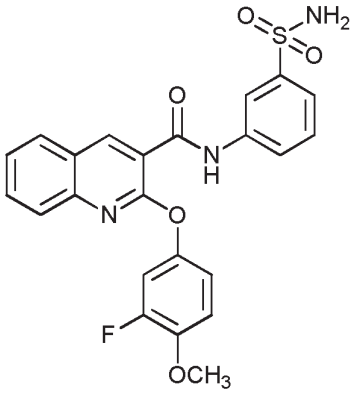
N-(3-carbamoylphenyl)-3-(4-fluoro-2-methoxyphenoxy)quinoxaline-2-carboxamide;



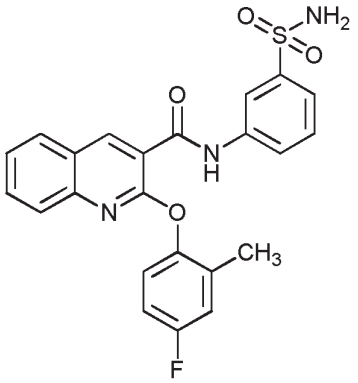
2-(4-fluorophenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



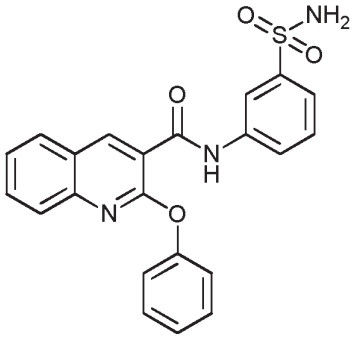
2-(4-fluoro-2-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



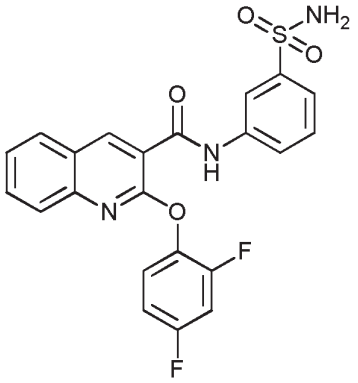
2-(3-fluoro-4-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



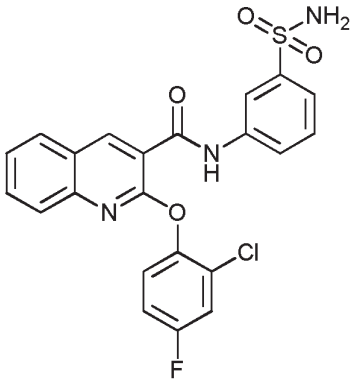
2-(4-fluoro-2-methylphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



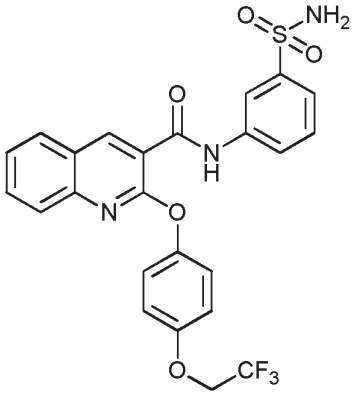
2-phenoxy-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



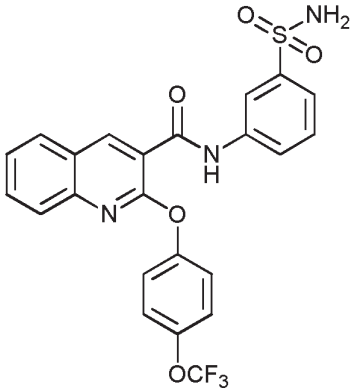
2-(2,4-difluorophenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



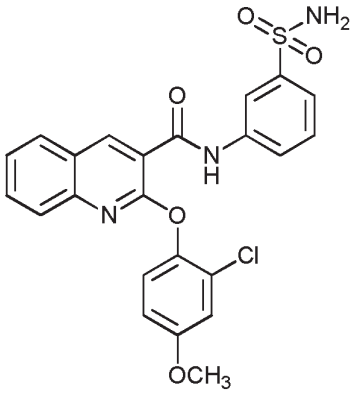
2-(2-chloro-4-fluorophenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



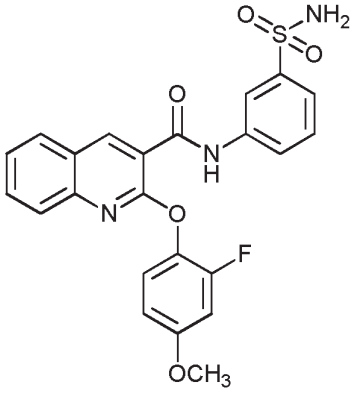
N-(3-sulfamoylphenyl)-2-(4-(2,2,2-trifluoroethoxy)phenoxy)quinoline-3-carboxamide;



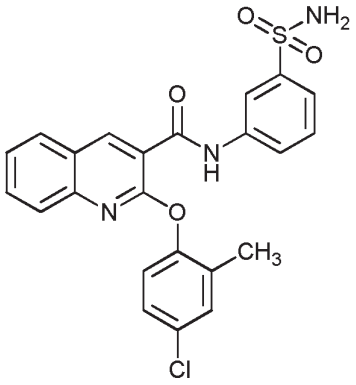
N-(3-sulfamoylphenyl)-2-(4-(trifluoromethoxy)phenoxy)quinoline-3-carboxamide;



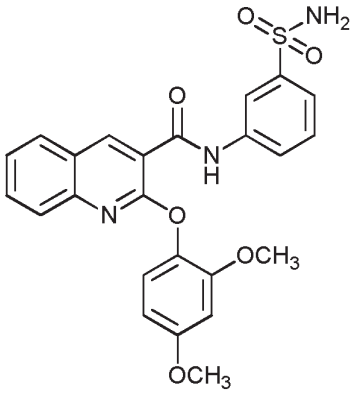
2-(2-chloro-4-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



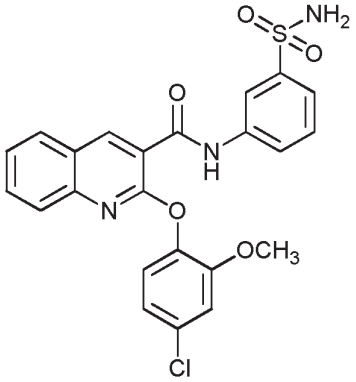
2-(2-fluoro-4-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



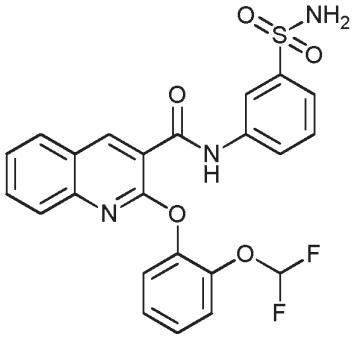
2-(4-chloro-2-methylphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



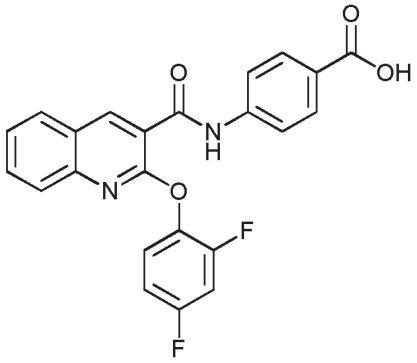
2-(2,4-dimethoxyphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



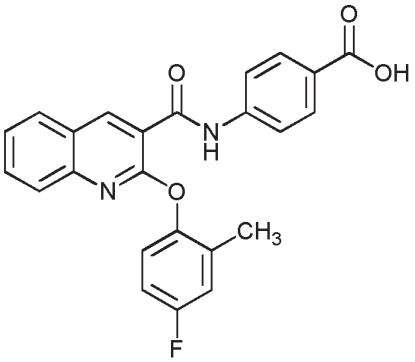
2-(4-chloro-2-methoxyphenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



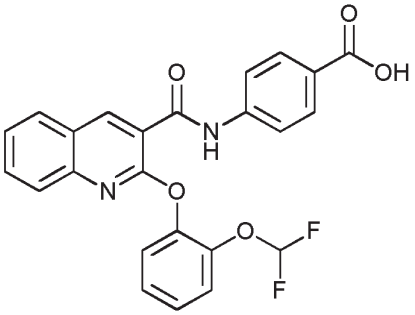
2-(2-(difluoromethoxy)phenoxy)-N-(3-sulfamoylphenyl)quinoline-3-carboxamide;



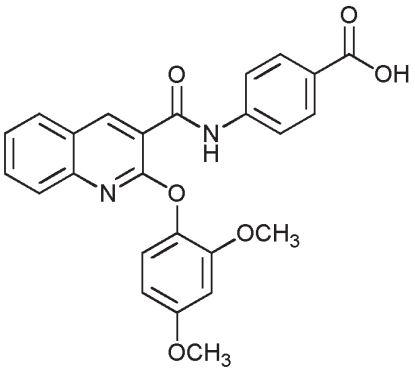
4-(2-(2,4-difluorophenoxy)quinoline-3-carboxamido)benzoic acid;



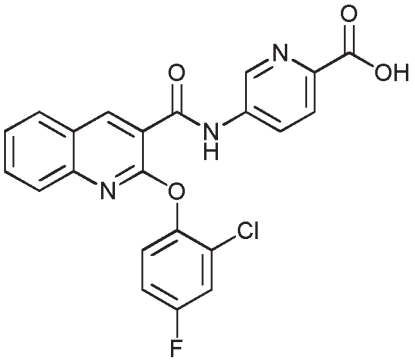
4-(2-(4-fluoro-2-methylphenoxy)quinoline-3-carboxamido)benzoic acid;



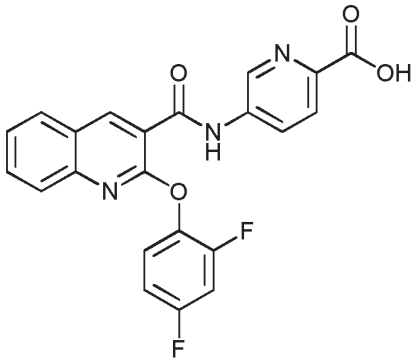
4-(2-(2-(difluoromethoxy)phenoxy)quinoline-3-carboxamido)benzoic acid;



4-(2-(2,4-dimethoxyphenoxy)quinoline-3-carboxamido)benzoic acid;



5-(2-(2-chloro-4-fluorophenoxy)quinoline-3-carboxamido)picolinic acid; and



5-(2-(2,4-difluorophenoxy)quinoline-3-carboxamido)picolinic acid;

or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a therapeutically effective amount of the compound or a pharmaceutically acceptable salt thereof of any one of claims 1 to 12 and one or more pharmaceutically acceptable carriers or vehicles.