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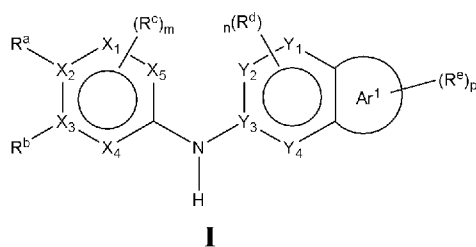
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(54) Title: FERROPTOSIS MODULATORS, PREPARATIONS, AND USES THEREOF

(57) Abstract: Provided are compounds of Formula I, compositions comprising the same, and methods of using the same, including use in treating various diseases and conditions, e.g., those involving ferroptosis.



I

FERROPTOSIS MODULATORS, PREPARATIONS, AND USES THEREOF

Related Application

5 This application claims priority to International Application No. PCT/CN2021/105449, filed on July 9, 2021, the content of which is incorporated by reference in its entirety.

Field of the Disclosure

10 The present disclosure relates to compounds that modulate ferroptosis, compositions comprising the compounds, methods of preparing the compounds, and methods of using the compounds to treat various diseases or conditions, e.g., those involving ferroptosis.

Background of the Disclosure

15 Ferroptosis is a type of programmed cell death dependent on iron and characterized by the accumulation of lipid peroxides, and is genetically and biochemically distinct from other forms of regulated cell death such as apoptosis, autophagy, and necrosis. (Dixon et al., Cell 149, 1060–1072
20 (2012).) Certain mechanisms of ferroptosis and key contributors to ferroptotic cell death is reviewed and illustrated by Conrad et al., Nature Chemical Biology, vol. 15, Dec. 2019, 1137–1147.

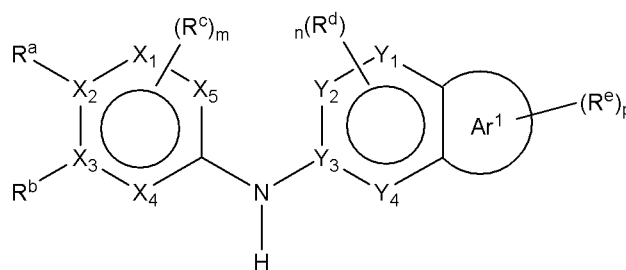
25 Ferroptosis has been implicated in a number of diseases or conditions, including neuropathy, stroke, neurodegenerative disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute
30 kidney failure. For example, inactivation of the the ferroptosis regulator Gpx4 triggers acute renal failure in mice. (Angeli, et al., Nature Cell Biology, published online Nov. 17, 2014; DOI: 10.1038/ncb3064.)

Ferroptosis has been considered to be implicated in several pathophysiological contexts such as tumor suppression, antiviral immunity, neurodegeneration, and ischemia/reperfusion injury (IRI). (Angeli et al., Trends in Pharmacological Sciences, May 2017, Vol. 38, No. 5, 489-498 (2017).)

Certain compounds that modulate ferroptosis are disclosed by Skouta et al., J. Am. Chem. Soc., dx.doi.org/10.1021/ja411006a; and in WO2013152039A1, WO2015084749A1, WO2019154795A1, WO2016075137A1, WO2020185738A1, and PCT/CN2021/078601.

Summary of the Disclosure

One aspect of this disclosure provides a compound selected from compounds of the Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, which can be employed in the treatment of various diseases or conditions, such as diseases or conditions involving ferroptosis. For example, disclosed herein is a compound of the following structural Formula I:



Formula I

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:

Ar¹ is aryl, cycloalkyl, heteroaryl, or 5- to 7-membered heterocyclyl;

X₁ is C, N, or S;

X₂, X₃, X₅, Y₁, Y₂, Y₃, and Y₄ are each independently C or N;

X₄ is C or N, but when X₁ is S, X₄ is nothing;

R^a is selected from H, halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted alkenyl, optionally

substituted alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is selected from H, halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^a and R^b may join together to form an optionally substituted 3- to 10-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring;

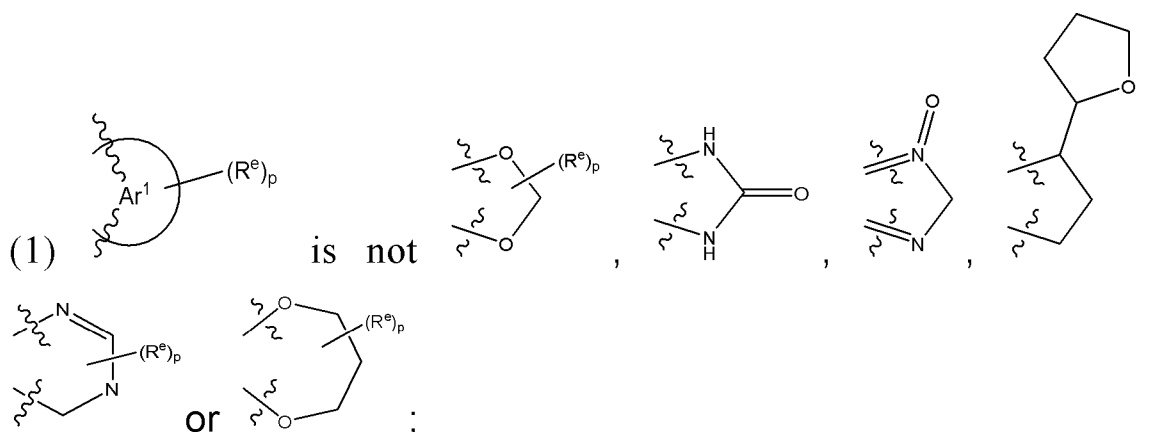
R^c, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, and optionally substituted alkyl;

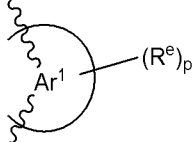
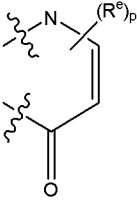
R^d, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, and optionally substituted alkyl;

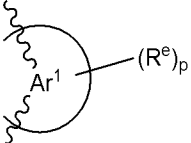
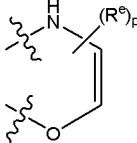
R^e, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl; and

m, n, and p are each an integer independently selected from 0, 1, 2, and 3;

provided that:



(2) when  is , R^e is not $-C(=O)OH$ or $-C(=O)O(C_1-C_3 \text{ alkyl})$;

(3) when  is , R^a is not OH; and

(4) when Ar^1 is a 5- to 6-membered cycloalkyl, 5- to 6-membered heteroaryl, or 5- to 7-membered heterocyclyl, (i) R^a is selected from optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl, (ii) R^a is selected from H, halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, provided that p is an integer selected from 1, 2, and 3 and that at least one of the R^e is =O, or (iii) R^a and R^b join together to form an optionally substituted 3- to 10-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring, provided that p is an integer selected from 1, 2, and 3 and that at least one of the R^e is =O.

In one aspect of the disclosure, the compounds of the Formulae disclosed herein are selected from Compounds 1 to 659 shown below, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

In some embodiments, the disclosure provides pharmaceutical compositions comprising a compound of the Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, and a pharmaceutically acceptable carrier. In some embodiments, the pharmaceutical compositions may comprise a compound selected from Compounds 1 to 659 shown below, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically

acceptable salt of the foregoing, and a pharmaceutically acceptable carrier. These compositions may further comprise an additional active pharmaceutical agent.

Another aspect of the disclosure provides methods of treating a disease or condition, comprising administering to a subject in need thereof, a therapeutically effective amount of a compound of the Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition comprising any of the foregoing, wherein the disease or condition is selected from neuropathy, stroke, neurodegenerative disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (AML), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute kidney failure.

A further aspect of the disclosure provides methods of treating a disease or condition involving ferroptosis, comprising administering to a subject in need thereof, a therapeutically effective amount of a compound of the Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition comprising any of the foregoing.

In some embodiments, the methods of treatment comprise administering to a subject in need thereof, a compound selected from Compounds 1 to 659 shown below, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition comprising any of the foregoing.

In some embodiments, the methods of treatment comprise administration of an additional active pharmaceutical agent to the subject

in need thereof, either in the same pharmaceutical composition as a compound of the Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or in a separate composition. In some
5 embodiments, the methods of treatment comprise administering a compound selected from Compounds 1 to 659 shown below, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing with an additional active pharmaceutical agent either in the same pharmaceutical composition or in a
10 separate composition. When administered as a separate composition, the additional therapeutic agent may be administered prior to, at the same time as, or following administration of the compound, tautomer, solvate, stereoisomer, or a pharmaceutically acceptable salt disclosed herein.

Also disclosed herein are methods of modulating, e.g., inhibiting,
15 ferroptosis in a subject in need thereof, comprising contacting the subject with a compound of the Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition comprising any of the foregoing. In some embodiments, the
20 methods of modulating, e.g., inhibiting, ferroptosis in a subject in need thereof comprise contacting the subject with a compound selected from Compounds 1 to 659 shown below, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition
25 comprising any of the foregoing.

Detailed Description of the Disclosure

I. Definitions

The term “a” or “an” when referring to a noun as used herein
30 encompasses the expression “at least one” and therefore encompasses both singular and plural units of the noun. For example, “an additional pharmaceutical agent” means a single or two or more additional

pharmaceutical agents.

The term "alkyl" refers to a hydrocarbon group selected from linear and branched saturated hydrocarbon groups, containing 1-20, e.g., 1-18, 1-12, 1-10, 1-8, 1-6, 1-4, or 1-3, carbon atoms. Examples of the alkyl group include methyl, ethyl, 1-propyl or n-propyl ("n-Pr"), 2-propyl or isopropyl ("i-Pr"), 1-butyl or n-butyl ("n-Bu"), 2-methyl-1-propyl or isobutyl ("i-Bu"), 1-methylpropyl or s-butyl ("s-Bu"), and 1,1-dimethylethyl or t-butyl ("t-Bu"). Other examples of an alkyl group include 1-pentyl, 2-pentyl, 3-pentyl, 2-methyl-2-butyl, 3-methyl-2-butyl, 3-methyl-1-butyl, 2-methyl-1-butyl, 1-hexyl, 2-hexyl, 3-hexyl, 2-methyl-2-pentyl, 3-methyl-2-pentyl, 4-methyl-2-pentyl, 3-methyl-3-pentyl, 2-methyl-3-pentyl, 2,3-dimethyl-2-butyl, and 3,3-dimethyl-2-butyl groups. Lower alkyl contains 1-8, preferably 1-6, more preferably 1-4 carbon atoms, and more preferably 1-3 carbon atoms.

The term "alkenyl" refers to a hydrocarbon group selected from linear and branched hydrocarbon groups, comprising at least one C=C double bond and 2-20, e.g., 2-18, 2-12, 2-10, 2-8, 2-6, or 2-4, carbon atoms. Examples of the alkenyl group may be selected from ethenyl or vinyl, prop-1-enyl, prop-2-enyl, 2-methylprop-1-enyl, but-1-enyl, but-2-enyl, but-3-enyl, buta-1,3-dienyl, 2-methylbuta-1,3-diene, hex-1-enyl, hex-2-enyl, hex-3-enyl, hex-4-enyl, and hexa-1,3-dienyl groups. Lower alkenyl contains 2-8, preferably 2-6, and more preferably 2-4 carbon atoms.

The term "alkynyl" refers to a hydrocarbon group selected from linear and branched hydrocarbon groups, comprising at least one C≡C triple bond and 2-20, e.g., 2-18, 2-12, 2-10, 2-8, 2-6, or 2-4, carbon atoms. Examples of the alkynyl group include ethynyl, 1-propynyl, 2-propynyl (propargyl), 1-butynyl, 2-butynyl, and 3-butynyl groups. Lower alkynyl contains 2-8, preferably 2-6, and more preferably 2-4 carbon atoms.

The term "heteroalkyl" refers to an alkyl group, as defined herein, in which one or more of the constituent carbon atoms have been replaced by a heteroatom, e.g., nitrogen, oxygen, or sulfur, e.g., CH₃CH₂OH,

CH₃CH₂OC₂H₅, CH₃CH₂SH, CH₃CH₂SC₂H₅, CH₃CH₂NH₂,
CH₃CH₂NHC₂H₅, etc. In some embodiments, in addition to the
replacement of one or more of the constituent carbon atoms by nitrogen,
oxygen, or sulfur, a heteroalkyl group is further optionally substituted as
5 defined herein.

The term "cycloalkyl" refers to a hydrocarbon group selected from
saturated and partially unsaturated cyclic hydrocarbon groups, e.g.,
monocyclic and polycyclic (e.g., bicyclic and tricyclic) groups. For
example, the cycloalkyl group may be of 3-12, or 3-8, or 3-6, or 3-4, or 5-6
10 carbon atoms. Even further for example, the cycloalkyl group may be a
monocyclic group of 3-12, or 3-8, or 3-6, or 3-4, or 5-6 carbon atoms.
Examples of the monocyclic cycloalkyl group include cyclopropyl,
cyclobutyl, cyclopentyl, 1-cyclopent-1-enyl, 1-cyclopent-2-enyl,
1-cyclopent-3-enyl, cyclohexyl, 1-cyclohex-1-enyl, 1-cyclohex-2-enyl,
15 1-cyclohex-3-enyl, cyclohexadienyl, cycloheptyl, cyclooctyl, cyclononyl,
cyclodecyl, cycloundecyl, and cyclododecyl groups. Examples of the
bicyclic cycloalkyl groups include those having 7-12 ring atoms arranged as
a bicycle ring selected from [4,4], [4,5], [5,5], [5,6] and [6,6] ring systems,
or as a bridged bicyclic ring selected from bicyclo[2.2.1]heptane,
20 bicyclo[2.2.2]octane, and bicyclo[3.2.2]nonane. The ring may be saturated
or have at least one double bond (i.e., partially unsaturated), but is not fully
conjugated, and is not aromatic, as aromatic is defined herein.

The term "heterocyclic" or "heterocycle" or "heterocyclyl" refers to a
ring selected from 4- to 12-membered, e.g., 3- to 6-membered, 3- to
25 5-membered, 4- to 5-membered, or 5- to 6-membered, monocyclic, bicyclic,
and tricyclic, saturated and partially unsaturated rings comprising at least
one carbon atom in addition to 1, 2, 3, or 4 heteroatoms, selected from
oxygen, sulfur, and nitrogen. "Heterocycle" also refers to a 5- to
7-membered heterocyclic ring comprising at least one heteroatom selected
30 from N, O, and S fused with 5-, 6-, and/or 7-membered cycloalkyl,
carbocyclic aromatic, or heteroaromatic ring, provided that the point of
attachment is at the heterocyclic ring when the heterocyclic ring is fused

with a carbocyclic aromatic or a heteroaromatic ring, and that the point of attachment can be at the cycloalkyl or heterocyclic ring when the heterocyclic ring is fused with cycloalkyl.

“Heterocycle” also refers to an aliphatic spirocyclic ring comprising at least one heteroatom selected from N, O, and S, provided that the point of attachment is at the heterocyclic ring. The rings may be saturated or have at least one double bond (i.e., partially unsaturated). A heterocycle may be substituted with oxo. The point of the attachment may be carbon or heteroatom in the heterocyclic ring. A heterocycle is not a heteroaryl as defined herein.

Examples of heterocycles include, but are not limited to, (as numbered from the linkage position assigned priority 1) 1-pyrrolidinyl, 2-pyrrolidinyl, 2,4-imidazolidinyl, 2,3-pyrazolidinyl, 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-piperidinyl, 2,5-piperazinyl, pyranlyl, 2-morpholinyl, 3-morpholinyl, oxiranyl, aziridinyl, thiranyl, azetidyl, oxetanyl, thietanyl, 1,2-dithietanyl, 1,3-dithietanyl, dihydropyridinyl, tetrahydropyridinyl, thiomorpholinyl, thioxanyl, piperazinyl, homopiperazinyl, homopiperidinyl, azepanyl, oxepanyl, thiepanyl, 1,4-oxathianyl, 1,4-dioxepanyl, 1,4-oxathiepanyl, 1,4-oxaazepanyl, 1,4-dithiepanyl, 1,4-thiazepanyl, 1,4-diazepanyl, 1,4-dithianyl, 1,4-azathianyl, oxazepinyl, diazepinyl, thiazepinyl, dihydrothienyl, dihydropyranyl, dihydrofuranyl, tetrahydrofuranyl, tetrahydrothienyl, tetrahydropyranyl, tetrahydrothiopyranyl, 1-pyrrolinyl, 2-pyrrolinyl, 3-pyrrolinyl, indolinyl, 2H-pyranyl, 4H-pyranyl, 1,4-dioxanyl, 1,3-dioxolanyl, pyrazolinyl, pyrazolidinyl, dithianyl, dithiolanyl, pyrazolidinyl, imidazolinyl, pyrimidinonyl, 1,1-dioxo-thiomorpholinyl, 3-azabicyclo[3.1.0]hexanyl, 3-azabicyclo[4.1.0]heptanyl and azabicyclo[2.2.2]hexanyl. Substituted heterocycle also includes ring systems substituted with one or more oxo moieties, such as piperidinyl N-oxide, morpholinyl-N-oxide, 1-oxo-1-thiomorpholinyl, and 1,1-dioxo-1-thiomorpholinyl.

The term "fused ring" herein refers to a polycyclic ring system, e.g., a

bicyclic or tricyclic ring system, in which two rings share only two ring atoms and one bond in common. Examples of fused rings may comprise a fused bicyclic cycloalkyl ring such as those having from 7 to 12 ring atoms arranged as a bicyclic ring selected from [4,4], [4,5], [5,5], [5,6] and [6,6] ring systems as mentioned above; a fused bicyclic aryl ring such as 7 to 12 membered bicyclic aryl ring systems as mentioned above, a fused tricyclic aryl ring such as 10 to 15 membered tricyclic aryl ring systems mentioned above; a fused bicyclic heteroaryl ring such as 8- to 12-membered bicyclic heteroaryl rings as mentioned above, a fused tricyclic heteroaryl ring such as 11- to 14-membered tricyclic heteroaryl rings as mentioned above; and a fused bicyclic or tricyclic heterocyclyl ring as mentioned above.

The term “heteroatom” means one or more of oxygen, sulfur, nitrogen, and phosphorus, including, any oxidized form of nitrogen or sulfur; the quaternized form of any basic nitrogen or a substitutable nitrogen of a heterocyclic ring, for example N (as in 3,4-dihydro-2H-pyrrolyl), NH (as in pyrrolidinyl) or NR^+ (wherein R is, e.g., an optionally substituted alkyl group) (as in N-substituted pyrrolidinyl).

The term “unsaturated”, as used herein, means that a moiety has one or more units or degrees of unsaturation. Unsaturation is the state in which not all of the available valence bonds in a compound are satisfied by substituents and thus the compound contains one or more double or triple bonds.

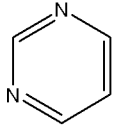
The term “alkoxy” as used herein, refers to an alkyl group, as defined above, wherein one carbon of the alkyl group is replaced by an oxygen atom, provided that the oxygen atom is linked between two carbon atoms.

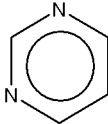
The term “halogen” includes F, Cl, Br, and I, i.e., fluoro, chloro, bromo, and iodo, respectively.

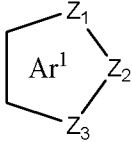
As used herein, a “CN”, “cyano” or “nitrile” group refers to $-\text{C}\equiv\text{N}$.

As used herein, an “aromatic ring” refers to a carbocyclic or heterocyclic ring that contains conjugated, planar ring systems with delocalized pi electron orbitals comprised of $[4n+2]$ p orbital electrons, wherein n is an integer of 0 to 6. A “non-aromatic” ring refers to a

carbocyclic or heterocyclic that does not meet the requirements set forth above for an aromatic ring, and can be either completely or partially saturated. Non-limiting examples of aromatic rings include aryl and heteroaryl rings that are further defined as follows. An “aromatic ring”

5 may be depicted as a cycle with conjugated double bonds, such as ,

or as a cycle with an inside circle such as , or as otherwise

indicated, such as , wherein Ar¹ is indicated as aromatic or non-aromatic.

The term “aryl” herein refers to a group selected from: monocyclic carbocyclic aromatic rings, for example, phenyl; bicyclic ring systems such as 7-12 membered bicyclic ring systems wherein at least one ring is carbocyclic and aromatic, selected, for example, from naphthalene, indane, and 1,2,3,4-tetrahydroquinoline; and tricyclic ring systems such as 10-15 membered tricyclic ring systems wherein at least one ring is carbocyclic and aromatic, for example, fluorene.

For example, the aryl group may be a 6-membered carbocyclic aromatic ring fused to a 5- to 7-membered cycloalkyl or heterocyclic ring optionally comprising at least one heteroatom selected from N, O, and S, provided that the point of attachment is at the carbocyclic aromatic ring when the carbocyclic aromatic ring is fused with a heterocyclic ring, and the point of attachment can be at the carbocyclic aromatic ring or at the cycloalkyl group when the carbocyclic aromatic ring is fused with a cycloalkyl group. Bivalent radicals formed from substituted benzene derivatives and having the free valences at ring atoms are named as substituted phenylene radicals. Bivalent radicals derived from univalent polycyclic hydrocarbon radicals whose names end in “-yl” by removal of

one hydrogen atom from the carbon atom with the free valence are named by adding "-idene" to the name of the corresponding univalent radical, e.g., a naphthyl group with two points of attachment is termed naphthylidene.

The term "heteroaryl" refers to a group selected from: 5- to 7-membered, e.g., 5- to 6-membered, aromatic, monocyclic rings comprising 1, 2, 3, or 4 heteroatoms selected from N, O, and S, with the remaining ring atoms being carbon; 8- to 12-membered bicyclic rings comprising 1, 2, 3, or 4 heteroatoms, selected from N, O, and S, with the remaining ring atoms being carbon and wherein at least one ring is aromatic and at least one heteroatom is present in the aromatic ring; and 11- to 14-membered tricyclic rings comprising 1, 2, 3, or 4 heteroatoms, selected from N, O, and S, with the remaining ring atoms being carbon and wherein at least one ring is aromatic and at least one heteroatom is present in an aromatic ring.

For example, the heteroaryl group may be a 5- to 7-membered heterocyclic aromatic ring fused to a 5- to 7-membered cycloalkyl ring. For such fused, bicyclic heteroaryl ring systems wherein only one of the rings comprises at least one heteroatom, the point of attachment may be at the heteroaromatic ring or at the cycloalkyl ring.

When the total number of S and O atoms in the heteroaryl group exceeds 1, those heteroatoms are not adjacent to one another. In some embodiments, the total number of S and O atoms in the heteroaryl group is not more than 2. In some embodiments, the total number of S and O atoms in the aromatic heterocycle is not more than 1.

Examples of the heteroaryl group include, but are not limited to, (as numbered from the linkage position assigned priority 1) pyridyl (such as 2-pyridyl, 3-pyridyl, or 4-pyridyl), cinnolinyl, pyrazinyl, 2,4-pyrimidinyl, 3,5-pyrimidinyl, 2,4-imidazolyl, imidazopyridinyl, isoxazolyl, oxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, tetrazolyl, thienyl, triazinyl, benzothienyl, furyl, benzofuryl, benzoimidazolyl, indolyl, isoindolyl, indolinyl, phthalazinyl, pyrazinyl, pyridazinyl, pyrrolyl, triazolyl, quinolinyl, isoquinolinyl, pyrazolyl, pyrrolopyridinyl (such as

1H-pyrrolo[2,3-b]pyridin-5-yl), pyrazolopyridinyl (such as 1H-pyrazolo[3,4-b]pyridin-5-yl), benzoxazolyl (such as benzo[d]oxazol-6-yl), pteridinyl, purinyl, 1-oxa-2,3-diazolyl, 1-oxa-2,4-diazolyl, 1-oxa-2,5-diazolyl, 1-oxa-3,4-diazolyl, 1-thia-2,3-diazolyl, 1-thia-2,4-diazolyl, 1-thia-2,5-diazolyl, 1-thia-3,4-diazolyl, furazanyl, benzofurazanyl, benzothiophenyl, benzothiazolyl, benzoxazolyl, quinazolinyl, quinoxalinyl, naphthyridinyl, furopyridinyl, benzothiazolyl (such as benzo[d]thiazol-6-yl), indazolyl (such as 1H-indazol-5-yl) and 5,6,7,8-tetrahydroisoquinolinyl.

10 The term “acyl” refers to a substituent group where a point of attachment in the substituent group is a carbonyl. Exemplary acyl groups include, but are not limited to, -C(=O)R', -C(=O)NR'R'', or -C(=O)OR', wherein R' and R'' are independently selected from hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, cycloalkyl, aryl, 15 heterocyclyl, or heteroaryl, any of which may be further substituted by one or more substituents.

Some of the compounds may exist with different points of attachment of hydrogen, referred to as “tautomers.” For example, compounds including carbonyl -CH₂C(O)- groups (keto forms) may undergo 20 tautomerism to form hydroxyl -CH=C(OH)- groups (enol forms). Both keto and enol forms, individually as well as mixtures thereof, are also intended to be included where applicable.

The compounds, tautomers, solvates, or pharmaceutically acceptable salts of the disclosure may contain an asymmetric center and may thus 25 exist as enantiomers. For example, where the compounds possess two or more asymmetric centers, they may additionally exist as diastereoisomers. Enantiomers and diastereoisomers fall within the broader class of stereoisomers. All such possible stereoisomers as substantially pure resolved enantiomers, racemic mixtures thereof, as well as mixtures of 30 diastereoisomers are intended to be included in this disclosure. All stereoisomers of the compounds, tautomers, solvates, and pharmaceutically acceptable salts thereof are intended to be included. Unless specifically

mentioned otherwise, reference to one isomer applies to any of the possible isomers. Whenever the isomeric composition is unspecified, all possible isomers are included.

Diastereoisomeric mixtures can be separated into their individual
5 diastereoisomers on the basis of their physical chemical differences by methods well known to those skilled in the art, such as by chromatography and/or fractional crystallization. Enantiomers can be separated by converting the enantiomeric mixture into a diastereoisomeric mixture by reaction with an appropriate optically active compound (e.g., chiral
10 auxiliary such as a chiral alcohol or Mosher's acid chloride), separating the diastereoisomers and converting (e.g., hydrolyzing) the individual diastereoisomers to the corresponding pure enantiomers. Enantiomers can also be separated by use of a chiral HPLC column.

A single stereoisomer, e.g., a substantially pure enantiomer, may be
15 obtained by resolution of the racemic mixture using a method such as formation of diastereoisomers using optically active resolving agents. Racemic mixtures of chiral compounds of the disclosure can be separated and isolated by any suitable method, including: (1) formation of ionic, diastereoisomeric salts with chiral compounds and separation by fractional
20 crystallization or other methods, (2) formation of diastereoisomeric compounds with chiral derivatizing reagents, separation of the diastereoisomers, and conversion to the pure stereoisomers, and (3) separation of the substantially pure or enriched stereoisomers directly under chiral conditions.

25 The term “substantially pure” in the context of stereoisomers means that the target stereoisomer contains no more than 35%, such as no more than 30%, further such as no more than 25%, even further such as no more than 20%, by weight of any other stereoisomer(s). In some embodiments, the term “substantially pure” means that the target stereoisomer contains
30 no more than 10%, for example, no more than 5%, such as no more than 1%, by weight of any other stereoisomer(s).

Unless otherwise indicated, structures depicted herein are meant to

include all isomeric forms of the structure, e.g., racemic mixtures, cis/trans isomers, geometric (or conformational) isomers, such as (*Z*) and (*E*) double bond isomers, and (*Z*) and (*E*) conformational isomers. Therefore, geometric and conformational mixtures of the compounds disclosed herein are within the scope of the disclosure. Unless otherwise stated, all tautomeric forms of the compounds of the disclosure are within the scope of the disclosure.

The disclosure provides pharmaceutically acceptable salts of the disclosed compounds, tautomers, solvates, and stereoisomers. A salt of a compound is formed between an acid and a basic group of the compound, such as an amino functional group, or a base and an acidic group of the compound, such as a carboxyl functional group.

The term “pharmaceutically acceptable,” as used herein, refers to a component that is, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and other mammals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. A “pharmaceutically acceptable salt” means any non-toxic salt that, upon administration to a recipient, is capable of providing, either directly or indirectly, a compound of this disclosure.

“Pharmaceutically acceptable salts” include, but are not limited to salts with inorganic acids, selected, for example, from hydrochlorates, phosphates, diphosphates, hydrobromates, sulfates, sulfinates, and nitrates; as well as salts with organic acids, selected, for example, from malates, maleates, fumarates, tartrates, succinates, citrates, lactates, methanesulfonates, p-toluenesulfonates, 2-hydroxyethylsulfonates, benzoates, salicylates, stearates, alkanoates such as acetate, and salts with $\text{HOOC}-(\text{CH}_2)_n\text{-COOH}$, wherein *n* is selected from 0 to 4. Similarly, examples of pharmaceutically acceptable cations include, but are not limited to, sodium, potassium, calcium, magnesium, aluminum, lithium, and ammonium. Suitable pharmaceutically acceptable salts are, for example, those disclosed in S. M. Berge, *et al. J. Pharmaceutical Sciences*, 1977, 66,

pp. 1 to 19.

Acids commonly employed to form pharmaceutically acceptable salts include inorganic acids such as hydrogen bisulfide, hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid and phosphoric acid, as well as organic acids such as para-toluenesulfonic acid, salicylic acid, tartaric acid, bitartaric acid, ascorbic acid, maleic acid, benzenesulfonic acid, fumaric acid, gluconic acid, glucuronic acid, formic acid, glutamic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, lactic acid, oxalic acid, para-bromophenylsulfonic acid, carbonic acid, succinic acid, citric acid, benzoic acid and acetic acid. Such pharmaceutically acceptable salts thus include sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, propionate, decanoate (i.e., caprate), caprylate, acrylate, formate, isobutyrate, heptanoate, propiolate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, butyne-1,4-dioate, hexyne-1,6-dioate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, phthalate, terephthalate, sulfonate, xylene sulfonate, phenylacetate, phenylpropionate, phenylbutyrate, citrate, lactate, β -hydroxybutyrate, glycolate, tartrate, methanesulfonate, propanesulfonate, naphthalene-1-sulfonate, naphthalene-2-sulfonate, mandelate and other salts. In some embodiments, pharmaceutically acceptable acid addition salts include those formed with mineral acids such as hydrochloric acid and hydrobromic acid, and those formed with organic acids such as maleic acid.

Pharmaceutically acceptable salts derived from appropriate bases include alkali metal, alkaline earth metal, ammonium, and $N^+(C_{1-4}alkyl)_4$ salts. This disclosure also envisions the quaternization of any basic nitrogen-containing groups of the compounds disclosed herein. Suitable non-limiting examples of alkali and alkaline earth metal salts include sodium, lithium, potassium, calcium, and magnesium salts. Further non-limiting examples of pharmaceutically acceptable salts include salts of

ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, lower alkyl sulfonate and aryl sulfonate. Other suitable, non-limiting examples of pharmaceutically acceptable salts include
5 besylate and glucosamine salts.

If a compound is obtained as an acid addition salt, the free base can be obtained by basifying a solution of the acid addition salt. Conversely, if the product is a free base, an addition salt, such as a pharmaceutically acceptable addition salt, may be produced by dissolving the free base in a
10 suitable organic solvent and treating the solution with an acid, in accordance with conventional procedures for preparing acid addition salts from base compounds. Those skilled in the art will recognize various synthetic methodologies that may be used without undue experimentation to prepare non-toxic pharmaceutically acceptable addition salts.

The compounds, tautomers, solvates, stereoisomers, and pharmaceutically acceptable salts of the disclosure may also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, $-CD_3$, $-CD_2H$ or $-CDH_2$ contains one or more deuteriums in place of hydrogen. For example, the
20 compounds may be radiolabeled with radioactive isotopes, such as for example tritium (^3H), iodine-125 (^{125}I) or carbon-14 (^{14}C). All isotopic variations of the compounds of the disclosure, whether radioactive or not, are intended to be encompassed within the scope of the disclosure.

As used herein, "optionally substituted" is interchangeable with the
25 phrase "substituted or unsubstituted." In general, the term "substituted," refers to the replacement of a hydrogen radical in a given structure with the radical of a specified substituent. Unless otherwise indicated, an "optionally substituted" group may have a substituent at each substitutable position of the group, and when more than one position in any given
30 structure may be substituted with more than one substituent chosen from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this disclosure are

those that result in the formation of stable or chemically feasible compounds.

In some embodiments, substituents are independently selected from optionally substituted heteroatom and optionally substituted, optionally hetero-, optionally cyclic C₁-C₁₈ hydrocarbonyl, particularly wherein the optionally substituted, optionally hetero-, optionally cyclic C₁-C₁₈ hydrocarbonyl is optionally-substituted, optionally hetero-, optionally cyclic alkyl, alkenyl or alkynyl, or optionally-substituted, optionally hetero-, aryl; and/or the optionally substituted heteroatom is halogen, optionally substituted hydroxyl (such as alkoxy, aryloxy), optionally substituted acyl (such as formyl, alkanoyl, carbamoyl, carboxyl, amido), optionally substituted amino (such as amino, alkylamino, dialkylamino, amido, sulfamidyl), optionally substituted thiol (such as mercapto, alkylthiol, aryl thiol), optionally substituted sulfinyl or sulfonyl (such as alkylsulfinyl, arylsulfinyl, alkyl sulfonyl, arylsulfonyl), nitro, or cyano.

In some embodiments, substituents are independently selected from: halogen, -R', -OR', =O, =NR', =N-OR', -NR'R'', -SR', -SiR'R''R''', -OC(=O)R', -C(=O)R', -CO₂R', -C(=O)NR'R'', -OC(=O)NR'R'', -NR''C(=O)R', -NR'-C(=O)NR''R''', -NR'-SO₂NR''R''', -NR''CO₂R', -NH-C(NH₂)=NH, -NR'C(NH₂)=NH, -NH-C(NH₂)=NR', -S(O)R', -SO₂R', -SO₂NR'R'', -NR''SO₂R', -CN, -NO₂, -N₃, -CH(Ph)₂, perfluoro(C₁-C₄)alkoxy, and perfluoro(C₁-C₄)alkyl, in a number ranging from zero to three, with those groups having zero, one, or two substituents being particularly preferred. R', R'' and R''' each independently refer to hydrogen, unsubstituted C₁-C₈ alkyl and heteroalkyl, C₁-C₈ alkyl and heteroalkyl substituted with one to three halogens, unsubstituted aryl, aryl substituted with one to three halogens, unsubstituted alkyl, alkoxy, or thioalkoxy groups, or aryl-(C₁-C₄) alkyl groups. When R' and R'' are attached to the same nitrogen atom, they can be combined with the nitrogen atom to form a 5-, 6- or 7-membered ring. Hence, -NR'R'' includes, e.g., 1-pyrrolidinyl and 4-morpholinyl. When the aryl group is 1,2,3,4-tetrahydronaphthalenyl, it may be substituted with a substituted or

unsubstituted C₃-C₇ spirocycloalkyl group. The C₃-C₇ spirocycloalkyl group may be substituted in the same manner as defined herein for "cycloalkyl."

In some embodiments, substituents are selected from: halogen, -R',
5 -OR', =O, -NR'R'', -SR', -SiR'R''R''', -OC(=O)R', -C(=O)R', -CO₂R',
-C(=O)NR'R'', -OC(=O)NR'R'', -NR''C(=O)R', -NR''CO₂R',
-NR'-SO₂NR''R''', -S(=O)R', -SO₂R', -SO₂NR'R'', -NR''SO₂R, -CN, -NO₂,
perfluoro C₁-C₄ alkoxy and perfluoro C₁-C₄ alkyl, where R' and R'' are as
defined above.

10 In some embodiments, substituents are independently selected from
substituted or unsubstituted heteroatom, substituted or unsubstituted, 0-3
heteroatom-containing C₁-C₆ alkyl (e.g., C₁-C₃ alkyl or C₁-C₂ alkyl),
substituted or unsubstituted, 0-3 heteroatom-containing C₂-C₆ alkenyl (e.g.,
C₂-C₄ alkenyl), substituted or unsubstituted, 0-3 heteroatom-containing
15 C₂-C₆ alkynyl (e.g., C₂-C₄ alkynyl), or substituted or unsubstituted, 0-3
heteroatom-containing C₆-C₁₄ aryl (e.g., C₅-C₆ aryl), wherein each
heteroatom is independently oxygen, phosphorus, sulfur, or nitrogen.

In some embodiments, substituents are independently selected from
aldehyde, aldimine, alkanoyloxy, alkoxy, alkoxycarbonyl, alkyloxy, alkyl,
20 alkenyl, alkynyl, amine, azo, halogen, carbamoyl, carbonyl, carboxamido,
carboxyl, cyanyl, ester, haloformyl, hydroperoxyl, hydroxyl, imine,
isocyanide, iscyante, N-tert-butoxycarbonyl, nitrate, nitrile, nitrite, nitro,
nitroso, phosphate, phosphono, sulfide, sulfonyl, sulfo, sulfhydryl, thiol,
thiocyanyl, trifluoromethyl, and trifluoromethyl ether (OCF₃) groups.

25 Preferred substituents are disclosed herein and exemplified in the
tables, structures, examples, and claims, and may be applied across
different compounds of this disclosure. For example, substituents of a
given compound may be combinatorically used with other compounds.

It may be advantageous to separate reaction products from one
30 another and/or from starting materials. The desired products of each step or
series of steps is separated and/or purified (hereinafter separated) to the
desired degree of homogeneity by the techniques common in the art.

Typically such separations involve multiphase extraction, crystallization from a solvent or solvent mixture, distillation, sublimation, or chromatography. Chromatography can involve any number of methods including, for example, reverse-phase and normal phase; size exclusion;
5 ion exchange; high, medium and low pressure liquid chromatography methods and apparatus; small scale analytical; simulated moving bed ("SMB") and preparative thin or thick layer chromatography, as well as techniques of small scale thin layer and flash chromatography. One skilled in the art may apply such techniques to achieve a desired separation.

10 Non-limiting examples of suitable solvents that may be used in this disclosure include water, methanol (MeOH), ethanol (EtOH), dichloromethane or methylene chloride (CH₂Cl₂), toluene, acetonitrile (MeCN), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), methyl acetate (MeOAc), ethyl acetate (EtOAc), heptanes, isopropyl acetate
15 (IPAc), *tert*-butyl acetate (*t*-BuOAc), isopropyl alcohol (IPA), tetrahydrofuran (THF), 2-methyl tetrahydrofuran (2-Me THF), methyl ethyl ketone (MEK), *tert*-butanol, diethyl ether (Et₂O), methyl-*tert*-butyl ether (MTBE), 1,4-dioxane, and *N*-methyl pyrrolidone (NMP).

Non-limiting examples of suitable bases that may be used in this
20 disclosure include 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), potassium *tert*-butoxide (KO^tBu), potassium carbonate (K₂CO₃), *N*-methyldmorpholine (NMM), triethylamine (Et₃N; TEA), diisopropyl-ethyl amine (*i*-Pr₂EtN; DIPEA), pyridine, potassium hydroxide (KOH), sodium hydroxide (NaOH), lithium hydroxide (LiOH), and sodium methoxide (NaOMe; NaOCH₃).

25 The term "subject" refers to an animal including a human.

The term "therapeutically effective amount" refers to the amount of a compound that produces a desired effect for which it is administered (*e.g.*, improvement in a disease or condition, lessening the severity of a disease or condition, and/or reducing progression of a disease or condition, *e.g.*, a
30 disease or condition selected from neuropathy, stroke, neurodegenerative disease (*e.g.*, Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (AML), multiple sclerosis, Huntington's Disease, dementia

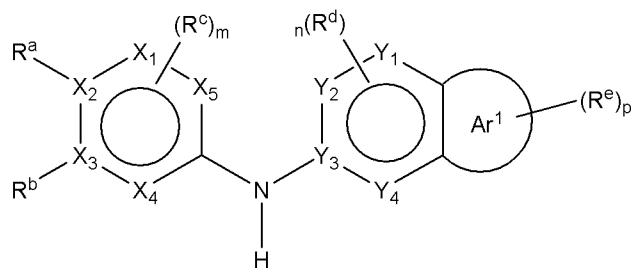
with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute kidney failure. The disease or condition
5 may be involved with dysregulated, e.g., abnormal, ferroptosis. The exact amount of a therapeutically effective amount will depend on the purpose of the treatment and will be ascertainable by one skilled in the art using known techniques (see, e.g., Lloyd (1999), The Art, Science and Technology of Pharmaceutical Compounding).

10 As used herein, the term "treatment" and its cognates refer to slowing or stopping disease progression. "Treatment" and its cognates as used herein include, but are not limited to the following: complete or partial remission, curing a disease or condition or a symptom thereof, lower risk of a disease or condition, e.g., neuropathy, stroke, neurodegenerative
15 disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and
20 kidney dysfunction such as acute kidney failure. The disease or condition may be involved with dysregulated, e.g., abnormal, ferroptosis. Improvements in or lessening the severity of any of these symptoms can be assessed according to methods and techniques known in the art.

The terms "about" and "approximately," when used in connection
25 with a number such as a percentage include the number as specified, and a range of the number (e.g., a range of percentages, for example, a range of $\pm 10\%$ with respect to a specific point value) that is recognized by one of ordinary skill in the art.

II. Compounds and Compositions

30 In a first embodiment, a compound of this disclosure is a compound of the following structural Formula I:

**Formula I**

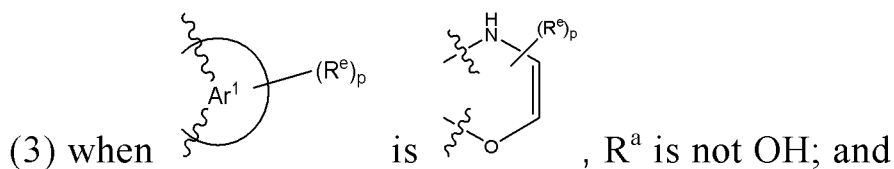
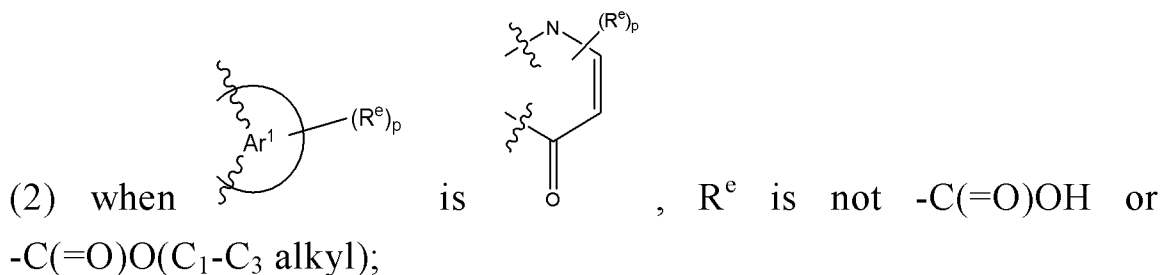
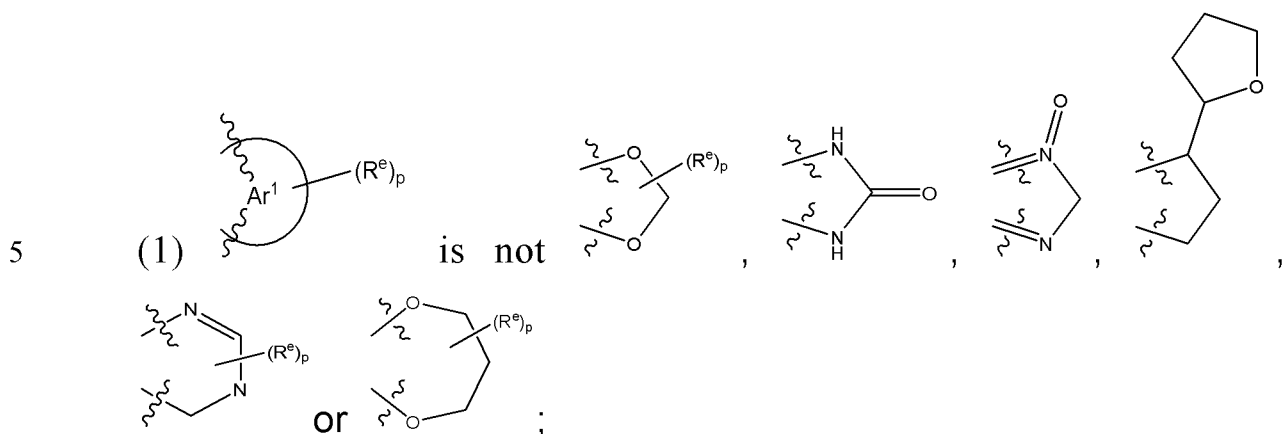
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:

- 5 Ar¹ is aryl, cycloalkyl, heteroaryl, or 5- to 7-membered heterocyclyl;
- X₁ is C, N, or S;
- X₂, X₃, X₅, Y₁, Y₂, Y₃, and Y₄ are each independently C or N;
- X₄ is C or N, but when X₁ is S, X₄ is nothing;
- R^a is selected from H, halogen, CN, optionally substituted heteroatom,
- 10 optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;
- R^b is selected from H, halogen, CN, optionally substituted heteroatom,
- 15 optionally substituted alkyl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;
- R^a and R^b may join together to form an optionally substituted 3- to 10-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring;
- 20 R^c, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, and optionally substituted alkyl;
- R^d, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, and optionally substituted alkyl;
- R^e, for each occurrence, is independently selected from halogen, CN,
- 25 optionally substituted heteroatom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and

optionally substituted heteroaryl; and

m, n, and p are each an integer independently selected from 0, 1, 2, and 3;

provided that:

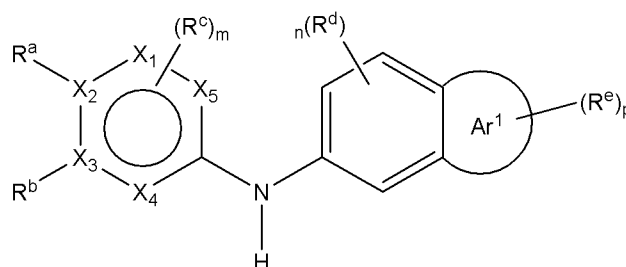


- 10 (4) when Ar^1 is a 5- to 6-membered cycloalkyl, 5- to 6-membered heteroaryl, or 5- to 7-membered heterocyclyl, (i) R^a is selected from optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl, (ii) R^a is selected from H, halogen, CN, optionally substituted heteroatom,
- 15 optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, provided that p is an integer selected from 1, 2, and 3 and that at least one of the R^e is =O, or (iii) R^a and R^b join together to form an optionally substituted 3- to 10-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring, provided
- 20 that p is an integer selected from 1, 2, and 3 and that at least one of the R^e is =O.

Combinations of substituents as disclosed herein are those that result in the formation of stable or chemically feasible compounds. For abbreviation or according to common practice, certain hydrogen atoms attached to a certain atom (e.g., a carbon atom C or a nitrogen atom N) are not specifically spelled out in a chemical structure, formula, or notation; hydrogen atoms are deemed to be present to the extent the valences of the certain atom (e.g., C or N) are completed.

In a second embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, Ar¹ is 5- to 6-membered heteroaryl or 5- to 7-membered heterocyclyl; and all other variables not specifically defined herein are as defined in the preceding embodiment.

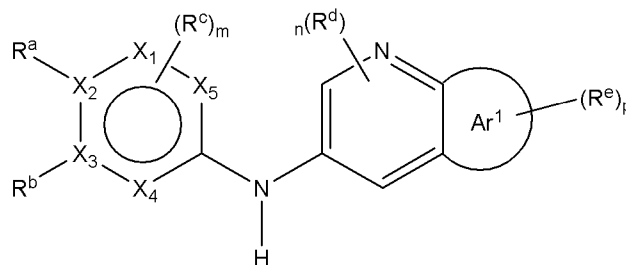
In a third embodiment, a compound of the disclosure is a compound of the following structural Formula IIa:



Formula IIa

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

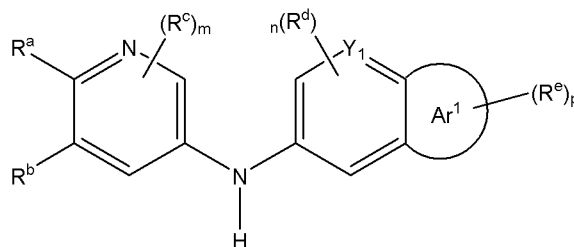
In a fourth embodiment, a compound of the disclosure is a compound of the following structural Formula IIb:



Formula IIb

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

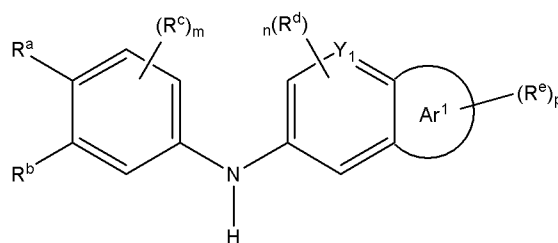
- 5 In a fifth embodiment, a compound of the disclosure is a compound of the following structural Formula IIIa:



Formula IIIa

- a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

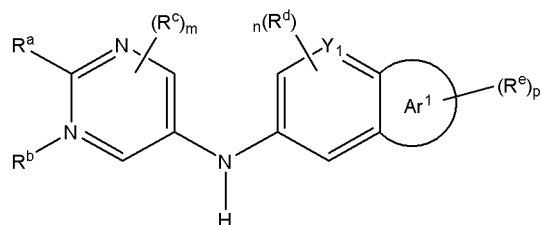
In a sixth embodiment, a compound of the disclosure is a compound of the following structural Formula IIIb:



Formula IIIb

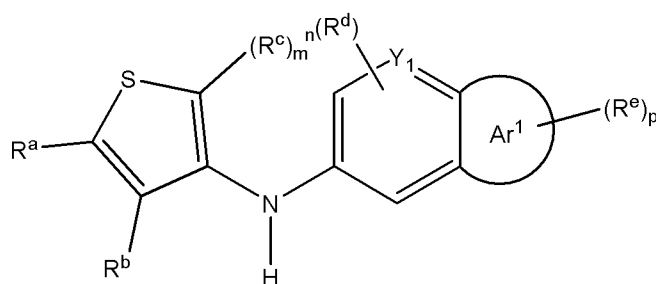
- a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a seventh embodiment, a compound of the disclosure is a compound of the following structural Formula IIIc:

**Formula IIIc**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; and all
 5 other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In an eighth embodiment, a compound of the disclosure is a compound of the following structural Formula IIIId:

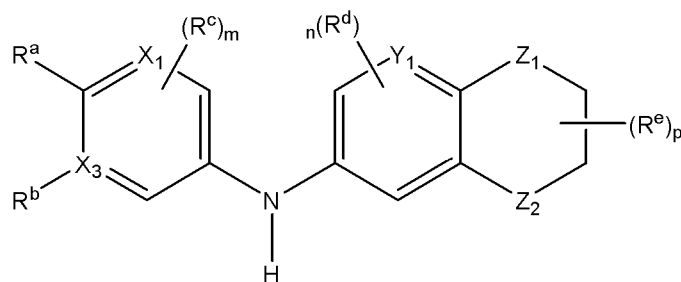


10

Formula IIIId

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; and all
 other variables not specifically defined herein are as defined in any one of the preceding embodiments.

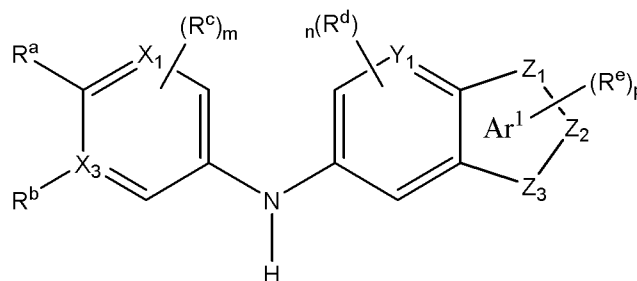
15 In a ninth embodiment, a compound of the disclosure is a compound of the following structural Formula IVa:

**Formula IVa**

a tautomer thereof, a solvate or stereoisomer of the compound or the

tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X_1 and X_3 are each independently C or N; and Z_1 and Z_2 are each independently N or O; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

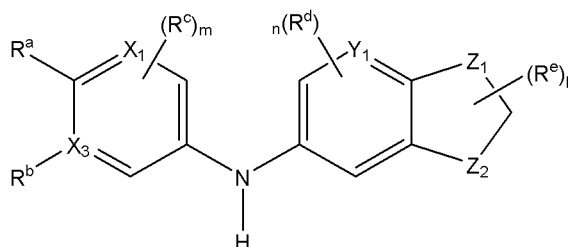
- 5 In a tenth embodiment, a compound of the disclosure is a compound of the following structural Formula IVb:



Formula IVb

- a tautomer thereof, a solvate or stereoisomer of the compound or the
 10 tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X_1 and X_3 are each independently C or N; Ar^1 is aromatic or non-aromatic; and Z_1 , Z_2 , and Z_3 are each independently N or C; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

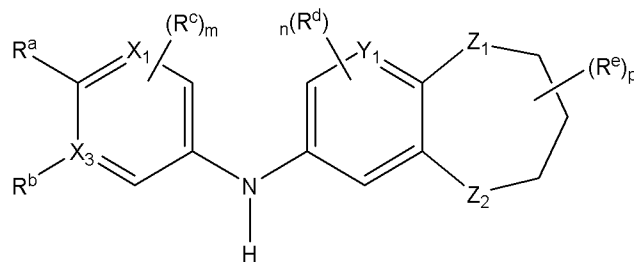
- 15 In an eleventh embodiment, a compound of the disclosure is a compound of the following structural Formula IVc:



Formula IVc

- a tautomer thereof, a solvate or stereoisomer of the compound or the
 20 tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X_1 and X_3 are each independently C or N; and Z_1 and Z_2 are each independently O or N; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

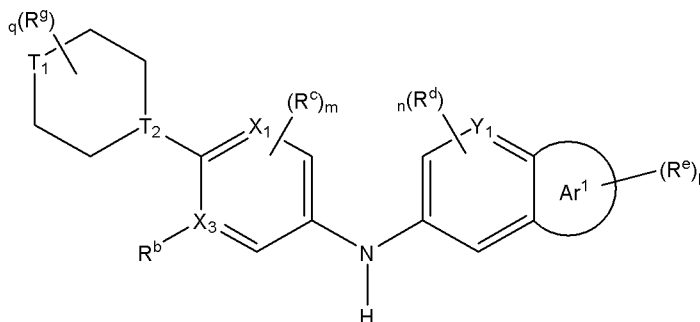
In a twelfth embodiment, a compound of the disclosure is a compound of the following structural Formula IVd:



Formula IVd

5 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X_1 and X_3 are each independently C or N; and Z_1 and Z_2 are each independently O or N; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

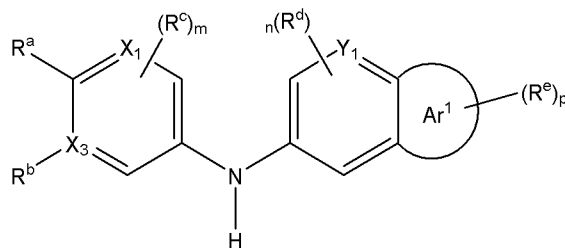
10 In a thirteenth embodiment, a compound of the disclosure is a compound of the following structural Formula Va:



Formula Va

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^e , for each occurrence, is selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

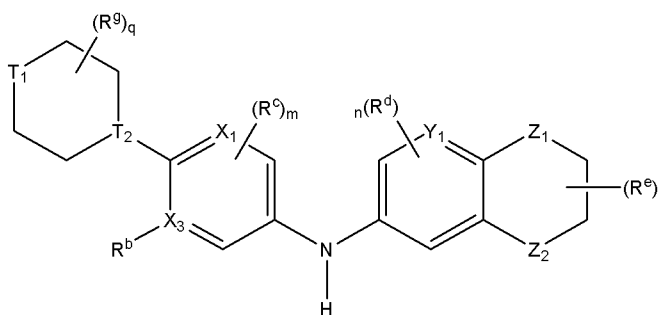
In a fourteenth embodiment, a compound of the disclosure is a compound of the following structural Formula Vb:



Formula Vb

5 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X₁ and X₃ are each independently N or C; R^a is selected from C₁ to C₃ alkoxy and C₁ to C₃ alkyl; R^b is selected from H, halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; and R^c is selected from halogen, C₁ to C₃ alkoxy, and
10 C₁ to C₃ alkyl; wherein the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^a, R^b, and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a fifteenth embodiment, a compound of the disclosure is a
15 compound of the following structural Formula VIa:

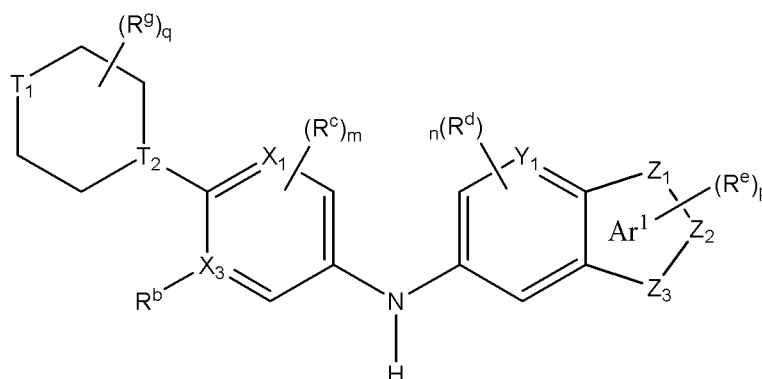


Formula VIa

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein
20 X₁ and X₃ are each independently N or C; T₁ is C or O; T₂ is C or N; R^g,
for each occurrence, is independently selected from CF₃, -CH₃, -OCH₃, and
-CH₂CH₃; q is 0, 1, or 2; R^b is selected from H, halogen, C₁ to C₃ alkoxy,
and C₁ to C₃ alkyl; and R^c is selected from halogen, C₁ to C₃ alkoxy, and

C₁ to C₃ alkyl; the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^b and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; Z₁ and Z₂ are each independently N or O; and all other variables not specifically defined herein are as defined in any one of the preceding
5 embodiments.

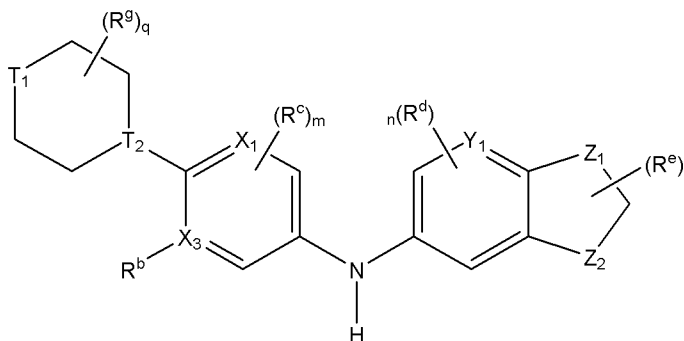
In a sixteenth embodiment, a compound of the disclosure is a compound of the following structural Formula VIb:



Formula VIb

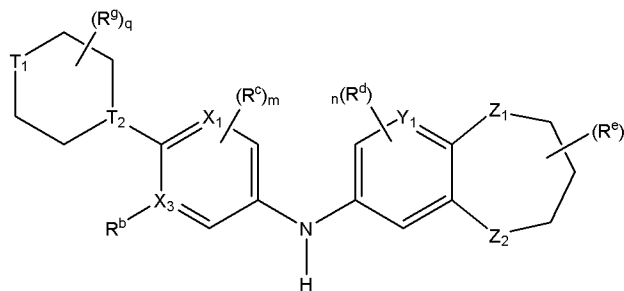
10 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein X₁ and X₃ are each independently N or C; T₁ is C or O; T₂ is C or N; R^g, for each occurrence, is independently selected from CF₃, -CH₃, -OCH₃, and -CH₂CH₃; q is 0, 1, or 2; R^b is selected from H, halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; and R^c is selected from halogen, C₁ to C₃ alkoxy, and
15 C₁ to C₃ alkyl; the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^b and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; Ar¹ is aromatic or non-aromatic; and Z₁, Z₂, and Z₃ are each independently N or C; and all other variables not specifically defined herein are as
20 defined in any one of the preceding embodiments.

In a seventeenth embodiment, a compound of the disclosure is a compound of the following structural Formula VIc:

**Formula VIc**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein
 5 X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is independently selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each
 10 occurrence, are each optionally substituted with 1 to 3 groups of halogen; and Z_1 and Z_2 are each independently O or N; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

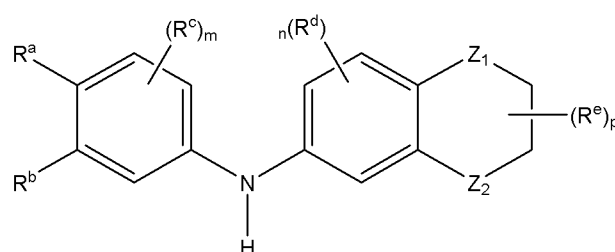
In an eighteenth embodiment, a compound of the disclosure is a
 15 compound of the following structural Formula VIId:

**Formula VIId**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein
 20 X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is independently selected from CF_3 , $-CH_3$, $-OCH_3$, and

-CH₂CH₃; q is 0, 1, or 2; R^b is selected from H, halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; and R^c is selected from halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^b and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and Z₁ and Z₂ are each independently O or N; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

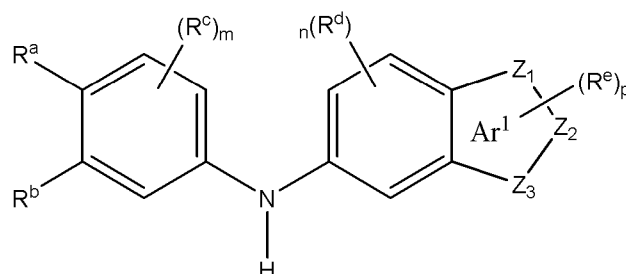
In a nineteenth embodiment, a compound of the disclosure is a compound of the following structural Formula VIIa:



Formula VIIa

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein Z₁ and Z₂ are each independently N or O; R^a is selected from C₁ to C₃ alkoxy and C₁ to C₃ alkyl; R^b is selected from H, halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; and R^c is selected from halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; wherein the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^a, R^b, and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

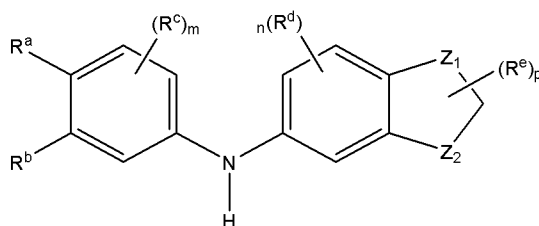
In a twentieth embodiment, a compound of the disclosure is a compound of the following structural Formula VIIb:



Formula VIIb

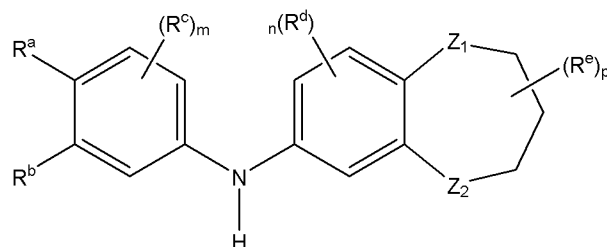
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing; wherein Ar^1 is aromatic or non-aromatic; Z_1 , Z_2 , and Z_3 are each independently N or C; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^a , R^b , and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a twenty-first embodiment, a compound of the disclosure is a compound of the following structural Formula VIIc:

**Formula VIIc**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein Z_1 and Z_2 are each independently O or N; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^a , R^b , and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a twenty-second embodiment, a compound of the disclosure is a compound of the following structural Formula VIId:

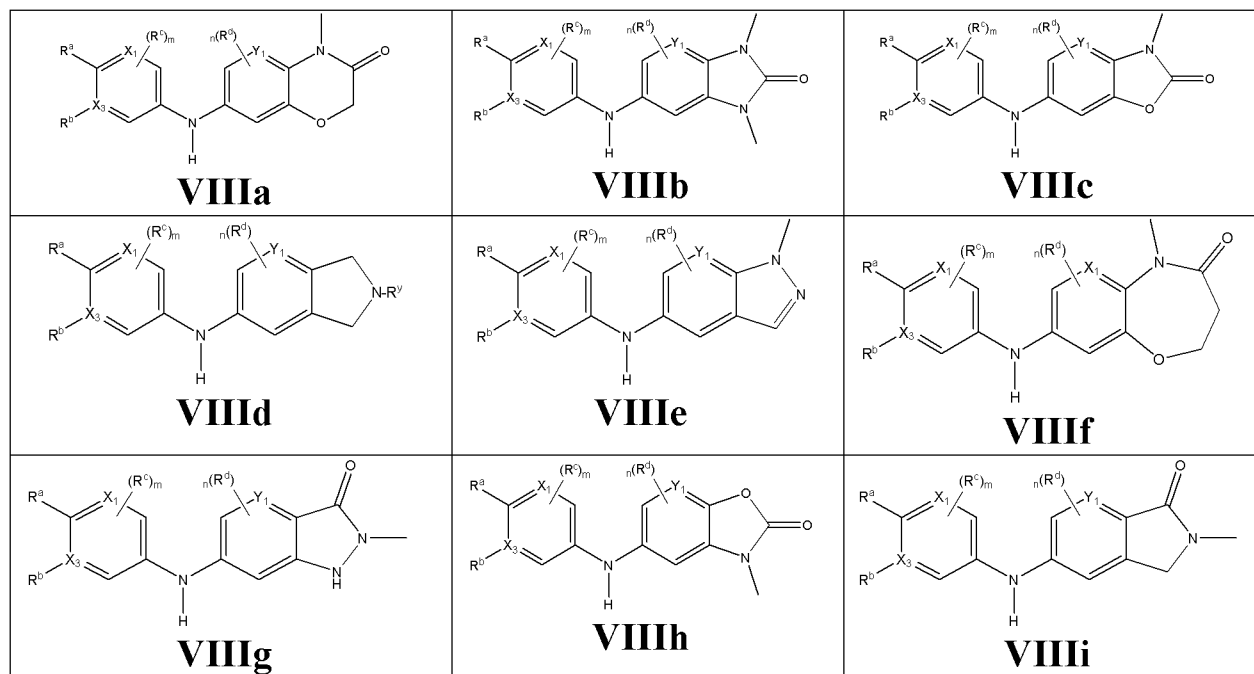
**Formula VIId**

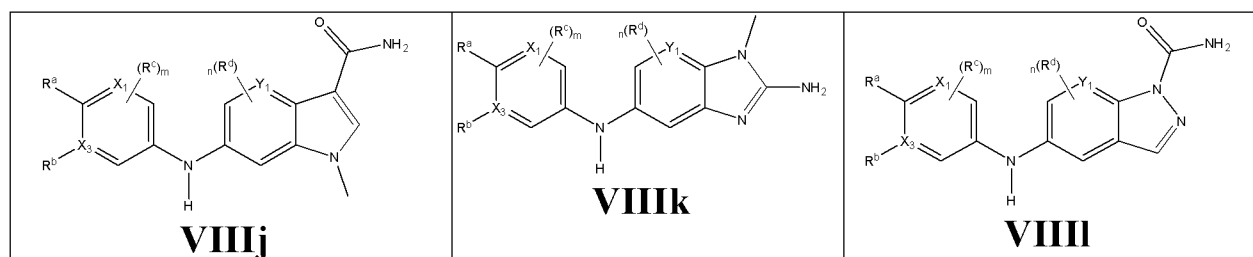
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein

5 Z_1 and Z_2 are each independently O or N; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^a , R^b , and R^c , for each occurrence, are each optionally substituted with 1 to 3

10 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

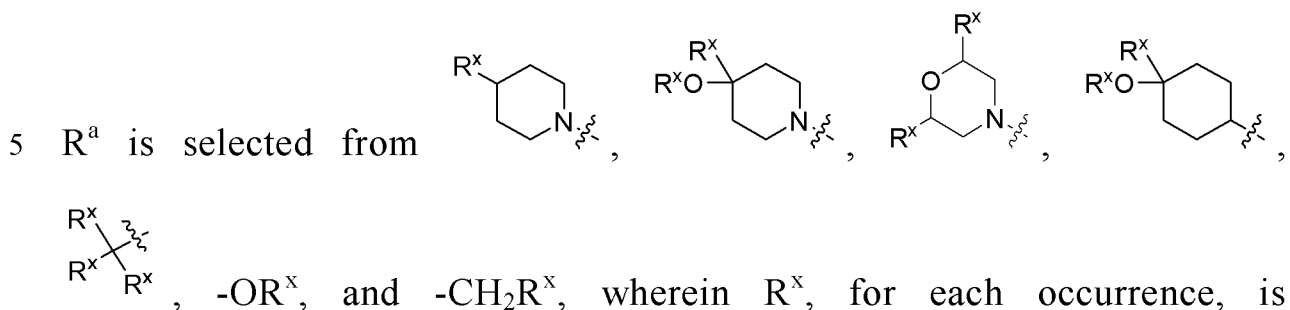
In a twenty-third embodiment, a compound of the disclosure is a compound of the following structural Formulae VIIIa-VIIIi:





a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:

X_1 and X_3 are each independently C or N;



independently selected from CF_3 , $-CH_3$, and $-CH_2CH_3$;

R^b is selected from H, halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy;

R^c is selected from halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy;

10 R^d is selected from halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy;

R^y is selected from H and C_1 to C_2 alkyl;

m is 0, 1, or 2; and

n is 0 or 1;

and all other variables not specifically defined herein are as defined in any

15 one of the preceding embodiments.

In a twenty-fourth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^a is selected from hydrogen, halogen, cyano, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_{10} cycloalkyl, 3- to 10- membered heterocyclyl, phenyl, 5- to 7- membered heteroaryl, $-C(=O)R^s$, $-C(=O)OR^s$, $-NR^pR^q$, $-OR^s$, wherein

20 the C_3 - C_{10} cycloalkyl, 3- to 10- membered heterocyclyl, phenyl, and 5- to 7- membered heteroaryl of R^a are each optionally substituted with 1-3 groups selected from halogen, OR^s , and C_1 - C_{10} alkyl optionally substituted

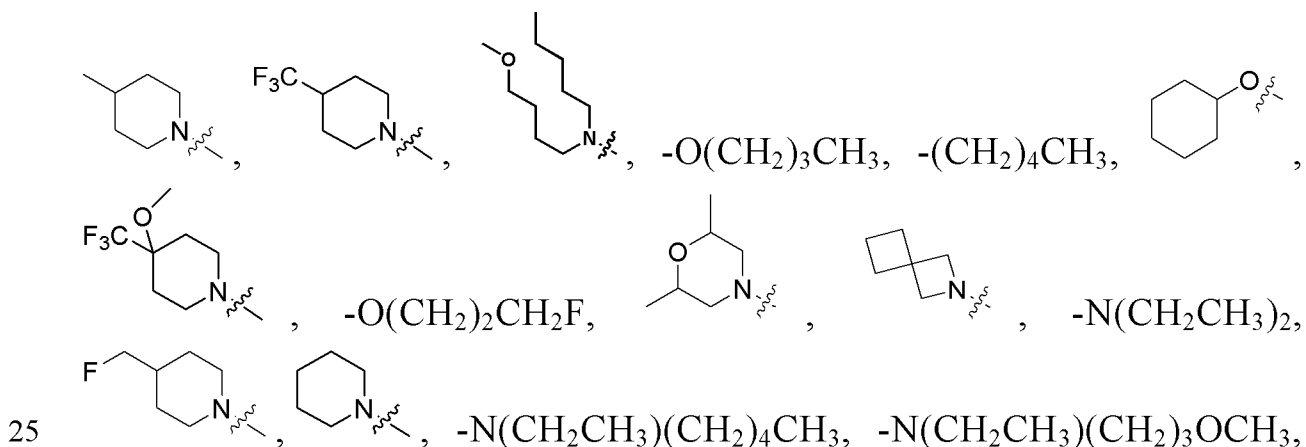
with 1 to 3 groups of halogen;

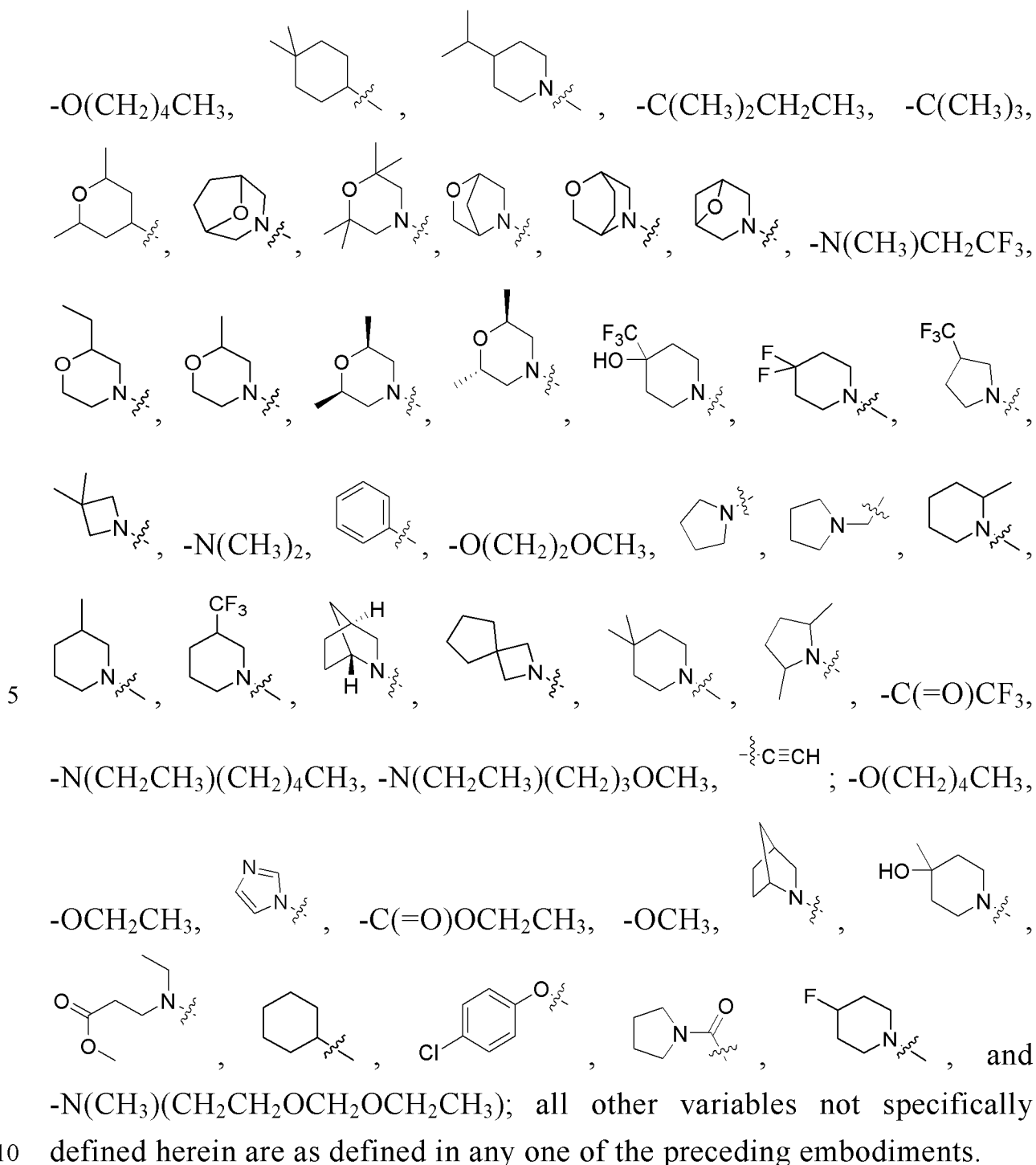
the C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, and C₂-C₁₀ alkynyl of R^a are each optionally substituted with 1 to 3 groups selected from halogen, 3- to 10-membered heterocyclyl, and -OR^s;

- 5 R^p and R^q, for each occurrence, are independently selected from hydrogen, C₃-C₁₀ cycloalkyl, and C₁-C₁₀ alkyl, wherein the C₃-C₁₀ cycloalkyl and C₁-C₁₀ alkyl of R^p and R^q are each optionally substituted with 1 to 3 groups selected from halogen, -OR^s and -C(=O)OR^s;

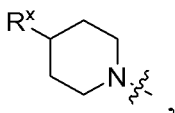
- R^s, for each occurrence, is selected from H, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 5- to 6-membered aryl, and C₁-C₁₀ alkyl optionally substituted with 1 to 3 groups selected from halogen, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, and C₁-C₆ alkoxy, wherein the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of R^s and the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of the C₁-C₁₀ alkyl of R^s are each optionally substituted with 1 to 3 groups of C₁-C₆ alkyl optionally substituted with halogen, and the C₁-C₆ alkoxy of the C₁-C₁₀ alkyl of R^s is optionally substituted with 1 to 3 groups of halogen; and all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

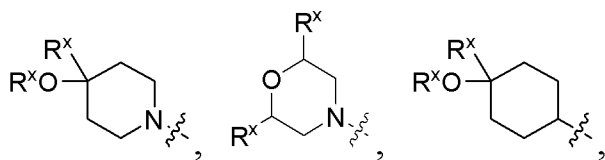
- 20 In a twenty-fifth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^a is selected from H, F, methyl,





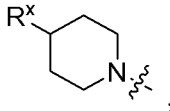
In a twenty-sixth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically

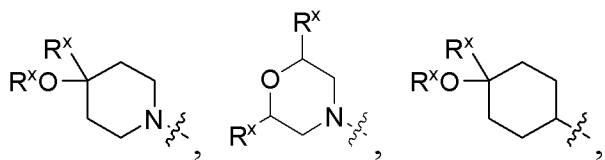
acceptable salt of this disclosure, R^a is selected from ,



5 R^x , for each occurrence, is independently selected from C_1 to C_2 alkyl optionally substituted with 1 to 3 groups of halogen; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a twenty-seventh embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically

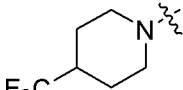
acceptable salt of this disclosure, R^a is selected from 



10 R^x , for each occurrence, is independently selected from CF_3 , $-CH_3$, and $-CH_2CH_3$; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a twenty-eighth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^b is selected from is H, halogen, C_1 to C_6 alkyl, $-NR^pR^q$, CN, C_1 - C_6 alkoxy, and 5- to 6- membered heterocyclyl optionally substituted with C_1 - C_3 alkyl optionally substituted with 1 to 3 groups selected from halogen, wherein R^p and R^q are each selected from C_1 to C_6 alkyl, and wherein the C_1 - C_6 alkyl and C_1 - C_6 alkoxy of R^b and the C_1 - C_6 alkyl of R^p and R^q are each optionally substituted with 1 to 3 groups selected from halogen; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a twenty-ninth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^b is H, methyl, $-NHCH_3$, $-N(CH_3)_2$,

-O(CH₂)₂CH₃, F, -OCH₃, -CF₃, Cl, -N(CH₃)₂, and ; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirtieth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^b is selected from halogen, C₁-C₂ alkyl, and C₁-C₂ alkoxy; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-first embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^b is selected from F, methyl, and -OCH₃; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-second embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^c, for each occurrence, is independently selected from is halogen, C₁-C₆ alkyl, -NR^pR^q, CN, and C₁-C₆ alkoxy, wherein R^p and R^q are each selected from C₁ to C₆ alkyl, and wherein the C₁-C₆ alkyl and C₁-C₆ alkoxy of R^c and the C₁-C₆ alkyl of R^p and R^q are each optionally substituted with 1 to 3 groups selected from halogen; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-third embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^c is selected from methyl, F, -OCH₃, Cl, -N(CH₃)₂, and CN; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-fourth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^c is selected from halogen, C₁-C₂ alkyl,

and C₁-C₂ alkoxy; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-fifth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^c is selected from F, methyl, and -OCH₃; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-sixth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^d, for each occurrence, is independently selected from halogen, C₁-C₆ alkyl, NO₂, CN, and C₁-C₆ alkoxy, wherein the C₁-C₆ alkyl and C₁-C₆ alkoxy of R^d are each optionally substituted with 1 to 3 groups selected from halogen; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-seventh embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^d is selected from F, methyl, Cl, NO₂, and -OCH₃; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-eighth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^d is selected from halogen, C₁-C₂ alkyl, and C₁-C₂ alkoxy; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a thirty-ninth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^d is selected from F, methyl, and -OCH₃; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

In a fortieth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^e, for each occurrence, is independently

selected from halogen, cyano, C₁-C₁₀ alkyl, phenyl, 5- to 7-membered heteroaryl, 3- to 10-membered heterocyclyl, C₃-C₁₀ cycloalkyl, -C(=O)R^s, C₂-C₁₀ alkenyl, =O, =NR^p; -C(=O)OR^s, -C(=O)NR^pR^q, -NR^pR^q, and -NR^pC(=O)R^s, wherein

5 the C₁-C₁₀ alkyl and C₂-C₁₀ alkenyl of R^e are each optionally substituted with 1 to 3 groups selected from 5- to 7-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, -OR^s, -C(=O)NR^pR^q, -NR^pC(=O)NR^qR^r, and -NR^pR^q;

10 the 3- to 10-membered heterocyclyl and C₃-C₁₀ cycloalkyl of R^e and the 3- to 10-membered heterocyclyl and C₃-C₁₀ cycloalkyl of the C₁-C₁₀ alkyl and C₂-C₁₀ alkenyl of R^e, are each optionally substituted with 1 to 3 groups selected from =O and C₁-C₆ alkyl optionally substituted with 1 to 3 groups selected from halogen and -OR^s;

15 the phenyl and 5- to 7-membered heteroaryl of R^e and the 5- to 7-membered heteroaryl of the C₁-C₁₀ alkyl and C₂-C₁₀ alkenyl of R^e are each optionally substituted with 1 to 3 groups selected from C₁-C₆ alkyl optionally substituted with 1 to 3 groups selected from halogen and -OR^s;

20 R^p, R^q, and R^r, for each occurrence, are independently selected from hydrogen, C₃-C₁₀ cycloalkyl, and C₁-C₁₀ alkyl, wherein the C₃-C₁₀ cycloalkyl and C₁-C₁₀ alkyl of R^p, R^q, and R^r are each optionally substituted with 1 to 3 groups selected from halogen, -OR^s and -C(=O)OR^s;

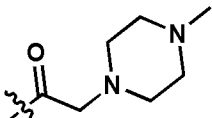
25 R^s, for each occurrence, is independently selected from H, C₃-C₁₀ cycloalkyl, 3- to 10- membered heterocyclyl, and C₁-C₁₀ alkyl optionally substituted with 1 to 3 groups selected from halogen, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, and C₁-C₆ alkoxy, wherein

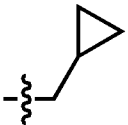
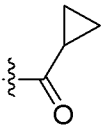
30 the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of R^s and the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of the C₁-C₁₀ alkyl of R^s are each optionally substituted with 1 to 3 groups of C₁-C₆ alkyl optionally substituted by halogen, and the C₁-C₆ alkoxy of

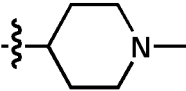
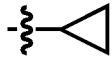
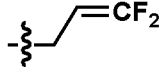
the C₁-C₁₀ alkyl of R^s is optionally substituted with 1 to 3 groups of halogen; and

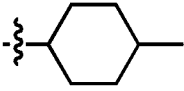
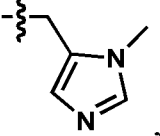
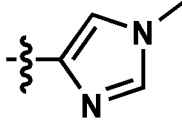
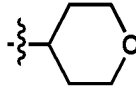
all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

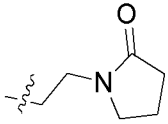
- 5 In a forty-first embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^e, for each occurrence, is selected from methyl, ethyl, =O, -(CH₂)₃OCH₃, -(CH₂)₂OCH₃, -CH₂C(=O)NH₂, -(CH₂)₂C(=O)NH₂, -C(=O)C(CH₃)₃, -C(=O)NHC(CH₃)₃,
 10 -(CH₂)₂NHC(=O)NH₂, -(CH₂)₃NHCH₃, -(CH₂)₂NHCH₃, -(CH₂)₃C(=O)NH₂,

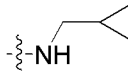
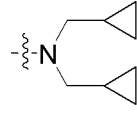
-(CH₂)₂N(CH₃)₂, -(CH₂)₂OH, , -C(=O)CH₃, -(CH₂)₂NH₂,

, -C(=O)OC(CH₃)₃, , -C(CH₃)₃, -(CH₂)₂O(CH₂)₂OCH₃, Bn

(benzyl), -(CH₂)₃N(CH₃)₂, , , -CH(CH₃)₂, ,

, , , , =NH, =NCH₃, -C(=O)OH,

- 15 -C(=O)CF₃, -C(=O)NHCH₂CH₃, -NHC(=O)CH₃, ,

-N(CH₃)(CH₂)₂OCH₂OCH₂CH₃, -NH₂, -C(=O)NH₂, , ,

-N(CH₃)₂, -NHCH₂CH₃, and ; all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

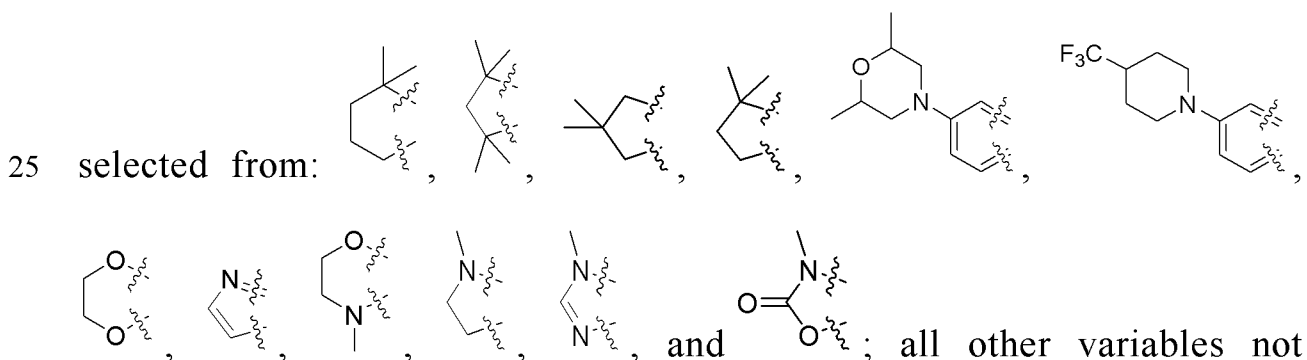
- In a forty-second embodiment, in a compound, tautomer, a solvate or
 20 stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^e is selected from =O, -C(=O)NR^pR^q,

and C₁-C₆ alkyl, wherein the C₁-C₆ alkyl is optionally substituted with 1 to 3 groups selected from C₁-C₃ alkoxy, -C(=O)NR^PR^Q, and -NR^PR^Q, wherein R^P and R^Q are each selected from H and C₁-C₃ alkyl; all other variables not specifically defined herein are as defined in any one of the preceding
5 embodiments.

In a forty-third embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^e is selected from C₁-C₂ alkyl, =O, and -C(=O)NH₂; all other variables not specifically defined herein are as
10 defined in any one of the preceding embodiments.

In a forty-fourth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^a and R^b join to form a 5- to 6-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring
15 optionally substituted with 1 to 3 groups selected from =O, C₁-C₆ alkyl, and 5- to 7-membered heterocyclyl, wherein the C₁-C₆ alkyl is optionally substituted with 1 to 3 groups of halogen, and the 5- to 7-membered heterocyclyl is optionally substituted with 1 to 3 groups of C₁-C₃ alkyl optionally substituted with 1 to 3 groups of halogen; all other variables not
20 specifically defined herein are as defined in any one of the preceding embodiments.

In a forty-fifth embodiment, in a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt of this disclosure, R^a and R^b join to form a structure

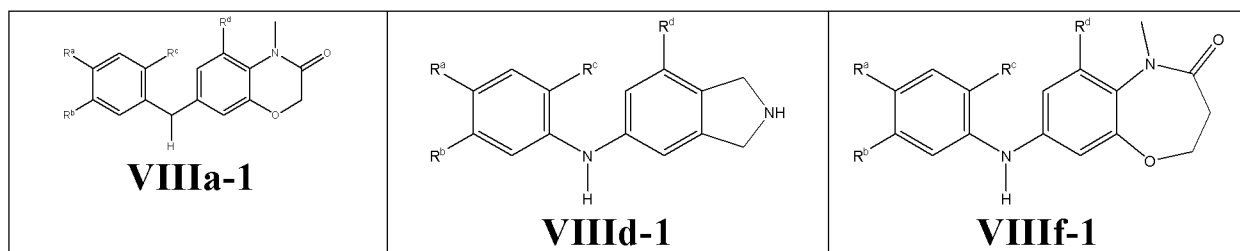


; all other variables not specifically defined herein are as defined in any one of the preceding

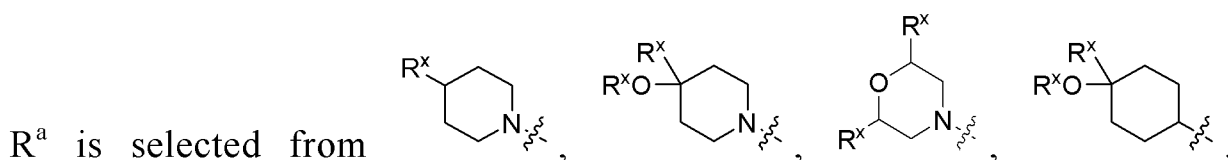
embodiments.

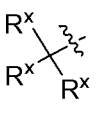
In a forty-sixth embodiment, a compound of the disclosure is a compound of the following structural formulae VIIId-1, VIIIf-1, and VIIIf-1:

5



a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:



10 R^x is selected from , $-OR^x$, and $-CH_2R^x$, wherein R^x , for each occurrence, is

independently selected from CF_3 and C_1 to C_2 alkyl;

R^b is selected from H, halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy;

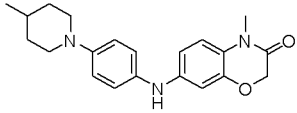
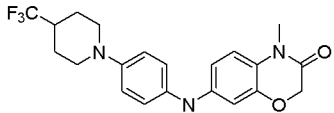
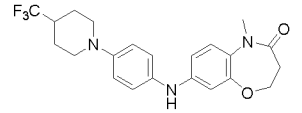
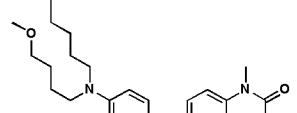
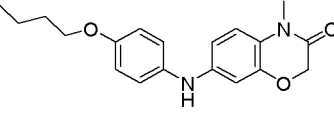
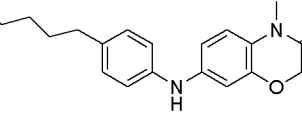
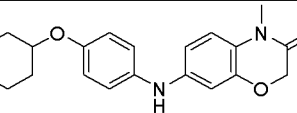
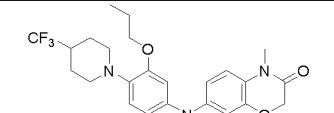
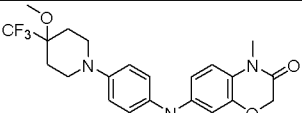
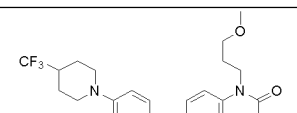
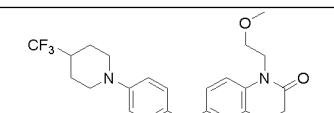
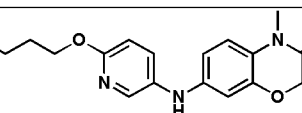
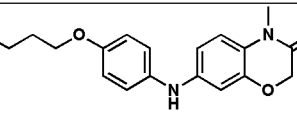
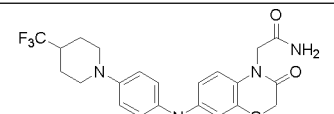
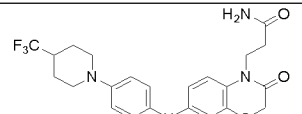
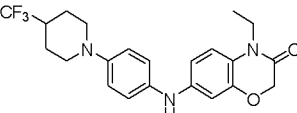
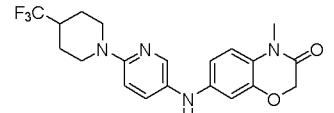
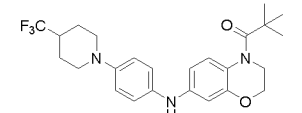
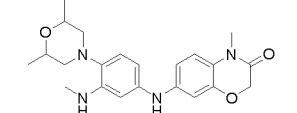
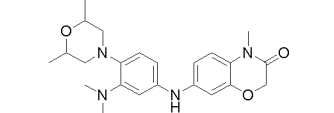
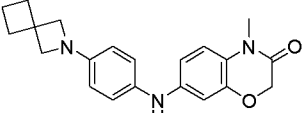
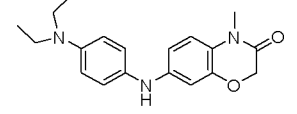
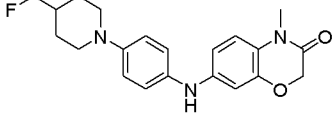
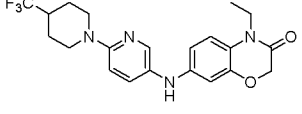
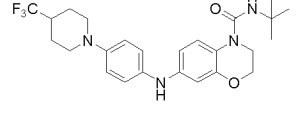
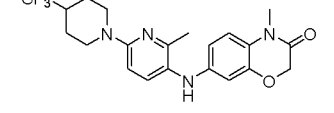
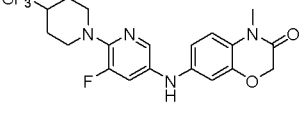
R^c is selected from halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy; and

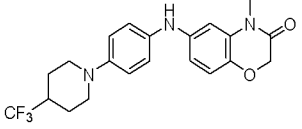
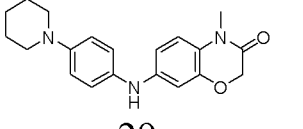
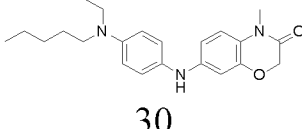
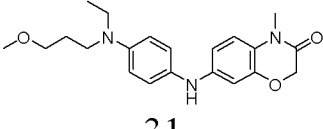
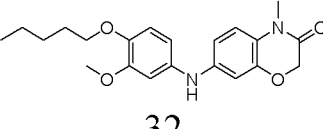
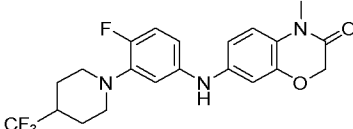
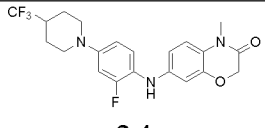
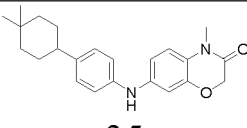
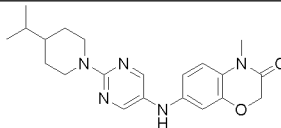
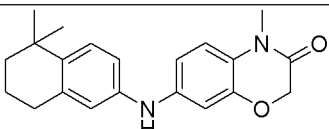
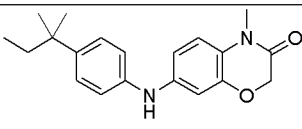
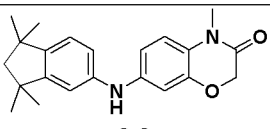
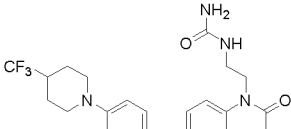
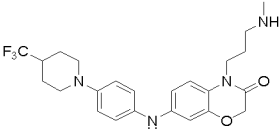
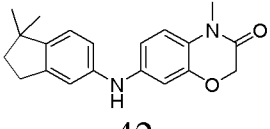
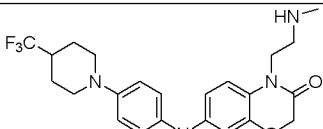
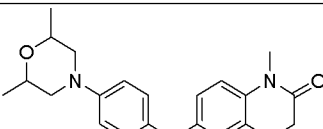
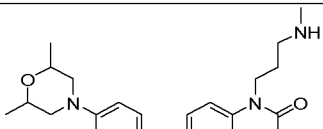
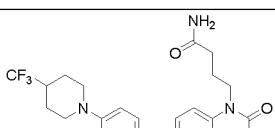
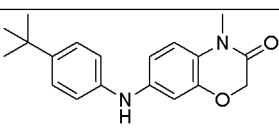
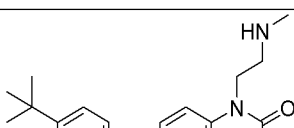
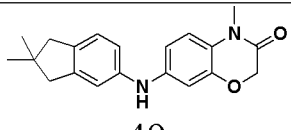
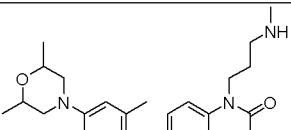
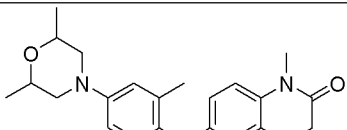
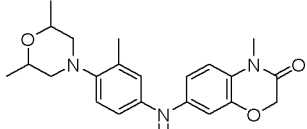
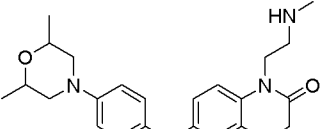
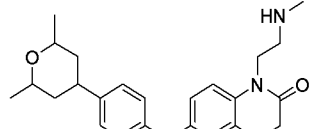
R^d is selected from halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy; and

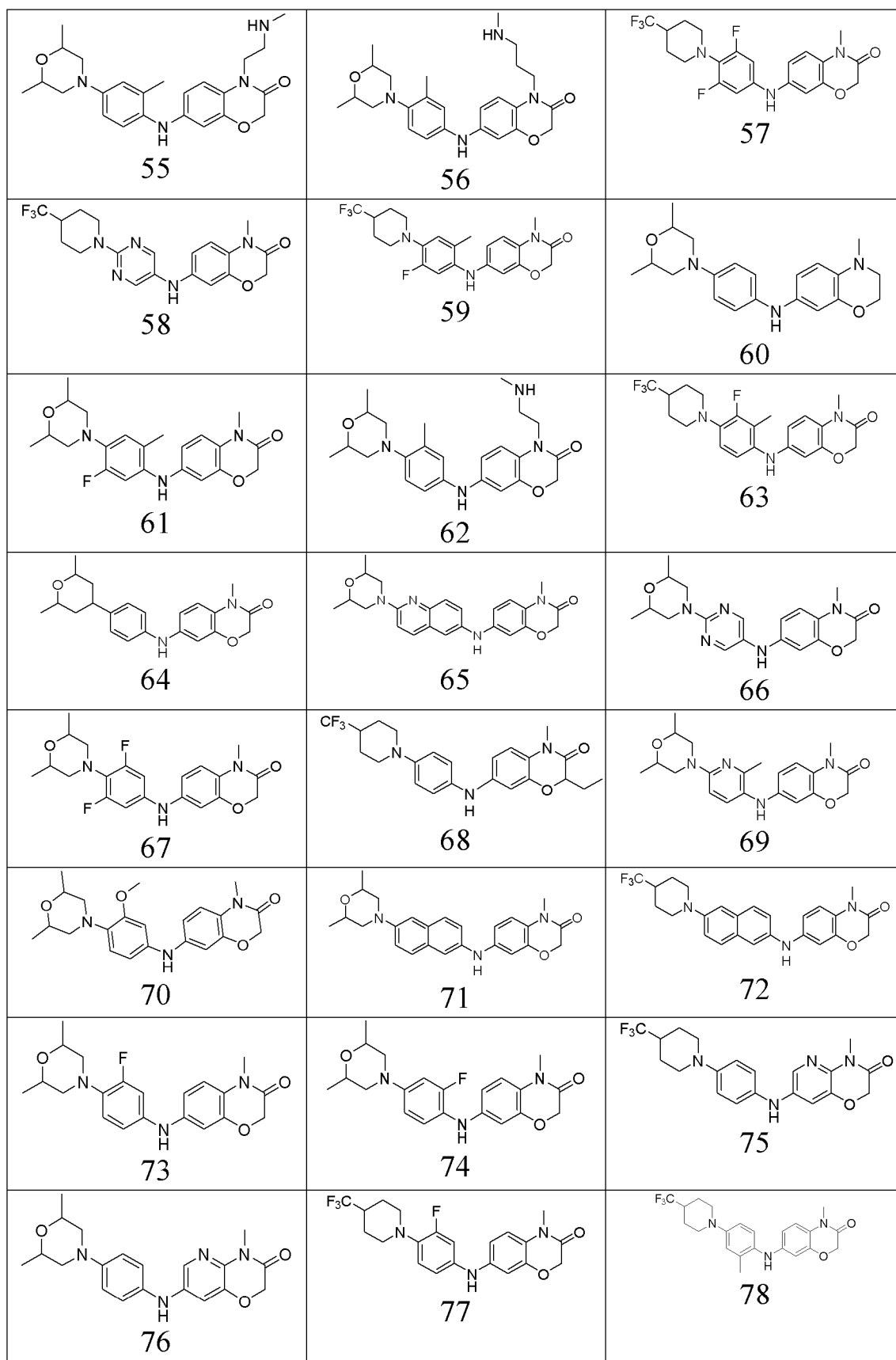
15 all other variables not specifically defined herein are as defined in any one of the preceding embodiments.

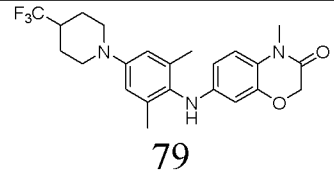
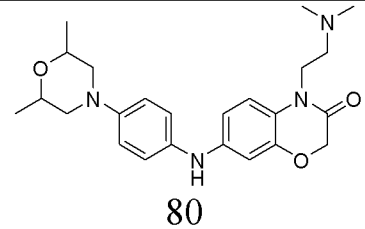
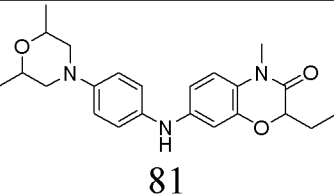
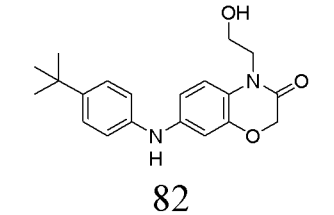
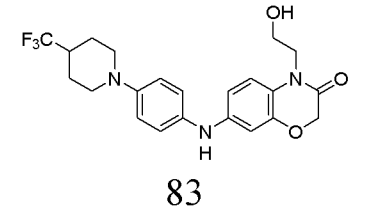
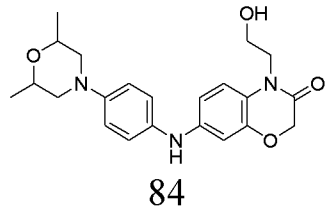
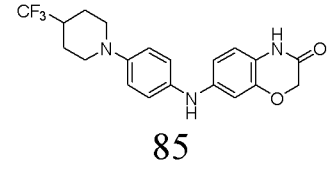
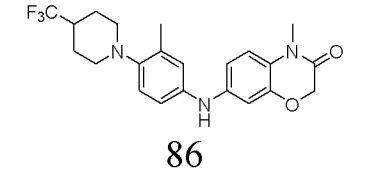
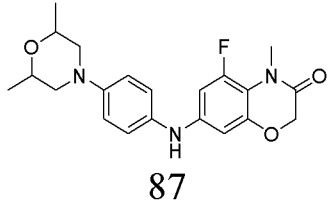
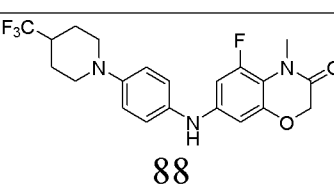
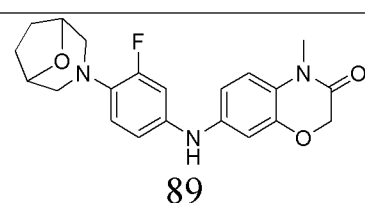
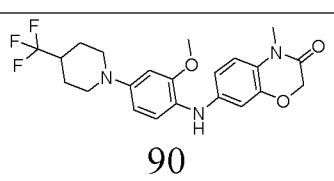
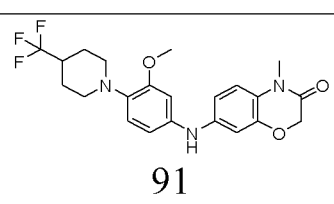
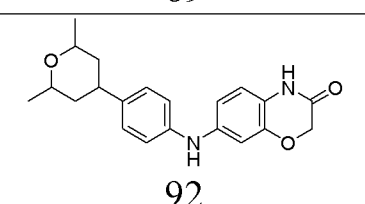
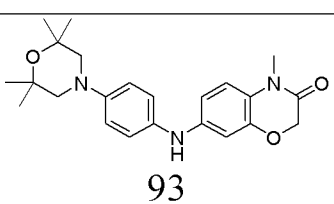
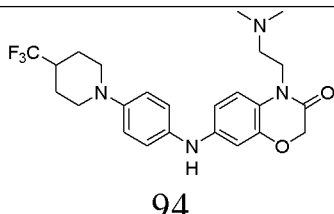
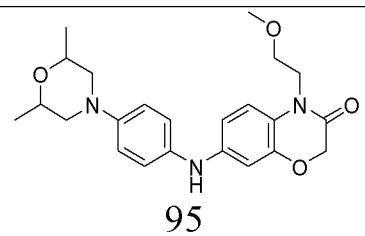
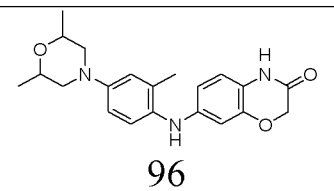
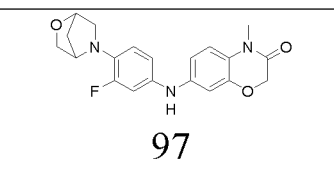
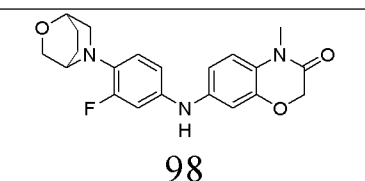
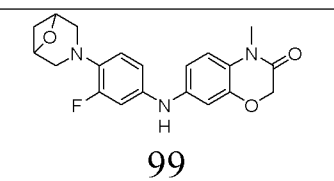
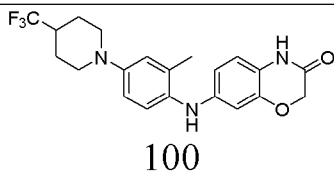
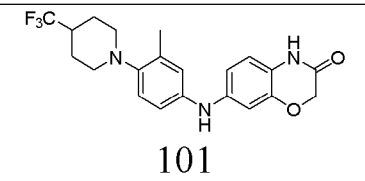
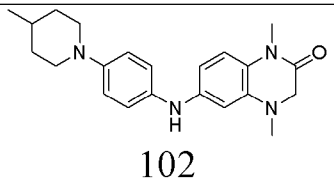
In certain embodiments, the at least one compound of the disclosure is selected from Compounds 1 to 659 depicted in Table 1, a tautomer thereof, a solvate or stereoisomer of the compound depicted in Table 1 or the
20 tautomer, or a pharmaceutically acceptable salt of the foregoing.

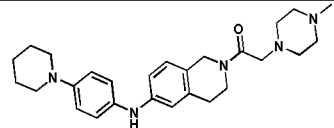
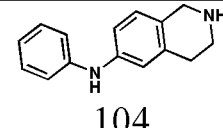
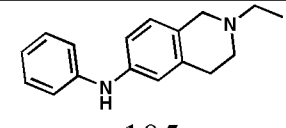
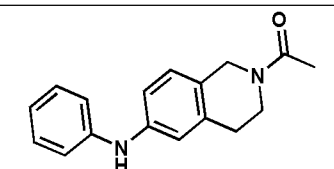
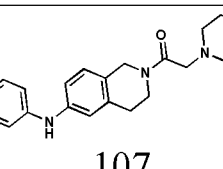
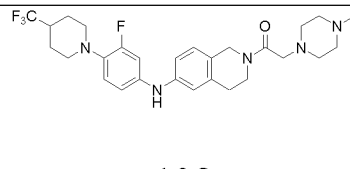
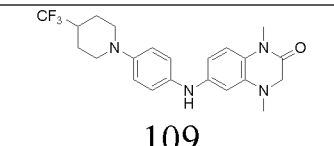
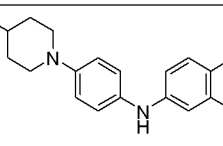
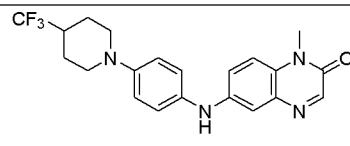
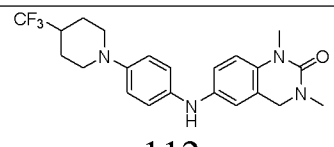
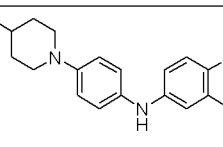
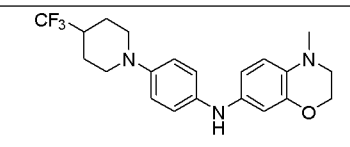
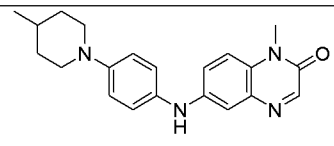
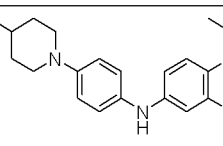
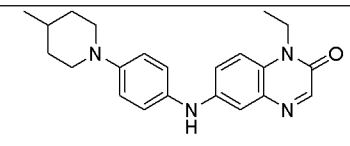
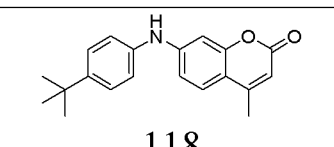
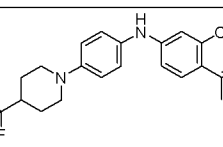
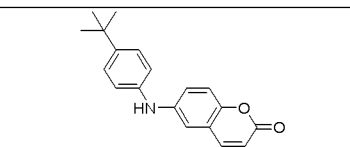
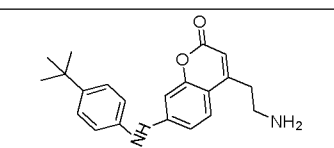
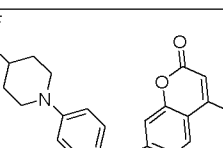
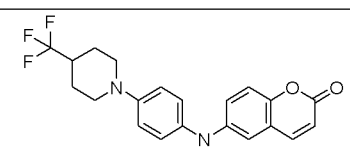
Table 1. Compounds 1 to 659

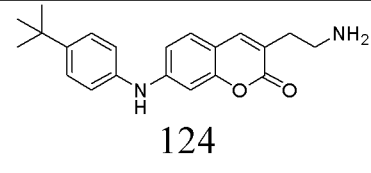
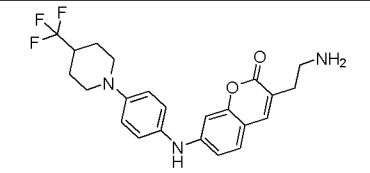
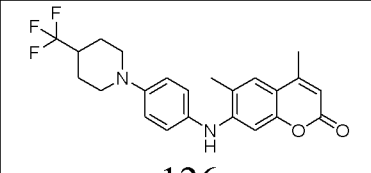
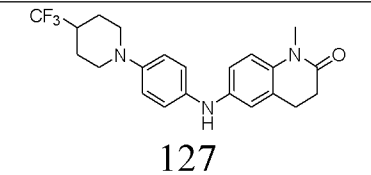
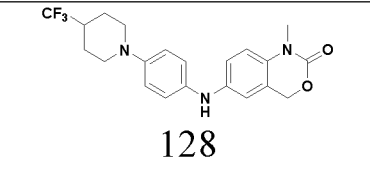
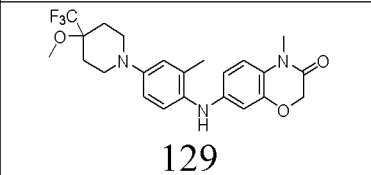
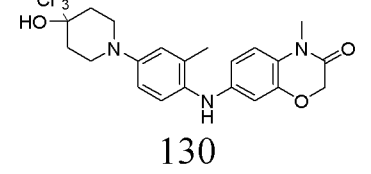
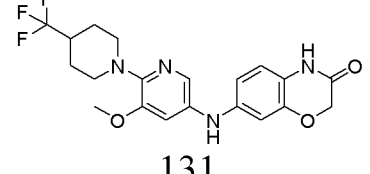
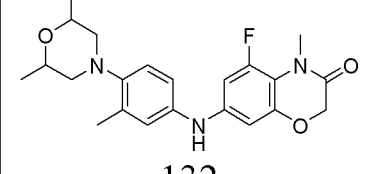
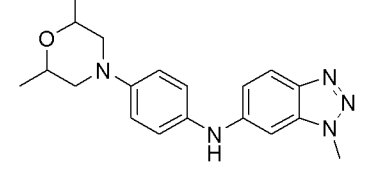
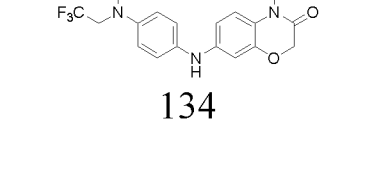
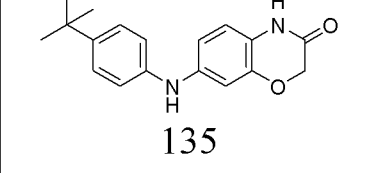
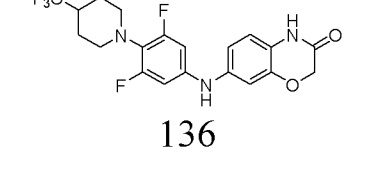
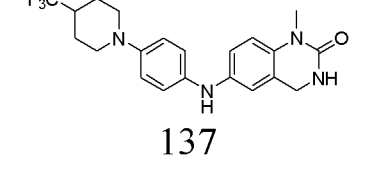
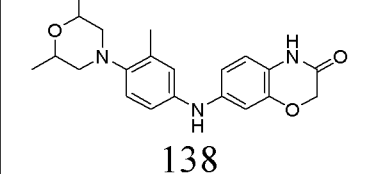
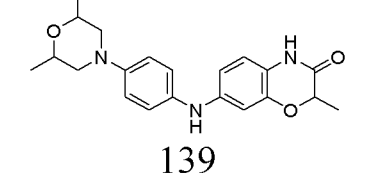
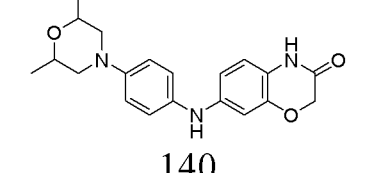
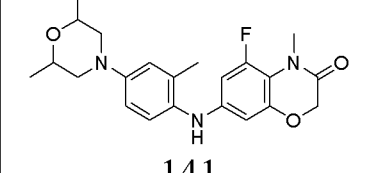
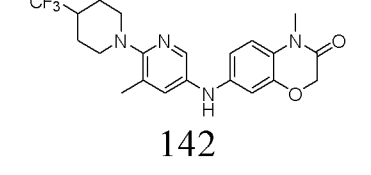
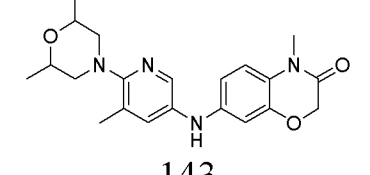
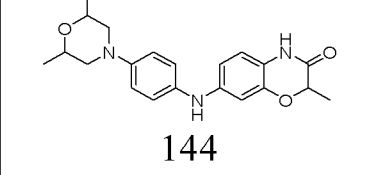
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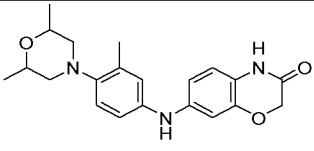
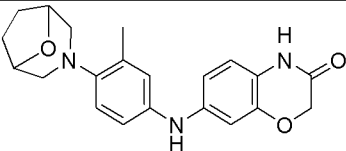
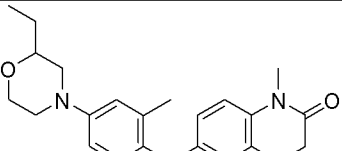
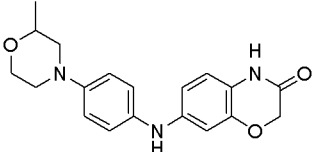
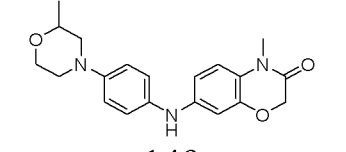
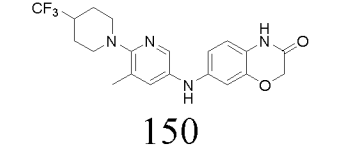
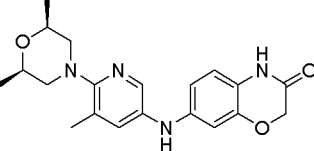
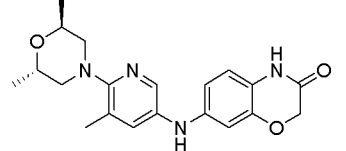
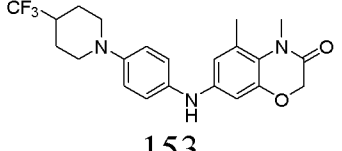
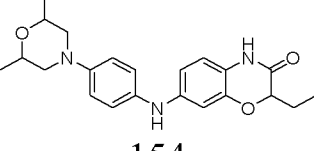
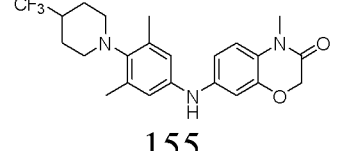
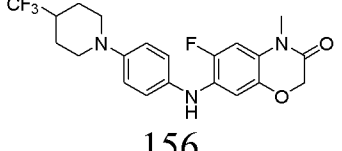
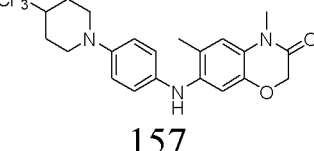
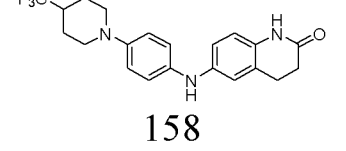
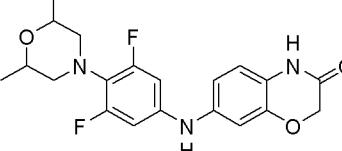
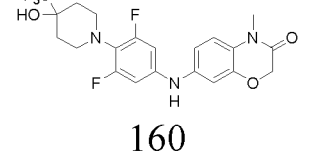
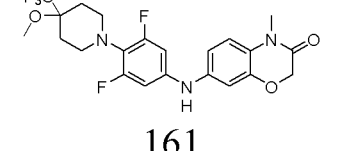
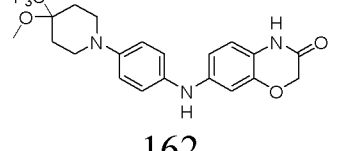
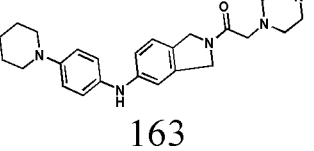
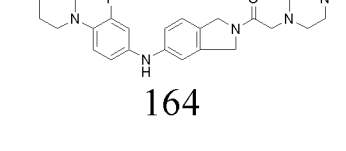
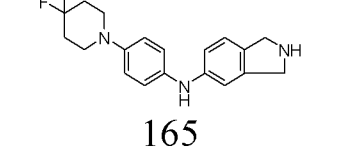
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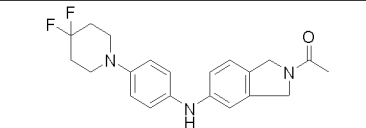
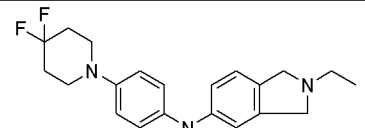
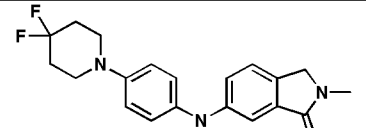
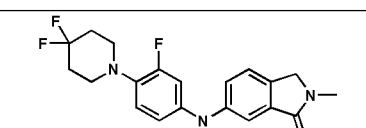
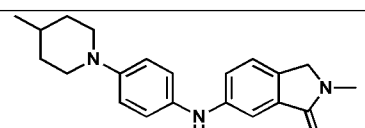
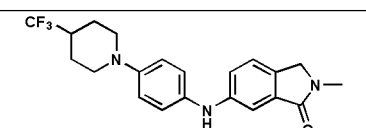
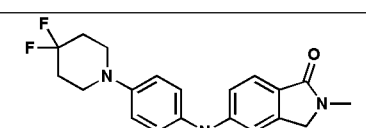
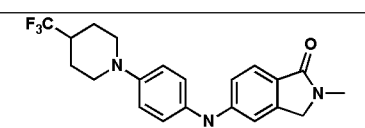
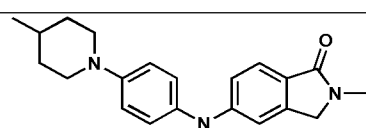
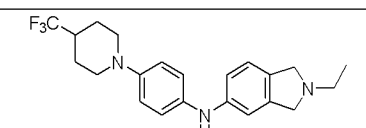
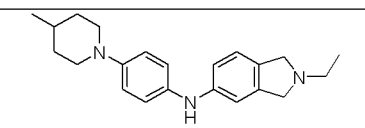
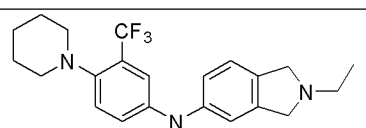
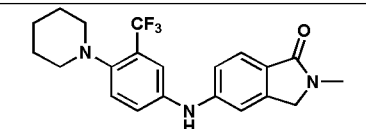
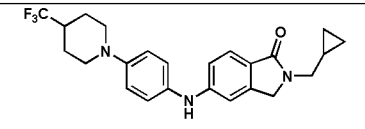
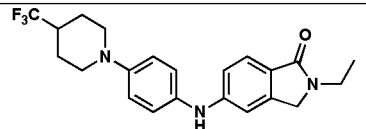
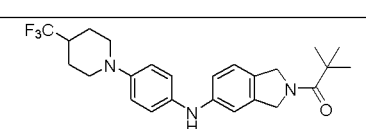
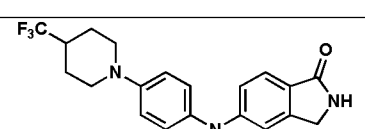
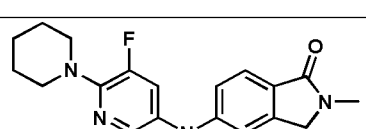
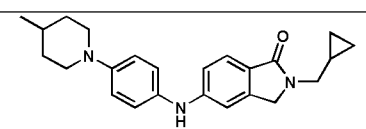
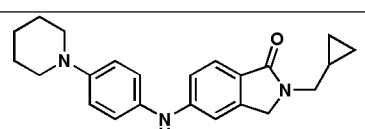
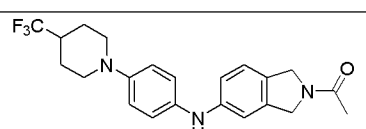
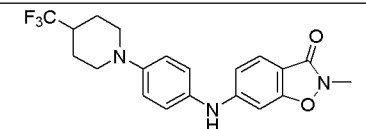
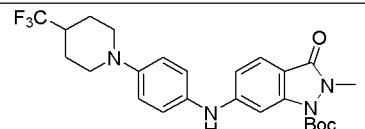
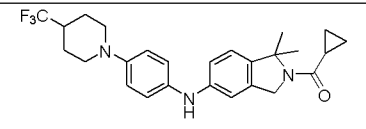
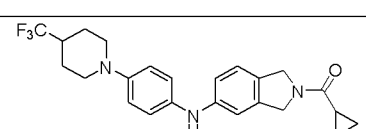
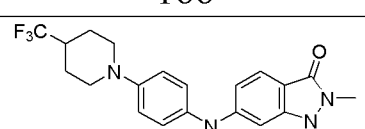
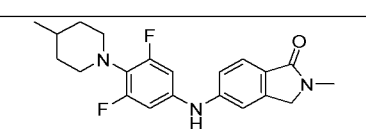


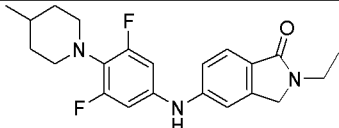
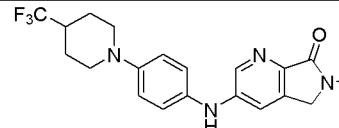
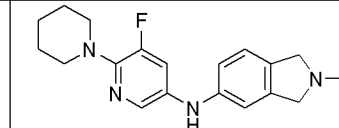
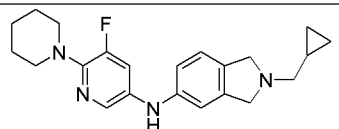
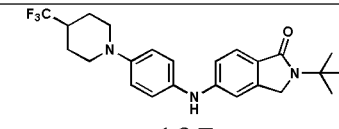
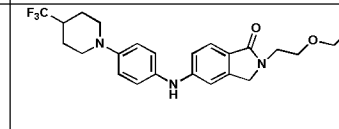
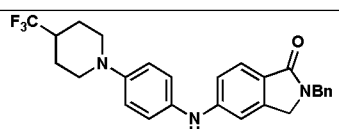
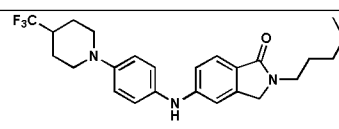
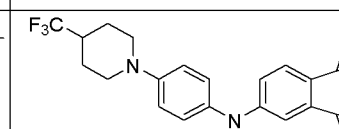
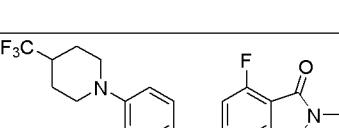
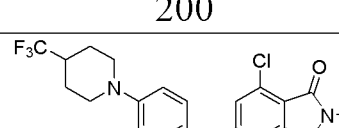
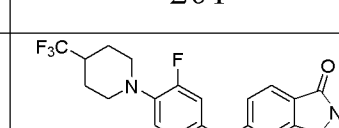
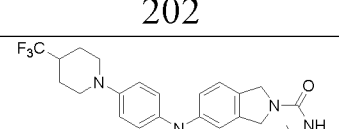
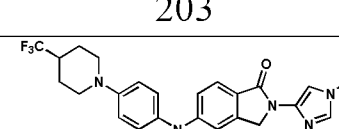
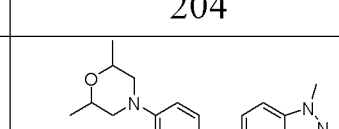
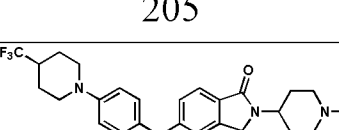
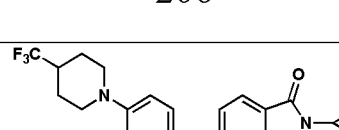
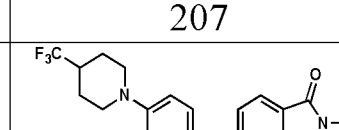
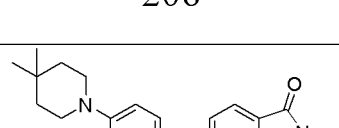
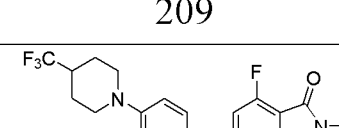
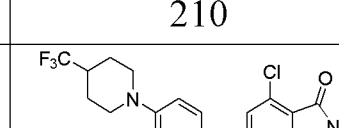
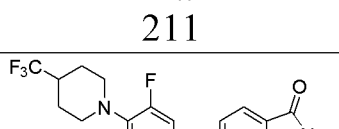
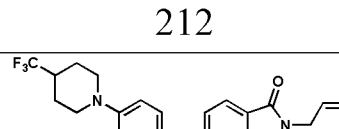
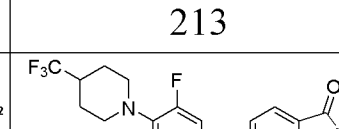
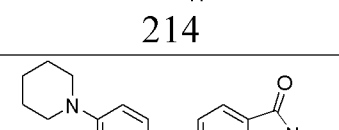
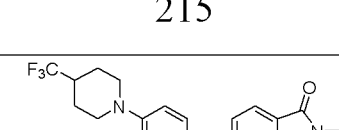
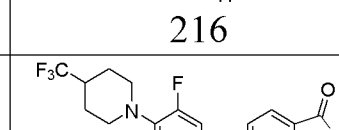
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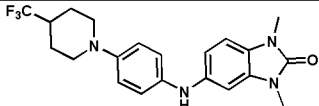
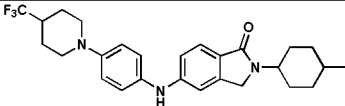
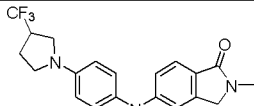
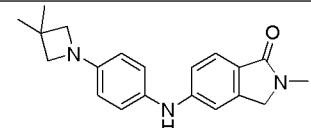
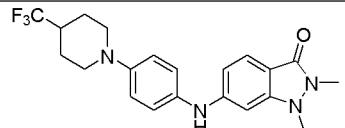
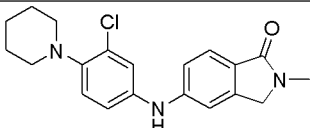
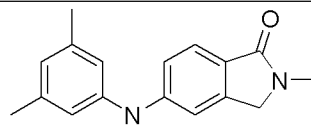
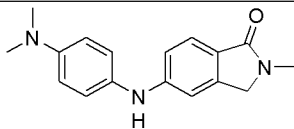
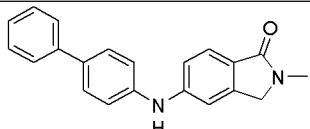
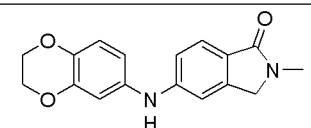
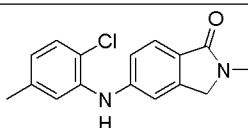
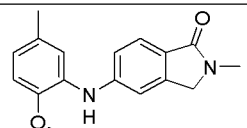
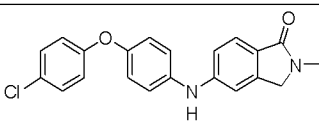
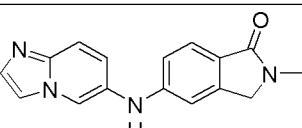
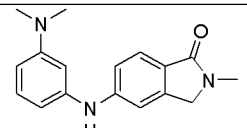
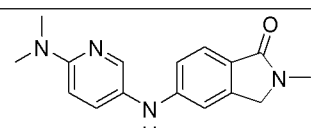
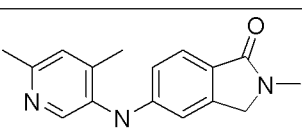
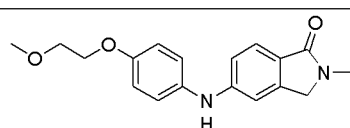
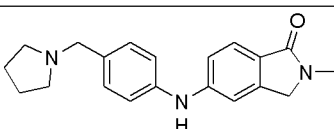
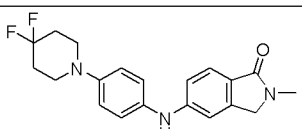
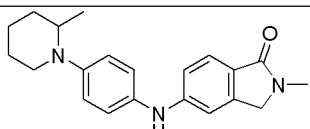
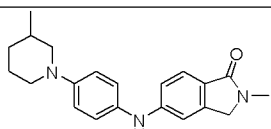
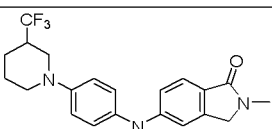
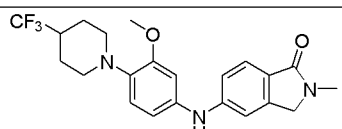
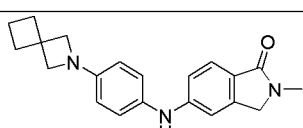
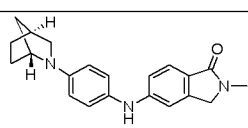
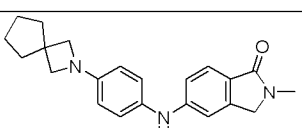
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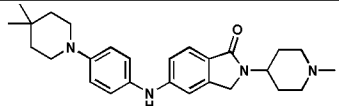
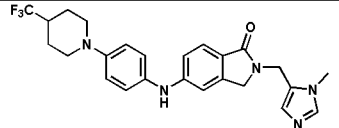
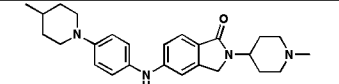
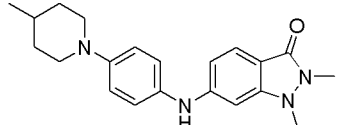
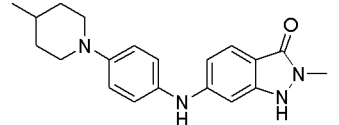
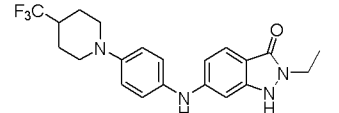
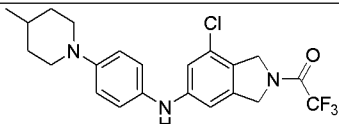
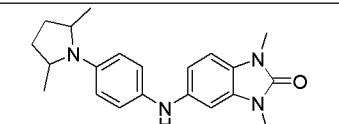
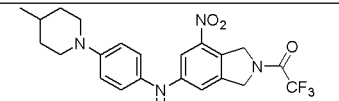
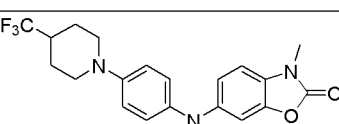
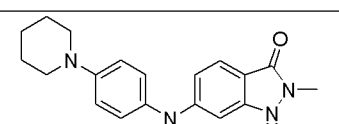
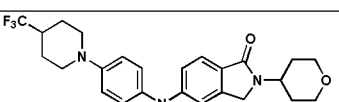
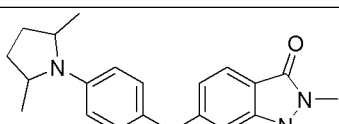
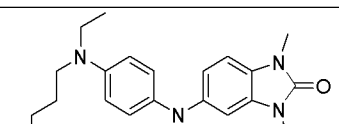
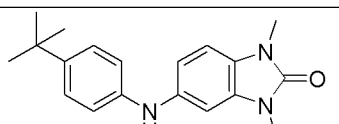
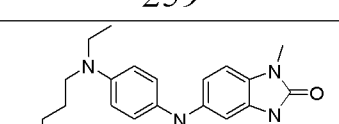
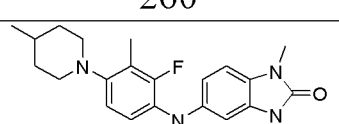
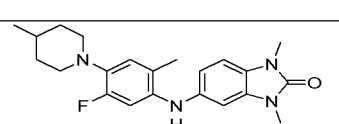
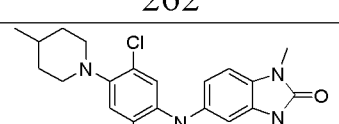
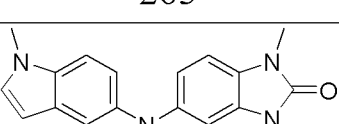
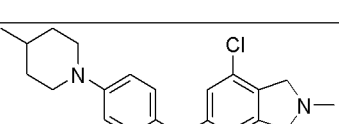
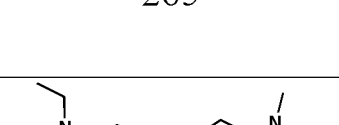
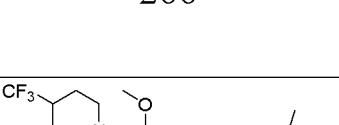
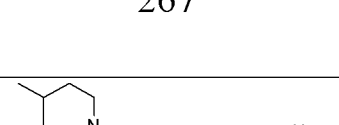
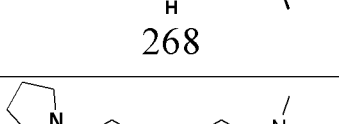
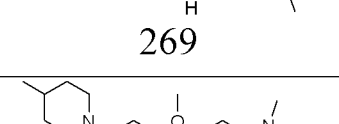
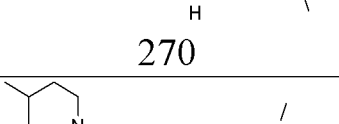
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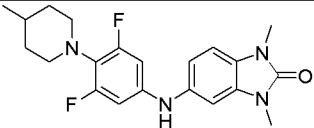
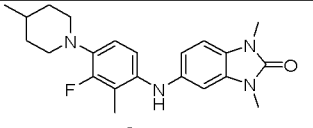
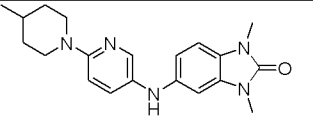
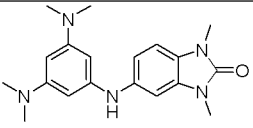
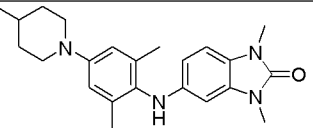
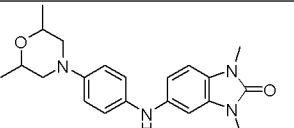
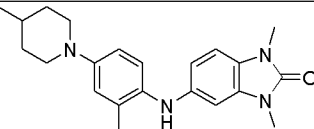
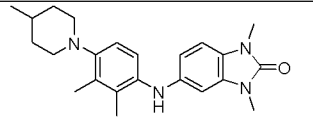
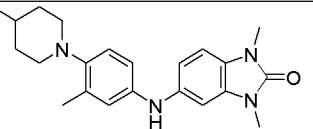
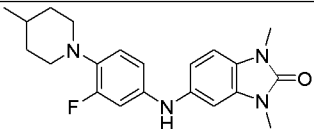
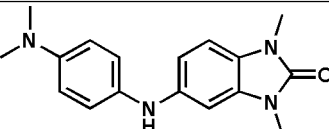
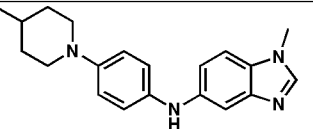
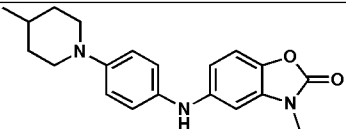
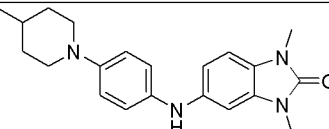
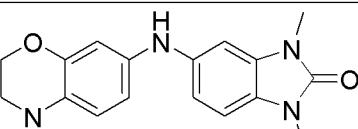
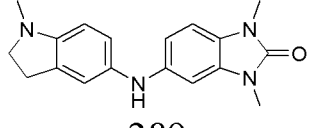
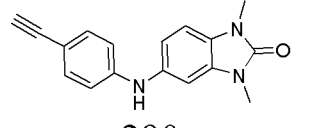
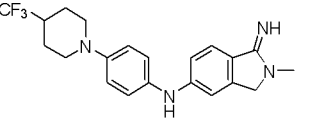
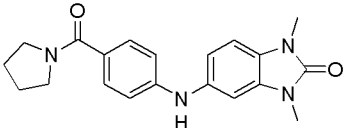
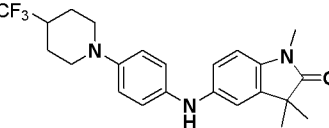
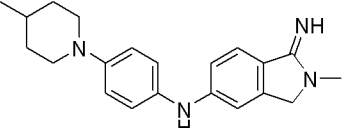
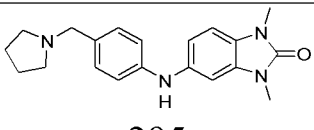
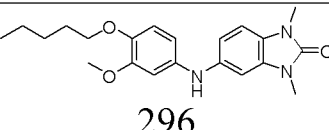
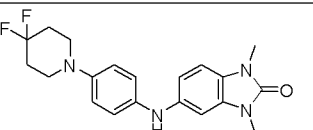
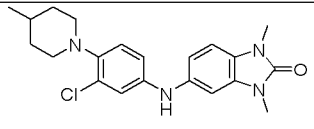
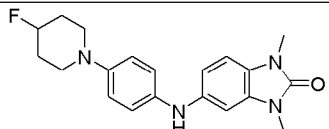
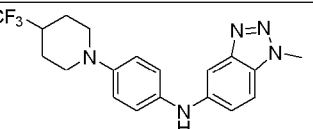
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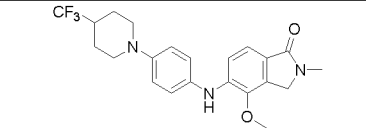
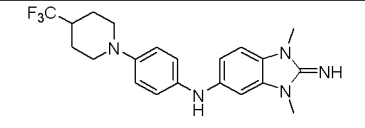
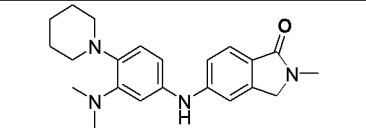
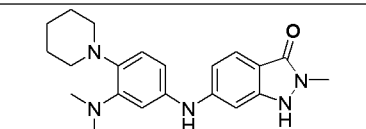
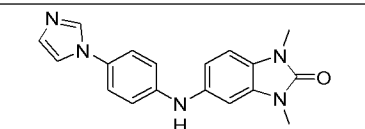
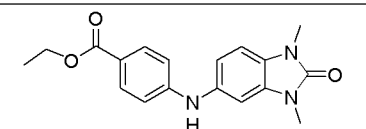
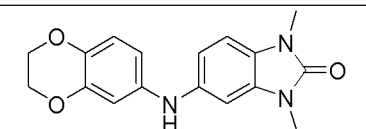
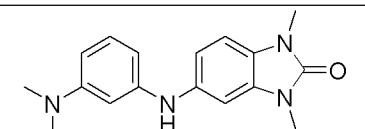
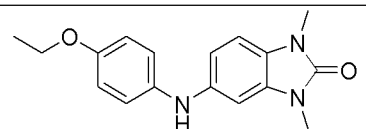
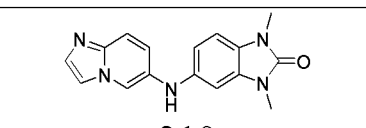
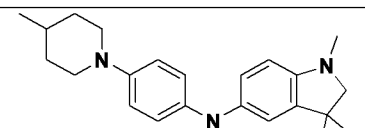
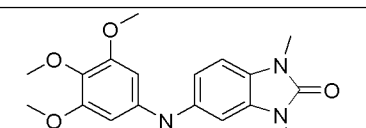
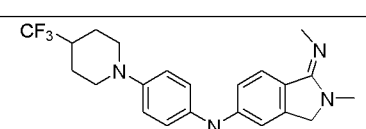
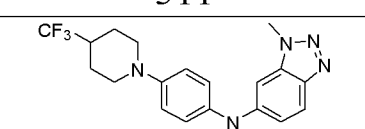
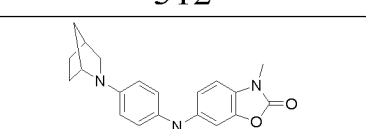
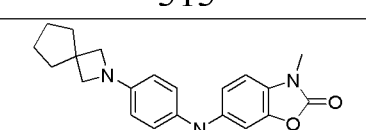
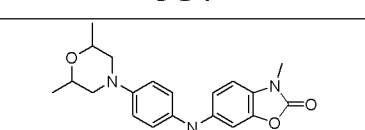
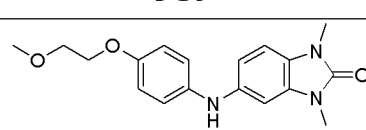
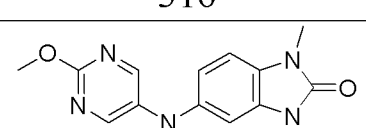
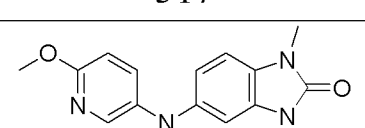
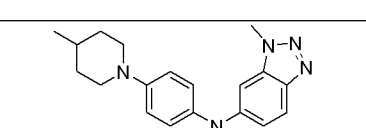
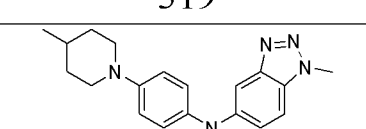
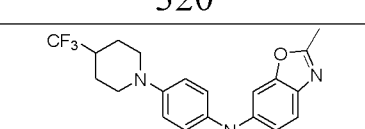
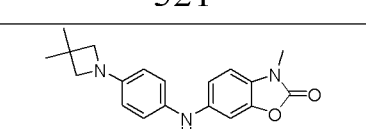
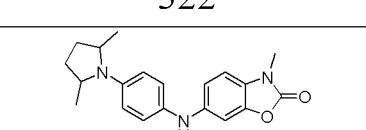
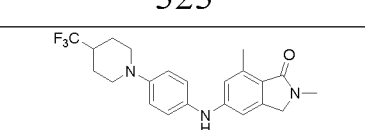
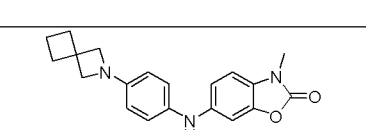
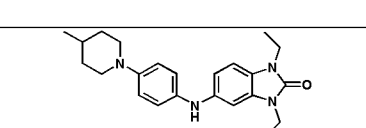
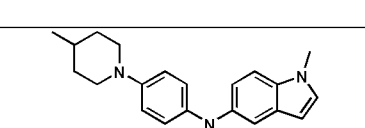
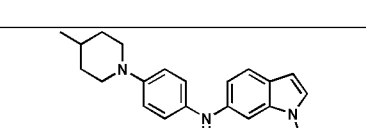
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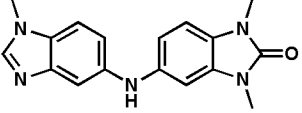
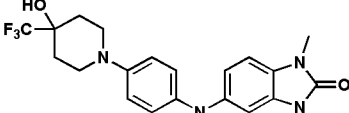
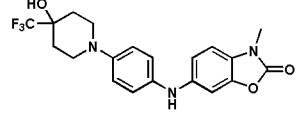
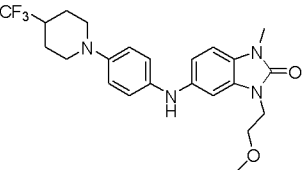
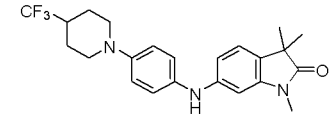
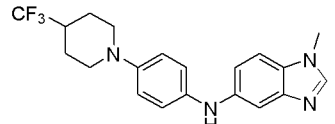
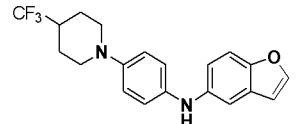
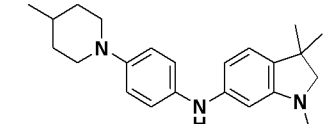
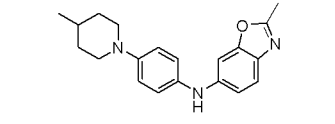
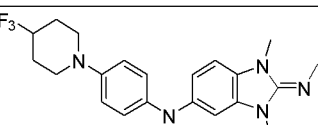
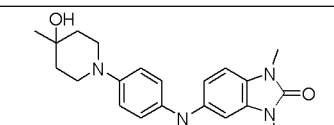
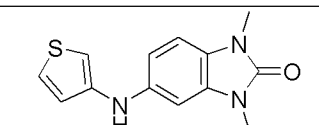
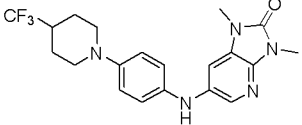
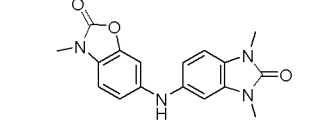
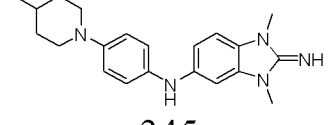
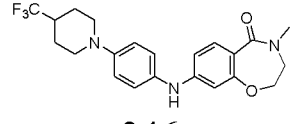
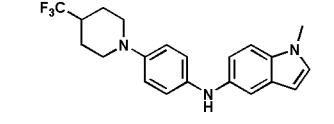
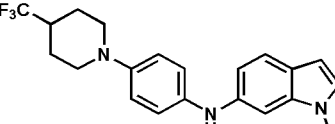
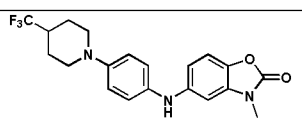
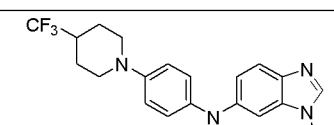
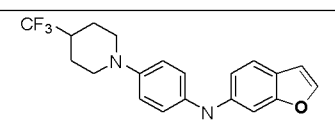
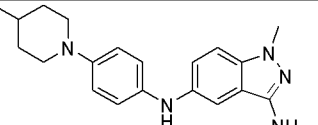
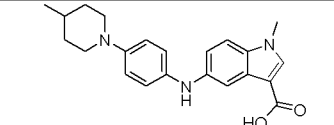
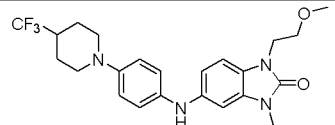
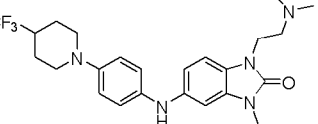
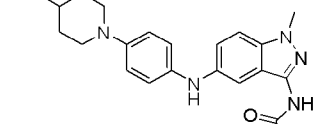
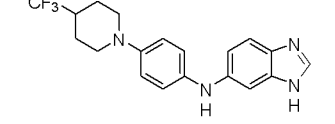
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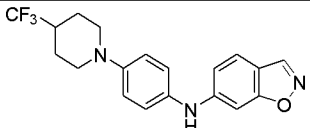
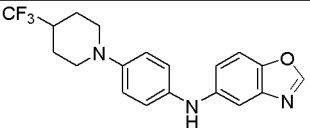
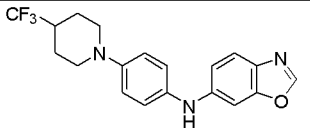
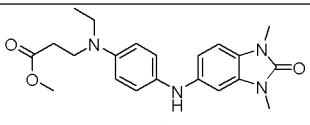
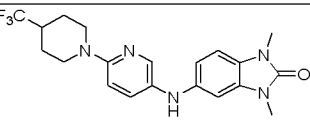
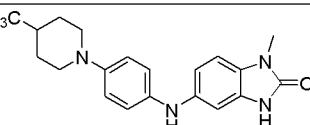
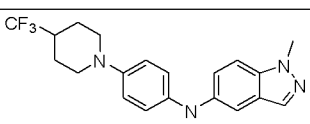
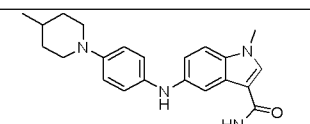
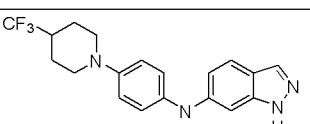
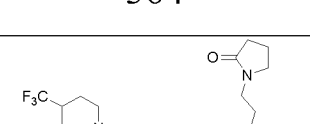
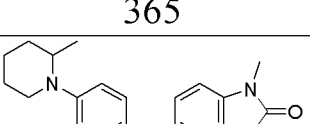
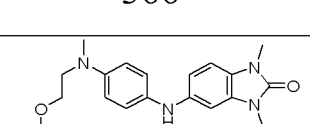
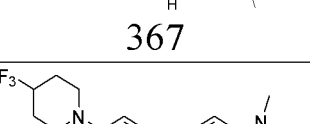
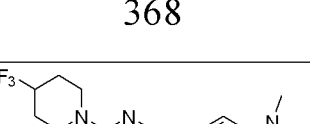
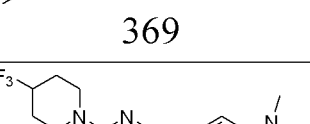
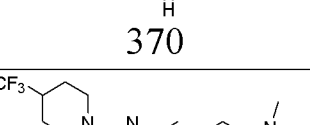
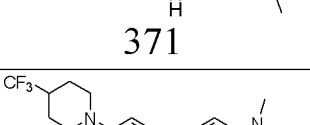
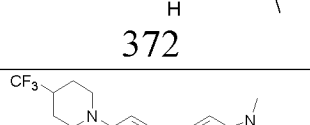
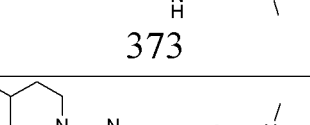
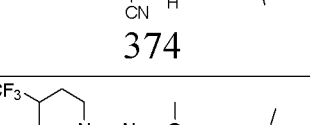
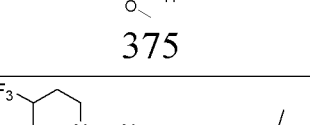
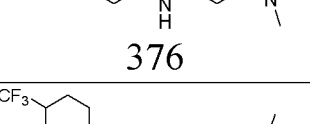
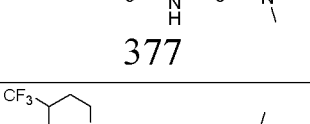
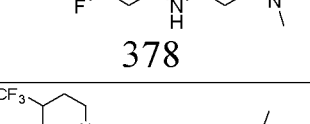
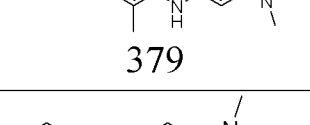
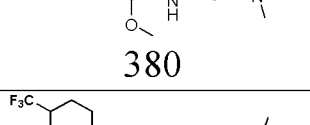
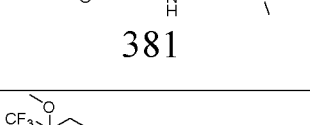
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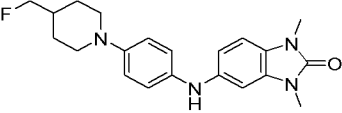
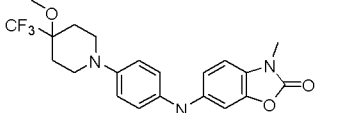
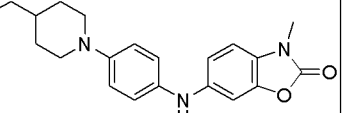
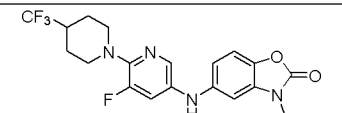
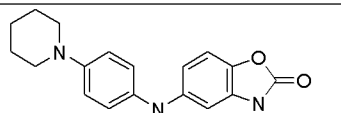
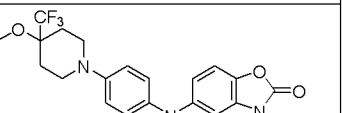
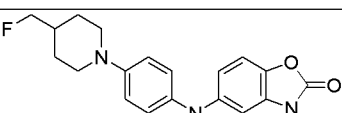
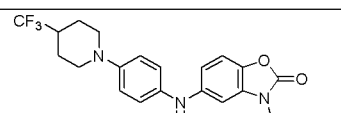
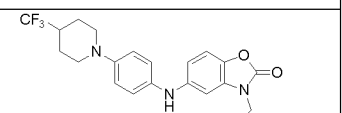
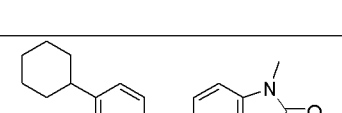
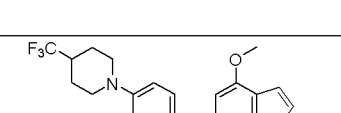
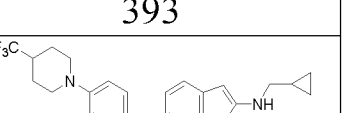
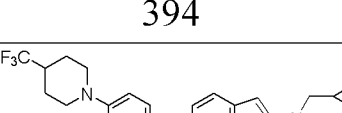
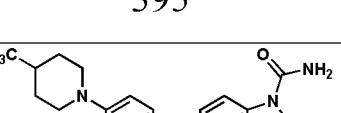
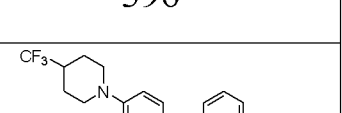
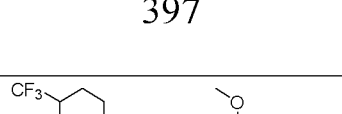
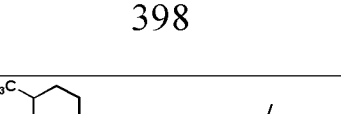
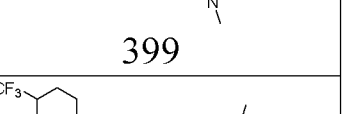
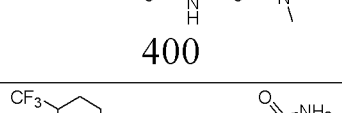
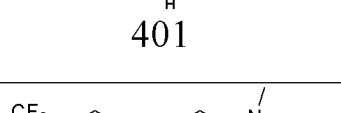
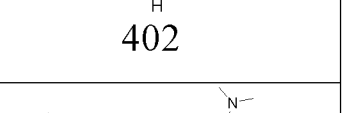
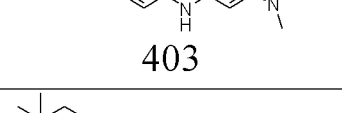
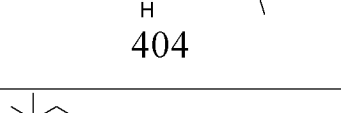
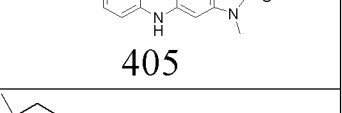
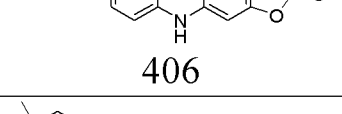
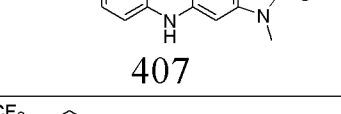
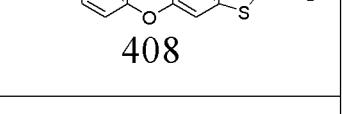
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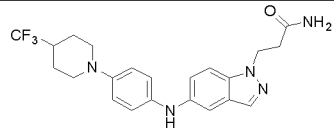
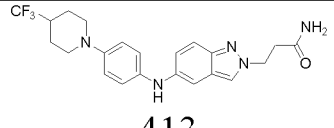
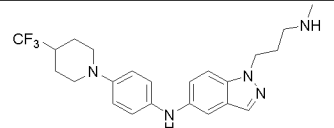
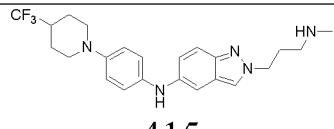
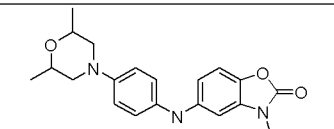
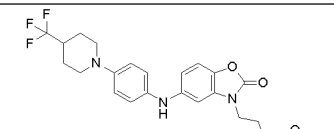
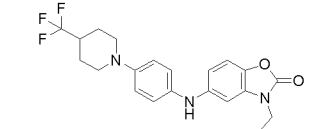
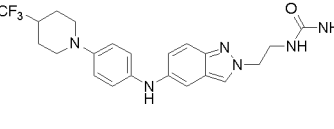
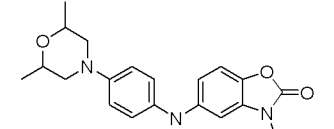
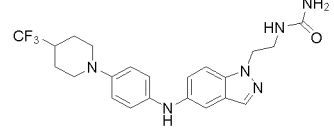
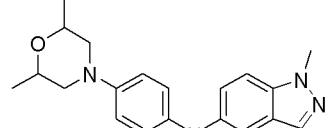
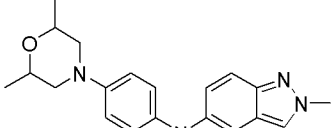
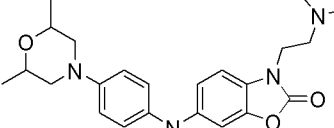
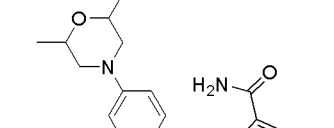
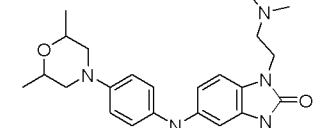
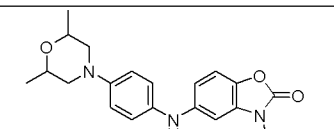
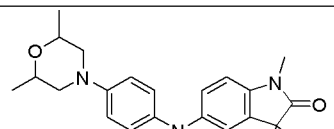
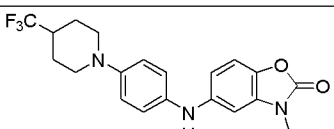
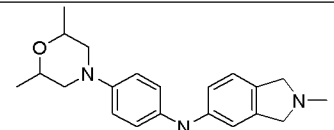
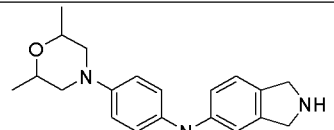
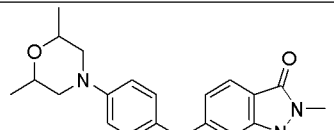
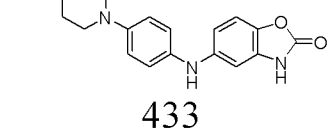
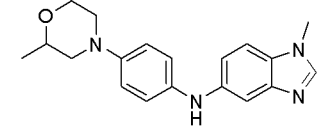
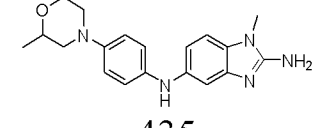
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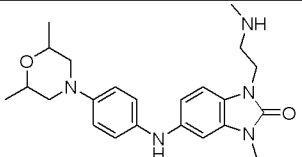
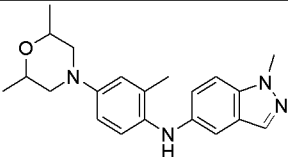
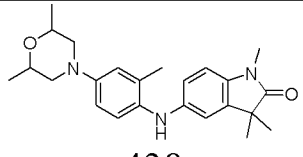
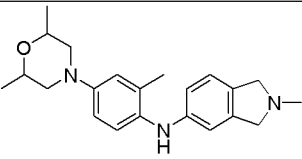
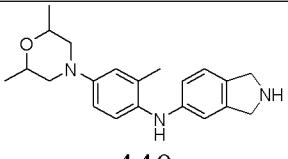
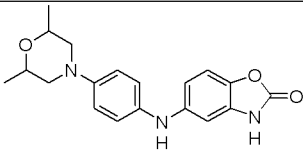
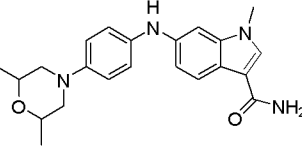
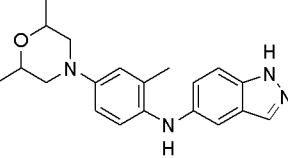
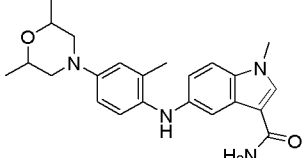
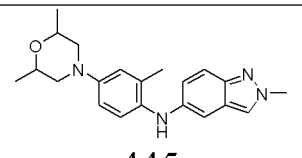
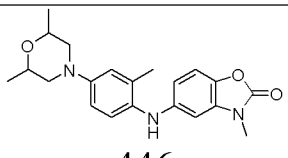
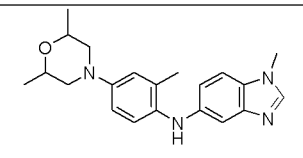
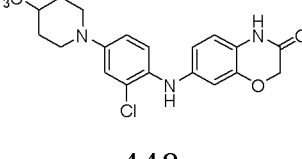
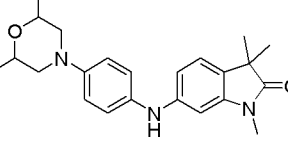
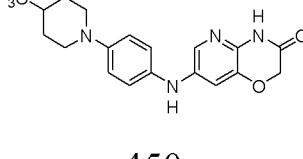
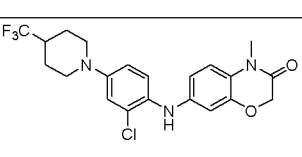
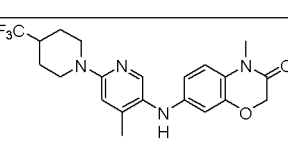
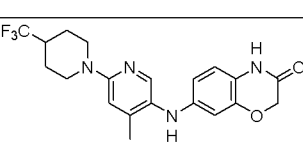
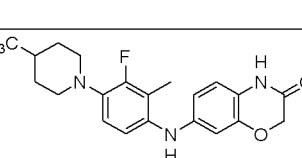
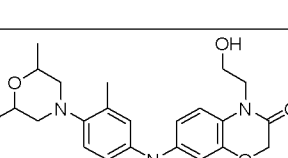
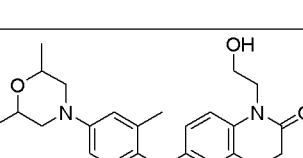
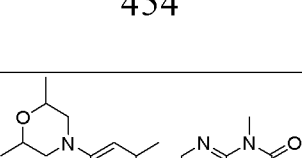
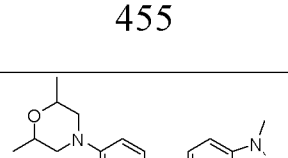
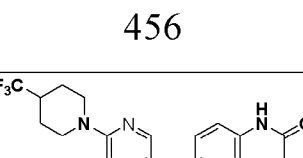
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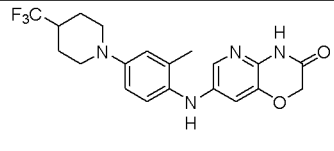
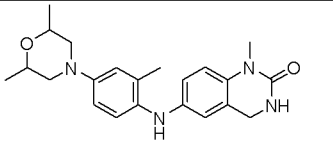
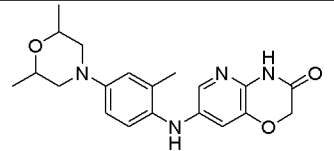
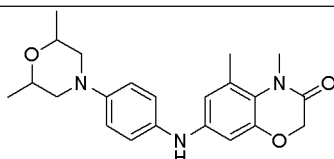
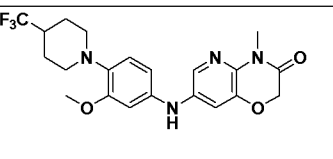
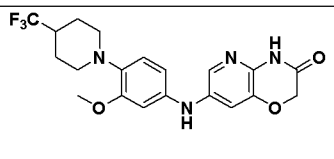
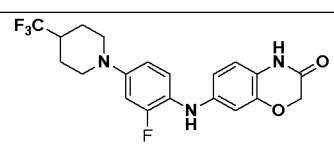
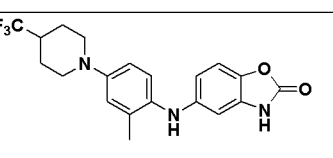
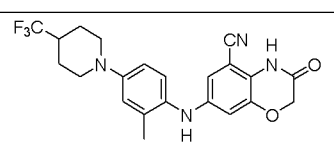
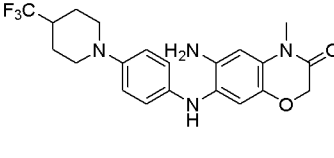
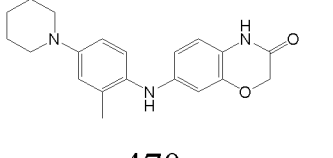
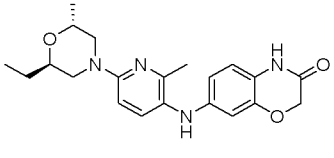
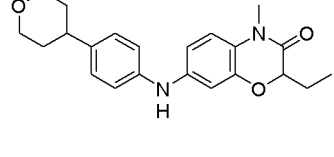
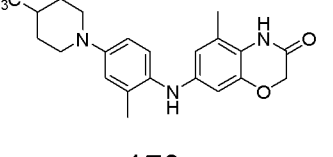
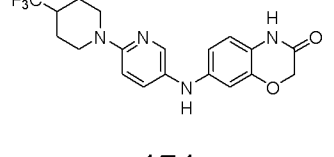
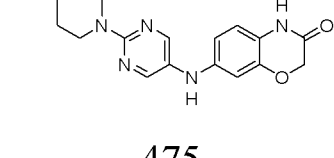
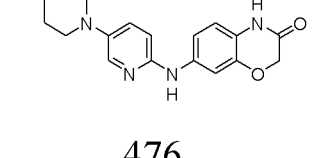
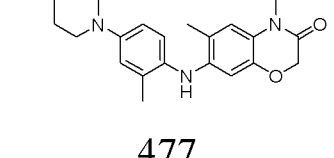
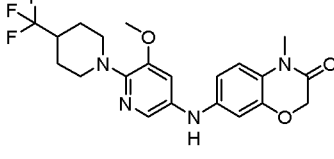
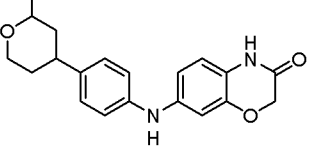
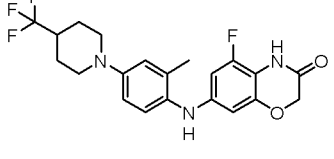
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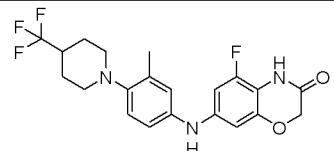
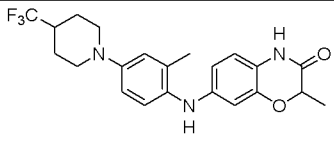
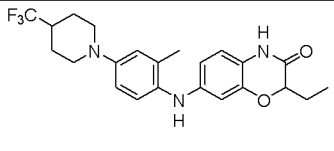
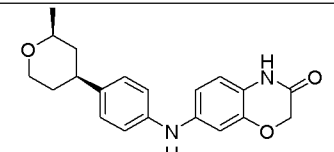
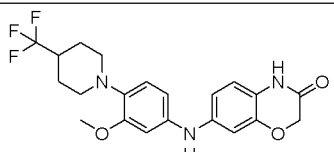
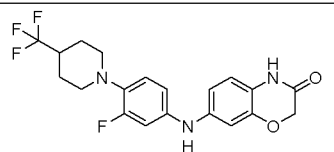
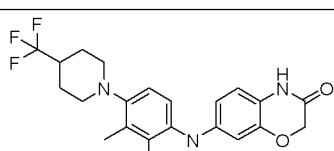
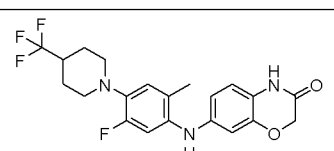
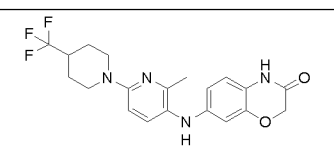
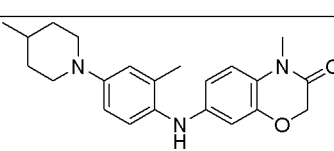
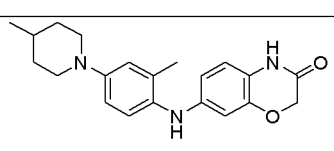
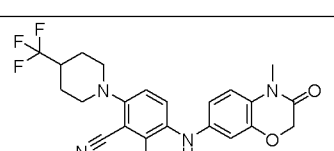
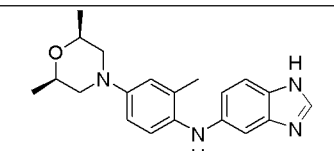
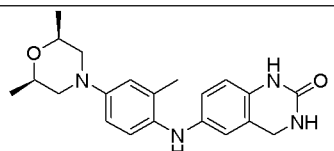
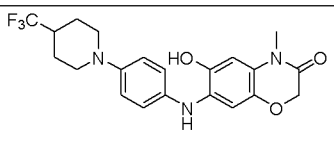
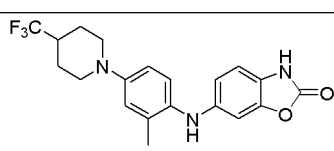
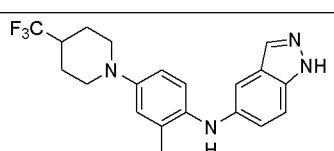
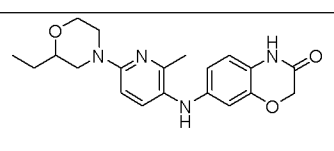
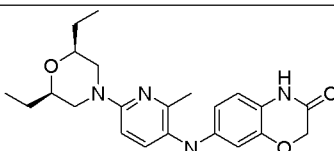
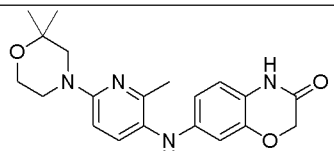
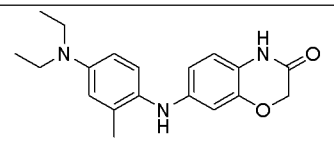
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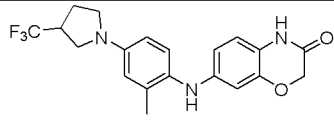
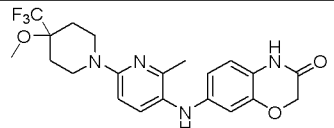
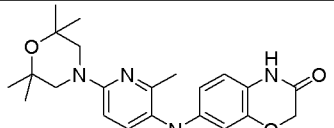
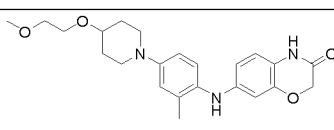
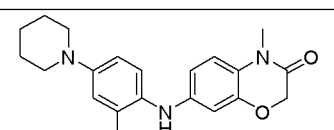
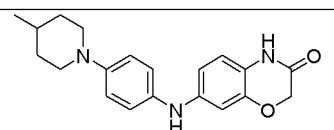
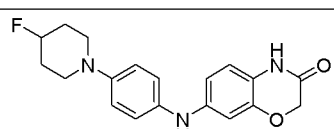
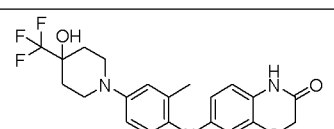
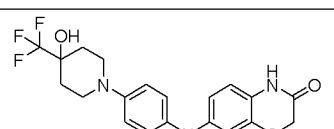
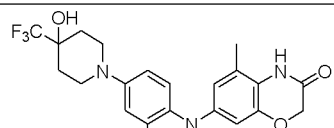
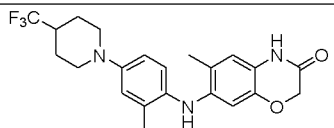
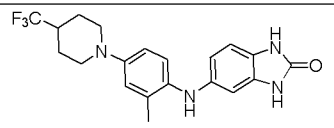
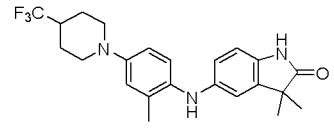
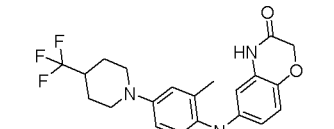
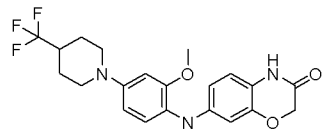
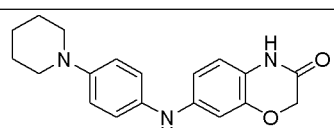
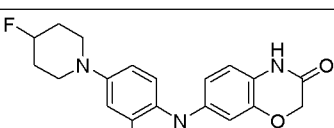
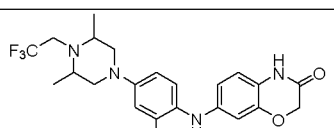
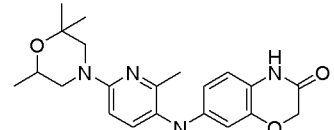
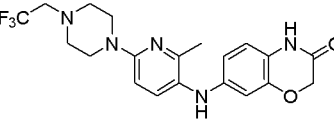
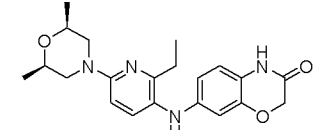
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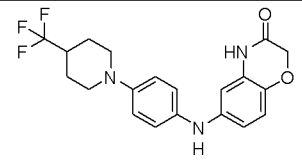
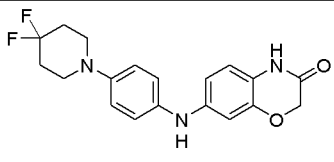
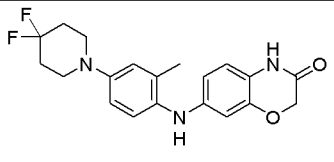
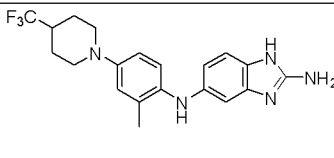
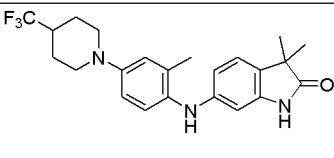
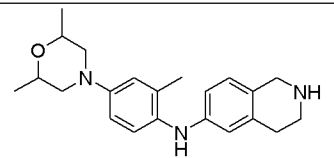
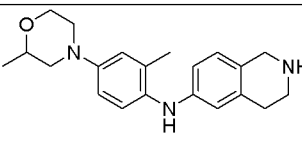
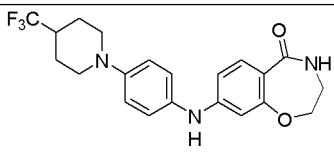
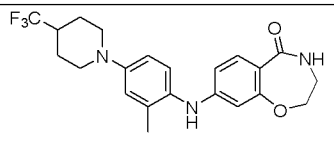
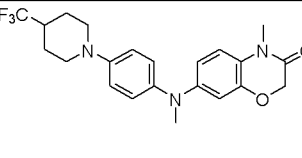
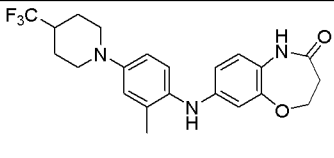
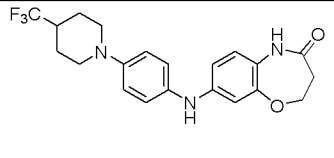
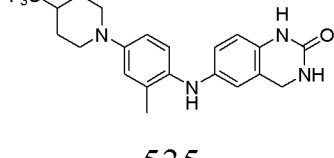
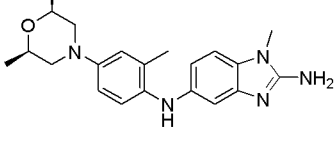
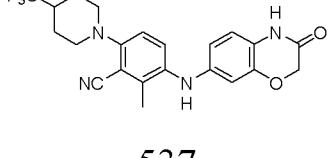
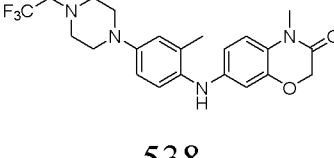
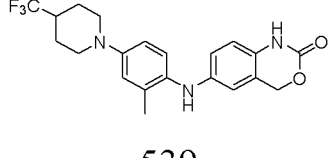
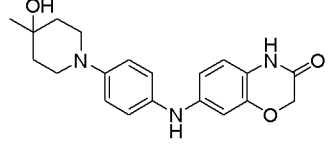
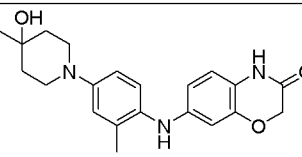
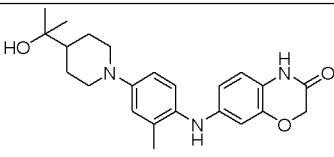
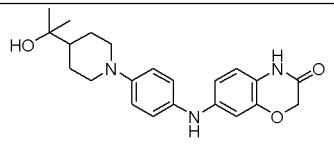
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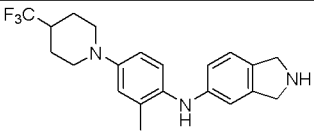
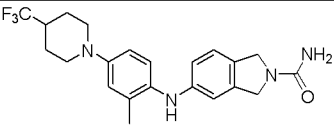
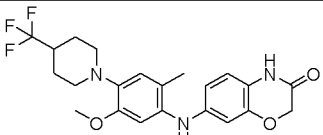
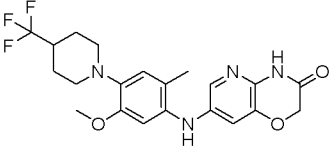
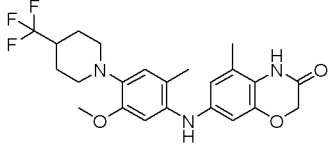
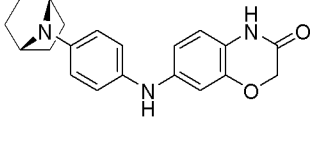
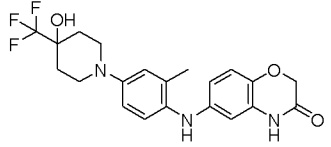
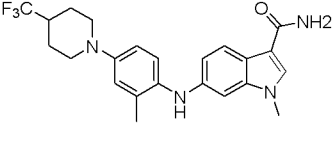
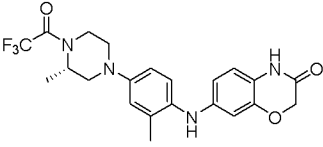
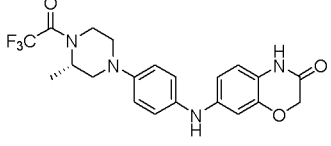
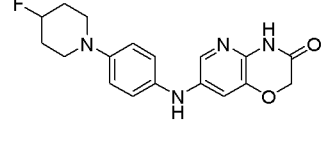
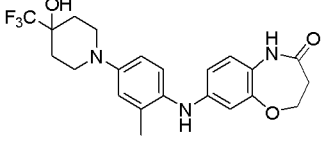
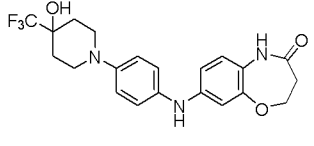
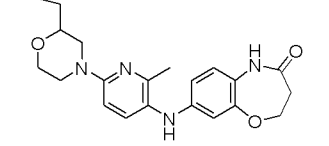
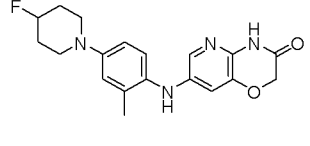
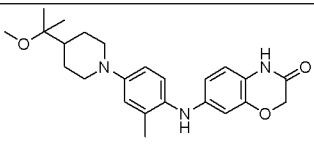
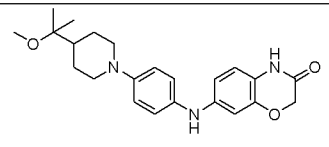
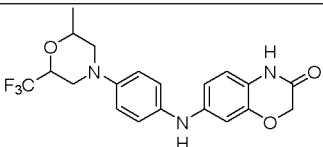
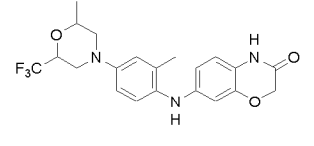
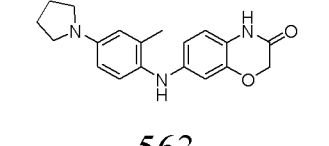
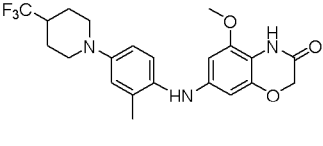
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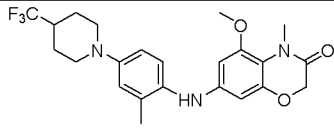
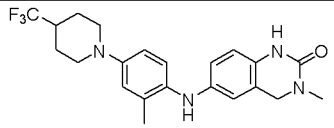
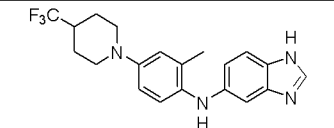
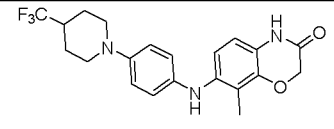
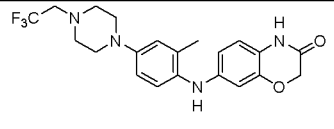
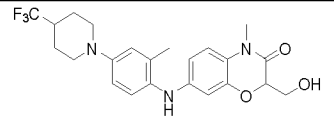
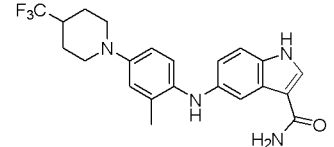
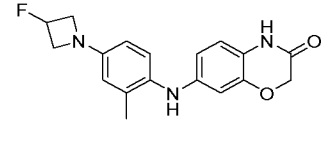
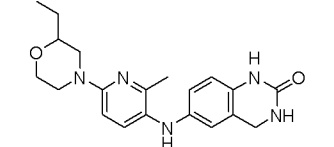
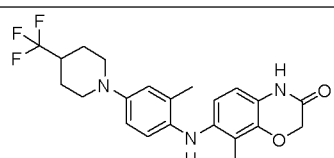
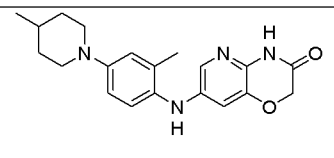
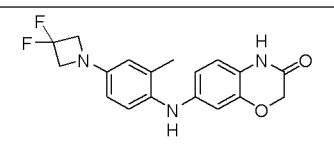
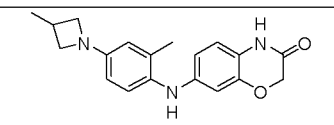
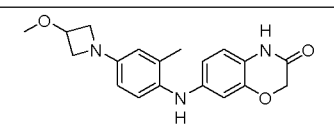
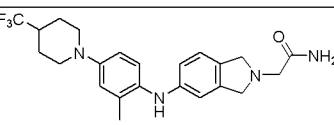
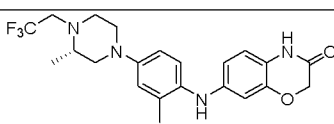
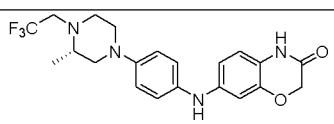
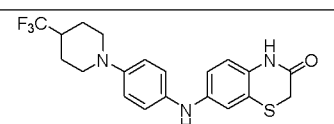
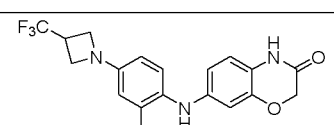
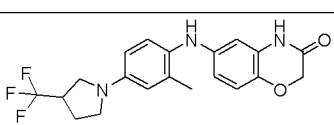
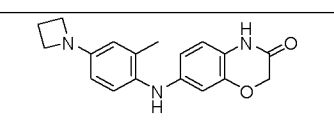
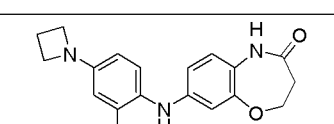
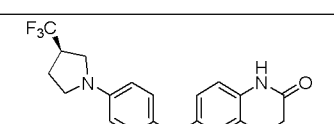
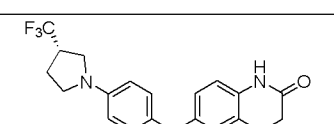
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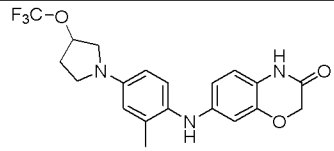
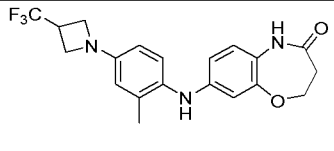
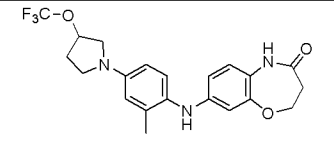
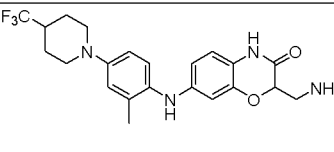
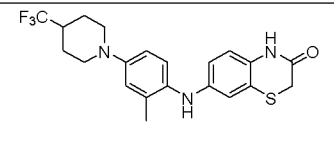
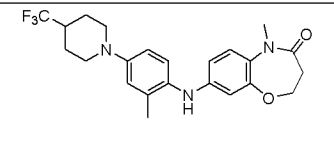
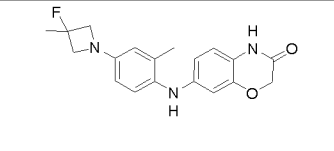
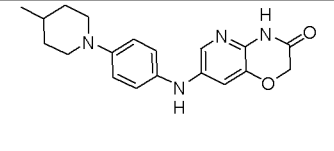
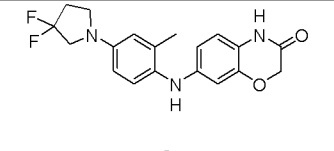
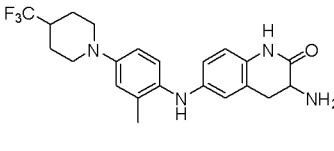
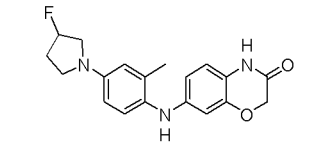
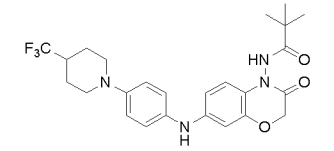
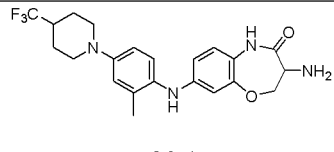
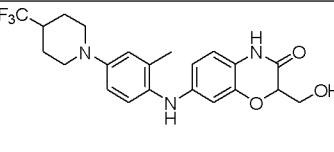
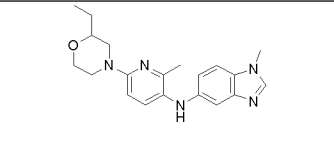
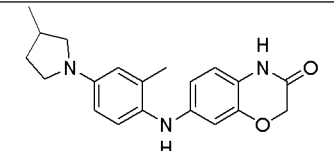
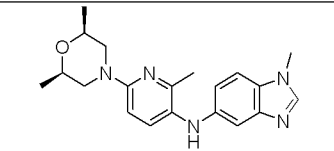
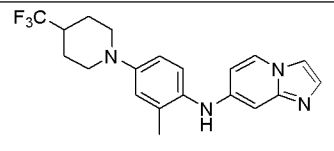
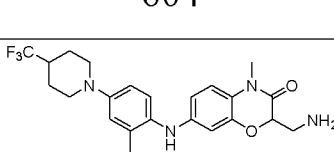
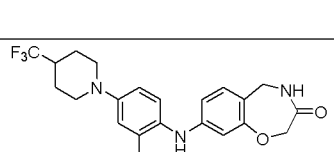
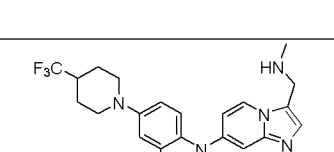
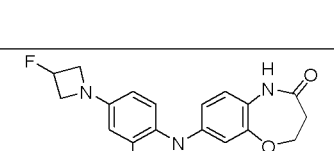
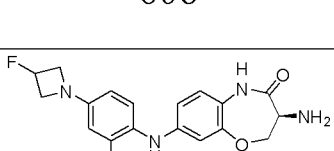
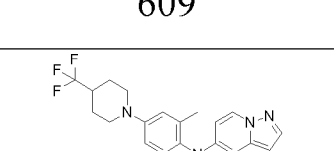
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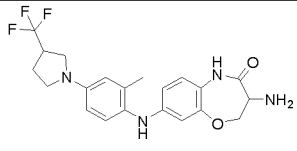
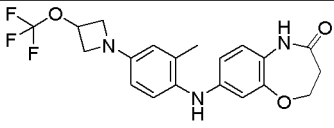
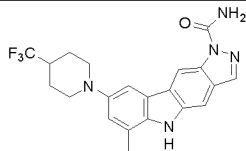
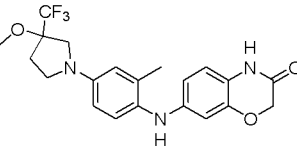
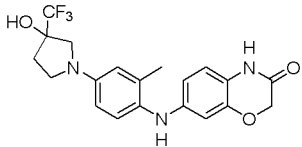
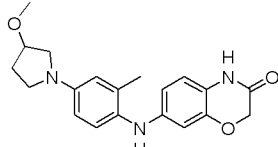
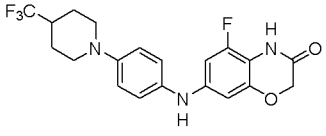
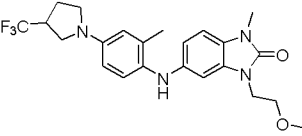
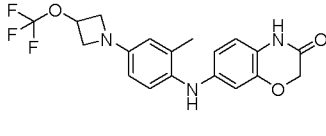
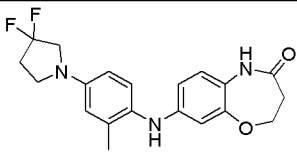
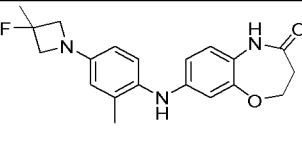
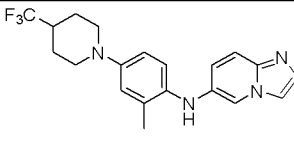
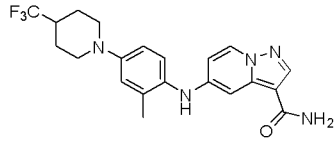
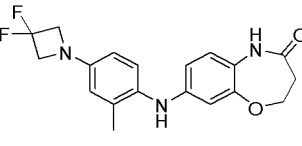
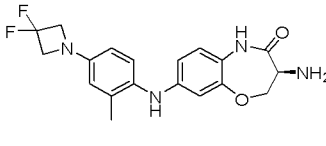
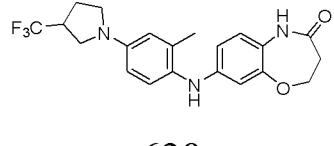
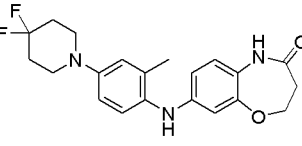
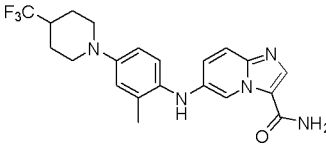
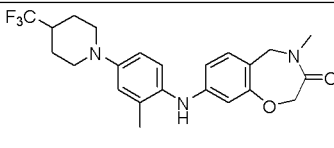
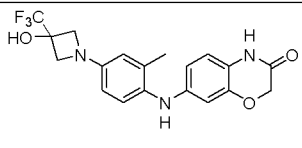
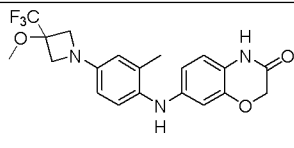
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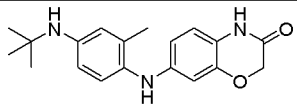
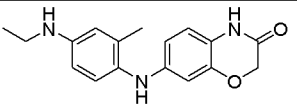
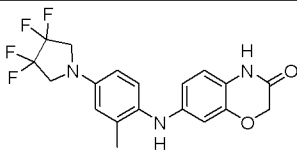
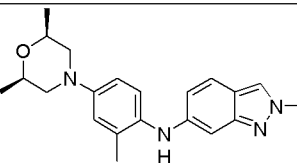
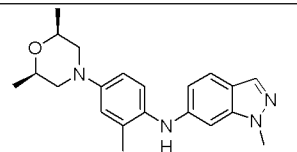
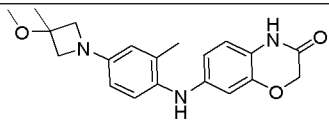
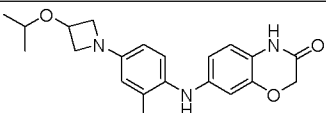
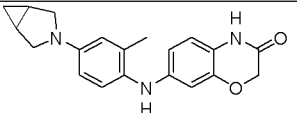
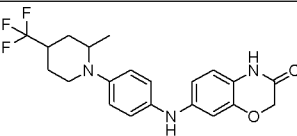
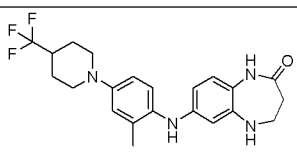
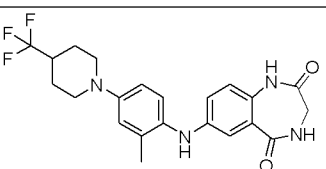
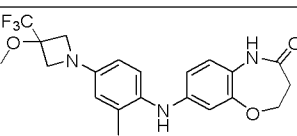
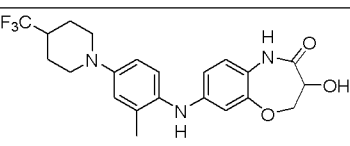
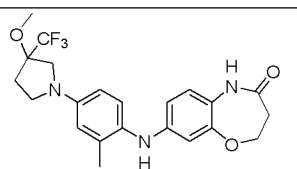
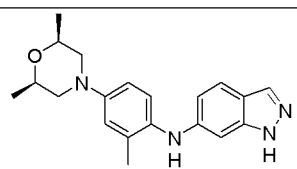
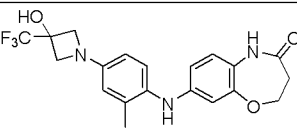
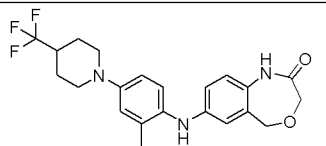
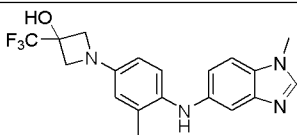
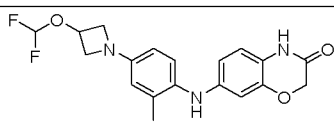
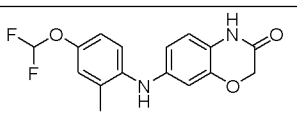
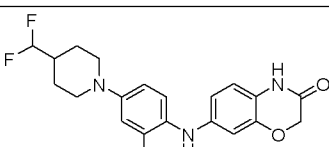
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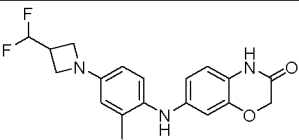
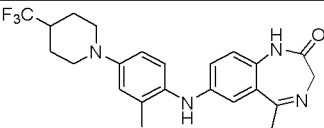
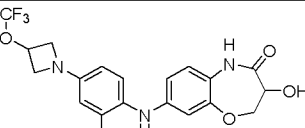
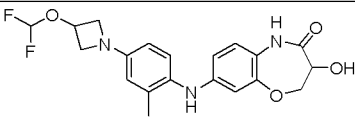
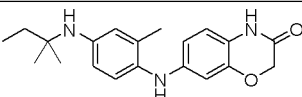
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 613	 614	 615
 616	 617	 618
 619	 620	 621
 622	 623	 624
 625	 626	 627
 628	 629	 630
 631	 632	 633

 634	 635	 636
 637	 638	 639
 640	 641	 642
 643	 644	 645
 646	 647	 648
 649	 650	 651
 652	 653	 654

 655	 656	 657
 658	 659	

Another aspect of the disclosure provides a pharmaceutical composition comprising at least one compound selected from a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, and at least one pharmaceutically acceptable carrier.

In some embodiments, the pharmaceutically acceptable carrier is selected from pharmaceutically acceptable vehicles and pharmaceutically acceptable adjuvants. In some embodiments, the pharmaceutically acceptable carrier is chosen from pharmaceutically acceptable fillers, disintegrants, surfactants, binders, and lubricants.

It will also be appreciated that a pharmaceutical composition of this disclosure can be employed in combination therapies; that is, the pharmaceutical compositions described herein can further include an additional active pharmaceutical agent. Alternatively, a pharmaceutical composition comprising a compound selected from a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing can be administered as a separate composition concurrently with, prior to, or subsequent to, a composition comprising an additional active pharmaceutical agent.

In some embodiments, the pharmaceutically acceptable carrier may be

chosen from adjuvants and vehicles. The pharmaceutically acceptable carrier, as used herein, can be chosen, for example, from any and all solvents, diluents, other liquid vehicles, dispersion aids, suspension aids, surface active agents, isotonic agents, thickening agents, emulsifying agents, preservatives, solid binders, and lubricants, which are suited to the particular dosage form desired. Remington: *The Science and Practice of Pharmacy*, 21st edition, 2005, ed. D.B. Troy, Lippincott Williams & Wilkins, Philadelphia, and *Encyclopedia of Pharmaceutical Technology*, eds. J. Swarbrick and J. C. Boylan, 1988 to 1999, Marcel Dekker, New York discloses various carriers used in formulating pharmaceutical compositions and known techniques for the preparation thereof. Except insofar as any conventional carrier is incompatible with the compounds of this disclosure, such as by producing any undesirable biological effect or otherwise interacting in a deleterious manner with any other component(s) of the pharmaceutical composition, its use is contemplated to be within the scope of this disclosure. Non-limiting examples of suitable pharmaceutically acceptable carriers include ion exchangers, alumina, aluminum stearate, lecithin, serum proteins (such as human serum albumin), buffer substances (such as phosphates, glycine, sorbic acid, and potassium sorbate), partial glyceride mixtures of saturated vegetable fatty acids, water, salts, and electrolytes (such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, and zinc salts), colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, wool fat, sugars (such as lactose, glucose and sucrose), starches (such as corn starch and potato starch), cellulose and its derivatives (such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate), powdered tragacanth, malt, gelatin, talc, excipients (such as cocoa butter and suppository waxes), oils (such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil), glycols (such as propylene glycol and polyethylene glycol), esters (such as ethyl oleate and ethyl laurate), agar, buffering agents (such as magnesium hydroxide and

aluminum hydroxide), alginic acid, pyrogen-free water, isotonic saline, Ringer's solution, ethyl alcohol, phosphate buffer solutions, non-toxic compatible lubricants (such as sodium lauryl sulfate and magnesium stearate), coloring agents, releasing agents, coating agents, sweetening
5 agents, flavoring agents, perfuming agents, preservatives, and antioxidants.

A compound selected from a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition disclosed herein can be
10 administered orally in solid dosage forms, such as capsules, tablets, troches, dragées, granules and powders, or in liquid dosage forms, such as elixirs, syrups, emulsions, dispersions, and suspensions. The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein can also be administered parenterally, in sterile liquid dosage forms, such
15 as dispersions, suspensions or solutions. Other dosages forms that can also be used to administer the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein as an ointment, cream, drops, transdermal patch or powder for topical administration, as an ophthalmic solution or suspension formation, e.g., eye drops, for ocular
20 administration, as an aerosol spray or powder composition for inhalation or intranasal administration, or as a cream, ointment, spray or suppository for rectal or vaginal administration.

Gelatin capsules containing a compound, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, and/or a
25 pharmaceutically acceptable salt of the foregoing disclosed herein and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like, can also be used. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for
30 continuous release of medication over a period of time. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective

disintegration in the gastrointestinal tract.

Liquid dosage forms for oral administration can further comprise at least one agent selected from coloring and flavoring agents to increase patient acceptance.

5 In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols can be examples of suitable carriers for parenteral solutions. Solutions for parenteral administration may comprise a water soluble salt of the at least one compound describe herein, at least one
10 suitable stabilizing agent, and if necessary, at least one buffer substance. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, can be examples of suitable stabilizing agents. Citric acid and its salts and sodium EDTA can also be used as examples of suitable stabilizing agents. In addition, parenteral solutions
15 can further comprise at least one preservative, selected, for example, from benzalkonium chloride, methyl- and propylparaben, and chlorobutanol.

A pharmaceutically acceptable carrier is, for example, selected from carriers that are compatible with active ingredients of the composition (and in some embodiments, capable of stabilizing the active ingredients) and not
20 deleterious to the subject to be treated. For example, solubilizing agents, such as cyclodextrins (which can form specific, more soluble complexes with the at least one compound and/or at least one pharmaceutically acceptable salt disclosed herein), can be utilized as pharmaceutical excipients for delivery of the active ingredients. Examples of other carriers
25 include colloidal silicon dioxide, magnesium stearate, cellulose, sodium lauryl sulfate, and pigments such as D&C Yellow # 10. Suitable pharmaceutically acceptable carriers are described in *Remington's Pharmaceutical Sciences*, A. Osol.

For administration by inhalation, the compound, tautomer, solvate,
30 stereoisomer, or pharmaceutically acceptable salt described herein may be conveniently delivered in the form of an aerosol spray presentation from pressurized packs or nebulisers. The compound, tautomer, solvate,

stereoisomer, or pharmaceutically acceptable salt described herein may also be delivered as powders, which may be formulated, and the powder composition may be inhaled with the aid of an insufflation powder inhaler device. One exemplary delivery system for inhalation can be metered dose
5 inhalation (MDI) aerosol, which may be formulated as a suspension or solution of a compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein in at least one suitable propellant, selected, for example, from fluorocarbons and hydrocarbons.

For ocular administration, an ophthalmic preparation may be
10 formulated with an appropriate weight percentage of a solution or suspension of the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein in an appropriate ophthalmic vehicle, such that the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein is
15 maintained in contact with the ocular surface for a sufficient time period to allow the compound to penetrate the corneal and internal regions of the eye.

Useful pharmaceutical dosage-forms for administration of the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable
20 salt described herein include, but are not limited to, hard and soft gelatin capsules, tablets, parenteral injectables, and oral suspensions. In some embodiments, the pharmaceutical compositions disclosed herein may be in the form of controlled release or sustained release compositions as known in the art.

25 The term "unit dosage forms" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical excipient. Typical unit dosage forms include prefilled,
30 premeasured ampules or syringes of the liquid compositions or pills, tablets, capsules, lozenges or the like in the case of solid compositions. In such compositions, the active material is usually a component ranging from

about 0.1 to about 50% by weight or preferably from about 1 to about 40% by weight with the remainder being various vehicles or carriers and processing aids helpful for forming the desired dosing form. Unit dosage formulations are preferably about of 5, 10, 25, 50, 100, 250, 500, or 1,000 mg per unit. In a particular embodiment, unit dosage forms are packaged in a multipack adapted for sequential use, such as blisterpack comprising sheets of at least 6, 9 or 12 unit dosage forms.

In some embodiments, unit capsules can be prepared by filling standard two-piece hard gelatin capsules each with, for example, 100 milligrams of the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein in powder, 150 milligrams of lactose, 50 milligrams of cellulose, and 6 milligrams magnesium stearate.

In some embodiments, a mixture of the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein and a digestible oil such as soybean oil, cottonseed oil or olive oil can be prepared and injected by means of a positive displacement pump into gelatin to form soft gelatin capsules containing 100 milligrams of the active ingredient. The capsules are washed and dried.

In some embodiments, tablets can be prepared by conventional procedures so that the dosage unit comprises, for example, 100 milligrams of the compound, stereoisomers thereof, or pharmaceutically acceptable salts thereof, 0.2 milligrams of colloidal silicon dioxide, 5 milligrams of magnesium stearate, 275 milligrams of microcrystalline cellulose, 11 milligrams of starch and 98.8 milligrams of lactose. Appropriate coatings may be applied to increase palatability or delay absorption.

In some embodiments, a parenteral composition suitable for administration by injection can be prepared by stirring 1.5% by weight of the compound and/or at least an enantiomer, a diastereoisomer, or pharmaceutically acceptable salt thereof disclosed herein in 10% by volume propylene glycol. The solution is made to the expected volume with water for injection and sterilized.

In some embodiment, an aqueous suspension can be prepared for oral administration. For example, each 5 milliliters of an aqueous suspension comprising 100 milligrams of finely divided compound, stereoisomers thereof, or pharmaceutically acceptable salts thereof, 100 milligrams of sodium carboxymethyl cellulose, 5 milligrams of sodium benzoate, 1.0 grams of sorbitol solution, U.S.P., and 0.025 milliliters of vanillin can be used.

The same dosage forms can generally be used when the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein is administered stepwise or in conjunction with at least one other therapeutic agent. When drugs are administered in physical combination, the dosage form and administration route should be selected depending on the compatibility of the combined drugs. Thus, the term "coadministration" is understood to include the administration of at least two agents concomitantly or sequentially, or alternatively as a fixed dose combination of the at least two active components.

The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt disclosed herein can be administered as the sole active ingredient or in combination with at least one second active ingredient.

The compound, tautomer, solvate, or stereoisomer described herein may be used per se, or in the form of their pharmaceutically acceptable salts, such as hydrochlorides, hydrobromides, acetates, sulfates, citrates, carbonates, trifluoroacetates and the like. When the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein contain relatively acidic functionalities, salts can be obtained by addition of the desired base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amine, or magnesium salts, or the like. When the compound, tautomer, solvate, or stereoisomer described herein contain relatively basic functionalities, salts can be obtained by addition of the desired acid, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable acid addition salts include those derived from

inorganic acids like hydrochloric, hydrobromic, nitric, carbonic, monohydrogencarbonic, phosphoric, monohydrogenphosphoric, dihydrogenphosphoric, sulfuric, monohydrogensulfuric, hydriodic, or phosphorous acids and the like, as well as the salts derived from relatively
5 nontoxic organic acids like acetic, propionic, isobutyric, maleic, malonic, benzoic, succinic, suberic, fumaric, lactic, mandelic, phthalic, benzenesulfonic, p-tolylsulfonic, citric, tartaric, methanesulfonic acids, and the like. Also included are salts of amino acids such as arginate and the like, and salts of organic acids like glucuronic or galacturonic acids and the
10 like (see, for example, Berge et al., "Pharmaceutical Salts," Journal of Pharmaceutical Science, 1977, 66, 1-19).

Neutral forms of the pharmaceutically acceptable salt described herein may be regenerated by contacting the salt with a base or acid, and isolating the parent compound in the conventional manner.

15 This disclosure provides prodrugs. Prodrugs of the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt described herein that readily undergo chemical changes under physiological conditions to provide the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of the present disclosure.
20 Additionally, prodrugs can be converted to the compound, tautomer, solvate, stereoisomer, or a pharmaceutically acceptable salt of the present disclosure by chemical or biochemical methods in an ex vivo environment. For example, prodrugs can be slowly converted to the compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of the present
25 disclosure when placed in a transdermal patch reservoir with a suitable enzyme or chemical reagent. Prodrugs are often useful because, in some situations, they may be easier to administer than the parent drug. They may, for instance, be more bioavailable by oral administration than the parent drug. The prodrug may also have improved solubility in pharmacological
30 compositions over the parent drug. A wide variety of prodrug derivatives are known in the art, such as those that rely on hydrolytic cleavage or oxidative activation of the prodrug. An example, without limitation, of a

prodrug would be a compound of the present disclosure which is administered as an ester (the "prodrug"), but then is metabolically hydrolyzed to the carboxylic acid, i.e. the active entity.

Certain compound, tautomer, stereoisomer, or pharmaceutically acceptable salt of the disclosure can exist in unsolvated forms as well as solvated forms, including hydrate forms. Certain compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of the disclosure may exist in multiple crystalline or amorphous forms.

Certain compound, tautomer, solvate, or pharmaceutically acceptable salt in this disclosure possesses asymmetric carbon atoms (optical centers) or double bonds; the racemates, enantiomers, diastereoisomers, geometric isomers and individual isomers are all intended to be encompassed within the scope of the present disclosure.

III. Methods of Treatment and Uses

Another aspect of the disclosure provides a method of treating a disease or condition, comprising administering to a subject in need thereof, a therapeutically effective amount of a compound of Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition comprising any of the foregoing, wherein the disease or condition is selected from neuropathy, stroke, neurodegenerative disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute kidney failure. In some embodiments, the disease or condition is involved with dysregulated ferroptosis, e.g., abnormal ferroptosis.

In another aspect, disclosed herein is a compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt as described herein, including a compound of the Formulae disclosed herein, Compounds 1 to

659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof, for use as a medicament.

In another aspect, disclosed herein is use of a compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt as described herein, including a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof, for the manufacture of a medicament for treating a disease or condition selected from neuropathy, stroke, neurodegenerative disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (AML), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute kidney failure. In some embodiments, the disease or condition is involved with dysregulated ferroptosis, e.g., abnormal ferroptosis.

In a further aspect of this disclosure, a compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt as described herein, including a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof, is for use in treating a disease or condition selected from neuropathy, stroke, neurodegenerative disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral sclerosis (AML), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute kidney failure. In some embodiments, the disease or condition is involved with dysregulated ferroptosis, e.g., abnormal

ferroptosis.

Another aspect of the disclosure provides a method of modulating, e.g., inhibiting, ferroptosis in a subject in need thereof, comprising administering to the subject, a therapeutically effective amount of a
5 compound of Formulae disclosed herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition comprising any of the foregoing.

In another aspect, disclosed herein is use of a compound, tautomer,
10 solvate, stereoisomer, or pharmaceutically acceptable salt as described herein, including a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof, for modulating, e.g.,
15 inhibiting, ferroptosis in a subject in need thereof.

In another aspect of this disclosure, a compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, or pharmaceutically acceptable salt as described herein, including a compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or
20 stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof, is for use in modulating, e.g., inhibiting, ferroptosis in a subject in need thereof by contacting the subject with the compound, tautomer, a solvate or stereoisomer of the compound or the tautomer, pharmaceutically
25 acceptable salt, or pharmaceutical composition.

A compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof may be administered once daily, twice
30 daily, or three times daily, for example, for the treatment of a disease or condition, selected from neuropathy, stroke, neurodegenerative disease (e.g., Alzheimer's disease), Parkinson's Disease, amyotrophic lateral

sclerosis (AML), multiple sclerosis, Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction such as acute kidney failure. In some embodiments, the disease or condition is involved with dysregulated ferroptosis, e.g., abnormal ferroptosis.

A compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof may be administered, for example, various manners, such as orally, topically, rectally, parenterally, by inhalation spray, or via an implanted reservoir, although the most suitable route in any given case will depend on the particular host, and nature and severity of the conditions for which the active ingredient is being administered. The term "parenteral" as used herein includes subcutaneous, intracutaneous, intravenous, intramuscular, intraarticular, intraarterial, intrasynovial, intrasternal, intrathecal, intralesional and intracranial injection or infusion techniques. The compositions disclosed herein may be conveniently presented in unit dosage form and prepared by any of the methods well known in the art. Parenteral administration can be by continuous infusion over a selected period of time. Other forms of administration contemplated in this disclosure are as described in International Patent Application Nos. WO 2013/075083, WO 2013/075084, WO 2013/078320, WO 2013/120104, WO 2014/124418, WO 2014/151142, and WO 2015/023915.

The contacting is generally effected by administering to the subject an effective amount of one or more compounds, tautomers, solvates, stereoisomers, and pharmaceutically acceptable salt disclosed herein. Generally, administration is adjusted to achieve a therapeutic dosage of about 0.1 to 50, preferably 0.5 to 10, more preferably 1 to 10 mg/kg, though optimal dosages are compound specific, and generally empirically

determined for each compound.

The dosage administered will be dependent on factors, such as the age, health and weight of the recipient, the extent of disease, type of concurrent treatment, if any, frequency of treatment, and the nature of the effect
5 desired. In general, a daily dosage of the active ingredient can vary, for example, from 0.1 to 2000 milligrams per day. For example, 10-500 milligrams once or multiple times per day may be effective to obtain the desired results.

In some embodiments, 2 mg to 1500 mg or 5 mg to 1000 mg of a
10 compound of the Formulae disclosed herein, Compounds 1 to 659, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, or a pharmaceutical composition thereof are administered once daily, twice daily, or three times daily. The compound, tautomer, solvate, stereoisomer,
15 or pharmaceutically acceptable salt described herein is administered for morning/daytime dosing, with off period at night.

Examples

In order that the disclosure described herein may be more fully
20 understood, the following examples are disclosed herein. It should be understood that these examples are for illustrative purposes only and are not to be construed as limiting this disclosure in any way.

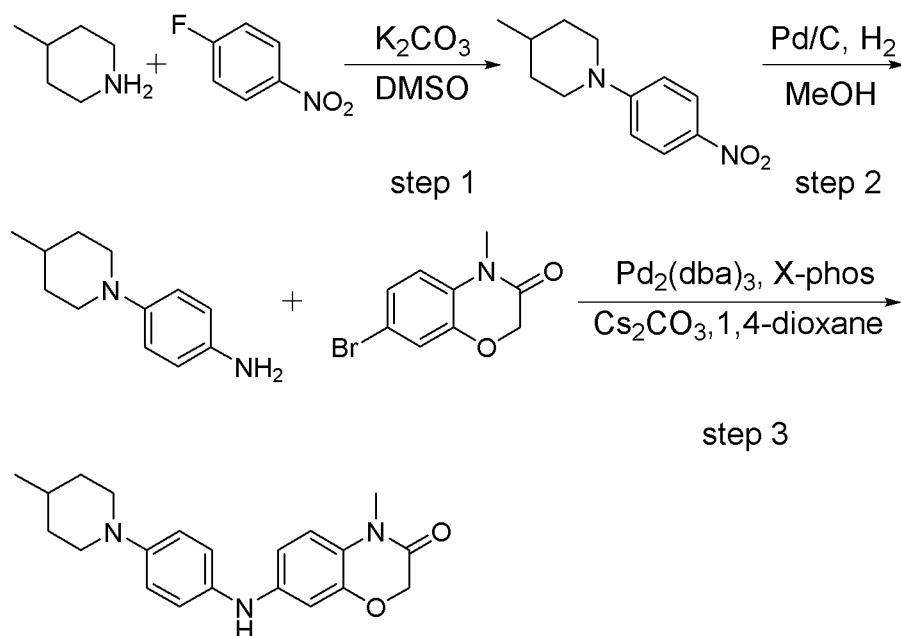
Example 1. Synthesis of Exemplary Compounds

The compounds of the disclosure, selected from a compound of the
25 Formulae depicted herein, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, can be made according to standard chemical practices or as illustrated herein, including the following synthetic schemes for Compounds 1 to 659 as representative examples of Formula I.

30

Compound 1

4-methyl-7-((4-(4-methylpiperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. 4-methyl-1-(4-nitrophenyl)piperidine

To a solution of 4-methylpiperidine (252 mg, 2.55 mmol) and 1-fluoro-4-nitrobenzene (300 mg, 2.13 mmol) in DMSO (5 mL) was added K_2CO_3 (440 mg, 3.20 mmol). Then the reaction was stirred overnight at 80 °C. The mixture was extracted by ethyl acetate (EA) (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by silica gel chromatography (EA/petroleum ether (PE) = 1:3) to give the desired product as a yellow solid (445 mg, 95%). Mass (m/z): 221.2 $[M+H]^+$.

Step 2. 4-(4-methylpiperidin-1-yl)aniline

To a solution of 4-methyl-1-(4-nitrophenyl)piperidine (445 mg, 2.02 mmol) in MeOH (10 mL) was added Pd/C (50 mg). The solution was stirred for 3 hours at room temperature (r.t.) under H_2 . The reaction mixture was filtered and concentrated under vacuum to afford the desired product as a purple solid. (326 mg, 85%). Mass (m/z): 190.3 $[M+H]^+$.

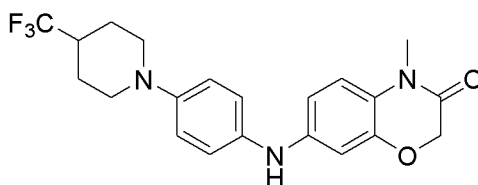
Step 3. 4-methyl-7-((4-(4-methylpiperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of 4-(4-methylpiperidin-1-yl)aniline (49.4 mg, 0.26 mmol) and 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (48.4 mg, 0.2

mmol) in 1,4-dioxane (5 mL) was added $\text{Pd}_2(\text{dba})_3$ (9.2 mg, 0.01 mmol), X-Phos (23.8 mg, 0.05 mmol) and Cs_2CO_3 (98.4 mg, 0.3 mmol) respectively under an argon atmosphere. The resulting mixture was heated to 110 °C and stirred for overnight at the same temperature. The reaction
 5 was diluted with water (10 mL) and extracted with ethyl acetate (5 mL) 3 times. The organic layer was combined and washed with water, saturated NaHCO_3 (aq) and brine respectively, and then dried over MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/AcOEt, 1/4) to give
 10 46.0 mg of compound **1** in a yield of 65.3% as a dark khaki powder. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.02 - 6.85 (m, 5H), 6.66 - 6.54 (m, 2H), 4.57 (s, 2H), 3.70 - 3.57 (m, 2H), 3.22 (s, 3H), 2.71 - 2.55 (m, 2H), 1.81 - 1.62 (m, 2H), 1.46 (m, 1H), 1.37 - 1.10 (m, 2H), 0.94 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 352.3 $[\text{M}+\text{H}]^+$.

Compound 2

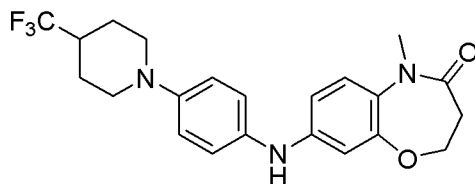
4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **2** (910 mg) was prepared in a total yield of 74.6% as a
 20 yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (878 mg, 3.6 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (726 mg, 3.0 mmol), $\text{Pd}_2(\text{dba})_3$ (27.5 mg, 0.03 mmol), X-Phos (71.55 mg, 0.15 mmol), and Cs_2CO_3 (1.47 g, 4.5 mmol) in 1,4-dioxane (30 mL) according to the procedure for compound **1**. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.01 - 6.83 (m, 5H), 6.67 - 6.52 (m, 2H), 4.56 (s, 2H), 3.68 - 3.57 (m, 2H), 3.22 (s, 3H), 2.68 - 2.56 (m, 2H), 2.45 - 2.34 (m, 1H), 1.94 - 1.81 (m, 2H), 1.65 - 1.47 (m, 2H). Mass (m/z): 406.2 $[\text{M}+\text{H}]^+$.

Compound 3

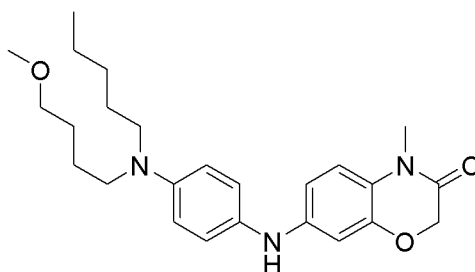
5-methyl-8-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-

dihydrobenzo[b][1,4]oxazepin-4(5H)-one

The title compound **3** (9.4 mg) was prepared in a total yield of 44.9% as a sky blue solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (12.8 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.14 (d, *J* = 8.8 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.74 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.62 (d, *J* = 2.4 Hz, 1H), 4.40 (t, *J* = 6.4 Hz, 2H), 3.68 - 3.59 (m, 2H), 3.15 (s, 3H), 2.69 - 2.57 (m, 2H), 2.55 - 2.52 (m, 2H), 2.42 (m, 1H), 1.96 - 1.79 (m, 2H), 1.64 - 1.50 (m, 2H). Mass (*m/z*): 420.2 [M+H]⁺.

Compound 4

7-((4-((4-methoxybutyl)(pentyl)amino)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

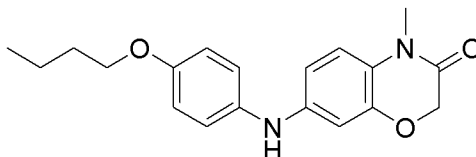


The title compound **4** (17 mg) was prepared in a total yield of 21.1% as brown oil from N¹-(4-methoxybutyl)-N¹-pentylbenzene-1,4-diamine (50 mg, 0.19 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (46 mg, 0.19 mmol), tris(dibenzylidenacetone)palladium (0) (4.5 mg, 0.009 mmol), dicyclohexyl(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphane (1.73 mg, 0.019 mmol, 0.08 equivs) and sodium tert-butoxide (27 mg, 0.28 mmol, 1.5 equivs) in dry 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.57 (s, 1H), 6.99 –

6.85 (m, 3H), 6.64 (dd, $J = 22.2, 5.5$ Hz, 2H), 6.52 (s, 1H), 6.44 (s, 1H), 4.54 (s, 2H), 3.21 (d, $J = 3.6$ Hz, 1H), 1.51 (s, 7H), 1.40 – 1.17 (m, 3H), 0.87 (t, $J = 7.0$ Hz, 4H). Mass (m/z): 426.7 [M+H]⁺.

Compound 5

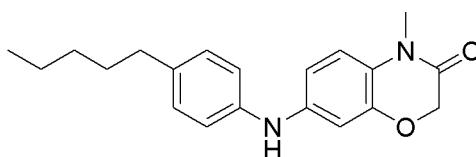
5 7-((4-butoxyphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **5** (26.0 mg) was prepared in a total yield of 38.3% as a grey solid from 4-butoxyaniline (41 mg, 0.250 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (102 mg, 0.318 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.84 (s, 1H), 6.98 (dd, $J = 8.4, 5.6$ Hz, 3H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.62 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.54 (d, $J = 2.4$ Hz, 1H), 4.57 (s, 2H), 3.90 (t, $J = 6.4$ Hz, 2H), 3.22 (s, 3H), 1.72 – 1.63 (m, 2H), 1.43 (h, $J = 7.6$ Hz, 2H), 0.93 (t, $J = 7.6$ Hz, 3H). Mass (m/z): 327.3 [M+H]⁺.

Compound 6

4-methyl-7-((4-pentylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

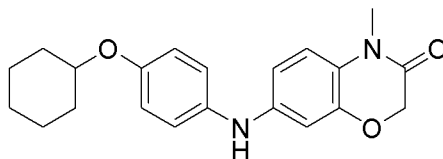


The title compound **6** (29.7 mg) was prepared in a total yield of 44.1% as an off-white solid from 4-pentylaniline (41 mg, 0.250 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (102 mg, 0.318 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.02 (s, 1H), 7.05 (d, $J = 8.4$ Hz, 2H), 7.01 (d, $J = 8.8$ Hz, 1H), 6.95 (d, $J = 8.4$ Hz, 2H), 6.73 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.64 (d, $J = 2.4$ Hz, 1H), 4.58 (s, 2H), 3.23 (s, 3H), 2.47 (d, $J = 7.6$ Hz, 1H), 1.53 (p, $J = 7.6$ Hz, 2H), 1.28 (tq, $J = 8.8,$

5.2, 4.0 Hz, 5H), 0.86 (t, $J = 6.8$ Hz, 3H). Mass (m/z): 325.3 $[M+H]^+$.

Compound 7

7-((4-(cyclohexyloxy)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



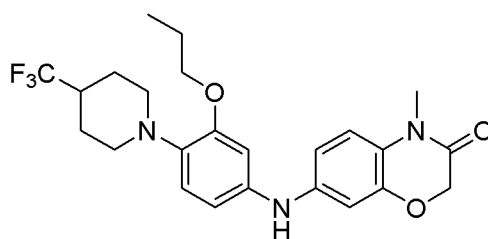
5

The title compound **7** (31.5 mg) was prepared in a total yield of 43.0% as a brown solid from 4-(cyclohexyloxy)aniline (48 mg, 0.250 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (106 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 7.85 (s, 1H), 6.98 (d, $J = 8.8$ Hz, 3H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.63 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.55 (d, $J = 2.4$ Hz, 1H), 4.57 (s, 2H), 4.19 (td, $J = 8.4, 4.0$ Hz, 1H), 3.22 (s, 3H), 1.95 – 1.86 (m, 2H), 1.75 – 1.66 (m, 2H), 1.53 (dd, $J = 11.2, 5.6$ Hz, 1H), 1.45 – 1.21 (m, 6H). Mass (m/z): 353.3 $[M+H]^+$.

15

Compound 8

4-methyl-7-((3-propoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



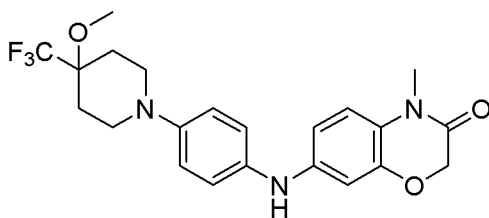
20 The title compound **8** (28.1 mg) was prepared in a total yield of 29.3% as a brown solid from 3-propoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (75 mg, 0.248 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (106 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (300 MHz, $DMSO-d_6$) δ 7.91 (s, 1H), 6.98 (d, $J = 8.7$ Hz, 1H), 6.78 (d, $J =$

25

8.1 Hz, 1H), 6.69 (dd, $J = 8.7, 2.4$ Hz, 1H), 6.61 – 6.54 (m, 3H), 4.57 (s, 2H), 3.85 (t, $J = 6.3$ Hz, 2H), 3.22 (s, 3H), 2.54 (s, 1H), 2.39 (ddd, $J = 19.2, 9.6, 5.1$ Hz, 2H), 1.87 (d, $J = 11.4$ Hz, 2H), 1.75 (q, $J = 6.6$ Hz, 2H), 1.58 (qd, $J = 12.3, 3.9$ Hz, 3H), 1.02 (t, $J = 7.2$ Hz, 3H). Mass (m/z):
 5 464.3 $[M+H]^+$.

Compound 9

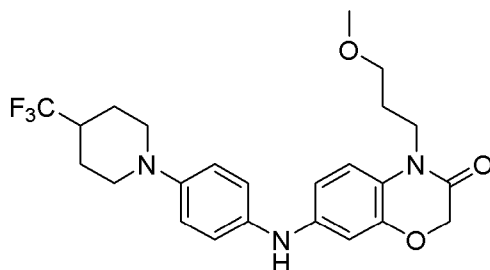
7-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



10 The title compound **9** (50.7 mg) was prepared in a total yield of 56.3% as a green solid from 4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)aniline (68 mg, 0.248 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4] oxazin-3(4H)-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs_2CO_3 (106 mg, 0.312 mmol) and 1,4-dioxane (5 mL)
 15 according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.04 (s, 1H), 7.27 – 6.83 (m, 5H), 6.65 (d, $J = 34.0$ Hz, 2H), 4.58 (s, 2H), 3.50 (s, 2H), 3.41 (d, $J = 1.6$ Hz, 3H), 3.23 (s, 3H), 2.99 (s, 2H), 2.16 – 1.91 (m, 4H). Mass (m/z): 436.3 $[M+H]^+$.

Compound 10

20 4-(3-methoxypropyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



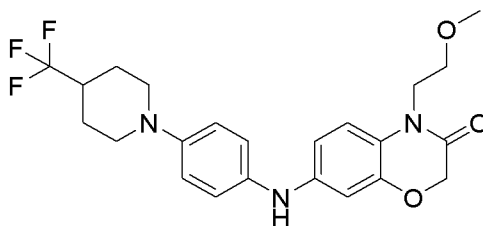
The title compound **10** (30.4 mg) was prepared in a total yield of 39.3% as a brown solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (49 mg, 0.200 mmol), 7-bromo-4-(3-methoxypropyl)-2H-benzo[b][1,4]oxazin-3(4H)-one
 25 0.200 mmol),

-3(4H)-one (50 mg, 0.167 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (82 mg, 0.251 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.92 (s, 1H), 7.02 – 6.94 (m, 3H), 6.92 – 6.87 (m, 2H), 6.63 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.56 (d, *J* = 2.4 Hz, 1H), 4.54 (s, 2H), 3.91 – 3.83 (m, 2H), 3.62 (d, *J* = 12.0 Hz, 2H), 3.34 (d, *J* = 6.0 Hz, 2H), 3.23 (s, 3H), 2.62 (td, *J* = 12.4, 2.4 Hz, 2H), 2.42 (ddt, *J* = 16.0, 7.6, 4.0 Hz, 1H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.61 – 1.50 (m, 2H). Mass (m/z): 464.3 [M+H]⁺.

10

Compound 11

4-(2-methoxyethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

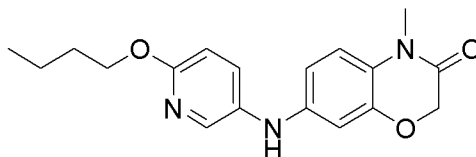


The title compound 11 (53.7 mg) was prepared in a total yield of 68.3% as a brown solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (51 mg, 0.210 mmol), 7-bromo-4-(2-methoxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.175 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (86 mg, 0.262 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.96 (s, 1H), 7.07 (d, *J* = 8.8 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.92 – 6.87 (m, 2H), 6.63 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.57 (d, *J* = 2.4 Hz, 1H), 4.55 (s, 2H), 4.02 (t, *J* = 5.6 Hz, 2H), 3.67 – 3.57 (m, 2H), 3.50 (t, *J* = 5.6 Hz, 2H), 3.24 (s, 3H), 2.62 (td, *J* = 12.4, 2.4 Hz, 2H), 2.42 (tp, *J* = 12.4, 4.0 Hz, 1H), 1.92 – 1.83 (m, 2H), 1.57 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (m/z): 450.3 [M+H]⁺.

25

Compound 12

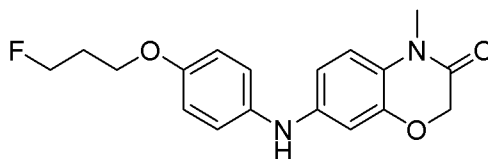
7-((6-butoxypyridin-3-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **12** (9.6 mg) was prepared in a yield of 14.2% as a pale yellow powder from 6-butoxypyridin-3-amine (50 mg, 0.21 mmol) and 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (38 mg, 0.24 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.93 (s, 1H), 7.90 (d, *J* = 2.8 Hz, 1H), 7.46 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 1H), 6.60 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.51 (d, *J* = 2.5 Hz, 1H), 4.57 (s, 2H), 4.18 (t, *J* = 6.6 Hz, 2H), 3.22 (s, 3H), 1.67 (dq, *J* = 8.6, 6.7 Hz, 2H), 1.51 – 1.32 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). Mass (*m/z*): 328.5 [M+H]⁺.

Compound 13

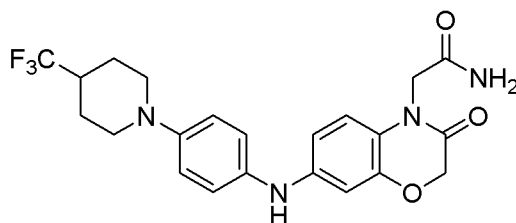
7-((4-(3-fluoropropoxy)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **13** (57.2 mg) was prepared in a yield of 48.83% as a brown oil from 4-(3-fluoropropoxy)aniline (60 mg, 0.35 mmol) and 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (86 mg, 0.35 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.85 (s, 1H), 6.98 (t, *J* = 8.5 Hz, 3H), 6.91 – 6.83 (m, 2H), 6.64 – 6.60 (m, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 4.65 (q, *J* = 5.8 Hz, 1H), 4.56 (d, *J* = 2.2 Hz, 2H), 4.52 (dd, *J* = 11.5, 5.9 Hz, 1H), 4.00 (t, *J* = 6.3 Hz, 2H), 3.22 (s, 3H), 2.14 – 2.01 (m, 2H). Mass (*m/z*): 331.2 [M+H]⁺.

Compound 14

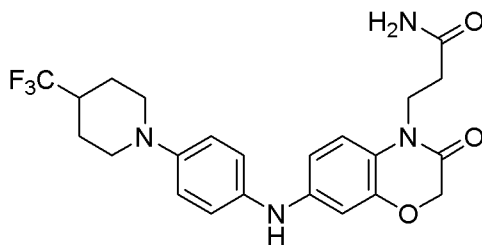
2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)acetamide



The title compound **14** (12.6 mg) was prepared in a total yield of 56.1% as a light gray solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)acetamide (14.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.00 - 6.72 (m, 5H), 6.63 - 6.51 (m, 2H), 4.61 (s, 2H), 4.38 (s, 2H), 3.66 - 3.57 (m, 2H), 2.68 - 2.56 (m, 2H), 2.41 (m, 1H), 1.92 - 1.82 (m, 2H), 1.63 - 1.50 (m, 2H). Mass (m/z): 449.2 [M+H]⁺.

Compound 15

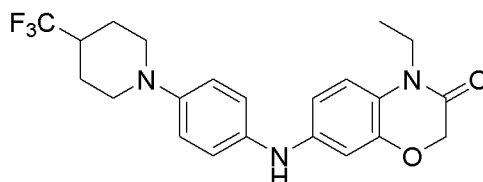
3-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)propanamide



The title compound **15** (20.1 mg) was prepared in a total yield of 87.0% as a rosy brown solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 3-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)propanamide (14.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.04 - 6.86 (m, 5H), 6.65 - 6.53 (m, 2H), 4.54 (s, 2H), 4.05 (t, *J* = 7.6 Hz, 2H), 3.66 - 3.58 (m, 2H), 2.67 - 2.55 (m, 2H), 2.45 - 2.30 (m, 3H), 1.95 - 1.79 (m, 2H), 1.63 - 1.50 (m, 2H). Mass (m/z): 463.3 [M+H]⁺.

Compound 16

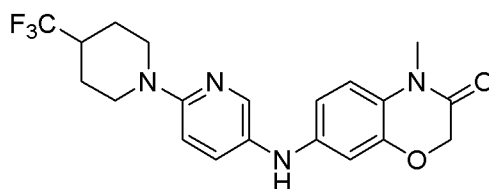
4-ethyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **16** (71.5 mg) was prepared in a total yield of 73.0% as
 5 a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (57 mg, 0.234 mmol), 7-bromo-4-ethyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.195 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs₂CO₃ (96 mg, 0.292 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H),
 10 7.01 (d, *J* = 8.8 Hz, 1H), 6.99 – 6.94 (m, 2H), 6.92 – 6.88 (m, 2H), 6.63 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 4.54 (s, 2H), 3.86 (q, *J* = 7.2 Hz, 2H), 3.62 (d, *J* = 12.0 Hz, 2H), 2.62 (td, *J* = 12.4, 2.4 Hz, 2H), 2.42 (qd, *J* = 10.4, 8.8, 6.0 Hz, 1H), 1.88 (dt, *J* = 10.4, 3.2 Hz, 2H), 1.57 (qd, *J* = 12.4, 4.0 Hz, 2H), 1.13 (t, *J* = 7.2 Hz, 3H). Mass (*m/z*): 420.3 [M+H]⁺.

Compound 17

4-methyl-7-((6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

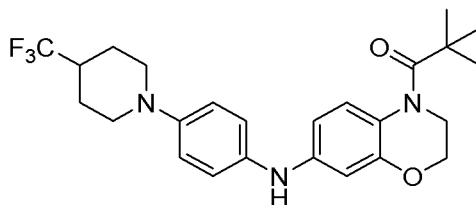


The title compound **17** (17.1 mg) was prepared in a total yield of 84.0% as
 20 a light orange solid from 6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (15.9 mg, 0.065 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (12.1 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.76 (s, 1H), 7.40 - 7.33 (m, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.53 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.45 (d, *J* = 2.4 Hz, 1H), 4.55

(s, 2H), 4.36 - 4.18 (m, 2H), 3.21 (s, 3H), 2.81 - 2.72 (m, 2H), 2.54 (m, 1H), 1.90 - 1.78 (m, 2H), 1.51 - 1.38 (m, 2H). Mass (m/z): 407.2 [M+H]⁺.

Compound 18

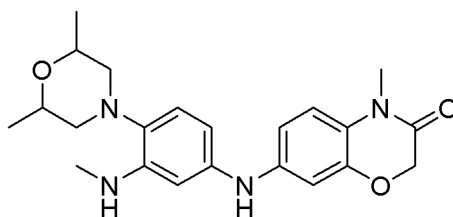
2,2-dimethyl-1-(7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-
2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)propan-1-one



The title compound **18** (18.7 mg) was prepared in a total yield of 81.1% as a light gray solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 1-(7-bromo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)-2,2-dimethylpropan-1-one (14.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.35 (d, *J* = 8.8 Hz, 1H), 7.02 - 6.83 (m, 4H), 6.48 - 6.33 (m, 2H), 4.21 (t, *J* = 4.4 Hz, 2H), 3.92 (t, *J* = 4.4 Hz, 2H), 3.67 - 3.55 (m, 2H), 2.69 - 2.54 (m, 2H), 2.41 (m, 1H), 1.93 - 1.82 (m, 2H), 1.63 - 1.50 (m, 2H), 1.27 (s, 9H). Mass (m/z): 462.2 [M+H]⁺.

Compound 19

7-((4-(2,6-dimethylmorpholino)-3-(methylamino)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



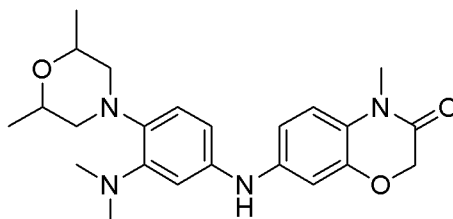
The title compound **19** (9.3 mg) was prepared in a total yield of 46.9% as a yellow solid from 6-(2,6-dimethylmorpholino)-N¹-methylbenzene-1,3-diamine (15.3 mg, 0.065 mmol), 1-(7-bromo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)-2,2-dimethylpropan-1-one (14.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR

(400 MHz, DMSO- d_6) δ 6.98 (d, J = 8.8 Hz, 1H), 6.82 - 6.59 (m, 3H), 6.35 - 6.15 (m, 2H), 4.57 (s, 2H), 3.83 - 3.72 (m, 2H), 3.22 (s, 3H), 2.81 - 2.74 (m, 2H), 2.69 (d, J = 5.2 Hz, 3H), 2.30 - 2.15 (m, 2H), 1.08 (d, J = 6.4 Hz, 6H). Mass (m/z): 397.2 [M+H]⁺.

5

Compound 20

7-((3-(dimethylamino)-4-(2,6-dimethylmorpholino)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

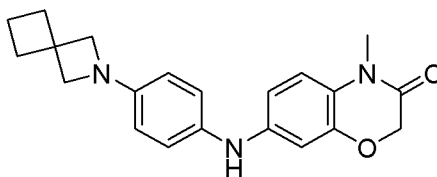


The title compound **20** (14.3 mg) was prepared in a total yield of 69.5% as a yellow solid from 6-(2,6-dimethylmorpholino)-N¹,N¹-dimethylbenzene-1,3-diamine (16.2 mg, 0.065 mmol), 1-(7-bromo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)-2,2-dimethylpropan-1-one (14.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO- d_6) δ 6.98 (d, J = 8.8 Hz, 1H), 6.81 - 6.66 (m, 2H), 6.64 - 6.56 (m, 3H), 4.57 (s, 2H), 3.85 - 3.65 (m, 2H), 3.34 - 3.29 (m, 2H), 3.22 (s, 3H), 2.76 (s, 6H), 2.18 - 2.09 (m, 2H), 1.10 (d, J = 6.4 Hz, 6H). Mass (m/z): 411.3 [M+H]⁺.

15

Compound 21

7-((4-(2-azaspiro[3.3]heptan-2-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



20

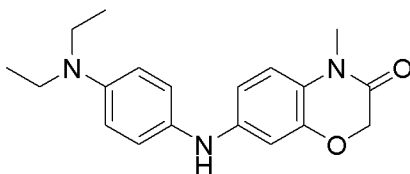
The title compound **21** (73.8 mg) was prepared in a total yield of 64.0% as a yellow solid from 4-(2-azaspiro[3.3]heptan-2-yl)aniline (81 mg, 0.43 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μ mol), X-Phos (7.9 mg, 16.5 μ mol) and

25

Cs₂CO₃ (163 mg, 0.50 mmol) in 1,4-dioxane (3.0 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.07 – 6.88 (m, 2H), 6.61 – 6.47 (m, 2H), 4.54 (s, 2H), 3.34 (s, 3H), 2.24 (t, *J* = 7.6 Hz, 4H), 1.96 – 1.88 (m, 2H), 1.41 – 1.19 (m, 4H). Mass (*m/z*):
 5 350.2[M+H]⁺.

Compound 22

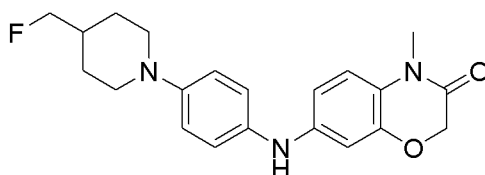
7-((4-(diethylamino)phenyl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one



10 The title compound **22** (43.0 mg) was prepared in a total yield of 40.2% as a dark yellow solid from a mixture of *N*¹,*N*¹-diethylbenzene-1,4-diamine (70.5 mg, 0.43 mmol), 7-bromo-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.9 mg, 16.5 μmol) and Cs₂CO₃ (163 mg, 0.50 mmol) in 1,4-dioxane (3.0 mL)
 15 according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.26 – 5.99 (m, 5H), 4.51 (s, 2H), 3.92 – 3.63 (m, 4H), 3.34 (s, 3H), 1.10 (t, *J* = 7.0 Hz, 6H). Mass (*m/z*): 326.2 [M+H]⁺.

Compound 23

7-((4-(4-(fluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benz
 20 o[*b*][1,4]oxazin-3(4H)-one

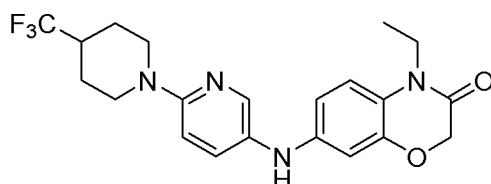


The title compound **23** (63.3 mg) was prepared in a total yield of 82.9% as a brown solid from 4-(4-(fluoromethyl)piperidin-1-yl)aniline (52 mg, 0.248 mmol), 7-bromo-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one (50
 25 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (102 mg, 0.310 mmol) and 1,4-dioxane (5 mL)

according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.86 (d, $J = 7.6$ Hz, 1H), 6.96 (dd, $J = 8.8, 2.4$ Hz, 3H), 6.91 – 6.86 (m, 2H), 6.62 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.54 (d, $J = 2.4$ Hz, 1H), 4.56 (s, 2H), 4.39 (d, $J = 6.0$ Hz, 1H), 4.27 (d, $J = 5.6$ Hz, 1H), 3.56 (dt, $J = 12.8, 3.2$ Hz, 2H), 3.22 (s, 3H), 2.58 (td, $J = 12.0, 2.4$ Hz, 2H), 1.80 – 1.69 (m, 3H), 1.35 (qd, $J = 12.0, 4.0$ Hz, 2H). Mass (m/z): 370.3 $[\text{M}+\text{H}]^+$.

Compound 24

4-ethyl-7-((6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



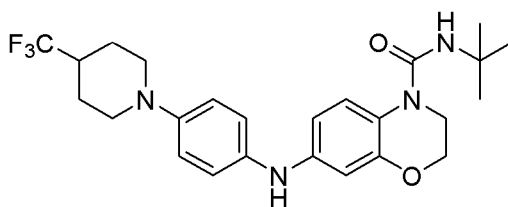
10

The title compound **24** (12.6 mg) was prepared in a total yield of 60.0 % as a wheat solid from 6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (15.9 mg, 0.065 mmol), 7-bromo-4-ethyl-2H-benzo[b][1,4]oxazin-3(4H)-one (12.8 mg, 0.05 mmol), $\text{Pd}_2(\text{dba})_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.96 (d, $J = 2.8$ Hz, 1H), 7.37 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.99 (d, $J = 8.8$ Hz, 1H), 6.84 (d, $J = 8.8$ Hz, 1H), 6.54 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.46 (d, $J = 2.8$ Hz, 1H), 4.53 (s, 2H), 4.24 - 4.32 (m, 2H), 3.85 (q, $J = 7.2$ Hz, 2H), 2.80 - 2.71 (m, 2H), 2.54 (m, 1H), 1.90 - 1.89 (m, 2H), 1.51 - 1.38 (m, 2H), 1.12 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 421.2 $[\text{M}+\text{H}]^+$.

20

Compound 25

4-ethyl-7-((6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



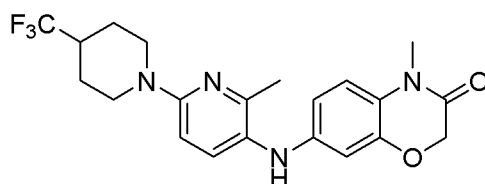
25

The title compound **25** (15.4 mg) was prepared in a total yield of 64.6% as

a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 7-bromo-N-(tert-butyl)-2,3-dihydro-4H-benzo[b][1,4]oxazine-4-carboxamide (15.7 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.20 (d, *J* = 8.8 Hz, 1H), 7.03 - 6.80 (m, 4H), 6.53 - 6.36 (m, 2H), 4.08 (t, *J* = 4.4 Hz, 2H), 3.66 - 3.57 (m, 4H), 2.68 - 2.55 (m, 2H), 2.41 (m, 1H), 1.92 - 1.81 (m, 2H), 1.64 - 1.51 (m, 2H), 1.28 (s, 9H). Mass (m/z): 477.3 [M+H]⁺.

Compound 26

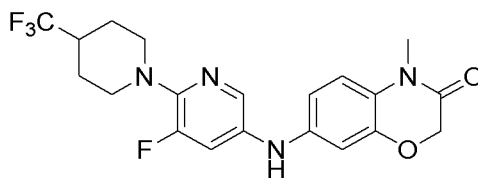
4-methyl-7-((2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title Compound 26 (93.1 mg) was prepared in a total yield of 66.5% as a light yellow solid from 2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (111 mg, 0.43 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.9 mg, 16.5 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.31 (d, *J* = 8.6 Hz, 1H), 7.26 (s, 1H), 6.92 (d, *J* = 8.6 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 1H), 6.27 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.22 (d, *J* = 2.6 Hz, 1H), 4.54 (s, 2H), 4.40 - 4.32 (m, 2H), 3.21 (s, 3H), 2.83 - 2.73 (m, 2H), 2.60 - 2.53 (m, 1H), 2.23 (s, 3H), 1.91 - 1.84 (m, 1H), 1.44 (qd, *J* = 12.6, 4.2 Hz, 2H). Mass (m/z): 421.3 [M+H]⁺.

Compound 27

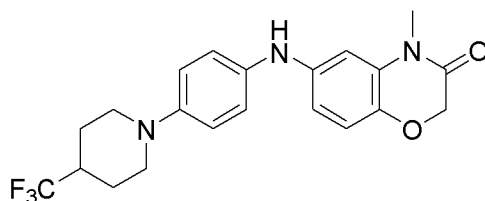
7-((5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title Compound **27** (62.2 mg) was prepared in a total yield of 44.4% as a Light yellow powder from 5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (113 mg, 0.43 mmol), 7-bromo-4-methyl-2H-benzo
 5 [b][1,4]oxazin-3(4H)-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 umol), X-Phos (7.9 mg, 16.5 umol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.15 (s, 1H), 7.85 (dd, *J* = 2.4, 1.0 Hz, 1H), 7.28 (dd, *J* = 14.2, 2.3 Hz, 1H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.71 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.61 (d, *J* =
 10 2.5 Hz, 1H), 4.60 (s, 2H), 3.83 – 3.75 (m, 2H), 3.24 (s, 3H), 2.81 (td, *J* = 12.7, 2.4 Hz, 2H), 2.53 (d, *J* = 10.3 Hz, 1H), 1.92 – 1.84 (m, 2H), 1.57 (qd, *J* = 12.6, 4.1 Hz, 2H). Mass (m/z): 425.2 [M+H]⁺.

Compound 28

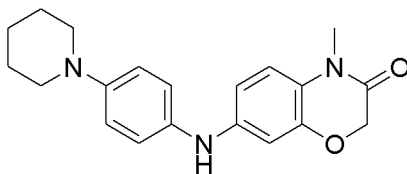
4-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-
 15 benzo[b][1,4]oxazin-3(4H)-one



The title compound **28** (39.4 mg) was prepared in a total yield of 47.0% as a brown solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (60 mg, 0.248 mmol), 6-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50
 20 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.75 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.83 – 6.77 (m, 3H), 6.66 (d, *J* = 2.4 Hz, 1H), 6.52 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.47 (s, 2H), 3.53 (d, *J* = 12.0
 25 Hz, 2H), 3.14 (s, 3H), 2.55 (t, *J* = 11.6 Hz, 2H), 2.40 – 2.34 (m, 1H), 1.81 (d, *J* = 12.4 Hz, 2H), 1.56 – 1.43 (m, 3H). Mass (m/z): 406.3 [M+H]⁺.

Compound 29

4-methyl-7-((4-(piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

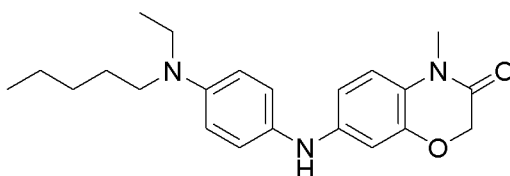


- 5 The title compound **29** (64.9 mg) was prepared in a total yield of 93.0% as a brown solid from 4-(piperidin-1-yl)aniline (43 mg, 0.248 mmol), 6-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the
10 procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.80 (s, 1H), 6.96 (dd, *J* = 8.8, 6.4 Hz, 3H), 6.89 – 6.84 (m, 2H), 6.61 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.53 (d, *J* = 2.5 Hz, 1H), 4.56 (s, 2H), 3.22 (s, 3H), 3.04 – 2.98 (m, 4H), 1.62 (q, *J* = 4.1, 2.4 Hz, 4H), 1.51 (q, *J* = 6.8, 6.4 Hz, 2H). Mass (*m/z*): 338.3 [M+H]⁺.

15

Compound 30

7-((4-(ethyl(pentyl)amino)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

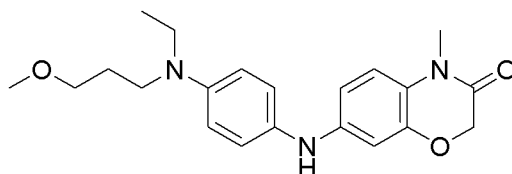


- The title compound **30** (33.1 mg) was prepared in a total yield of 43.5% as
20 a white solid from N¹-ethyl-N¹-pentylbenzene-1,4-diamine (51 mg, 0.248 mmol), 6-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.64 (s,
25 1H), 6.93 (d, *J* = 8.4 Hz, 3H), 6.62 (d, *J* = 8.4 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 1H), 6.45 (d, *J* = 2.4 Hz, 1H), 4.54 (s, 2H), 3.28 (d, *J* = 7.2 Hz, 2H), 3.21 (s,

3H), 3.16 (d, $J = 7.6$ Hz, 2H), 1.54 – 1.46 (m, 2H), 1.29 (td, $J = 12.0, 10.0, 5.6$ Hz, 4H), 1.05 (t, $J = 6.8$ Hz, 3H), 0.88 (t, $J = 6.8$ Hz, 3H). Mass (m/z): 368.3 $[M+H]^+$.

Compound 31

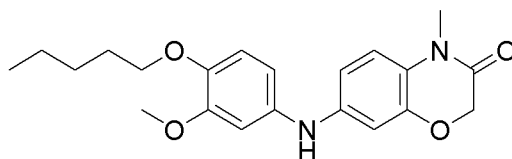
5 7-((4-(ethyl(3-methoxypropyl)amino)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **31** (53.6 mg) was prepared in a total yield of 70.2% as a black oil from N¹-ethyl-N¹-(3-methoxypropyl)benzene-1,4-diamine (51 mg, 0.248 mmol), 6-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.66 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 3H), 6.67 – 6.62 (m, 2H), 6.54 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 4.54 (s, 2H), 3.37 (s, 1H), 3.36 – 3.34 (m, 2H), 3.31 – 3.25 (m, 3H), 3.24 (s, 3H), 3.21 (s, 3H), 1.77 – 1.66 (m, 2H), 1.05 (t, $J = 6.8$ Hz, 3H). Mass (m/z): 370.3 $[M+H]^+$.

Compound 32

20 7-((3-methoxy-4-(pentyloxy)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



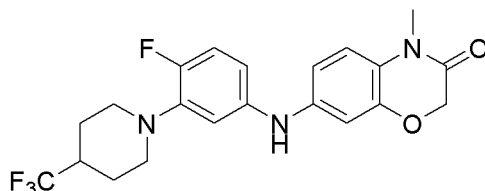
The title compound **32** (38.8 mg) was prepared in a total yield of 50.7% as a pink solid from 3-methoxy-4-(pentyloxy)aniline (52 mg, 0.248 mmol), 6-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol) and Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.93 (s, 1H),

6.99 (d, $J = 8.8$ Hz, 1H), 6.84 (d, $J = 8.8$ Hz, 1H), 6.71 – 6.64 (m, 2H), 6.61 – 6.54 (m, 2H), 4.57 (s, 2H), 3.87 (t, $J = 6.4$ Hz, 2H), 3.71 (s, 3H), 3.23 (s, 3H), 1.68 (p, $J = 6.8$ Hz, 2H), 1.43 – 1.28 (m, 4H), 0.90 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 371.3 $[M+H]^+$.

5

Compound 33

7-((4-fluoro-3-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

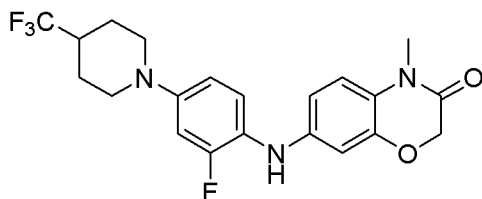


The title compound **33** (16.9 mg) was prepared in a total yield of 15.9% as a light pink solid from 4-fluoro-3-(4-(trifluoromethyl) piperidin-1-yl) aniline (86 mg, 0.33 mmol), 7-bromo-4-methyl-2H- benzo[b][1,4]oxazin-3(4H)-one (60 mg, 0.25 mmol), $Pd_2(dba)_3$ (2.3 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), and Cs_2CO_3 (122 mg, 0.75 mmol) according to the procedure for compound 1. ^1H NMR (300 MHz, $DMSO-d_6$) δ 8.03 (s, 1H), 7.03 – 6.95 (m, 2H), 6.72 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.68 – 6.58 (m, 3H), 4.59 (s, 2H), 3.36 – 3.29 (m, 4H), 3.24 (s, 3H), 2.70 – 2.62 (m, 2H), 2.48 – 2.41 (m, 1H), 1.94 – 1.86 (m, 2H), 1.61 (qd, $J = 12.4, 4.1$ Hz, 2H). Mass (m/z): 424.2 $[M+H]^+$.

15

Compound 34

7-((2-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



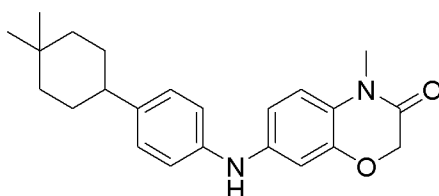
The title compound **34** (38.1 mg) as prepared in a total yield of 28.2% as a light gray solid from 2-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.38 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4] oxazin-3(4H)-one (76 mg, 0.32 mmol), $Pd_2(dba)_3$ (2.9 mg, 3.2 μ mol), X-Phos (7.6 mg, 16

25

umol), and Cs_2CO_3 (156 mg, 0.48 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.54 (s, 1H), 7.14 – 7.07 (m, 1H), 6.95 (d, $J = 8.7$ Hz, 1H), 6.87 (dd, $J = 14.3, 2.7$ Hz, 1H), 6.74 (dd, $J = 8.7, 2.7$ Hz, 1H), 6.46 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.37 (d, $J = 2.5$ Hz, 1H), 4.55 (s, 2H), 3.78 – 3.68 (m, 2H), 3.21 (s, 3H), 2.69 (td, $J = 12.5, 2.6$ Hz, 2H), 2.49 – 2.40 (m, 1H), 1.90 – 1.83 (m, 2H), 1.54 (qd, $J = 12.6, 4.1$ Hz, 2H). Mass (m/z): 424.3 $[\text{M}+\text{H}]^+$.

Compound 35

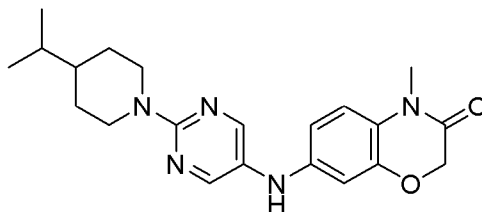
7-((4-(4,4-dimethylcyclohexyl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **35** (15.9 mg) was prepared in a total yield of 87.1% as a yellow powder from 4-(4,4-dimethylcyclohexyl)aniline (13.2 mg, 0.065 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (12.1 mg, 0.05 mmol), $\text{Pd}_2(\text{dba})_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.14 - 7.03 (m, 2H), 7.02 - 6.90 (m, 3H), 6.72 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.63 (d, $J = 2.4$ Hz, 1H), 4.57 (s, 2H), 3.23 (s, 3H), 2.31 (m, 1H), 1.63 - 1.49 (m, 4H), 1.49 - 1.37 (m, 2H), 1.35 - 1.22 (m, 2H), 0.95 (s, 3H), 0.93 (s, 3H). Mass (m/z): 365.2 $[\text{M}+\text{H}]^+$.

Compound 36

7-((2-(4-isopropylpiperidin-1-yl)pyrimidin-5-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

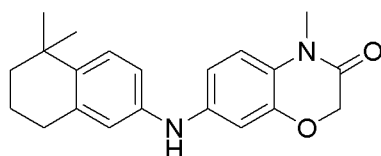


The title compound **36** (62.1 mg) was prepared in a total yield of 78.6% as a yellow solid from 2-(4-isopropylpiperidin-1-yl)pyrimidin-5-amine (55

mg, 0.248 mmol), 6-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-Phos (6 mg, 0.01 mmol), Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.17 (s, 2H), 7.67 (d, *J* = 4.4 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 6.42 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.35 (d, *J* = 2.4 Hz, 1H), 4.60 (dt, *J* = 12.8, 2.4 Hz, 2H), 4.52 (s, 2H), 3.17 (s, 3H), 2.71 (td, *J* = 12.8, 2.4 Hz, 2H), 1.65 (dd, *J* = 12.4, 2.8 Hz, 2H), 1.39 (dq, *J* = 13.2, 6.8 Hz, 1H), 1.29 – 1.00 (m, 4H), 0.83 (d, *J* = 6.8 Hz, 6H). Mass (m/z): 382.3 [M+H]⁺.

Compound 37

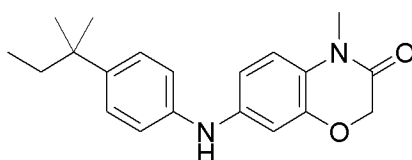
7-((5,5-dimethyl-5,6,7,8-tetrahydronaphthalen-2-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **37** (125.0 mg) was prepared in a total yield of 88.1% as a yellow solid from 6-bromo-1,1-dimethyl-1,2,3,4-tetrahydronaphthalene (0.1 g, 0.42 mmol), 7-amino-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (0.09 g, 0.5 mmol), Ruphos (39 mg, 0.08 mmol), Pd₂(dba)₃ (38 mg, 0.04 mmol) and Cs₂CO₃ (0.41 g, 1.26 mmol) in 1,4-dioxane (10 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, CDCl₃) δ 7.23 (d, *J* = 8.4 Hz, 1H), 6.88 – 6.83 (m, 2H), 6.73 (d, *J* = 13.6 Hz, 3H), 4.59 (s, 2H), 3.49 (s, 1H), 3.34 (s, 3H), 2.71 (t, *J* = 6.4 Hz, 2H), 1.81 – 1.76 (m, 2H), 1.66 – 1.64 (m, 2H), 1.27 (s, 6H). Mass (m/z): 337.2 [M+H]⁺.

Compound 38

4-methyl-7-((4-(tert-pentyl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

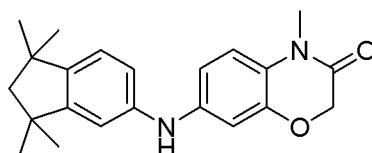


The title compound **38** (60.0 mg) was prepared in a total yield of 33.2% as

a white solid from 4-(tert-pentyl)aniline (100 mg, 0.613 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (134 mg, 0.558 mmol), Pd₂(dba)₃ (25.5 mg, 0.028 mmol), X-Phos (26.6 mg, 0.056 mmol) and Cs₂CO₃ (364 mg, 1.12 mmol) in dioxane (15 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.27 (m, 4H), 7.12 (t, J = 10.6 Hz, 2H), 6.59 (t, J = 8.6 Hz, 2H), 4.36 – 4.23 (m, 2H), 3.85 (d, J = 15.9 Hz, 2H), 1.64 – 1.54 (m, 3H), 1.24 (d, J = 10.9 Hz, 7H), 0.68 (t, J = 7.4 Hz, 3H). Mass (m/z): 325.4 [M+H]⁺.

Compound 39

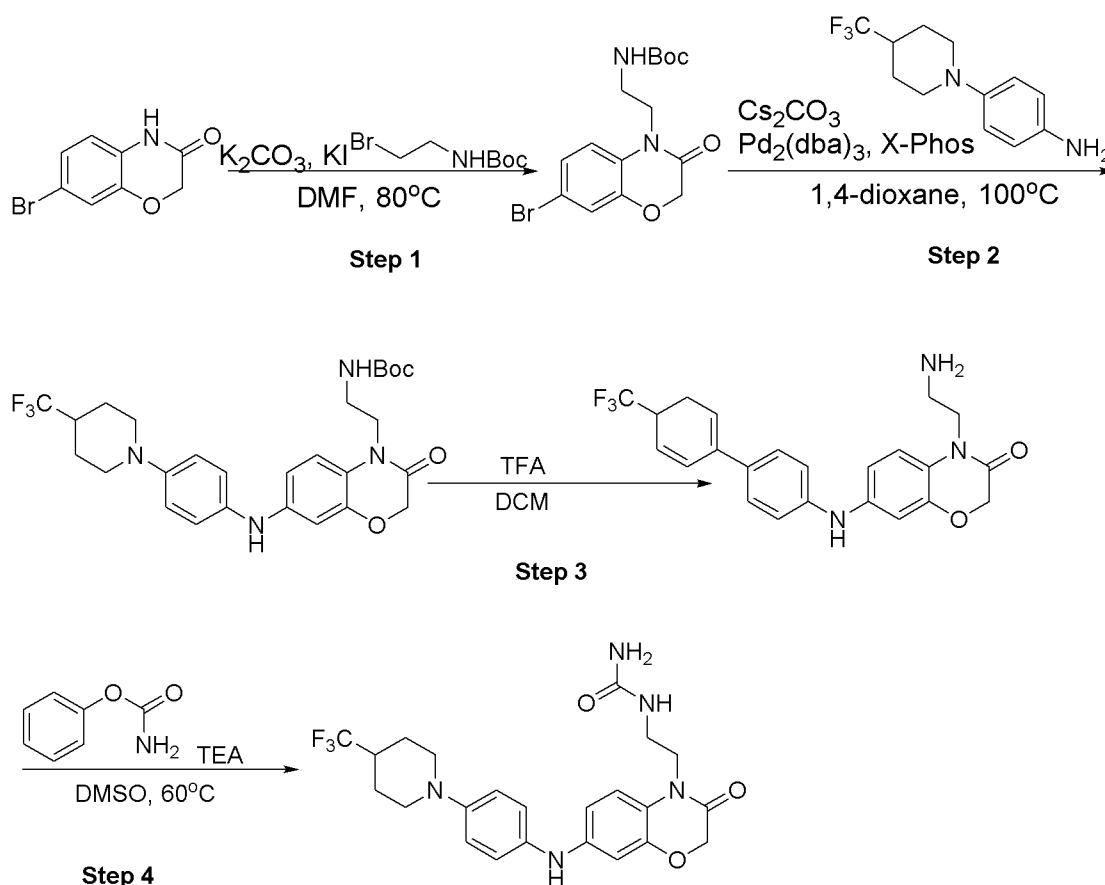
4-methyl-7-((1,1,3,3-tetramethyl-2,3-dihydro-1H-inden-5-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **39** (8 mg) was prepared as a yellow solid from 5-bromo-1,1,3,3-tetramethyl-2,3-dihydro-1H-indene (300 mg, 1.19 mmol), 7-amino-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (211 mg, 1.19 mmol), Cs₂CO₃ (772 mg, 2.38 mmol), Pd₂(dba)₃ (108 mg, 0.12 mmol) and Ruphos (110 mg, 0.24 mmol) in 1,4-dioxane (15 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, CD₃OD) δ 6.97 (dd, J = 8.4, 3.2 Hz, 2H), 6.88 (dd, J = 8.2, 2.2 Hz, 1H), 6.79 (d, J = 2.0 Hz, 1H), 6.70 (dd, J = 8.6, 2.6 Hz, 1H), 6.64 (d, J = 2.6 Hz, 1H), 4.53 (s, 2H), 3.30 (s, 3H), 1.89 (s, 2H), 1.26 (d, J = 1.8 Hz, 12H). Mass (m/z): 351.3 [M+H]⁺.

Compound 40

1-(2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)urea



Step 1. Preparation of tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)carbamate

A mixture of 7-bromo-2H-1,4-benzoxazine-3(4H)-one (454 mg, 2.0 mmol),
 5 tert-Butyl N-(2-bromoethyl)carbamate (892 mg, 4.0 mmol), KI (33.2 mg, 0.2 mmol) and K₂CO₃ (828 mg, 6.0 mmol) in DMF (10.0 mL) was stirred for 18 hours at 80°C. After cooling to r.t., 10 mL of water was added. The resulting solution was extracted with 3x10 mL of ethyl acetate. The organic layers were combined, washed with water (3x15 mL), dried and
 10 concentrated under vacuum. The residue was purified by a silica gel column (EA/PE=0-1/2) to afford the desired product as a yellow solid (250 mg, 33.8 %). Mass (m/z): 371.2 [M+H]⁺.

Step 2. Preparation of tert-butyl (2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)carbamate
 15

The title compound (220 mg) as prepared in a total yield of 60.6% as a light yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (214

mg, 0.89 mmol), tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo
[b][1,4] oxazin-4-yl)ethyl)carbamate (250 mg, 0.68 mmol), Pd₂(dba)₃ (5.0
mg, 6.8 μ mol), X-Phos (16.3 mg, 34 μ mol), and Cs₂CO₃ (333 mg, 1.02
mmol) according to the procedure for compound 1. Mass (m/z): 535.2
5 [M+H]⁺.

Step 3. Preparation of 4-(2-aminoethyl)-7-((4'-(trifluoromethyl)-3',4'-
dihydro-[1,1'-biphenyl]-4-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of tert-butyl (2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin
-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)carba
10 mate (220 mg, 0.41 mmol) in DCM (5 mL) was added TFA (5 mL). Then
the solution was stirred for 30 mins at r.t. and concentrated. 10 ml water
was added. The pH of the filtration was adjusted to 8-9 with sodium
carbonate solution. Then the mixture was extracted by DCM (15 mL x 3).
The combined organic layers were washed with water (10 mL), dried over
15 Na₂SO₄ and concentrated. The residue was purified by prep-TLC
(MeOH/DCM=1/5) to afford the desired product as a yellow solid. Mass
(m/z):435.1 [M+H]⁺.

Step 4. Preparation of 1-(2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin
-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)urea

20 **(40)**

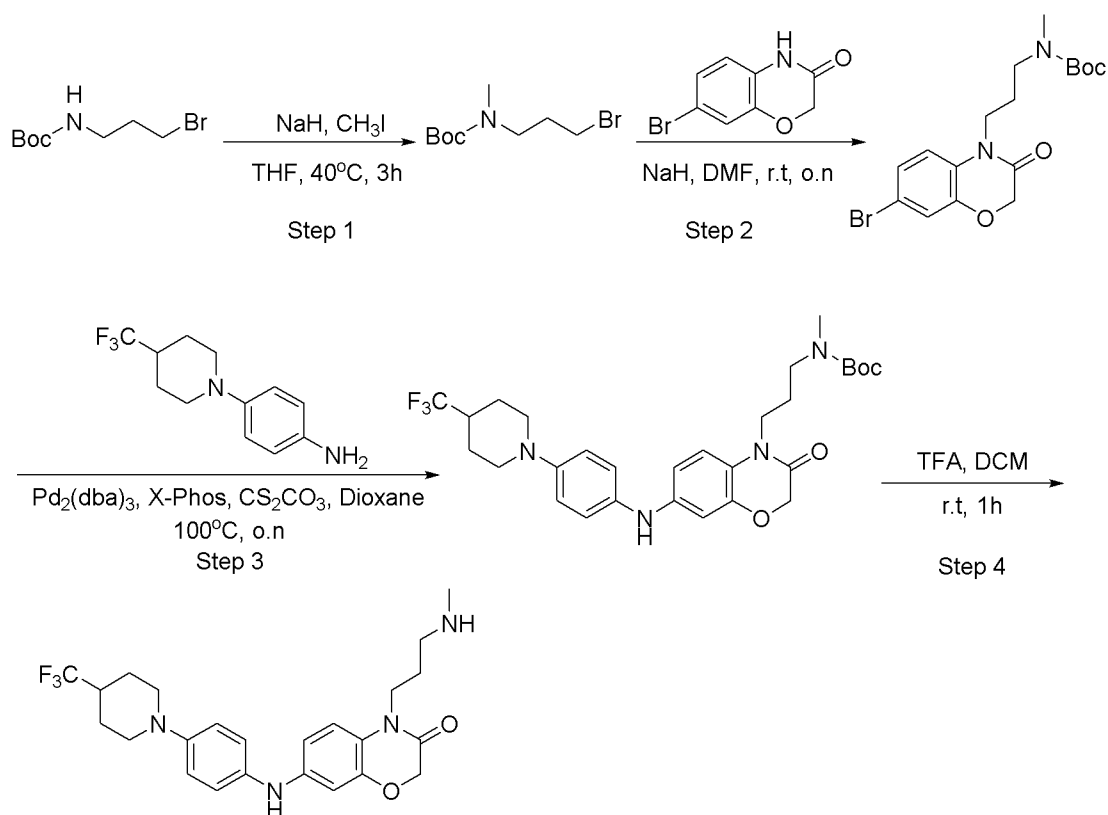
To a solution of 4-(2-aminoethyl)-7-((4'-(trifluoromethyl)-3',4'-dihydro
-[1,1'-biphenyl]-4-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (160 mg,
0.37 mmol) and TEA (112 mg, 1.11 mmol) in DMSO (3.0 mL) was added
phenyl carbamate (60.6 mg, 0.44 mmol). Then the mixture was stirred
25 overnight at 60°C. After cooling to rt., 10 mL of water was added. The
resulting solution was extracted with 3x10 mL of ethyl acetate. The
organic layers were combined, washed with water (3x15 mL), dried and
concentrated under vacuum. The residue was purified by prep-TLC
(MeOH/DCM=1/10) to afford the desired product (compound 40) as a
30 yellow solid (17.5 mg, 9.9 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.81 (s,
1H), 7.18 (d, *J* = 8.8 Hz, 1H), 6.99 – 6.94 (m, 2H), 6.93 – 6.87 (m, 2H),
6.60 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 6.14 (t, *J* = 5.9 Hz,

1H), 5.52 (s, 2H), 4.54 (s, 2H), 3.81 (t, $J = 7.0$ Hz, 2H), 3.67 – 3.57 (m, 2H), 3.15 (q, $J = 6.5$ Hz, 2H), 2.66 – 2.58 (m, 2H), 2.46 – 2.36 (m, 1H), 1.94 – 1.84 (m, 2H), 1.57 (qd, $J = 12.5, 4.1$ Hz, 2H). Mass (m/z): 478.2 $[M+H]^+$.

5

Compound 41

4-(3-(methylamino)propyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. Preparation of tert-butyl (3-bromopropyl)(methyl)carbamate

- 10 To a solution of tert-butyl (3-bromopropyl)carbamate (1.00g, 4.20 mmol) in THF (10 mL) was added NaH (60%, 252 mg, 6.30 mmol) in portions at 0°C. The mixture was stirred at r.t. for 1 h. CH₃I was then added to the above mixture and stirred at 35°C for 12h. The reaction mixture was quenched by the addition of water (20 mL) and extracted with ethyl acetate
- 15 (3x 50 mL). The combined organic phase was dried and concentrated to give the titled compound (1.06 g, theoretical yield) as a light yellow oil. LC-MS (m/z) 252.2 $[M+H]^+$.

Step 2. Preparation of tert-butyl(3-(7-bromo-3-oxo-2,3-dihydro-4H-

benzo[b][1,4]oxazin-4-yl)propyl)(methyl)carbamate

To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (200 mg, 0.88 mmol) in DMF (3 mL) was added NaH (60%, 52.6 mg, 1.31 mmol) in portions at 0 °C. The mixture was stirred at r.t. for 1h. Tert-butyl
5 (3-bromopropyl)(methyl)carbamate (221.13 mg, 0.877 mmol) was then added to the above mixture and stirred at room temperature for 12h. The reaction mixture was quenched by the addition of water (20mL) and extracted with ethyl acetate (3x 50 mL). The combined organic phase was dried and concentrated. The residue was purified by TLC (Petroleum ether:
10 Ethyl acetate=3:1) to give the titled compound (340 mg, 97% yield) as a light yellow oil. LC-MS (m/z) 399.2 [M+H]⁺.

Step 3. Preparation of tert-butylmethyl(3-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)propyl)carbamate

15 The title compound (60 mg) as prepared in a total yield of 42.6% as light yellow oil from tert-butyl (3-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4] oxazin-4-yl)propyl)(methyl)carbamate (100 mg, 0.25 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (67.3 mg, 0.27 mmol), Pd₂(dba)₃ (11.5 mg, 0.013 mmol), X-phos (11 mg, 0.025 mmol) and
20 Cs₂CO₃ (163 mg, 0.5 mmol) according to the procedure for compound 1. LC-MS (m/z) 563.2 [M+H]⁺.

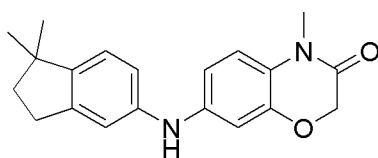
Step 4. 4-(3-(methylamino)propyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (**41**)

To a solution of 4-(3-(methylamino)propyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (60 mg,
25 0.11 mmol) in DCM (3 mL) was added TFA (1 mL). The mixture was stirred at r.t. for 1h. The reaction mixture was concentrated under vacuum. The residue was quenched by the addition of a saturated solution of NaHCO₃ (10 mL) and extracted with ethyl acetate (3x 20 mL). The
30 combined organic phase was dried and concentrated. The residue was purified by Prep TLC (Dichloromethane: Methanol: Ammonia=5:1:0.1) to give the titled compound **41** (18.7 mg, 37.9% yield) as a light green solid.

¹H NMR (400 MHz, DMSO-*d*₆): δ 8.82 (s, 2H), 7.88 (s, 1H), 7.09 (d, *J* = 8.7 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 2H), 6.91 (s, 2H), 6.63 (d, *J* = 8.7 Hz, 1H), 6.57 (s, 1H), 4.58 (s, 2H), 3.94-3.90 (t, *J* = 7.2 Hz, 2H), 3.62 (d, *J* = 12.1 Hz, 2H), 2.93 (d, *J* = 8.5 Hz, 2H), 2.68-2.58 (m, 2H), 2.47-2.39 (m, 2H), 2.53 (s, 1H), 1.94-1.84 (m, 4H), 1.58 (s, 2H). LC-MS (*m/z*) 463.2 [M+H]⁺.

Compound 42

7-((1,1-dimethyl-2,3-dihydro-1H-inden-5-yl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one



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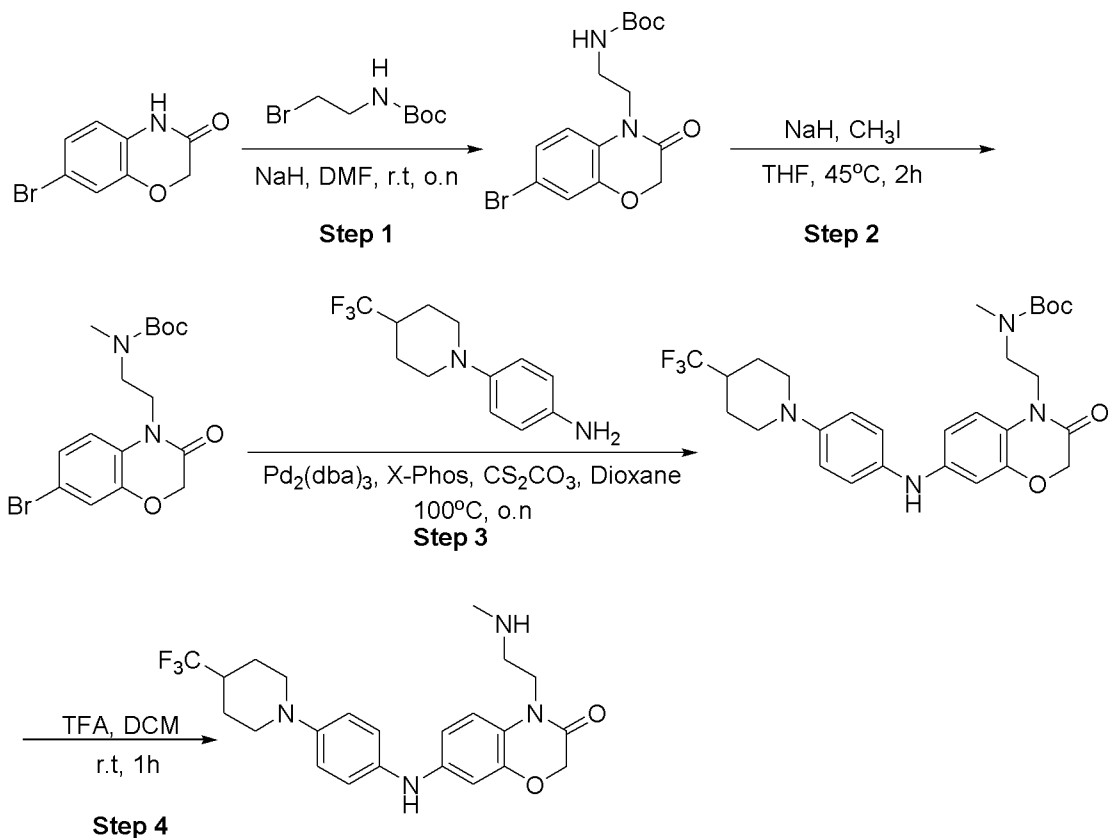
The title compound (16 mg) was prepared in a total yield of 8% as a yellow solid from 1,1-dimethyl-2,3-dihydro-1H-inden-5-amine (0.1 g, 0.6 mmol), 7-bromo-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one (0.15 g, 0.6 mmol), Xantphos (69 mg, 0.12 mmol), Cs₂CO₃ (0.39 g, 1.2 mmol), Pd₂(dba)₃ (50 mg, 0.06 mmol) and toluene (10 mL) according to the procedure for compound 1. MS (ESI) *m/z* 322.8 [M+H]⁺. ¹H NMR (300 MHz, CD₃OD) δ 7.11 – 6.80 (m, 4H), 6.72 – 6.62 (m, 2H), 4.55 (s, 2H), 3.32 – 3.27 (m, 3H), 2.80 (q, *J* = 6 Hz, 2H), 1.91 (q, *J* = 6 Hz, 2H), 1.23 (s, 6H).

15

Compound 43

4-(2-(methylamino)ethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one

20



Step 1. Preparation of tert-butyl(2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)carbamate

To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (150 mg, 0.66 mmol) in DMF (10 mL) was added NaH (60%, 162 mg, 0.72 mmol) in portions at 0°C. The mixture was stirred at r.t. for 1h. Tert-butyl (2-bromoethyl)carbamate (31.6 mg, 0.79 mmol) was then added to the above mixture and stirred at room temperature for 12h. The reaction mixture was quenched by the addition of water (20 mL) and extracted with ethyl acetate (3x 50 mL). The combined organic phase was dried and concentrated. The residue was purified by Prep-TLC (petroleum ether: ethyl acetate=1:1) to afford the titled compound (236 mg, 96.6% yield) as a light yellow oil. LC-MS (m/z) 371.2 [M+H]⁺.

Step 2. Preparation of tert-butyl(2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate

To a solution of tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4] oxazin-4-yl)ethyl)carbamate (236 mg, 0.64 mmol) in THF

(3 mL) was added NaH (60%, 30.5 mg, 0.76 mmol) in portions at 0°C. The mixture was stirred at r.t. for 1 h. CH₃I (108.33 mg, 0.76 mmol) was then added to the above mixture and stirred at room temperature for 2 h. The reaction mixture was quenched by the addition of water (20 mL) and
 5 extracted with ethyl acetate (3x 50 mL). The combined organic phase was dried and concentrated to give the titled compound (228 mg, 93.1% yield) as brown oil. LC-MS (m/z) 385.2 [M+H]⁺.

Step 3. Preparation of tert-butylmethyl(2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)carbamate
 10

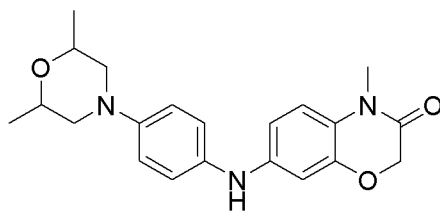
The title compound (70 mg) was prepared in a total yield of 42.7% as light yellow oil from tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate (115 mg, 0.30 mmol), 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (80.2 mg, 0.33 mmol), Pd₂(dba)₃
 15 (13.7 mg, 0.015 mmol), X-phos (14.2 mg, 0.03 mmol) and Cs₂CO₃ (195 mg, 0.60 mmol) in 1,4-dioxane (5 mL) according to the procedure for compound 1. LC-MS (m/z) 549.2 [M+H]⁺.

Step 4. Preparation of 4-(2-(methylamino)ethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

The title compound **43** (20.1 mg) was prepared in a total yield of 35.1 % as a khaki solid from methyl(2-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)carbamate (70 mg, 0.13 mmol), TFA (1 mL) and DCM (3 mL) according to the procedure for compound **41**. ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.82 (s, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.96 – 6.89 (m, 2H), 6.91 – 6.83 (m, 2H), 6.61 – 6.49 (m, 2H), 4.55 (s, 2H), 4.05 (t, *J* = 6.4 Hz, 2H), 3.59 (d, *J* = 12.3 Hz, 2H), 3.26 (s, 3H), 2.96 (t, *J* = 6.4 Hz, 2H), 2.59 (td, *J* = 12.3, 2.5 Hz, 2H), 2.45 – 2.35 (m, 2H), 1.90 – 1.81 (m, 2H), 1.53 (qd, *J* = 12.4, 4.1 Hz, 2H). LC-MS (m/z) 449.2 [M+H]⁺.
 25

Compound 44

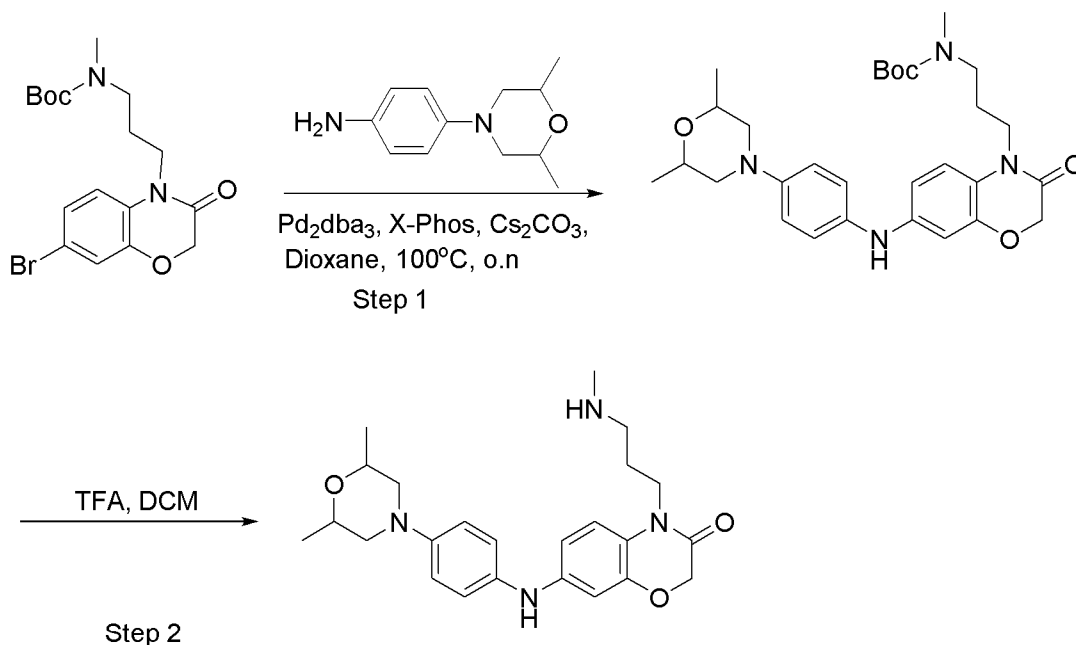
7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **44** (68.5 mg) was prepared in a total yield of 34.7 % as a khaki solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (130 mg, 0.54 mmol), 4-(2,6-dimethylmorpholino)aniline (122 mg, 0.59 mmol), Pd₂(dba)₃ (24.6 mg, 0.03 mmol), X-Phos (25.6 mg, 0.054 mmol) and Cs₂CO₃ (350 mg, 1.07 mmol) in 1,4-dioxane (5 mL) according to the procedure for compound **1**. LC-MS (m/z) 368.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.75 (s, 1H), 6.96 – 6.87 (m, 3H), 6.87 – 6.80 (m, 2H), 6.58 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.49 (d, *J* = 2.5 Hz, 1H), 4.53 (s, 2H), 3.69-3.61 (m, 2H), 3.40 (dt, *J* = 11.1, 2.3 Hz, 2H), 3.18 (s, 3H), 2.15 (t, *J* = 11.2 Hz, 2H), 1.10 (d, *J* = 6.2 Hz, 6H).

Compound 45

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. Preparation of 7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of tert-butyl (3-(7-bromo-3-oxo-2,3-dihydro-4H-

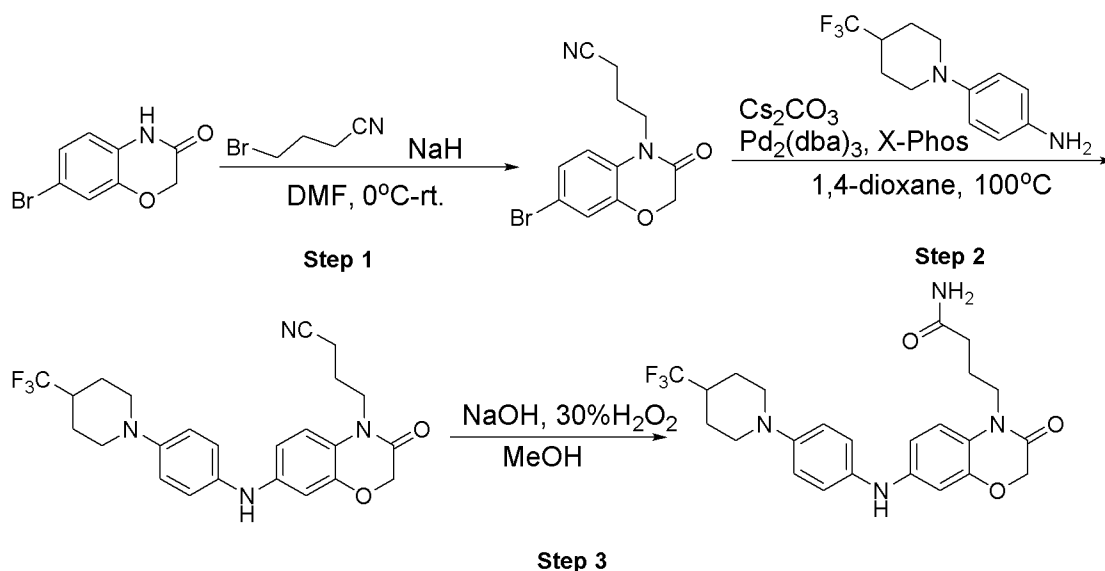
benzo[b][1,4]oxazin-4-yl)propyl)(methyl)carbamate (120 mg, 0.30 mmol) and 4-(2,6-dimethylmorpholino)aniline (68.2 mg, 0.33 mmol) in 1,4-dioxane (5 mL) was added Pd₂(dba)₃ (13.8 mg, 0.015 mmol), X-Phos (14.3 mg, 0.03 mmol) and Cs₂CO₃ (196 mg, 0.60 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3x 50 mL). The combined organic phase was dried and concentrated. The residue was purified by Prep-TLC (Petroleum ether: Ethyl acetate=1:5) to give the titled compound (75 mg, 47.6%) as a brown oil. LC-MS (m/z) 525.3 [M+H]⁺.

Step 2. Preparation of 7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of tert-butyl (3-(7-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)propyl)(methyl)carbamate (75 mg, 0.14 mmol) in dichloromethane (5 mL) was added TFA (1.0mL). The mixture was stirred at room temperature for 2h. The reaction mixture was concentrated and adjusted PH to 7-8 with sat. NaHCO₃ and extracted with dichloromethane (3x 50 mL). The combined organic phase was dried and concentrated. The residue was purified by Prep-TLC (Dichloromethane: Methanol: Ammonia=5:1:0.1) to give the titled compound **45** (27 mg, 44.5%) as a khaki solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.45 (s, 1H), 7.80 (s, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.96 – 6.90 (m, 2H), 6.88 – 6.82 (m, 2H), 6.57 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.51 (d, *J* = 2.5 Hz, 1H), 4.55 (s, 2H), 3.88 (t, *J* = 7.0 Hz, 2H), 3.65 (ddd, *J* = 10.3, 6.3, 2.3 Hz, 2H), 3.45 – 3.37 (m, 2H), 2.93 – 2.85 (m, 2H), 2.51 (s, 3H), 2.15 (dd, *J* = 11.8, 10.3 Hz, 2H), 1.83 (q, *J* = 7.5 Hz, 2H), 1.11 (d, *J* = 6.2 Hz, 6H). LC-MS (m/z) 425.2 [M+H]⁺.

Compound 46

4-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)butanamide



Step 1. Preparation of 4-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)butanenitrile

To a solution of 7-bromo-2H-1,4-benzoxazine-3(4H)-one (227 mg, 1 mmol) in DMF (10 mL) stirred at 0°C under nitrogen atmosphere was added NaH (60%, 60 mg, 1.5 mmol). Then the mixture was stirred for 1 hour at 0°C. 4-Bromobutyronitrile (194 mg, 2 mmol) was added, the mixture was stirred overnight at r.t. 20 mL of water was added dropwise at 0°C. The precipitate was collected by filtration and washed with 10 mL of water. Target product was obtained as a yellow solid. (238 mg, 81.0%). Mass (m/z): 295.0 [M+H]⁺.

Step 2. Preparation of 4-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)butanenitrile

The title compound (161 mg) as prepared in a total yield of 43.4% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (198 mg, 0.81 mmol), 4-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)butanenitrile (238 mg, 0.81 mmol), Pd₂(dba)₃ (11.8 mg, 16 μmol), X-Phos (18.5 mg, 32 μmol), and Cs₂CO₃ (396 mg, 1.22 mmol) according to the procedure for compound 1. Mass (m/z): 459.2 [M+H]⁺.

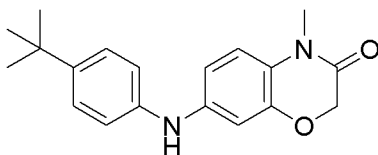
Step 3. Preparation of 4-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)butanamide (**46**)

To a solution of 4-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)

phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)butanenitrile in MeOH (3 mL) was added 1 mL of 10% NaOH solution at 0 °C. Followed by the addition of 0.3 mL of 30% H₂O₂ solution then the mixture was stirred for 3 hours at r.t. 10 mL of water was added. The resulting solution was extracted with 3x10 mL of ethyl acetate. The organic layers were combined, washed with water (3x15 mL), dried and concentrated under vacuum. The residue was purified by prep-TLC (MeOH/DCM=1/10) to afford the desired product as a yellow solid (9.6 mg, 15.5 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.78 (s, 1H), 7.27 (s, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.95 – 6.91 (m, 2H), 6.89 – 6.83 (m, 2H), 6.74 (s, 1H), 6.58 (dd, *J* = 8.9, 2.2 Hz, 1H), 6.51 (d, *J* = 2.4 Hz, 1H), 4.51 (s, 2H), 3.77 (t, *J* = 7.5 Hz, 2H), 3.62 – 3.55 (m, 2H), 2.60 – 2.53 (m, 2H), 2.43 – 2.37 (m, 1H), 2.08 (t, *J* = 7.4 Hz, 2H), 1.88– 1.82 (m, 2H), 1.74 – 1.66 (m, 2H), 1.60 – 1.44 (m, 2H). Mass (m/z): 477.2 [M+H]⁺.

Compound 47

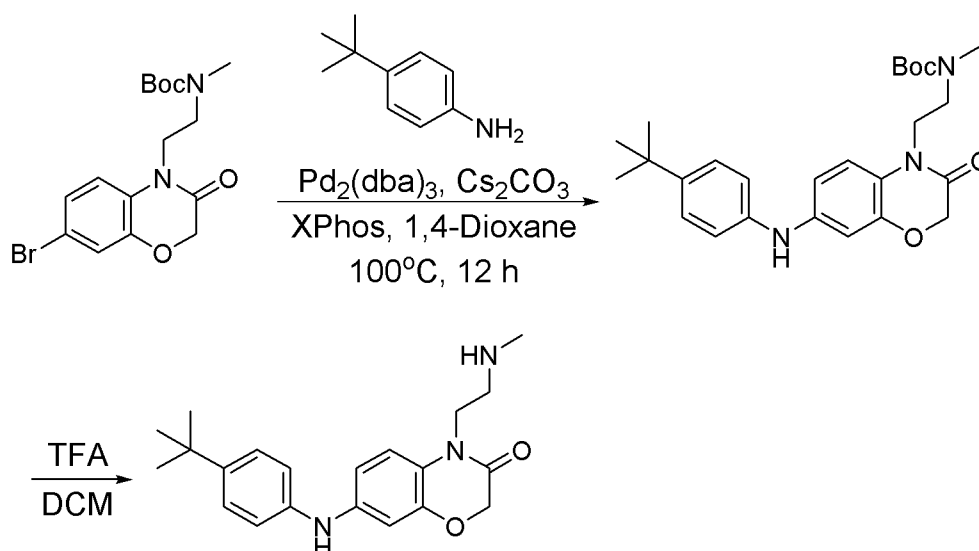
7-((4-(tert-butyl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **47** (26.0 mg) was prepared in a yield of 20.0% as a light blue solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.42 mmol), 4-(tert-butyl)aniline (68 mg, 0.46 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (38 mg, 0.04 mmol), Xphos (39 mg, 0.08 mmol) and Cs₂CO₃ (277 mg, 0.83 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.99 (s, 1H), 7.26 – 7.16 (m, 2H), 7.00 – 6.89 (m, 3H), 6.70 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.61 (d, *J* = 2.4 Hz, 1H), 4.55 (s, 2H), 3.20 (s, 3H), 1.22 (s, 9H). Mass (m/z): 310.2 [M+H]⁺.

Compound 48

7-((4-(tert-butyl)phenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1 . Preparation of tert-butyl (2-(7-((4-(tert-butyl)phenyl)amino)-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate

To a solution of tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate (120 mg, 0.31 mmol) and 4-(tert-butyl)aniline (61 mg, 0.34 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (28 mg, 0.03 mmol), Xphos (29 mg, 0.06 mmol) and Cs_2CO_3 (203 mg, 0.63 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC to give tert-butyl (2-(7-((4-(tert-butyl)phenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)ethyl)(methyl)carbamate (50 mg, 35%) as a brown solid. Mass (m/z): 454.2 $[\text{M}+\text{H}]^+$.

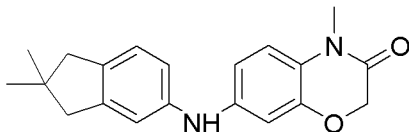
Step 2. Preparation of 7-((4-(tert-butyl)phenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (48)

To a solution of tert-butyl (2-(7-((4-(tert-butyl)phenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)ethyl)(methyl)carbamate (50 mg, 0.11 mmol) in DCM (3 mL) was added 2,2,2-trifluoroacetic acid (1 mL). The mixture was stirred at r.t. for 1h, the mixture was concentrated and purified by prep TLC to give 7-((4-(tert-butyl)phenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (16.9 mg, 43%) as a white solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.63 (s, 1H), 8.20 (s, 1H), 7.32 (d, $J = 8.6$ Hz, 1H), 7.07 – 6.99 (m, 2H), 6.94 – 6.86 (m, 2H), 6.57 (dd, $J = 8.6, 1.9$ Hz, 1H), 6.46 (d, $J = 1.8$ Hz, 1H), 3.72 – 3.60 (m,

2H), 3.51 – 3.43 (m, 2H), 3.18 (s, 3H), 2.23 – 2.13 (m, 2H), 1.12 (d, J = 6.2 Hz, 6H). Mass (m/z): 354.2 $[M+H]^+$.

Compound 49

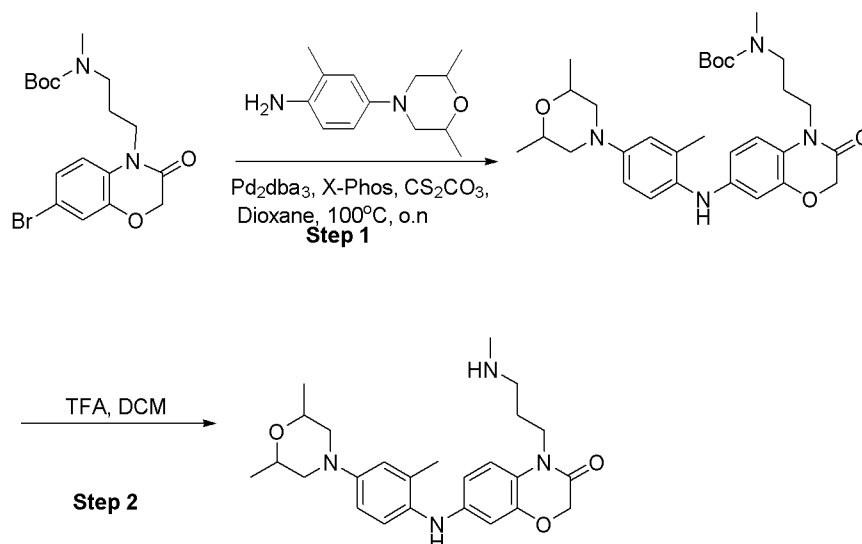
7-((2,2-dimethyl-2,3-dihydro-1H-inden-5-yl)amino)-4-methyl-2H-
benzo[b][1,4]oxazin-3(4H)-one



To a stirred solution of compound 5-bromo-2,2-dimethyl-2,3-dihydro-1H-indene (80 mg, 0.355 mmol) and 7-amino-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (69.66 mg, 0.391 mmol) in dioxane under N_2 was added NaOtBu (68.31 mg, 0.711 mmol), $Pd_2(dba)_3$ (32.54 mg, 0.036) and BINAP (44.26 mg, 0.071 mmol). The reaction mixture was stirred at 90°C for 16 hrs. Then the mixture was filtered and concentrated. To the residue was added water (10 mL), extracted with EA (10 mL x 3). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by prep-HPLC (column-Xbridge-C18, 150 x 21.2 mm, 5um; Mobile phase: ACN- H_2O (0.1% trifluoroacetic acid (TFA)), 60%-80%) to afford compound **49** as a yellow solid (12.6 mg). ^1H NMR (400 MHz, CD_3OD) δ 6.99 (dd, J = 13.4, 8.3 Hz, 2H), 6.88 (s, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.71 (dd, J = 8.7, 2.5 Hz, 1H), 6.65 (d, J = 2.4 Hz, 1H), 4.54 (s, 2H), 3.32 (s, 3H), 2.65 (d, J = 6.3 Hz, 4H), 1.14 (s, 6H). MS (m/z): 322.17 $[M+H]^+$.

Compound 50

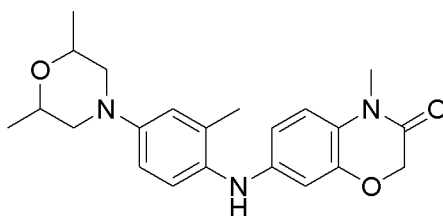
7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **50** (4.2 mg, 12.3 %) as a white solid was prepared according to the procedure outlined for compound **48**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.41 (s, 1H), 7.22 (s, 1H), 6.96 (t, *J* = 8.9 Hz, 2H), 6.81 (d, *J* = 2.9 Hz, 1H), 6.72 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.31 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.23 (d, *J* = 2.5 Hz, 1H), 4.52 (s, 2H), 3.86 (t, *J* = 7.1 Hz, 1H), 3.70 – 3.65 (m, 1H), 3.65 – 3.53 (m, 1H), 3.51 – 3.43 (m, 2H), 2.93 – 2.80 (m, 2H), 2.50 (s, 3H), 2.27 – 2.10 (m, 2H), 2.09 (s, 3H), 1.89–1.76 (m, 1H), 1.21 (s, 2H), 1.11 (d, *J* = 6.3 Hz, 6H). LC-MS (*m/z*) 439.2 [M+H]⁺.

Compound 51

7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



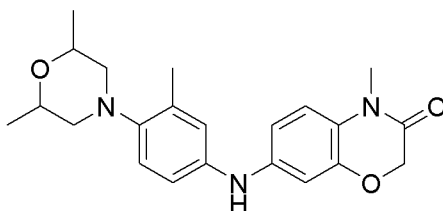
The title compound **51** (95 mg) was prepared in a yield of 24.1% as a white solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (250 mg, 1.03 mmol), 4-(2,6-dimethylmorpholino)-2-methylaniline (250.3 mg, 1.14 mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (47.3 mg, 0.05 mmol), X-phos (49.2 mg, 0.103 mmol) and Cs₂CO₃ (674 mg, 2.06 mmol) according to the procedure of compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.17 (s, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.80 (d, *J* = 2.9 Hz, 1H),

6.71 (dd, $J = 8.6, 2.9$ Hz, 1H), 6.30 (dd, $J = 8.7, 2.5$ Hz, 1H), 6.22 (d, $J = 2.4$ Hz, 1H), 4.50 (s, 2H), 3.68-3.61 (m, 2H), 3.47 (dt, $J = 10.7, 2.1$ Hz, 2H), 3.16 (s, 3H), 2.17 (t, $J = 10.3$ Hz, 2H), 2.08 (s, 3H), 1.11 (d, $J = 6.3$ Hz, 6H). LC-MS (m/z) 382.2 $[M+H]^+$.

5

Compound 52

7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

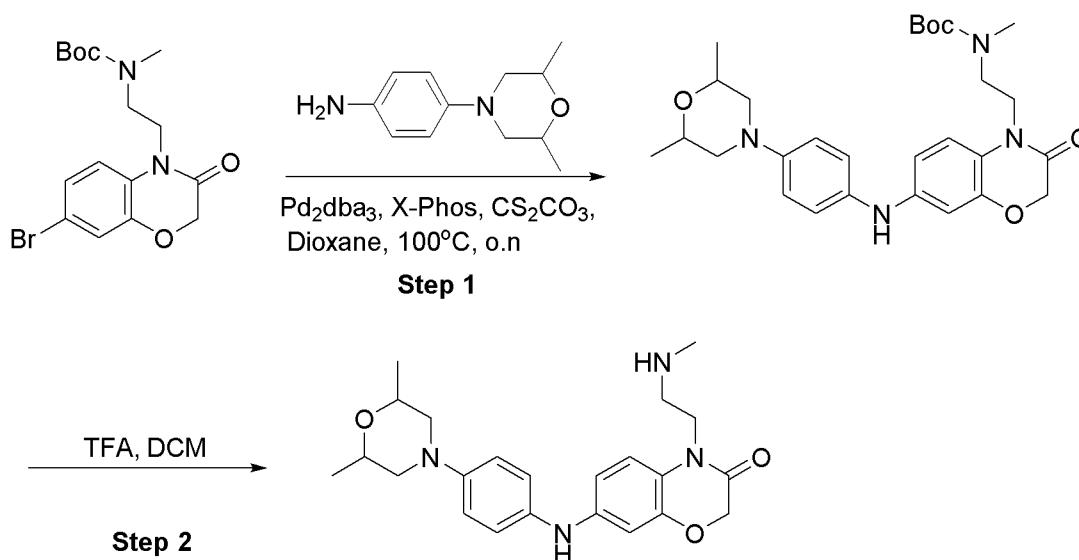


The title compound **52** (37.4 mg) was prepared from in a yield of 23% as
 10 an off-white solid from 4-(2,6-dimethylmorpholino)-3-methylaniline
 (100 mg, 0.45 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]
 oxazin-3(4H)-one (120 mg, 0.50 mmol), 1,4-dioxane (2 mL), $Pd_2(dba)_3$
 (41 mg, 0.05 mmol), Xphos (43 mg, 0.09 mmol) and Cs_2CO_3 (296 mg,
 0.91 mmol) according to the procedure of compound 1. ^1H NMR (400
 15 MHz, $DMSO-d_6$) δ 7.89 (s, 1H), 6.99 (d, $J = 8.7$ Hz, 1H), 6.92 (d, $J = 8.3$
 Hz, 1H), 6.86 (s, 1H), 6.92 – 6.81 (m, 1H), 6.69 (dd, $J = 8.7, 2.5$ Hz, 1H),
 6.60 (d, $J = 2.5$ Hz, 1H), 4.58 (s, 2H), 3.77 – 3.65 (m, 2H), 3.33 (s, 2H),
 3.23 (s, 3H), 2.88 – 2.80 (m, 2H), 2.33 – 2.23 (m, 2H), 2.21 (s, 3H), 1.10
 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 382.2 $[M+H]^+$.

20

Compound 53

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. Preparation of tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate

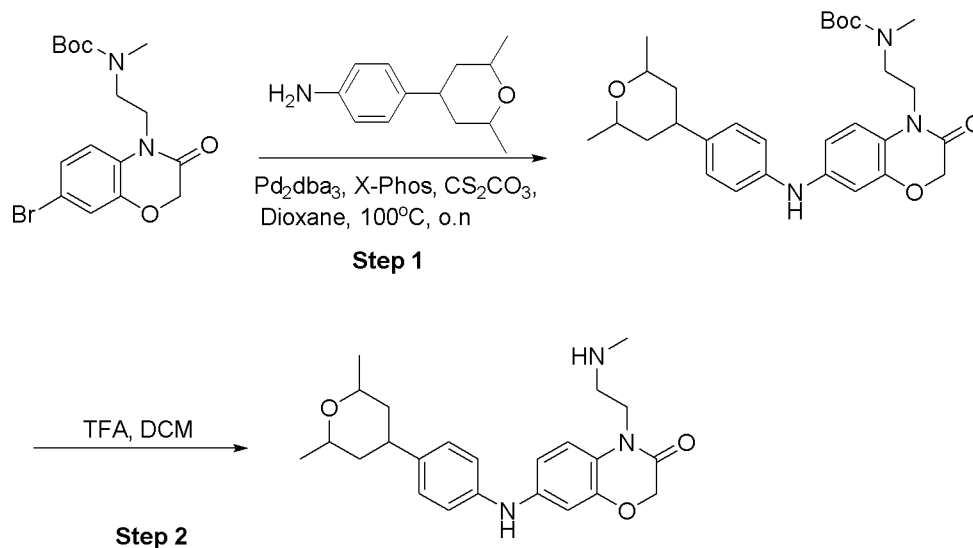
- 5 To a solution of tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate (120 mg, 0.31 mmol) and 4-(2,6-dimethylmorpholino)aniline (71.0 mg, 0.34 mmol) in 1,4-dioxane (5 mL) was added $\text{Pd}_2(\text{dba})_3$ (14.3 mg, 0.016 mmol), X-phos (14.8 mg, 0.031 mmol) and Cs_2CO_3 (203 mg, 0.623 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3x 50 mL). The combined organic phase was dried and concentrated to give the titled compound (150 mg, crude) as a brown oil. LC-MS (m/z) 511.2 $[\text{M}+\text{H}]^+$.

- Step 2.** Preparation of 7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one
- 15 To a solution of tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate (140 mg, 0.27 mmol) in dichloromethane (5 mL) was added trifluoroacetic acid (TFA, 1.0mL). The mixture was stirred at room temperature for 2h. The reaction mixture was concentrated and adjusted PH to 7-8 with sat. NaHCO_3 and extracted with dichloromethane (3x 50 mL). The combined organic phase was dried and concentrated. The residue

was purified by Prep-TLC (Petroleum ether: Ethyl acetate=1:5) and further purified by Prep-HPLC with the following conditions: Column: Spherical C18 40-60 μm , 40 g; Mobile phase A: water (0.5% NH_4HCO_3); Mobile phase B: acetonitrile or ACN; Flow rate: 50 mL/min; Gradient: 30%B-65%B in 20 min; Detector: 254 nm. The fractions containing desired product were collected at 60% B and concentrated under reduce pressure to give the titled compound **53** (33.3 mg, 29.6%) as a white solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.78 (s, 1H), 7.04 (d, $J = 8.8$ Hz, 1H), 7.01 – 6.92 (m, 2H), 6.92 – 6.84 (m, 2H), 6.60 (dd, $J = 8.7, 2.5$ Hz, 1H), 6.52 (d, $J = 2.5$ Hz, 1H), 4.54 (s, 2H), 3.89 (t, $J = 6.9$ Hz, 2H), 3.72-3.64 (m, 2H), 3.44 (dt, $J = 10.8, 2.1$ Hz, 2H), 2.63 (t, $J = 6.9$ Hz, 2H), 2.28 (s, 3H), 2.19 (dd, $J = 11.8, 10.2$ Hz, 2H), 1.14 (d, $J = 6.3$ Hz, 6H). LC-MS (m/z) 411.2 $[\text{M}+\text{H}]^+$.

Compound 54

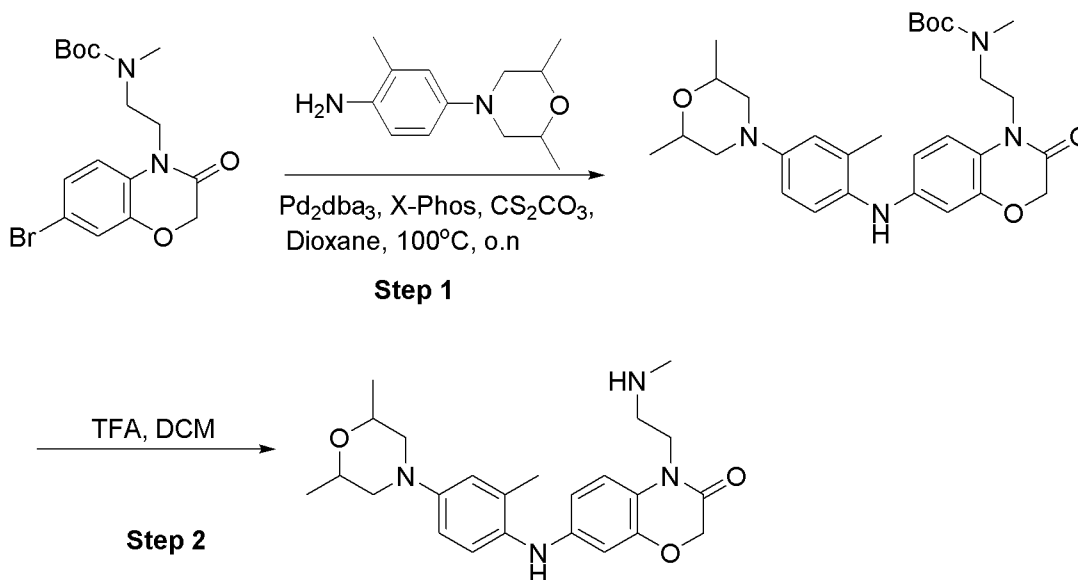
7-((4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)phenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **54** (30.9 mg, 35%) as a white solid was prepared according to the procedure outlined for compound **53**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.03 (s, 1H), 7.09 (d, $J = 8.4$ Hz, 3H), 7.03 – 6.93 (m, 2H), 6.72 (dd, $J = 8.7, 2.5$ Hz, 1H), 6.64 (d, $J = 2.5$ Hz, 1H), 4.56 (s, 2H), 3.90 (t, $J = 6.9$ Hz, 2H), 3.59 – 3.46 (m, 2H), 2.76 – 2.61 (m, 3H), 2.28 (s, 3H), 1.75 – 1.66 (m, 2H), 1.25 – 1.04 (m, 8H). LC-MS (m/z) 410.2 $[\text{M}+\text{H}]^+$.

Compound 55

7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



- 5 **Step 1.** Preparation of tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate

To a solution of tert-butyl (2-(7-bromo-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate (120 mg, 0.31 mmol) and 4-(2,6-dimethylmorpholino)-2-methylaniline (75.5 mg, 0.34 mmol) in 1,4-dioxane (5 mL) was added Pd₂(dba)₃ (14.3 mg, 0.016 mmol), X-phos (14.8 mg, 0.031 mmol) and Cs₂CO₃ (203 mg, 0.623 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3x 50 mL). The combined organic phase was dried and concentrated to give the titled compound (120 mg, crude) as a brown oil. LC-MS (m/z) 525.3 [M+H]⁺.

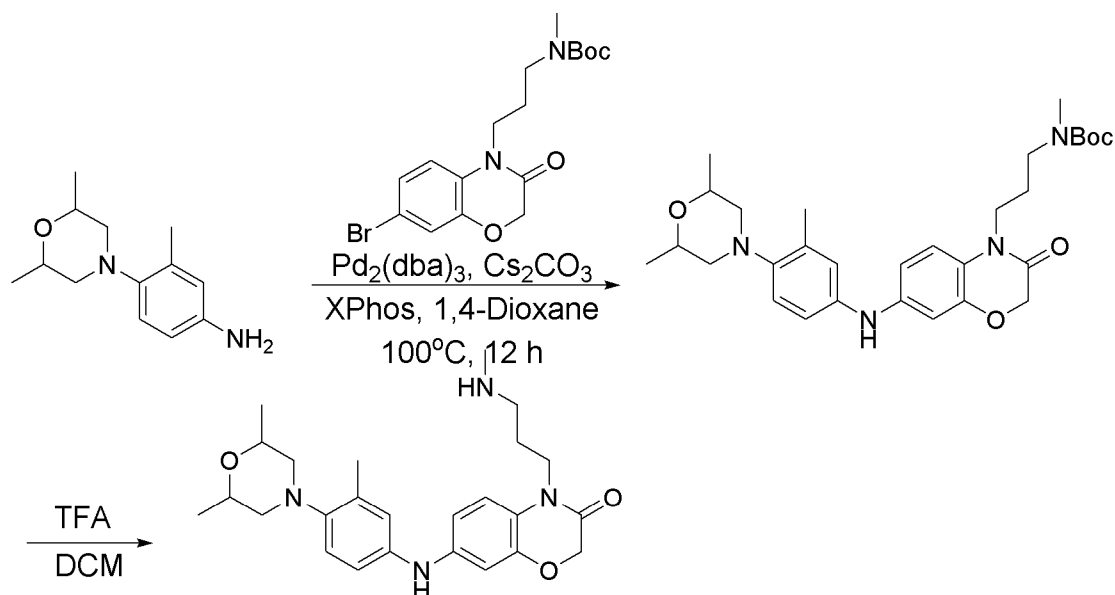
Step 2. Preparation of 7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-3-oxo-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)ethyl)(methyl)carbamate (120 mg, 0.23 mmol) in dichloromethane (5 mL)

was added TFA (1.0 mL) The mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated and adjusted pH to 7-8 with sat. NaHCO₃ and extracted with dichloromethane (3x 50 mL). The combined organic phase was dried and concentrated. The residue was purified by
 5 Prep-HPLC with the following conditions: Column: Spherical C18 40-60 μ m, 40 g; Mobile phase A: water (0.5% NH₄HCO₃); Mobile phase B: acetonitrile or ACN; Flow rate: 50 mL/min; Gradient: 30%B-65%B in 20 min; Detector: 254 nm. The fractions containing desired product were collected at 57% B and concentrated under reduce pressure to give the
 10 titled compound **55** (25 mg, 25.7%) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.19 (s, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 2.8 Hz, 1H), 6.75 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.34 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.25 (d, *J* = 2.5 Hz, 1H), 4.51 (s, 2H), 3.88 (t, *J* = 6.9 Hz, 2H), 3.68 (dtt, *J* = 12.4, 6.2, 3.7 Hz, 2H), 3.54 – 3.46 (m, 2H), 2.65 (t, *J* = 7.0 Hz, 2H), 2.29 (s, 3H),
 15 2.20 (dd, *J* = 11.9, 10.2 Hz, 2H), 2.12 (s, 3H), 1.15 (d, *J* = 6.2 Hz, 6H). LC-MS (*m/z*) 425.2 [M+H]⁺.

Compound 56

7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. Preparation of tert-butyl (3-(7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)propyl)

(methyl)carbamate

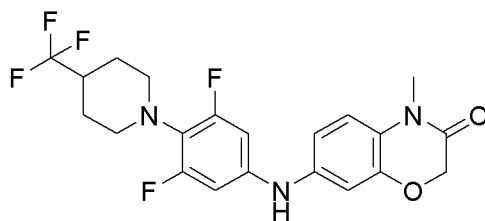
To a solution of tert-butyl (3-(7-bromo-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)propyl)(methyl)carbamate (150 mg, 0.37 mmol) and 4-(2,6-dimethylmorpholino)-3-methylaniline (75 mg, 0.34 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (31 mg, 0.03 mmol), Xphos (29 mg, 0.07 mmol) and Cs₂CO₃ (222 mg, 0.68 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC to give tert-butyl (3-(7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)propyl)(methyl)carbamate (50 mg, 27%) as a brown solid. Mass (m/z): 539.3 [M+H]⁺.

Step 2. Preparation of 7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of tert-butyl (3-(7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)propyl)(methyl)carbamate (50 mg, 0.09 mmol) in DCM (3 mL) was added 2,2,2-trifluoroacetic acid (1 mL). The mixture was stirred at r.t. for 1h, the mixture was concentrated and purified by prep HPLC to give 7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(3-(methylamino)propyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (16.8 mg, 41%) as an off-white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.87 (s, 1H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.86 – 6.77 (m, 2H), 6.68 – 6.61 (m, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 4.53 (s, 2H), 3.85 (t, *J* = 7.2 Hz, 2H), 3.74 – 3.62 (m, 2H), 2.85 – 2.74 (m, 2H), 2.54 – 2.48 (m, 2H), 2.26 (s, 3H), 2.29 – 2.19 (m, 2H), 2.17 (s, 3H), 1.66 (p, *J* = 7.1 Hz, 2H), 1.07 (d, *J* = 6.3 Hz, 6H). Mass (m/z): 439.3 [M+H]⁺.

Compound 57

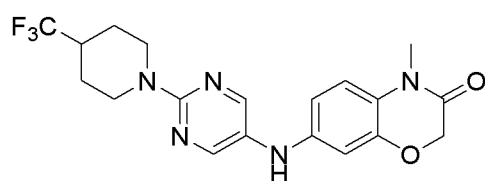
7-((3,5-difluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **57** (108.7 mg) was prepared in a yield of 34.0% as an off-white solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (190 mg, 0.79 mmol), 3,5-difluoro-4-(4-(trifluoromethyl) piperidin-1-yl)aniline (202 mg, 0.72 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (66 mg, 0.07 mmol), Xphos (68 mg, 0.14 mmol) and Cs₂CO₃ (470 mg, 1.44 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.37 (s, 1H), 7.04 (d, *J* = 8.7 Hz, 1H), 6.77 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.67 (d, *J* = 2.4 Hz, 1H), 6.60 – 6.47 (m, 2H), 4.59 (s, 2H), 3.22 (s, 3H), 3.09 – 2.91 (m, 4H), 2.45 – 2.32 (m, 1H), 1.84 – 1.75 (m, 2H), 1.50 (qd, *J* = 12.2, 4.9 Hz, 2H). Mass (*m/z*): 442.4 [M+H]⁺.

Compound 58

4-methyl-7-((2-(4-(trifluoromethyl)piperidin-1-yl)pyrimidin-5-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

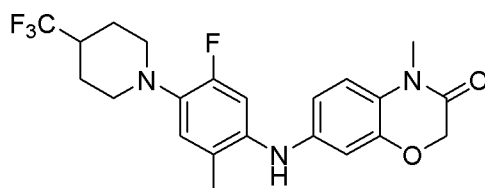


The title compound **58** (56.6 mg) was prepared in a yield of 30.6% as a white solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (110 mg, 0.45 mmol), 2-(4-(trifluoromethyl) piperidin-1-yl) pyrimidin-5-amine (112 mg, 0.45 mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (20.8 mg, 0.023 mmol), X-phos (21.6 mg, 0.045 mmol) and Cs₂CO₃ (296.3 mg, 0.91 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.25 (s, 2H), 7.70 (s, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 6.49 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.41 (d, *J* = 2.5 Hz, 1H), 4.69 (d, *J* = 13.3 Hz, 2H), 4.56 (s, 2H), 3.21 (s, 3H), 2.89 (td, *J* = 13.0, 2.6 Hz, 2H), 2.63 (dq, *J* = 7.8, 4.2, 3.6 Hz, 1H), 1.87 (dd, *J* = 13.6, 3.6 Hz, 2H), 1.38 (qd, *J* = 12.5,

4.3 Hz, 2H). LC-MS (m/z) 408.2 [M+H]⁺.

Compound 59

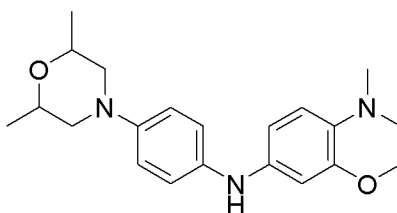
7-((5-fluoro-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **59** (67.5 mg) was prepared in a yield of 30.6% as a light yellow solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (110mg, 0.45 mmol), 2-(4-(trifluoromethyl)piperidin-1-yl)pyrimidin-5-amine (125.5 mg, 0.45mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (20.8 mg, 0.023 mmol), X-phos (21.6 mg, 0.045 mmol) and Cs₂CO₃ (296.3 mg, 0.91 mmol) according to the procedure for compound **1**. ¹HNMR (400 MHz, DMSO-*d*₆) δ 7.35 (s, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 6.91 – 6.81 (m, 2H), 6.53 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.46 (d, *J* = 2.4 Hz, 1H), 4.57 (s, 2H), 3.35 (s, 1H), 3.32 (s, 1H), 3.22 (s, 3H), 2.67 (td, *J* = 12.1, 2.4 Hz, 2H), 2.47 – 2.38 (m, 1H), 2.12 (s, 3H), 1.90 (dd, *J* = 12.1, 3.2 Hz, 2H), 1.60 (qd, *J* = 12.4, 4.0 Hz, 2H). LC-MS (m/z) 438.2 [M+H]⁺.

Compound 60

N-(4-(2,6-dimethylmorpholino)phenyl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-amine



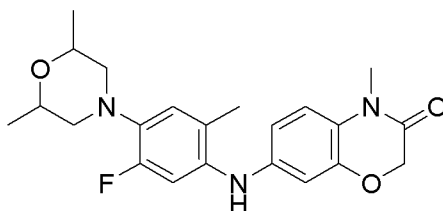
The title compound **60** (18 mg) was prepared in a yield of 5% as a grey solid from 7-bromo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazine (121 mg, 0.53 mmol), 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.48 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (44 mg, 0.05 mmol), Xphos (46 mg, 0.10 mmol) and Cs₂CO₃ (316 mg, 0.97 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Pyr) δ 8.16 (s, 1H), 7.40 – 7.32 (m, 2H),

7.06 (d, $J = 2.5$ Hz, 1H), 7.06 – 6.99 (m, 2H), 6.97 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.78 (d, $J = 8.5$ Hz, 1H), 4.27 – 4.21 (m, 2H), 3.86 – 3.74 (m, 2H), 3.45 – 3.37 (m, 2H), 3.03 (t, $J = 4.4$ Hz, 2H), 2.71 (s, 3H), 2.35 (t, $J = 10.9$ Hz, 2H), 1.21 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 354.4 $[M+H]^+$.

5

Compound 61

7-((4-(2,6-dimethylmorpholino)-5-fluoro-2-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



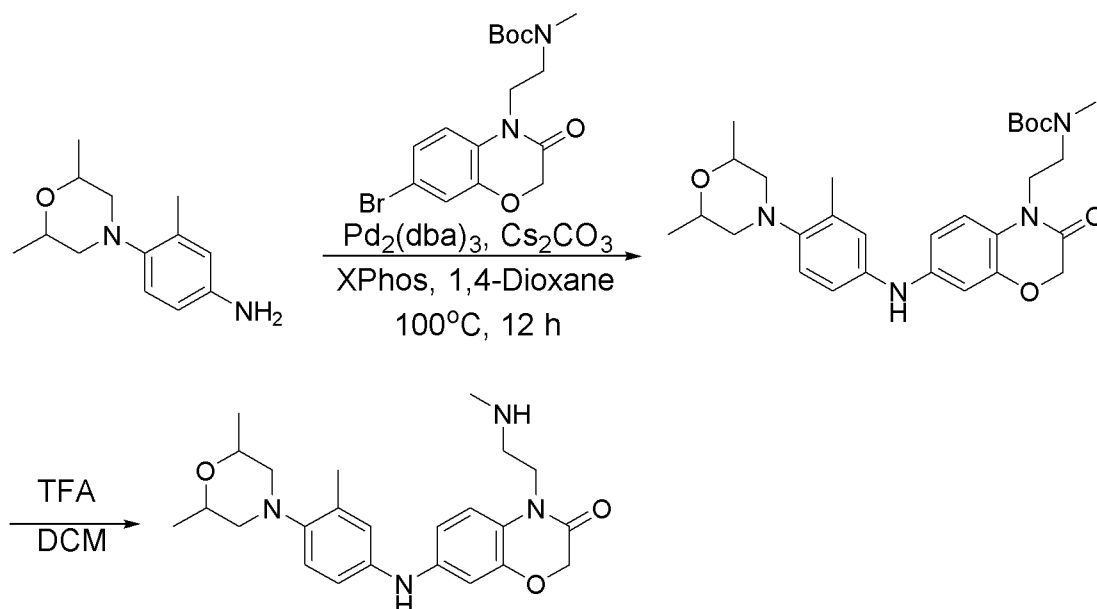
The title compound **61** (77 mg) was prepared in a yield of 45% as a white solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (121 mg, 0.50 mmol), 4-(2,6-dimethylmorpholino)-5-fluoro-2-methylaniline (100 mg, 0.42 mmol), 1,4-dioxane (2 mL), $Pd_2(dba)_3$ (38 mg, 0.04 mmol), Xphos (40 mg, 0.08 mmol) and Cs_2CO_3 (274 mg, 0.84 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, DMSO) δ 7.34 (s, 1H), 6.98 (d, $J = 8.7$ Hz, 1H), 6.91 – 6.81 (m, 2H), 6.52 (dd, $J = 8.7, 2.5$ Hz, 1H), 6.44 (d, $J = 2.4$ Hz, 1H), 4.57 (s, 2H), 3.79 – 3.67 (m, 2H), 3.22 (s, 3H), 3.19 – 3.11 (m, 2H), 2.37 – 2.27 (m, 2H), 2.12 (s, 3H), 1.11 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 400.4 $[M+H]^+$.

15

Compound 62

20

7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1 . Preparation of tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)ethyl)(methyl)carbamate

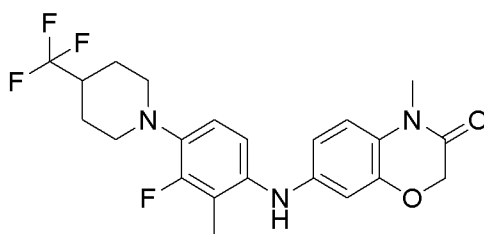
- 5 To a solution of tert-butyl (2-(7-bromo-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)ethyl)(methyl)carbamate (146 mg, 0.38 mmol) and 4-(2,6-dimethylmorpholino)-3-methylaniline (70 mg, 0.32 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (29 mg, 0.03 mmol), Xphos (30 mg, 0.06 mmol) and Cs_2CO_3 (207 mg, 0.63 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was
10 purified by prep TLC to give tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)ethyl)(methyl)carbamate (50 mg, 30%) as a brown solid. Mass (m/z): 525.3 $[\text{M}+\text{H}]^+$.

- 15 **Step 2.** Preparation of 7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(2-(methylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (**62**)
To a solution of tert-butyl (2-(7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-3-oxo-2H-benzo[b][1,4]oxazin-4(3H)-yl)ethyl)(methyl)carbamate (50 mg, 0.09 mmol) in DCM (3 mL) was added
20 2,2,2-trifluoroacetic acid (1 mL). The mixture was stirred at r.t. for 1h, the mixture was concentrated and purified by prep HPLC to give 7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(2-(methylami

no)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (20 mg, 49%) as an off-white solid. ^1H NMR (400 MHz, DMSO- d_6) δ 7.86 (s, 1H), 7.03 (d, J = 8.8 Hz, 1H), 6.92 – 6.77 (m, 3H), 6.64 (dd, J = 8.7, 2.5 Hz, 1H), 6.56 (d, J = 2.4 Hz, 1H), 4.52 (s, 2H), 3.86 (t, J = 6.9 Hz, 2H), 3.74 – 3.62 (m, 2H), 2.85 – 2.74 (m, 2H), 2.60 (d, J = 6.9 Hz, 2H), 2.29 – 2.15 (m, 8H), 1.07 (d, J = 6.2 Hz, 6H). Mass (m/z): 425.3 $[\text{M}+\text{H}]^+$.

Compound 63

7-((3-fluoro-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



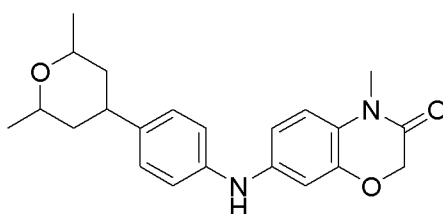
10

The title compound **63** (127.7 mg) was prepared in a yield of 40% as a pink solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (191 mg, 0.80 mmol), 3-fluoro-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (200 mg, 0.72 mmol), 1,4-dioxane (2 mL), $\text{Pd}_2(\text{dba})_3$ (66 mg, 0.07 mmol), Xphos (68 mg, 0.14 mmol) and Cs_2CO_3 (472 mg, 1.45 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.40 (s, 1H), 6.92 (d, J = 8.7 Hz, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.85 – 6.76 (m, 1H), 6.44 (dd, J = 8.6, 2.5 Hz, 1H), 6.37 (d, J = 2.4 Hz, 1H), 4.52 (s, 2H), 3.34 – 3.31 (m, 1H), 3.29 – 3.26 (m, 1H), 3.18 (s, 3H), 2.68 – 2.57 (m, 2H), 2.45 – 2.34 (m, 1H), 2.02 (d, J = 2.5 Hz, 3H), 1.91 – 1.82 (m, 2H), 1.65 – 1.50 (m, 2H). Mass (m/z): 438.2 $[\text{M}+\text{H}]^+$.

20

Compound 64

7-((4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

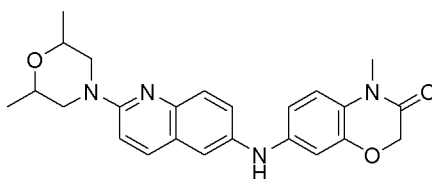


25

The title compound **64** (56 mg) was prepared in a yield of 44% as a light yellow solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (90 mg, 0.38 mmol), 4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)aniline (70 mg, 0.34 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (31 mg, 0.03 mmol), Xphos (31 mg, 0.07 mmol) and Cs₂CO₃ (223 mg, 0.68 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*D*₆) δ 8.00 (s, 1H), 7.10 – 7.02 (m, 2H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.97 – 6.89 (m, 2H), 6.70 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.61 (d, *J* = 2.4 Hz, 1H), 4.55 (s, 2H), 3.55 – 3.43 (m, 2H), 3.20 (s, 3H), 2.73 – 2.62 (m, 1H), 1.71 – 1.62 (m, 2H), 1.22 – 1.12 (m, 2H), 1.09 (d, *J* = 6.1 Hz, 6H). Mass (*m/z*): 367.4 [M+H]⁺.

Compound 65

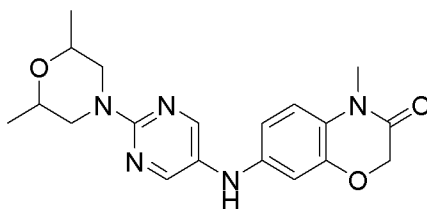
7-((2-(2,6-dimethylmorpholino)quinolin-6-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **65** (66.5 mg) was prepared in a yield of 27% as a yellow solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (154 mg, 0.64 mmol), 2-(2,6-dimethylmorpholino)quinolin-6-amine (150 mg, 0.58 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (53 mg, 0.06 mmol), Xphos (55 mg, 0.12 mmol) and Cs₂CO₃ (381 mg, 1.17 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.21 (s, 1H), 7.93 (d, *J* = 9.1 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.34 – 7.25 (m, 2H), 7.18 (d, *J* = 9.2 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 6.82 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.73 (d, *J* = 2.4 Hz, 1H), 4.61 (s, 2H), 4.33 – 4.24 (m, 2H), 3.69 – 3.59 (m, 2H), 3.25 (s, 3H), 2.48 – 2.40 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 6H). Mass (*m/z*): 419.4 [M+H]⁺.

Compound 66

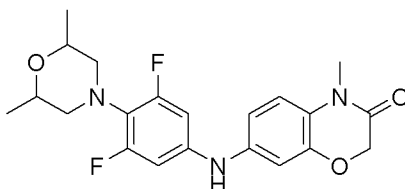
7-((2-(2,6-dimethylmorpholino)pyrimidin-5-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **66** (61.5 mg) was prepared in a yield of 43.4% as a green solid from 2-(2,6-dimethylmorpholino)pyrimidin-5-amine (80 mg, 0.385 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (92.7 mg, 0.385 mmol), dioxane (15 mL), Pd₂(dba)₃ (17.6 mg, 0.0193 mmol), X-phos (18.4 mg, 0.0385 mmol) and Cs₂CO₃ (188 mg, 0.578 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO) δ 8.25 (d, J = 5.0 Hz, 2H), 7.69 (d, J = 10.3 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H), 6.48 (dd, J = 8.7, 2.5 Hz, 1H), 6.41 (d, J = 2.5 Hz, 1H), 4.56 (s, 2H), 4.40 (dd, J = 13.0, 1.7 Hz, 2H), 3.64 – 3.46 (m, 2H), 3.21 (s, 3H), 2.46 (s, 1H), 2.08 (s, 1H), 1.15 (d, J = 6.2 Hz, 6H). Mass (m/z): 370.4 [M+H]⁺

Compound 67

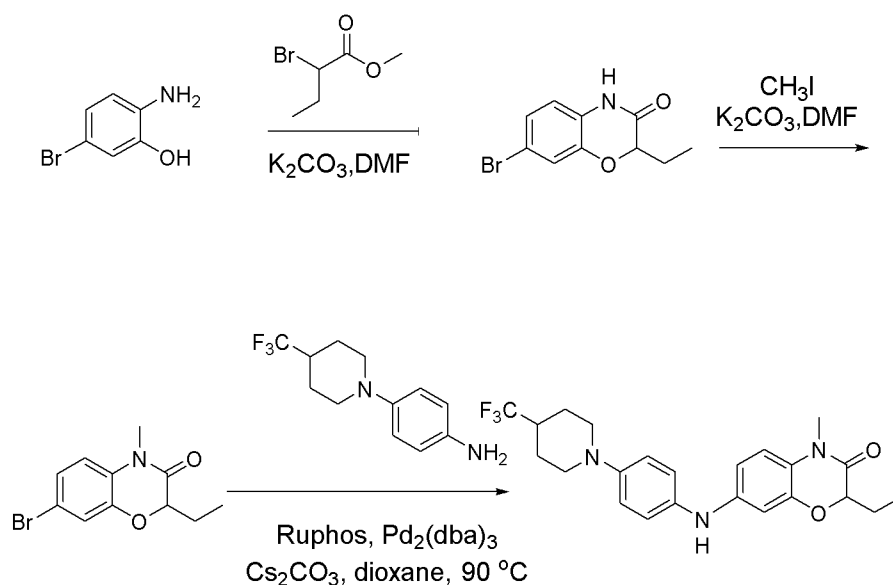
4-methyl-7-((4-(tert-pentyl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **67** (69 mg) was prepared in a yield of 41.6% as a yellow solid from 4-(2,6-dimethylmorpholino)-3,5-difluoroaniline (100 mg, 0.413 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (99.6 mg, 0.413 mmol), dioxane (15 mL), Pd₂(dba)₃ (18.9 mg, 0.021 mmol), X-phos (19.7 mg, 0.0413 mmol) and Cs₂CO₃ (202 mg, 0.619 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO) δ 8.41 (s, 1H), 7.08 (d, J = 8.7 Hz, 1H), 6.81 (dd, J = 8.6, 2.4 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 6.64 – 6.51 (m, 2H), 4.63 (s, 2H), 3.65 (dd, J = 11.4, 4.6 Hz, 2H), 3.25 (s, 3H), 2.86 (d, J = 10.0 Hz, 2H), 2.68 (t, J = 10.7 Hz, 2H), 1.06 (d, J = 6.3 Hz, 6H). Mass (m/z): 404.4 [M+H]⁺

Compound 68

2-ethyl-4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. Preparation of 7-bromo-2-ethyl-2H-benzo[b][1,4]oxazin-3(4H)-one

To a solution of compound 2-amino-5-bromophenol (200 mg, 1.06 mmol) in DMF (5 mL) was added K_2CO_3 (367.53 mg, 2.659 mmol) and methyl 2-bromobutanoate (231 g, 1.28 mmol) at r.t. Then the mixture was stirred at $90^\circ C$ for 16 hrs. After cooling to rt, the reaction solution was diluted with water (20 mL), extracted with ethyl acetate (20 mL*3). The organic layers were combined, washed with brine (20 mL), concentrated under vacuum and the residue was purified by silica gel chromatography (PE:EA=5:1) to give the title compound as a white solid (220 mg, 80.8%). Mass (m/z): 255.7 $[M+H]^+$.

Step 2. Preparation of 7-bromo-2-ethyl-4-methyl-2H-benzo [b][1,4]oxazin -3(4H)-one

To a solution of 7-bromo-2-ethyl-2H-benzo[b][1,4]oxazin-3(4H)-one (220 mg, 0.86 mmol) in DMF (5 mL) was added K_2CO_3 (118.7 mg, 0.859 mmol) and MeI (365.82 mg, 2.57 mmol) at $25^\circ C$. Then the mixture was stirred at $25^\circ C$ for 2 hrs, diluted with water (20 mL), extracted with ethyl acetate (20 mL*3), the organic layers were combined, washed with brine (20 mL), concentrated under vacuum to give the title compound as a white solid (220 mg, 74.49%). Mass (m/z): 269.7 $[M+H]^+$.

Step 3. Preparation 2-ethyl-4-methyl-7-((4-(4-(trifluoromethyl) piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (**68**)

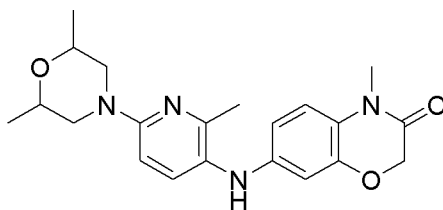
To a solution of compound 7-bromo-2-ethyl-4-methyl -2H-benzo[b][1,4]oxazin-3(4H)-one

- 5 To a solution of 7-bromo-2-ethyl-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.37 mmol), compound 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (108 mg, 0.444 mmol), Cs₂CO₃ (241 mg, 0.74 mmol) and Ruphos (17 mg, 0.037 mmol) in 1,4-dioxane (15 mL) was added Pd₂(dba)₃ (68 mg, 0.074 mmol). The mixture was stirred at 90°C for 3 hours under N₂ atmosphere.
- 10 After cooling to ambient temperature, ethyl acetate (20 mL) was added to the reaction mixture and the mixture was filtered through celite. The filtrate was washed with water and saturated brine. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The residue was purified by silica gel column to provide 8 mg of
- 15 compound **68** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*⁶) δ 7.82 (s, 1H), 6.96 (m, 5H), 6.59 (d, *J* = 25.6 Hz, 2H), 4.47 (dd, *J* = 8.0, 4.5 Hz, 10H), 3.62 (s, 2H), 3.22 (s, 3H), 2.65 (d, *J* = 14.9 Hz, 2H), 2.47 – 2.35 (m, 1H), 1.97 – 1.82 (m, 2H), 1.80 – 1.67 (m, 2 H), 1.58 (brs, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). Mass (*m/z*): 434.2 [M+H]⁺.

20

Compound 69

7-((6-(2,6-dimethylmorpholino)-2-methylpyridin-3-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

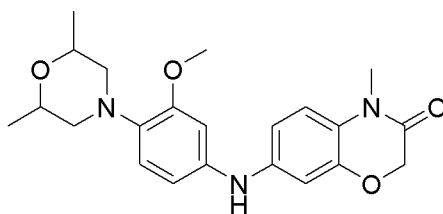


- The title compound **69** (19.1mg) was prepared in a yield of 9% as a light
- 25 yellow solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (143 mg, 0.60 mmol), 6-(2,6-dimethylmorpholino) -2-methylpyridin-3-amine (120 mg, 0.54 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (50 mg, 0.05 mmol), Xphos (51 mg, 0.11 mmol) and Cs₂CO₃ (354 mg, 1.09 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, MeOD)

δ 7.35 (d, J = 8.7 Hz, 1H), 6.92 (d, J = 8.7 Hz, 1H), 6.63 (d, J = 8.8 Hz, 1H), 6.32 (dd, J = 8.6, 2.5 Hz, 1H), 6.24 (d, J = 2.5 Hz, 1H), 4.51 (s, 2H), 4.05 (dt, J = 11.5, 2.0 Hz, 2H), 3.79 – 3.66 (m, 2H), 3.30 (s, 3H), 2.46 – 2.35 (m, 2H), 2.28 (s, 3H), 1.23 (d, J = 6.2 Hz, 6H). Mass (m/z): 383.4 [M+H]⁺.

Compound 70

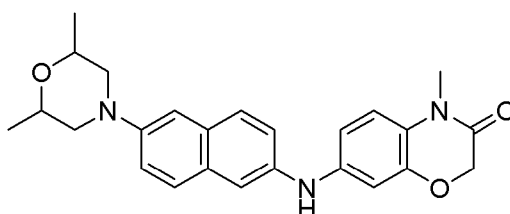
7-((4-(2,6-dimethylmorpholino)-3-methoxyphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **70** (20.8 mg) was prepared in a yield of 15.5% as a pink solid from 4-(2,6-dimethylmorpholino)-3-methoxyaniline (80 mg, 0.339 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (81.7 mg, 0.339 mmol), dioxane (15 mL), Pd₂(dba)₃ (15.5 mg, 0.017 mmol), X-phos (16.2 mg, 0.034 mmol) and Cs₂CO₃ (166 mg, 0.509 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO) δ 7.95 (s, 1H), 7.00 (d, J = 8.7 Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 6.71 (dd, J = 8.7, 2.4 Hz, 1H), 6.64 – 6.55 (m, 3H), 4.58 (s, 2H), 3.73 (s, 3H), 3.72 – 3.65 (m, 2H), 3.23 (s, 3H), 3.13 (d, J = 10.6 Hz, 2H), 2.20 (t, J = 10.8 Hz, 2H), 1.09 (d, J = 6.2 Hz, 6H). Mass (m/z): 398.5 [M+H]⁺.

Compound 71

7-((6-(2,6-dimethylmorpholino)naphthalen-2-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

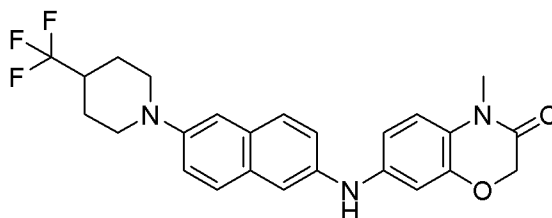


The title compound **71** (45.8 mg) was prepared in a yield of 28% as a grey solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (112 mg, 0.47 mmol), 6-(2,6-dimethylmorpholino)naphthalen-2-amine (100 mg,

0.39 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (36 mg, 0.04 mmol), Xphos (37 mg, 0.08 mmol) and Cs₂CO₃ (255 mg, 0.78 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO) δ 8.20 (s, 1H), 7.61 (dd, *J* = 19.6, 9.0 Hz, 2H), 7.34 (d, *J* = 2.2 Hz, 1H), 7.29 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.17 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.10 – 7.02 (m, 2H), 6.83 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.74 (d, *J* = 2.4 Hz, 1H), 4.61 (s, 2H), 3.81 – 3.69 (m, 2H), 3.67 – 3.59 (m, 2H), 3.25 (s, 3H), 2.33 – 2.23 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 6H). Mass (*m/z*): 418.4 [M+H]⁺.

Compound 72

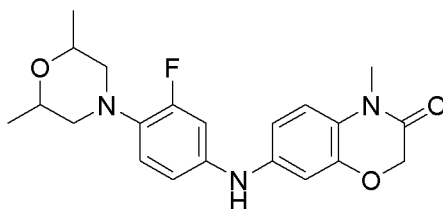
10 *4-methyl-7-((6-(4-(trifluoromethyl)piperidin-1-yl)naphthalen-2-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one*



The title compound **72** (44.7 mg) was prepared in a yield of 29.5% as an off-white solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (97 mg, 0.41 mmol), 6-(2,6-dimethylmorpholino)naphthalen-2-amine (100 mg, 0.34 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (31 mg, 0.03 mmol), Xphos (32 mg, 0.07 mmol) and Cs₂CO₃ (221 mg, 0.68 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.20 (s, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.58 (d, *J* = 9.1 Hz, 1H), 7.34 (d, *J* = 2.2 Hz, 1H), 7.27 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.17 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.74 (d, *J* = 2.4 Hz, 1H), 4.61 (s, 2H), 3.83 (d, *J* = 12.4 Hz, 2H), 3.26 (s, 3H), 2.79 – 2.68 (m, 2H), 2.54 – 2.51 (m, 1H), 1.97 – 1.88 (m, 2H), 1.69 – 1.54 (m, 2H). Mass (*m/z*): 446.4 [M+H]⁺.

Compound 73

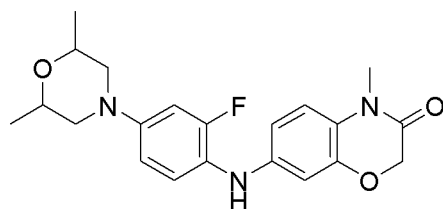
7-((4-(2,6-dimethylmorpholino)-3-fluorophenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **73** (66.1 mg) was prepared in a yield of 32% as a brown solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (154 mg, 0.64 mmol), 4-(2,6-dimethylmorpholino)-3-fluoroaniline (120 mg, 0.54 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (49 mg, 0.05 mmol), Xphos (51 mg, 0.11 mmol) and Cs₂CO₃ (349 mg, 1.07 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO) δ 8.10 (s, 1H), 7.03 (d, *J* = 8.7 Hz, 1H), 6.93 (dd, *J* = 9.9, 8.4 Hz, 1H), 6.83 – 6.75 (m, 2H), 6.73 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 4.60 (s, 2H), 3.79 – 3.66 (m, 2H), 3.24 (s, 3H), 3.13 – 3.05 (m, 2H), 2.35 – 2.25 (m, 2H), 1.11 (d, *J* = 6.2 Hz, 6H). Mass (*m/z*): 386.4 [M+H]⁺.

Compound 74

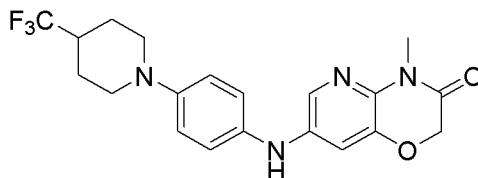
7-((4-(2,6-dimethylmorpholino)-2-fluorophenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **74** (97.2 mg) was prepared in a yield of 43% as an off-white solid from 7-bromo-4-methyl-2H-benzo[b][1,4] oxazin-3(4H)-one (139 mg, 0.58 mmol), 6-(2,6-dimethylmorpholino) naphthalen-2-amine (130 mg, 0.58 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (53 mg, 0.06 mmol), Xphos (55 mg, 0.12 mmol) and Cs₂CO₃ (378 mg, 1.16 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO) δ 7.53 (s, 1H), 7.11 (t, *J* = 9.3 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 6.85 (dd, *J* = 14.3, 2.7 Hz, 1H), 6.72 (dd, *J* = 9.0, 2.7 Hz, 1H), 6.44 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.36 (d, *J* = 2.4 Hz, 1H), 4.55 (s, 2H), 3.73 – 3.61 (m, 2H), 3.59 – 3.50 (m, 2H), 3.21 (s, 3H), 2.28 – 2.18 (m, 2H), 1.15 (d, *J* = 6.2 Hz, 6H). Mass (*m/z*): 386.4 [M+H]⁺.

Compound 75

4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one

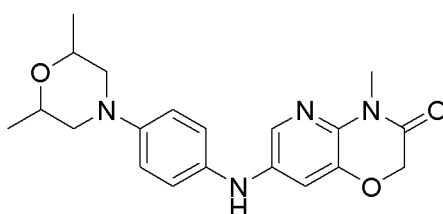


- 5 The title compound **75** (50.3 mg) was prepared in a yield of 20.1% as a white solid from 7-bromo-4-methyl-2H-pyrido[3,2-b][1,4] oxazin-3(4H)-one (150mg, 0.62 mmol), 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (166 mg, 0.68mmol) in 1,4-dioxane (5 mL), Pd₂(dba)₃ (28 mg, 0.03 mmol), X-phos (29.4 mg, 0.06 mmol) and Cs₂CO₃ (402 mg, 1.23 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.96 (s, 1H), 7.71 (d, *J* = 2.3 Hz, 1H), 7.01 – 6.95 (m, 2H), 6.95 – 6.87 (m, 3H), 4.69 (s, 2H), 3.63 (d, *J* = 12.3 Hz, 2H), 3.28 (s, 3H), 2.63 (td, *J* = 12.2, 2.4 Hz, 2H), 2.42 (td, *J* = 8.6, 4.1 Hz, 1H), 1.93 – 1.83 (m, 2H), 1.57 (qd, *J* = 12.5, 4.1 Hz, 2H). LC-MS (*m/z*) 407.2 [M+H]⁺.

15

Compound 76

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-methyl-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one

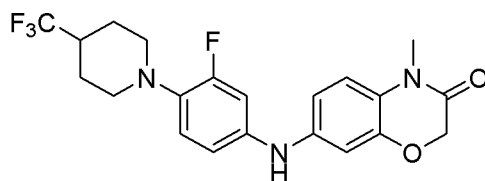


- The title compound **76** (100 mg) was prepared in a yield of 44% as a light yellow solid from 7-bromo-4-methyl-2H-pyrido[3,2-b][1,4] oxazin-3(4H)-one (150 mg, 0.62 mmol), 4-(2,6-dimethylmorpholino) aniline (140 mg, 0.68mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (28 mg, 0.03 mmol), X-phos (29.4 mg, 0.06 mmol) and Cs₂CO₃ (402 mg, 1.23 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.94 (s, 1H), 7.70 (d, *J* = 2.4 Hz, 1H), 6.99 (d, *J* = 2.2 Hz, 1H), 6.98 – 6.84 (m, 4H), 4.69 (s, 2H), 3.69 (dq, *J* = 12.4, 6.1, 2.1 Hz,

2H), 3.45 (dt, $J = 10.9, 2.1$ Hz, 2H), 3.34 (s, 3H), 2.19 (dd, $J = 11.8, 10.2$ Hz, 2H), 1.24 – 1.11 (m, 6H). LC-MS (m/z) 369.2 $[M+H]^+$.

Compound 77

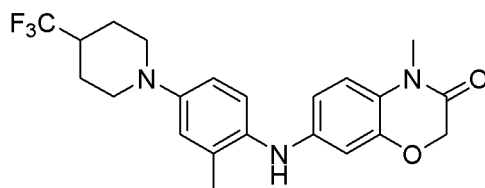
7-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-
2H-benzo[*b*][1,4]oxazin-3(4H)-one



The title compound **77** (13 mg) was prepared in a yield of 44% as a white solid from 7-bromo-4-methyl-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one (120 mg, 0.49 mmol), 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl) aniline (130 mg, 0.49mmol), 1,4-dioxane (5 mL), $Pd_2(dba)_3$ (22.7 mg, 0.025 mmol), X-phos (23.6 mg, 0.049 mmol) and Cs_2CO_3 (323.2 mg, 0.991 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.11 (s, 1H), 7.03 (d, $J = 8.7$ Hz, 1H), 6.97 (dd, $J = 10.0, 8.4$ Hz, 1H), 6.79 (s, 1H), 6.77 (t, $J = 2.7$ Hz, 1H), 6.73 (dd, $J = 8.6, 2.5$ Hz, 1H), 6.64 (d, $J = 2.5$ Hz, 1H), 4.60 (s, 2H), 3.28 (d, $J = 11.7$ Hz, 2H), 3.24 (s, 3H), 2.65 (dd, $J = 12.6, 10.2$ Hz, 2H), 2.46 – 2.36 (m, 1H), 1.93 – 1.84 (m, 2H), 1.60 (qd, $J = 12.4, 4.0$ Hz, 2H). LC-MS (m/z) 424.2 $[M+H]^+$.

Compound 78

4-methyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one

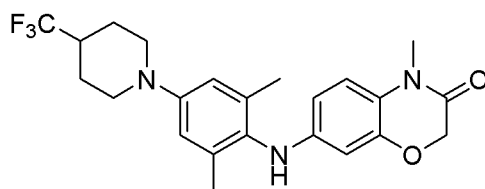


The title compound **78** (32 mg) was prepared in a yield of 15.4% as a white solid from 7-bromo-4-methyl-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one (120 mg, 0.49 mmol), 2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (130 mg, 0.49mmol), 1,4-dioxane (5 mL), $Pd_2(dba)_3$

(22.7 mg, 0.025 mmol), X-phos (23.6 mg, 0.049 mmol) and Cs₂CO₃ (323.2 mg, 0.991 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.20 (s, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 1H), 6.85 (d, *J* = 2.8 Hz, 1H), 6.76 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.35 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.27 (d, *J* = 2.4 Hz, 1H), 4.53 (s, 2H), 3.70 (d, *J* = 12.1 Hz, 2H), 3.20 (s, 3H), 2.65 (td, *J* = 12.3, 2.5 Hz, 2H), 2.48 – 2.41 (m, 1H), 2.12 (s, 3H), 1.92 – 1.83 (m, 2H), 1.56 (qd, *J* = 12.5, 4.1 Hz, 2H). LC-MS (*m/z*) 420.2 [M+H]⁺.

Compound 79

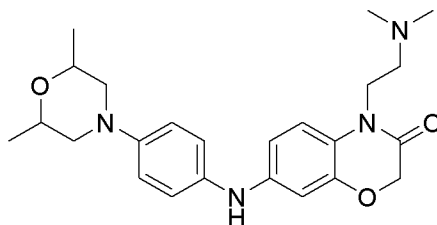
7-((2,6-dimethyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The title compound **79** (38 mg) was prepared in a yield of 16.3% as a white solid from 7-bromo-4-methyl-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one (130 mg, 0.54 mmol), 2,6-dimethyl-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (146 mg, 0.54 mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (24.6 mg, 0.027 mmol), X-phos (25.6 mg, 0.054 mmol) and Cs₂CO₃ (350 mg, 1.07 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.06 (s, 1H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.72 (s, 2H), 6.05 (dd, *J* = 8.6, 2.5 Hz, 1H), 5.98 (d, *J* = 2.4 Hz, 1H), 4.51 (s, 2H), 3.75 (d, *J* = 12.3 Hz, 2H), 3.18 (s, 3H), 2.67 (td, *J* = 12.0, 2.4 Hz, 2H), 2.47 – 2.39 (m, 1H), 2.07 (d, *J* = 2.8 Hz, 6H), 1.92 – 1.83 (m, 2H), 1.55 (qd, *J* = 12.6, 4.1 Hz, 2H). LC-MS (*m/z*) 434.2 [M+H]⁺.

Compound 80

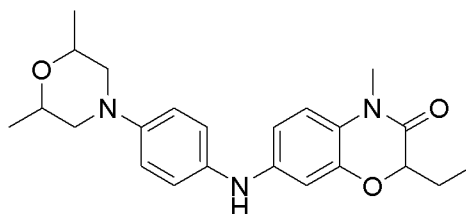
4-(2-(dimethylamino)ethyl)-7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The title compound **80** (35.2 mg) was prepared in a yield of 24.4% as a pink solid from 4-(2,6-dimethylmorpholino)aniline (70 mg, 0.339 mmol), 7-bromo-4-(2-(dimethylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (101 mg, 0.339 mmol), dioxane (5 mL), Pd₂(dba)₃ (15.6 mg, 0.017 mmol), X-phos (16.2 mg, 0.034 mmol) and Cs₂CO₃ (166 mg, 0.509 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO) δ 7.81 (s, 1H), 6.99 (dd, J = 15.6, 8.9 Hz, 3H), 6.88 (d, J = 9.0 Hz, 2H), 6.61 (dd, J = 8.7, 2.4 Hz, 1H), 6.53 (d, J = 2.4 Hz, 1H), 4.54 (s, 2H), 3.93 (t, J = 6.9 Hz, 2H), 3.68 (dd, J = 11.5, 5.0 Hz, 2H), 3.44 (d, J = 10.6 Hz, 2H), 2.39 (t, J = 6.9 Hz, 2H), 2.29 (dd, J = 19.8, 10.7 Hz, 1H), 2.23 – 2.13 (m, 7H), 1.15 (t, J = 5.7 Hz, 6H). Mass (m/z): 425.6 [M+H]⁺

Compound 81

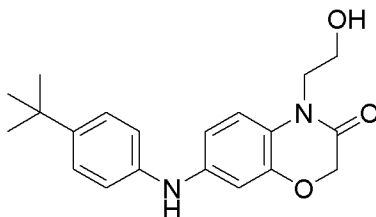
7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-ethyl-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **81** (12.5 mg) was prepared in a yield of 17% as a pink solid from 4-(2,6-dimethylmorpholino)aniline (38.3 mg, 0.186 mmol), 7-bromo-2-ethyl-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.186 mmol), dioxane (5 mL), Pd₂(dba)₃ (8.52 mg, 0.0093 mmol), X-phos (8.9 mg, 0.0186 mmol) and Cs₂CO₃ (91 mg, 0.279 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.79 (s, 1H), 7.00 – 6.85 (m, 4H), 6.63 – 6.49 (m, 2H), 4.46 (dd, J = 8.0, 4.6 Hz, 1H), 3.76 – 3.61 (m, 2H), 3.45 (d, J = 10.8 Hz, 2H), 3.22 (s, 3H), 2.25 – 2.13 (m, 2H), 1.15 (t, J = 5.7 Hz, 5H), 1.02 – 0.85 (m, 3H). Mass (m/z): 396.5

[M+H]⁺**Compound 82**

7-((4-(*tert*-butyl)phenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[b][1,4]
oxazin-3(4H)-one

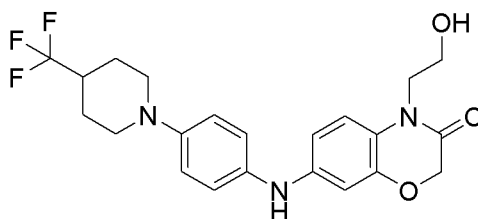


5

To a solution of 7-((4-(*tert*-butyl)phenyl)amino)-4-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.24 mmol) in methanol (3 mL) was added 4-methylbenzenesulfonic acid (44 mg, 0.26 mmol). The mixture was stirred at r.t. for 1h, the mixture was
10 concentrated and purified by prep HPLC to give 7-((4-(*tert*-butyl)phenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (16.9 mg, 43%) as a light yellow solid. Mass (m/z): 341.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.98 (s, 1H), 7.26 – 7.17 (m, 2H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.98 – 6.89 (m, 2H), 6.68 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 4.83 (t, *J* = 5.7 Hz, 1H), 4.53 (s, 2H),
15 3.87 (t, *J* = 6.3 Hz, 2H), 3.53 (q, *J* = 6.1 Hz, 2H), 1.22 (s, 9H).

Compound 83

4-(2-hydroxyethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



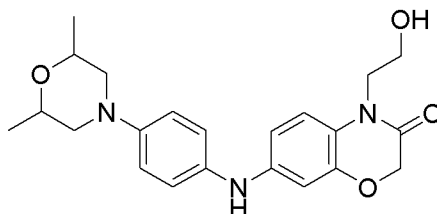
20

To a solution of 4-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.19 mmol) in methanol (3 mL) was added 4-methylbenzenesulfonic acid (36 mg, 0.21 mmol). The mixture was
25 stirred at r.t. for 1h, concentrated and purified by prep HPLC to give 4-(2-hydroxyethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (16.9 mg, 43%) as a light yellow solid. Mass (m/z): 341.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.98 (s, 1H), 7.26 – 7.17 (m, 2H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.98 – 6.89 (m, 2H), 6.68 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 4.83 (t, *J* = 5.7 Hz, 1H), 4.53 (s, 2H), 3.87 (t, *J* = 6.3 Hz, 2H), 3.53 (q, *J* = 6.1 Hz, 2H), 1.22 (s, 9H).

)-2H-benzo[b][1,4]oxazin-3(4H)-one (16.9 mg, 43%) as a grey solid. ¹H NMR (400 MHz, DMSO) δ 7.81 (s, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.96 – 6.86 (m, 2H), 6.60 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.53 (d, *J* = 2.5 Hz, 1H), 4.86 (t, *J* = 5.7 Hz, 1H), 4.54 (s, 2H), 3.89 (t, *J* = 6.3 Hz, 2H), 3.64 (s, 1H), 3.62 – 3.51 (m, 3H), 2.68 – 2.57 (m, 2H), 2.47 – 2.36 (m, 1H), 1.93 – 1.83 (m, 2H), 1.64 – 1.49 (m, 2H). Mass (*m/z*): 436.4 [M+H]⁺.

Compound 84

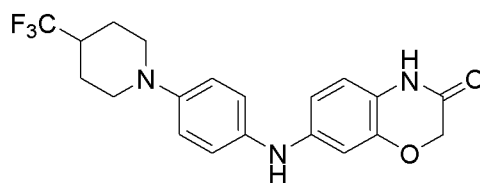
7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 4-(2-hydroxyethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.21 mmol) in methanol (3 mL) was added 4-methylbenzenesulfonic acid (39 mg, 0.23 mmol). The mixture was stirred at r.t. for 1h, the mixture was concentrated and purified by prep HPLC to give 7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (16.9 mg, 43%) as a grey solid. ¹H NMR (400 MHz, DMSO) δ 7.75 (s, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.90 – 6.82 (m, 2H), 6.57 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.50 (d, *J* = 2.4 Hz, 1H), 4.82 (s, 1H), 4.51 (s, 2H), 3.87 (t, *J* = 6.3 Hz, 2H), 3.73 – 3.61 (m, 2H), 3.53 (t, *J* = 6.4 Hz, 2H), 3.46 – 3.38 (m, 2H), 2.17 (t, *J* = 11.0 Hz, 2H), 1.12 (d, *J* = 6.2 Hz, 6H). Mass (*m/z*): 398.4 [M+H]⁺.

Compound 85

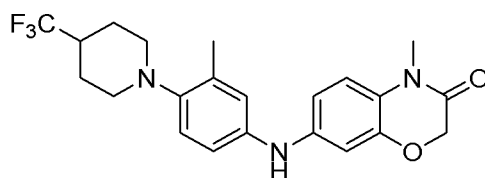
7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **85** (8.6 mg) was prepared in a total yield of 10.0% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (59 mg, 0.241 mmol), 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs₂CO₃ (108 mg, 0.329 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.46 (s, 1H), 7.71 (s, 1H), 6.96 – 6.84 (m, 4H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.57 – 6.49 (m, 2H), 4.48 (s, 2H), 3.61 (d, *J* = 12.4 Hz, 2H), 2.61 (td, *J* = 12.4, 2.4 Hz, 2H), 2.42 (ddt, *J* = 12.4, 8.8, 4.0 Hz, 1H), 1.91 – 1.82 (m, 2H), 1.57 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (*m/z*): 392.3 [M+H]⁺.

Compound 86

4-methyl-7-((3-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



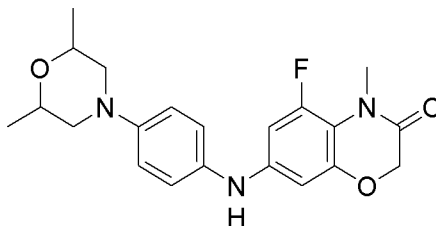
15

The title compound **86** (156 mg) was prepared in a yield of 60% as a light yellow solid from 7-bromo-4-methyl-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one (150 mg, 0.62 mmol), 3-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (160 mg, 0.62 mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (28.3 mg, 0.03 mmol), X-phos (29.5 mg, 0.06 mmol) and Cs₂CO₃ (404 mg, 1.24 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.89 (s, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.89 – 6.81 (m, 2H), 6.69 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 4.58 (s, 2H), 3.23 (s, 3H), 3.04 (d, *J* = 11.4 Hz, 2H), 2.61 (td, *J* = 12.0, 2.3 Hz, 2H), 2.45 – 2.36 (m, 1H), 2.19 (s, 3H), 1.93 – 1.84 (m, 2H), 1.60 (qd, *J* = 12.3, 4.0 Hz, 2H). LC-MS (*m/z*) 420.2 [M+H]⁺.

25

Compound 87

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-5-fluoro-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

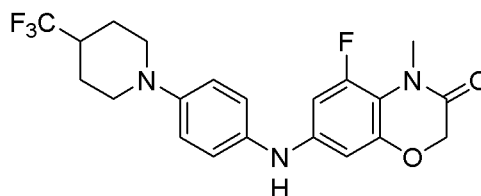


- 5 The title compound **87** (39.4 mg) was prepared in a yield of 22.2% as a white solid from 7-bromo-5-fluoro-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (120 mg, 0.46 mmol), 4-(2,6-dimethylmorpholino)aniline (95 mg, 0.46mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (21 mg, 0.023 mmol), X-phos (22 mg, 0.046 mmol) and Cs₂CO₃ (301 mg, 0.92 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.06 (s, 1H), 7.04 – 6.96 (m, 2H), 6.96 – 6.87 (m, 2H), 6.44 – 6.32 (m, 2H), 4.54 (s, 2H), 3.72 – 3.64 (m, 2H), 3.48 (dt, *J* = 11.0, 2.1 Hz, 2H), 3.29 (d, *J* = 5.5 Hz, 3H), 2.20 (dd, *J* = 11.8, 10.2 Hz, 2H), 1.14 (d, *J* = 6.2 Hz, 6H). LC-MS (*m/z*) 386.2 [M+H]⁺.

15

Compound 88

5-fluoro-4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

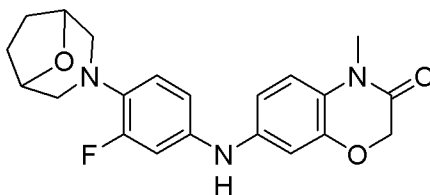


- The titled compound **88** (46.5 mg, 23.8 %) as an off-white solid was prepared according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.08 (s, 1H), 7.00 (d, *J* = 6.5 Hz, 1H), 6.98 – 6.90 (m, 3H), 6.41 (dd, *J* = 15.1, 2.5 Hz, 1H), 6.36 (dd, *J* = 2.5, 1.2 Hz, 1H), 4.54 (s, 2H), 3.67 (d, *J* = 12.3 Hz, 2H), 3.29 (d, *J* = 5.5 Hz, 3H), 2.63 (dd, *J* = 12.3, 2.5 Hz, 2H), 2.46 – 2.36 (m, 1H), 1.93 – 1.84 (m, 2H), 1.56 (qd, *J* = 12.5, 4.1 Hz, 2H). LC-MS (*m/z*) 424.2 [M+H]⁺.

25

Compound 89

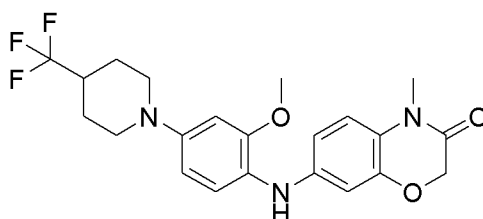
7-((4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-3-fluorophenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



- 5 The title compound **89** (51.1 mg) was prepared in a yield of 26.9% as a light yellow solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (120 mg, 0.49 mmol), 4-(2,6-dimethylmorpholino)aniline (110 mg, 0.49mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (22.7 mg, 0.025 mmol), X-phos (23.6 mg, 0.049 mmol) and Cs₂CO₃ (323 mg, 0.99
10 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.07 (s, 1H), 7.02 (d, *J* = 8.7 Hz, 1H), 6.88 (dd, *J* = 10.0, 8.4 Hz, 1H), 6.82 – 6.66 (m, 3H), 6.62 (d, *J* = 2.5 Hz, 1H), 4.59 (s, 2H), 4.32 (dt, *J* = 4.4, 2.2 Hz, 2H), 3.23 (s, 3H), 2.94 (dd, *J* = 10.6, 1.5 Hz, 2H), 2.86 (dd, *J* = 11.4, 2.0 Hz, 2H), 1.95 (q, *J* = 6.2, 5.6 Hz, 2H), 1.81 (dd, *J* = 7.8,
15 4.2 Hz, 2H). LC-MS (*m/z*) 384.2 [M+H]⁺.

Compound 90

7-((2-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



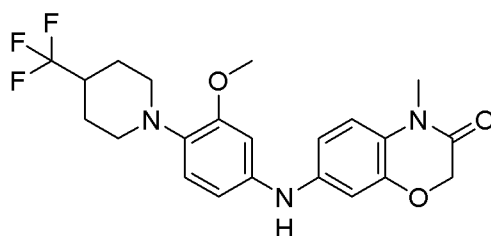
- 20 The title compound **90** (48 mg) was prepared in a yield of 37.8% as a gray solid from 2-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (80 mg, 0.292 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (70.4 mg, 0.292mmol), dioxane (15 mL), Pd₂(dba)₃ (13.4 mg, 0.015 mmol), X-phos (14 mg, 0.0292 mmol) and Cs₂CO₃ (143 mg, 0.438mmol)
25 according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO) δ 7.10 (s, 1H), 7.01 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 1H), 6.65 (d, *J* =

2.5 Hz, 1H), 6.55 – 6.39 (m, 3H), 4.53 (s, 2H), 3.78 (d, J = 13.8 Hz, 3H), 3.72 (d, J = 12.4 Hz, 2H), 3.21 (s, 3H), 2.67 (dd, J = 12.2, 10.5 Hz, 2H), 2.44 (dd, J = 11.7, 8.3 Hz, 1H), 1.89 (d, J = 13.4 Hz, 2H), 1.58 (qd, J = 12.5, 3.9 Hz, 2H). Mass (m/z): 436.5 [M+H]⁺

5

Compound 91

7-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

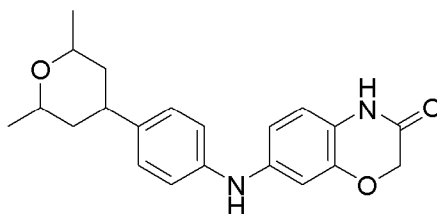


The title compound **91** (27.8 mg) was prepared in a yield of 21.9% as a gray solid from 3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (80 mg, 0.292 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (70.4 mg, 0.292mmol), dioxane (15 mL), Pd₂(dba)₃ (13.4 mg, 0.015 mmol), X-phos (14 mg, 0.0292 mmol) and Cs₂CO₃ (143 mg, 0.438mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.93 (s, 1H), 6.96 (d, J = 8.8 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 6.68 (dd, J = 8.7, 2.4 Hz, 1H), 6.62 – 6.47 (m, 3H), 4.54 (s, 2H), 3.73 (d, J = 20.5 Hz, 3H), 3.26 (s, 2H), 3.19 (s, 3H), 2.51 – 2.48 (m, 2H), 1.82 (d, J = 11.7 Hz, 2H), 1.55 (dt, J = 13.1, 8.7 Hz, 2H). Mass (m/z): 436.5 [M+H]⁺

20

Compound 92

7-((4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



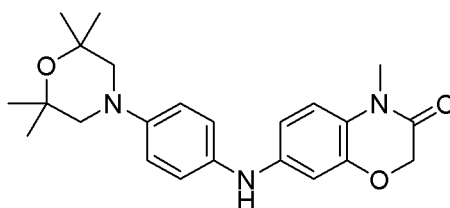
The title compound **92** (23 mg) was prepared in a yield of 11% as a white solid from 4-(2,6-dimethyltetrahydro-2H-pyran-4-yl)aniline (100 mg,

0.488 mmol), 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (122 mg, 0.536 mmol), t-BuOH (5 mL), Pd₂(dba)₃ (22.4 mg, 0.0244 mmol), Brettphos (26.2 mg, 0.0488 mmol) and Cs₂CO₃ (239 mg, 0.732 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.51 (s, 1H), 7.93 (s, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.94 (t, *J* = 10.7 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.66 – 6.55 (m, 2H), 4.50 (s, 2H), 3.52 (dq, *J* = 12.2, 6.1 Hz, 2H), 2.73 – 2.61 (m, 1H), 1.70 (d, *J* = 15.8 Hz, 2H), 1.25 – 1.14 (m, 2H), 1.11 (t, *J* = 12.2 Hz, 6H). Mass (*m/z*): 353.4 [M+H]⁺

10

Compound 93

4-methyl-7-((4-(2,2,6,6-tetramethylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



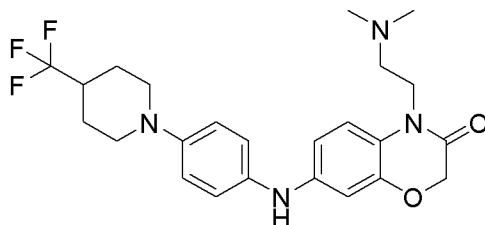
The title compound **93** (32 mg) was prepared in a yield of 31% as an olive solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (68 mg, 0.28 mmol), 4-(2,2,6,6-tetramethylmorpholino)aniline (60 mg, 0.26 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (23 mg, 0.03 mmol), Xphos (24 mg, 0.05 mmol) and Cs₂CO₃ (167 mg, 0.51 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.81 (s, 1H), 7.02 – 6.92 (m, 3H), 6.91 – 6.82 (m, 2H), 6.62 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.53 (d, *J* = 2.4 Hz, 1H), 4.56 (s, 2H), 3.22 (s, 3H), 2.84 (s, 4H), 1.22 (s, 12H). Mass (*m/z*): 396.4 [M+H]⁺.

20

Compound 94

4-(2-(dimethylamino)ethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

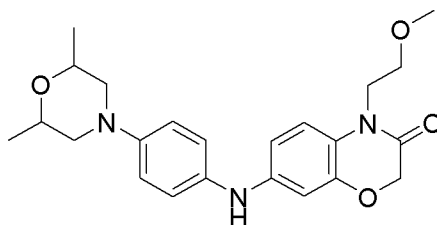
25



The title compound **94** (36 mg) was prepared in a yield of 31% as a light pink solid from 7-bromo-4-(2-(dimethylamino)ethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.36 mmol), 4-(4-(trifluoromethyl) piperidin-1-yl)aniline (80 mg, 0.32 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (30 mg, 0.03 mmol), Xphos (31 mg, 0.07 mmol) and Cs₂CO₃ (213 mg, 0.66 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H), 7.01 (d, *J* = 8.8 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.93 – 6.86 (m, 2H), 6.62 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.54 (d, *J* = 2.5 Hz, 1H), 4.54 (s, 2H), 3.93 (t, *J* = 7.0 Hz, 2H), 3.66 – 3.59 (m, 2H), 2.68 – 2.57 (m, 2H), 2.46 – 2.35 (m, 3H), 2.18 (s, 6H), 1.92 – 1.83 (m, 2H), 1.64 – 1.49 (m, 2H).

Compound 95

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-4-(2-methoxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one

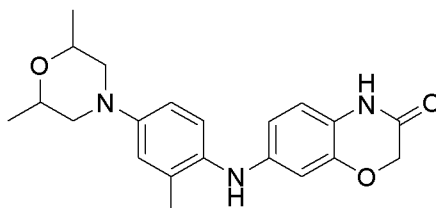


The title compound **95** (56 mg) was prepared in a yield of 25% as a grey solid from 7-bromo-4-(2-methoxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one (150 mg, 0.59 mmol), 4-(2,6-dimethylmorpholino)aniline (110 mg, 0.53 mmol), 1,4-dioxane (2 mL), Pd₂(dba)₃ (49 mg, 0.05 mmol), Xphos (51 mg, 0.11 mmol) and Cs₂CO₃ (348 mg, 1.06 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.77 (s, 1H), 7.03 (d, *J* = 8.8 Hz, 1H), 6.97 – 6.89 (m, 2H), 6.89 – 6.80 (m, 2H), 6.55 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.49 (d, *J* = 2.5 Hz, 1H), 4.51 (s, 2H), 3.98 (t, *J* =

5.8 Hz, 2H), 3.71 – 3.59 (m, 2H), 3.46 (t, $J = 5.8$ Hz, 2H), 3.44 – 3.37 (m, 2H), 3.20 (s, 3H), 2.20 – 2.10 (m, 2H), 1.10 (d, $J = 6.2$ Hz, 6H).

Compound 96

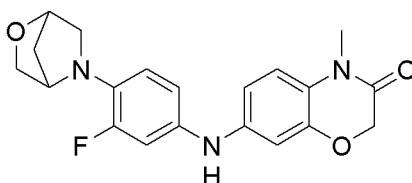
7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **96** (20 mg) was prepared in a yield of 8% as a grey solid from 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (154 mg, 0.68 mmol), 4-(2,6-dimethylmorpholino)-2-methylaniline (150 mg, 0.68 mmol), 1,4-dioxane (2 mL), Brettphos Pd G3 (62 mg, 0.14 mmol), Brettphos (73 mg, 0.13 mmol) and Cs_2CO_3 (444 mg, 1.36 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.38 (s, 1H), 7.08 (s, 1H), 6.96 (d, $J = 8.6$ Hz, 1H), 6.82 (d, $J = 2.8$ Hz, 1H), 6.73 (dd, $J = 8.6, 2.8$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 6.26 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.23 (d, $J = 2.3$ Hz, 1H), 4.45 (s, 2H), 3.74 – 3.62 (m, 2H), 3.53 – 3.45 (m, 2H), 2.29 – 2.14 (m, 2H), 2.11 (s, 3H), 1.14 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 368.4 $[\text{M}+\text{H}]^+$.

Compound 97

7-((4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-3-fluorophenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

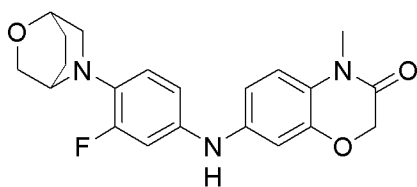


The title compound **97** (47.5 mg) was prepared in a yield of 26% as a light yellow solid from 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (120 mg, 0.49 mmol), 4-((1S,4S)-2-oxa-5-azabicyclo[2.2.1] heptan-5-yl)-3-fluoroaniline (103.2 mg, 0.49mmol), 1,4-dioxane (5 mL), $\text{Pd}_2(\text{dba})_3$ (22.7 mg, 0.025 mmol), X-phos (23.6 mg, 0.049 mmol) and Cs_2CO_3 (323

mg, 0.99 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.91 (s, 1H), 6.99 (d, *J* = 8.7 Hz, 1H), 6.85 – 6.76 (m, 1H), 6.76 – 6.68 (m, 2H), 6.65 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.56 (d, *J* = 2.4 Hz, 1H), 4.58 (s, 2H), 4.53 (t, *J* = 1.9 Hz, 1H), 4.37 (s, 1H), 3.81 (d, *J* = 7.6 Hz, 1H), 3.72 (dd, *J* = 7.7, 1.6 Hz, 1H), 3.56 (ddd, *J* = 9.7, 4.0, 1.7 Hz, 1H), 3.23 (s, 3H), 2.99 (dd, *J* = 9.8, 3.5 Hz, 1H), 1.88 (dd, *J* = 9.6, 2.3 Hz, 1H), 1.83 – 1.75 (m, 1H). LC-MS (*m/z*) 370.2 [M+H]⁺.

Compound 98

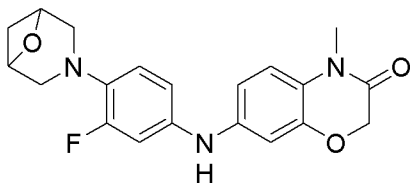
7-((4-(2-oxa-5-azabicyclo[2.2.2]octan-5-yl)-3-fluorophenyl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The title compound **98** (34.5 mg) was prepared in a yield of 16.7% as an off-white solid from 7-bromo-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one (120 mg, 0.49 mmol), 4-(2-oxa-5-azabicyclo[2.2.2]octan-5-yl)-3-fluoroaniline (110 mg, 0.49 mmol), 1,4-dioxane (5 mL), Pd₂(dba)₃ (22.7 mg, 0.025 mmol), X-phos (23.6 mg, 0.049 mmol) and Cs₂CO₃ (323 mg, 0.99 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.94 (s, 1H), 7.00 (d, *J* = 8.7 Hz, 1H), 6.89 – 6.84 (m, 1H), 6.84 – 6.81 (m, 1H), 6.80 – 6.73 (m, 1H), 6.66 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.57 (d, *J* = 2.5 Hz, 1H), 4.58 (s, 2H), 4.09 (dt, *J* = 8.9, 2.4 Hz, 1H), 3.92 – 3.84 (m, 2H), 3.69 (dq, *J* = 10.5, 2.8 Hz, 1H), 3.54 (d, *J* = 3.0 Hz, 1H), 3.32 (d, *J* = 2.5 Hz, 1H), 3.23 (s, 3H), 2.08 (s, 1H), 2.02 – 1.93 (m, 1H), 1.88 – 1.67 (m, 2H). LC-MS (*m/z*) 384.2 [M+H]⁺.

Compound 99

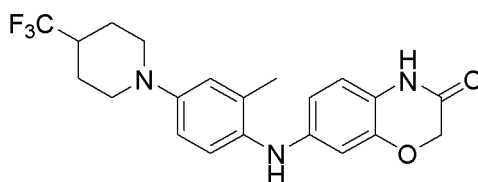
7-((4-(6-oxa-3-azabicyclo[3.1.1]heptan-3-yl)-3-fluorophenyl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **99** (21.7 mg, 14.2 %) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.00 (s, 1H), 7.01 (d, $J = 8.7$ Hz, 1H), 6.97 (dd, $J = 10.4, 8.6$ Hz, 1H), 6.86 – 6.77 (m, 2H), 6.69 (dd, $J = 8.7, 2.5$ Hz, 1H), 6.60 (d, $J = 2.4$ Hz, 1H), 4.58 (d, $J = 3.7$ Hz, 4H), 3.55 (d, $J = 11.3$ Hz, 2H), 3.23 (s, 3H), 3.43 (d, $J = 11.4$ Hz, 2H), 3.04 (dt, $J = 8.1, 6.3$ Hz, 1H), 2.17 (d, $J = 8.2$ Hz, 1H). LC-MS (m/z) 370.2 $[\text{M}+\text{H}]^+$.

Compound 100

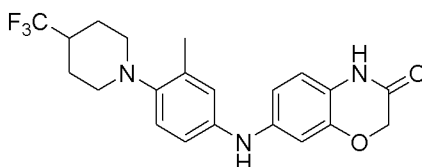
7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The title compound **100** (32 mg) was prepared in a yield of 9.0% as a white solid from 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (200 mg, 0.88 mmol), 2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (226 mg, 0.88 mmol), $t\text{-BuOH}$ (5 mL), $\text{Pd}_2(\text{dba})_3$ (40 mg, 0.045 mmol), Brettphos (47.1 mg, 0.088 mmol) and Cs_2CO_3 (572 mg, 1.75 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.39 (s, 1H), 7.08 (s, 1H), 6.96 (d, $J = 8.6$ Hz, 1H), 6.84 (d, $J = 2.8$ Hz, 1H), 6.75 (dd, $J = 8.7, 2.8$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 6.28 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.24 (d, $J = 2.3$ Hz, 1H), 4.45 (s, 2H), 3.68 (d, $J = 12.3$ Hz, 2H), 2.62 (dd, $J = 12.4, 2.5$ Hz, 2H), 2.47 – 2.38 (m, 1H), 2.11 (s, 3H), 1.92 – 1.83 (m, 2H), 1.56 (qd, $J = 12.5, 4.1$ Hz, 2H). LC-MS (m/z) 406.2 $[\text{M}+\text{H}]^+$.

Compound 101

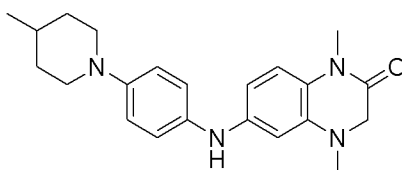
7-((3-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-

benzo[b][1,4]oxazin-3(4H)-one

The titled compound **101** (113 mg, 31.8 %) as a white solid was prepared according to the procedure outlined for compound **1**. LC-MS (m/z) 406.2
 5 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.48 (s, 1H), 7.79 (s, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.60 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.56 (d, *J* = 2.3 Hz, 1H), 4.49 (s, 2H), 3.02 (d, *J* = 11.5 Hz, 2H), 2.60 (td, *J* = 11.9, 2.3 Hz, 2H), 2.43 – 2.32 (m, 1H), 2.18 (s, 3H), 1.92 – 1.84 (m, 2H), 1.60 (qd, *J* = 12.3, 4.0 Hz, 2H).

Compound 102

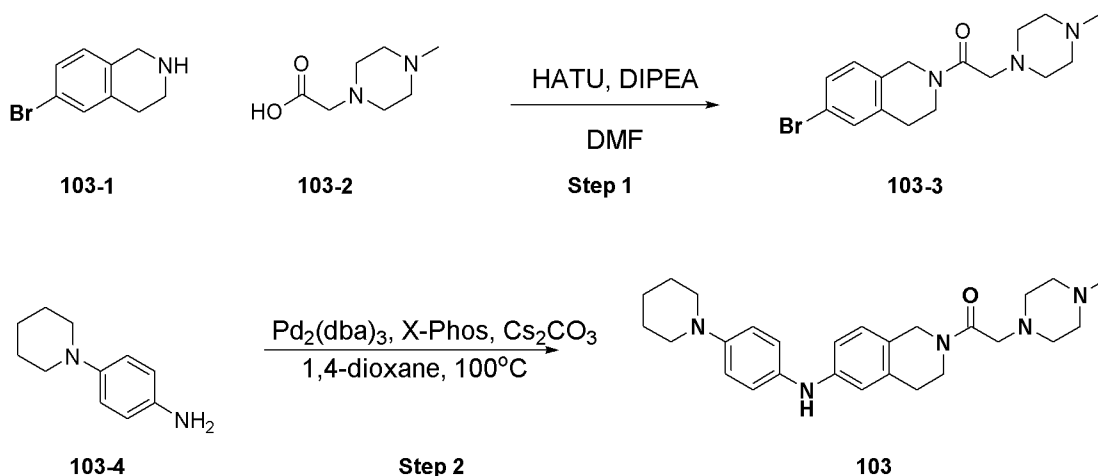
1,4-dimethyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)-3,4-dihydroquinoxalin-2(1H)-one



The title compound **102** (8.5 mg) was prepared in a total yield of 11.9% as
 15 a purple solid from 4-(4-methylpiperidin-1-yl)aniline (48 mg, 0.256 mmol) and 6-bromo-1,4-dimethyl-3,4-dihydroquinoxalin-2(1H)-one (50 mg, 0.197 mmol) in 1,4-dioxane (5 mL), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (97 mg, 0.295 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz,
 20 Methanol-*d*₄) δ 7.07 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 3H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.54 (s, 1H), 3.63 (d, *J* = 7.2 Hz, 2H), 3.42 (s, 3H), 3.37 (s, 2H), 3.10 (s, 3H), 2.69 (s, 2H), 2.29 (dq, *J* = 8.4, 4.8, 4.4 Hz, 1H), 2.01 (s, 1H), 1.98 (s, 1H), 1.76 (d, *J* = 4.0 Hz, 1H), 1.73 (d, *J* = 4.0 Hz, 1H), 1.73 (d, *J* = 4.0 Hz, 1H). Mass (m/z): 365.3 [M+H]⁺.

Compound 103

2-(4-methylpiperazin-1-yl)-1-(6-((4-(piperidin-1-yl)phenyl)amino)-3,4-

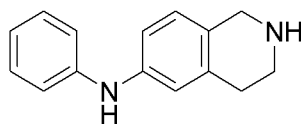
dihydroisoquinolin-2(1H)-yl)ethan-1-one

Step 1. Preparation of 1-(6-bromo-3,4-dihydroisoquinolin-2(1H)-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one (**103-3**)

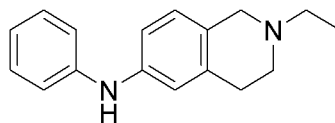
To a solution of 6-bromo-1,2,3,4-tetrahydroisoquinoline (212 mg, 1.0 mmol) and 2-(4-methylpiperazin-1-yl)acetic acid (205 mg, 1.3 mmol) in DMF (5 mL) was added DIEA (0.33 mL, 2.0 mmol). Followed by the addition of HATU (501 mg, 1.3 mmol) then the reaction mixture was stirred for 3 hours at r.t. Then 40 mL of water was added. Then the mixture was extracted by DCM (20 mL x 3). The combined organic layers were washed with water (20 mL x 3), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by prep-TLC to give the desired product as yellow solid (301 mg, 85.2 %). Mass (m/z): 352.1 [M+H]⁺.

Step 2. Preparation of 2-(4-methylpiperazin-1-yl)-1-(6-((4-(piperidin-1-yl)phenyl)amino)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (**103**)

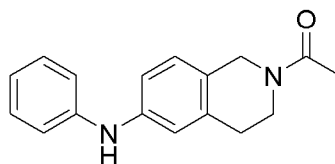
The title compound **103** (18.5 mg) was prepared in a total yield of 82.6% as a yellow solid from 4-(piperidin-1-yl)aniline (11.4 mg, 0.065 mmol), 1-(6-bromo-3,4-dihydroisoquinolin-2(1H)-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one (17.6 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.40 – 6.73 (m, 7H), 4.72 (s, 2H), 3.83 (s, 2H), 3.51 – 3.39 (m, 4H), 3.06 – 2.87 (m, 4H), 2.85 – 2.63 (m, 8H), 2.50 (s, 3H), 1.90 – 1.76 (m, 4H), 1.71 – 1.60 (m, 2H). Mass (m/z): 448.3 [M+H]⁺.

Compound 104*N*-phenyl-1,2,3,4-tetrahydroisoquinolin-6-amine

The title compound **104** (8.6 mg) was prepared in a total yield of 76.4% as
 5 an orange solid from 6-bromo-1,2,3,4-tetrahydroisoquinoline (10.6 mg, 0.05 mmol), aniline (6.1 mg, 0.065 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.29 - 7.18 (m, 2H), 7.09 - 6.79 (m, 6H), 4.10 (s, 2H), 3.29
 10 (t, *J* = 6.4 Hz, 2H), 2.93 (t, *J* = 6.4 Hz, 2H). Mass (m/z): 225.3 [M+H]⁺.

Compound 105*2*-ethyl-*N*-phenyl-1,2,3,4-tetrahydroisoquinolin-6-amine

The title compound **105** (9.8 mg) was prepared in a total yield of 77.8% as
 15 a orange solid from 6-bromo-2-ethyl-1,2,3,4-tetrahydroisoquinoline (12.0 mg, 0.05 mmol), aniline (6.1 mg, 0.065 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.24 - 7.17 (m, 2H), 7.08 - 7.02 (m, 2H), 7.00 - 6.80 (m, 4H), 3.89 (s, 2H), 3.08 (t, *J* = 6.4 Hz, 2H), 2.97 (t, *J* = 6.4 Hz, 2H), 2.91 (q,
 20 *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). Mass (m/z): 253.2 [M+H]⁺.

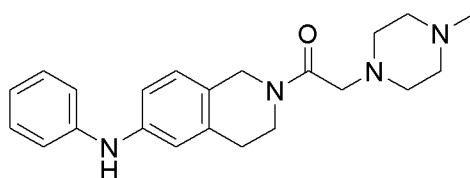
Compound 106*1*-(6-(phenylamino)-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one

25 The title compound **106** (9.2 mg) was prepared in a total yield of 68.9% as

a orange solid from 1-(6-bromo-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (12.7 mg, 0.05 mmol), aniline (6.1 mg, 0.065 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.23 - 7.16 (m, 2H), 7.07 - 6.78 (m, 6H), 4.57 (s, 2H), 3.66 (t, *J* = 6.4 Hz, 2H), 2.79 (t, *J* = 6.4 Hz, 2H), 2.15 (s, 3H). Mass (m/z): 267.2 [M+H]⁺.

Compound 107

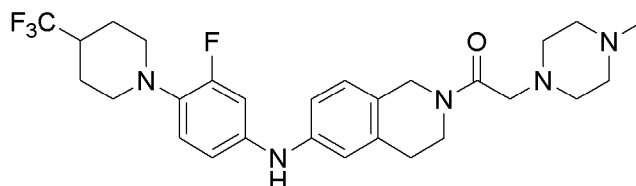
2-(4-methylpiperazin-1-yl)-1-(6-(phenylamino)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one



The title compound **107** (15.3 mg) was prepared in a total yield of 83.8% as an orange solid from 1-(6-bromo-3,4-dihydroisoquinolin-2(1H)-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one (17.6 mg, 0.05 mmol), aniline (6.1 mg, 0.065 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.25 - 7.14 (m, 2H), 7.08 - 6.78 (m, 6H), 4.62 (s, 2H), 3.72 (s, 2H), 3.36 (t, *J* = 6.0 Hz, 2H), 2.84 (t, *J* = 6.0 Hz, 2H), 2.80 - 2.58 (m, 8H), 2.44 (s, 3H). Mass (m/z): 365.2 [M+H]⁺.

Compound 108

1-(6-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroisoquinolin-2(1H)-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one

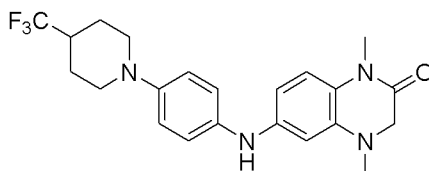


The title compound **108** (20.1 mg) was prepared in a total yield of 75.3% as a yellow solid from 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)

aniline (17.1 mg, 0.065 mmol), 1-(6-bromo-3,4-dihydroisoquinolin-2(1H)-yl) -2-(4-methylpiperazin-1-yl)ethan-1-one (17.6 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.14 - 6.72 (m, 6H), 4.63 (s, 2H), 3.76 (s, 2H), 3.41 - 3.33 (m, 4H), 2.96 - 2.75 (m, 4H), 2.73 - 2.55 (m, 8H), 2.41(s, 3H), 2.25 (m, 1H), 1.98 - 1.90 (m, 2H), 1.79 - 1.68 (m, 2H). Mass (m/z): 534.3 [M+H]⁺

Compound 109

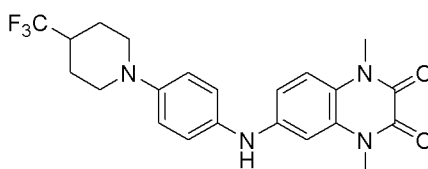
1,4-dimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinoxalin-2(1H)-one



The title compound **109** (29.5 mg) was prepared in a total yield of 35.8% as a purple solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (62 mg, 0.256 mmol), 6-bromo-1,4-dimethyl-3,4-dihydroquinoxalin-2(1H)-one (50 mg, 0.197 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (97 mg, 0.295 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.07 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 3H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.54 (s, 1H), 3.63 (d, *J* = 7.2 Hz, 2H), 3.42 (s, 3H), 3.37 (s, 2H), 3.10 (s, 3H), 2.69 (s, 2H), 2.29 (dq, *J* = 8.4, 4.8, 4.4 Hz, 1H), 2.01 (s, 1H), 1.98 (s, 1H), 1.76 (d, *J* = 4.0 Hz, 1H), 1.73 (d, *J* = 4.0 Hz, 1H). Mass (m/z): 419.3 [M+H]⁺.

Compound 110

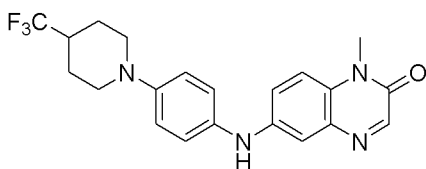
1,4-dimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,4-dihydroquinoxaline-2,3-dione



The title compound **110** (8.8 mg) as prepared in a total yield of 43.4% as a yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (80 mg, 0.33 mmol), 6-bromo-1,4-dimethyl-1,4-dihydroquinoxaline-2,3-dione (67 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), t-BuOK (36 mg, 0.38 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.30 (d, *J* = 8.8 Hz, 1H), 7.16 – 7.08 (m, 2H), 7.04 – 6.94 (m, 4H), 3.72 – 3.66 (m, 2H), 3.65 (s, 3H), 3.60 (s, 3H), 2.76 – 2.65 (m, 2H), 2.35 – 2.25 (m, 1H), 2.03 – 1.96 (m, 1H), 1.75 (qd, *J* = 12.5, 4.1 Hz, 2H). Mass (*m/z*): 433.3 [M+H]⁺.

Compound 111

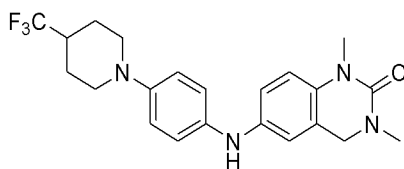
1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)quinoxalin-2(1H)-one



The title compound **111** (37.9 mg) was prepared in a total yield of 22.6% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (122 mg, 0.502 mmol), 6-bromo-1-methylquinoxalin-2(1H)-one (100 mg, 0.418 mmol), Pd₂(dba)₃ (4 mg, 0.004 mmol), X-phos (10 mg, 0.02 mmol) and Cs₂CO₃ (206 mg, 0.628 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.16 (s, 1H), 8.06 (s, 1H), 7.48 – 7.42 (m, 1H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.06 – 7.03 (m, 2H), 6.97 – 6.92 (m, 2H), 3.66 (d, *J* = 12.0 Hz, 2H), 3.57 (s, 3H), 2.65 (td, *J* = 12.0, 2.4 Hz, 2H), 2.43 (ddd, *J* = 12.4, 8.4, 3.6 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.58 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (*m/z*): 403.3 [M+H]⁺.

Compound 112

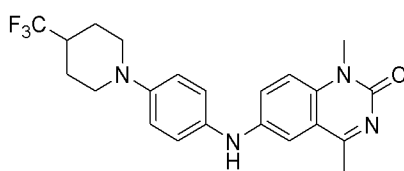
1,3-dimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinazolin-2(1H)-one



The title compound **112** (11.3 mg) was prepared in a total yield of 6.9% as a purple solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (115 mg, 0.470 mmol), 6-bromo-1,3-dimethyl-3,4-dihydroquinazolin-2(1H)-one (100 mg, 0.392 mmol), Pd₂(dba)₃ (4 mg, 0.004 mmol), X-phos (10 mg, 0.02 mmol) and Cs₂CO₃ (193 mg, 0.588 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.07 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 3H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.54 (s, 1H), 3.63 (d, *J* = 7.2 Hz, 2H), 3.42 (s, 3H), 3.37 (s, 2H), 3.10 (s, 3H), 2.69 (s, 2H), 2.29 (dq, *J* = 8.4, 4.8, 4.4 Hz, 1H), 2.01 (s, 1H), 1.98 (s, 1H), 1.76 (d, *J* = 4.0 Hz, 1H), 1.73 (d, *J* = 4.0 Hz, 1H). Mass (m/z): 419.3 [M+H]⁺.

Compound 113

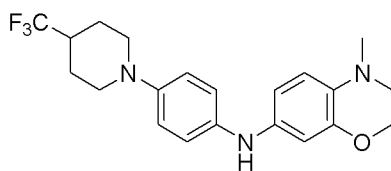
1,4-dimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)quinazolin-2(1H)-one



The title compound **113** (33.4 mg) was prepared in a total yield of 20.3% as a pink solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (116 mg, 0.474 mmol), 6-bromo-1,4-dimethylquinazolin-2(1H)-one (100 mg, 0.395 mmol), Pd₂(dba)₃ (4 mg, 0.004 mmol), X-phos (10 mg, 0.02 mmol), Cs₂CO₃ (194 mg, 0.592 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.01 (s, 1H), 8.72 (s, 1H), 7.85 (s, 2H), 7.50 (s, 1H), 7.11 (s, 5H), 3.88 – 3.65 (m, 6H), 2.92 (d, *J* = 44.4 Hz, 4H), 1.94 (s, 3H), 1.65 (s, 2H). Mass (m/z): 417.3 [M+H]⁺.

Compound 114

4-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-amine

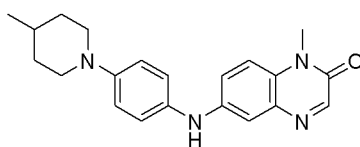


The title compound **114** (46.7 mg) was prepared in a total yield of 54.6%
 5 as a green solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (64 mg, 0.263 mmol), 7-bromo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazine (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (108 mg, 0.328 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.82 (s, 1H), 6.97 (dt, *J* = 10.0, 3.2 Hz, 3H), 6.94 – 6.87 (m, 2H), 6.63 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 4.57 (s, 2H), 3.77 (d, *J* = 12.0, 2H), .63 (d, *J* = 11.6 Hz, 2H), 3.23 (s, 3H), 2.63 (td, *J* = 12.4, 2.4 Hz, 2H), 2.43 (dp, *J* = 12.4, 4.0 Hz, 1H), 1.88 (d, *J* = 12.0 Hz, 2H), 1.57 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (*m/z*): 392.3 [M+H]⁺.

15

Compound 115

1-methyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)quinoxalin-2(1H)-one

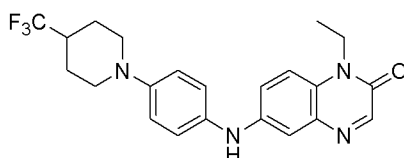


The title compound **115** (101.2 mg) was prepared in a total yield of 69.5%
 20 as a yellow solid from 4-(4-methylpiperidin-1-yl)aniline (95 mg, 0.502 mmol), 6-bromo-1-methylquinoxalin-2(1H)-one (100 mg, 0.418 mmol), Pd₂(dba)₃ (4 mg, 0.004 mmol), X-phos (12 mg, 0.02 mmol), Cs₂CO₃ (206 mg, 0.627 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.74 (s, 1H), 8.22 (s, 1H), 7.63 – 7.40 (m, 5H), 7.19 (d, *J* = 8.5 Hz, 2H), 4.71 (s, 4H), 3.60 (s, 3H), 1.90 (d, *J* = 13.8 Hz, 2H), 1.77 (d, *J* = 7.8 Hz, 1H), 1.59 (d, *J* = 12.6 Hz, 2H), 0.99 (d, *J* = 6.3 Hz, 3H). Mass (*m/z*): 349.3 [M+H]⁺.

25

Compound 116

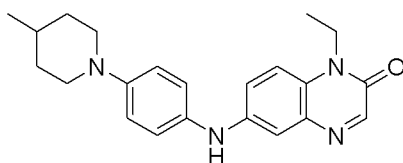
1-ethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)quinoxalin-2(1H)-one



- 5 The title compound **116** (31.6 mg) was prepared in a total yield of 38.1% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (58 mg, 0.239 mmol), 6-bromo-1-ethylquinoxalin-2(1H)-one (50 mg, 0.199 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (98 mg, 0.299 mmol) and 1,4-dioxane (5 mL) according to the procedure for
 10 compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.17 (s, 1H), 7.69 – 6.81 (m, 7H), 4.22 (q, *J* = 7.2 Hz, 4H), 3.07 (s, 2H), 2.62 (d, *J* = 10.0 Hz, 1H), 2.10 – 1.92 (m, 2H), 1.80 (d, *J* = 36.0 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H). Mass (m/z): 417.3 [M+H]⁺.

Compound 117

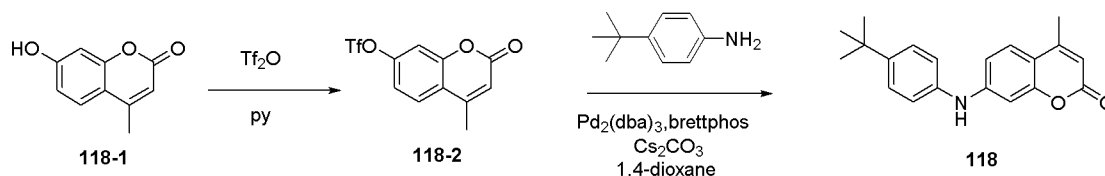
- 15 *1-ethyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)quinoxalin-2(1H)-one*



- The title compound **117** (40.2 mg) was prepared in a total yield of 55.8% as a yellow solid from 4-(4-methylpiperidin-1-yl)aniline (45 mg, 0.239 mmol), 6-bromo-1-ethylquinoxalin-2(1H)-one (50 mg, 0.199 mmol),
 20 Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (98 mg, 0.299 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.81 – 8.54 (m, 1H), 8.20 (s, 1H), 7.72 – 7.03 (m, 7H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.71 – 3.60 (m, 4H), 2.00 – 1.46 (m, 5H), 1.24 (t, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 6.0 Hz, 3H).
 25 Mass (m/z): 363.3 [M+H]⁺.

Compound 118

7-((4-(tert-butyl)phenyl)amino)-4-methyl-2H-chromen-2-one



Step 1. Preparation of 4-methyl-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (**118-2**)

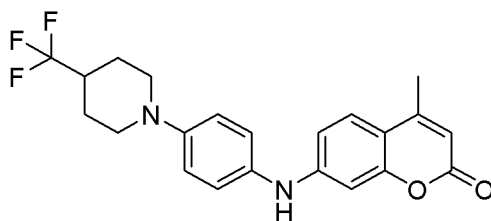
To a solution of 7-hydroxy-4-methyl-2H-chromen-2-one (500 mg, 2.84 mmol) in pyridine (10 mL) was added trifluoromethanesulfonic anhydride (881 mg, 3.13 mmol) at 0 °C. Then the mixture was stirred at room temperature for 1 hour. The mixture was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 600 mg as a yellow solid. Mass (m/z): 309.3 [M+H]⁺

Step 2. Preparation of 7-((4-(tert-butyl)phenyl)amino)-4-methyl-2H-chromen-2-one (**118**)

To a solution of 4-methyl-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (100 mg, 0.324 mmol) and 4-(tert-butyl)aniline (53.2 mg, 0.356 mmol) in dioxane (5 mL) was added Pd₂(dba)₃ (14.8 mg, 0.016 mmol), Brettphos (17.4 mg, 0.0324 mmol) and Cs₂CO₃ (212 mg, 0.648 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (48.8 mg, 49.0%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.78 (s, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.37 – 7.29 (m, 2H), 7.15 – 7.07 (m, 2H), 6.92 (dd, J = 8.8, 2.3 Hz, 1H), 6.78 (d, J = 2.3 Hz, 1H), 6.01 (d, J = 1.3 Hz, 1H), 2.31 (d, J = 1.2 Hz, 3H), 1.25 (s, 9H). Mass (m/z): 308.4 [M+H]⁺.

Compound 119

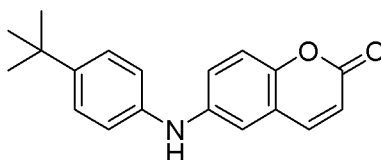
4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one



The title compound **119** was prepared according to the procedure for compound **118**. To a solution of 4-methyl-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (100 mg, 0.325 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (79.2 mg, 0.325 mmol) in dioxane (5 mL) was added $\text{Pd}_2(\text{dba})_3$ (14.9 mg, 0.0163 mmol), Brettphos (17.5 mg, 0.0325 mmol) and Cs_2CO_3 (212 mg, 0.65 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (34.1 mg, 26.1%). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.59 (s, 1H), 7.49 (d, $J = 8.8$ Hz, 1H), 7.10 – 7.02 (m, 2H), 6.99 – 6.90 (m, 2H), 6.80 (dd, $J = 8.8, 2.3$ Hz, 1H), 6.64 (d, $J = 2.2$ Hz, 1H), 5.96 (d, $J = 1.3$ Hz, 1H), 3.68 (d, $J = 12.3$ Hz, 2H), 2.65 (td, $J = 12.4, 2.5$ Hz, 2H), 2.30 (d, $J = 1.2$ Hz, 3H), 1.90 – 1.81 (m, 2H), 1.54 (qd, $J = 12.5, 4.1$ Hz, 2H). Mass (m/z): 403.4 $[\text{M}+\text{H}]^+$.

Compound 120

6-((4-(tert-butyl)phenyl)amino)-2H-chromen-2-one

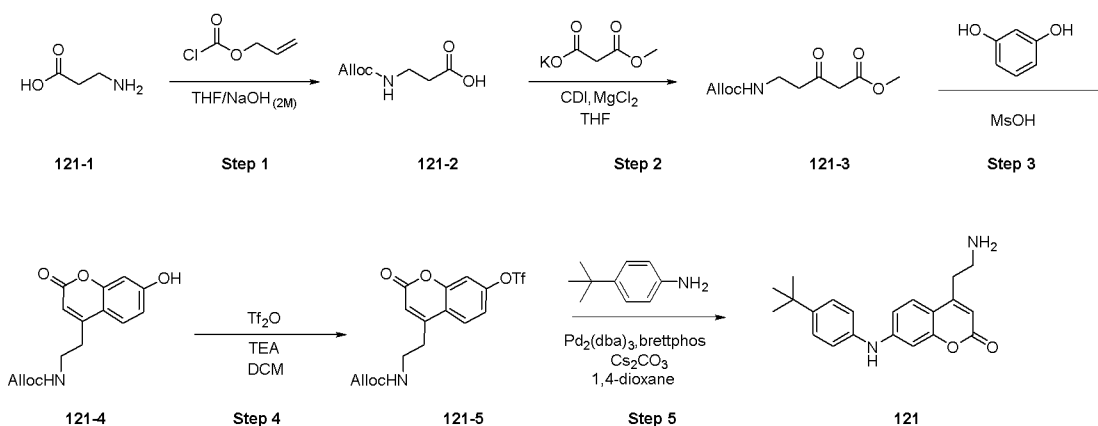


The title compound **120** (40.2 mg) was prepared according to the procedure for compound **118**. To a solution of 2-oxo-2H-chromen-6-yl trifluoromethanesulfonate (100 mg, 0.34 mmol) and 4-(tert-butyl)aniline (55.8 mg, 0.374 mmol) in dioxane (5 mL) was added $\text{Pd}_2(\text{dba})_3$ (15.6 mg, 0.017 mmol), Brettphos (18.3 mg, 0.034 mmol) and Cs_2CO_3 (222 mg, 0.68 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The

combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (80 mg, 80%).
¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, J = 9.5 Hz, 1H), 7.33 (d, J = 8.5 Hz, 2H), 7.21 (dd, J = 11.1, 8.9 Hz, 2H), 7.13 (s, 1H), 7.02 (t, J = 9.7 Hz, 2H), 6.40 (d, J = 9.5 Hz, 1H), 1.32 (s, 9H). Mass (m/z): 294.3 [M+H]⁺.

Compound 121

4-(2-aminoethyl)-7-((4-(tert-butyl)phenyl)amino)-2H-chromen-2-one



Step 1. Preparation of 3-(((allyloxy)carbonyl)amino)propanoic acid (121-2)

To a solution of 3-aminopropanoic acid (3.0 g, 33.7 mmol) in THF (60 mL)/H₂O (30 mL) was added NaOH (2N) (33.7 mL, 67.4 mmol), allyl chloroformate (5.9 mL, 33.7 mmol). Then the mixture was stirred at room temperature overnight. The mixture was diluted with water and extracted by DCM (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 3.2 g as colorless oil. Mass (m/z): 174.2 [M+H]⁺.

Step 2. Preparation of methyl 5-(((allyloxy)carbonyl)amino)-3-oxopentanoate (121-3)

To a solution of 3-(((allyloxy)carbonyl)amino)propanoic acid (2.0 g, 11.6 mmol) in THF (50 mL) was added CDI (2.26 g, 13.9 mmol) under argon atmosphere, the mixture was stirred at room temperature for 2 hours. Then a mixture of MgCl₂ (1.1 g, 11.6 mmol) and potassium

3-methoxy-3-oxopropanoate (2.71 g, 17.3 mmol) was added. The mixture was stirred at room temperature overnight. Then it was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 1.86 g as colorless oil. Mass (m/z): 230.2 [M+H]⁺.

Step 3. Preparation of allyl (2-(7-hydroxy-2-oxo-2H-chromen-4-yl)ethyl) carbamate (**121-4**)

To a solution of methyl 5-(((allyloxy)carbonyl)amino)-3-oxopentanoate (1.86 g, 8.12 mmol) in MsOH (20 mL) was added resorcinol (893 g, 8.12 mmol) under argon atmosphere at 0°C, the mixture was stirred at 0°C for 3 hours. Then saturated NaHSO₄ solution was added. The mixture was stirred from turbidity to clarification. Then it was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 1.0g as yellow solid. Mass (m/z): 290.3 [M+H]⁺.

Step 4. Preparation of 4-(2-(((allyloxy)carbonyl)amino)ethyl)-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (**121-5**)

To a solution of allyl (2-(7-hydroxy-2-oxo-2H-chromen-4-yl)ethyl) carbamate (1.0 g, 3.46 mmol) in DCM (20 mL) was added trifluoromethanesulfonic anhydride (1.07 g, 3.8mmol), TEA (700 mg, 6.92mmol) at 0°C. Then the mixture was stirred at room temperature for 3 hours. The mixture was diluted with water and extracted by DCM (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 600mg as yellow solid. Mass (m/z): 422.4 [M+H]⁺.

Step 5. Preparation of 4-(2-aminoethyl)-7-((4-(tert-butyl)phenyl)amino)-2H-chromen-2-one (**121**)

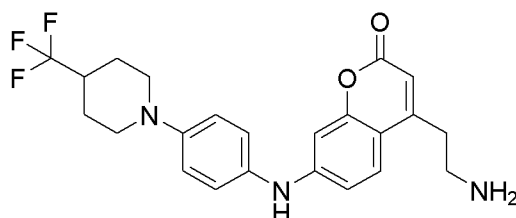
To a solution of 4-(2-(((allyloxy)carbonyl)amino)ethyl)-2-

oxo-2H-chromen-7-yl trifluoromethanesulfonate (100 mg, 0.238 mmol) and 4-(tert-butyl)aniline (35.4 mg, 0.238mmol) in dioxane (5 mL) was added Pd₂(dba)₃ (10.9 mg, 0.012 mmol), Brettphos (12.8 mg, 0.0238 mmol) and Cs₂CO₃ (117 mg, 0.357mmol) under nitrogen atmosphere.

5 Then the mixture was stirred at 100 °C for 2 hours. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (4.7 mg, 5.9%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.81 (s, 1H), 8.32 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.15 – 7.07 (m, 2H), 6.91 (dd, J = 8.8, 2.3 Hz, 1H), 6.80 (d, J = 2.3 Hz, 1H), 6.00 (s, 1H), 2.94 – 2.79 (m, 4H), 1.25 (s, 9H). Mass (m/z): 337.4 [M+H]⁺.

Compound 122

15 4-(2-aminoethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one

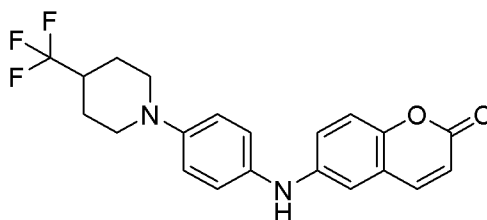


To a solution of 4-(2-(((allyloxy)carbonyl)amino)ethyl)-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (150 mg, 0.356 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (130 mg, 0.534 mmol) in dioxane (5 mL) was added Pd₂(dba)₃ (16.3 mg, 0.018 mmol), Brettphos (19.1 mg, 0.0356 mmol) and Cs₂CO₃ (174 mg, 0.534mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C for 2 hours. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (21.0 mg, 13.7%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.59 (s, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.06 (d, J = 8.9 Hz, 2H), 6.98 – 6.91 (m, 2H), 6.80 (dd, J = 8.8, 2.4 Hz, 1H), 6.64

(d, $J = 2.3$ Hz, 1H), 5.93 (s, 1H), 3.69 (d, $J = 12.1$ Hz, 2H), 2.81 (dd, $J = 21.2, 6.4$ Hz, 4H), 2.70 – 2.59 (m, 4H), 1.86 (d, $J = 12.6$ Hz, 2H), 1.61 – 1.46 (m, 2H). Mass (m/z): 432.4 $[M+H]^+$.

Compound 123

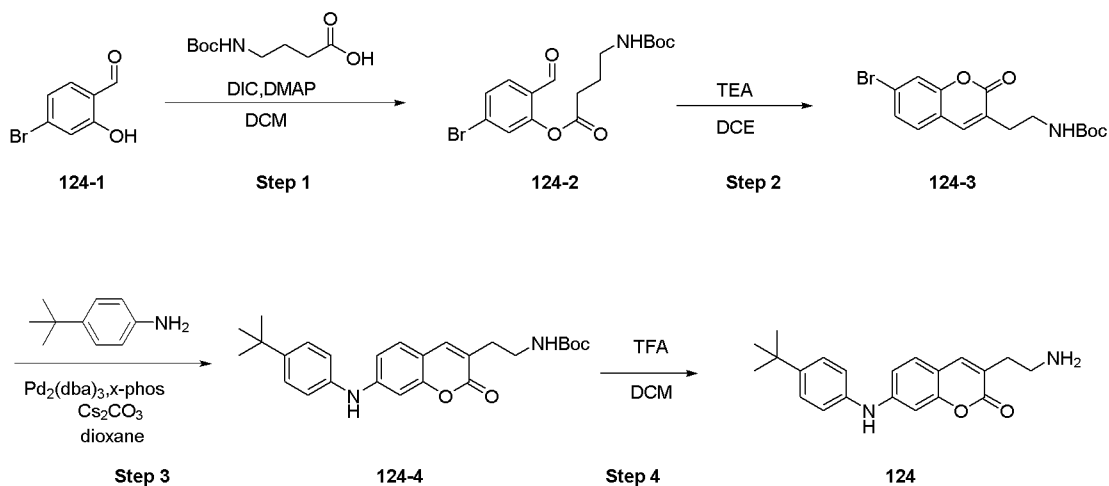
5 6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one



To a solution of 2-oxo-2H-chromen-6-yl trifluoromethanesulfonate (100 mg, 0.34 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (91.2 mg, 0.374 mmol) in dioxane (5 mL) was added $Pd_2(dba)_3$ (15.6 mg, 0.017 mmol), Brettphos (18.3 mg, 0.034 mmol) and Cs_2CO_3 (222 mg, 0.68 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (22.0 mg, 15.2%). ^1H NMR (400 MHz, $DMSO-d_6$) δ 7.94 (d, $J = 9.9$ Hz, 2H), 7.21 (d, $J = 8.8$ Hz, 1H), 7.16 – 7.07 (m, 2H), 7.03 – 6.95 (m, 2H), 6.93 – 6.85 (m, 2H), 6.37 (d, $J = 9.5$ Hz, 1H), 3.61 (d, $J = 12.3$ Hz, 2H), 2.59 (dd, $J = 12.3, 2.5$ Hz, 2H), 2.43 – 2.39 (m, 1H), 1.85 (d, $J = 12.7$ Hz, 2H), 1.54 (qd, $J = 12.5, 4.1$ Hz, 2H). Mass (m/z): 389.3 $[M+H]^+$.

Compound 124

3-(2-aminoethyl)-7-((4-(tert-butyl)phenyl)amino)-2H-chromen-2-one



Step 1. Preparation of 5-bromo-2-formylphenyl 4-((tert-butoxycarbonyl)amino)butanoate (124-2)

To a solution of 4-bromo-2-hydroxybenzaldehyde (3.5 g, 17.4 mmol) in DCM (50 mL) was added 4-((tert-butoxycarbonyl)amino)butanoic acid (4.24g, 20.9 mmol), DIC (2.85 g, 22.6 mmol) and DMAP (637 mg, 5.22mmol). Then the mixture was stirred at room temperature overnight. The mixture was diluted with water and extracted by DCM (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 2.1 g as yellow solid. Mass (m/z): 386.3 [M+H]⁺.

Step 2. Preparation of tert-butyl (2-(7-bromo-2-oxo-2H-chromen-3-yl)ethyl)carbamate (124-3)

To a solution of 5-bromo-2-formylphenyl 4-((tert-butoxycarbonyl)amino)butanoate (2.1 g, 5.44 mmol) in DCE (20 mL) was added TEA (1.1 g, 10.9 mmol), the mixture was reflux for 3 hours. Then it was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 300 mg as white solid. Mass (m/z): 369.3[M+H]⁺.

Step 3. Preparation of Preparation of tert-butyl (2-(7-((4-(tert-butyl)phenyl)amino)-2-oxo-2H-chromen-3-yl)ethyl)carbamate (124-4)

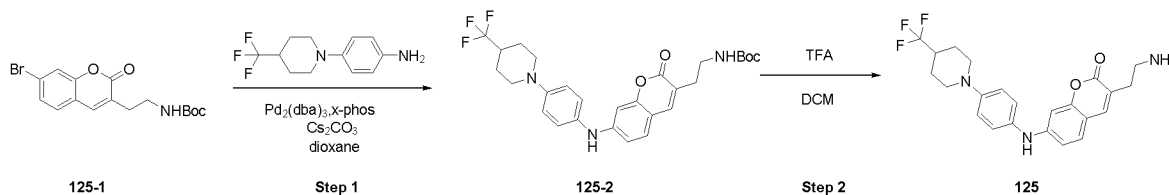
To a solution of tert-butyl (2-(7-bromo-2-oxo-2H-chromen-3-yl)ethyl)carbamate (100 mg, 0.272 mmol) and 4-(tert-butyl)aniline (57 mg, 0.326 mmol) in dioxane (5 mL) was added Pd₂(dba)₃ (2.5 mg, 0.00272 mmol), X-phos (6.5 mg, 0.0136 mmol) and Cs₂CO₃ (133 mg, 0.408 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by TLC to give the desired product as yellow solid 50 mg. Mass (m/z): 437.6 [M+H]⁺.

Step 4. Preparation of 3-(2-aminoethyl)-7-((4-(tert-butyl)phenyl)amino)-2H-chromen-2-one (124)

To a solution of tert-butyl(2-(7-((4-(tert-butyl)phenyl)amino)-2-oxo-2H-chromen-3-yl)ethyl)carbamate (50 mg, 0.114 mmol) in DCM (9 mL) was added 2,2,2-trifluoroacetic acid (3 mL). Then the mixture was concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (12.5 mg, 32.9%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.81 (s, 1H), 8.32 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.15 – 7.07 (m, 2H), 6.91 (dd, J = 8.8, 2.3 Hz, 1H), 6.80 (d, J = 2.3 Hz, 1H), 6.00 (s, 1H), 2.94 – 2.79 (m, 4H), 1.25 (s, 9H). Mass (m/z): 337.2 [M+H]⁺.

Compound 125

3-(2-aminoethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one



Step 1. Preparation of

tert-butyl(2-(2-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-3-yl)ethyl)carbamate (125-2)

To a solution of tert-butyl (2-(7-bromo-2-oxo-2H-chromen

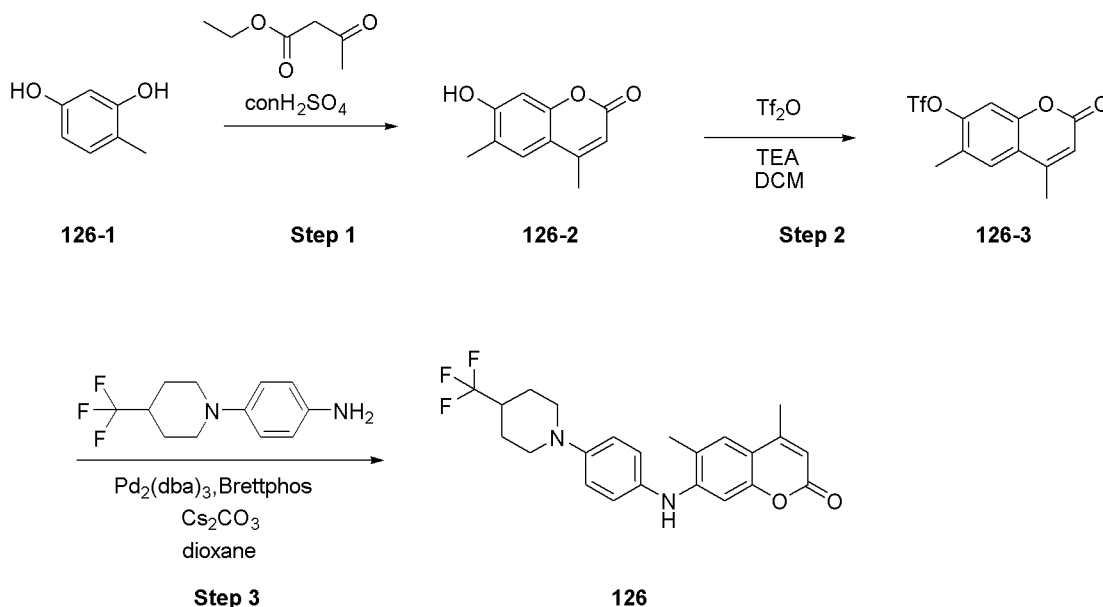
-3-yl)ethyl)carbamate (85 mg, 0.231 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (67.6 mg, 0.277 mmol) in DMF (5 mL) was added Pd₂(dba)₃ (2.5 mg, 0.00272 mmol), X-phos (6.6 mg, 0.0139 mmol) and Cs₂CO₃ (135 mg, 0.416 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by TLC to give the desired product as yellow solid (40 mg). Mass (m/z): 532.6 [M+H]⁺.

Step 2. Preparation of 3-(2-aminoethyl)-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one (**125**)

To a solution of tert-butyl(2-(2-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-3-yl)ethyl)carbamate (40 mg, 0.0752 mmol) in DCM (9 mL) was added 2,2,2-trifluoroacetic acid (3 mL). Then the mixture was concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (5 mg, 15.6%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.56 (s, 1H), 8.34 (s, 1H), 7.65 (s, 1H), 7.36 (d, J = 8.7 Hz, 1H), 7.05 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 9.0 Hz, 2H), 6.78 (dd, J = 8.6, 2.2 Hz, 1H), 6.65 (d, J = 2.2 Hz, 1H), 3.68 (dd, J = 12.1, 3.1 Hz, 3H), 2.86 (t, J = 7.0 Hz, 2H), 2.77 – 2.51 (m, 7H), 1.86 (d, J = 13.0 Hz, 3H), 1.55 (td, J = 12.5, 4.1 Hz, 2H). Mass (m/z): 432.2 [M+H]⁺.

Compound 126

4,6-dimethyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one



Step 1. Preparation of 7-hydroxy-4,6-dimethyl-2H-chromen-2-one

To a solution of 4-methylbenzene-1,3-diol (2.0 g, 16.1 mmol) in ethyl 3-oxobutanoate (3 mL) was added con.H₂SO₄ (5 mL) at 0°C. Then the mixture was stirred at 0°C for 5 hours. The mixture was filtered and washed with water till PH to 7-8 and dried to give the desired product 1.1 g as grey solid. Mass (m/z): 191.2 [M+H]⁺.

Step 2. Preparation of 4,6-dimethyl-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate

To a solution of 7-hydroxy-4,6-dimethyl-2H-chromen-2-one (200 mg, 1.05 mmol) in DCM (10 mL) was added trifluoromethanesulfonic anhydride (356 mg, 1.26 mmol) and TEA (159 mg, 1.58 mmol) at 0°C. Then the mixture was stirred at room temperature for 3 hours. The mixture was diluted with water and extracted by DCM (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product which was purified by Column chromatography to give the desired product 200mg as yellow solid. Mass (m/z): 323.3 [M+H]⁺.

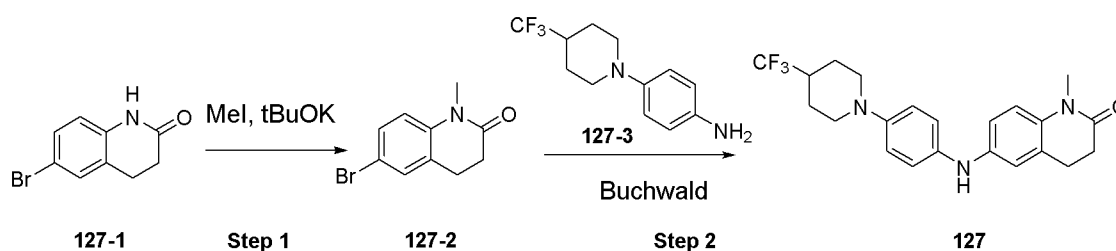
Step 3. Preparation of 4,6-dimethyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-chromen-2-one (126)

To a solution of 4,6-dimethyl-2-oxo-2H-chromen-7-yl trifluoromethanesulfonate (87 mg, 0.270 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (87 mg, 0.270 mmol) was added Pd₂(dba)₃, Brettphos, Cs₂CO₃ and dioxane. The mixture was stirred at 100°C for 24 hours. The mixture was filtered and washed with water till PH to 7-8 and dried to give the desired product 126 as yellow solid. Mass (m/z): 454.3 [M+H]⁺.

piperidin-1-yl)aniline (60 mg, 0.246mmol) in dioxane (3 mL) was added Pd₂(dba)₃ (11.3 mg, 0.0123 mmol), Brettphos (13.2 mg, 0.0246 mmol) and Cs₂CO₃ (120 mg, 0.369mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as yellow solid (34.5 mg, 33.8%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.62 (s, 1H), 7.45 (s, 1H), 7.17 – 7.08 (m, 2H), 7.06 – 6.92 (m, 2H), 6.57 (s, 1H), 5.98 (d, J = 1.3 Hz, 1H), 3.75 (d, J = 12.4 Hz, 2H), 2.72 (dd, J = 12.3, 2.5 Hz, 2H), 2.35 (d, J = 1.2 Hz, 3H), 2.29 (s, 3H), 1.96 – 1.83 (m, 2H), 1.58 (qd, J = 12.5, 4.0 Hz, 2H). Mass (m/z): 417.4 [M+H]⁺.

Compound 127

1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinolin-2(1H)-one



Step 1. Preparation of 6-bromo-1-methyl-3,4-dihydroquinolin-2(1H)-one (127-2)

To a solution of 6-bromo-3,4-dihydroquinolin-2(1H)-one 127-1 (500 mg, 2.21 mmol) and t-BuOK (496 mg, 4.42 mmol) in DMF (10 mL) was added MeI (408 mg, 2.88 mmol). Then the mixture was stirred at room temperature for overnight. The mixture was poured into H₂O and extracted with EA (30 mL*3). The organic layer was washed with brine, dried over Na₂SO₄, filtered and concentrated, the residue was purified by silica gel chromatography with EA/PE (20:1 to 5:1) to give 6-bromo-1-methyl-3,4-dihydroquinolin-2(1H)-one 127-2 (493 mg, 93% yield) as a yellow solid. MS (ESI) m/z 239.8, 241.8 [M+H]⁺.

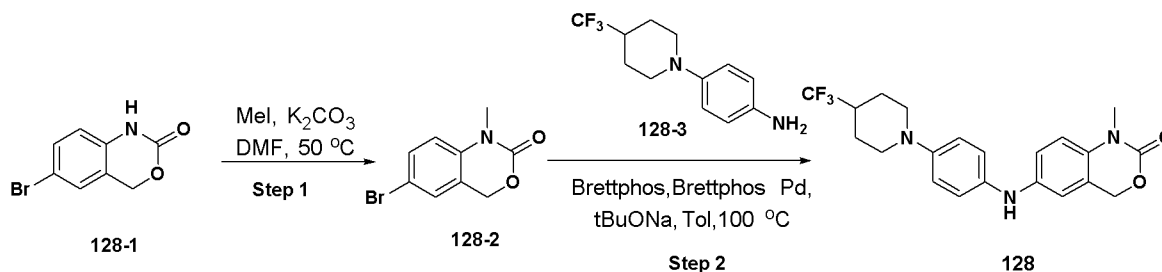
Step 2. Preparation of 1-methyl-6-((4-(4-(trifluoromethyl) piperidin-1-yl)

phenyl)amino)-3,4-dihydroquinolin-2(1H)-one (**127**)

A mixture solution of 4-(4-(trifluoromethyl)piperidin-1-yl)aniline **127-3** (300 mg, 1.23 mmol), 6-bromo-1-methyl-3,4-dihydroquinolin-2(1H)-one **127-2** (295 mg, 1.23 mmol), Ruphos (115 mg, 0.25 mmol), Pd₂(dba)₃ (112 mg, 0.12 mmol) and Cs₂CO₃ (600 mg, 1.84 mmol) in 1,4-dioxane (10 mL) was stirred at 100°C under N₂ atmosphere for 12 hrs. The mixture was concentrated and the residue was purified by pre-HPLC to give compound **127** as a yellow solid (25.3 mg, 5%). Mass (m/z): 404.2 [M+H]⁺. ¹H NMR (400 MHz, CD₃OD) δ 6.98 (d, J = 9.0 Hz, 2H), 6.92 (dd, J = 8.8, 4.2 Hz, 3H), 6.89 – 6.84 (m, 1H), 6.81 (d, J = 2.5 Hz, 1H), 3.57 (dd, J = 13.1, 0.6 Hz, 2H), 3.28 (s, 3H), 2.78 (dd, J = 8.5, 6.2 Hz, 2H), 2.63 (td, J = 12.2, 1.7 Hz, 2H), 2.54 (dd, J = 8.5, 6.2 Hz, 2H), 2.33 – 2.15 (m, 1H), 1.99 – 1.89 (m, 2H), 1.77-1.64 (m, 2H).

Compound 128

1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one



Step 1. Preparation of 6-bromo-1-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one (128-2**)**

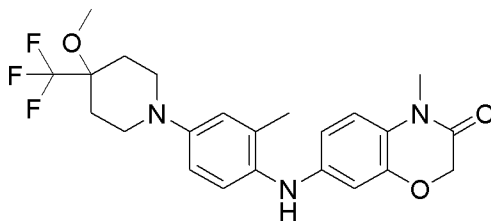
To a solution of compound **128-1** (300 mg, 1.316 mmol) in DMF (10 mL) was added K₂CO₃ (363.63 mg, 2.631 mmol) and MeI (280 mg, 1.973 mmol) at 50°C. Then the mixture was stirred at 50°C for 16 hrs. After cooling to rt, the reaction solution was washed with water, extracted with ethyl acetate (20 mL*3). The organic layers were combined and concentrated under vacuum, the residue was purified through silica gel chromatography (PE:EA=5:1) to give 6-bromo-1-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one as white solid (150 mg, 37.68%). Mass (m/z): 377.3 [M+H]⁺.

Step 2. Preparation of 1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one (**128**)

A mixture of 6-bromo-1-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one (150 mg, 0.6197 mmol), 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (151.37 mg, 0.6197 mmol), NaOtBu (119.11 mg, 1.2394 mmol), Brettphos (33.26 mg, 0.062 mmol), Brettphos-Pd-G1 (49.44 mg, 0.062 mmol) in toluene (10 mL) was stirred 10 hrs at 100 °C under N₂ atmosphere. After cooling to rt, the reaction solution was washed with water, extracted with ethyl acetate (20 mL*3), the organic layers were combined and concentrated under vacuum, the residue was purified by prep-HPLC(column-Xbridge-C18 150 x 21.2 mm, 5 um; Mobile phase: ACN-H₂O (0.1%FA), 30%-35%) to afford compound 128 as yellow solid. (12.2 mg, 4.71%). Mass (m/z): 406 [M+H]⁺. ¹H NMR (400 MHz, CD₃OD) δ 7.07 – 6.93 (m, 6H), 6.86 (d, *J* = 2.1 Hz, 1H), 5.17 (s, 2H), 3.63 (d, *J* = 12.2 Hz, 2H), 3.34 (s, 3H), 2.68 (td, *J* = 12.3, 2.2 Hz, 2H), 2.34 – 2.25 (m, 1H), 1.99 (d, *J* = 13.3 Hz, 2H), 1.79 – 1.69 (m, 2H).

Compound 129

7-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

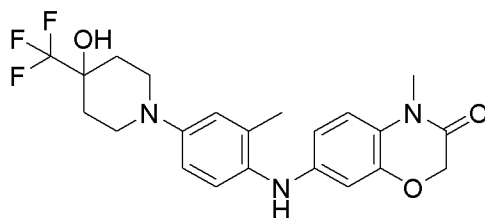


To a solution of 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (138 mg, 0.57 mmol) and 4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylaniline (150 mg, 0.52 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (47 mg, 0.05 mmol), Xphos (49 mg, 0.10 mmol) and Cs₂CO₃ (339 mg, 1.04 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (57.9 mg, 29.1%) as a red solid. Mass

(m/z): 450.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.21 (s, 1H), 7.07 – 6.86 (m, 4H), 6.83 – 6.75 (m, 1H), 6.39 – 6.32 (m, 1H), 6.27 (d, *J* = 2.5 Hz, 1H), 4.54 (s, 2H), 3.58 – 3.50 (m, 2H), 3.40 (s, 3H), 3.20 (s, 3H), 2.92 – 2.73 (m, 2H), 2.49 – 2.44 (m, 1H), 2.12 (s, 3H), 2.06 – 1.95 (m, 2H), 1.88 – 1.76 (m, 2H).

Compound 130

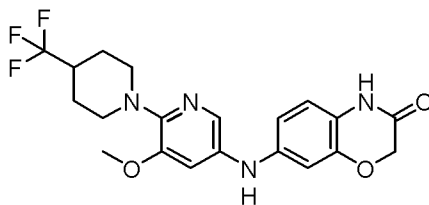
7-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one (48 mg, 0.20 mmol) and 1-(4-amino-3-methylphenyl)-4-(trifluoromethyl)piperidin-4-ol (50 mg, 0.18 mmol) in 1,4-dioxane (1 mL) was added Pd₂(dba)₃ (17 mg, 0.02 mmol), Xphos (17 mg, 0.04 mmol) and Cs₂CO₃ (119 mg, 0.36 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-4-methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one (20.5 mg, 29.4%) as a pink solid. Mass (m/z): 436.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.20 (s, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 2.8 Hz, 1H), 6.82 – 6.74 (m, 1H), 6.39 – 6.31 (m, 1H), 6.27 (d, *J* = 2.4 Hz, 1H), 5.95 (s, 1H), 4.53 (s, 2H), 3.57 – 3.50 (m, 2H), 3.20 (s, 3H), 3.01 – 2.81 (m, 2H), 2.12 (s, 3H), 1.85 – 1.68 (m, 4H).

Compound 131

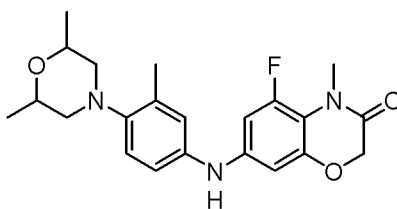
7-((5-methoxy-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (66 mg, 0.291 mmol) and 5-methoxy-6-(4-(trifluoromethyl) piperidin-1-yl) pyridin-3-amine (80 mg, 0.291 mmol) in t-BuOH (5 mL) was added
 5 Pd₂(dba)₃ (13.3 mg, 0.0146 mmol), Brettphos (15.6 mg, 0.0291 mmol) and Cs₂CO₃ (142 mg, 0.437mmol) under nitrogen atmosphere. Then the mixture was stirred at 100°C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude
 10 product, which was purified by pre-HPLC to give the desired product as pink solid (51.9 mg, 42.3%). ¹H NMR (400 MHz, DMSO) δ 10.50 (s, 1H), 7.87 (s, 1H), 7.59 (d, J = 2.2 Hz, 1H), 6.95 (t, J = 9.7 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 6.62 – 6.57 (m, 1H), 6.55 (d, J = 2.3 Hz, 1H), 4.50 (s, 2H), 3.85 – 3.68 (m, 5H), 2.73 – 2.56 (m, 2H), 2.43 (s, 1H), 1.84 (d, J = 11.0
 15 Hz, 2H), 1.56 (qd, J = 12.5, 3.9 Hz, 2H). Mass(m/z): 423.2 [M+H]⁺.

Compound 132

7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-5-fluoro-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

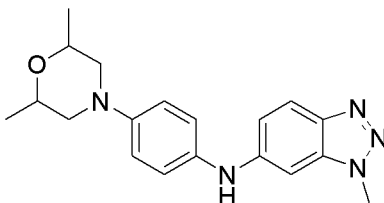


To a solution of 7-bromo-5-fluoro-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (70.7 mg, 0.273 mmol) and 4-(2,6-dimethylmorpholino)-3-methylaniline (60 mg, 0.273 mmol) in t-BuOH (5 mL) was added Pd₂(dba)₃ (12.5 mg, 0.0136 mmol), X-phos (13 mg, 0.0273 mmol) and Cs₂CO₃ (133 mg, 0.41mmol) under a nitrogen
 20 atmosphere. Then the mixture was stirred at 100°C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers

were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as a pink solid (12.6 mg, 11.6%). ¹H NMR (400 MHz, DMSO) δ 8.17 (s, 1H), 6.96 (d, J = 9.4 Hz, 1H), 6.89 (d, J = 7.0 Hz, 2H), 6.55 – 6.37 (m, 2H), 4.56 (s, 2H), 3.77 – 3.66 (m, 2H), 3.30 (d, J = 5.5 Hz, 2H), 2.87 (d, J = 10.8 Hz, 2H), 2.37 – 2.24 (m, 3H), 2.22 (s, 3H), 1.12 (dd, J = 14.3, 10.1 Hz, 6H). Mass(m/z): 400.2 [M+H]⁺.

Compound 133

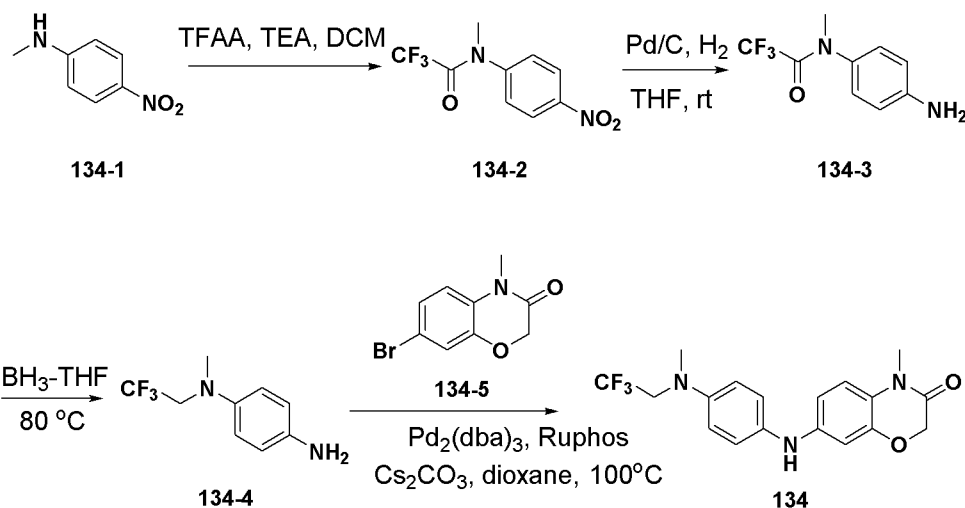
N-(4-(2,6-dimethylmorpholino)phenyl)-1-methyl-1H-benzo[d][1,2,3]triazol-6-amine



To a solution of 4-(2,6-dimethylmorpholin-4-yl) aniline (107 mg, 0.52 mmol), 6-bromo-1-methyl-1,2,3-benzotriazole (121 mg, 0.57 mmol) and t-BuONa (100 mg, 1.1 mmol) in toluene (2 mL) was added BrettPhos Pd G3 (47 mg, 0.052 mmol). The mixture was heated to 100°C and stirred under nitrogen for 18 h. The resulting mixture was concentrated and the residue was purified by column chromatography (EA:PE = 1:1) to give the product (27.5 mg, 15.56%) as a white solid. MS (ESI) m/z: 338 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.28 (s, 1H), 7.72 (d, J = 9.2 Hz, 1H), 7.14 (d, J = 9.2 Hz, 2H), 6.98 - 6.94 (m, 4H), 4.09 (s, 2H), 3.72 - 3.68 (m, 2H), 3.51 (d, J = 10.4 Hz, 2H), 2.25-2.20 (m, 2H), 1.15 (d, J = 6.4 Hz, 6H).

Compound 134

1-hydroxy-5-oxo-*N*-(4-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzyl)pyrrolidine-3-carboxamide



Step 1. Preparation of 2,2,2-trifluoro-N-methyl-N-(4-nitrophenyl)acetamide (**134-2**)

A mixture solution of N-methyl-4-nitroaniline (1 g, 6.58 mmol),
 5 Trifluoroacetic anhydride (TFAA, 1.52 g, 7.24 mmol), TEA (1.33 g, 13.16 mmol) in DCM (20 mL) was stirred at 25°C for 12 hrs. The mixture was concentrated and the residue was purified by flash chromatography, eluting with PE : EA = 10:1 to 1 : 1 to give 2,2,2-trifluoro-N-methyl-N-(4-nitrophenyl)acetamide as a yellow oil (1.5 g,
 10 91.2%). Mass (m/z): 249.1 [M+H]⁺.

Step 2. Preparation of N-(4-aminophenyl)-2,2,2-trifluoro-N-methylacetamide (**134-3**)

A mixture solution of 2,2,2-trifluoro-N-methyl-N-(4-nitrophenyl)acetamide **134-2** (1.5 g, 6.05 mmol), Pd/C (0.4 g) in THF (20 mL) was
 15 stirred under 1 atm of H₂ atmosphere at 25°C for 2 hrs. After filtration, the filtrate was removed under vacuum and the residue was purified by flash, eluting with PE : EA = 10:1 to 1 : 1 to give N-(4-aminophenyl)-2,2,2-trifluoro-N-methylacetamide **134-3** as yellow solid. (1.2 g, 91.7%). Mass (m/z): 218.07 [M+H]⁺.

20 **Step 3.** Preparation of N¹-methyl-N¹-(2,2,2-trifluoroethyl)benzene-1,4-diamine (417-4):

A solution of N-(4-aminophenyl)-2,2,2-trifluoro-N-methylacetamide **134-3** (0.5 g, 2.29 mmol) in BH₃-THF (5 mL, 1.0 mol/L) and THF (2 mL) was

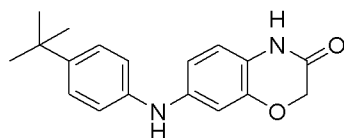
stirred at 80°C for 12 hrs. Quenched with MeOH (30 mL), concentrated, to the residue was added H₂O (30 mL), extracted with EA (20 mL*3), the organic phase was concentrated under vacuum, the residue was purified by flash, eluting with PE : EA = 10:1 to 1 : 1 to give N¹-methyl-N¹-(2,2,2-trifluoroethyl)benzene-1,4-diamine **134-4** as yellow solid. (0.16 g, 34.1%). Mass (m/z): 205.0 [M+H]⁺.

Step 4. Preparation of 1-hydroxy-5-oxo-N-(4-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzyl)pyrrolidine-3-carboxamide (**134**)

A mixture solution of N¹-methyl-N¹-(2,2,2-trifluoroethyl)benzene-1,4-diamine **134-4** (0.16 g, 0.78 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (**134-5**) (0.2 g, 0.83 mmol), Ruphos (73 mg, 0.16 mmol), Pd₂(dba)₃ (72 mg, 0.08 mmol) and Cs₂CO₃ (0.76 g, 2.34 mmol) in 1,4-dioxane (10 mL) was stirred at 100°C under N₂ atmosphere for 12 hrs. The mixture was concentrated and the residue was purified by prep-HPLC to give compound **134** as a yellow solid (0.134 g, 47.1%). Mass (m/z): 365.7 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.72 (s, 1H), 6.96 (t, *J* = 8.6 Hz, 3H), 6.81 (d, *J* = 8.0 Hz, 2H), 6.57 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.49 (d, *J* = 2.4 Hz, 1H), 4.55 (s, 2H), 4.13 (q, *J* = 9.6 Hz, 2H), 3.22 (s, 3H), 2.96 (s, 3H).

Compound 135

7-((4-(*tert*-butyl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

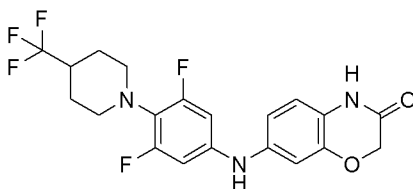


To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (333 mg, 1.48 mmol) and 4-(*tert*-butyl)aniline (60 mg, 0.26 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (122 mg, 0.13 mmol), Brettphos (144 mg, 0.26 mmol) and Cs₂CO₃ (875 mg, 2.68 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((4-(*tert*-butyl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (32 mg, 31%) as a yellow solid. Mass (m/z): 297.3 [M+H]⁺. ¹H NMR (400

MHz, DMSO) δ 10.50 (s, 1H), 7.93 (s, 1H), 7.27 – 7.19 (m, 2H), 6.98 – 6.90 (m, 2H), 6.75 (d, $J = 8.4$ Hz, 1H), 6.65 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.60 (d, $J = 2.3$ Hz, 1H), 4.50 (s, 2H), 1.24 (s, 9H).

Compound 136

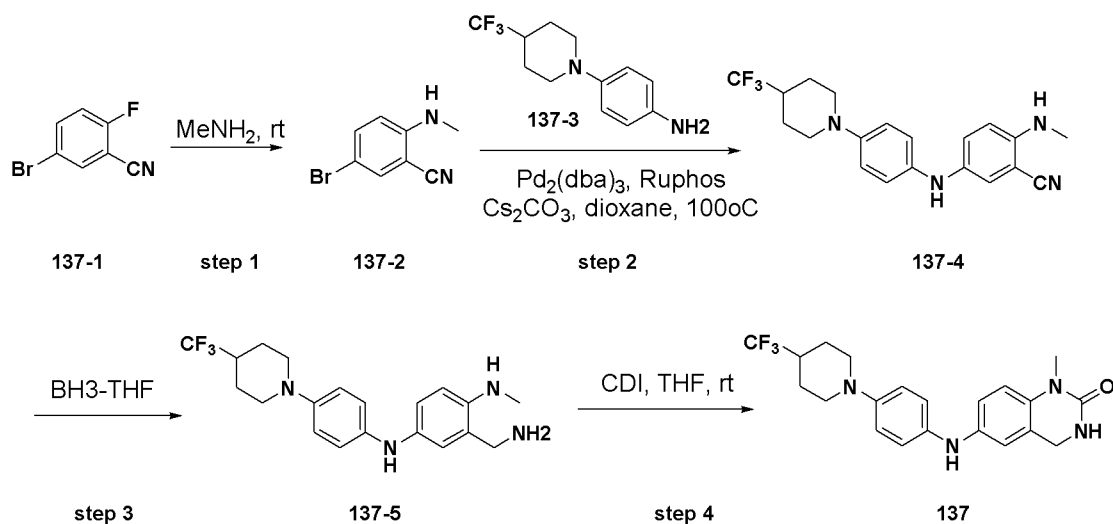
5 7-((3,5-difluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-
-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (151 mg, 0.67 mmol) and 3,5-difluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline
10 (170 mg, 0.61 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (55 mg, 0.06 mmol), Brettphos (65 mg, 0.12 mmol) and Cs_2CO_3 (396 mg, 1.21 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((3,5-difluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (28 mg, 10.8%) as a white
15 solid. Mass (m/z): 428.3 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.61 (s, 1H), 8.31 (s, 1H), 6.82 (d, $J = 8.4$ Hz, 1H), 6.71 (dd, $J = 8.4, 2.3$ Hz, 1H), 6.66 (d, $J = 2.4$ Hz, 1H), 6.58 – 6.46 (m, 2H), 4.54 (s, 2H), 3.11 – 2.92 (m, 4H), 2.49 – 2.35 (m, 1H), 1.88 – 1.79 (m, 2H), 1.61 –
20 1.46 (m, 2H).

Compound 137

1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinazolin-2(1H)-one



Step 1. Preparation of 5-bromo-2-(methylamino)benzonitrile (**137-2**)

A mixture solution of 5-bromo-2-fluorobenzonitrile (5 g, 25mmol) in MeNH₂ in MeOH (1 mol/L, 50 mL) was stirred at r.t. 2 hrs. Then the solvent was removed under reduced pressure, the residue was diluted with EA (50 mL), washed with water (50 mL x 3), dried with Na₂SO₄, filtered and evaporated. The residue was purified by column chromatography to give 5-bromo-2-(methylamino)benzonitrile **137-2** (5 g, 94.76%).

Step 2. Preparation of 2-(methylamino)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzonitrile (**137-4**)

A mixture solution of 5-bromo-2-(methylamino)benzonitrile (200 mg, 0.95 mmol), 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (255 mg, 1.04 mmol), Cs₂CO₃ (926 mg, 2.84 mmol), Ruphos (88 mg, 0.19 mmol) and Pd₂(dba)₃ (87 mg, 0.09 mmol) in dioxane was stirred at 100°C for 16 hrs. Then the solvent was removed under vacuo, the residue was purified by silica gel column with PE:EA (3:1) to give 2-(methylamino)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzonitrile **137-4** (300 mg, 84.56%). Mass (m/z): 374.7 [M+H]⁺.

Step 3. Preparation of 2-(aminomethyl)-N¹-methyl-N⁴-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzene-1,4-diamine (**137-5**)

A solution of 2-(methylamino)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzonitrile (300 mg, 0.80 mmol) in BH₃ in THF (1M, 20 mL) was stirred at r.t. for 16 hrs. Then the solvent was removed under

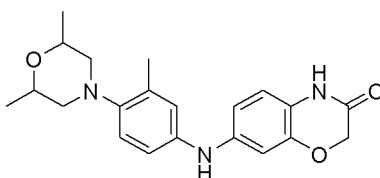
vacuo, the residue was diluted with EA (20 mL), washed with water (20 mL x 3), dried with Na₂SO₄, filtered and evaporated. The residue was purified by column chromatography to give **137-5** (300 mg, 98.93%). Mass (m/z): 378.8 [M+H]⁺.

5 **Step 4.** Preparation of 1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinazolin-2(1H)-one (**137**)

A solution of 2-(aminomethyl)-N¹-methyl-N4-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzene-1,4-diamine (300 mg, 0.79 mmol) and CDI (141 mg, 0.87 mmol) in THF was stirred at r.t. for 16 hrs. Then the solvent
10 was removed under vacuo, the residue was purified by prep-HPLC to give 1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinazolin-2(1H)-one compound **137** (90 mg, 28.07%). Mass (m/z): 404.7 [M+H]⁺. ¹H NMR (400 MHz, CD₃OD) δ 6.89 - 6.76 (m, 7H), 4.29 (s, 2H), 3.57 (s, 2H), 3.23 (s, 3H), 2.65 (s, 2H), 2.37 – 2.17 (m, 1H), 1.96 (d, *J*
15 = 12.1 Hz, 2H), 1.72 (dd, *J* = 12.6, 3.5 Hz, 2H).

Compound 138

7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



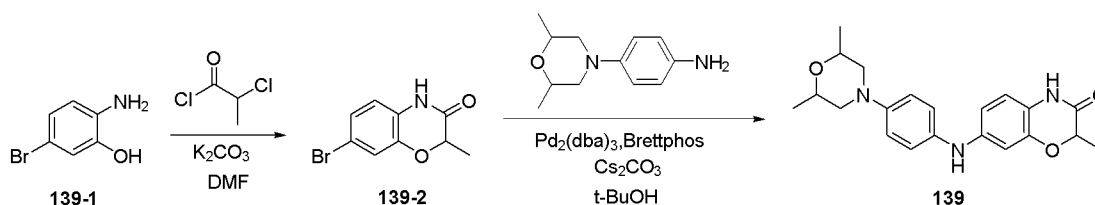
20 To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (114 mg, 0.500 mmol) and 4-(2,6-dimethylmorpholino)-3-methylaniline (100 mg, 0.455mmol) in t-BuOH (5 mL) was added Pd₂(dba)₃ (20.8 mg, 0.0228 mmol), Brettphos (24.4 mg, 0.0455 mmol) and Cs₂CO₃ (223 mg, 0.683mmol) under nitrogen atmosphere. Then the mixture was stirred at
25 100 °C for 2 hours. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as white solid (37.2 mg, 22.3%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.48 (s, 1H), 7.79 (s, 1H), 6.90 (d, *J* = 8.2

Hz, 1H), 6.85 – 6.76 (m, 2H), 6.73 (d, $J = 8.4$ Hz, 1H), 6.62 – 6.50 (m, 2H), 4.49 (s, 2H), 3.78 – 3.60 (m, 2H), 2.81 (t, $J = 16.9$ Hz, 2H), 2.37 – 2.22 (m, 2H), 2.20 (s, 3H), 1.10 (d, $J = 6.3$ Hz, 6H). Mass (m/z): 368.2 $[M+H]^+$.

5

Compound 139

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



Step 1. Preparation of 7-bromo-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (**139-2**)

10

To a solution of 2-amino-5-bromophenol (5.0 g, 26.6 mmol) in DMF (30 mL) was added K_2CO_3 (7.34 g, 53.2 mmol), 2-chloropropanoyl chloride (3.72 g, 29.3 mmol) was added at $0^\circ C$. Then the mixture was stirred at r.t. for 0.5 hour then heated at $90^\circ C$ for 2 hours. The mixture was filtered and washed with water, dried over Na_2SO_4 and concentrated to give the desired product 4.1 g as grey solid. Mass (m/z): 242.1 $[M+H]^+$.

15

Step 2. Preparation of 7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (**139**)

20

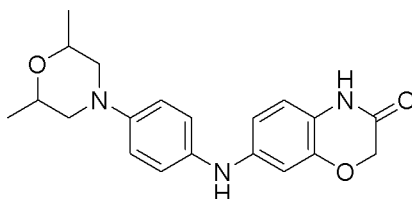
To a solution of 7-bromo-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (129 mg, 0.534 mmol) and 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.485 mmol) in t-BuOH (5 mL) was added $Pd_2(dba)_3$ (22.2 mg, 0.0243 mmol), Brettphos (26 mg, 0.0485 mmol) and Cs_2CO_3 (237 mg, 0.728 mmol) under nitrogen atmosphere. Then the mixture was stirred at $100^\circ C$ overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as gray solid (41.7 mg, 23.4%). ^1H NMR (400 MHz, $DMSO-d_6$) δ 10.45 (s, 1H), 7.69 (s, 1H), 6.90 (dd, $J = 29.6, 9.0$ Hz, 4H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.58 – 6.42 (m, 2H), 4.93 –

25

4.87 (m, 1H), 3.67 (tdd, $J = 25.5, 14.8, 10.7$ Hz, 2H), 3.43 (d, $J = 10.6$ Hz, 2H), 2.27 – 2.10 (m, 2H), 1.58 – 1.55 (m, 3H), 1.14 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 368.2 $[M+H]^+$.

Compound 140

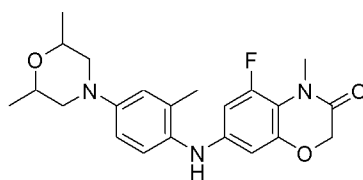
5 7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (110.2 mg, 0.485 mmol) and 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.485mmol) in t-BuOH (5 mL) was added $Pd_2(dba)_3$ (22.2 mg, 0.0243 mmol), Brettphos (26 mg, 0.0485 mmol) and Cs_2CO_3 (237 mg, 0.728mmol) under nitrogen atmosphere. Then the mixture was stirred at 100°C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as white solid (50 mg, 29.2%). ^1H NMR (400 MHz, $DMSO-d_6$) δ 10.45 (s, 1H), 7.69 (s, 1H), 6.90 (dd, $J = 29.6, 9.0$ Hz, 4H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.58 – 6.42 (m, 2H), 4.48 (s, 2H), 3.67 (tdd, $J = 25.5, 14.8, 10.7$ Hz, 2H), 3.43 (d, $J = 10.6$ Hz, 2H), 2.27 – 2.10 (m, 2H), 1.14 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 354.2 $[M+H]^+$.

Compound 141

((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-5-fluoro-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

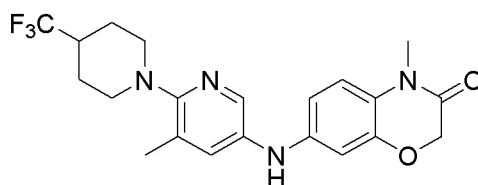


25 To a solution of 7-bromo-5-fluoro-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (90 mg, 0.347 mmol) and 4-(2,6-dimethylmorpholino)

-2-methylaniline (77 mg, 0.347mmol) in dioxane (5 mL) was added Pd₂(dba)₃ (16 mg, 0.0174 mmol), X-phos (16.6 mg, 0.0347 mmol) and Cs₂CO₃ (170 mg, 0.520mmol) under nitrogen atmosphere. Then the mixture was stirred at 100°C overnight. The mixture was extracted by EA
 5 (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as pink solid (45 mg, 32.6%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.55 (s, 1H), 6.99 (d, *J* = 8.6 Hz, 1H), 6.89 – 6.72 (m, 2H), 6.16 – 6.03 (m, 2H), 4.52 (s, 2H), 3.74 – 3.63 (m,
 10 2H), 3.53 (d, *J* = 10.6 Hz, 2H), 3.27 (d, *J* = 5.5 Hz, 3H), 2.23 (dd, *J* = 21.8, 10.8 Hz, 2H), 2.10 (d, *J* = 15.7 Hz, 3H), 1.15 (d, *J* = 6.2 Hz, 6H). Mass (m/z): 400.2 [M+H]⁺.

Compound 142

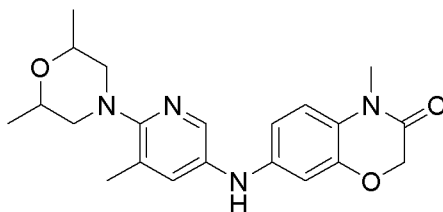
4-methyl-7-((5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one
 15



To a solution of 5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (100 mg, 0.39 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (112 mg, 0.46 mmol) in toluene (2 mL) was added
 20 tBuONa (74 mg, 0.77 mmol) and BrettPhos-Pd-G3 (35 mg, 0.038 mmol). The mixture was heated to 100°C and stirred under nitrogen overnight. The resulting mixture was concentrated and the residue was purified by prep-HPLC to give compound 425 as a light yellow solid (14 mg, 8.22 %). MS (ESI) m/z 421.0 [M+H]⁺. ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, *J* =
 25 2.4 Hz, 1H), 7.29 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 6.62 (s, 1H), 4.59 (s, 2H), 3.45 – 3.39 (m, 1H), 3.34 (s, 3H), 2.80 (t, *J* = 12.0 Hz, 2H), 2.26 (s, 2H), 2.23 - 2.16 (m, 1H), 1.99 - 1.96 (m, 4H), 1.80 - 1.70 (m, 2H).

Compound 143

7-((6-(2,6-dimethylmorpholino)-5-methylpyridin-3-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

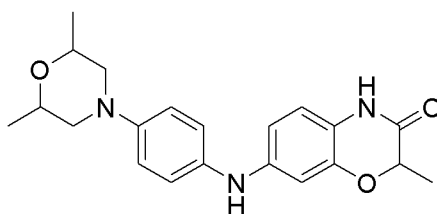


To a solution of 6-(2,6-dimethylmorpholino)-5-methylpyridin-3-amine (90 mg, 0.41 mmol), 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (118 mg, 0.49 mmol) in toluene (2 mL) was added t-BuONa (78 mg, 0.81 mmol) and BrettPhos-Pd-G3 (36.7 mg, 0.041 mmol). The mixture was heated to 100 °C and stirred under nitrogen overnight. The resulting mixture was concentrated and the residue was purified by prep-HPLC to give **143** (14.6 mg, 8.80 %) as a light yellow solid. MS (ESI) m/z 421.0 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 2.4 Hz, 1H), 7.25 (d, J = 2.4 Hz, 1H), 6.83 (d, J = 8.4 Hz, 1H), 6.64 - 6.58 (m, 2H), 4.58 (s, 2H), 3.88 - 3.80 (m, 2H), 3.33 (s, 3H), 3.17 (d, J = 12.0 Hz, 2H), 2.60 (t, J = 10.2 Hz, 2H), 2.27 (s, 3H), 1.23 (d, J = 6.4 Hz, 6H).

15

Compound 144

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

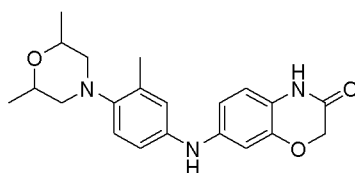


To a solution of 4-(2,6-dimethylmorpholin-4-yl)aniline (100 mg, 0.485 mmol), 7-bromo-2-methyl-2,4-dihydro-1,4-benzoxazin-3-one (129 mg, 0.533 mmol), and t-BuONa (93.2 mg, 0.970 mmol) in toluene (2 mL) was added BrettPhos-Pd-G3 (44.0 mg, 0.0484 mmol). The resulting solution was stirred for 16h at 100 °C under nitrogen atmosphere. The solution was diluted with water (20 mL) and EA (20 mL), then filtered through celite. The aqueous layer was extracted with EA (3 x 20 mL). The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4 , filtered,

and concentrated under reduced pressure. The residue was purified by pre-TLC (PE/EA=2/1) to provide compound 426 (28.2 mg, 15.43% yield) as a light yellow solid. MS (ESI) m/z 368.0 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 7.68 (s, 1H), 6.98 – 6.83 (m, 4H), 6.70 (d, J = 8.4 Hz, 1H), 6.57 - 6.45 (m, 2H), 4.56 (q, J = 6.8 Hz, 1H), 3.73 - 3.64 (m, 2H), 3.43 (d, J = 11.1 Hz, 2H), 2.18 (t, J = 10.9 Hz, 2H), 1.38 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 6.2 Hz, 6H).

Compound 145

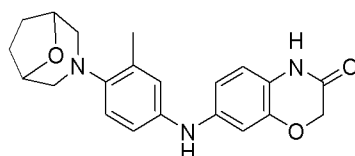
7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (154 mg, 0.57 mmol) and 4-(2,6-dimethylmorpholino)-3-methylaniline (115 mg, 0.52 mmol) in 1,4-dioxane (2 mL) was added $Pd_2(dba)_3$ (48 mg, 0.05 mmol), Brettphos (56 mg, 0.10 mmol) and Cs_2CO_3 (341 mg, 1.04 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (54 mg, 28%) as an off-white solid. Mass (m/z): 368.4 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 10.48 (s, 1H), 7.79 (s, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.85 – 6.77 (m, 2H), 6.73 (d, J = 8.3 Hz, 1H), 6.63 – 6.53 (m, 2H), 4.49 (s, 2H), 3.77 – 3.65 (m, 2H), 2.87 – 2.79 (m, 2H), 2.32 – 2.22 (m, 2H), 2.20 (s, 3H), 1.10 (d, J = 6.2 Hz, 6H).

Compound 146

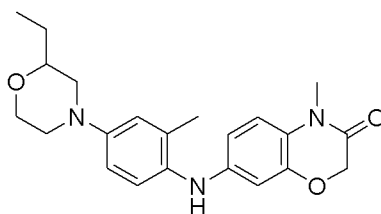
7-((4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-3-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (115 mg, 0.50 mmol) and 4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-3-methylaniline (100 mg, 0.46 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (42 mg, 0.05 mmol), Brettphos (49 mg, 0.09 mmol) and Cs₂CO₃ (299 mg, 0.92 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((4-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-3-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (23.5 mg, 14%) as a white solid. Mass (m/z): 366.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.47 (s, 1H), 7.79 (s, 1H), 6.99 – 6.92 (m, 1H), 6.84 – 6.78 (m, 2H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.63 – 6.54 (m, 2H), 4.49 (s, 2H), 4.30 (dt, *J* = 4.7, 2.2 Hz, 2H), 2.88 – 2.77 (m, 2H), 2.67 – 2.59 (m, 2H), 2.22 (s, 3H), 2.10 – 1.99 (m, 2H), 1.85 – 1.73 (m, 2H).

Compound 147

7-((4-(2-ethylmorpholino)-2-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

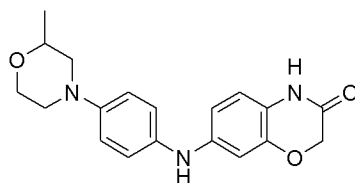


To a solution of 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (121 mg, 0.50 mmol) and 4-(2-ethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (42 mg, 0.05 mmol), Xphos (43 mg, 0.09 mmol) and Cs₂CO₃ (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC then purified by prep HPLC to give 7-((4-(2-ethylmorpholino)-2-methylphenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (62 mg, 35.7%) as a grey solid. Mass (m/z): 382.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO) δ 7.21 (s, 1H), 6.99 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 1H), 6.85 (d, *J* = 2.8 Hz, 1H), 6.76 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.34 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.26 (d, *J* = 2.5 Hz, 1H), 4.53 (s, 2H), 3.97 – 3.88 (m, 1H), 3.66 – 3.55 (m, 1H), 3.54 – 3.46 (m, 1H), 3.46

– 3.36 (m, 2H), 3.20 (s, 3H), 2.61 (td, $J = 11.8, 3.4$ Hz, 1H), 2.36 – 2.26 (m, 1H), 2.12 (s, 3H), 1.55 – 1.42 (m, 2H), 0.95 (t, $J = 7.5$ Hz, 3H).

Compound 148

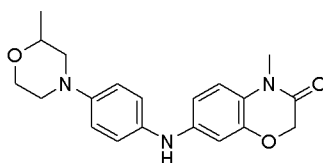
7-((4-(2-methylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (129 mg, 0.57 mmol) and 4-(2-methylmorpholino)aniline (100 mg, 0.52 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (47 mg, 0.05 mmol), Brettphos (56 mg, 0.10 mmol) and Cs_2CO_3 (339 mg, 1.04 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC then purified by flash chromatography to give 7-((4-(2-methylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (62 mg, 35%) as a light blue solid. Mass (m/z): 340.4 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.44 (s, 1H), 7.69 (s, 1H), 6.98 – 6.90 (m, 2H), 6.90 – 6.82 (m, 2H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.56 – 6.47 (m, 2H), 4.48 (s, 2H), 3.93 – 3.84 (m, 1H), 3.69 – 3.57 (m, 2H), 3.48 – 3.39 (m, 1H), 3.38 – 3.30 (m, 1H), 2.62 – 2.51 (m, 1H), 2.25 (dd, $J = 11.7, 10.1$ Hz, 1H), 1.14 (d, $J = 6.2$ Hz, 3H).

Compound 149

4-methyl-7-((4-(2-methylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

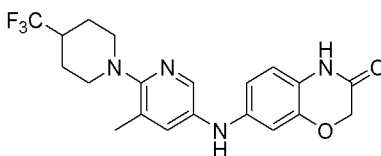


To a solution of 7-bromo-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one (138 mg, 0.57 mmol) and 4-(2-methylmorpholino)aniline (100 mg, 0.52 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (47 mg, 0.05 mmol), Xphos (49 mg, 0.10 mmol) and Cs_2CO_3 (339 mg, 1.04 mmol) under

nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC then purified by flash chromatography to give 4-methyl-7-((4-(2-methylmorpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (117 mg, 63%) as a light yellow solid. Mass (m/z): 354.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.80 (s, 1H), 7.01 – 6.93 (m, 3H), 6.92 – 6.84 (m, 2H), 6.61 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.53 (d, *J* = 2.4 Hz, 1H), 4.56 (s, 2H), 3.93 – 3.85 (m, 1H), 3.70 – 3.57 (m, 2H), 3.49 – 3.41 (m, 1H), 3.36 (d, *J* = 11.1 Hz, 1H), 3.22 (s, 3H), 2.63 – 2.52 (m, 1H), 2.31 – 2.21 (m, 1H), 1.14 (d, *J* = 6.2 Hz, 3H).

Compound 150

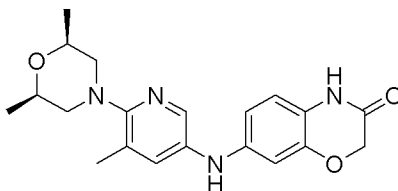
7-((5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of 5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (100 mg, 0.39 mmol) and 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (105 mg, 0.46 mmol) in toluene (2 mL) was added t-BuONa (74 mg, 0.77 mmol) and BrettPhos-Pd-G3 (35 mg, 0.039 mmol). The mixture was heated to 100 °C and stirred under nitrogen overnight. The resulting mixture was concentrated and the residue was purified by prep-HPLC to give compound **150** as a light yellow solid (12.2 mg, 7.74 %). MS (ESI) m/z 407.0 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.59 (s, 1H), 8.26 (s, 1H), 7.76 (s, 1H), 7.53 (s, 1H), 6.84 – 6.61 (m, 3H), 4.53 (s, 2H), 3.90 – 3.70 (m, 1H), 3.50 – 3.35 (m, 2H), 2.90 – 2.82 (m, 2H), 2.27 (s, 3H), 1.97 – 1.86 (m, 2H), 1.70 – 1.55 (m, 2H).

Compound 151

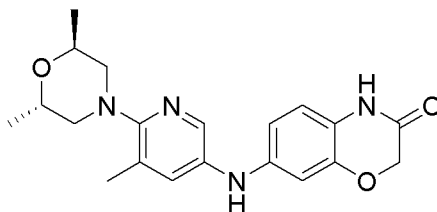
7-((6-(2,6-dimethylmorpholino)-5-methylpyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



To a solution of *cis*-6-(2,6-dimethylmorpholino)-5-methylpyridin-3-amine (90 mg, 0.41 mmol) and 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (112 mg, 0.49 mmol) in toluene (2 mL) was added tBuONa (78 mg, 0.81 mmol) and BrettPhos-Pd-G3 (37 mg, 0.041 mmol). The mixture was heated to 100 °C and stirred under nitrogen overnight. The resulting mixture was concentrated and the residue was purified by prep-HPLC to give **151** as a light yellow solid (8.6 mg, 5.54 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 7.88 (s, 1H), 7.86 (d, *J* = 2.8 Hz, 1H), 7.23 (d, *J* = 2.8 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.61 - 6.52 (m, 2H), 4.49 (s, 2H), 3.76 - 3.66 (m, 2H), 3.08 (d, *J* = 11.6 Hz, 2H), 2.40 - 2.34 (m, 2H), 2.20 (s, 3H), 1.09 (d, *J* = 2.4 Hz, 6H). MS (ESI) *m/z* 369.0 [M+H]⁺.

Compound 152

7-((6-(2,6-dimethylmorpholino)-5-methylpyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

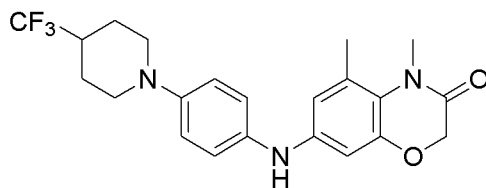


To a solution of *trans*-6-(2,6-dimethylmorpholino)-5-methylpyridin-3-amine (40 mg, 0.18 mmol) and 7-bromo-2H-benzo[b][1,4]oxazin-3(4H)-one (49 mg, 0.22 mmol) in toluene (2 mL) was added tBuONa (35 mg, 0.36 mmol) and BrettPhos-Pd-G3 (16 mg, 0.018 mmol). The mixture was heated to 100 °C and stirred under nitrogen overnight. The resulting mixture was concentrated and the residue was purified by prep-HPLC to give compound **152** as a light yellow solid (5.0mg, 3.32 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 7.88 (s, 1H), 7.86 (d, *J* = 2.8 Hz, 1H), 7.23 (d, *J* = 2.8 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.61 - 6.52 (m, 2H), 4.49 (s, 2H), 3.76 - 3.66 (m, 2H), 3.08 (d, *J* = 11.6 Hz, 2H), 2.40 -

2.34 (m, 2H), 2.20 (s, 3H), 1.09 (d, $J = 2.4$ Hz, 6H). MS (ESI) m/z 369.0 $[M+H]^+$.

Compound 153

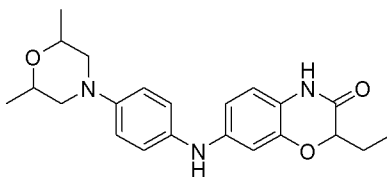
7-((5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



A solution of 7-bromo-4,5-dimethyl-2H-1,4-benzoxazin-3-one (100 mg, 0.35 mmol), 4-[4-(trifluoromethyl)piperidin-1-yl]aniline (86 mg, 0.35 mmol), t-BuONa (75 mg, 0.78 mmol) and BrettPhos-Pd-G3 (35.4 mg, 0.039 mmol) in toluene (2 mL) was heated to 100 °C and stirred under nitrogen for 18 hrs. The resulting mixture was concentrated under reduced pressure and the residue was purified by prep-HPLC (0.05% NH_3) to give compound **153** as a light yellow solid (9.0 mg, 10.93% yield). ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.04 (s, 1H), 7.13-7.08 (m, 3H), 7.14 – 7.06 (m, 3H), 6.96 (d, $J = 8.4$ Hz, 2H), 6.71 (dd, $J = 8.4, 2.0$ Hz, 1H), 6.63 (d, $J = 2.4$ Hz, 1H), 4.88 (t, $J = 5.6$ Hz, 1H), 4.56 (s, 2H), 3.90 (t, $J = 6.0$ Hz, 2H), 3.59 - 3.49 (m, 4H), 2.74 - 2.67 (m, 1H), 1.74 - 1.66 (m, 2H), 1.23 - 1.17 (m, 2H), 1.12 (d, $J = 6.4$ Hz, 6H). MS (ESI) m/z 397.0 $[M+H]^+$.

Compound 154

7-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-ethyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one

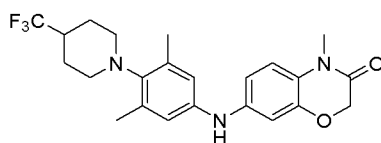


To a solution of 4-(2,6-dimethylmorpholin-4-yl)aniline (100 mg, 0.485 mmol), 7-bromo-2-methyl-2,4-dihydro-1,4-benzoxazin-3-one (137 mg, 0.533 mmol), and t-BuONa (93.2 mg, 0.970 mmol) in toluene (2 mL) was added BrettPhos-Pd-G3 (44.0 mg, 0.0484 mmol). The resulting solution

was stirred for 16 hrs at 100°C under nitrogen atmosphere. The solution was diluted with water (20 mL) and EA (20 mL), then filtered through celite. The aqueous layer was extracted with EA (3 x 20 mL). The organic layers were combined, washed with brine, dried over anhydrous Na₂SO₄,
 5 filtered, and concentrated under reduced pressure. The residue was purified by pre-TLC (PE/EA=2/1) to provide compound 436 (31.1 mg, 15.64% yield) as a light pink solid. MS (ESI) *m/z* 382.0 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.39 (s, 1H), 7.68 (s, 1H), 6.94 (d, *J* = 9.0 Hz, 2H), 6.87 (d, *J* = 9.0 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 1H), 6.54 – 6.48 (m, 2H),
 10 4.40 (dd, *J* = 7.9, 4.5 Hz, 1H), 3.72 – 3.65 (m, 2H), 3.43 (d, *J* = 10.5 Hz, 2H), 2.18 (t, *J* = 10.2 Hz, 2H), 1.80 – 1.68 (m, 2H), 1.14 (d, *J* = 6.2 Hz, 6H), 0.96 (t, *J* = 7.4 Hz, 3H).

Compound 155

7-((3,5-dimethyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-
 15 methyl-2H-benzo[*b*][1,4]oxazin-3(4H)-one

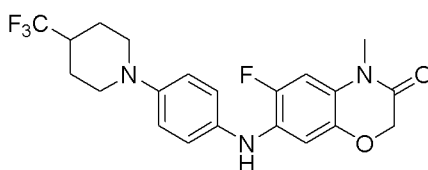


To a solution of 3,5-dimethyl-4-[4-(trifluoromethyl)piperidin-1-yl]aniline (100 mg, 0.367 mmol), 7-bromo-4-methyl-2H-1,4-benzoxazin-3-one (97.8 mg, 0.404 mmol), and t-BuONa (70.58 mg, 0.734 mmol) in toluene (2 mL)
 20 was added BrettPhos-Pd-G3 (33.3 mg, 0.0367 mmol). The resulting solution was stirred for 16h at 100°C under nitrogen atmosphere. The solution was diluted with water (20 mL) and EA (20 mL), then filtered through celite. The aqueous layer was extracted with EA (3 x 20 mL). The organic layers were combined, washed with brine, dried over anhydrous
 25 Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by prep-HPLC with CH₃CN/H₂O (0.05%NH₃) to provide compound **155** (8.7 mg, 5.42% yield) as a light pink solid. MS (ESI) *m/z* 434.0 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.89 (s, 1H), 7.00 (d, *J* = 8.7 Hz, 1H), 6.72 (dd, *J* = 8.8, 2.4 Hz, 2H), 6.61 (dd, *J* = 8.8, 2.4 Hz, 2H),
 30 4.58 (s, 2H), 3.23 (s, 3H), 3.15 (t, *J* = 10.8 Hz, 2H), 2.94 - 2.86 (m, 2H),

2.41 – 2.32 (m, 1H), 2.19 (d, $J = 10.5$ Hz, 6H), 1.84 - 1.77 (m, 2H), 1.60 - 1.49 (m, 2H).

Compound 156

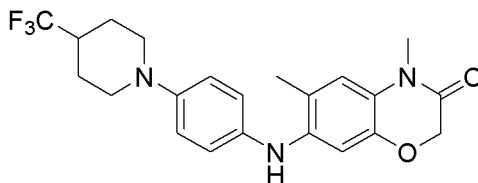
6-fluoro-4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-
2H-benzo[*b*][1,4]oxazin-3(4H)-one



The mixture of 7-bromo-6-fluoro-4-methyl-2H-1,4-benzoxazin-3-one (100 mg, 0.384 mmol), 4-[4-(trifluoromethyl)piperidin-1-yl]aniline (85 mg, 0.346 mmol), t-BuONa (74 mg, 0.769 mmol) and BrettPhos Pd G3 (35.4 mg, 0.039 mmol) in toluene (2 mL) was heated to 100°C and stirred for 18 h under nitrogen atmosphere. The resulting mixture was concentrated under reduced pressure and the residue was purified by column chromatography (EA:PE = 1:1) to give compound **156** (45.5 mg, 26.84% yield) as a white solid. Mass (m/z): 424 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 7.55 (s, 1H), 7.12 (d, $J = 12.4$ Hz, 1H), 6.94 - 6.88 (m, 4H), 6.67 (d, $J = 8.0$ Hz, 1H), 4.56 (s, 2H), 3.62 (d, $J = 12.4$ Hz, 2H), 3.23 (s, 3H), 2.65 - 2.62 (m, 2H), 2.45 - 2.39 (m, 1H), 1.92 - 1.83 (m, 2H), 1.63 - 1.50 (m, 2H).

Compound 157

4,6-dimethyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)cyclohexa-1,5-dien-1-yl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one

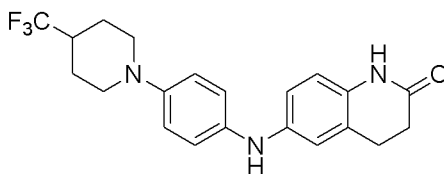


The mixture of 7-bromo-4,6-dimethyl-2H-1,4-benzoxazin-3-one (100 mg, 0.35 mmol), 4-[4-(trifluoromethyl)piperidin-1-yl]aniline (86 mg, 0.35 mmol), t-BuONa (75 mg, 0.78 mmol) and BrettPhos-Pd-G3 (35.4 mg, 0.039 mmol) in toluene (2 mL) was heated to 100°C and stirred under

nitrogen for 18 hrs. The resulting mixture was concentrated under reduced pressure and the residue was purified by column chromatography (EA:PE = 1:1) to give compound **157** (30 mg, 16.85% yield) as a white solid. Mass (m/z): 420 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.93 (d, *J* = 10.8 Hz, 2H), 6.86 - 6.81 (m, 4H), 6.52 (s, 1H), 4.49 (s, 2H), 3.57 (d, *J* = 12 Hz, 2H), 3.17 (s, 3H), 2.65 - 2.52 (m, 2H), 2.41 - 2.35 (m, 1H), 2.13 (s, 3H), 1.84 (d, *J* = 12 Hz, 2H), 1.58-1.45 (m, 2H).

Compound 158

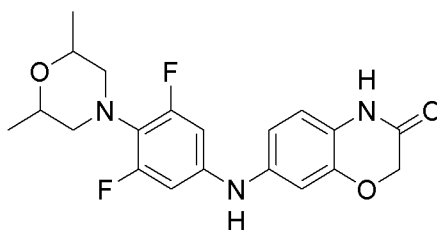
6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinolin-2(1H)-one



The mixture of compound 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (200 mg, 0.82 mmol), 6-bromo-3,4-dihydroquinolin-2(1H)-one (200 mg, 0.88 mmol), *t*-BuONa (250 mg, 2.60 mmol), and Brettphos-Pd-G3 (75 mg, 0.083 mmol) in toluene (10 mL) was heated to 100°C and stirred for six hours at N₂ atmosphere. TLC showed the reaction was completed. The resulting mixture was concentrated and the residue was purified through pre-TLC to give compound **158** (60 mg, 18.8% yield) as a white solid. MS (ESI) m/z 389.9 [M+H]⁺. ¹H NMR (400 MHz, CD₃OD) δ 9.85 (s, 1H), 7.58 (s, 1H), 7.00 - 6.65 (m, 7H), 3.57 (d, *J* = 10.4 Hz, 2H), 3.16 (d, *J* = 5.2 Hz, 1H), 2.82 - 2.72 (m, 2H), 2.70 - 2.54 (m, 2H), 2.42 - 2.35 (m, 2H), 1.92 - 1.82 (m, 2H), 1.65 - 1.50 (m, 2H).

Compound 159

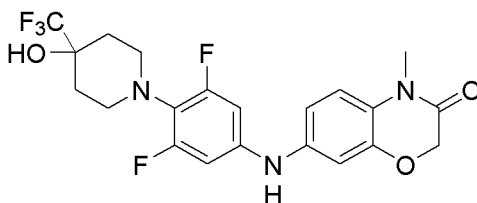
7-((4-(2,6-dimethylmorpholino)-3,5-difluorophenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **159** (60 mg, 29.3 %) as a white solid was prepared according to the procedure outlined for compound **1**. LC-MS (m/z) 390.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.61 (s, 1H), 8.31 (s, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.66 (d, *J* = 2.3 Hz, 1H), 6.58 – 6.46 (m, 2H), 4.54 (s, 2H), 3.65 (dtt, *J* = 8.7, 6.3, 3.7 Hz, 2H), 2.89 – 2.81 (m, 2H), 2.72 – 2.62 (m, 2H), 1.06 (d, *J* = 6.3 Hz, 6H).

Compound 160

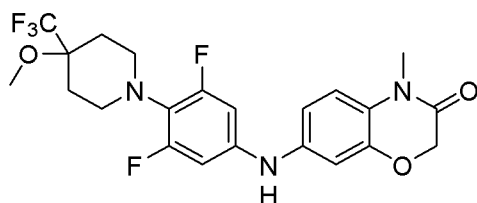
7-((3,5-difluoro-4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **160** (16.3 mg, 36%) as a white solid was prepared according to the procedure outlined for compound **1**. LC-MS (m/z) 458.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.41 (s, 1H), 7.08 (d, *J* = 8.7 Hz, 1H), 6.81 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.71 (d, *J* = 2.4 Hz, 1H), 6.62 – 6.51 (m, 2H), 5.91 (s, 1H), 4.63 (s, 2H), 3.29 (d, *J* = 12.8 Hz, 2H), 3.25 (s, 3H), 2.90 – 2.82 (m, 2H), 1.73 (dt, *J* = 22.4, 8.5 Hz, 4H).

Compound 161

7-((3,5-difluoro-4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

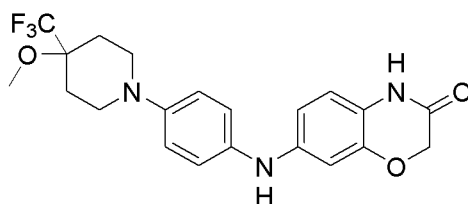


The titled compound **161** (80.6 mg, 30.2%) as a white solid was prepared

according to the procedure outlined for compound **1**. LC-MS (m/z) 472.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 8.41 (s, 1H), 7.08 (d, $J = 8.7$ Hz, 1H), 6.81 (dd, $J = 8.7, 2.4$ Hz, 1H), 6.71 (d, $J = 2.4$ Hz, 1H), 6.63 – 6.51 (m, 2H), 4.63 (s, 2H), 3.43 (s, 3H), 3.25 (s, 3H), 3.16 (t, $J = 11.7$ Hz, 2H), 2.95 – 2.87 (m, 2H), 1.97 (dt, $J = 14.0, 2.4$ Hz, 2H), 1.79 (td, $J = 13.0, 4.7$ Hz, 2H).

Compound 162

7-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
-2H-benzo[b][1,4]oxazin-3(4H)-one



10

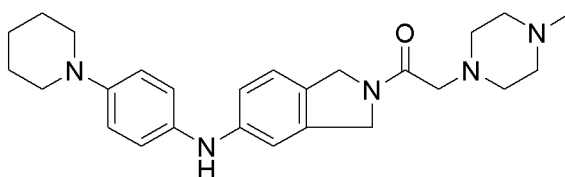
The titled compound **162** (6 mg, 2.2 %) as a saddle brown solid was prepared according to the procedure outlined for compound **1**. LC-MS (m/z) 422.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 10.45 (s, 1H), 7.71 (s, 1H), 6.97 – 6.87 (m, 4H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.58 – 6.48 (m, 2H), 4.48 (s, 2H), 3.45 (d, $J = 12.3$ Hz, 2H), 3.41 – 3.36 (m, 3H), 2.74 (td, $J = 12.4, 2.4$ Hz, 2H), 1.99 (dd, $J = 14.2, 2.6$ Hz, 2H), 1.83 (td, $J = 13.1, 4.5$ Hz, 2H).

15

Compound 163

2-(4-methylpiperazin-1-yl)-1-(5-((4-(piperidin-1-yl)phenyl)amino)
isoindolin-2-yl)ethan-1-one

20



The title compound **163** (16.8 mg) was prepared in a total yield of 78.0% as an orange solid from 4-(piperidin-1-yl)aniline (11.4 mg, 0.065 mmol), 1-(5-bromoisindolin-2-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one (16.9 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the

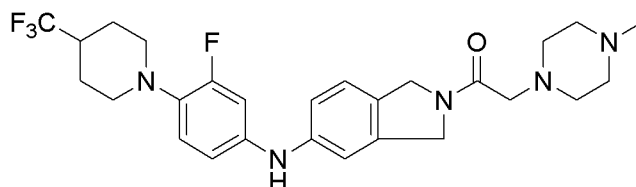
25

procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.08 - 6.96 (m, 3H), 6.94 - 6.83 (m, 4H), 4.70 (s, 2H), 4.56 (s, 2H), 3.24 (s, 2H), 3.08 - 2.86 (m, 4H), 2.76 - 2.54 (m, 8H), 2.34 (s, 3H), 1.73 - 1.64 (m, 4H), 1.57 - 1.48 (m, 2H). Mass (m/z): 434.3 $[\text{M}+\text{H}]^+$.

5

Compound 164

1-(5-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-2-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one

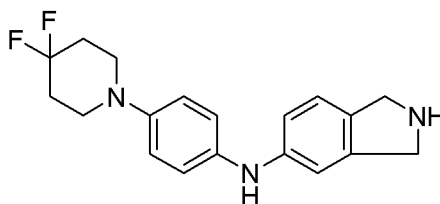


The title compound **164** (17.2 mg) was prepared in a total yield of 66.3% as an orange solid from 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (17.1 mg, 0.065 mmol), 1-(5-bromoisoindolin-2-yl)-2-(4-methylpiperazin-1-yl)ethan-1-one (16.9 mg, 0.05 mmol), $\text{Pd}_2(\text{dba})_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.18 - 7.10 (m, 1H), 7.00 - 6.91 (m, 3H), 6.84 - 6.75 (m, 2H), 4.81 (s, 2H), 4.65 (s, 2H), 3.39 - 3.32 (m, 4H), 2.86 - 2.58 (m, 10H), 2.25 (m, 1H), 1.98 - 1.89 (m, 2H), 1.79 - 1.66 (m, 2H). Mass (m/z): 520.3 $[\text{M}+\text{H}]^+$.

15

Compound 165

N-(4-(4,4-difluoropiperidin-1-yl)phenyl)isoindolin-5-amine



20

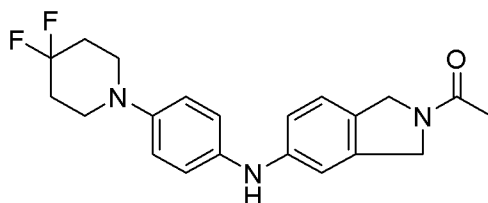
The title compound **165** (11.8 mg) was prepared in a total yield of 71.7% as a yellow solid from 4-(4,4-difluoropiperidin-1-yl)aniline (13.8 mg, 0.065 mmol), 5-bromoisoindoline (9.9 mg, 0.05 mmol), $\text{Pd}_2(\text{dba})_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz,

25

Methanol- d_4) δ 7.17 - 6.89 (m, 7H), 4.48 (s, 2H), 4.43 (s, 2H), 3.27 - 3.21 (m, 4H), 2.14 - 2.01 (m, 4H). Mass (m/z): 330.2 [M+H]⁺.

Compound 166

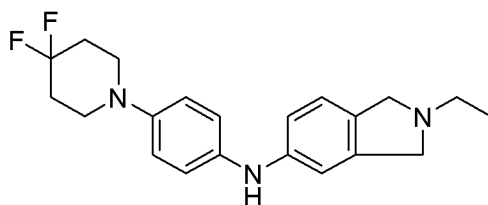
1-(5-((4-(4,4-difluoropiperidin-1-yl)phenyl)amino)isoindolin-2-yl)ethan-1-one



The title compound **166** (15.2 mg) was prepared in a total yield of 81.9% as a yellow solid from 4-(4,4-difluoropiperidin-1-yl)aniline (13.8 mg, 0.065 mmol), 1-(5-bromoisoindolin-2-yl)ethan-1-one (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol- d_4) δ 7.15 - 6.78 (m, 7H), 4.75 (s, 2H), 4.61 (s, 2H), 3.26 - 3.18 (m, 4H), 2.15 (s, 3H), 2.12 - 1.97 (m, 4H). Mass (m/z): 372.2 [M+H]⁺.

Compound 167

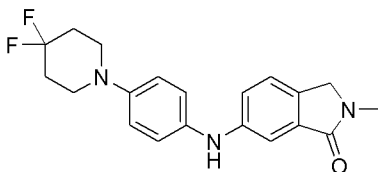
N-(4-(4,4-difluoropiperidin-1-yl)phenyl)-2-ethylisoindolin-5-amine



The title compound **167** (12.8 mg) was prepared in a total yield of 71.7% as a yellow solid from 4-(4,4-difluoropiperidin-1-yl)aniline (13.8 mg, 0.065 mmol), 5-bromo-2-ethylisoindoline (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol- d_4) δ 7.22 - 6.61 (m, 7H), 4.68 (s, 2H), 4.55 (s, 2H), 3.47 (q, J = 7.2 Hz, 2H), 3.27 - 3.15 (m, 4H), 2.37 - 2.16 (m, 4H), 1.42 (t, J = 7.2 Hz, 3H). Mass (m/z): 358.2 [M+H]⁺.

Compound 168

6-((4-(4,4-difluoropiperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one

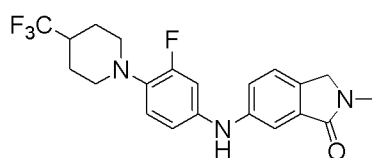


The title compound **168** (3.3 mg) was prepared in a total yield of 3.9% as a pale yellow solid from 4-(4,4-difluoropiperidin-1-yl)aniline (50 mg, 0.23 mmol), 6-bromo-2-methylisoindolin-1-one (53 mg, 0.23 mmol), (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane) (10.91 mg, 0.019 mmol, 0.08 equivs), [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium (II) (6.9 mg, 0.009 mmol, 0.04 equivs) and cesium carbonate (153.5 mg, 0.47 mmol, 2.0 equivs) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.36 (dd, *J* = 5.2, 2.9 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.17 – 7.13 (m, 1H), 7.08 (d, *J* = 8.7 Hz, 2H), 7.03 – 6.97 (m, 2H), 4.38 (s, 2H), 3.25 (s, 3H), 3.17 (d, *J* = 3.0 Hz, 4H), 2.16-2.00 (m, 4H). ¹⁹F NMR (376 MHz, Methanol-*d*₄) δ -99.32. LC-MS (*m/z*) 358.6 [M+H]⁺.

15

Compound 169

6-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one

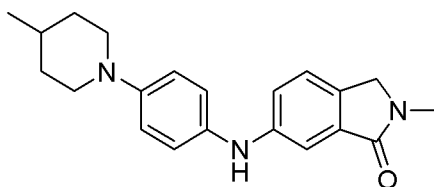


The title compound **169** (4.5 mg) was prepared in a total yield of 5.0% as a pale yellow solid from 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.24 mmol, 1.0 equivs), 6-bromo-2-methylisoindolin-1-one (53 mg, 0.24 mmol, 1.0 equivs), (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane) (10.91 mg, 0.019 mmol, 0.08 equivs), dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) (6.9 mg, 0.009 mmol, 0.04 equivs) and cesium carbonate (92 mg, 0.28 mmol, 1.2 equivs) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.74 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.71 (dd, *J* = 5.7, 3.3 Hz, 1H),

7.64 – 7.58 (m, 2H), 7.55 (ddd, $J = 7.6, 5.7, 1.0$ Hz, 2H), 7.48 (ddd, $J = 8.3, 7.1, 1.5$ Hz, 1H), 4.48 (s, 2H), 3.22 (d, $J = 2.3$ Hz, 1H), 3.19 (s, 3H), 3.17 (d, $J = 5.1$ Hz, 1H), 1.78 – 1.65 (m, 2H), 1.50 – 1.40 (m, 2H), 1.01 – 0.94 (m, 3H). ^{19}F NMR (376 MHz, Methanol- d_4) δ -75.43 (d, $J = 8.3$ Hz),
 5 -76.95, -123.72, -123.75. Mass (m/z): 408.3 $[\text{M}+\text{H}]^+$.

Compound 170

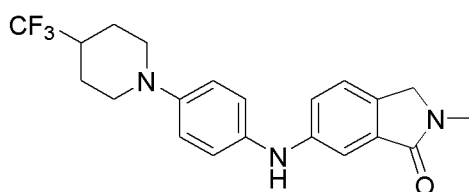
2-methyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **170** (21.4 mg) was prepared in a yield of 24.38% as a
 10 pale yellow solid from 6-bromo-2-methylisoindolin-1-one (50 mg, 0.22 mmol) and 4-(4-methylpiperidin-1-yl)aniline (42 mg, 0.22 mmol), according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.75 – 7.46 (m, 2H), 7.36 (d, $J = 8.9$ Hz, 2H), 7.28 – 6.95 (m, 3H), 4.40 (s, 2H), 3.67-3.45 (m, 2H), 3.16 (s, 3H), 3.04-2.96 (m, 1H),
 15 1.86 (d, $J = 11.7$ Hz, 2H), 1.64 (q, $J = 13.2, 11.6$ Hz, 2H), 1.56 – 1.42 (m, 2H), 1.03 (d, $J = 6.4$ Hz, 3H). LC-MS (m/z) 336.2 $[\text{M}+\text{H}]^+$.

Compound 171

2-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



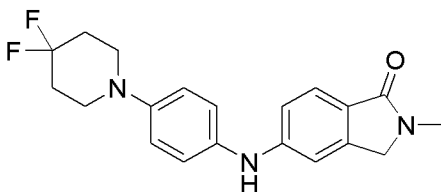
20

The title compound **171** (12.2 mg) was prepared in a yield of 14.17% as a
 pale yellow solid from 6-bromo-2-methylisoindolin-1-one (50 mg, 0.22 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (54 mg, 0.22 mmol), according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.67 – 7.46 (m, 2H), 7.42 – 7.28 (m, 2H), 7.24 – 7.04 (m, 2H), 6.99 (d, $J = 7.9$ Hz, 1H), 4.36 (d, $J = 7.9$ Hz, 2H), 3.65 (d, $J = 12.3$ Hz,
 25

1H), 3.16 (s, 3H), 2.68 (t, $J = 11.8$ Hz, 1H), 2.28 (s, 1H), 1.80 – 1.65 (m, 2H), 1.46 (h, $J = 7.3$ Hz, 1H), 1.39 – 1.18 (m, 3H). LC-MS (m/z) 390.3 $[M+H]^+$.

Compound 172

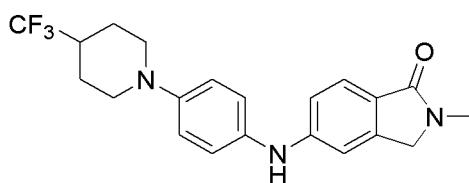
5 5-((4-(4,4-difluoropiperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



The title compound **172** (93.8 mg) was prepared in a yield of 59.33% as a pale yellow powder from 5-bromo-2-methylisoindolin-1-one (100 mg, 0.44 mmol) and 4-(4,4-difluoropiperidin-1-yl)aniline (94 mg, 0.44 mmol),
 10 according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.50 (d, $J = 8.5$ Hz, 1H), 7.14 – 6.96 (m, 6H), 4.32 (s, 2H), 3.27 (s, 3H), 3.12 (s, 4H), 2.09 (m, 4H). LC-MS (m/z) 358.2 $[M+H]^+$.

Compound 173

2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
 15 isoindolin-1-one



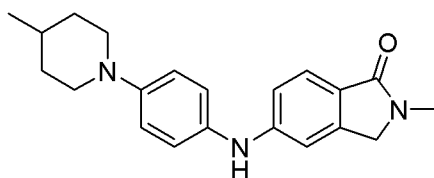
To a solution of 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (108 mg, 0.44 mmol, 1.0 equivs) and 5-bromo-2-methylisoindolin-1-one (100 mg, 0.44 mmol, 1.0 equivs) in 1,4-dioxane (5 mL) was added
 20 (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane) (20.48 mg, 0.035 mmol, 0.08 equivs), [1,1'-Bis(diphenylphosphino)ferrocene] dichloropalladium (II) (12.95 mg, 0.018 mmol, 0.04 equivs) and cesium carbonate (216.18 mg, 0.66 mmol, 2.0 equivs) respectively under argon atmosphere. The resulting mixture was heated to 110°C and stirred for
 25 overnight at the same temperature. The reaction was diluted with water (10 mL) and extracted with ethyl acetate (5 mL) 3 times. The organic layer was

combined and washed with water, sat. NaHCO₃ (aq), and brine respectively. Then dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/AcOEt, 1/4) to give 58.4 mg of compound **1** in a yield of 33.90% as a blue powder. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.50 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.04 – 6.96 (m, 3H), 6.95 – 6.90 (m, 1H), 4.33 (s, 2H), 3.68 (d, *J* = 12.4 Hz, 2H), 3.11 (s, 3H), 2.69 (s, 2H), 2.34-2.21 (m, 1H), 2.05 – 1.89 (m, 2H), 1.79 – 1.64 (m, 2H). LC-MS (*m/z*) 390.2 [M+H]⁺.

10

Compound 174

2-methyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)isoindolin-1-one

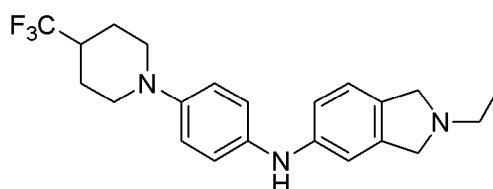


The title compound **174** (37.9 mg) was prepared in a yield of 25.54% as a pale yellow powder from 5-bromo-2-methylisoindolin-1-one (100 mg, 0.44 mmol) and 4-(4-methylpiperidin-1-yl)aniline (84 mg, 0.44 mmol), according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.14 – 7.05 (m, 2H), 7.02 – 6.95 (m, 3H), 6.92 (dd, *J* = 8.4, 2.1 Hz, 1H), 4.30 (s, 2H), 3.54 (d, *J* = 11.8 Hz, 2H), 3.10 (s, 3H), 2.64 (t, *J* = 12.1 Hz, 2H), 1.82 – 1.68 (m, 2H), 1.57 – 1.42 (m, 1H), 1.41 – 1.30 (m, 2H), 0.99 (d, *J* = 6.3 Hz, 3H). LC-MS (*m/z*) 336.3 [M+H]⁺.

20

Compound 175

2-ethyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)isoindolin-5-amine



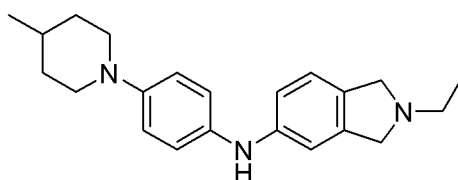
The title compound **175** (14.7 mg) was prepared in a total yield of 75.6% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9

25

mg, 0.065 mmol), 5-bromo-2-ethylisoindoline (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.07 (d, *J* = 8.0 Hz, 1H), 7.04 - 7.00 (m, 2H), 6.97 - 6.93 (m, 2H), 6.90 - 6.83 (m, 2H), 4.05 (s, 4H), 3.65 - 3.55 (m, 2H), 2.97 (q, *J* = 7.2 Hz, 2H), 2.70 - 2.61 (m, 2H), 2.26 (m, 1H), 2.00 - 1.89 (m, 2H), 1.79 - 1.64 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H). Mass (*m/z*): 390.3 [M+H]⁺.

Compound 176

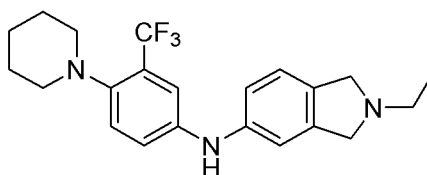
2-ethyl-N-(4-(4-methylpiperidin-1-yl)phenyl)isoindolin-5-amine



The title compound **176** (13.9 mg) was prepared in a total yield of 82.9 % as a yellow solid from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 5-bromo-2-ethylisoindoline (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.10 - 6.81 (m, 7H), 4.03 (s, 4H), 3.55 - 3.43 (m, 2H), 2.96 (q, *J* = 7.2 Hz, 2H), 2.71 - 2.54 (m, 2H), 1.79 - 1.71 (m, 2H), 1.56 - 1.43 (m, 1H), 1.42 - 1.29 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H), 0.99 (d, *J* = 6.4 Hz, 3H). Mass (*m/z*): 336.2 [M+H]⁺.

Compound 177

2-ethyl-N-(4-(piperidin-1-yl)-3-(trifluoromethyl)phenyl)isoindolin-5-amine

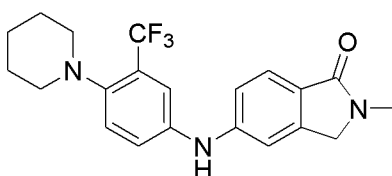


The title compound **177** (17.3 mg) was prepared in a total yield of 88.7 % as a yellow solid from 4-(piperidin-1-yl)-3-(trifluoromethyl)aniline (15.9 mg, 0.065 mmol), 5-bromo-2-ethylisoindoline (11.3 mg, 0.05 mmol),

Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.37 - 7.23 (m, 3H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.07 - 6.98 (m, 2H), 4.38 (s, 2H), 4.36 (s, 2H), 3.25 (q, *J* = 7.2 Hz, 2H), 2.85 - 2.70 (m, 4H), 1.71 - 1.62 (m, 4H), 1.58 - 1.50 (m, 2H), 1.35 (t, *J* = 7.2 Hz, 3H). Mass (m/z): 390.3 [M+H]⁺.

Compound 178

2-methyl-5-((4-(piperidin-1-yl)-3-(trifluoromethyl)phenyl)amino)isoindolin-1-one



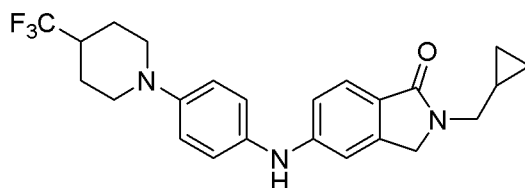
10

The title compound **178** (58.4 mg) was prepared in a yield of 25.72% as a white powder from 5-bromo-2-methylisoindolin-1-one (100 mg, 0.44 mmol) and 4-(piperidin-1-yl)-3-(trifluoromethyl)aniline (108 mg, 0.44 mmol), according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.58 (d, *J* = 8.4 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.37 (t, *J* = 1.5 Hz, 1H), 7.16-7.12 (m, 1H), 7.06 (dd, *J* = 8.4, 2.1 Hz, 1H), 4.40 (s, 2H), 3.14 (s, 3H), 2.87 – 2.78 (m, 4H), 1.69 (p, *J* = 5.7 Hz, 4H), 1.58 (d, *J* = 6.0 Hz, 2H). LC-MS (m/z) 387.9 [M-H]⁻.

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Compound 179

2-(cyclopropylmethyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



20

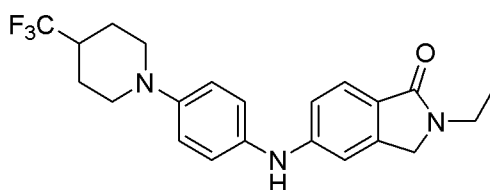
The title compound **179** (17.2 mg) was prepared in a yield of 9.78% as a pale yellow powder from 5-bromo-2-(cyclopropylmethyl)isoindolin-1-one (100 mg, 0.41 mmol) and 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (120 mg, 0.41 mmol), according to the procedure for compound 1. ¹H NMR

25

(400 MHz, DMSO- d_6) δ 8.31 (s, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.07 (d, J = 8.9 Hz, 2H), 6.99 (d, J = 2.1 Hz, 1H), 6.98 – 6.92 (m, 2H), 6.90 (dt, J = 8.4, 2.0 Hz, 1H), 4.40 (s, 2H), 3.69 (d, J = 12.3 Hz, 2H), 2.71 – 2.61 (m, 2H), 1.89 (d, J = 13.6 Hz, 2H), 1.57 (qd, J = 12.4, 4.0 Hz, 2H), 1.24 (s, 2H),
 5 1.04 – 0.94 (m, 1H), 0.89-0.82 (d, J = 7.2 Hz, 1H), 0.51 – 0.44 (m, 2H), 0.30 – 0.22 (m, 2H). LC-MS (m/z) 430.3 $[M+H]^+$.

Compound 180

2-ethyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
 isoindolin-1-one

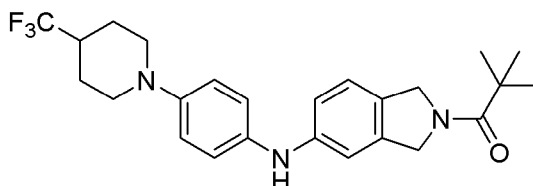


10

The title compound **180** (73.1 mg) was prepared in a yield of 44.26% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-ethylisoindolin-1-one (98 mg, 0.41 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Chloroform- d) δ 7.58 (d, J = 8.4 Hz, 1H), 7.49 – 7.35 (m, 1H), 7.15 (s, 2H), 6.98 (d, J = 10.0 Hz, 4H), 4.32 (d, J = 4.1 Hz, 2H), 3.69 (d, J = 12.3 Hz, 2H), 3.61 (qd, J = 7.3, 2.8 Hz, 2H), 3.42 – 3.33 (m, 1H), 2.71 (t, J = 12.3 Hz, 2H), 2.19 (ddt, J = 12.6, 8.3, 4.0 Hz, 1H), 2.00 (d, J = 13.1 Hz, 2H), 1.87 – 1.70 (m, 2H), 1.25 (td, J = 7.2, 3.1 Hz, 2H). Mass (m/z): 404.2
 15
 20 $[M+H]^+$.

Compound 181

2,2-dimethyl-1-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
 isoindolin-2-yl)propan-1-one

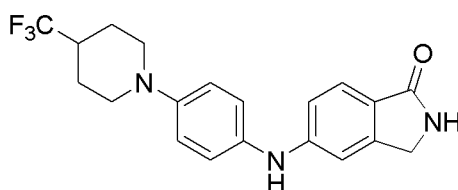


25 The title compound **181** (17.0 mg) was prepared in a total yield of 76.4 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9

mg, 0.065 mmol), 1-(5-bromoisindolin-2-yl)-2,2-dimethylpropan-1-one (14.1 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.27 - 6.75 (m, 7H), 4.96 (s, 2H), 4.67 (s, 2H), 3.83 - 3.41 (m, 2H), 2.71 - 2.57 (m, 2H), 2.27 (m, 1H), 2.07 - 1.89 (m, 2H), 1.81 - 1.62 (m, 2H), 1.32 (s, 9H). Mass (m/z): 446.3 [M+H]⁺.

Compound 182

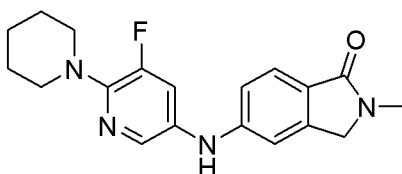
5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isindolin-1-one



The title compound **182** (1.1 mg) was prepared in a yield of 1.4% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromoisindolin-1-one (43 mg, 0.20 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.53 (d, *J* = 8.4 Hz, 1H), 7.15 - 7.09 (m, 2H), 7.03 - 6.98 (m, 3H), 6.95 (dd, *J* = 8.3, 2.1 Hz, 1H), 4.32 (s, 2H), 3.69 (d, *J* = 12.4 Hz, 2H), 2.70 (td, *J* = 12.5, 2.4 Hz, 2H), 1.98 (d, *J* = 13.4 Hz, 2H), 1.72 (qd, *J* = 12.4, 4.5 Hz, 3H). Mass (m/z): 376.2 [M+H]⁺.

Compound 183

5-((5-fluoro-6-(piperidin-1-yl)pyridin-3-yl)amino)-2-methylisindolin-1-one



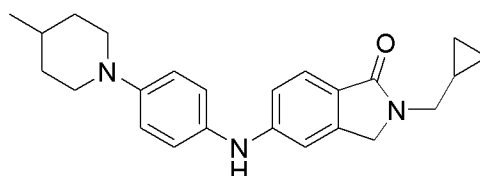
The title compound **183** (24.6 mg) was prepared in a yield of 28.22% as a pale yellow powder from 5-fluoro-6-(piperidin-1-yl)pyridin-3-amine (50 mg, 0.26 mmol) and 5-bromo-2-methylisindolin-1-one (58 mg, 0.26 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz,

DMSO- d_6) δ 8.53 (s, 1H), 7.94 (dt, $J = 2.3, 1.2$ Hz, 1H), 7.44 (d, $J = 8.3$ Hz, 1H), 7.42 – 7.36 (m, 1H), 7.04 (d, $J = 2.2$ Hz, 1H), 6.93 (dt, $J = 8.3, 1.9$ Hz, 1H), 4.31 (s, 2H), 2.99 (s, 3H), 1.66 – 1.52 (m, 6H). Mass (m/z): 341.7 $[M+H]^+$.

5

Compound 184

2-(cyclopropylmethyl)-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)isoindolin-1-one



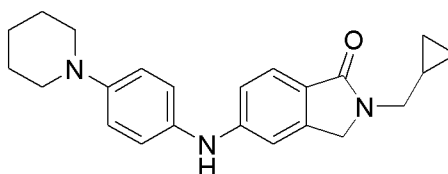
The title compound **184** (46.3 mg) was prepared in a yield of 46.92% as a pale yellow powder from 4-(4-methylpiperidin-1-yl)aniline (50 mg, 0.26 mmol) and 5-bromo-2-(cyclopropylmethyl)isoindolin-1-one (58 mg, 0.26 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.28 (s, 1H), 7.41 (d, $J = 8.3$ Hz, 1H), 7.09 – 7.02 (m, 2H), 6.97 (d, $J = 2.1$ Hz, 1H), 6.94 (s, 1H), 6.92 – 6.87 (m, 2H), 4.40 (s, 2H), 3.65 – 3.50 (m, 2H), 3.29 (d, $J = 7.1$ Hz, 2H), 2.60 (t, $J = 11.9$ Hz, 2H), 1.74 – 1.65 (m, 2H), 1.47 (dq, $J = 11.0, 6.6, 5.3$ Hz, 1H), 1.26 (dd, $J = 12.7, 9.0$ Hz, 3H), 0.95 (d, $J = 6.5$ Hz, 3H), 0.53 – 0.45 (m, 2H), 0.31 – 0.22 (m, 2H). Mass (m/z): 376.3 $[M+H]^+$.

15

Compound 185

2-(cyclopropylmethyl)-5-((4-(piperidin-1-yl)phenyl)amino)isoindolin-1-one

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The title compound **185** (72.1 mg) was prepared in a yield of 70.31% as a pale yellow powder from 4-(piperidin-1-yl)aniline (50 mg, 0.28 mmol) and 5-bromo-2-(cyclopropylmethyl)isoindolin-1-one (83 mg, 0.31 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6)

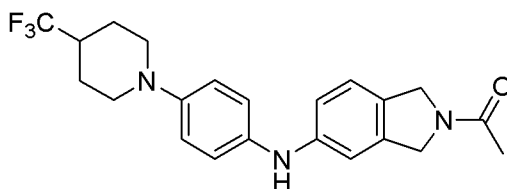
25

δ 7.41 (d, J = 8.3 Hz, 1H), 7.09 – 7.02 (m, 2H), 6.97 (t, J = 2.3 Hz, 1H), 6.95 – 6.86 (m, 3H), 4.39 (s, 2H), 3.29 (d, J = 7.1 Hz, 2H), 3.05 (d, J = 10.9 Hz, 4H), 1.71 – 1.57 (m, 4H), 1.56 – 1.45 (m, 2H), 1.04 – 0.93 (m, 1H), 0.52 – 0.42 (m, 2H), 0.29 – 0.21 (m, 2H). Mass (m/z): 362.1 $[M+H]^+$.

5

Compound 186

1-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-2-yl)ethan-1-one

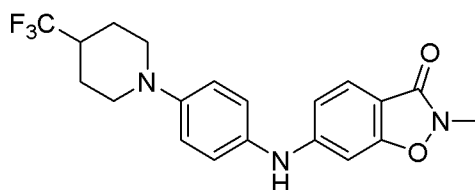


The title compound **186** (16.7 mg) was prepared in a total yield of 82.6% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 1-(5-bromoisoindolin-2-yl)ethan-1-one (12.0 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, Chloroform- d) δ 7.18 - 6.68 (m, 7H), 4.70 (s, 4H), 3.75 - 3.58 (m, 2H), 2.79 - 2.68 (m, 2H), 2.18 (m, 1H), 2.15 (s, 3H), 2.04 - 1.93 (m, 2H), 1.85 - 1.70 (m, 2H). Mass (m/z): 404.2 $[M+H]^+$.

15

Compound 187

2-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]isoxazol-3(2H)-one



20

The title compound **187** (16.4 mg) was prepared in a total yield of 83.9% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-2-methylbenzo[d]isoxazol-3(2H)-one (11.4 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, Chloroform- d) δ 7.56 (d, J = 8.8 Hz, 1H),

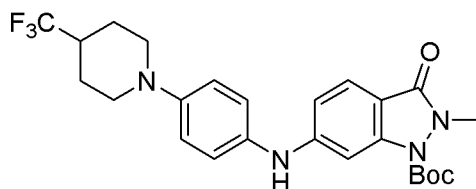
25

7.13 (d, $J = 8.8$ Hz, 2H), 6.95 (d, $J = 8.8$ Hz, 2H), 6.66 (d, $J = 8.8$ Hz, 1H), 6.55 - 6.49 (m, 1H), 3.77 - 3.69 (m, 2H), 3.54 (s, 3H), 2.77 - 2.67 (m, 2H), 2.17 (m, 1H), 2.05 - 1.95 (m, 2H), 1.88 - 1.70 (m, 2H). Mass (m/z): 392.2 $[M+H]^+$.

5

Compound 188

tert-butyl 2-methyl-3-oxo-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-1H-indazole-1-carboxylate

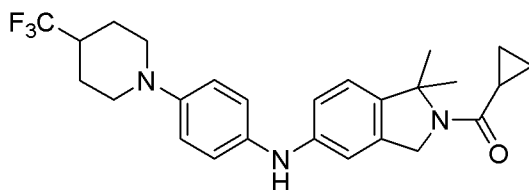


The title compound **188** (26.4 mg) was prepared in a total yield of 53.8% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (31.8 mg, 0.13 mmol), *tert-butyl* 6-bromo-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (32.8 mg, 0.1 mmol), $Pd_2(dba)_3$ (1.84 mg, 0.002 mmol), X-Phos (4.76 mg, 0.01 mmol) and Cs_2CO_3 (48.8 mg, 0.15 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Chloroform- d) δ 7.62 (d, $J = 8.4$ Hz, 1H), 7.21 (s, 1H), 7.16 - 7.12 (m, 2H), 6.95 (d, $J = 8.4$ Hz, 2H), 6.72 (m, 1H), 3.75 - 3.68 (m, 2H), 3.53 (s, 3H), 2.77 - 2.62 (m, 2H), 2.17 (m, 1H), 2.03 - 1.95 (m, 2H), 1.84 - 1.74 (m, 2H), 1.53 (s, 9H). Mass (m/z): 491.3 $[M+H]^+$.

15

Compound 189

cyclopropyl(1,1-dimethyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-2-yl)methanone



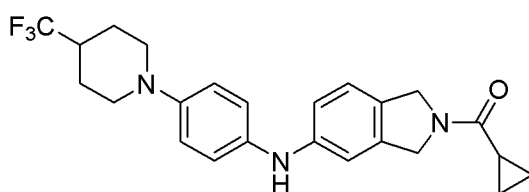
The title compound **189** (17.7 mg) was prepared in a total yield of 77.3% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), (5-bromo-1,1-dimethylisoindolin-2-yl) (cyclopropyl) methanone (14.7 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol),

25

X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.12 - 7.00 (m, 3H), 6.96 - 6.88 (m, 2H), 6.89 - 6.83 (m, 1H), 6.73 (s, 1H), 4.92 (s, 2H), 3.72 - 3.62 (m, 2H), 2.73 - 2.59 (m, 2H),
 5 2.14 (m, 1H), 2.03 - 1.91 (m, 2H), 1.83 - 1.75 (m, 3H), 1.70 (s, 6H), 1.06 - 0.97 (m, 2H), 0.83 - 0.72 (m, 2H). Mass (m/z): 458.1 [M+H]⁺.

Compound 190

cyclopropyl(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-2-yl)methanone



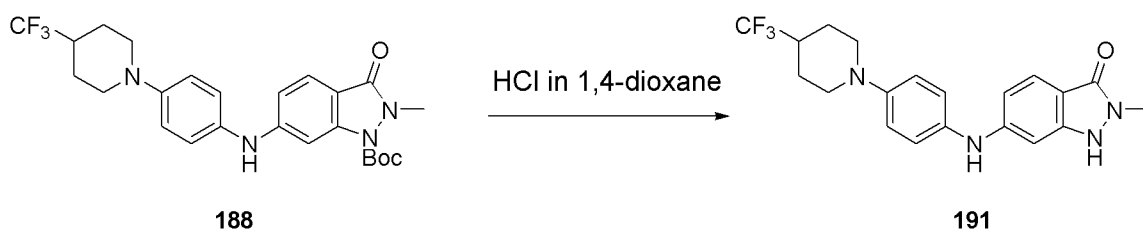
10

The title compound **190** (16.5 mg) was prepared in a total yield of 76.7% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), (5-bromoisoindolin-2-yl)(cyclopropyl)methanone (13.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the
 15 procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.19 - 6.72 (m, 7H), 4.91 (s, 2H), 4.72 (s, 2H), 3.73 - 3.62 (m, 2H), 2.78 - 2.57 (m, 2H), 2.14 (m, 1H), 2.04 - 1.93 (m, 2H), 1.86 - 1.64 (m, 3H), 1.09 - 1.03 (m, 2H), 0.86 - 0.80 (m, 2H). Mass (m/z): 430.2 [M+H]⁺.

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Compound 191

2-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-indazol-3-one



188

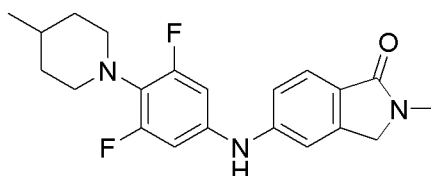
191

A solution of tert-butyl 2-methyl-3-oxo-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-1H-indazole-1-carboxylate
 25

(12.3 mg, 0.025 mmol) in 1 mL of a solution of HCl in 1,4-dioxane was stirred for 30 mins at r.t. and concentrated. 5 ml water was added. The pH of the filtrate was adjusted to 8-9 with sodium carbonate solution. Then the mixture was extracted by DCM (3 mL x 3). The combined organic layers were washed with water (5 mL), dried over Na₂SO₄ and concentrated. The residue was purified by prep-TLC (MeOH/DCM=1/10) to afford the desired product as a yellow solid (8.3 mg, 85.2 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.36 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.62 (d, *J* = 8.8 Hz, 1H), 6.52 (s, 1H), 3.73 - 3.65 (m, 2H), 3.22 (s, 3H), 2.73 - 2.61 (m, 2H), 2.11 (m, 1H), 1.93 - 1.85 (m, 2H), 1.65 - 1.51 (m, 2H). Mass (m/z): 391.2 [M+H]⁺.

Compound 192

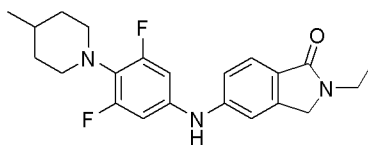
5-((3,5-difluoro-4-(4-methylpiperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



The title compound **192** (37.3 mg) was prepared in a total yield of 45.4% as a white solid from 3,5-difluoro-4-(4-methylpiperidin-1-yl)aniline (65 mg, 0.288 mmol), 5-bromo-2-methylisoindolin-1-one (50 mg, 0.221 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs₂CO₃ (109 mg, 0.332 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.61 – 7.50 (m, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 2.0 Hz, 1H), 7.09 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.82 – 6.69 (m, 2H), 2.98 (s, 3H), 2.96 – 2.86 (m, 4H), 1.56 (dd, *J* = 12.8, 3.2 Hz, 2H), 1.37 (dq, *J* = 13.2, 8.0, 6.8, 2.8 Hz, 1H), 1.18 (tq, *J* = 11.6, 4.8 Hz, 2H), 0.88 (d, *J* = 6.4 Hz, 3H). Mass (m/z): 372.3 [M+H]⁺.

Compound 193

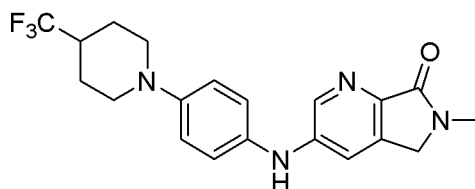
5-((3,5-difluoro-4-(4-methylpiperidin-1-yl)phenyl)amino)-2-ethylisoindolin-1-one



The title compound **193** (27.1 mg) was prepared in a total yield of 33.8% as a white solid from 3,5-difluoro-4-(4-methylpiperidin-1-yl)aniline (61 mg, 0.271 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.208 mmol),
 5 Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.77 (s, 1H), 7.49 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.21 (d, *J* = 1.6 Hz, 1H), 7.05 (dt, *J* = 8.0, 1.6 Hz, 1H), 6.76 – 6.66 (m, 2H), 4.36 (s, 2H), 3.54 – 3.40 (m, 2H), 3.02 – 2.88 (m, 4H),
 10 1.68 – 1.55 (m, 2H), 1.48 – 1.34 (m, 1H), 1.21 (qd, *J* = 11.6, 4.4 Hz, 2H), 1.12 (td, *J* = 7.2, 1.2 Hz, 3H), 0.91 (dd, *J* = 6.4, 1.2 Hz, 3H). Mass (*m/z*): 386.3 [M+H]⁺.

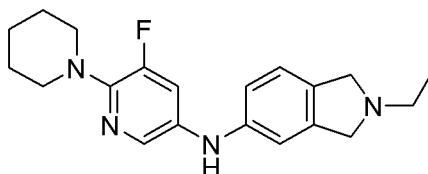
Compound 194

15 6-methyl-3-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-5,6-dihydro-7H-pyrrolo[3,4-*b*]pyridin-7-one

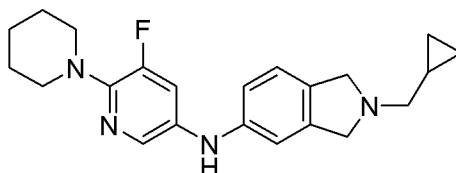


The title compound **194** (13.2 mg) was prepared in a total yield of 67.7 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 3-bromo-6-methyl-5,6-dihydro-7H-pyrrolo[3,4-*b*]pyridin-7-one (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.30 (s, 1H), 7.17 (s, 1H), 7.12 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.24 (s, 2H), 3.76 - 3.69 (m, 2H), 3.19 (s, 3H), 2.77 - 2.67
 20 (m, 2H), 2.19 (m, 1H), 2.04 - 1.95 (m, 2H), 1.85 - 1.70 (m, 2H). Mass (*m/z*): 391.2 [M+H]⁺.

Compound 195

2-ethyl-N-(5-fluoro-6-(piperidin-1-yl)pyridin-3-yl)isoindolin-5-amine

The title compound **195** (15.0 mg) was prepared in a total yield of 88.2 % as a yellow solid from 5-fluoro-6-(piperidin-1-yl)pyridin-3-amine (12.7 mg, 0.065 mmol), 5-bromo-2-ethylisoindoline (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 2.0 Hz, 1H), 7.10 - 6.99 (m, 2H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.74 (s, 1H), 4.06 (s, 2H), 4.02 (s, 2H), 3.33 - 3.23 (m, 4H), 2.93 (q, *J* = 7.2 Hz, 2H), 1.75 - 1.65 (m, 4H), 1.65 - 1.56 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). Mass (*m/z*): 341.2 [M+H]⁺.

Compound 196*2-(cyclopropylmethyl)-N-(5-fluoro-6-(piperidin-1-yl)pyridin-3-yl)isoindolin-5-amine*

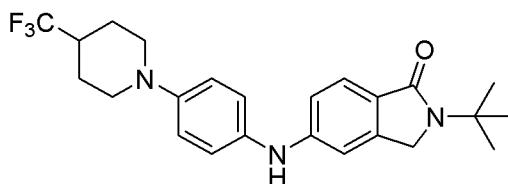
15

The title compound **196** (15.3 mg) was prepared in a total yield of 83.4 % as a yellow solid from 5-fluoro-6-(piperidin-1-yl)pyridin-3-amine (12.7 mg, 0.065 mmol), 5-bromo-2-(cyclopropylmethyl)isoindoline (12.6 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 2.0 Hz, 1H), 7.09 - 6.94 (m, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.71 (s, 1H), 4.18 (s, 2H), 4.12 (s, 2H), 3.30 - 3.21 (m, 4H), 2.82 (d, *J* = 6.8 Hz, 2H), 1.71 - 1.63 (m, 4H), 1.63 - 1.55 (m, 2H), 1.11 (m, 1H), 0.67 - 0.58 (m, 2H), 0.33 - 0.27 (m, 2H). Mass (*m/z*): 367.3 [M+H]⁺.

25

Compound 197

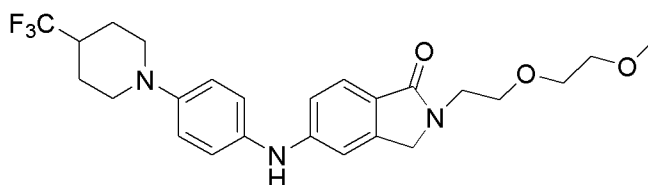
2-(tert-butyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **197** (32.6 mg) was prepared in a yield of 18.45% as a
 5 pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100
 mg, 0.41 mmol) and 5-bromo-2-(tert-butyl)isoindolin-1-one (121 mg, 0.45
 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz,
 Methanol-*d*₄) δ 7.66 – 7.58 (m, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.34 – 7.25
 (m, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.95 – 6.89 (m, 1H), 4.44 (d, *J* = 0.9 Hz,
 10 2H), 3.67 (d, *J* = 12.5 Hz, 2H), 2.76 – 2.60 (m, 2H), 2.29 (dtq, *J* = 16.7, 8.4,
 4.3 Hz, 1H), 2.01 – 1.93 (m, 2H), 1.74 (td, *J* = 12.6, 4.1 Hz, 2H), 1.53 (s,
 9H). Mass (*m/z*): 432.5 [M+H]⁺.

Compound 198

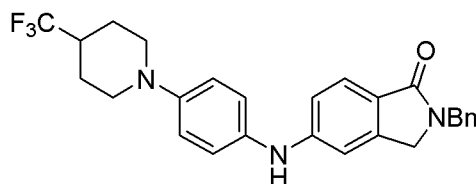
2-(2-(2-methoxyethoxy)ethyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **198** (41.6 mg) was prepared in a yield of 21.28% as a
 white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg,
 0.41 mmol) and 5-bromo-2-(2-(2-methoxyethoxy)ethyl)isoindolin-1-one
 20 (141 mg, 0.45 mmol) according to the procedure for compound **1**. ¹H NMR
 (400 MHz, Methanol-*d*₄) δ 7.53 (d, *J* = 8.4 Hz, 1H), 7.16 – 7.08 (m, 2H),
 7.03 – 6.89 (m, 4H), 4.44 (s, 2H), 3.73 – 3.69 (m, 4H), 3.69 – 3.63 (m, 2H),
 3.62 – 3.59 (m, 2H), 3.53 – 3.49 (m, 2H), 2.68 (s, 2H), 2.27 (tdt, *J* = 12.3,
 7.8, 3.9 Hz, 1H), 2.00 – 1.92 (m, 2H), 1.71 (qd, *J* = 12.6, 4.1 Hz, 2H).
 25 Mass (*m/z*): 478.3 [M+H]⁺.

Compound 199

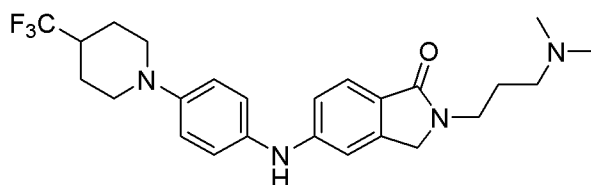
2-benzyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **199** (75.2 mg) was prepared in a yield of 39.37% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 2-benzyl-5-bromoisindolin-1-one (123 mg, 0.45 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.57 (d, *J* = 9.0 Hz, 1H), 7.39 – 7.31 (m, 3H), 7.31 – 7.25 (m, 3H), 7.14 – 7.08 (m, 2H), 7.03 – 6.98 (m, 2H), 6.96 (dq, *J* = 4.6, 2.1 Hz, 2H), 4.74 (s, 2H), 4.23 (s, 2H), 3.72 – 3.65 (m, 2H), 2.69 (td, *J* = 12.4, 2.5 Hz, 2H), 2.29 (dtd, *J* = 16.1, 8.1, 3.9 Hz, 1H), 1.97 (dt, *J* = 12.9, 3.0 Hz, 2H), 1.72 (qd, *J* = 12.6, 4.2 Hz, 2H). Mass (*m/z*): 466.3 [M+H]⁺.

Compound 200

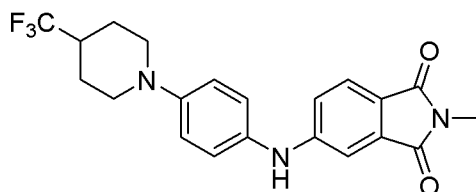
2-(3-(dimethylamino)propyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **200** (52.9 mg) was prepared in a yield of 28.06% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-(3-(dimethylamino)propyl)isoindolin-1-one (121 mg, 0.41 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.51 (dd, *J* = 8.4, 0.5 Hz, 1H), 7.14 – 7.09 (m, 2H), 7.00 (dt, *J* = 4.3, 1.5 Hz, 2H), 6.98 (d, *J* = 2.2 Hz, 1H), 6.95 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.39 (s, 2H), 3.73 – 3.58 (m, 4H), 2.96 – 2.86 (m, 2H), 2.71 (s, 8H), 2.27 (dtq, *J* = 17.0, 8.5, 4.2 Hz, 1H), 2.08 – 1.91 (m, 4H), 1.77 – 1.63 (m, 2H). Mass (*m/z*): 461.8 [M+H]⁺.

Compound 201

*2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
isoindoline-1,3-dione*

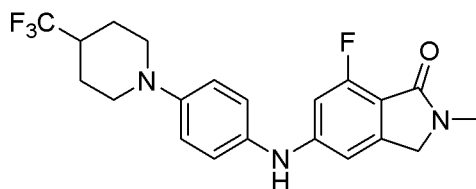


The title compound **201** (16.3 mg) was prepared in a total yield of 80.9 %
5 as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9
mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05
mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol)
and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for
compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.45 (m, 1H), 7.15 -
10 6.88 (m, 3H), 6.87 - 6.70 (m, 3H), 3.67 - 3.43 (m, 2H), 2.94 (s, 3H), 2.65 -
2.45 (m, 2H), 2.01 (m, 1H), 1.87 - 1.77 (m, 2H), 1.67 - 1.52 (m, 2H). Mass
(*m/z*): 404.2 [M+H]⁺.

Compound 202

*7-fluoro-2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
isoindolin-1-one*

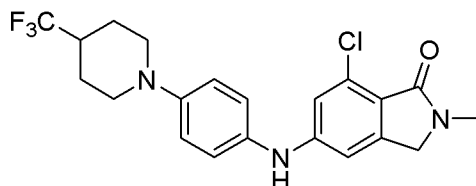
15



The title compound **202** (17.7 mg) was prepared in a total yield of 86.8 %
as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9
mg, 0.065 mmol), 5-bromo-7-fluoro-2-methylisoindolin-1-one (12.2 mg,
20 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005
mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for
compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.10 (d, *J* = 8.4 Hz, 2H),
6.94 (d, *J* = 8.4 Hz, 2H), 6.82 - 6.76 (m, 2H), 4.22 (s, 2H), 3.77 - 3.66 (m,
2H), 3.09 (s, 3H), 2.78 - 2.62 (m, 2H), 2.17 (m, 1H), 2.04 - 1.95 (m, 2H),
25 1.83 - 1.71 (m, 2H). Mass (*m/z*): 408.2 [M+H]⁺.

Compound 203

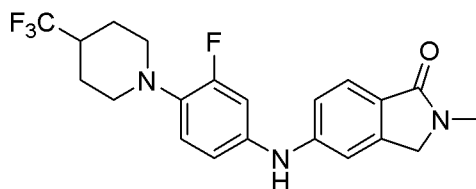
7-chloro-2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **203** (18.6 mg) was prepared in a total yield of 87.9 %
 5 as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-7-chloro-2-methylisoindolin-1-one (13.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.13 - 7.07 (m, 2H),
 10 6.99 - 6.92 (m, 2H), 6.84 - 6.77 (m, 2H), 4.23 (s, 2H), 3.72 - 3.64 (m, 2H), 3.08 (s, 3H), 2.75 - 2.63 (m, 2H), 2.19 (m, 1H), 2.01 - 1.93 (d, *J* = 3.8 Hz, 2H), 1.80 - 1.66 (m, 2H). Mass (*m/z*): 424.1 [M+H]⁺.

Compound 204

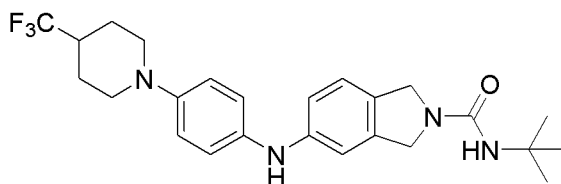
5-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



The title compound **204** (16.2 mg) was prepared in a total yield of 79.4 %
 as a yellow solid from 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline
 (17.0 mg, 0.065 mmol), 5-bromo-2-methylisoindolin-1-one (11.3 mg, 0.05
 20 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.4 Hz, 1H),
 7.02 - 6.85 (m, 4H), 6.51 (s, 1H), 4.25 (s, 2H), 3.54 - 3.41 (m, 2H), 3.13 (s,
 3H), 2.71 - 2.62 (m, 2H), 2.14 (m, 1H), 2.01 - 1.92 (m, 2H), 1.89 - 1.76 (m,
 25 2H). Mass (*m/z*): 408.2 [M+H]⁺.

Compound 205

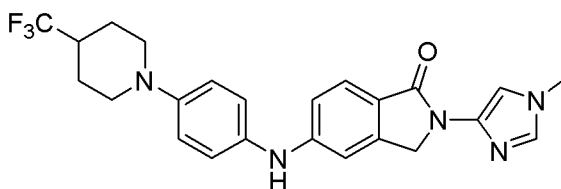
N-(tert-butyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindoline-2-carboxamide



The title compound **205** (19.0 mg) was prepared in a total yield of 82.6 %
 5 as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-N-(tert-butyl)isoindoline-2-carboxamide (14.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.14 - 6.81
 10 (m, 7H), 4.54 (s, 4H), 3.69 - 3.57 (m, 2H), 2.74 - 2.62 (m, 2H), 2.27 (m, 1H), 2.02 - 1.93 (m, 2H), 1.79 - 1.67 (m, 2H), 1.39 (s, 9H). Mass (m/z): 461.3 [M+H]⁺.

Compound 206

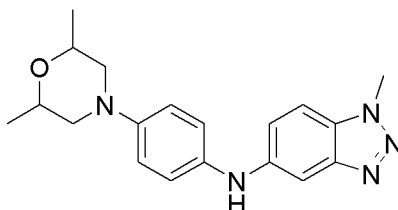
2-(1-methyl-1H-imidazol-4-yl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **206** (7.1 mg) was prepared in a yield of 7.61% as a yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-2-(1-methyl-1H-imidazol-4-yl)isoindolin-1-one (60 mg, 0.20 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.75 - 7.68 (m, 1H), 7.52 (s, 1H), 7.40 (tdd, *J* = 8.6, 6.4, 1.7 Hz, 4H), 7.29 (d, *J* = 3.4 Hz, 1H), 7.04 (td, *J* = 7.7, 2.6 Hz, 1H), 7.00 - 6.95 (m, 1H), 6.69 (ddd, *J* = 15.6, 7.6, 1.6 Hz, 1H), 4.83 (s, 2H), 2.12 (d, *J* = 37.6 Hz, 2H), 2.04 (s, 1H), 1.99 (s, 2H), 1.78 (s, 2H), 1.73
 20 (s, 3H), 1.56 (s, 1H), 1.25 (t, *J* = 7.1 Hz, 1H). Mass (m/z): 456.2 [M+H]⁺.

Compound 207

N-(4-(2,6-dimethylmorpholino) phenyl)-1-methyl-1*H*-benzo[d]
[1,2,3]triazol-5-amine

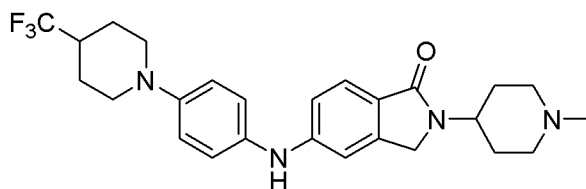


To a solution of 4-(2,6-dimethylmorpholin-4-yl)aniline (107 mg, 0.518 mmol), 5-bromo-1-methyl-1,2,3-benzotriazole (109 mg, 0.518 mmol) in toluene (2 mL) was added Cs₂CO₃ (338 mg, 1.04 mmol), Pd₂(dba)₃ (48 mg, 0.052 mmol) and Ru-Phos (48 mg, 0.104 mmol). The reaction mixture was stirred at 100 °C for 18 h under N₂ atmosphere. The resulting mixture was concentrated under reduced pressure. The residue was purified by column chromatography (EA:PE = 1:3) to give the target compound (61.8 mg, 34.55%) as a green solid. MS (ESI) *m/z*: 338 [M+H]⁺.

¹H NMR (400 MHz, DMSO-*d*₆) δ 7.99 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.28 (s, 1H), 7.19 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 4.22 (s, 3H), 3.70 - 3.68 (m, 2H), 3.47 (d, *J* = 10.4 Hz, 2H), 2.24 - 2.18 (m, 2H), 1.16 (d, *J* = 6.0 Hz, 6H).

Compound 208

2-(1-methylpiperidin-4-yl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl) phenyl)amino)isoindolin-1-one

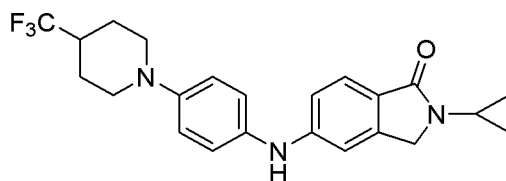


The title compound **208** (66.5 mg) was prepared in a yield of 34.37% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-(1-methylpiperidin-4-yl)isoindolin-1-one (127 mg, 0.41 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.50 (d, *J* = 8.4 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.04 – 6.86 (m, 4H), 4.39 – 4.28 (m, 3H), 3.75 – 3.59 (m, 2H), 3.59 – 3.47 (m, 2H), 3.13 (td, *J* = 12.9, 2.9 Hz, 2H), 2.85 (s, 3H), 2.64 (s, 2H), 2.34 –

2.11 (m, 3H), 2.10 – 1.87 (m, 4H), 1.67 (qd, $J = 12.6, 4.1$ Hz, 2H). Mass (m/z): 473.2 $[M+H]^+$.

Compound 209

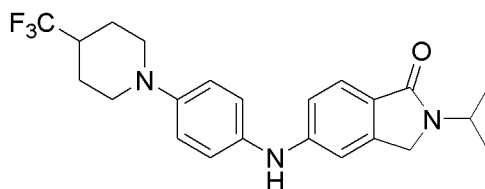
2-cyclopropyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
isoindolin-1-one



The title compound **209** (67.2 mg) was prepared in a yield of 39.51% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-cyclopropylisoindolin-1-one (103 mg, 0.41 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.30 (s, 1H), 7.44 – 7.34 (m, 1H), 7.08 – 7.03 (m, 2H), 6.98 – 6.93 (m, 2H), 6.92 (q, $J = 1.4, 0.8$ Hz, 1H), 6.88 (dt, $J = 8.3, 2.0$ Hz, 1H), 4.22 (s, 2H), 3.69 (d, $J = 12.5$ Hz, 2H), 2.83 (tt, $J = 6.8, 4.3$ Hz, 1H), 2.73 – 2.60 (m, 2H), 2.46 (d, $J = 3.2$ Hz, 1H), 1.93 – 1.82 (m, 2H), 1.57 (qd, $J = 12.5, 4.1$ Hz, 2H), 0.79 – 0.65 (m, 4H). Mass (m/z): 473.2 $[M+H]^+$.

Compound 210

2-isopropyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
isoindolin-1-one

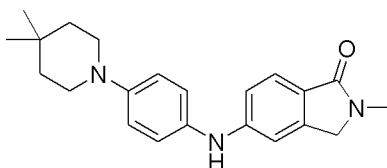


The title compound **210** (32.4 mg) was prepared in a yield of 18.96% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-isopropylisoindolin-1-one (104 mg, 0.41 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.51 (dd, $J = 8.4, 0.9$ Hz, 1H), 7.29 (dt, $J = 15.2, 7.2$ Hz, 2H), 7.14 – 7.10 (m, 2H), 7.04 – 6.99 (m, 3H), 4.33 (s, 2H), 3.74 – 3.63 (m, 2H), 2.74 – 2.66 (m, 2H), 2.30 (dtt, $J = 15.8, 7.6, 3.9$ Hz, 1H), 1.98 (d, $J =$

12.6 Hz, 2H), 1.74 (td, $J = 12.5, 4.3$ Hz, 3H), 1.28 (dd, $J = 6.8, 1.1$ Hz, 6H).
Mass (m/z): 418.7 $[M+H]^+$.

Compound 211

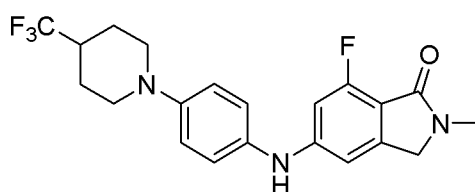
5-((4-(4,4-dimethylpiperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



The title compound **211** (35.6 mg) was prepared in a yield of 20.3% as a yellow powder from 4-(4,4-dimethylpiperidin-1-yl)aniline (107 mg, 0.5 mmol), 5-bromo-2-methylisoindolin-1-one (87 mg, 0.38 mmol), Pd(dppf)Cl₂ (5.6 mg, 7.6 μ mol), Xantphos (8.8 mg, 15.2 μ mol), Cs₂CO₃ (245 mg, 0.75 mmol) and 1,4-dioxane (3.0 mL) according to the procedure for compound **1**. (35.6 mg, 20.3%). ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.49 (d, $J = 8.4$ Hz, 1H), 7.13 – 7.08 (m, 2H), 7.02 – 6.96 (m, 3H), 6.92 (dd, $J = 8.4, 2.1$ Hz, 1H), 4.33 (s, 2H), 3.15 – 3.05 (m, 7H), 1.57 – 1.52 (m, 4H), 1.00 (s, 6H). Mass (m/z): 350.3 $[M+H]^+$.

Compound 212

7-fluoro-2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one

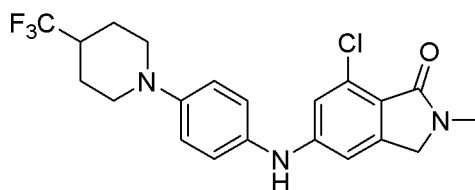


The title compound **212** (17.7 mg) was prepared in a total yield of 86.8 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-7-fluoro-2-methylisoindolin-1-one (12.2 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.10 (d, $J = 8.4$ Hz, 2H), 6.94 (d, $J = 8.4$ Hz, 2H), 6.82 - 6.76 (m, 2H), 4.22 (s, 2H), 3.77 - 3.66 (m, 2H), 3.09 (s, 3H), 2.78 - 2.62 (m, 2H), 2.17 (m, 1H), 2.04 - 1.95 (m, 2H),

1.83 - 1.71 (m, 2H). Mass (m/z): 408.2 [M+H]⁺.

Compound 213

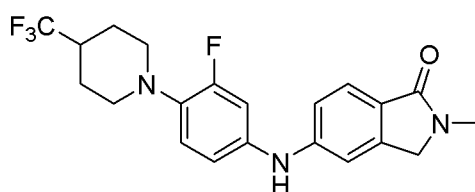
7-chloro-2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **213** (18.6 mg) was prepared in a total yield of 87.9 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-7-chloro-2-methylisoindolin-1-one (13.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.13 - 7.07 (m, 2H), 6.99 - 6.92 (m, 2H), 6.84 - 6.77 (m, 2H), 4.23 (s, 2H), 3.72 - 3.64 (m, 2H), 3.08 (s, 3H), 2.75 - 2.63 (m, 2H), 2.19 (m, 1H), 2.01 - 1.93 (d, J = 3.8 Hz, 2H), 1.80 - 1.66 (m, 2H). Mass (m/z): 424.1 [M+H]⁺.

Compound 214

5-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one

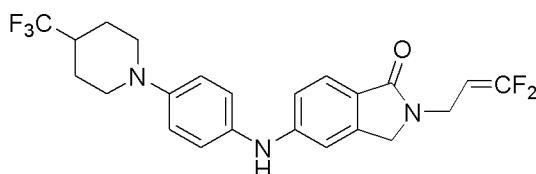


The title compound **214** (16.2 mg) was prepared in a total yield of 79.4 % as a yellow solid from 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (17.0 mg, 0.065 mmol), 5-bromo-2-methylisoindolin-1-one (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, J = 8.4 Hz, 1H), 7.02 - 6.85 (m, 4H), 6.51 (s, 1H), 4.25 (s, 2H), 3.54 - 3.41 (m, 2H), 3.13 (s, 3H), 2.71 - 2.62 (m, 2H), 2.14 (m, 1H), 2.01 - 1.92 (m, 2H), 1.89 - 1.76 (m,

2H). Mass (m/z): 408.2 [M+H]⁺.

Compound 215

2-(3,3-difluoroallyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



5

The title compound **215** (23.5 mg) was prepared in a yield of 12.72% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-(3,3-difluoroallyl)isoindolin-1-one (118 mg, 0.41 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ: 8.35 (s, 1H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.12 – 7.02 (m, 2H), 7.01 – 6.93 (m, 3H), 6.90 (dd, *J* = 8.4, 2.1 Hz, 1H), 4.76 (dtd, *J* = 26.2, 7.7, 2.3 Hz, 1H), 4.30 (s, 2H), 4.07 (dt, *J* = 7.7, 1.9 Hz, 2H), 3.69 (d, *J* = 12.1 Hz, 2H), 2.66 (td, *J* = 12.5, 2.5 Hz, 2H), 2.45 (td, *J* = 12.4, 10.5, 6.3 Hz, 1H), 1.88 (d, *J* = 12.3 Hz, 2H), 1.57 (qd, *J* = 12.5, 4.1 Hz, 2H). ¹⁹F NMR (DMSO-*d*₆) δ: -72.49 (d, *J* = 8.8 Hz), -86.58 (d, *J* = 2.2 Hz), -86.69 (d, *J* = 2.2 Hz), -88.75, -88.84 (d, *J* = 15.8 Hz), -88.93. Mass (m/z): 452.3 [M+H]⁺.

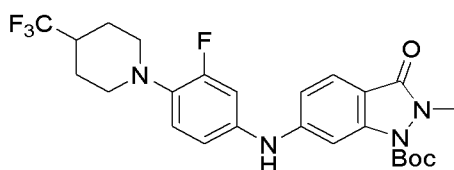
10

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Compound 216

tert-butyl 6-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate

20



25

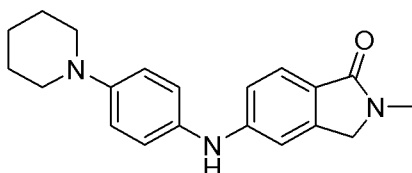
The title compound **216** (18.4 mg) was prepared in a total yield of 72.3% as a yellow solid from 3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (17.0 mg, 0.065 mmol), tert-butyl 6-bromo-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (16.4 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075

mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.57 (d, $J = 8.4$ Hz, 1H), 7.38 (s, 1H), 7.07 - 6.95 (m, 3H), 6.85 (d, $J = 8.4$ Hz, 1H), 3.53 (s, 3H), 3.48 - 3.42 (m, 2H), 2.76 - 2.66 (m, 2H), 2.24 (m, 1H), 2.02 - 1.93 (m, 2H), 1.83 - 1.72 (m, 2H), 1.56 (s, 9H).

5 Mass (m/z): 509.3 $[\text{M}+\text{H}]^+$.

Compound 217

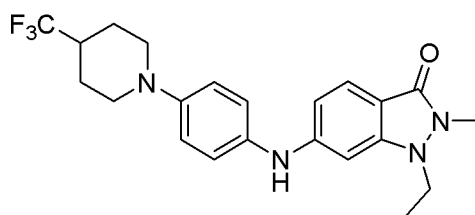
2-methyl-5-((4-(piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **217** (13.6 mg) was prepared in a total yield of 85.0% as a yellow solid from 4-(piperidin-1-yl)aniline (11.4 mg, 0.065 mmol), 5-bromo-2-methylisoindolin-1-one (11.3 mg, 0.05 mmol), $\text{Pd}_2(\text{dba})_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Chloroform- d) δ 7.53 (d, $J = 8.4$ Hz, 1H), 7.04 (d, $J = 8.8$ Hz, 2H), 6.94 - 6.76 (m, 4H), 4.15 (s, 2H), 3.67 - 3.61 (m, 2H), 3.13 - 3.02 (m, 5H), 1.74 - 1.65 (m, 4H), 1.59 - 1.46 (m, 2H). Mass (m/z): 322.2 $[\text{M}+\text{H}]^+$.

Compound 218

1-ethyl-2-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-indazol-3-one



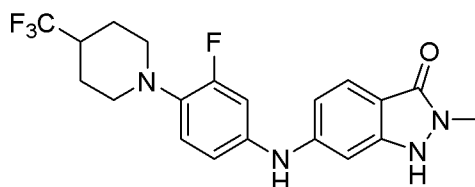
The title compound **218** (17.8 mg) was prepared in a total yield of 85.2% as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-1-ethyl-2-methyl-1,2-dihydro-3H-indazol-3-one (12.8 mg, 0.05 mmol), $\text{Pd}_2(\text{dba})_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.45 (d,

$J = 8.8$ Hz, 1H), 7.06 (d, $J = 8.8$ Hz, 2H), 6.90 (d, $J = 8.8$ Hz, 2H), 6.67 (d, $J = 8.8$ Hz, 1H), 6.59 (s, 1H), 3.72 (q, $J = 6.8$ Hz, 2H), 3.63 - 3.55 (m, 2H), 3.26 (s, 3H), 2.67 - 2.46 (m, 2H), 2.17 (m, 1H), 1.94 - 1.81 (m, 2H), 1.69 - 1.56 (m, 2H), 0.75 (t, $J = 6.8$ Hz, 3H). Mass (m/z): 419.2 [M+H]⁺.

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Compound 219

6-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methyl-1,2-dihydro-3H-indazol-3-one

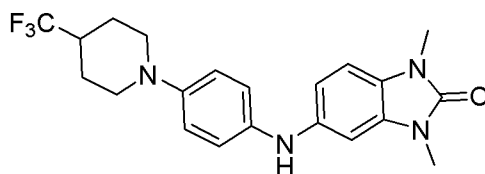


The title compound **219** (8.9 mg) was prepared in a total yield of 87.0 % as a yellow solid from tert-butyl 6-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (12.7 mg, 0.025 mmol) and HCl in 1,4-dioxane according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.52 (d, $J = 8.8$ Hz, 1H), 7.05 - 6.88 (m, 3H), 6.79 - 6.72 (m, 2H), 3.46 - 3.35 (m, 5H), 2.73 - 2.64 (m, 2H), 2.26 (m, 1H), 2.01 - 1.89 (m, 2H), 1.81 - 1.68 (m, 2H). Mass (m/z): 409.2 [M+H]⁺.

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Compound 220

1,3-dimethyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



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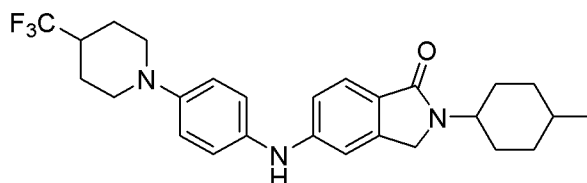
The title compound **220** (32.9 mg) was prepared in a yield of 19.87% as a pale blue powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (99 mg, 0.41 mmol) according to the procedure for compound **1**. ¹H NMR (Methanol-*d*₄) δ 7.13 - 6.85 (m, 8H), 3.61 (dddd, $J = 24.5, 12.6, 5.5, 3.1$ Hz, 4H), 3.15 (pd, $J = 6.7, 4.3$ Hz, 1H), 2.74 - 2.60

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(m, 3H), 2.32 – 2.14 (m, 2H), 1.82 – 1.65 (m, 2H), 1.16 – 1.05 (m, 2H), 0.96 (t, $J = 7.3$ Hz, 1H). Mass (m/z): 405.4 $[M+H]^+$.

Compound 221

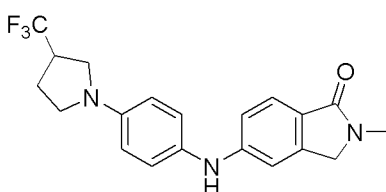
2-(4-methylcyclohexyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **221** (14.6 mg) was prepared in a yield of 7.56% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (100 mg, 0.41 mmol) and 5-bromo-2-(4-methylcyclohexyl)isoindolin-1-one (126 mg, 0.41 mmol) according to the procedure for compound **1**. ^1H NMR (Methanol- d_4) δ 7.86 – 6.26 (m, 7H), 4.07 (s, 2H), 1.97 (d, $J = 17.1$ Hz, 3H), 1.87 – 1.65 (m, 8H), 1.64 – 1.47 (m, 5H), 1.13 (q, $J = 13.9, 13.1$ Hz, 1H), 1.02 (dd, $J = 7.2, 2.4$ Hz, 2H), 0.98 – 0.77 (m, 2H). Mass (m/z): 472.3 $[M+H]^+$.

Compound 222

2-methyl-5-((4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)isoindolin-1-one

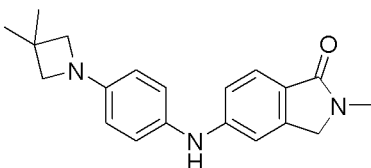


The title compound **222** (17.6 mg) was prepared in a total yield of 21.2% as a white solid from 4-(3-(trifluoromethyl)pyrrolidin-1-yl)aniline (66 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $\text{Pd}_2(\text{dba})_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.18 (s, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 2H), 6.88 – 6.75 (m, 2H), 6.61 (d, $J = 8.4$ Hz, 2H), 4.24 (s, 2H), 3.47 (t, $J = 8.8$ Hz, 1H), 3.39 – 3.33 (m, 1H), 3.32 –

3.23 (m, 3H), 2.95 (s, 3H), 2.25 (dtd, $J = 12.8, 7.6, 5.0$ Hz, 1H), 2.11 – 1.99 (m, 1H). Mass (m/z): 376.3 $[M+H]^+$.

Compound 223

5-((4-(3,3-dimethylazetidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



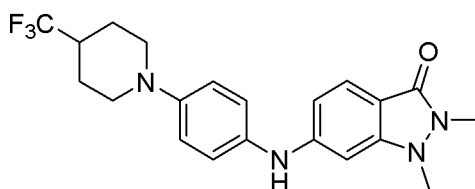
5

The title compound **223** (21.9 mg) was prepared in a total yield of 31.0% as a white solid from 4-(3,3-dimethylazetidin-1-yl)aniline (51 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.21 (s, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 6.98 (d, $J = 8.4$ Hz, 2H), 6.84 – 6.76 (m, 2H), 6.41 – 6.34 (m, 2H), 4.24 (s, 2H), 3.46 (s, 3H), 3.32 (s, 1H), 2.95 (s, 3H), 1.25 (s, 6H). Mass (m/z): 322.3 $[M+H]^+$.

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Compound 224

1,2-dimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-indazol-3-one



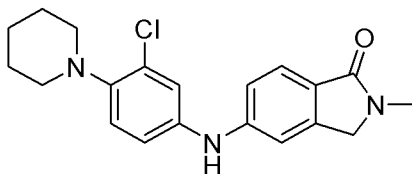
The title compound **224** (13.4 mg) was prepared in a total yield of 66.3 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-1,2-dimethyl-1,2-dihydro-3H-indazol-3-one (12.1 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, $Methanol-d_4$) δ 7.52 (d, $J = 8.8$ Hz, 1H), 7.24 - 6.53 (m, 6H), 3.75 - 3.62 (m, 2H), 3.35 (s, 3H), 3.16 (s, 3H), 2.78 - 2.63 (s, 2H), 2.18 (m, 1H), 2.03 - 1.93 (m, 2H), 1.83 - 1.66

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(m, 2H). Mass (m/z): 405.2 [M+H]⁺.

Compound 225

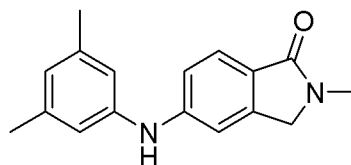
5-((3-chloro-4-(piperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



- 5 The title compound **225** (12.5 mg) was prepared in a total yield of 70.4 % as a yellow solid from 3-chloro-4-(piperidin-1-yl)aniline (13.7 mg, 0.065 mmol), 5-bromo-2-methylisoindolin-1-one (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**.
 10 ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.54 (d, *J* = 8.4 Hz, 1H), 7.17 (s, 1H), 7.09 - 6.93 (m, 4H), 4.30 (s, 2H), 3.11 (s, 3H), 2.95 - 2.87 (m, 4H), 1.77 - 1.67 (m, 4H), 1.60 - 1.51 (m, 2H). Mass (m/z): 356.1 [M+H]⁺.

Compound 226

5-((3,5-dimethylphenyl)amino)-2-methylisoindolin-1-one

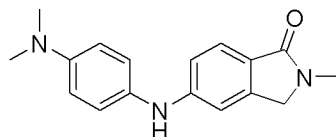


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- The title compound **226** (33.5 mg) was prepared in a total yield of 37.8% as a yellow solid from 3,5-dimethylaniline (52.2 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.53 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.11 (s, 1H), 7.02 (dt, *J* = 8.4, 1.8 Hz, 1H), 6.80 (s, 2H), 6.64 (s, 1H), 4.37 (s, 2H), 3.13 (d, *J* = 1.4 Hz, 3H), 2.26 (d, *J* = 1.3 Hz, 6H). Mass (m/z): 267.2 [M+H]⁺.

Compound 227

- 25 *5-((4-(dimethylamino)phenyl)amino)-2-methylisoindolin-1-one*

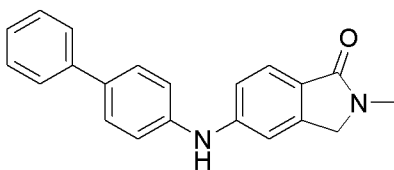


The title compound **227** (41.1 mg) was prepared in a total yield of 43.9% as a yellow solid from *N,N*-dimethyl-*p*-phenylenediamine (58.0 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.48 (d, *J* = 8.3 Hz, 1H), 7.11 – 7.05 (m, 2H), 6.93 – 6.76 (m, 5H), 4.32 (s, 2H), 3.11 (s, 3H), 2.90 (s, 6H). Mass (m/z): 282.2 [M+H]⁺.

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Compound 228

5-([1,1'-biphenyl]-4-ylamino)-2-methylisoindolin-1-one

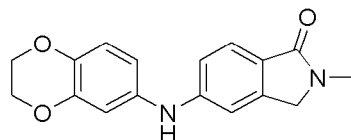


The title compound **228** (33.6 mg) was prepared in a total yield of 32.0% as a yellow solid from 4-aminobiphenyl (73.0 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.62 – 7.54 (m, 5H), 7.44 – 7.37 (m, 2H), 7.31 – 7.21 (m, 4H), 7.12 (dd, *J* = 8.3, 2.0 Hz, 1H), 4.40 (s, 2H), 3.15 (s, 3H). Mass (m/z): 315.3 [M+H]⁺.

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Compound 229

*5-((2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)amino)-2-methylisoindolin-1-one*



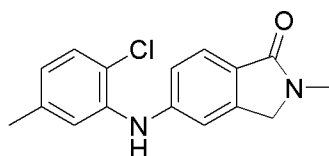
The title compound **229** (47.4 mg) was prepared in a total yield of 32.0% as a yellow solid from 1,4-benzodioxan-6-amine (65.0 mg, 0.43 mmol),

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5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.50 (dd, *J* = 8.3, 0.6 Hz, 1H), 7.00 – 6.97 (m, 1H), 6.92 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.69 – 6.62 (m, 2H), 4.34 (s, 2H), 4.26 – 4.16 (m, 4H), 3.12 (s, 3H). Mass (m/z): 297.2 [M+H]⁺.

Compound 230

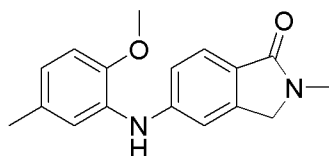
5-((2-chloro-5-methylphenyl)amino)-2-methylisoindolin-1-one



The title compound **230** (38.6 mg) was prepared in a total yield of 41.1% as a yellow solid from 2-Chloro-5-methylaniline (61.0 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.59 – 7.55 (m, 1H), 7.32 – 7.26 (m, 1H), 7.22 (s, 1H), 7.07 – 7.00 (m, 1H), 6.89 – 6.83 (m, 1H), 4.38 (s, 2H), 3.14 (s, 3H), 2.29 (s, 3H). Mass (m/z): 287.1 [M+H]⁺.

Compound 231

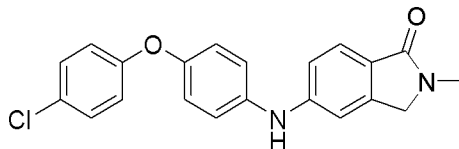
5-((2-methoxy-5-methylphenyl)amino)-2-methylisoindolin-1-one



The title compound **231** (30.6 mg) was prepared in a total yield of 32.9% as a yellow solid from 2-Methoxy-5-methylaniline (59.0 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)₂Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.52 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.13 (d, *J* = 2.1 Hz, 1H), 7.05 – 6.98 (m, 2H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.83 – 6.79 (m, 1H), 4.34 (s, 2H), 3.81 (s, 3H), 3.12 (s, 3H), 2.26 (s, 3H). Mass (m/z): 283.2 [M+H]⁺.

Compound 232

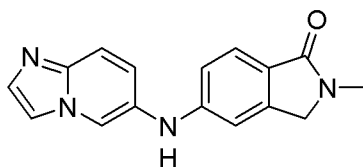
5-((4-(4-chlorophenoxy)phenyl)amino)-2-methylisoindolin-1-one



The title compound **232** (26.5 mg) was prepared in a total yield of 21.9% as a yellow solid from 4-(4-Chlorophenoxy)aniline (94.0 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)₂Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.55 (d, *J* = 8.4 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.24 – 7.19 (m, 2H), 7.12 – 7.09 (m, 2H), 7.04 – 6.92 (m, 5H), 4.37 (s, 2H), 3.13 (s, 3H). Mass (*m/z*): 365.1 [M+H]⁺.

Compound 233

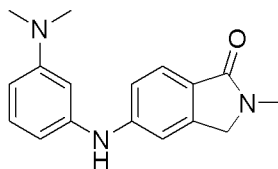
*5-(imidazo[1,2-*a*]pyridin-6-ylamino)-2-methylisoindolin-1-one*



The title compound **233** (31.7 mg) was prepared in a total yield of 34.2% as a yellow solid from imidazo[1,2-*a*]pyridin-6-amine (94.0 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)₂Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (161 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.43 – 8.40 (m, 1H), 7.84 (d, *J* = 1.4 Hz, 1H), 7.64 – 7.55 (m, 3H), 7.34 (dt, *J* = 9.6, 1.9 Hz, 1H), 7.13 – 7.08 (m, 1H), 7.07 – 7.01 (m, 1H), 4.39 (s, 2H), 3.14 (s, 3H). Mass (*m/z*): 279.2 [M+H]⁺.

Compound 234

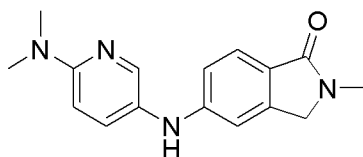
5-((3-(dimethylamino)phenyl)amino)-2-methylisoindolin-1-one



The title compound **234** (34.6 mg) was prepared in a total yield of 36.9% as a yellow solid from *N,N*-dimethyl-*m*-phenylenediamine (58 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol),
 5 Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**.
¹H NMR (400 MHz, Methanol-*d*₄) δ 7.54 – 7.50 (m, 1H), 7.15 – 7.09 (m, 2H), 7.05 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.60 – 6.56 (m, 1H), 6.55 (t, *J* = 2.3 Hz, 1H), 6.47 – 6.41 (m, 1H), 4.36 (s, 2H), 3.13 (s, 3H), 2.91 (d, *J* = 0.8 Hz, 6H). Mass (*m/z*): 282.2 [M+H]⁺.

Compound 235

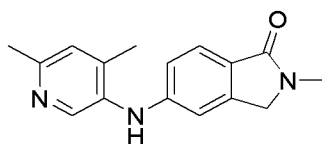
5-((6-(dimethylamino)pyridin-3-yl)amino)-2-methylisoindolin-1-one



The title compound **235** (29.8 mg) was prepared in a total yield of 31.7% as a yellow solid from *N*²,*N*²-dimethylpyridine-2,5-diamine (59 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol),
 Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**.
¹H NMR (400 MHz, Methanol-*d*₄) δ 7.94 (dt, *J* = 2.7, 0.7 Hz, 1H), 7.51 – 7.42 (m, 2H), 6.84 – 6.79 (m, 2H), 6.71 (dt, *J* = 9.0, 0.7 Hz, 1H), 4.32 (s, 2H), 3.11 (s, 3H), 3.07 (s, 6H). Mass (*m/z*): 283.2 [M+H]⁺.

Compound 236

5-((4,6-dimethylpyridin-3-yl)amino)-2-methylisoindolin-1-one

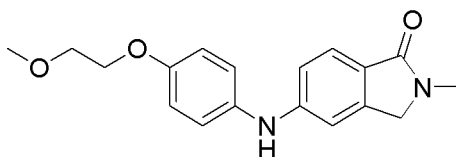


The title compound **236** (21.7 mg) was prepared in a total yield of 24.4%

as a yellow solid from 4,6-dimethylpyridin-3-amine (52 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)₂Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.94 (dt, *J* = 2.7, 0.7 Hz, 1H), 7.51 – 7.42 (m, 2H), 6.84 – 6.79 (m, 2H), 6.71 (dt, *J* = 9.0, 0.7 Hz, 1H), 4.32 (s, 2H), 3.11 (s, 3H), 3.07 (s, 6H). Mass (*m/z*): 268.2 [M+H]⁺.

Compound 237

5-((4-(2-methoxyethoxy)phenyl)amino)-2-methylisoindolin-1-one



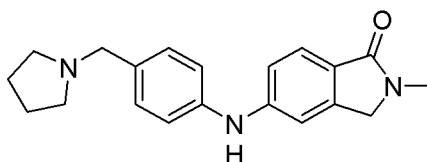
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The title compound **237** (51.0 mg) was prepared in a total yield of 49.0% as a yellow solid from 4-(2-methoxyethoxy)aniline (72 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.15 – 7.06 (m, 2H), 6.98 – 6.85 (m, 5H), 4.32 (s, 2H), 4.14 – 4.04 (m, 2H), 3.76 – 3.72 (m, 2H), 3.42 (s, 3H), 3.11 (s, 3H). Mass (*m/z*): 313.3 [M+H]⁺.

15

Compound 238

2-methyl-5-((4-(pyrrolidin-1-ylmethyl)phenyl)amino)isoindolin-1-one



20

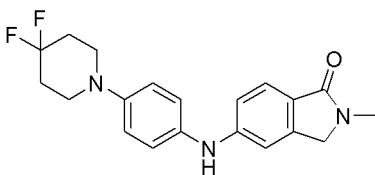
The title compound **238** (24.6 mg) was prepared in a total yield of 23.0% as a yellow solid from 4-(Pyrrolidin-1-ylmethyl)aniline (76 mg, 0.43 mmol), 5-bromo-2-methylisoindolin-1-one (75 mg, 0.33 mmol), Pd(dppf)₂Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.59 (d, *J* = 8.3 Hz, 1H), 7.46 – 7.41

25

(m, 2H), 7.27 – 7.23 (m, 3H), 7.15 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.40 (s, 2H), 4.30 (s, 2H), 3.37 – 3.31 (m, 4H), 3.14 (s, 3H), 2.15 – 2.01 (m, 4H). Mass (m/z): 322.3 $[M+H]^+$.

Compound 239

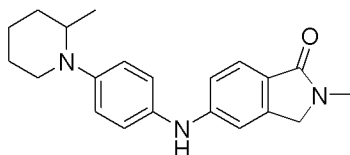
5 *2-methyl-5-((4-(2-methylpiperidin-1-yl)phenyl)amino)isoindolin-1-one*



The title compound **239** (22.7 mg) was prepared in a total yield of 28.7% as a white solid from 4-(4,4-difluoropiperidin-1-yl)aniline (61 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.63 (d, $J = 8.4$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 2.0$ Hz, 1H), 7.19 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.43 (s, 2H), 3.77 (s, 1H), 3.61 (d, $J = 6.4$ Hz, 2H), 3.16 (s, 3H), 2.09 – 1.91 (m, 3H), 1.80 (q, $J = 11.2, 10.0$ Hz, 2H). Mass (m/z): 358.3 $[M+H]^+$.

Compound 240

2-methyl-5-((4-(2-methylpiperidin-1-yl)phenyl)amino)isoindolin-1-one

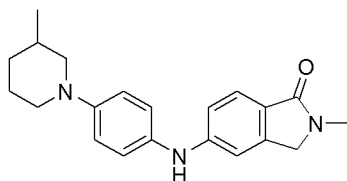


20 The title compound **240** (46.4 mg) was prepared in a total yield of 62.7% as a white solid from 4-(2-methylpiperidin-1-yl)aniline (55 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.63 (d, $J = 8.4$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 2.0$ Hz, 1H), 7.19 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.43 (s, 2H), 3.77 (s, 1H), 3.61 (d, $J = 6.4$ Hz, 2H), 3.16

(s, 3H), 2.16 (d, $J = 10.0$ Hz, 1H), 2.09 – 1.91 (m, 3H), 1.80 (q, $J = 11.2$, 10.0 Hz, 2H), 1.11 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 336.3 $[M+H]^+$.

Compound 241

2-methyl-5-((4-(3-methylpiperidin-1-yl)phenyl)amino)isoindolin-1-one



5

The title compound **241** (32.5 mg) was prepared in a total yield of 43.9% as a white solid from 4-(3-methylpiperidin-1-yl)aniline (55 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**.

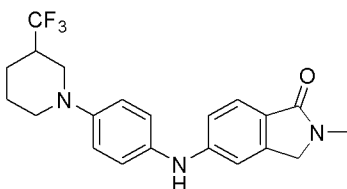
10

^1H NMR (400 MHz, Methanol- d_4) δ 7.63 (d, $J = 8.4$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 2.0$ Hz, 1H), 7.19 (dd, $J = 8.4$, 2.0 Hz, 1H), 4.43 (s, 2H), 3.77 (s, 1H), 3.61 (d, $J = 6.4$ Hz, 2H), 3.16 (s, 3H), 2.16 (d, $J = 10.0$ Hz, 1H), 2.09 – 1.91 (m, 3H), 1.80 (q, $J = 11.2$, 10.0 Hz, 2H), 1.11 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 336.3 $[M+H]^+$.

15

Compound 242

2-methyl-5-((4-(3-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



20

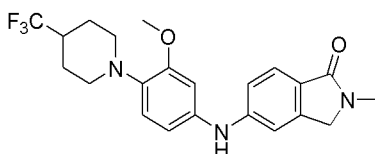
The title compound **242** (16.9 mg) was prepared in a total yield of 19.7% as a white solid from 4-(3-(trifluoromethyl)piperidin-1-yl)aniline (70 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.63 (d, $J = 8.4$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.28 (d, $J = 2.0$ Hz, 1H),

25

7.19 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.43 (s, 2H), 3.77 (s, 1H), 3.61 (d, $J = 6.4$ Hz, 2H), 3.16 (s, 3H), 2.16 (d, $J = 10.0$ Hz, 1H), 2.09 – 1.91 (m, 3H), 1.80 (q, $J = 11.2, 10.0$ Hz, 2H). Mass (m/z): 390.3 $[M+H]^+$.

Compound 243

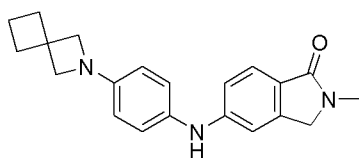
5 5-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one



The title compound **243** (49.0 mg) was prepared in a total yield of 52.9% as a white solid from 3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (79 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Chloroform- d) δ 7.55 (d, $J = 8.0$ Hz, 1H), 6.90 – 6.79 (m, 3H), 6.68 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.62 (d, $J = 2.4$ Hz, 1H), 4.16 (s, 2H), 3.74 (s, 3H), 3.45 (d, $J = 11.2$ Hz, 2H), 3.05 (s, 3H), 2.56 – 2.42 (m, 2H), 2.07 (tdt, $J = 11.6, 7.6, 3.6$ Hz, 1H), 1.92 – 1.75 (m, 4H). Mass (m/z): 420.3 $[M+H]^+$.

Compound 244

20 5-((4-(2-azaspiro[3.3]heptan-2-yl)phenyl)amino)-2-methylisoindolin-1-one

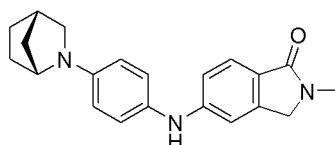


The title compound **244** (35.5 mg) was prepared in a total yield of 48.2% as a white solid from 4-(2-azaspiro[3.3]heptan-2-yl)aniline (54 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Chloroform- d) δ 7.57 (d, $J = 8.4$ Hz, 1H), 7.03 (s, 2H),

6.83 – 6.68 (m, 2H), 6.43 (s, 2H), 5.90 (s, 1H), 4.18 (s, 2H), 3.46 (s, 1H), 3.10 (s, 3H), 2.20 (t, $J = 7.6$ Hz, 4H), 1.93 – 1.83 (m, 2H). Mass (m/z): 334.3 $[M+H]^+$.

Compound 245

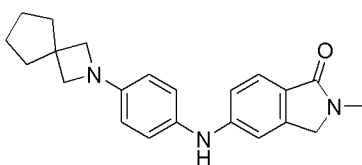
5 5-((4-((1*R*,4*S*)-2-azabicyclo[2.2.1]heptan-2-yl)phenyl)amino)-2-methylisoindolin-1-one



The title compound **245** (32.9 mg) was prepared in a total yield of 44.6% as a white solid from 4-((1*R*,4*S*)-2-azabicyclo[2.2.1]heptan-2-yl)aniline (54 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.52 (m, 1H), 7.03 (s, 2H), 6.73 (s, 3H), 6.52 (s, 1H), 4.17 (s, 3H), 3.47 (s, 1H), 3.10 (s, 3H), 2.59 (s, 1H), 1.85 – 1.64 (m, 4H), 1.50 (s, 1H), 1.41 – 1.31 (m, 1H). Mass (m/z): 334.3 $[M+H]^+$.

Compound 246

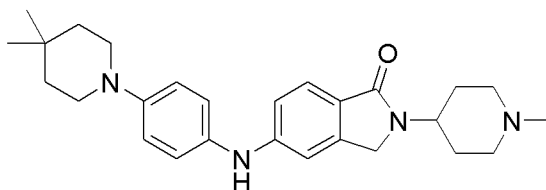
5-((4-(2-azaspiro[3.4]octan-2-yl)phenyl)amino)-2-methylisoindolin-1-one



20 The title compound **246** (35.5 mg) was prepared in a total yield of 43.7% as a purple solid from 4-(2-azaspiro[3.4]octan-2-yl)aniline (56 mg, 0.288 mmol), 5-bromo-2-ethylisoindolin-1-one (50 mg, 0.221 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (109 mg, 0.332 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, $J = 8.4$ Hz, 1H), 7.03 (s, 2H), 6.83 – 6.68 (m, 2H), 6.43 (s, 2H), 5.90 (s, 1H), 4.18 (s, 2H), 3.46 (s, 1H), 3.10 (s, 3H), 2.56 – 2.42 (m, 2H), 2.20 (t, $J = 7.6$ Hz, 4H), 1.93 – 1.83 (m, 2H). Mass (m/z): 348.3 $[M+H]^+$.

Compound 247

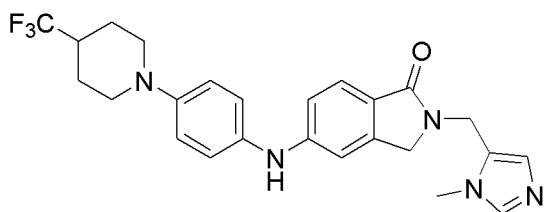
5-((4-(4,4-dimethylpiperidin-1-yl)phenyl)amino)-2-(1-methylpiperidin-4-yl)isoindolin-1-one



- 5 The title compound **247** (24.8 mg) was prepared in a yield of 35.45% as a pale yellow powder from 4-(4,4-dimethylpiperidin-1-yl)aniline (32 mg, 0.16 mmol) and 5-bromo-2-(1-methylpiperidin-4-yl)isoindolin-1-one (50 mg, 0.16 mmol) according to the procedure for compound 1. ¹H NMR (Methanol-*d*₄) δ 7.51 (d, *J* = 8.4 Hz, 1H), 7.11 (s, 2H), 6.97 (d, *J* = 29.5 Hz, 4H), 4.37 (s, 2H), 4.30 (ddt, *J* = 11.9, 8.1, 4.2 Hz, 2H), 3.52 (dt, *J* = 12.4, 2.5 Hz, 2H), 3.22 – 3.00 (m, 5H), 2.82 (s, 3H), 2.16 (qd, *J* = 13.1, 4.0 Hz, 2H), 2.08 – 1.96 (m, 2H), 1.55 (t, *J* = 5.7 Hz, 4H), 1.00 (s, 6H). Mass (*m/z*): 433.5 [M+H]⁺.

Compound 248

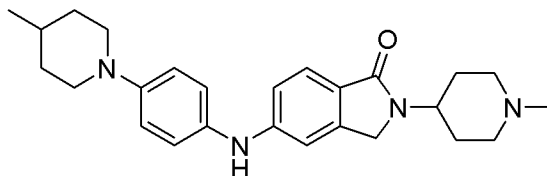
- 15 *2-((1-methyl-1H-imidazol-5-yl)methyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one*



- The title compound **248** (24.5 mg) was prepared in a yield of 25.49% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-2-((1-methyl-1H-imidazol-5-yl)methyl)isoindolin-1-one (63 mg, 0.20 mmol) according to the procedure for compound 1. ¹H NMR (Methanol-*d*₄) δ 7.94 (s, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.18 – 7.09 (m, 3H), 7.05 – 6.94 (m, 4H), 4.83 (s, 2H), 4.26 (s, 2H), 3.74 (s, 5H), 2.71 (t, *J* = 12.0 Hz, 2H), 2.35 (dtd, *J* = 12.3, 8.4, 3.8 Hz, 1H), 1.98 (d, *J* = 13.1 Hz, 2H), 1.71 (qd, *J* = 12.5, 4.1 Hz, 2H). Mass (*m/z*): 470.3 [M+H]⁺.

Compound 249

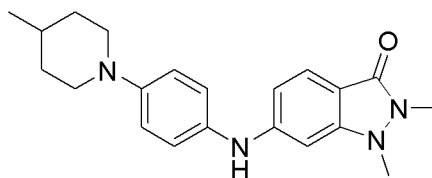
5-((4-(4-methylpiperidin-1-yl)phenyl)amino)-2-(1-methylpiperidin-4-yl)isoindolin-1-one



- 5 The title compound **249** (19.6 mg) was prepared in a yield of 28.96% as a pale yellow powder from 4-(4-methylpiperidin-1-yl)aniline (30 mg, 0.16 mmol) and 5-bromo-2-(1-methylpiperidin-4-yl)isoindolin-1-one (50 mg, 0.16 mmol) according to the procedure for compound **1**. ¹H NMR (Methanol-*d*₄) δ: 7.51 (d, *J* = 8.4 Hz, 1H), 7.14 – 7.08 (m, 2H), 7.05 – 6.97 (m, 3H), 6.94 (dd, *J* = 8.5, 2.0 Hz, 1H), 4.37 (s, 2H), 4.28 (ddt, *J* = 11.9, 8.3, 4.0 Hz, 1H), 3.55 (d, *J* = 12.0 Hz, 2H), 3.45 (d, *J* = 12.6 Hz, 2H), 2.96 (td, *J* = 12.6, 2.9 Hz, 2H), 2.76 (s, 3H), 2.65 (s, 2H), 2.13 (qd, *J* = 12.8, 3.7 Hz, 2H), 2.05 – 1.94 (m, 2H), 1.76 (dd, *J* = 13.0, 3.0 Hz, 2H), 1.61 – 1.42 (m, 1H), 1.44 – 1.25 (m, 3H), 0.99 (d, *J* = 6.4 Hz, 3H). Mass (*m/z*): 419.3
- 15 [M+H]⁺.

Compound 250

1,2-dimethyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-indazol-3-one

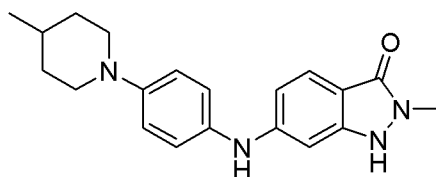


- 20 The title compound **250** (15.6 mg) was prepared in a total yield of 89.1 % as a yellow solid from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 6-bromo-1,2-dimethyl-1,2-dihydro-3H-indazol-3-one (12.1 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (300 MHz, Chloroform-*d*) δ 7.46 (m, 1H), 7.15 - 6.45 (m, 6H), 3.83 (s, 3H), 3.63 - 3.45 (m, 2H), 3.05 (s, 3H), 2.76 - 2.48 (m,
- 25

2H), 1.76 - 1.28 (m, 5H), 0.90 (d, $J = 5.7$ Hz, 3H). Mass (m/z): 351.2 [M+H]⁺.

Compound 251

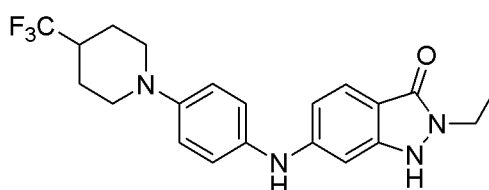
2-methyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-indazol-3-one



The title compound **251** (30.7 mg) was prepared in a total yield of 91.1 % as a yellow solid from tert-butyl 2-methyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (43.6 mg, 0.1 mmol) and HCl in 1,4-dioxane according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.71 - 7.59 (m, 3H), 7.41 - 7.33 (m, 2H), 7.01 - 6.94 (m, 2H), 3.72 - 3.61 (m, 7H), 2.13 - 2.01 (m, 2H), 1.91 (m, 1H), 1.83 - 1.72 (m, 2H), 1.10 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 337.2 [M+H]⁺.

Compound 252

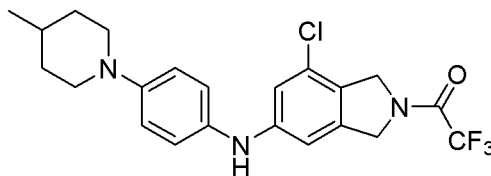
2-ethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-indazol-3-one



The title compound **252** (18.3 mg) was prepared in a total yield of 90.6 % as a yellow solid from tert-butyl 2-ethyl-3-oxo-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-1H-indazole-1-carboxylate (25.2 mg, 0.05 mmol) and HCl in 1,4-dioxane according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.68 - 7.60 (m, 3H), 7.38 - 7.33 (m, 2H), 7.00 - 6.90 (m, 2H), 3.98 (q, $J = 7.2$ Hz, 2H), 3.85 - 3.65 (m, 4H), 2.80 (m, 1H), 2.34 - 2.26 (m, 2H), 2.23 - 2.11 (m, 2H), 1.37 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 405.2 [M+H]⁺.

Compound 253

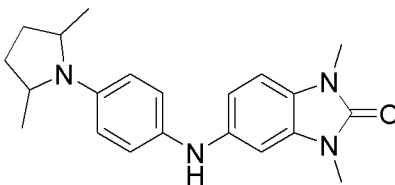
1-(4-chloro-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)isoindolin-2-yl)-2,2,2-trifluoroethan-1-one



- 5 The title compound **253** (19.1 mg) was prepared in a total yield of 87.4 % as a red solid from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 1-(6-bromo-4-chloroisoindolin-2-yl)-2,2,2-trifluoroethan-1-one (16.4 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the
10 procedure for compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.33 - 6.78 (m, 6H), 4.90 (s, 2H), 4.78 (s, 2H), 3.74 - 3.65 (m, 2H), 2.79 - 2.67 (m, 2H), 1.91 - 1.70 (m, 2H), 1.55 (m, 1H), 1.47 - 1.36 (m, 2H), 1.02 (d, *J* = 6.4 Hz, 3H). Mass (m/z): 438.1 [M+H]⁺.

Compound 254

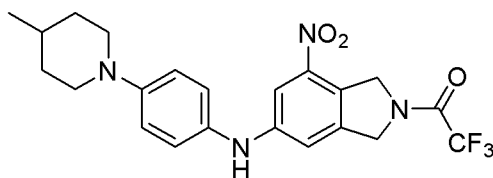
- 15 *5-((4-(2,5-dimethylpyrrolidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one*



- The title compound **254** (13.4 mg) was prepared in a total yield of 76.4 % as a white solid from 4-(2,5-dimethylpyrrolidin-1-yl)aniline (12.4 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.61 - 6.57 (m, 7H), 3.55 - 3.51 (m, 2H), 3.45 (s, 3H), 3.37 (s, 3H), 2.16 - 1.67 (m, 4H), 1.15 (d, *J* =
25 6.4 Hz, 6H). Mass (m/z): 351.2 [M+H]⁺.

Compound 255

2,2,2-trifluoro-1-(6-((4-(4-methylpiperidin-1-yl)phenyl)amino)-4-nitroisindolin-2-yl)ethan-1-one

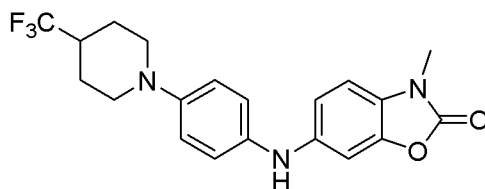


The title compound **255** (18.7 mg) was prepared in a total yield of 83.5 %
 5 as a red solid from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 1-(6-bromo-4-nitroisindolin-2-yl)-2,2,2-trifluoroethan-1-one (16.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.65 - 6.81
 10 (m, 6H), 4.94 (s, 2H), 4.79 (s, 2H), 3.51 - 3.40 (m, 2H), 2.72 - 2.66 (m, 2H), 1.79 - 1.68 (m, 2H), 1.48 (m, 1H), 1.43 - 1.31 (m, 2H), 0.99 (d, *J* = 6.4 Hz, 3H). Mass (*m/z*): 449.3 [M+H]⁺.

Compound 256

6-((4-(2,5-dimethylpyrrolidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

15

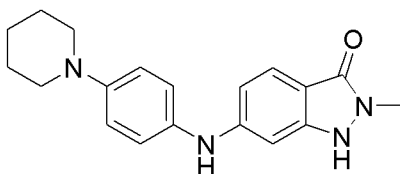


The title compound **256** (11.3 mg) was prepared in a total yield of 66.7 %
 as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (11.4 mg, 0.05
 20 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.21 - 6.78 (m, 7H), 3.68 - 3.57 (m, 2H), 3.35 (s, 3H), 2.75 - 2.57 (m, 2H), 2.27 (m, 1H), 2.03 - 1.93 (m, 2H), 1.83 - 1.67 (m, 2H). Mass (*m/z*): 392.1 [M+H]⁺.

25

Compound 257

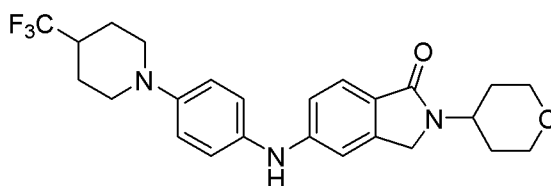
2-methyl-6-((4-(piperidin-1-yl)phenyl)amino)-1,2-dihydro-3H-

indazol-3-one

The title compound **257** (28.7 mg) was prepared in a total yield of 88.9 % as a white solid from tert-butyl 2-methyl-3-oxo-6-((4-(piperidin-1-yl)phenyl)amino)-2,3-dihydro-1H-indazole-1-carboxylate (42.2 mg, 0.1 mmol) and HCl according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.61 - 6.81 (m, 7H), 3.26 (s, 3H), 2.96 - 2.85 (m, 4H), 1.93 - 1.74 (m, 4H), 1.68 - 1.57 (m, 2H). Mass (m/z): 323.2 [M+H]⁺.

Compound 258

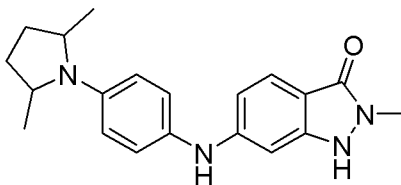
2-(tetrahydro-2H-pyran-4-yl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **258** (10.4 mg) was prepared in a yield of 11.06% as a pale yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-2-(tetrahydro-2H-pyran-4-yl)isoindolin-1-one (60 mg, 0.20 mmol) according to the procedure for compound **1**. ¹H NMR (DMSO-*d*₆) δ 8.30 (s, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.9 Hz, 2H), 6.95 (dd, J = 9.0, 2.5 Hz, 3H), 6.89 (dd, J = 8.3, 2.0 Hz, 1H), 4.30 (s, 2H), 4.24 - 4.12 (m, 2H), 3.95 - 3.87 (m, 2H), 3.68 (d, J = 12.3 Hz, 2H), 3.42 (t, J = 11.6 Hz, 2H), 2.62 (s, 2H), 1.88 (d, J = 13.2 Hz, 2H), 1.82 - 1.68 (m, 2H), 1.64 - 1.51 (m, 4H). Mass (m/z): 460.3 [M+H]⁺.

Compound 259

6-((4-(2,5-dimethylpyrrolidin-1-yl)phenyl)amino)-2-methyl-1,2-dihydro-3H-indazol-3-one

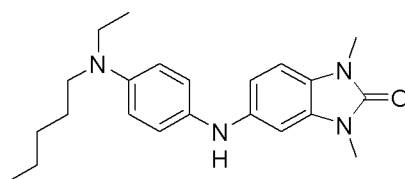


The title compound **259** (30.7 mg) was prepared in a total yield of 91.1 % as a white solid from tert-butyl 6-((4-(2,5-dimethylpyrrolidin-1-yl)phenyl)amino)-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate

- 5 (43.6 mg, 0.1 mmol) and HCl according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.77 - 7.18 (m, 5H), 6.89 - 6.78 (m, 2H), 4.04 - 3.83 (m, 2H), 3.37 (s, 3H), 2.37 - 2.31 (m, 2H), 1.98 - 1.89 (m, 2H), 1.25 (d, J = 6.4 Hz, 6H). Mass (m/z): 337.2 $[\text{M}+\text{H}]^+$.

Compound 260

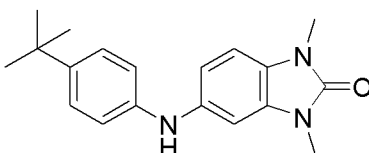
- 10 5-((4-(ethyl(pentyl)amino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **260** (11.3 mg) was prepared in a total yield of 12.3% as a yellow solid from N^1 -ethyl- N^1 -pentylbenzene-1,4-diamine (67 mg, 0.33 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), Pd(dppf)Cl₂ (3.7 mg, 5 μ mol), Xantphos (5.8 mg, 10.0 μ mol), and Cs₂CO₃ (122 mg, 0.38 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.72 - 6.81 (m, 8H), 3.65-3.29 (m, 10H), 1.49 - 1.15 (m, 4H), 1.07 - 0.99 (m, 2H), 0.93- 0.77 (m, 20 6H). Mass (m/z): 367.3 $[\text{M}+\text{H}]^+$.

Compound 261

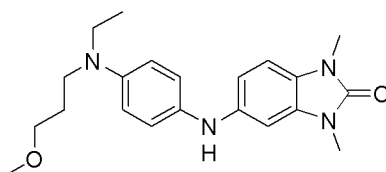
5-((4-(tert-butyl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **261** (39.9 mg) was prepared in a total yield of 31.0 % as a white solid from 4-(tert-butyl)aniline (80 mg, 0.542 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (100 mg, 0.417 mmol), Pd₂(dba)₃ (4 mg, 0.004 mmol), X-phos (12 mg, 0.02 mmol), Cs₂CO₃ (205 mg, 0.625 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.92 (s, 1H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 2.0 Hz, 1H), 6.78 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.28 (d, *J* = 7.6 Hz, 6H), 1.24 (s, 9H). Mass (m/z): 310.3 [M+H]⁺.

Compound 262

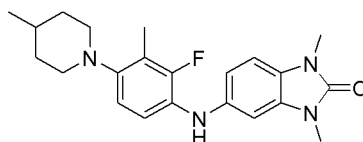
5-((4-(ethyl(3-methoxypropyl)amino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **262** (8.3 mg) was prepared in a total yield of 6.8% as a gray powder from *N*¹-ethyl-*N*¹-(3-methoxypropyl)benzene-1,4-diamine (89 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 umol), Xantphos (7.6 mg, 13.2 umol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.75 – 6.69 (m, 8H), 3.65– 3.29 (m, 15H), 1.10 – 1.02 (m, 2H), 0.93– 0.77 (m, 3H). Mass (m/z): 369.2 [M+H]⁺.

Compound 263

5-((2-fluoro-3-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

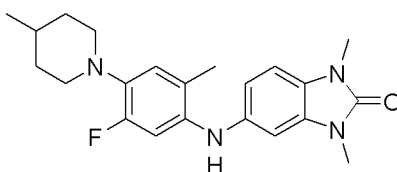


The title compound **263** (21.4 mg) was prepared in a total yield of 16.9% as a pink powder from 2-fluoro-3-methyl-4-(4-methylpiperidin-1-yl)aniline

(95 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (301 MHz, Methanol-*d*₄) δ 7.27 – 6.91 (m, 5H), 3.69 – 3.49 (m, 4H), 3.42 (s, 3H), 3.39 (s, 3H), 2.43 (s, 3H), 2.10 – 1.97 (m, 2H), 1.89 – 1.71 (m, 3H), 1.09 (d, *J* = 5.9 Hz, 3H). Mass (*m/z*): 383.3 [M+H]⁺.

Compound 264

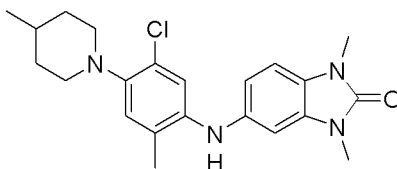
5-((5-fluoro-2-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **264** (12.1 mg) was prepared in a total yield of 10.0% as a light pink powder from 5-fluoro-2-methyl-4-(4-methylpiperidin-1-yl)aniline (95 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (300 MHz, Methanol-*d*₄) δ 6.99 (d, *J* = 8.2 Hz, 1H), 6.89 (d, *J* = 9.6 Hz, 1H), 6.79 – 6.67 (m, 3H), 3.39 (s, 3H), 3.35 (s, 3H), 3.27 (s, 2H), 2.65 (t, *J* = 11.3 Hz, 2H), 2.19 (s, 3H), 1.79 – 1.71 (m, 2H), 1.50 – 1.37 (m, 3H), 1.00 (d, *J* = 6.0 Hz, 3H). Mass (*m/z*): 383.3 [M+H]⁺.

Compound 265

5-((5-chloro-2-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

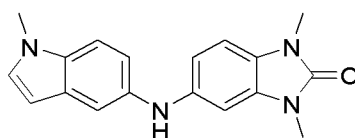


The title compound **265** (28.9 mg) was prepared in a total yield of 21.8%

as a white powder from 5-chloro-2-methyl-4-(4-methylpiperidin-1-yl) aniline (102 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 umol), Xantphos (7.6 mg, 13.2 umol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (300 MHz, Methanol-*d*₄) δ 7.14 – 6.94 (m, 3H), 6.72 – 6.65 (m, 2H), 3.39 (s, 3H), 3.34 (s, 3H), 3.24 (d, *J* = 11.4 Hz, 2H), 2.62 (t, *J* = 11.4 Hz, 2H), 2.20 (s, 3H), 1.77 – 1.70 (m, 2H), 1.49 – 1.37 (m, 3H), 1.01 (d, *J* = 5.9 Hz, 4H). Mass (m/z): 399.3 [M+H]⁺.

Compound 266

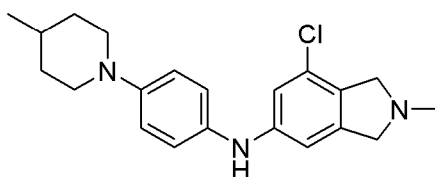
1,3-dimethyl-5-((1-methyl-1H-indol-5-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **266** (28.9 mg) was prepared in a total yield of 21.8% as a white powder from 1-methyl-1H-indol-5-amine (63 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd(dppf)Cl₂ (4.8 mg, 6.6 umol), Xantphos (7.6 mg, 13.2 umol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.31 (d, *J* = 7.0 Hz, 1H), 7.30 (s, 1H), 7.12 (d, *J* = 3.0 Hz, 1H), 7.02 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.76 (d, *J* = 2.1 Hz, 1H), 6.33 (dd, *J* = 3.0, 0.8 Hz, 1H), 3.80 (s, 3H), 3.39 (s, 3H), 3.34 (s, 3H). Mass (m/z): 307.3 [M+H]⁺.

Compound 267

7-chloro-2-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)isoindolin-5-amine



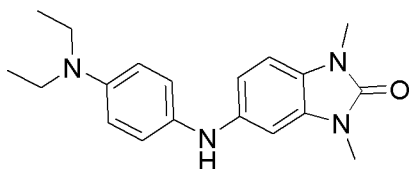
The title compound **267** (12.6 mg) was prepared in a total yield of 70.8 %

as a dim gray powder from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 6-bromo-4-chloro-2-methylisoindoline (12.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1.

¹H NMR (400 MHz, Methanol-*d*₄) δ 7.29 (s, 1H), 7.14 - 6.86 (m, 5H), 4.30 (s, 2H), 4.24 (s, 2H), 3.65 - 3.53 (m, 2H), 2.88 (s, 3H), 2.73 - 2.59 (m, 2H), 1.85 - 1.73 (m, 2H), 1.52 (m, 1H), 1.44 - 1.27 (m, 2H), 1.00 (d, *J* = 6.4 Hz, 3H). Mass (m/z): 356.2 [M+H]⁺.

Compound 268

5-((4-(diethylamino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

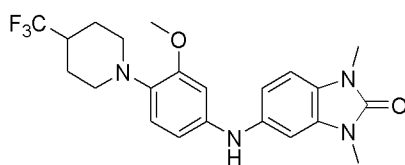


The title compound **268** (14.1 mg) was prepared in a yield of 14.28% as a pale yellow powder from N¹,N¹-diethylbenzene-1,4-diamine (50 mg, 0.30 mmol) and 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (73 mg, 0.30 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 8.41 (s, 1H), 7.61 (s, 1H), 7.40 (s, 1H), 7.06 (s, 2H), 6.97 (s, 1H), 6.52 (s, 1H), 3.53 (m, 4H), 1.24 (s, 6H), 1.17 (d, *J* = 12.0 Hz, 6H). Mass (m/z): 325.6 [M+H]⁺.

20

Compound 269

5-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

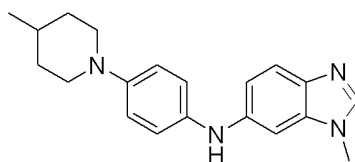


The title compound **269** (27.1 mg) was prepared in a total yield of 15.0 % as a white solid from 3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (148 mg, 0.542 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (100 mg, 0.417 mmol), Pd₂(dba)₃ (4 mg, 0.004

mmol), X-phos (12 mg, 0.02 mmol), Cs₂CO₃ (205 mg, 0.625 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.0 Hz, 1H), 6.90 – 6.79 (m, 3H), 6.68 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.62 (d, *J* = 2.4 Hz, 1H), 3.89 (d, *J* = 7.6 Hz, 6H), 3.74 (s, 3H), 3.45 (d, *J* = 11.2 Hz, 2H), 2.56 – 2.42 (m, 2H), 2.07 (tdt, *J* = 11.6, 7.6, 3.6 Hz, 1H), 1.92 – 1.75 (m, 4H). Mass (m/z): 435.3 [M+H]⁺.

Compound 270

1-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-1H-benzo[d]imidazol-6-amine



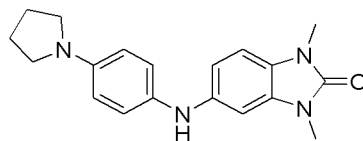
10

The title compound **270** (19.4 mg) was prepared in a total yield of 12.1% as a gray solid from 4-(4-methylpiperidin-1-yl)aniline (124 mg, 0.65 mmol), 6-bromo-1-methyl-1H-1,3-benzodiazole (105 mg, 0.50 mmol), Pd(dppf)Cl₂ (7.3 mg, 10 μmol), Xantphos (11.6 mg, 20 μmol), and Cs₂CO₃ (245 mg, 0.75 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.21 (s, 1H), 7.89 (s, 1H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.08 – 7.00 (m, 3H), 6.98 – 6.82 (m, 3H), 3.77 (s, 3H), 3.55 – 3.48 (m, 2H), 2.61 – 2.52 (m, 2H), 1.73 – 1.65 (m, 2H), 1.53 – 1.38 (m, 1H), 1.31 – 1.20 (m, 2H), 0.95 (d, *J* = 6.5 Hz, 3H). Mass (m/z): 321.3 [M+H]⁺.

20

Compound 271

1,3-dimethyl-5-((4-(pyrrolidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



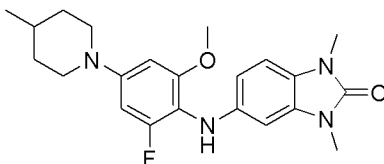
The title compound **271** (19.4 mg) was prepared in a total yield of 12.1% as a gray solid from 4-(pyrrolidin-1-yl)aniline (73 mg, 0.45 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd(dppf)₂Cl₂ (4.8 mg, 6.6 μmol), Xantphos (7.6 mg, 13.2 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for

25

compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.86 – 6.01 (m, 8H), 3.56 – 3.33 (m, 8H), 3.30 – 3.14 (m, 2H), 2.11 – 1.89 (m, 4H). Mass (m/z): 323.2 $[\text{M}+\text{H}]^+$.

Compound 272

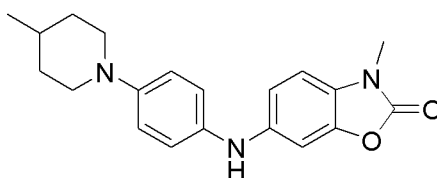
5 *5-((2-fluoro-6-methoxy-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one*



The title compound **272** (2.4 mg) was prepared in a total yield of 2.1% as a gray solid from 2-fluoro-6-methoxy-4-(4-methylpiperidin-1-yl)aniline (90 mg, 0.38 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (70 mg, 0.29 mmol), Pd(dppf)Cl₂ (4.2 mg, 5.8 μmol), Xantphos (6.7 mg, 11.6 μmol), and Cs₂CO₃ (142 mg, 0.44 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.18 – 6.84 (m, 3H), 6.73 – 6.45 (m, 2H), 4.00 – 3.89 (m, 2H), 3.49 – 3.36 (m, 5H), 3.35 (s, 3H), 3.34 (s, 3H), 2.13 – 1.98 (m, 2H), 1.88 – 1.76 (m, 1H), 1.68 – 1.57 (m, 2H), 1.10 (d, J = 6.3 Hz, 3H). Mass (m/z): 399.3 $[\text{M}+\text{H}]^+$.

Compound 273

3-methyl-6-((4-(4-methylpiperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one

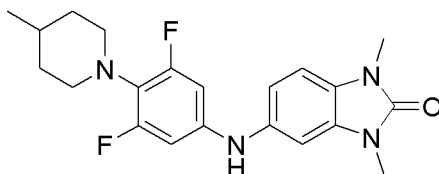


The title compound **273** (12.6 mg) was prepared in a total yield of 70.8 % as a dim gray powder from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (11.4 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.58 – 6.64 (m, 7H), 3.53

- 3.37 (m, 2H), 3.26 (s, 3H), 2.77 - 2.63 (m, 2H), 1.87 - 1.72 (m, 2H), 1.55 (m, 1H), 1.46 - 1.29 (m, 2H), 1.01 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 338.3 $[M+H]^+$.

Compound 274

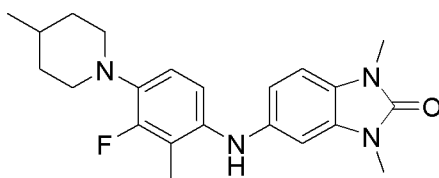
5 5-((3,5-difluoro-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **274** (15.2 mg) was prepared in a total yield of 78.6 % as a violet solid from 3,5-difluoro-4-(4-methylpiperidin-1-yl)aniline (14.7 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.01 - 6.65 (m, 5H), 3.65 - 3.56 (m, 2H), 3.39 (s, 3H), 3.35 (s, 3H), 2.76 - 2.61 (m, 2H), 1.81 - 1.73 (m, 2H), 1.54 (m, 1H), 1.48 - 1.35 (m, 3H), 1.01 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 387.2 $[M+H]^+$.

Compound 275

5-((3-fluoro-2-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

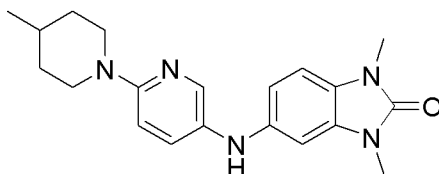


20 The title compound **275** (15.2 mg) was prepared in a total yield of 78.6 % as a violet solid from 3-fluoro-2-methyl-4-(4-methylpiperidin-1-yl)aniline (14.4 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 6.97 (d, $J = 8.4$ Hz, 1H),

6.87 - 6.82 (m, 2H), 6.69 - 6.64 (m, 2H), 3.67 - 3.55 (m, 2H), 3.38 (s, 3H), 3.33 (s, 3H), 2.70 - 2.59 (m, 2H), 2.14 (s, 3H), 1.80 - 1.72 (m, 2H), 1.58 - 1.35 (m, 3H), 1.01 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 383.2 [M+H]⁺.

Compound 276

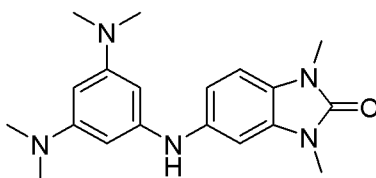
5 *1,3-dimethyl-5-((6-(4-methylpiperidin-1-yl)pyridin-3-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one*



The title compound **276** (14.3 mg) was prepared in a total yield of 81.3 % as a white solid from 6-(4-methylpiperidin-1-yl)pyridin-3-amine (12.4 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.51 (d, $J = 2.0$ Hz, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 6.94 - 6.58 (m, 4H), 4.14 - 4.05 (m, 2H), 3.31 (s, 3H), 3.26 (s, 3H), 2.72 - 2.64 (m, 2H), 1.71 - 1.64 (m, 2H), 1.58 (m, 1H), 1.52 - 1.43 (m, 2H), 1.11 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 352.2 [M+H]⁺.

Compound 277

5-((3,5-bis(dimethylamino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

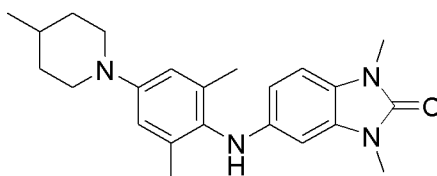


20 The title compound **277** (13.3 mg) was prepared in a total yield of 78.5 % as a gray solid from N¹,N¹,N³,N³-tetramethylbenzene-1,3,5-triamine (11.6 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.44 - 6.57 (m, 6H), 3.39

(s, 3H), 3.36 (s, 3H), 3.22 (s, 12H). Mass (m/z): 340.2 [M+H]⁺.

Compound 278

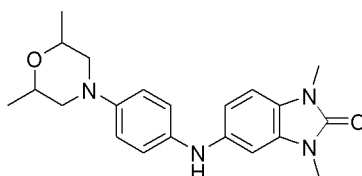
5-((2,6-dimethyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **278** (12.4 mg) was prepared in a total yield of 65.6 % as a gray solid from 2,6-dimethyl-4-(4-methylpiperidin-1-yl)aniline (14.2 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.33 - 7.05 (m, 2H), 6.83 (s, 1H), 6.26 (s, 1H), 6.05 (s, 1H), 3.66 - 3.54 (m, 4H), 3.23 (s, 3H), 3.19 (s, 3H), 2.14 (s, 6H), 1.97 - 1.86 (m, 2H), 1.70 (m, 1H), 1.49 - 1.39 (m, 2H), 0.98 (d, *J* = 6.4 Hz, 3H). Mass (m/z): 379.3 [M+H]⁺.

Compound 279

5-((4-(2,6-dimethylmorpholino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

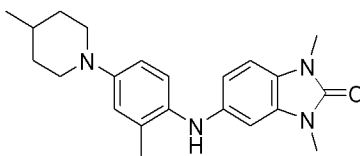


The title compound **279** (9.8 mg) was prepared in a total yield of 12.9 % as a blue solid from 4-(2,6-dimethylmorpholino)aniline (56 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.07 - 6.76 (m, 7H), 3.82 (ddt, *J* = 12.8, 6.4, 3.2 Hz, 2H), 3.44 (s, 2H), 3.40 (s, 3H), 3.36 (s, 3H), 2.38 - 2.21 (m, 2H), 1.24 (d, *J* = 6.4 Hz, 6H). Mass (m/z):

367.3 [M+H]⁺.

Compound 280

1,3-dimethyl-5-((2-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



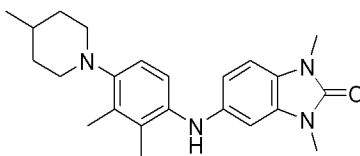
5

The title compound **280** (9.2 mg) was prepared in a total yield of 12.1 % as a blue solid from 2-methyl-4-(4-methylpiperidin-1-yl)aniline (55 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.00 – 6.88 (m, 3H), 6.59 – 6.49 (m, 2H), 3.38 (s, 3H), 3.34 (s, 3H), 3.03 (d, *J* = 11.8 Hz, 2H), 2.79 (t, *J* = 12.4 Hz, 1H), 2.63 (t, *J* = 11.6 Hz, 2H), 2.29 (s, 3H), 1.01 (dd, *J* = 14.8, 6.4 Hz, 4H), 1.02 (d, *J* = 6.0 Hz, 3H). Mass (*m/z*): 365.3 [M+H]⁺.

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Compound 281

5-((2,3-dimethyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



20

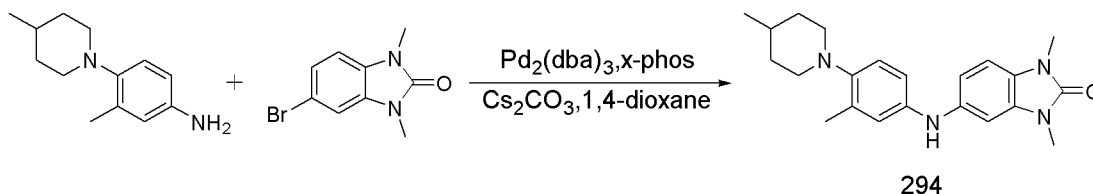
The title compound **281** (5.0 mg) was prepared in a total yield of 6.4 % as a yellow solid from 2,3-dimethyl-4-(4-methylpiperidin-1-yl)aniline (59 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.00 – 6.88 (m, 3H), 6.59 – 6.49 (m, 2H), 3.38 (s, 3H), 3.34 (s, 3H), 3.03 (d, *J* = 11.8 Hz, 2H), 2.79 (t, *J* = 12.4 Hz, 1H), 2.63 (t, *J* =

25

11.6 Hz, 2H), 2.29 (s, 3H), 2.16 (s, 3H), 1.01 (dd, $J = 14.8, 6.4$ Hz, 4H), 1.02 (d, $J = 6.0$ Hz, 3H). Mass (m/z): 379.3 $[M+H]^+$.

Compound 282

1,3-dimethyl-5-((3-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



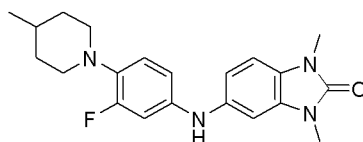
The title compound **282** (8.7 mg) was prepared in a total yield of 11.5 % as a yellow solid from 3-methyl-4-(4-methylpiperidin-1-yl)aniline (55 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.00 – 6.88 (m, 3H), 6.59 – 6.49 (m, 2H), 3.38 (s, 3H), 3.34 (s, 3H), 3.03 (d, $J = 11.8$ Hz, 2H), 2.79 (t, $J = 12.4$ Hz, 1H), 2.63 (t, $J =$ 11.6 Hz, 2H), 2.16 (s, 3H), 1.01 (dd, $J = 14.8, 6.4$ Hz, 4H), 1.02 (d, $J = 6.0$ Hz, 3H). Mass (m/z): 365.3 $[M+H]^+$.

10

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Compound 283

5-((3-fluoro-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **283** (3.9 mg) was prepared in a total yield of 5.1 % as a yellow solid from 3-fluoro-4-(4-methylpiperidin-1-yl)aniline (56 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.07 – 7.03 (m, 1H), 6.98 (t, $J = 9.3$ Hz, 1H), 6.90 (dd, $J =$

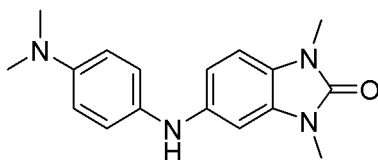
25

6.4, 2.4 Hz, 2H), 6.79 – 6.72 (m, 2H), 3.42 (s, 3H), 3.39 (s, 3H), 2.66 (t, J = 11.2 Hz, 2H), 2.21 (t, J = 7.6 Hz, 1H), 2.05 (d, J = 6.0 Hz, 1H), 1.76 (d, J = 12.4 Hz, 2H), 1.48 – 1.39 (m, 3H), 1.02 (d, J = 6.0 Hz, 3H). Mass (m/z): 369.3 $[M+H]^+$.

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Compound 284

5-((4-(dimethylamino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

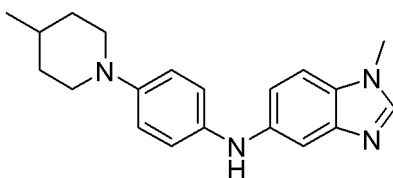


The title compound **284** (12.1 mg) was prepared in a yield of 11.12% as a gray powder from N^1,N^1 -dimethylbenzene-1,4-diamine (50 mg, 0.37 mmol) and 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (88 mg, 0.37 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, DMSO- d_6) δ 7.42 (s, 1H), 6.93 (s, 3H), 6.66 (s, 5H), 3.22 (s, 6H), 2.81 (s, 6H). Mass (m/z): 297.5 $[M+H]^+$.

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Compound 285

1-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-1H-benzo[d]imidazol-5-amine



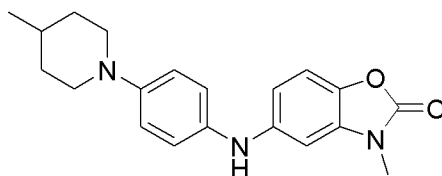
The title compound **285** (14.0 mg) was prepared in a yield of 16.63% as a violet powder from 4-(4-methylpiperidin-1-yl)aniline (50 mg, 0.26 mmol) and 5-bromo-1-methyl-1H-benzo[d]imidazole (55 mg, 0.26 mmol) according to the procedure for compound 1. ^1H NMR (DMSO- d_6) δ 8.08 (s, 1H), 7.84 (s, 1H), 7.51 (s, 1H), 6.95 (d, J = 58.4 Hz, 6H), 3.74 (s, 3H), 3.50 (s, 2H), 2.56 (s, 1H), 1.69 (s, 2H), 1.45 (s, 1H), 1.24 (s, 3H), 0.94 (d, J = 6.4 Hz, 3H). Mass (m/z): 321.6 $[M+H]^+$.

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Compound 286

3-methyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)benzo[d]

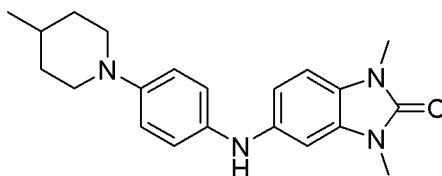
oxazol-2(3H)-one



The title compound **286** (5.1 mg) was prepared in a yield of 5.75% as a wheat powder from 4-(4-methylpiperidin-1-yl)aniline (50 mg, 0.26 mmol) and 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (60 mg, 0.26 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 7.80 (s, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.04 – 6.80 (m, 4H), 6.73 (s, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 3.51 (d, *J* = 11.8 Hz, 2H), 3.26 (s, 3H), 2.59 (s, 1H), 1.69 (d, *J* = 12.6 Hz, 2H), 1.45 (s, 1H), 1.25 (d, *J* = 9.0 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H). Mass (*m/z*): 338.3 [M+H]⁺.

Compound 287

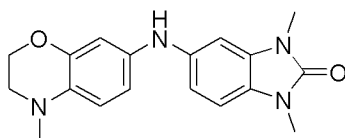
1,3-dimethyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



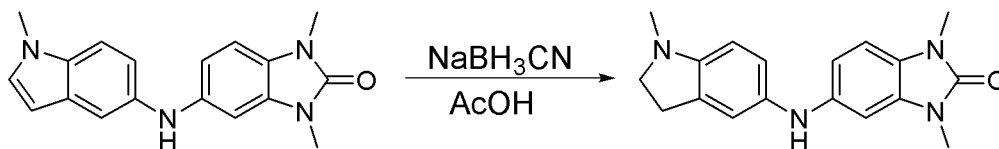
The title compound **287** (13.9 mg) was prepared in a total yield of 79.2 % as a yellow solid from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.93 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 3.60 - 3.42 (m, 4H), 3.32 (s, 3H), 3.29 (s, 3H), 1.96 - 1.84 (m, 2H), 1.76 (m, 1H), 1.65 - 1.48 (m, 2H), 0.98 (d, *J* = 6.4 Hz, 3H). Mass (*m/z*): 351.3 [M+H]⁺.

Compound 288

1,3-dimethyl-5-((4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)

amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one

The title compound **288** (30.5 mg) was prepared in a total yield of 37.7% as a gray solid from 5-amino-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (89 mg, 0.50 mmol), 7-bromo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazine (57 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 umol), X-Phos (6.0 mg, 12.5 umol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.50 (s, 1H), 7.01 – 6.90 (m, 1H), 6.77 – 6.59 (m, 3H), 6.54 (s, 1H), 6.42 (s, 1H), 4.28 – 4.15 (m, 2H), 3.27 (s, 3H), 3.25 (s, 3H), 3.17 – 3.04 (m, 2H), 2.75 (s, 3H). Mass (m/z): 325.2 [M+H]⁺.

Compound 289*1,3-dimethyl-5-((1-methylindolin-5-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one*

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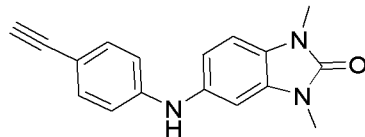
266**Step 1****289**

To a solution of 1,3-dimethyl-5-((1-methyl-1H-indol-5-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one (70 mg, 0.23 mmol) in AcOH (2.0 mL) was added NaBH₃CN (29 mg, 0.46 mmol). Then the mixture was stirred overnight at r.t. 5 mL of water was added. The PH of the filtration was adjusted to 8-9 with sodium carbonate solution. Then the mixture was extracted by DCM (15 mL x 3). The combined organic layers were washed with water (10 mL), dried over Na₂SO₄ and concentrated. The residue was purified by prep-HPLC to afford the desired product as a blue solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.49 (s, 1H), 7.06 – 6.98 (m, 1H), 6.77 – 6.59 (m, 3H), 6.54 (s, 1H), 4.28 – 4.15 (m, 2H), 3.34 (s, 3H), 3.27 (s, 3H), 3.25 (s, 3H), 3.17 – 3.04 (m, 2H). Mass (m/z): 309.2 [M+H]⁺.

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Compound 290

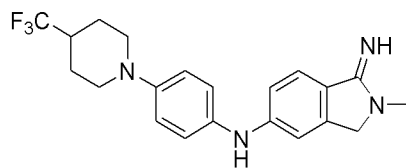
5-((4-ethynylphenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **290** (6.6 mg) was prepared in a total yield of 7.2% as a gray solid from 4-ethynylaniline (90 mg, 0.38 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (70 mg, 0.29 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.29 – 7.21 (m, 4H), 7.12 (d, *J* = 8.0 Hz, 1H), 6.71 – 6.65 (m, 2H), 3.43 (d, *J* = 1.4 Hz, 6H). Mass (*m/z*): 278.2 [M+H]⁺.

Compound 291

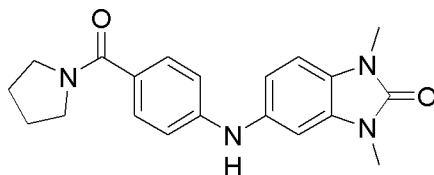
1-imino-2-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)isoindolin-5-amine



The title compound **291** (3.3 mg) was prepared in a total yield of 3.4% as a gray solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (122 mg, 0.50 mmol), 5-bromo-2-methylisoindolin-1-imine (56 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 μmol), X-Phos (5.9 mg, 12.5 μmol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.69 – 7.59 (m, 1H), 7.12 – 6.82 (m, 6H), 4.60 (s, 2H), 3.74 – 3.56 (m, 2H), 3.24 (s, 3H), 2.74 – 2.59 (m, 2H), 2.30 – 2.20 (m, 1H), 1.94 – 1.85 (m, 2H), 1.67 – 1.57 (m, 2H). Mass (*m/z*): 389.3 [M+H]⁺.

Compound 292

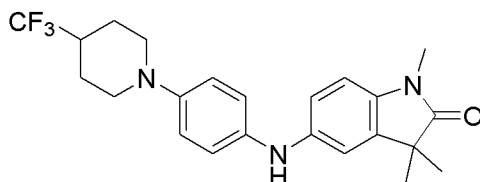
1,3-dimethyl-5-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **292** (14.5 mg) was prepared in a total yield of 20.7% as a light green solid from 5-amino-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (71 mg, 0.40 mmol), (4-bromophenyl) (pyrrolidin-1-yl)methanone (63 mg, 0.25 mmol), Pd₂(dba)₃ (1.8 mg, 2 umol), X-Phos (4.8 mg, 10.0 umol), and t-BuONa (29 mg, 0.30 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.36 – 7.27 (m, 2H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.89 (dt, *J* = 6.9, 2.2 Hz, 4H), 3.52 – 3.44 (m, 4H), 3.31 (s, 3H), 3.29 (s, 3H), 1.94 – 1.74 (m, 4H). Mass (m/z): 351.2 [M+H]⁺.

Compound 293

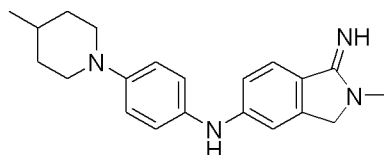
1,3,3-trimethyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)indolin-2-one



The title compound **293** (11.1 mg) was prepared in a total yield of 9.0% as a light gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (122 mg, 0.50 mmol), 5-bromo-1,3,3-trimethylindolin-2-one (84 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 umol), X-Phos (7.8 mg, 16.5 umol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 6.94 – 6.82 (m, 6H), 6.76 (d, *J* = 8.2 Hz, 1H), 3.56 – 3.44 (m, 2H), 3.09 (s, 3H), 2.63 – 2.49 (m, 2H), 2.25 – 2.10 (m, 1H), 1.95 – 1.83 (m, 2H), 1.63 (qd, *J* = 12.5, 4.1 Hz, 3H), 1.22 (s, 6H). Mass (m/z): 418.2 [M+H]⁺.

Compound 294

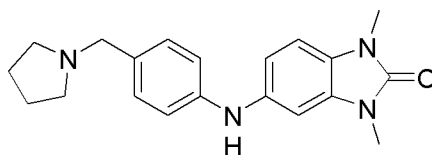
1-imino-2-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)isoindolin-5-amine



The title compound **294** (11.1 mg) was prepared in a total yield of 10.0% as a yellow powder from 4-(4-methylpiperidin-1-yl)aniline (95 mg, 0.50 mmol), 5-bromo-2-methylisoindolin-1-imine (75 mg, 0.33 mmol),
 5 Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.5 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.62 (d, *J* = 8.6 Hz, 1H), 7.05 – 7.00 (m, 2H), 6.95 – 6.85 (m, 4H), 4.59 (s, 2H), 3.50 (dt, *J* = 12.7, 3.3 Hz, 2H), 2.58 (td, *J* = 12.1, 2.6 Hz, 2H), 1.73 – 1.64 (m, 2H), 1.48 – 1.38 (m, 1H), 1.26 (qd, *J* = 12.1, 3.9 Hz, 2H), 0.90 (d, *J* = 6.5 Hz, 3H). Mass (m/z): 335.3 [M+H]⁺.

Compound 295

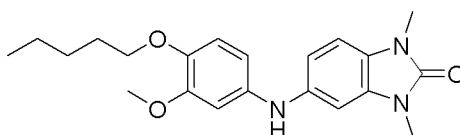
1,3-dimethyl-5-((4-(pyrrolidin-1-ylmethyl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **295** (31.3 mg) was prepared in a total yield of 37.2% as a Rosy Brown green solid from 1-(4-bromobenzyl)pyrrolidine (71 mg, 0.40 mmol), 5-amino-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (60 mg, 0.25 mmol), Pd₂(dba)₃ (1.8 mg, 2 μmol), X-Phos (4.8 mg, 10.0 μmol), and t-BuONa (29 mg, 0.30 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.17 – 7.11 (m, 2H), 6.98 – 6.88 (m, 3H), 6.86 – 6.81 (m, 2H), 3.86 (s, 2H), 3.30 (s, 3H), 3.27 (s, 3H), 2.95 – 2.85 (m, 4H), 1.91 – 1.83 (m, 4H). Mass (m/z): 337.2 [M+H]⁺.

Compound 296

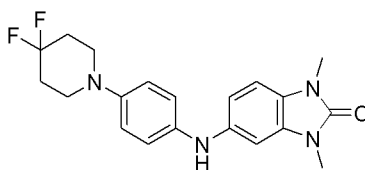
5-((3-methoxy-4-(pentyloxy)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **296** (7.4 mg) was prepared in a total yield of 9.6 % as a yellow solid from 3-methoxy-4-(pentyloxy)aniline (56 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.71 (s, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.81 (dd, *J* = 5.3, 3.3 Hz, 2H), 6.73 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.66 (d, *J* = 2.6 Hz, 1H), 6.53 (dd, *J* = 8.5, 2.5 Hz, 1H), 3.85 (t, *J* = 6.6 Hz, 2H), 3.70 (s, 2H), 3.32 (s, 3H), 3.28 (s, 3H), 3.26 (s, 3H), 1.67 (p, *J* = 6.8 Hz, 2H), 1.42 – 1.31 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H). Mass (*m/z*): 370.3 [M+H]⁺.

Compound 297

5-((4-(4,4-difluoropiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



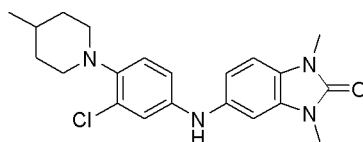
15

The title compound **297** (10.4 mg) was prepared in a total yield of 13.4 % as a blue solid from 4-(4,4-difluoropiperidin-1-yl)aniline (58 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.89 – 6.79 (m, 5H), 6.68 (d, *J* = 2.0 Hz, 1H), 6.62 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 3.12 (d, *J* = 10.0 Hz, 2H), 2.85 - 2.93 (m, 2H), 1.92 (dd, *J* = 10.4, 5.2 Hz, 2H), 1.75 (d, *J* = 10.4 Hz, 2H). Mass (*m/z*): 373.3 [M+H]⁺.

25

Compound 298

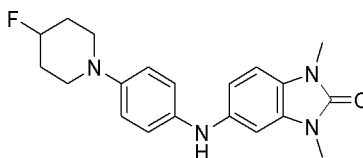
5-((3-chloro-4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **298** (15.2 mg) was prepared in a total yield of 19.0 % as a white solid from 3-chloro-4-(4-methylpiperidin-1-yl)aniline (60 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.92 (s, 1H), 6.96 (t, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.78 (d, *J* = 2.0 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.26 (s, 1H), 3.23 (s, 3H), 3.21 (s, 3H), 3.01 (d, *J* = 11.6 Hz, 2H), 2.48 (d, *J* = 2.4 Hz, 1H), 1.66 – 1.56 (m, 2H), 1.42 – 1.32 (m, 1H), 1.22 (dd, *J* = 12.0, 3.6 Hz, 2H), 0.88 (d, *J* = 6.4 Hz, 3H). Mass (*m/z*): 386.3 [M+H]⁺.

Compound 299

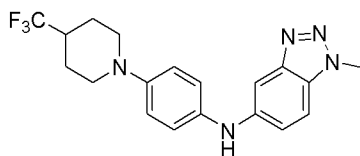
5-((4-(4-fluoropiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **299** (10.3 mg) was prepared in a total yield of 14.1 % as a white solid from 4-(4-fluoropiperidin-1-yl)aniline (49 mg, 0.271 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.89 – 6.79 (m, 5H), 6.68 (d, *J* = 2.0 Hz, 1H), 6.62 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 3.12 (d, *J* = 10.0 Hz, 2H), 2.91 (td, *J* = 8.4, 7.6, 4.0 Hz, 3H), 1.92 (dd, *J* = 10.4, 5.2 Hz, 2H), 1.75 (d, *J* = 10.4 Hz, 2H). Mass (*m/z*): 355.3 [M+H]⁺.

Compound 300

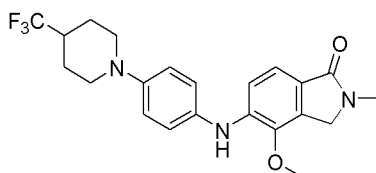
1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-

benzo[d][1,2,3]triazol-5-amine

The title compound **300** (19.7 mg) was prepared in a total yield of 22.2 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (69 mg, 0.283 mmol), 5-bromo-1-methyl-1H-benzo[d][1,2,3]triazole (50 mg, 0.236 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (116 mg, 0.354 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.00 (s, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.15 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.03 – 6.97 (m, 2H), 6.90 – 6.84 (m, 2H), 4.15 (s, 3H), 3.59 (d, *J* = 12.0 Hz, 2H), 2.58 (td, *J* = 12.4, 2.6 Hz, 2H), 1.82 (d, *J* = 12.4 Hz, 2H), 1.52 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (*m/z*): 376.3 [M+H]⁺.

Compound 301

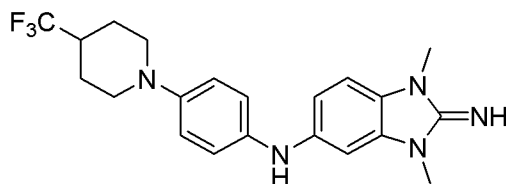
4-methoxy-2-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



The title compound **301** (44.6 mg) was prepared in a total yield of 54.5 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (57 mg, 0.234 mmol), 5-bromo-4-methoxy-2-methylisoindolin-1-one (50 mg, 0.195 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (96 mg, 0.293 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.50 (s, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.04 – 7.00 (m, 2H), 6.93 – 6.85 (m, 3H), 4.49 (s, 2H), 3.81 (s, 3H), 3.62 (d, *J* = 12.4 Hz, 2H), 2.95 (s, 3H), 2.60 (td, *J* = 12.4, 2.4 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.50 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (*m/z*): 420.3 [M+H]⁺.

Compound 302

2-imino-1,3-dimethyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-5-amine

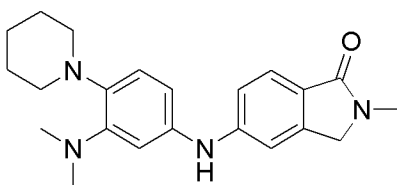


The title compound **302** (16.2 mg) was prepared in a total yield of 80.2 %
 5 as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-imine (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz,
 10 Methanol-*d*₄) δ 7.35 - 6.71 (m, 7H), 3.76 - 3.66 (m, 2H), 3.59 (s, 3H), 3.56 (s, 3H), 2.79 - 2.61 (m, 2H), 2.11 (m, 1H), 1.99 - 1.86 (m, 2H), 1.75 - 1.69 (m, 2H). Mass (m/z): 404.2 [M+H]⁺.

Compound 303

5-((3-(dimethylamino)-4-(piperidin-1-yl)phenyl)amino)-2-methylisoindolin-1-one

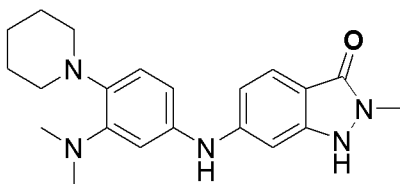
15



The title compound **303** (14.5 mg) was prepared in a total yield of 79.7 %
 as a white solid from N¹,N¹-dimethyl-6-(piperidin-1-yl)benzene-1,3-diamine (14.2 mg, 0.065 mmol), 5-bromo-2-methylisoindolin-1-one (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.67 - 7.57 (m, 2H), 7.41 (d, *J* = 2.4 Hz, 1H), 7.31 - 7.23 (m, 2H), 7.18 (dd, *J* = 8.4, 2.4 Hz, 1H), 4.44 (s, 2H), 3.25 - 3.18 (m, 4H), 3.16 (s, 3H), 3.03 (s,
 20 6H), 1.74 - 1.63 (m, 4H), 1.59 - 1.51 (m, 2H). Mass (m/z): 365.2 [M+H]⁺.

Compound 304

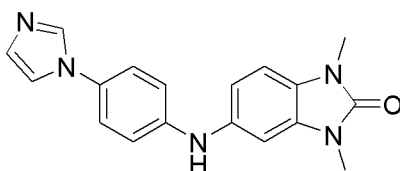
6-((3-(dimethylamino)-4-(piperidin-1-yl)phenyl)amino)-2-methyl-1,2-dihydro-3H-indazol-3-one



The title compound **304** (15.3 mg) was prepared in a total yield of 83.8 %
 5 as a light pink solid from tert-butyl 6-((3-(dimethylamino)-4-(piperidin-1-yl)phenyl)amino)-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (23.3 mg, 0.05 mmol) and 3 ml HCl (4.0 M) in 1,4-dioxane according to the procedure for compound **203**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.80 - 7.26 (m, 5H), 6.97 (s, 1H), 3.25 (s, 3H), 3.20 - 3.09
 10 (m, 4H), 3.02 (s, 6H), 1.86 - 1.68 (m, 4H), 1.56 - 1.34 (m, 2H). Mass (m/z): 366.2 [M+H]⁺.

Compound 305

5-((4-(1H-imidazol-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

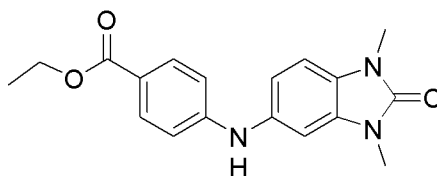


15 The title compound **305** (42.0 mg) was prepared in a total yield of 39.3% as a light blue powder from 4-(1H-Imidazol-1-yl)aniline (67 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 umol), X-Phos (7.8 mg, 16.5 umol),
 20 and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 9.20 (s, 1H), 7.84 (t, *J* = 1.8 Hz, 1H), 7.62 (t, *J* = 1.7 Hz, 1H), 7.42 - 7.32 (m, 2H), 7.06 - 6.98 (m, 3H), 6.94 - 6.86 (m, 2H), 3.32 (s, 3H), 3.29 (s, 3H). Mass (m/z): 320.3 [M+H]⁺.

25 **Compound 306**

ethyl 4-((1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)

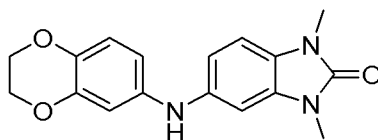
amino)benzoate



The title compound **306** (32.7 mg) was prepared in a total yield of 30.0% as a light yellow powder from 4-(ethoxycarbonyl)phenylamine (71 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.85 – 7.79 (m, 2H), 7.16 – 7.07 (m, 1H), 7.03 – 6.90 (m, 4H), 3.43 (s, 3H), 3.40 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). Mass (*m/z*): 326.2 [M+H]⁺.

Compound 307

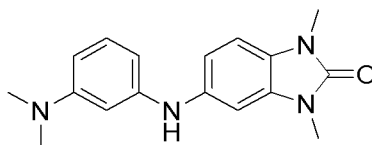
*5-((2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[*d*]imidazol-2-one*



The title compound **307** (34.9 mg) was prepared in a total yield of 33.7% as a light yellow powder from 1,4-benzodioxan-6-amine (85 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.00 (d, *J* = 8.6 Hz, 1H), 6.84 – 6.77 (m, 2H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.60 – 6.51 (m, 2H), 4.24 – 4.16 (m, 4H), 3.40 (s, 3H), 3.37 (s, 3H). Mass (*m/z*): 312.2 [M+H]⁺.

Compound 308

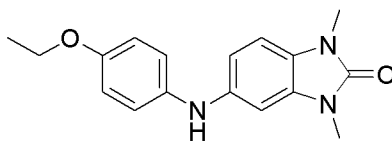
*5-((3-(dimethylamino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[*d*]imidazol-2-one*



The title compound **308** (12.6 mg) was prepared in a total yield of 12.8% as a light yellow powder from N,N-dimethyl-m-phenylenediamine (59 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 6.98 – 6.87 (m, 2H), 6.84 – 6.77 (m, 2H), 6.40 – 6.30 (m, 2H), 6.24 – 6.17 (m, 1H), 3.29 (s, 3H), 3.25 (s, 3H), 2.77 (s, 6H). Mass (m/z): 297.3 [M+H]⁺.

Compound 309

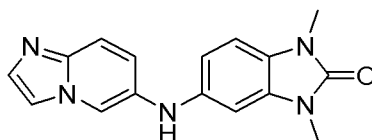
5-((4-ethoxyphenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **309** (36.5 mg) was prepared in a total yield of 36.9% as a light blue powder from 4-ethoxybenzenamine (59 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 6.96 – 6.82 (m, 3H), 6.76 – 6.58 (m, 4H), 3.89 (q, *J* = 7.0 Hz, 2H), 3.27 (s, 3H), 3.23 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 3H). Mass (m/z): 298.2 [M+H]⁺.

Compound 310

5-(imidazo[1,2-a]pyridin-6-ylamino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

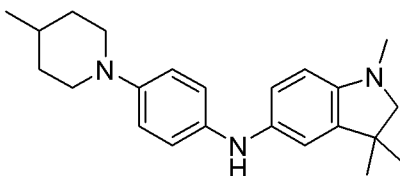


The title compound **310** (33.9 mg) was prepared in a total yield of 34.7%

as a yellow powder from H-imidazo[1,2-a]pyridin-6-amine (57 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.16 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.84 (d, *J* = 1.9 Hz, 1H), 7.67 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 9.6 Hz, 1H), 7.49 (dd, *J* = 9.7, 2.2 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 1H), 6.94 (d, *J* = 2.0 Hz, 1H), 6.91 (dd, *J* = 8.3, 2.1 Hz, 1H), 3.33 (s, 3H), 3.32 (s, 3H). Mass (m/z): 294.2 [M+H]⁺.

Compound 311

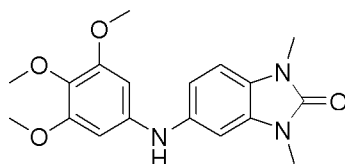
1,3,3-trimethyl-N-(4-(4-methylpiperidin-1-yl)phenyl)indolin-5-amine



The title compound **311** (28.1 mg) was prepared in a total yield of 24.1% as a light green powder from 4-(4-methylpiperidin-1-yl)aniline (82 mg, 0.43 mmol), 5-bromo-1,3,3-trimethylindoline (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.15 – 5.87 (m, 7H), 3.73 – 3.28 (m, 2H), 3.34 (s, 3H), 2.82 – 2.43 (m, 2H), 1.70 – 1.63 (m, 2H), 1.31 – 1.07 (m, 8H), 0.90 (d, *J* = 6.1 Hz, 6H), 0.83 – 0.74 (m, 2H). Mass (m/z): 350.4 [M+H]⁺.

Compound 312

1,3-dimethyl-5-((3,4,5-trimethoxyphenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **312** (34.4 mg) was prepared in a total yield of 30.2% as a white powder from 3,4,5-trimethoxyaniline (79 mg, 0.43 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (80 mg, 0.33

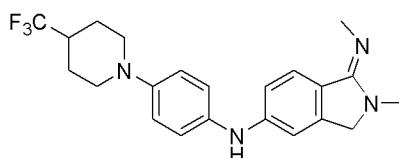
mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound 1.

¹H NMR (400 MHz, Methanol-*d*₄) δ 6.97 – 6.90 (m, 1H), 6.83 – 6.78 (m, 2H), 6.22 (s, 2H), 3.66 (s, 6H), 3.60 (s, 3H), 3.29 (s, 3H), 3.26 (s, 3H).

5 Mass (m/z): 344.2 [M+H]⁺.

Compound 313

2-methyl-1-(methylimino)-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)isoindolin-5-amine

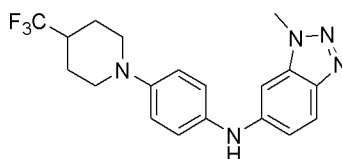


10 The title compound **313** (9.4 mg) was prepared in a total yield of 11.2 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (61 mg, 0.251 mmol), 5-bromo-N,2-dimethylisoindolin-1-imine (50 mg, 0.209 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (103 mg, 0.314 mmol) and 1,4-dioxane (5 mL) according to the procedure
15 for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.55 (s, 1H), 8.59 (s, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.14 – 7.05 (m, 4H), 6.99 (d, *J* = 8.8 Hz, 2H), 3.73 (d, *J* = 12.4 Hz, 2H), 3.08 (s, 3H), 2.73 – 2.66 (m, 2H), 1.90 (d, *J* = 12.8 Hz, 2H), 1.58 (qd, *J* = 12.4, 4.0 Hz, 3H), 1.24 (s, 2H). Mass (m/z): 403.3 [M+H]⁺.

20

Compound 314

1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[d][1,2,3]triazol-6-amine



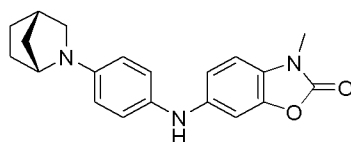
The title compound **314** (8.5 mg) was prepared in a total yield of 9.6 % as a
25 white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (69 mg, 0.283 mmol), 6-bromo-1-methyl-1H-benzo[d][1,2,3]triazole (50 mg, 0.236 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (116 mg, 0.354 mmol) and 1,4-dioxane (5 mL) according to the procedure

for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.31 (s, 1H), 7.77 (d, J = 9.6 Hz, 1H), 7.18 – 7.13 (m, 2H), 7.03 – 6.90 (m, 4H), 4.10 (s, 3H), 3.70 (d, J = 12.4 Hz, 2H), 2.68 (d, J = 23.6 Hz, 2H), 1.90 (d, J = 12.4 Hz, 2H), 1.59 (qd, J = 12.4, 4.0 Hz, 2H). Mass (m/z): 376.3 $[\text{M}+\text{H}]^+$.

5

Compound 315

6-((4-((1R,4S)-2-azabicyclo[2.2.1]heptan-2-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

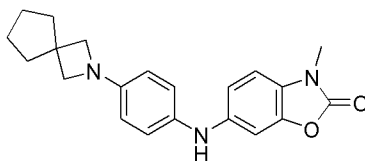


The title compound **315** (26.0 mg) was prepared in a total yield of 35.4 % as a white solid from 4-((1R,4S)-2-azabicyclo[2.2.1]heptan-2-yl)aniline (50 mg, 0.263 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), $\text{Pd}_2(\text{dba})_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (108 mg, 0.329 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.63 (s, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.93 (d, J = 8.0 Hz, 2H), 6.76 (s, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.48 (d, J = 8.4 Hz, 2H), 4.09 (s, 1H), 2.62 (d, J = 8.0 Hz, 1H), 2.54 (s, 1H), 1.69 (d, J = 9.2 Hz, 1H), 1.61 (s, 2H), 1.46 (d, J = 9.2 Hz, 1H), 1.25 (d, J = 12.0 Hz, 2H). Mass (m/z): 336.3 $[\text{M}+\text{H}]^+$.

15

Compound 316

6-((4-(2-azaspiro[3.4]octan-2-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one



20

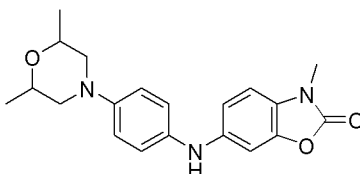
The title compound **316** (8.3 mg) was prepared in a total yield of 10.8 % as a white solid from 4-(2-azaspiro[3.4]octan-2-yl)aniline (53 mg, 0.263 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), $\text{Pd}_2(\text{dba})_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (108 mg, 0.329 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.63 (s, 1H), 6.95 (d, J =

25

8.4 Hz, 1H), 6.89 – 6.84 (m, 2H), 6.72 (d, $J = 2.0$ Hz, 1H), 6.63 (dd, $J = 8.4, 2.1$ Hz, 1H), 6.32 (d, $J = 8.8$ Hz, 2H), 3.54 (s, 3H), 3.21 (s, 2H), 1.71 (q, $J = 6.0, 4.4$ Hz, 4H), 1.55 – 1.48 (m, 4H). Mass (m/z): 350.3 $[M+H]^+$.

Compound 317

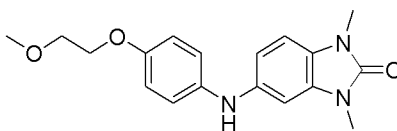
5 6-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one



The title compound **317** (19.4 mg) was prepared in a total yield of 25.1 % as a white solid from 4-(2,6-dimethylmorpholino)aniline (54 mg, 0.263 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (108 mg, 0.329 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.85 (s, 1H), 7.06 (d, $J = 8.4$ Hz, 1H), 6.99 – 6.94 (m, 2H), 6.91 – 6.86 (m, 3H), 6.79 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.69 (ddt, $J = 12.4, 6.4, 3.2$ Hz, 2H), 3.44 (d, $J = 11.2$ Hz, 2H), 2.23 – 2.15 (m, 2H), 1.14 (d, $J = 6.4$ Hz, 6H). Mass (m/z): 354.3 $[M+H]^+$.

Compound 318

5-((4-(2-methoxyethoxy)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

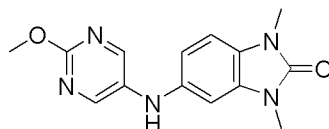


20 The title compound **318** (18.4 mg) was prepared in a total yield of 27.0 % as a white solid from 4-(2-methoxyethoxy)aniline (42 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.69 (s, 1H), 6.97 (dd, $J = 8.8, 2.4$ Hz, 3H), 6.86 – 6.81 (m, 2H), 6.75 (d, $J = 2.0$ Hz,

1H), 6.70 (dd, $J = 8.4, 2.1$ Hz, 1H), 4.04 – 3.99 (m, 2H), 3.66 – 3.60 (m, 2H), 3.31 (s, 3H), 3.28 (s, 3H), 3.25 (s, 3H). Mass (m/z): 328.3 $[M+H]^+$.

Compound 319

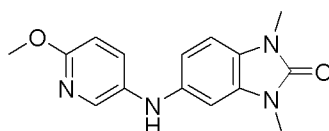
5-((2-methoxypyrimidin-5-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazole-2-one



The title compound **319** (9.9 mg) was prepared in a total yield of 16.7 % as a white solid from 2-methoxypyrimidin-5-amine (31 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.38 (s, 2H), 7.95 (s, 1H), 7.02 (d, $J = 8.4$ Hz, 1H), 6.83 (d, $J = 2.0$ Hz, 1H), 6.72 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.86 (s, 3H), 3.29 (d, $J = 4.4$ Hz, 6H). Mass (m/z): 286.3 $[M+H]^+$.

Compound 320

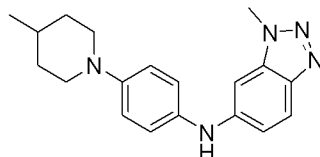
5-((6-methoxypyridin-3-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **320** (34.5 mg) was prepared in a total yield of 58.4 % as a white solid from 6-methoxypyridin-3-amine (31 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), Xphos (6 mg, 0.01 mmol), Cs_2CO_3 (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 7.93 (d, $J = 2.8$ Hz, 1H), 7.82 (s, 1H), 7.45 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.99 (d, $J = 8.4$ Hz, 1H), 6.78 – 6.72 (m, 2H), 6.69 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.79 (s, 3H), 3.27 (d, $J = 7.6$ Hz, 6H). Mass (m/z): 285.3 $[M+H]^+$.

Compound 321

1-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-1H-benzo[d][1,2,3]triazol-6-amine

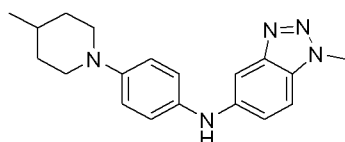


- 5 The title compound **321** (55.1 mg) was prepared in a total yield of 72.6 % as a white solid from 4-(4-methylpiperidin-1-yl)aniline (54 mg, 0.283 mmol), 6-bromo-1-methyl-1H-benzo[d][1,2,3]triazole (50 mg, 0.236 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (116 mg, 0.354 mmol) and 1,4-dioxane (5 mL) according to the procedure
 10 for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.36 – 8.29 (m, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.15 – 7.10 (m, 2H), 7.01 – 6.97 (m, 1H), 6.97 – 6.91 (m, 3H), 4.09 (s, 3H), 3.57 (dt, *J* = 12.4, 3.6 Hz, 2H), 2.60 (td, *J* = 12.0, 2.6 Hz, 2H), 1.74 – 1.65 (m, 2H), 1.53 – 1.41 (m, 1H), 1.31 – 1.18 (m, 2H), 0.95 (d, *J* = 6.4 Hz, 3H). Mass (*m/z*): 322.3 [M+H]⁺.

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Compound 322

1-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-1H-benzo[d][1,2,3]triazol-6-amine

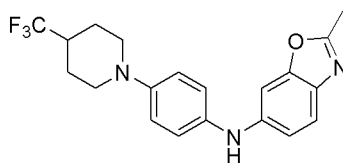


- The title compound **322** (24.8 mg) was prepared in a total yield of 32.7 %
 20 as a white solid from 4-(4-methylpiperidin-1-yl)aniline (54 mg, 0.283 mmol), 5-bromo-1-methyl-1H-benzo[d][1,2,3]triazole (50 mg, 0.236 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (116 mg, 0.354 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.04 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.09 – 7.02 (m, 2H), 6.94 – 6.89 (m, 2H), 4.22 (s, 3H), 3.53 (dt, *J* = 12.4, 3.2 Hz, 2H), 2.57 (td, *J* = 12.0, 2.4 Hz, 2H), 1.69 (d, *J* = 13.6 Hz, 2H), 1.45 (ddt, *J* = 10.4, 7.2, 3.6 Hz, 1H), 1.25 (dd, *J* = 12.4, 3.6 Hz, 2H), 0.94 (d, *J* = 6.4 Hz,

3H). Mass (m/z): 322.3 [M+H]⁺.

Compound 323

2-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzo[d]oxazol-6-amine



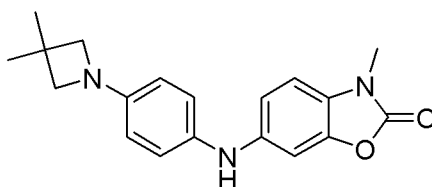
5

The title compound **323** (61.6 mg) was prepared in a total yield of 64.1 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (69 mg, 0.283 mmol), 6-bromo-2-methylbenzo[d]oxazole (50 mg, 0.256 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs₂CO₃ (126 mg, 0.384 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.03 (dt, *J* = 6.8, 2.8 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 7.00 – 6.94 (m, 2H), 6.88 – 6.80 (m, 3H), 3.57 (d, *J* = 12.4 Hz, 2H), 2.56 (td, *J* = 12.4, 2.4 Hz, 2H), 2.45(s, 3H), 2.36 (ddq, *J* = 12.4, 8.8, 3.6 Hz, 1H), 1.86 – 1.76 (m, 2H), 1.51 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (m/z): 376.3 [M+H]⁺.

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Compound 324

6-((4-(3,3-dimethylazetidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

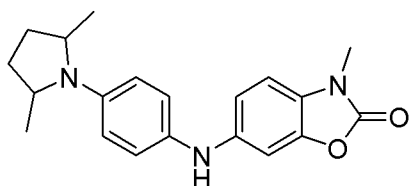


The title compound **324** (13.1 mg) was prepared in a total yield of 80.9 % as a yellow solid from 4-(3,3-dimethylazetidin-1-yl)aniline (11.4 mg, 0.065 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (11.4 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.14 - 6.58 (m, 7H), 3.64 (s, 4H), 3.37 (s, 3H), 1.25 (s, 6H). Mass (m/z): 324.1 [M+H]⁺.

25

Compound 325

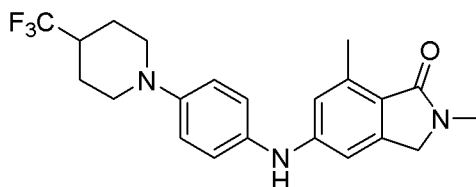
6-((4-(2,5-dimethylpyrrolidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one



The title compound **325** (11.3 mg) was prepared in a total yield of 66.7 %
 5 as a white solid from 4-(2,5-dimethylpyrrolidin-1-yl)aniline (12.4 mg, 0.065 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (11.4 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.05 - 6.87 (m, 3H), 6.78
 10 - 6.63 (m, 2H), 6.54 - 6.43 (m, 2H), 3.53 - 3.46 (m, 2H), 3.34 (s, 3H), 2.11 - 1.65 (m, 4H), 1.14 (d, *J* = 6.4 Hz, 6H). Mass (*m/z*): 338.2 [M+H]⁺.

Compound 326

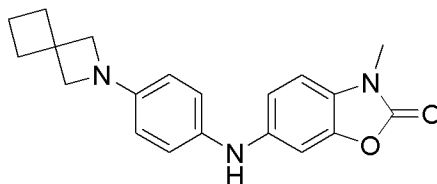
2,7-dimethyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-1-one



15 The title compound **326** (16.7 mg) was prepared in a total yield of 82.6 % as a light yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-2,7-dimethylisoindolin-1-one (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005
 20 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.34 - 6.75 (m, 6H), 4.29 (s, 2H), 3.76 - 3.61 (m, 2H), 3.11 (s, 3H), 2.79 - 2.66 (m, 2H), 2.53 (s, 3H), 2.15 (m, 1H), 2.06 - 1.93 (m, 2H), 1.79 - 1.66 (m, 2H). Mass (*m/z*): 404.2 [M+H]⁺.

25 **Compound 327**

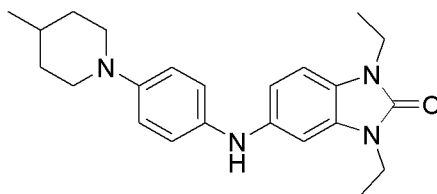
6-((4-(2-azaspiro[3.3]heptan-2-yl)phenyl)amino)-3-methylbenzo[d]

oxazol-2(3H)-one

The title compound **327** (15.8 mg) was prepared in a total yield of 78.2 % as a wheat solid from 4-(2-azaspiro[3.3]heptan-2-yl)aniline (12.2 mg, 0.065 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (11.4 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.41 - 6.74 (m, 6H), 3.71 (s, 4H), 3.15 (s, 3H), 2.19 - 2.11 (m, 4H), 1.89 - 1.77 (m, 2H). Mass (m/z): 404.2 [M+H]⁺.

Compound 328

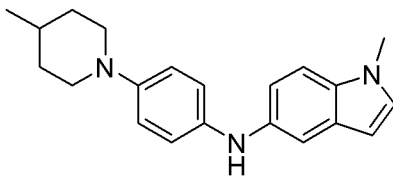
1,3-diethyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **328** (1.2 mg) was prepared in a yield of 1.21% as a grey solid from 4-(4-methylpiperidin-1-yl)aniline (50 mg, 0.26 mmol) and 5-bromo-1,3-diethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (70 mg, 0.26 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 7.61 (s, 1H), 7.21 (s, 1H), 7.01-6.72 (m, 4H), 6.65 (s, 1H), 3.79 (s, 2H), 1.99 (q, J = 6.9, 6.2 Hz, 5H), 1.65 (m, 1H), 1.45 (s, 3H), 1.19 - 1.13 (m, 5H), 0.94 (d, J = 6.4 Hz, 2H), 0.84 (d, J = 7.2 Hz, 4H). Mass (m/z): 379.3 [M+H]⁺.

Compound 329

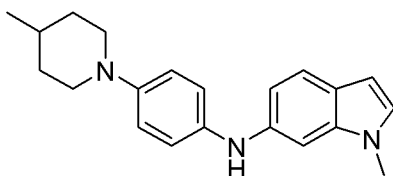
1-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-1H-indol-5-amine



The title compound **329** (1.5 mg) was prepared in a yield of 1.79% as a grey solid from 4-(4-methylpiperidin-1-yl)aniline (50 mg, 0.26 mmol) and 5-bromo-1-methyl-1H-indole (55 mg, 0.26 mmol) according to the procedure for compound **1**. ¹H NMR (DMSO-*d*₆) δ 7.20 (s, 5H), 7.02-6.82(m, 3), 6.64 (s, 2H), 2.10 – 1.80 (m, 5H), 1.44 (s, 3H), 1.14 (s, 3H), 0.83 (d, J = 6.8 Hz, 4H). Mass (m/z): 320.4 [M+H]⁺.

Compound 330

1-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-1H-indol-6-amine



10

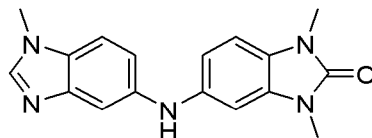
The title compound **330** (2.4 mg) was prepared in a yield of 2.86% as a grey powder from 4-(4-methylpiperidin-1-yl)aniline (50 mg, 0.26 mmol) and 6-bromo-1-methyl-1H-indole (55 mg, 0.26 mmol) according to the procedure for compound **1**. ¹H NMR (DMSO-*d*₆) δ 7.62-7.34 (m, 4H), 7.21-6.86 (m, 3H), 6.65 (s, 2H), 2.67 (s, 4H), 1.99 (q, J = 7.0, 6.4 Hz, 3H), 1.66 (s, 2H), 1.45 (s, 2H), 1.14 (s, 1H), 0.84 (d, J = 7.1 Hz, 3H). Mass (m/z): 320.6 [M+H]⁺.

15

Compound 331

1,3-dimethyl-5-((1-methyl-1H-benzo[d]imidazol-5-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one (847)

20



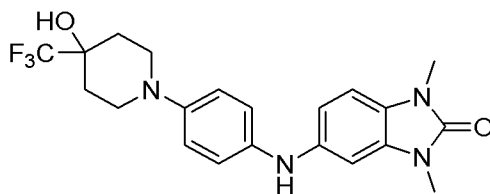
The title compound **331** (8.3 mg) was prepared in a yield of 11.4% as a white powder from 5-amino-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.24 mmol) and 5-bromo-1-methyl-1H-

benzo[d]imidazole (42 mg, 0.24 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.06 (s, 1H), 7.81 (s, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 7.27 (s, 1H), 7.07 – 6.96 (m, 2H), 6.81 (d, *J* = 1.9 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 3.79 (s, 3H), 3.29 (s, 3H), 3.25 (s, 3H).

5 Mass (m/z): 308.4 [M+H]⁺.

Compound 332

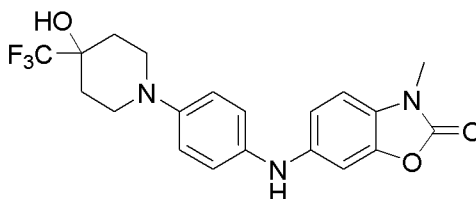
5-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



10 The title compound **332** (5.6 mg) was prepared in a yield of 6.42% as a grey powder from 1-(4-aminophenyl)-4-(trifluoromethyl)piperidin-4-ol (50 mg, 0.19 mmol) and 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (54 mg, 0.21 mmol) according to the procedure for compound 1. ¹H NMR (301 MHz, DMSO-*d*₆) δ 7.64 (s, 1H),
 15 7.01 – 6.83 (m, 5H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.72 – 6.64 (m, 1H), 5.92 (s, 1H), 3.26 (dd, *J* = 7.2, 1.5 Hz, 6H), 2.85 (t, *J* = 11.5 Hz, 3H), 1.88 – 1.61 (m, 5H). Mass (m/z): 421.6 [M+H]⁺.

Compound 333

6-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one



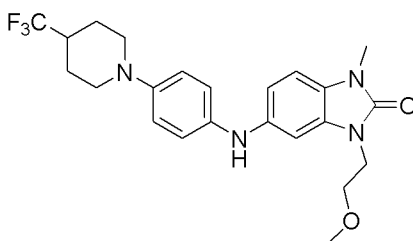
The title compound **333** (2.4 mg) was prepared in a yield of 3.07% as a pale yellow powder from 1-(4-aminophenyl)-4-(trifluoromethyl)piperidin-4-ol (50 mg, 0.19 mmol)
 25 and 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (48 mg, 0.21 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 7.81 (s,

1H), 7.21 (s, 1H), 7.05 (d, $J = 8.4$ Hz, 1H), 7.00 – 6.86 (m, 3H), 6.78 (d, $J = 9.0$ Hz, 1H), 6.66 (s, 1H), 5.93 (s, 1H), 2.88 (d, $J = 11.3$ Hz, 2H), 2.00 (q, $J = 7.0, 6.3$ Hz, 3H), 1.73 (s, 2H), 1.45 (s, 2H), 0.84 (d, $J = 7.0$ Hz, 2H). Mass (m/z): 408.6 $[M+H]^+$.

5

Compound 334

3-(2-methoxyethyl)-1-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one

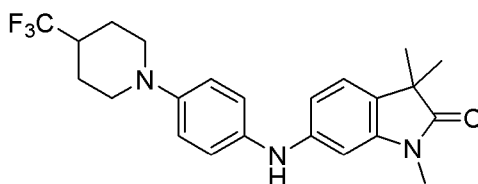


The title compound **334** (44.0 mg) was prepared in a total yield of 29.5% as a dark gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (79.3 mg, 0.33 mmol), 5-bromo-3-(2-methoxyethyl)-1-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (71 mg, 0.25 mmol), $Pd_2(dba)_3$ (2.3 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), and t-BuONa (36.8 mg, 0.38 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, Methanol- d_4) δ 7.06 – 6.91 (m, 6H), 6.84 – 6.78 (m, 1H), 4.01 (t, $J = 5.3$ Hz, 2H), 3.66 (t, $J = 5.3$ Hz, 3H), 3.63 – 3.55 (m, 2H), 3.39 (s, 3H), 3.33 (s, 3H), 2.83 – 2.53 (m, 2H), 2.36 – 2.22 (m, 2H), 2.01 – 1.92 (m, 2H), 1.74 (qd, $J = 12.5, 4.1$ Hz, 3H). Mass (m/z): 449.3 $[M+H]^+$.

15

Compound 335

1,3,3-trimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)indolin-2-one



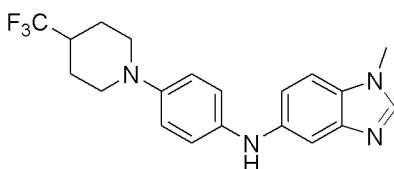
25

The title compound **335** (51.1 mg) was prepared in a total yield of 36.8% as a light gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (122 mg, 0.50 mmol), 6-bromo-1,3,3-trimethylindolin-2-one (84 mg, 0.33

mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**.
¹H NMR (400 MHz, Methanol-*d*₄) δ 8.09 – 5.93 (m, 7H), 3.16 (s, 3H), 2.53 – 2.31 (m, 1H), 2.21 – 1.66 (m, 4H), 1.31 (s, 6H). Mass (m/z): 418.3
 5 [M+H]⁺.

Compound 336

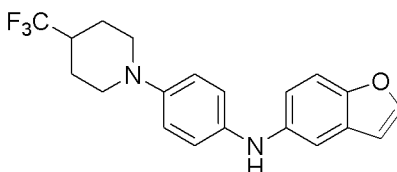
1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[d]imidazol-5-amine



10 The title compound **336** (35.1 mg) was prepared in a total yield of 28.1% as a yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (105 mg, 0.43 mmol), 5-bromo-1-methyl-1H-benzo[d]imidazole (70 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**.
 15 ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.02 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 1H), 7.32 – 7.20 (m, 1H), 7.13 – 6.75 (m, 5H), 3.85 (s, 3H), 3.69 – 3.49 (m, 2H), 2.79 – 2.48 (m, 2H), 2.35 – 2.16 (m, 2H), 2.01 – 1.87 (m, 2H), 1.80 – 1.65 (m, 2H). Mass (m/z): 375.3 [M+H]⁺.

Compound 337

20 *N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzofuran-5-amine*

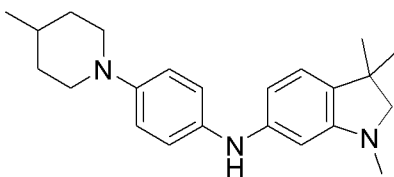


The title compound **337** (54.6 mg) was prepared in a total yield of 45.5% as a yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (105 mg, 0.43 mmol), 5-bromobenzofuran (66 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz,

Methanol- d_4) δ 7.64 (d, J = 2.2 Hz, 1H), 7.47 – 6.75 (m, 7H), 6.68 (d, J = 1.6 Hz, 1H), 3.86 – 3.40 (m, 2H), 3.04 – 2.16 (m, 3H), 2.04 – 1.91 (m, 2H), 1.81 – 1.61 (m, 2H). Mass (m/z): 361.2 [M+H]⁺.

Compound 338

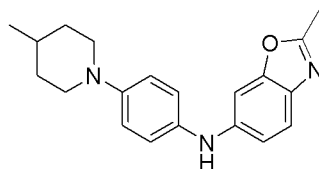
5 *1,3,3-trimethyl-N-(4-(4-methylpiperidin-1-yl)phenyl)indolin-6-amine*



The title compound **338** (43.2 mg) was prepared in a total yield of 45.5% as a yellow powder from 4-(4-methylpiperidin-1-yl)aniline (82 mg, 0.43 mmol), 6-bromo-1,3,3-trimethylindoline (80 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μ mol), X-Phos (7.8 mg, 16.5 μ mol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol- d_4) δ 6.92 – 6.86 (m, 2H), 6.85 – 6.80 (m, 2H), 6.69 (s, 1H), 6.09 (s, 1H), 3.38 – 3.31 (m, 2H), 2.90 (s, 2H), 2.56 (s, 3H), 2.54 – 2.44 (m, 2H), 1.70 – 1.59 (m, 2H), 1.42 – 1.21 (m, 3H), 1.14 (s, 6H), 0.88 (d, J = 6.3 Hz, 3H). Mass (m/z): 350.3 [M+H]⁺.

Compound 339

2-methyl-N-(4-(4-methylpiperidin-1-yl)phenyl)benzo[d]oxazol-6-amine

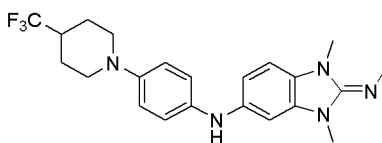


The title compound **339** (69.4 mg) was prepared in a total yield of 84.3 % as a white solid from 4-(4-methylpiperidin-1-yl)aniline (54 mg, 0.283 mmol), 6-bromo-2-methylbenzo[d]oxazole (50 mg, 0.256 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (126 mg, 0.384 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO- d_6) δ 8.05 (s, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.11 – 6.83 (m, 6H), 3.52 (s, 2H), 3.36 (s, 3H), 2.55 (s, 2H), 1.68 (s, 2H), 1.46 (s, 1H), 1.24 (d, J = 9.2 Hz, 2H), 0.94 (d, J = 6.4 Hz, 3H).

Mass (m/z): 322.3 [M+H]⁺.

Compound 340

1,3-dimethyl-2-(methylimino)-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-5-amine



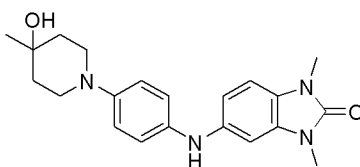
5

The title compound **340** (2.2 mg) was prepared in a total yield of 2.7 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (57 mg, 0.236 mmol), 5-bromo-N,1,3-trimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-imine (50 mg, 0.197 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (97 mg, 0.296 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.89 – 6.79 (m, 5H), 6.68 (d, *J* = 2.0 Hz, 1H), 6.62 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 3.12 (d, *J* = 10.0 Hz, 2H), 2.91 (td, *J* = 8.4, 7.6, 4.0 Hz, 3H), 1.92 (dd, *J* = 10.4, 5.2 Hz, 2H), 1.75 (d, *J* = 10.4 Hz, 2H), 1.02 (d, *J* = 6.0 Hz, 3H). Mass (m/z): 418.3 [M+H]⁺.

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Compound 341

5-((4-(4-hydroxy-4-methylpiperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



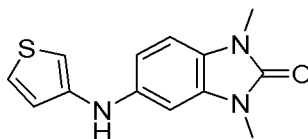
The title compound **341** (12.1 mg) was prepared in a total yield of 15.9 % as a green solid from 1-(4-aminophenyl)-4-methylpiperidin-4-ol (51 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.65 – 7.59 (m, 1H), 6.98 – 6.91 (m, 3H), 6.87 – 6.82 (m, 2H), 6.73 (d, *J* = 2.0 Hz, 1H), 6.68 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.27 (q, *J* = 1.6 Hz, 1H), 3.26 (d, *J* = 10.4 Hz, 6H), 3.10 (dt, *J* = 12.0, 4.4 Hz, 2H), 3.01 (dt, *J* = 12.4, 6.4

25

Hz, 2H), 1.57 (dd, $J = 6.4, 4.4$ Hz, 4H), 1.15 (s, 3H). Mass (m/z): 367.3 [M+H]⁺.

Compound 342

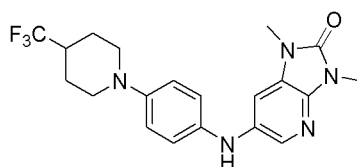
1,3-dimethyl-5-(thiophen-3-ylamino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **342** (6.4 mg) was prepared in a total yield of 11.9 % as a brown solid from thiophen-3-amine (34 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-d₆) δ 7.93 (d, $J = 2.8$ Hz, 1H), 7.82 (s, 1H), 7.45 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.99 (d, $J = 8.4$ Hz, 1H), 6.78 – 6.72 (m, 2H), 6.69 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.27 (d, $J = 7.6$ Hz, 6H). Mass (m/z): 260.3 [M+H]⁺.

Compound 343

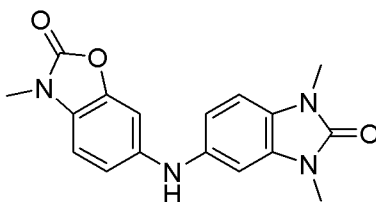
1,3-dimethyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-imidazo[4,5-b]pyridin-2-one



The title compound **343** (7.0 mg) was prepared in a total yield of 8.3 % as a green solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (60 mg, 0.248 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.310 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-d₆) δ 7.72 (s, 2H), 7.25 - 6.80 (m, 5H), 3.47 (s, 3H), 3.30 (s, 6H), 2.73 (s, 1H), 1.91 (s, 2H), 1.63 (s, 2H). Mass (m/z): 406.3 [M+H]⁺.

Compound 344

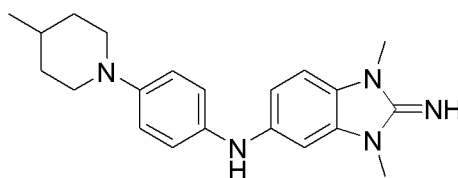
6-((1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)amino)
-3-methylbenzo[d]oxazol-2(3H)-one



- 5 The title compound **344** (11.3 mg) was prepared in a total yield of 16.8 % as a white solid from 6-amino-3-methylbenzo[d]oxazol-2(3H)-one (41 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL)
10 according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.89 (s, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 2.0 Hz, 1H), 6.78 (dd, *J* = 8.0, 2.1 Hz, 2H), 6.70 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.25 – 3.22 (m, 6H), 3.20 (s, 3H). Mass (m/z): 325.3 [M+H]⁺.

Compound 345

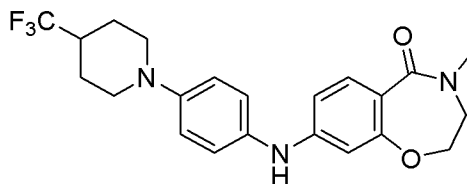
- 15 2-imino-1,3-dimethyl-N-(4-(4-methylpiperidin-1-yl)phenyl)-2,3-dihydro-1H-benzo[d]imidazol-5-amine



- The title compound **345** (13.9 mg) was prepared in a total yield of 79.2 % as a light blue solid from 4-(4-methylpiperidin-1-yl)aniline (12.4 mg, 0.065 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-imine (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.47 - 6.79 (m, 7H), 3.78 - 3.67 (m, 2H), 3.64 (s, 3H), 3.59 (s, 3H), 2.83 - 2.54 (m, 2H), 1.97 - 1.68 (m, 2H), 1.53 (m, 1H), 1.47 - 1.36 (m, 2H), 1.01 (d, *J* = 6.4 Hz, 3H). Mass (m/z): 350.2 [M+H]⁺.
- 20
25

Compound 346

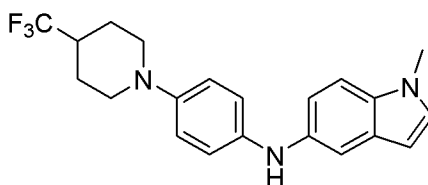
4-methyl-8-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydrobenzo[f][1,4]oxazepin-5(2H)-one



- 5 The title compound **346** (18.3 mg) was prepared in a total yield of 87.1 % as a wheat solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 8-bromo-4-methyl-3,4-dihydrobenzo[f][1,4]oxazepin-5(2H)-one (12.8 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the
 10 procedure for compound 1. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.59 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.43 (d, *J* = 2.4 Hz, 1H), 4.33 (t, *J* = 4.8 Hz, 2H), 3.74 - 3.63 (m, 2H), 3.53 (t, *J* = 4.8 Hz, 2H), 3.17 (s, 3H), 2.81 - 2.57 (m, 2H), 2.15 (m, 1H), 2.02 - 1.92 (m, 2H), 1.85 - 1.68 (m, 2H). Mass (*m/z*): 420.3
 15 [M+H]⁺.

Compound 347

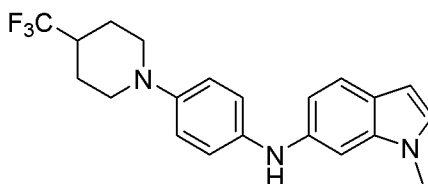
1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indol-5-amine



- 20 The title compound **347** (23.9 mg) was prepared in a yield of 31.27% as a pale gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-1-methyl-1H-indole (47 mg, 0.23 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 7.57-6.42 (br, 9H), 4.62-3.21 (br, 8H), 2.64-1.41 (br, 4H). Mass (*m/z*):
 25 374.2 [M+H]⁺.

Compound 348

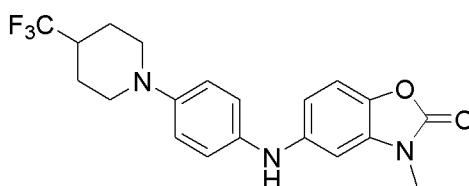
1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indol-6-amine



The title compound **348** (38.0 mg) was prepared in a yield of 49.71% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 6-bromo-1-methyl-1H-indole (47 mg, 0.22 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 7.86-6.63 (br, 9H), 4.51-3.04 (br, 8H), 2.36-1.52 (br, 4H). Mass (m/z): 374.1 [M+H]⁺.

Compound 349

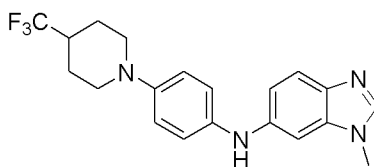
3-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one



The title compound **349** (8.8 mg) was prepared in a yield of 10.25% as a dim gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.22 mmol) and 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (59 mg, 0.22 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.84 (s, 1H), 7.12 (d, *J* = 8.6 Hz, 1H), 7.03 – 6.95 (m, 2H), 6.94 – 6.87 (m, 2H), 6.75 (d, *J* = 2.1 Hz, 1H), 6.63 (dt, *J* = 8.6, 1.9 Hz, 1H), 3.62 (d, *J* = 12.4 Hz, 2H), 3.26 (s, 3H), 2.63 (td, *J* = 12.3, 2.5 Hz, 2H), 1.93 – 1.79 (m, 2H), 1.57 (qd, *J* = 12.4, 4.2 Hz, 3H). Mass (m/z): 392.6 [M+H]⁺.

Compound 350

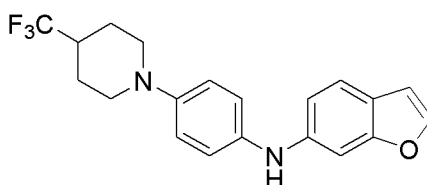
1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[d]imidazol-6-amine



The title compound **350** (35.6 mg) was prepared in a total yield of 28.5% as a yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (82 mg, 0.43 mmol), 6-bromo-1-methyl-1H-benzo[d]imidazole (70 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.26 (s, 1H), 7.96 (s, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.09 – 7.02 (m, 3H), 6.97 – 6.88 (m, 3H), 3.79 (d, *J* = 1.6 Hz, 3H), 3.67 – 3.60 (m, 2H), 2.64 (td, *J* = 12.4, 2.5 Hz, 2H), 2.47 – 2.40 (m, 1H), 1.93 – 1.84 (m, 2H), 1.58 (qd, *J* = 12.5, 4.1 Hz, 2H). Mass (*m/z*): 375.3 [M+H]⁺.

Compound 351

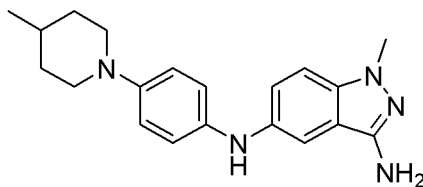
N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzofuran-6-amine



The title compound **351** (10.3 mg) was prepared in a total yield of 8.6% as a yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (105 mg, 0.43 mmol), 6-bromobenzofuran (66 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.55 (d, *J* = 2.2 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 8.9 Hz, 3H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.70 (dd, *J* = 2.2, 1.0 Hz, 1H), 3.67 – 3.54 (m, 2H), 2.78 – 2.59 (m, 2H), 2.38 – 2.23 (m, 2H), 2.03 – 1.91 (m, 2H), 1.75 (qd, *J* = 12.6, 4.1 Hz, 2H). Mass (*m/z*): 361.2 [M+H]⁺.

Compound 352

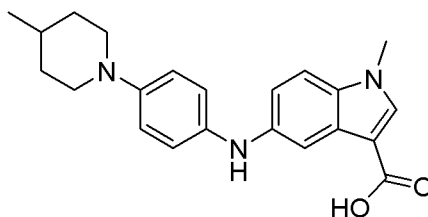
1-methyl-*N*5-(4-(4-methylpiperidin-1-yl)phenyl)-1H-indazole-3,5-diamine



The title compound **352** (9.9 mg) was prepared in a total yield of 8.9% as a yellow powder from 4-(4-methylpiperidin-1-yl)aniline (81.7 mg, 0.43 mmol), 5-bromo-1-methyl-1H-indazol-3-amine (75 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μ mol), X-Phos (7.8 mg, 16.5 μ mol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.38 – 6.52 (m, 7H), 3.76 (s, 3H), 3.61 – 3.35 (m, 2H), 2.98 – 2.43 (m, 2H), 1.87 – 1.71 (m, 2H), 1.58 – 1.35 (m, 3H), 1.01 (d, *J* = 6.2 Hz, 3H). Mass (m/z): 336.4 [M+H]⁺.

Compound 353

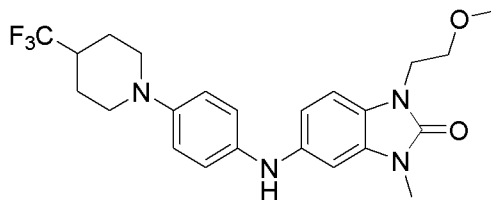
1-methyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1H-indole-3-carboxylic acid



The title compound **353** (11.1 mg) was prepared in a total yield of 9.2% as a yellow powder from 4-(4-methylpiperidin-1-yl)aniline (81.7 mg, 0.43 mmol), 5-bromo-1-methyl-1H-indole-3-carboxylic acid (85 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μ mol), X-Phos (7.8 mg, 16.5 μ mol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.18 – 6.47 (m, 8H), 4.17 – 3.61 (m, 7H), 1.75 – 1.45 (m, 5H), 1.02 (d, *J* = 6.1 Hz, 3H). Mass (m/z): 364.3 [M+H]⁺.

Compound 354

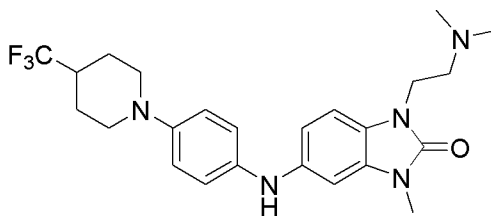
1-(2-methoxyethyl)-3-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **354** (59.1 mg) was prepared in a total yield of 40.0% as a gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (105 mg, 0.43 mmol), 5-bromo-1-(2-methoxyethyl)-3-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (94.7 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 umol), X-Phos (7.8 mg, 16.5 umol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.10 – 6.03 (m, 7H), 4.03 (t, *J* = 5.4 Hz, 2H), 3.87 – 3.42 (m, 4H), 3.33 – 3.31 (m, 5H), 2.34 – 2.21 (m, 1H), 2.05 – 1.91 (m, 2H), 1.80 – 1.65 (m, 2H). Mass (m/z): 449.3 [M+H]⁺.

Compound 355

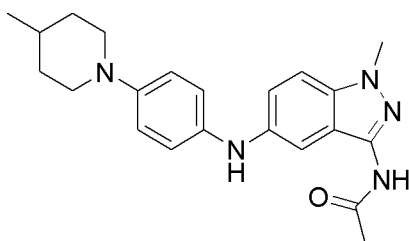
1-(2-(dimethylamino)ethyl)-3-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **355** (7.0 mg) was prepared in a total yield of 4.6% as a gray powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (80 mg, 0.43 mmol), 5-bromo-1-(2-(dimethylamino)ethyl)-3-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (74.5 mg, 0.25 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 umol), X-Phos (7.8 mg, 16.5 umol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.27 – 6.47 (m, 7H), 3.99 (t, *J* = 6.5 Hz, 2H), 3.64 – 3.36 (m, 2H), 3.24 (s, 3H), 2.87 (t, *J* = 6.5 Hz, 2H), 2.76 – 2.46 (m, 2H), 2.45 (s, 6H), 2.24 – 2.12 (m, 1H), 1.94 – 1.82 (m, 2H), 1.62 (q, *J* = 12.5, 11.9 Hz, 2H). Mass (m/z): 462.4 [M+H]⁺.

Compound 356

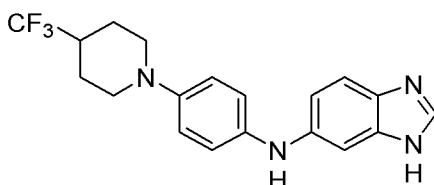
N-(1-methyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1H-indazol-3-yl)

acetamide

The title compound **356** (4.0 mg) was prepared in a total yield of 3.2% as a gray powder from 4-(4-methylpiperidin-1-yl)aniline (82 mg, 0.43 mmol),
 5 *N*-(5-bromo-1-methyl-1H-indazol-3-yl)acetamide (74.5 mg, 0.25 mmol),
 Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.84 – 6.71 (m, 7H), 4.24 – 3.43 (m, 7H), 2.20 (s, 3H), 2.07 – 2.00 (m, 1H), 1.93 – 1.40 (m, 7H), 1.06 (d, *J* = 6.0 Hz, 4H).
 10 Mass (*m/z*): 378.3 [M+H]⁺.

Compound 357

N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[*d*]imidazol-6-amine

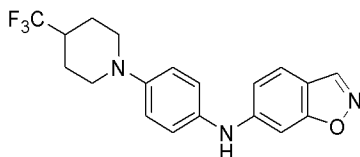


15 To a solution of tert-butyl 6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-benzo[*d*]imidazole-1-carboxylate (153 mg, 0.33 mmol) in EtOH (5 mL) was added a solution of HCl in 1,4-dioxane (5 mL). Then the solution was stirred for 30 mins at r.t. and concentrated. 10 ml water was added. The PH of the filtration was adjusted to 8-9 with sodium carbonate
 20 solution. Then the mixture was extracted by DCM (15 mL x 3). The combined organic layers were washed with water (10 mL), dried over Na₂SO₄ and concentrated. The residue was purified by perp-TLC (MeOH/DCM=1/10) to afford the desired product as a light gray solid. (6.1 mg, 5.0%). ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.56 (s, 1H), 8.04 – 6.31 (m, 7H), 4.01 – 3.51 (m, 2H), 3.11 – 2.57 (m, 2H), 2.41 – 2.27 (m, 1H),
 25

2.13 – 1.65 (m, 4H). Mass (m/z): 361.2 [M+H]⁺.

Compound 358

N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzo[d]isoxazol-6-amine

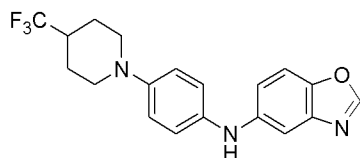


- 5 The title compound **358** (19.1 mg) was prepared in a total yield of 21.0 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (73 mg, 0.303 mmol), 6-bromobenzo[d]isoxazole (50 mg, 0.252 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (124 mg, 0.374 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**.
- 10 ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.64 (s, 1H), 8.46 (s, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.06 – 7.00 (m, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.45 (d, *J* = 2.0 Hz, 1H), 6.34 (dd, *J* = 8.4, 2.1 Hz, 1H), 3.71 (d, *J* = 12.0 Hz, 2H), 2.67 (td, *J* = 12.4, 2.4 Hz, 2H), 2.44 (ddd, *J* = 15.2, 7.6, 3.6 Hz, 1H), 1.94 – 1.84 (m, 2H), 1.57 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (m/z): 362.3 [M+H]⁺.

15

Compound 359

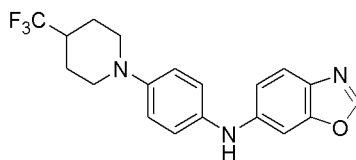
N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzo[d]oxazol-5-amine



- The title compound **359** (9.3 mg) was prepared in a total yield of 10.2 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (73 mg, 0.303 mmol), 5-bromobenzo[d]oxazole (50 mg, 0.252 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (124 mg, 0.374 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**.
- 20 ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.59 (s, 1H), 7.90 (s, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.04 – 6.99 (m, 3H), 6.96 – 6.90 (m, 2H), 3.63 (d, *J* = 12.4 Hz, 2H), 2.63 (td, *J* = 12.4, 2.4 Hz, 2H), 2.43 (dtd, *J* = 12.4, 8.4, 3.6 Hz, 1H), 1.93 – 1.84 (m, 2H), 1.58 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (m/z): 362.3 [M+H]⁺.
- 25

Compound 360

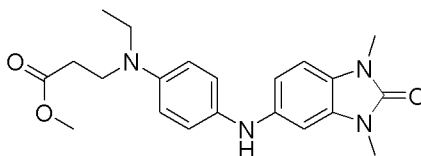
N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)benzo[d]oxazol-6-amine



The title compound **360** (27.3 mg) was prepared in a total yield of 30.0 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (73 mg, 0.303 mmol), 6-bromobenzo[d]oxazole (50 mg, 0.252 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol) and Cs₂CO₃ (124 mg, 0.374 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.38 (s, 1H), 8.08 (s, 1H), 7.48 (d, *J* = 8.8 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 7.04 – 6.96 (m, 2H), 6.88 (td, *J* = 8.8, 2.0 Hz, 3H), 3.59 (d, *J* = 11.6 Hz, 2H), 2.57 (td, *J* = 12.4, 2.4 Hz, 2H), 2.36 (dq, *J* = 12.4, 3.6 Hz, 1H), 1.88 – 1.76 (m, 2H), 1.51 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass (*m/z*): 362.3 [M+H]⁺.

Compound 361

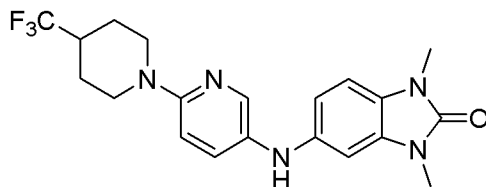
methyl 3-((4-((1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)amino)phenyl)(ethyl)amino)propanoate



The title compound **361** (10.3 mg) was prepared in a total yield of 53.9 % as a white solid from methyl 3-((4-aminophenyl)(ethyl)amino)propanoate (14.4 mg, 0.065 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.35 - 6.70 (m, 7H), 3.67 (s, 3H), 3.62 (s, 3H), 3.41 – 3.32 (m, 4H), 3.29 (s, 3H), 2.58 - 2.46 (m, 2H), 1.08 (t, *J* = 6.8 Hz, 3H). Mass (*m/z*): 383.2 [M+H]⁺.

Compound 362

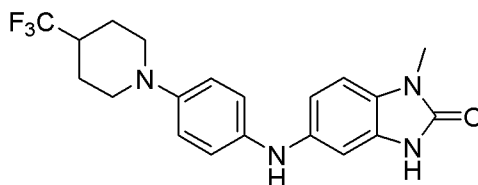
1,3-dimethyl-5-((6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **362** (13.7 mg) was prepared in a total yield of 67.6 % as a yellow solid from 6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (15.9 mg, 0.065 mmol), 5-bromo-2-methylisoindoline-1,3-dione (12.0 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.96 (d, *J* = 2.4 Hz, 1H), 7.43 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.77 - 6.70 (m, 2H), 4.25 - 4.17 (m, 2H), 3.37 (s, 3H), 3.34 (s, 3H), 2.86 - 2.73 (m, 2H), 2.38 (m, 1H), 1.99 - 1.88 (m, 2H), 1.67 - 1.53 (m, 2H). Mass (*m/z*): 406.2 [M+H]⁺.

Compound 363

1-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



15

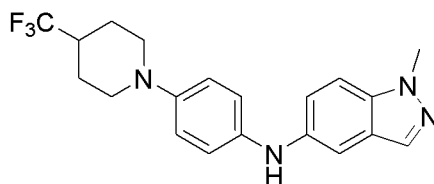
The title compound **363** (16.5 mg) was prepared in a total yield of 84.4 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-1-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (11.3 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.46 - 6.65 (m, 7H), 3.71 - 3.65 (m, 2H), 3.58 (s, 3H), 2.78 - 2.66 (m, 2H), 2.13 (m, 1H), 2.01 - 1.87 (m, 2H), 1.76 - 1.67 (m, 2H). Mass (*m/z*): 391.2 [M+H]⁺.

25

Compound 364

1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indazol

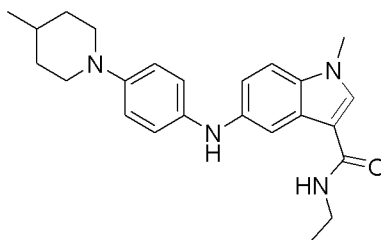
-5-amine



The title compound **364** (89.9 mg) was prepared in a total yield of 71.9% as a light yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (105 mg, 0.43 mmol), 5-bromo-1-methyl-1H-indazole (70 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.80 (s, 1H), 7.47 – 6.83 (m, 7H), 4.02 (s, 3H), 3.76 – 3.41 (m, 2H), 3.22 – 2.34 (m, 2H), 2.33 – 2.20 (m, 2H), 2.02 – 1.93 (m, 2H), 1.73 (qd, *J* = 12.7, 3.9 Hz, 2H). Mass (*m/z*): 375.3 [M+H]⁺.

Compound 365

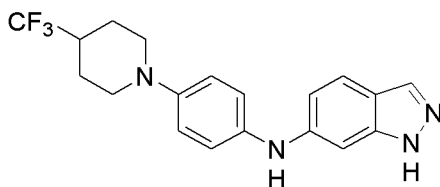
N-ethyl-1-methyl-5-((4-(4-methylpiperidin-1-yl)phenyl)amino)-1H-indole-3-carboxamide



The title compound **365** (12.0 mg) was prepared in a total yield of 9.2% as a gray solid from 4-(4-methylpiperidin-1-yl)aniline (81.7 mg, 0.43 mmol), 5-bromo-*N*-ethyl-1-methyl-1H-indole-3-carboxamide (93.3 mg, 0.33 mmol), Pd₂(dba)₃ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and Cs₂CO₃ (163 mg, 0.50 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.71 (s, 1H), 7.55 – 6.6 (m, 7H), 4.00 – 3.75 (m, 4H), 3.39 (q, *J* = 7.2 Hz, 2H), 3.33 (s, 3H), 1.88 – 1.34 (m, 5H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.02 (d, *J* = 6.1 Hz, 3H). Mass (*m/z*): 391.3 [M+H]⁺.

Compound 366

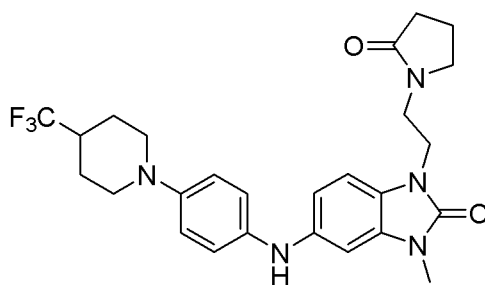
N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indazol-6-amine



To a solution of tert-butyl 6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indazole-1-carboxylate (45 mg, 0.10 mmol) in EtOH (5 mL) was added a solution of HCl in 1,4-dioxane (5 mL). Then the solution
 5 was stirred for 30 mins at r.t. and concentrated. 10 ml water was added. The pH of the filtration was adjusted to 8-9 with sodium carbonate solution. Then the mixture was extracted by DCM (15 mL x 3). The combined organic layers were washed with water (10 mL), dried over Na₂SO₄ and concentrated. The residue was purified by prep-TLC (MeOH/DCM=1/10)
 10 to afford the desired product as a light gray solid. (23.0 mg, 63.8%). ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.56 (s, 1H), 8.04 – 6.31 (m, 7H), 4.01 – 3.51 (m, 2H), 3.11 – 2.57 (m, 2H), 2.41 – 2.27 (m, 1H), 2.13 – 1.65 (m, 4H). ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.56 (s, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.78 – 7.70 (m, 2H), 7.50 – 7.41 (m, 2H), 7.23 – 7.14 (m, 1H), 3.85 –
 15 3.77 (m, 4H), 2.91 – 2.78 (m, 1H), 2.36 – 2.20 (m, 4H). Mass (*m/z*): 361.2 [M+H]⁺.

Compound 367

3-methyl-1-(2-(2-oxopyrrolidin-1-yl)ethyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



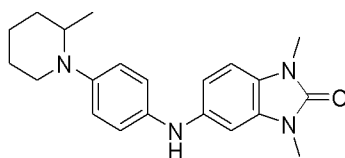
20

The title compound **367** (22.1 mg) was prepared in a total yield of 87.9 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 5-bromo-3-methyl-1-(2-(2-oxopyrrolidin-1-yl)ethyl)-1,3-dihydro-2H-benzo[d]imidazol-2-one (16.9 mg, 0.05 mmol),

Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.35 - 6.54 (m, 7H), 4.07 - 3.96 (m, 2H), 3.59 (t, *J* = 6.8 Hz, 2H), 3.43 (t, *J* = 6.8 Hz, 2H), 3.33 (s, 3H), 2.81 - 2.65 (m, 2H), 2.21 (m, 1H), 2.19 (t, *J* = 8.1 Hz, 2H), 2.05 - 1.86 (m, 4H), 1.82 - 1.62 (m, 2H). Mass (m/z): 502.3 [M+H]⁺

Compound 368

1,3-dimethyl-5-((4-(2-methylpiperidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one

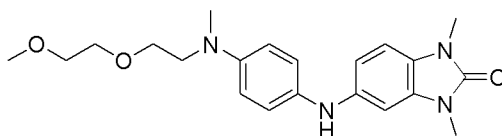


10

The title compound **368** (31.9 mg) was prepared in a total yield of 43.8 % as a green solid from 4-(2-methylpiperidin-1-yl)aniline (48 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.78 (s, 1H), 7.14 – 6.63 (m, 7H), 3.50 (s, 1H), 3.27 (s, 6H), 3.00 (s, 2H), 1.89 – 1.33 (m, 6H), 0.88 (s, 3H). Mass (m/z): 321.3 [M+H]⁺.

Compound 369

5-((4-((2-(2-methoxyethoxy)ethyl)(methyl)amino)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



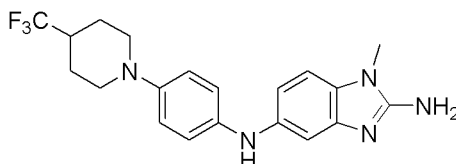
The title compound **369** (41.8 mg) was prepared in a total yield of 52.3 % as a brown solid from N¹-(2-(2-methoxyethoxy)ethyl)-N¹-methylbenzene-1,4-diamine (56 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1.

25

^1H NMR (400 MHz, DMSO- d_6) δ 7.45 (s, 1H), 6.94 (t, $J = 9.2$ Hz, 3H), 6.72 – 6.56 (m, 4H), 3.57 – 3.49 (m, 4H), 3.45 – 3.38 (m, 4H), 3.24 (d, $J = 3.2$ Hz, 6H), 2.86 (s, 3H). Mass (m/z): 385.3 $[\text{M}+\text{H}]^+$.

Compound 370

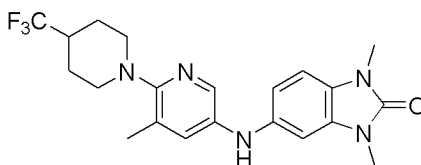
5 *1-methyl- N^5 -(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[d]imidazole-2,5-diamine*



The title compound **370** (2.0 mg) was prepared in a total yield of 1.5% as a light pink solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (105 mg, 0.43 mmol), 5-bromo-1-methyl-1H-benzo[d]imidazol-2-amine (75 mg, 0.33 mmol), $\text{Pd}_2(\text{dba})_3$ (3.0 mg, 3.3 μmol), X-Phos (7.8 mg, 16.5 μmol), and t-BuONa (48 mg, 0.50 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.13 – 6.52 (m, 7H), 3.73 – 3.44 (m, 5H), 2.85 – 2.49 (m, 2H), 2.34 – 2.21 (m, 1H), 2.02 – 1.91 (m, 2H), 1.80 – 1.67 (m, 2H). Mass (m/z): 390.3 $[\text{M}+\text{H}]^+$.

Compound 371

1,3-dimethyl-5-((5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one

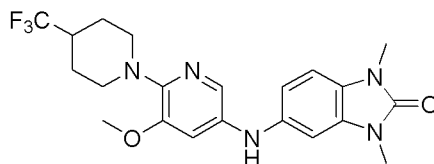


20 The title compound **371** (33.4 mg) was prepared in a total yield of 31.9% as a light yellow powder from 5-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (84 mg, 0.33 mmol), 5-bromo-1,3-dimethyl-1H-benzo[d]imidazol-2(3H)-one (60 mg, 0.25 mmol), $\text{Pd}_2(\text{dba})_3$ (2.0 mg, 2.5 μmol), X-Phos (6.0 mg, 12.5 μmol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.88 (d, $J = 2.8$ Hz, 1H), 7.31 (dd, $J = 2.8, 0.9$ Hz, 1H), 7.08 – 7.02 (m, 1H), 6.89 – 6.83 (m, 2H), 3.41 (s, 3H),

3.38 (s, 3H), 3.37 – 3.34 (m, 2H), 2.79 (td, $J = 12.4, 2.3$ Hz, 2H), 2.37 – 2.29 (m, 1H), 2.28 (s, 3H), 2.01 – 1.94 (m, 2H), 1.69 – 1.57 (m, 2H). Mass (m/z): 420.3 $[M+H]^+$.

Compound 372

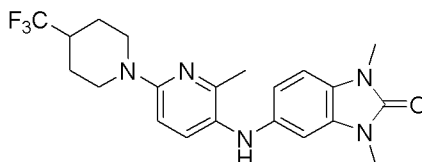
5 5-((5-methoxy-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **372** (21.7 mg) was prepared in a total yield of 19.9% as a light gray powder from 5-methoxy-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (84 mg, 0.33 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), $Pd_2(dba)_3$ (2.0 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.61 (d, $J = 2.3$ Hz, 1H), 7.06 (d, $J = 5.7$ Hz, 1H), 7.05 (s, 1H), 6.91 – 6.86 (m, 2H), 3.85 (s, 3H), 3.82 – 3.73 (m, 2H), 3.41 (s, 3H), 3.39 (s, 3H), 2.72 (td, $J = 12.5, 2.4$ Hz, 2H), 2.36 – 2.25 (m, 1H), 1.98 – 1.89 (m, 2H), 1.69 – 1.57 (m, 2H). Mass (m/z): 436.3 $[M+H]^+$.

Compound 373

1,3-dimethyl-5-((2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



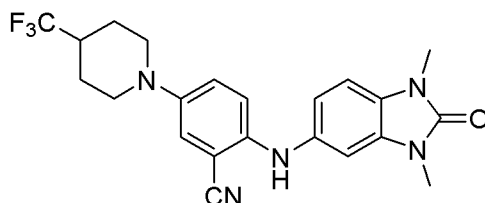
The title compound **373** (54.4 mg) was prepared in a total yield of 51.8% as a light yellow powder from 2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (84 mg, 0.33 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), $Pd_2(dba)_3$ (2.3 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.39 (d, $J = 8.7$ Hz, 1H), 6.94 (d, $J = 8.4$ Hz, 1H),

6.68 (d, $J = 8.8$ Hz, 1H), 6.52 (dd, $J = 8.4, 2.1$ Hz, 1H), 6.47 (d, $J = 2.1$ Hz, 1H), 4.35 (d, $J = 12.9$ Hz, 2H), 3.38 (s, 3H), 2.81 (t, $J = 12.7$ Hz, 2H), 2.47 – 2.35 (m, 1H), 2.33 (s, 3H), 2.00 – 1.89 (m, 1H), 1.69 – 1.57 (m, 2H). Mass (m/z): 420.3 $[M+H]^+$.

5

Compound 374

2-((1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-5-yl)amino)-5-(4-(trifluoromethyl)piperidin-1-yl)benzonitrile



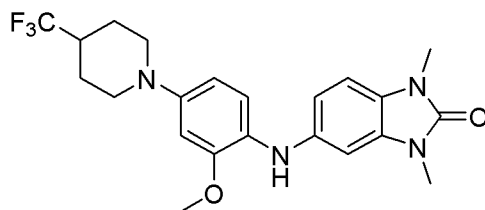
The title compound **374** (45.4 mg) was prepared in a yield of 56.93% as a white powder from 2-amino-5-(4-(trifluoromethyl)piperidin-1-yl)benzonitrile (50 mg, 0.19 mmol) and 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (49 mg, 0.20 mmol) according to the procedure for compound 1. ^1H NMR (Methanol- d_4) δ 7.20 (dd, $J = 9.1, 2.9$ Hz, 1H), 7.16 – 7.13 (m, 1H), 7.10 (d, $J = 9.1$ Hz, 1H), 7.06 (d, $J = 8.9$ Hz, 1H), 6.90 – 6.86 (m, 2H), 3.63 (d, $J = 11.9$ Hz, 2H), 3.41 (s, 3H), 3.37 (s, 3H), 2.68 (td, $J = 12.3, 2.5$ Hz, 2H), 2.29 (ddp, $J = 12.4, 7.9, 4.0$ Hz, 1H), 1.98 (d, $J = 12.9$ Hz, 2H), 1.78 – 1.62 (m, 2H). Mass (m/z): 430.5 $[M+H]^+$.

15

Compound 375

5-((2-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

20



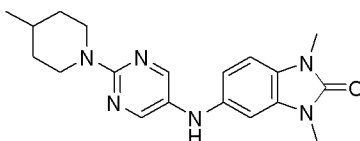
The title compound **375** (36.7 mg) was prepared in a yield of 46.34% as a white powder from 2-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.18 mmol) and 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (48 mg, 0.20 mmol) according to the procedure for compound 1. ^1H NMR (Methanol- d_4) δ : 7.30 – 6.28 (m, 6H), 3.87 (s, 5H),

25

3.41 – 3.36 (m, 3H), 2.21 (s, 2H), 2.11 – 1.85 (m, 4H), 1.66 (d, $J = 48.8$ Hz, 4H). Mass (m/z): 435.2 $[M+H]^+$.

Compound 376

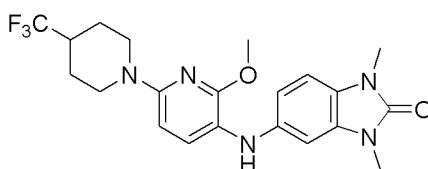
1,3-dimethyl-5-((2-(4-methylpiperidin-1-yl)pyrimidin-5-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **376** (10.1 mg) was prepared in a total yield of 13.8 % as a white solid from 2-(4-methylpiperidin-1-yl)pyrimidin-5-amine (48 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H- benzo[d]imidazol-2-one (50 mg, 0.208 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.23 (s, 2H), 7.49 (s, 1H), 6.94 (d, $J = 8.4$ Hz, 1H), 6.61 (d, $J = 2.0$ Hz, 1H), 6.54 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.55 (dt, $J = 12.4, 3.2$ Hz, 2H), 3.25 (d, $J = 7.2$ Hz, 6H), 2.82 (td, $J = 12.8, 2.4$ Hz, 2H), 1.70 – 1.60 (m, 3H), 1.12 – 1.00 (m, 2H), 0.93 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 353.3 $[M+H]^+$.

Compound 377

5-((2-methoxy-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



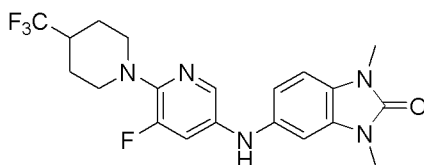
The title compound **377** (40.6 mg) was prepared in a total yield of 37.3% as a purple powder from 2-methoxy-6-(4-(trifluoromethyl) piperidin-1-yl) pyridin-3-amine (79 mg, 0.29 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), $Pd_2(dba)_3$ (2.3 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.38 (d, $J = 8.3$ Hz, 1H), 6.96 (d, $J = 8.4$ Hz, 1H), 6.71 (d, J

= 8.4 Hz, 1H), 6.67 (d, J = 2.1 Hz, 1H), 6.31 (d, J = 8.3 Hz, 1H), 4.38 – 4.32 (m, 2H), 3.93 (s, 3H), 3.38 (s, 3H), 3.34 (s, 3H), 2.79 (t, J = 12.8 Hz, 2H), 2.44 – 2.35 (m, 1H), 1.98 – 1.92 (m, 2H), 1.69 – 1.57 (m, 2H). Mass (m/z): 436.3 [M+H]⁺.

5

Compound 378

5-((5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

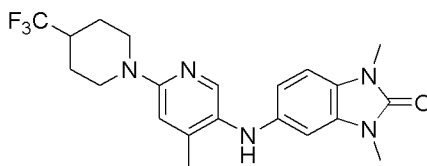


The title compound **378** (40.6 mg) was prepared in a total yield of 42.0% as a brown powder from 5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (75.6 mg, 0.29 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 umol), X-Phos (6.0 mg, 12.5 umol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.80 (d, J = 2.1 Hz, 1H), 7.18 (dd, J = 13.9, 2.4 Hz, 1H), 7.06 – 7.01 (m, 1H), 6.89 – 6.83 (m, 2H), 3.85 – 3.77 (m, 2H), 3.40 (s, 3H), 3.38 (s, 3H), 2.83 (td, J = 12.6, 2.4 Hz, 2H), 2.39 – 2.26 (m, 1H), 1.99 – 1.89 (m, 2H), 1.78 – 1.65 (m, 2H). Mass (m/z): 424.3 [M+H]⁺.

15

Compound 379

1,3-dimethyl-5-((4-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



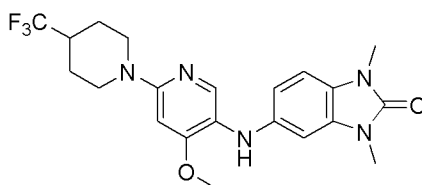
25

The title compound **379** (49.7 mg) was prepared in a total yield of 47.3% as a peach puff powder from 4-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (75.0 mg, 0.29 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 umol), X-Phos (6.0 mg, 12.5 umol), and t-BuONa (36 mg, 0.38 mmol) according to the procedure for compound **1**. ¹H NMR

(400 MHz, Methanol- d_4) δ 7.92 (s, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.82 (s, 1H), 6.51 (dd, J = 8.4, 2.1 Hz, 1H), 6.48 (d, J = 2.1 Hz, 1H), 4.34 – 4.24 (m, 2H), 3.38 (s, 3H), 3.32 (s, 3H), 2.90 – 2.81 (m, 2H), 2.48 – 2.36 (m, 1H), 2.21 (s, 3H), 2.00 – 1.92 (m, 2H), 1.68 – 1.55 (m, 2H). Mass (m/z):
 5 420.3 [M+H]⁺.

Compound 380

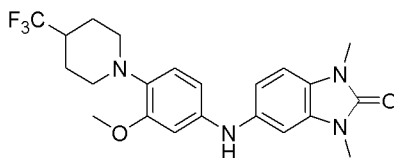
5-((4-methoxy-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



10 The title compound **380** (27.0 mg) was prepared in a total yield of 21.6% as a light yellow powder from 4-methoxy-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (69.0 mg, 0.29 mmol), 5-bromo-1,3-dimethyl-2,3-dihydro-1H-1,3-benzodiazol-2-one (60 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 umol), X-Phos (6.0 mg, 12.5 umol), and t-BuONa
 15 (36 mg, 0.38 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol- d_4) δ 7.85 (s, 1H), 6.98 (d, J = 8.3 Hz, 1H), 6.71 (dd, J = 8.3, 2.1 Hz, 1H), 6.68 (d, J = 2.1 Hz, 1H), 6.52 (d, J = 6.9 Hz, 1H), 4.32 – 4.24 (m, 2H), 3.92 (s, 3H), 3.39 (s, 3H), 3.35 (s, 3H), 2.92 – 2.85 (m, 2H), 2.48 – 2.40 (m, 1H), 2.02 – 1.99 (m, 2H), 1.67 – 1.61 (m, 2H). Mass
 20 (m/z): 436.3 [M+H]⁺.

Compound 381

5-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

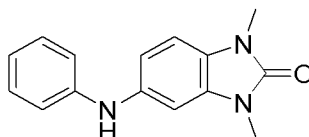


25 The title compound **381** (37.8 mg) was prepared in a total yield of 41.8 % as a yellow solid from 3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (65 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro

-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.10 – 6.46 (m, 6H), 3.82 (s, 3H), 3.48 (s, 3H),
 5 3.22 (s, 6H), 2.72 (s, 1H), 2.12 – 1.81 (m, 5H). Mass (m/z): 435.3 [M+H]⁺.

Compound 382

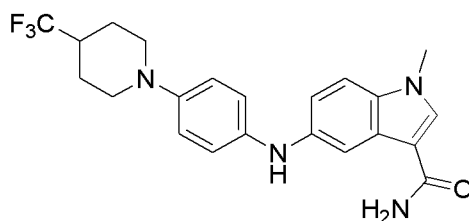
1,3-dimethyl-5-(phenylamino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **382** (41.7 mg) was prepared in a total yield of 79.1 %
 10 as a yellow solid from aniline (22 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.96 (s, 1H), 7.20 – 7.14 (m, 2H), 7.03 (d,
 15 *J* = 8.4 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.89 (d, *J* = 2.0 Hz, 1H), 6.81 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.72 (tt, *J* = 7.2, 1.1 Hz, 1H), 3.29 (d, *J* = 7.6 Hz, 6H). Mass (m/z): 254.3 [M+H]⁺.

Compound 383

1-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indole-3-carboxamide

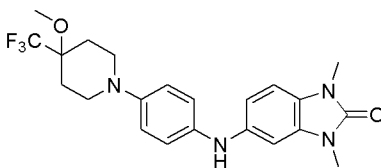


The title compound **383** (3.7 mg) was prepared in a yield of 4.5% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-1-methyl-1H-indole-3-carboxamide (48 mg, 0.20
 25 mmol) according to the procedure for compound 1. ¹H NMR (DMSO-*d*₆) δ 7.93 (s, 2H), 7.34 (s, 2H), 6.81 (d, *J* = 119.4 Hz, 4H), 3.92 (s, 4H), 3.16 (s, 1H), 2.72 – 2.63 (m, 1H), 2.32 (p, *J* = 1.9 Hz, 1H), 1.99 (q, *J* = 6.9, 6.3 Hz,

3H), 1.42 (s, 1H), 0.90 – 0.79 (m, 1H). Mass (m/z): 417.4 [M+H]⁺.

Compound 384

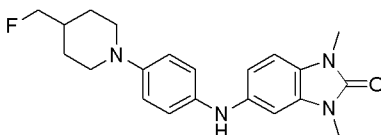
5-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one



The title compound **384** (30.2 mg) was prepared in a total yield of 33.4 % as a yellow solid from 4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)aniline (68 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, Pyridine-*d*₅) δ 8.90 (s, 2H), 8.60 (s, 3H), 8.46 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 4.95 (s, 2H), 4.86 (q, *J* = 1.2 Hz, 3H), 4.78 (s, 3H), 4.72 (s, 3H), 4.40 (s, 2H), 3.54 – 3.37 (m, 4H). Mass (m/z): 435.3 [M+H]⁺.

Compound 385

5-((4-(4-(fluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

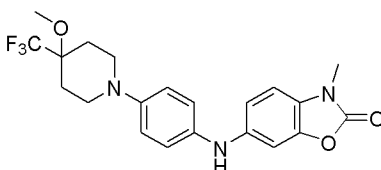


The title compound **385** (19.4 mg) was prepared in a total yield of 25.3 % as a blue solid from 4-(4-(fluoromethyl)piperidin-1-yl)aniline (52 mg, 0.250 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.208 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (102 mg, 0.312 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.74 (s, 1H), 6.63 (d, *J* = 8.8 Hz, 1H), 4.40 (d, *J* = 6.0 Hz, 1H), 4.28 (d, *J* = 5.6 Hz, 1H), 3.57 (d, *J* = 12.0 Hz, 2H), 3.24 (d, *J* = 3.2 Hz, 6H), 2.60 (t, *J* = 12.0 Hz, 2H), 1.74 (d, *J* = 13.2 Hz, 3H), 1.36 (d, *J* = 12.4

Hz, 2H). Mass (m/z): 369.3 [M+H]⁺.

Compound 386

6-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one



5

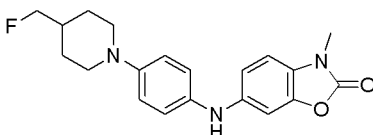
The title compound **386** (23.6 mg) was prepared in a total yield of 25.6 % as a yellow solid from 4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl) aniline (72 mg, 0.263 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (129 mg, 0.394 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.99 – 6.88 (m, 5H), 6.79 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.46 (d, *J* = 12.4 Hz, 2H), 3.39 (d, *J* = 1.2 Hz, 3H), 3.29 (s, 3H), 2.75 (td, *J* = 12.4, 2.4 Hz, 2H), 2.03 – 1.95 (m, 2H), 1.83 (td, *J* = 13.2, 4.4 Hz, 2H). Mass (m/z): 422.3 [M+H]⁺.

10

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Compound 387

6-((4-(4-(fluoromethyl)piperidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one



The title compound **387** (29.7 mg) was prepared in a total yield of 38.2 % as a white solid from 4-(4-(fluoromethyl)piperidin-1-yl)aniline (55 mg, 0.263 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (129 mg, 0.394 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.74 (s, 1H), 6.63 (d, *J* = 8.8 Hz, 1H), 4.40 (d, *J* = 6.0 Hz, 1H), 4.28 (d, *J* = 5.6 Hz,

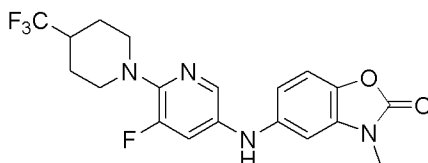
20

25

1H), 3.57 (d, $J = 11.6$ Hz, 2H), 3.27 (s, 3H), 2.60 (t, $J = 12.0$ Hz, 2H), 1.74 (d, $J = 13.2$ Hz, 3H), 1.36 (d, $J = 12.4$ Hz, 2H). Mass (m/z): 356.3 [M+H]⁺.

Compound 388

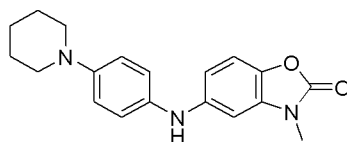
5-((5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)
-3-methylbenzo[d]oxazol-2(3H)-one



The title compound **388** (5.3 mg) was prepared in a total yield of 5.2% as a light yellow powder from 5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-amine (87.0 mg, 0.33 mmol), 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (57 mg, 0.25 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 umol), X-Phos (6.0 mg, 12.5 umol), and Cs₂CO₃ (122 mg, 0.38 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.19 (s, 1H), 7.89 (dd, $J = 2.4, 1.0$ Hz, 1H), 7.30 (dd, $J = 14.2, 2.4$ Hz, 1H), 7.19 (d, $J = 8.6$ Hz, 1H), 6.89 (d, $J = 2.3$ Hz, 1H), 6.71 (dd, $J = 8.6, 2.3$ Hz, 1H), 3.81 – 3.76 (m, 2H), 3.31 (s, 3H), 2.86 – 2.75 (m, 2H), 2.59 – 2.52 (m, 1H), 1.92 – 1.84 (m, 2H), 1.63 – 1.51 (m, 2H). Mass (m/z): 411.2 [M+H]⁺.

Compound 389

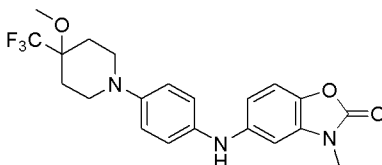
3-methyl-5-((4-(piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one



The title compound **389** (56.0 mg) was prepared in a total yield of 79.1 % as a white solid from 4-(piperidin-1-yl)aniline (46 mg, 0.263 mmol), 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (129 mg, 0.394 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.77 (s, 1H), 7.04 (d, $J = 8.4$ Hz, 1H), 6.96 – 6.88 (m, 2H), 6.80 (d, $J = 8.0$ Hz, 2H), 6.67 (s, 1H), 6.55 (d, $J = 8.8$ Hz, 1H), 3.19 (s, 3H), 2.94 (s, 4H), 1.55 (s, 4H), 1.43 (s, 2H). Mass (m/z): 324.3 [M+H]⁺.

Compound 390

5-((4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

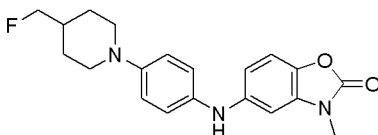


- 5 The title compound **390** (52.0 mg) was prepared in a total yield of 56.3 % as a white solid from 4-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)aniline (72 mg, 0.263 mmol), 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (129 mg, 0.394 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.87 (s, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.04 – 6.89 (m, 4H), 6.76 (s, 1H), 6.64 (d, *J* = 8.8 Hz, 1H), 3.47 (d, *J* = 12.0 Hz, 2H), 3.40 (d, *J* = 1.2 Hz, 3H), 3.27 (s, 3H), 2.78 (d, *J* = 10.4 Hz, 2H), 2.01 (d, *J* = 13.6 Hz, 2H), 1.86 (d, *J* = 13.6 Hz, 2H). Mass (m/z): 422.3 [M+H]⁺.

15

Compound 391

5-((4-(4-(fluoromethyl)piperidin-1-yl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

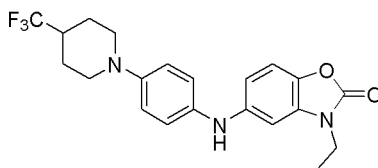


- The title compound **391** (25.9 mg) was prepared in a total yield of 33.3 % as a white solid from 4-(4-(fluoromethyl)piperidin-1-yl)aniline (55 mg, 0.263 mmol), 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.219 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (129 mg, 0.394 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.74 (s, 1H), 6.63 (d, *J* = 8.8 Hz, 1H), 4.40 (d, *J* = 6.0 Hz, 1H), 4.28 (d, *J* = 5.6 Hz, 1H), 3.57 (d, *J* = 11.6 Hz, 2H), 3.27 (s, 3H), 2.60 (t, *J* = 12.0 Hz, 2H), 1.74 (d, *J* = 13.2 Hz, 3H), 1.36 (d, *J* = 12.4 Hz, 2H). Mass (m/z): 356.3 [M+H]⁺.

25

Compound 392

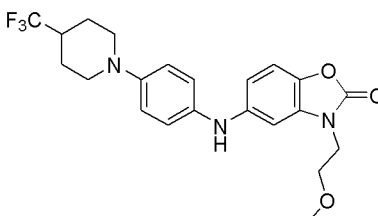
3-ethyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one



- 5 The title compound **392** (75.1 mg) was prepared in a total yield of 89.4 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (60 mg, 0.248 mmol), 5-bromo-3-ethylbenzo[d]oxazol-2(3H)-one (50 mg, 0.207 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (122 mg, 0.372 mmol) and 1,4-dioxane (5 mL) according to the procedure
- 10 for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.92 (t, *J* = 4.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.02 – 6.97 (m, 2H), 6.93 – 6.88 (m, 2H), 6.81 (d, *J* = 2.0 Hz, 1H), 6.65 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.78 (q, *J* = 7.2 Hz, 2H), 3.62 (d, *J* = 12.0 Hz, 2H), 2.63 (td, *J* = 12.4, 2.4 Hz, 2H), 2.43 (ddq, *J* = 12.4, 8.8, 4.0 Hz, 1H), 1.93 – 1.84 (m, 2H), 1.57 (qd, *J* = 12.4, 4.0 Hz, 2H),
- 15 1.22 (t, *J* = 7.2 Hz, 3H). Mass (*m/z*): 406.3 [M+H]⁺.

Compound 393

3-(2-methoxyethyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one

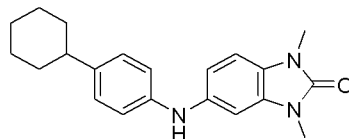


- 20 The title compound **393** (58.0 mg) was prepared in a total yield of 72.5 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (54 mg, 0.221 mmol), 5-bromo-3-(2-methoxyethyl)benzo[d]oxazol-2(3H)-one (50 mg, 0.184 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (91 mg, 0.276 mmol) and 1,4-dioxane (5 mL) according to
- 25 the procedure for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.92 (s, 1H), 7.13 (d, *J* = 8.4 Hz, 1H), 7.02 – 6.96 (m, 2H), 6.93 – 6.84 (m, 3H),

6.64 (dd, $J = 8.8, 2.0$ Hz, 1H), 3.91 (t, $J = 5.2$ Hz, 2H), 3.65 – 3.56 (m, 4H), 3.25 (s, 3H), 2.63 (t, $J = 12.0$ Hz, 2H), 2.47 – 2.37 (m, 1H), 1.88 (d, $J = 12.4$ Hz, 2H), 1.58 (d, $J = 12.8$ Hz, 2H). Mass (m/z): 436.3 $[M+H]^+$.

Compound 394

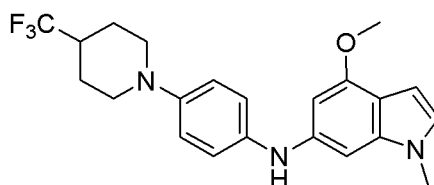
5 *5-((4-cyclohexylphenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one*



The title compound **394** (49.7 mg) was prepared in a total yield of 71.6 % as a yellow solid from 4-cyclohexylaniline (44 mg, 0.248 mmol),
 10 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (50 mg, 0.207 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (102 mg, 0.310 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 7.86 (s, 1H), 7.05 – 6.99 (m, 3H), 6.95 – 6.89 (m, 2H), 6.85 (d, $J = 2.1$ Hz, 1H), 6.78 (dd,
 15 $J = 8.3, 2.1$ Hz, 1H), 3.28 (d, $J = 7.9$ Hz, 6H), 2.42 – 2.42 (m, 1H), 1.82 – 1.66 (m, 5H), 1.42 – 1.28 (m, 4H), 1.22 (s, 1H). Mass (m/z): 336.3 $[M+H]^+$.

Compound 395

20 *4-methoxy-1-methyl-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indol-6-amine*

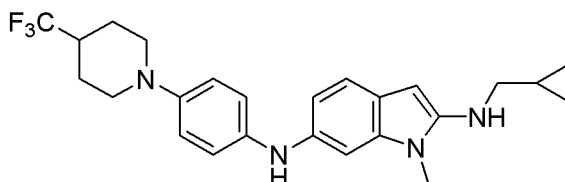


The title compound **395** (17.1 mg) was prepared in a total yield of 84.8 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-4-methoxy-1-methyl-1H-indole (12.0 mg, 0.05
 25 mmol), $Pd_2(dba)_3$ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs_2CO_3 (24.4 mg, 0.075 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, $DMSO-d_6$) δ 7.10 - 6.78 (m, 5H), 6.58 (s,

1H), 6.26 (d, $J = 2.8$ Hz, 2H), 3.80 (s, 3H), 3.60 (s, 3H), 3.58 - 3.51 (m, 2H), 2.69 - 2.52 (m, 2H), 2.38 (m, 1H), 1.94 - 1.79 (m, 2H), 1.66 - 1.49 (m, 2H). Mass (m/z): 404.2 [M+H]⁺.

Compound 396

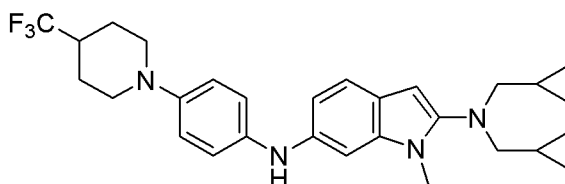
5 *N2-(cyclopropylmethyl)-1-methyl-N6-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indole-2,6-diamine*



The title compound **396** (17.1 mg) was prepared in a total yield of 84.8 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-N-(cyclopropylmethyl)-1-methyl-1H-indol-2-amine (13.9 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.43 - 6.58 (m, 7H), 3.75 - 3.45 (m, 5H), 3.40 - 3.22 (m, 2H), 2.80 - 2.54 (m, 2H), 2.41 (m, 1H), 1.98 - 1.82 (m, 2H), 1.69 - 1.47 (m, 2H), 1.29 - 1.14 (m, 1H), 0.57 - 0.46 (m, 2H), 0.43 - 0.24 (m, 2H). Mass (m/z): 443.2 [M+H]⁺

Compound 397

N2,N2-bis(cyclopropylmethyl)-1-methyl-N6-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indole-2,6-diamine



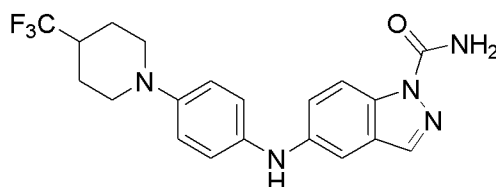
The title compound **397** (20.3mg) was prepared in a total yield of 81.8 % as a yellow solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (15.9 mg, 0.065 mmol), 6-bromo-N,N-bis(cyclopropylmethyl)-1-methyl-1H-indol-2-amine (16.7 mg, 0.05 mmol), Pd₂(dba)₃ (0.92 mg, 0.001 mmol), X-Phos (2.38 mg, 0.005 mmol) and Cs₂CO₃ (24.4 mg, 0.075 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, DMSO-*d*₆)

δ 7.40 - 6.49 (m, 8H), 3.70 - 3.42 (m, 5H), 3.16 (d, J = 6.8 Hz, 4H), 2.79 - 2.55 (m, 2H), 2.37 (m, 1H), 1.95 - 1.81 (m, 2H), 1.68 - 1.47 (m, 2H), 1.10 - 0.94 (m, 2H), 0.50 - 0.32 (m, 4H), 0.19 - 0.10 (m, 4H). Mass (m/z): 497.3 $[M+H]^+$.

5

Compound 398

5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indazole-1-carboxamide



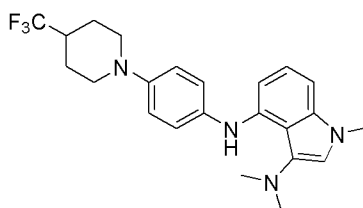
The title compound **398** (8.2 mg) was prepared in a yield of 9.9% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-1H-indazole-1-carboxamide (49 mg, 0.20 mmol) according to the procedure for compound **1**. ^1H NMR ($\text{DMSO}-d_6$) δ 8.13 (d, J = 0.8 Hz, 1H), 8.06 (d, J = 9.0 Hz, 1H), 7.89 (s, 1H), 7.58 (d, J = 45.8 Hz, 2H), 7.28 - 7.23 (m, 1H), 7.18 (dd, J = 9.0, 2.2 Hz, 1H), 7.02 (d, J = 8.9 Hz, 2H), 6.92 (d, J = 8.5 Hz, 2H), 3.63 (d, J = 12.2 Hz, 1H), 2.67 (q, J = 1.9 Hz, 2H), 2.32 (d, J = 1.9 Hz, 1H), 1.87 (s, 2H), 1.58 (dd, J = 12.2, 4.0 Hz, 2H). Mass (m/z): 404.6 $[M+H]^+$.

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Compound 399

N3,N3,1-trimethyl-N4-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indole-3,4-diamine

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The title compound **399** (34.3 mg) was prepared in a total yield of 41.6 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (58 mg, 0.237 mmol), 4-bromo-N,N,1-trimethyl-1H-indol-3-amine (50 mg, 0.198 mmol), $\text{Pd}_2(\text{dba})_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (97 mg, 0.297 mmol) and 1,4-dioxane (5 mL) according to the procedure

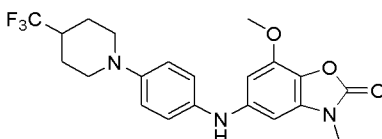
25

for compound **1**. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.69 (s, 1H), 7.31 – 7.01 (m, 6H), 6.90 (s, 1H), 3.78 (s, 3H), 3.65 (d, $J = 12.0$ Hz, 2H), 3.13 (s, 6H), 2.62 (s, 1H), 2.02 (d, $J = 13.6$ Hz, 2H), 1.77 (d, $J = 12.4$ Hz, 2H). Mass (m/z): 417.3 $[\text{M}+\text{H}]^+$.

5

Compound 400

7-methoxy-3-methyl-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo [d]oxazol-2(3H)-one

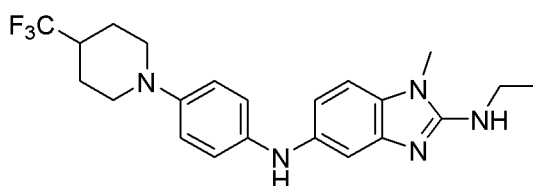


The title compound **400** (49.1 mg) was prepared in a total yield of 60.1 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (57 mg, 0.232 mmol), 5-bromo-7-methoxy-3-methylbenzo[d]oxazol-2(3H)-one (50 mg, 0.194 mmol), $\text{Pd}_2(\text{dba})_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (95 mg, 0.291 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.94 (s, 1H), 7.05 – 6.99 (m, 2H), 6.94 – 6.88 (m, 2H), 6.37 (s, 2H), 3.83 (s, 3H), 3.64 (d, $J = 12.4$ Hz, 2H), 3.24 (s, 3H), 2.63 (dd, $J = 13.2, 10.7$ Hz, 2H), 2.42 (td, $J = 8.8, 4.0$ Hz, 1H), 1.93 – 1.82 (m, 2H), 1.57 (qd, $J = 12.4, 4.0$ Hz, 2H). Mass (m/z): 422.3 $[\text{M}+\text{H}]^+$.

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Compound 401

N2-ethyl-1-methyl-N5-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[d]imidazole-2,5-diamine



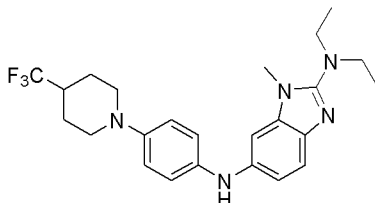
25

The title compound **401** (23.6 mg) was prepared in a yield of 28.7% as a white powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (50 mg, 0.20 mmol) and 5-bromo-N-ethyl-1-methyl-1H-benzo[d]imidazol-2-amine (48 mg, 0.20 mmol) according to the procedure for compound **1**. ^1H NMR ($\text{DMSO-}d_6$) δ 12.75 (s, 1H), 8.66 (s, 1H), 8.15 (s, 1H), 7.17 (d, $J = 87.5$ Hz,

6H), 4.22 (s, 5H), 3.59 (d, $J = 40.2$ Hz, 7H), 1.96 (s, 1H), 1.69 (s, 1H), 1.27 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 418.6 $[M+H]^+$.

Compound 402

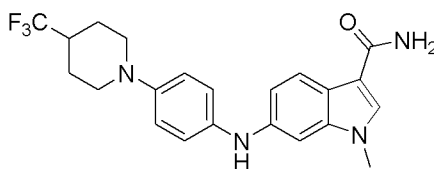
N2,N2-diethyl-1-methyl-N6-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-benzo[d]imidazole-2,6-diamine



The title compound **402** (28.5 mg) was prepared in a total yield of 36.1 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (52 mg, 0.213 mmol), 6-bromo-N,N-diethyl-1-methyl-1H-benzo[d]imidazole-2-amine (50 mg, 0.177 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (87 mg, 0.265 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, Pyridine- d_5) δ 7.76 (s, 1H), 7.05 (s, 2H), 3.56 (s, 2H), 3.36 (s, 3H), 3.33 – 3.20 (m, 4H), 2.52 (s, 2H), 2.12 (s, 1H), 1.78 (s, 2H), 1.66 (d, $J = 12.8$ Hz, 2H), 1.24 (d, $J = 6.4$ Hz, 1H), 1.09 (t, $J = 7.2$ Hz, 6H). Mass (m/z): 446.3 $[M+H]^+$.

Compound 403

1-methyl-6-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indole-3-carboxamide



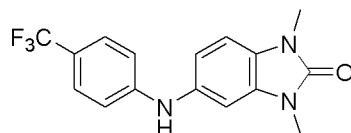
The title compound **403** (9.6 mg) was prepared in a total yield of 11.5% as a light yellow powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (63 mg, 0.26 mmol, 6-bromo-1-methyl-1H-indole-3-carboxamide (50 mg, 0.20 mmol), $Pd_2(dba)_3$ (2.3 mg, 2.5 μ mol), X-Phos (6.0 mg, 12.5 μ mol), and Cs_2CO_3 (122 mg, 0.38 mmol) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.91 (d, $J = 8.5$ Hz, 1H), 7.76 (d, $J = 7.3$

Hz, 2H), 7.22 (s, 1H), 7.05 – 7.01 (m, 2H), 6.96 (d, $J = 1.9$ Hz, 1H), 6.92 – 6.86 (m, 2H), 6.82 (dd, $J = 8.7, 2.0$ Hz, 1H), 6.68 (s, 1H), 3.67 (s, 3H), 3.64 – 3.58 (m, 2H), 2.69 – 2.59 (m, 2H), 2.46 – 2.38 (m, 1H), 1.92 – 1.85 (m, 2H), 1.64 – 1.50 (m, 2H). Mass (m/z): 417.2 $[M+H]^+$.

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Compound 404

1,3-dimethyl-5-((4-(trifluoromethyl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



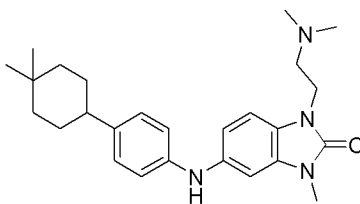
The title compound **404** (90.3 mg) was prepared in a total yield of 67.4 % as a white solid from 4-(trifluoromethyl)aniline (80 mg, 0.450 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (100 mg, 0.417 mmol), $Pd_2(dba)_3$ (4 mg, 0.004 mmol), X-phos (12 mg, 0.02 mmol), Cs_2CO_3 (200 mg, 0.625 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ^1H NMR (400 MHz, $DMSO-d_6$) δ 8.65 (s, 1H), 7.46 (d, $J = 8.4$ Hz, 2H), 7.11 (d, $J = 8.0$ Hz, 1H), 7.08 – 6.98 (m, 3H), 6.90 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.31 (d, $J = 6.8$ Hz, 6H). Mass (m/z): 322.3 $[M+H]^+$.

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Compound 405

1-(2-(dimethylamino)ethyl)-5-((4-(4,4-dimethylcyclohexyl)phenyl)amino)-3-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

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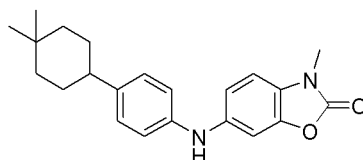
The title compound **405** (11.0 mg) was prepared in a total yield of 19.4 % as a green solid from 4-(4,4-dimethylcyclohexyl)aniline (30 mg, 0.148 mmol), 5-bromo-1-(2-(dimethylamino)ethyl)-3-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (40 mg, 0.135 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (66 mg, 0.202 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound 1. ^1H NMR

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(400 MHz, DMSO- d_6) δ 9.44 (s, 1H), 7.90 (s, 1H), 7.15 (d, $J = 8.4$ Hz, 1H), 7.08 (d, $J = 8.4$ Hz, 2H), 6.97 – 6.89 (m, 3H), 6.79 (dd, $J = 8.4, 2.0$ Hz, 1H), 4.18 (t, $J = 6.0$ Hz, 2H), 3.29 (s, 3H), 2.89 (s, 6H), 2.29 (dt, $J = 10.4, 5.2$ Hz, 1H), 1.61 – 1.38 (m, 6H), 1.28 (ddd, $J = 23.2, 11.6, 4.4$ Hz, 3H),
 5 0.95 (d, $J = 9.6$ Hz, 6H). Mass (m/z): 421.3 $[M+H]^+$.

Compound 406

6-((4-(4,4-dimethylcyclohexyl)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

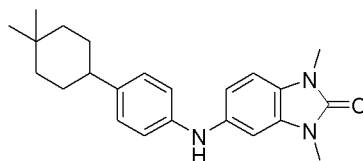


10 The title compound **406** (6.8 mg) was prepared in a total yield of 11.1 % as a white solid from 4-(4,4-dimethylcyclohexyl)aniline (39 mg, 0.193 mmol), 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (40 mg, 0.175 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (84 mg, 0.262 mmol) and 1,4-dioxane (5 mL) according to the procedure for
 15 compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.01 (s, 1H), 7.10 (dd, $J = 8.4, 2.0$ Hz, 3H), 7.00 (d, $J = 2.0$ Hz, 1H), 6.96 – 6.92 (m, 2H), 6.89 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.30 (s, 3H), 2.31 (tt, $J = 10.4, 5.2$ Hz, 1H), 1.60 – 1.54 (m, 3H), 1.48 – 1.41 (m, 2H), 1.35 – 1.21 (m, 3H), 0.95 (d, $J = 10.0$ Hz, 6H). Mass (m/z): 351.3 $[M+H]^+$.

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Compound 407

5-((4-(4,4-dimethylcyclohexyl)phenyl)amino)-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

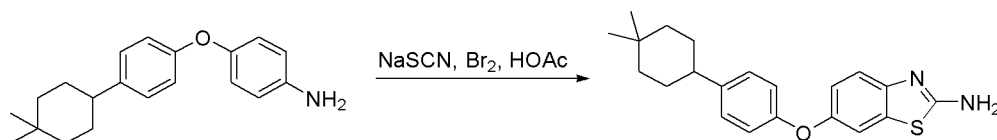


The title compound **407** (4.4 mg) was prepared in a total yield of 7.2 % as a
 25 green solid from 4-(4,4-dimethylcyclohexyl)aniline (37 mg, 0.183 mmol), 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (40 mg, 0.167 mmol), $Pd_2(dba)_3$ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs_2CO_3 (80 mg, 0.250 mmol) and 1,4-dioxane (5 mL) according to the

procedure for compound 1. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.83 (s, 1H), 7.09 – 7.03 (m, 2H), 7.00 (d, $J = 8.4$ Hz, 1H), 6.94 – 6.89 (m, 2H), 6.85 (d, $J = 2.0$ Hz, 1H), 6.77 (dd, $J = 8.4, 2.0$ Hz, 1H), 3.28 (d, $J = 8.0$ Hz, 6H), 2.28 (dt, $J = 10.4, 5.2$ Hz, 1H), 1.61 – 1.54 (m, 3H), 1.44 (d, $J = 12.8$ Hz, 2H), 1.29 (td, $J = 12.8, 6.0$ Hz, 3H), 0.94 (d, $J = 10.0$ Hz, 6H). Mass (m/z): 364.3 $[\text{M}+\text{H}]^+$.

Compound 408

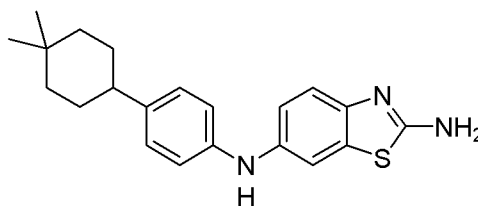
6-(4-(4,4-dimethylcyclohexyl)phenoxy)benzo[d]thiazol-2-amine



A solution of 4-(4-(4,4-dimethylcyclohexyl)phenoxy)aniline (50 mg, 0.17 mmol), NaSCN (16.5 mg, 0.20 mmol) and Br_2 (32 mg, 0.20 mmol) in HOAc (1 mL) was stirred at r.t. for 18 hours. After filtration, the filtrate was concentrated under vacuum. The residue was purified by prep-HPLC (column-Xbridge-C18 150 x 19 mm, 5 μm ; Mobile phase: ACN- H_2O (0.1%FA), 25%-40%) to afford **408** (22.3 mg) as a white solid. Mass (m/z): 353.2 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.43 (d, $J = 2.6$ Hz, 1H), 7.34 (d, $J = 8.8$ Hz, 1H), 7.22 – 7.19 (m, 2H), 6.96 (dd, $J = 8.8, 2.5$ Hz, 1H), 6.87 – 6.84 (m, 2H), 2.36 (td, $J = 10.6, 4.9$ Hz, 1H), 1.54 (dt, $J = 16.4, 5.9$ Hz, 4H), 1.41 (d, $J = 12.4$ Hz, 2H), 1.31 – 1.24 (m, 2H), 0.91 (d, $J = 10.0$ Hz, 6H).

Compound 409

N⁶-(4-(4,4-dimethylcyclohexyl)phenyl)benzo[d]thiazole-2,6-diamine

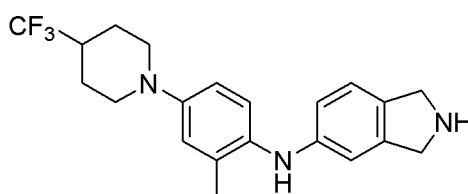


A solution of N^1 -(4-(4,4-dimethylcyclohexyl)phenyl)benzene-1,4-diamine (60 mg, 0.20 mmol), NaSCN (20.0 mg, 0.24 mmol) and Br_2 (39.0 mg, 0.24 mmol) in MeOH (2 mL) was stirred at r.t. for 18 hours. The solids were filtered, the filtrate was concentrated under vacuum. The residue was

purified by prep-HPLC (column-Xbridge-C18 150 x 19 mm, 5 μ m; Mobile phase: ACN-H₂O (0.1%FA), 25%-40%) to afford compound **409** (5.0 mg) as a white solid. Mass (m/z): 352.2 [M+H]⁺. ¹H NMR (400 MHz, CD₃OD) δ 7.29 (d, *J* = 2.2 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.98 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 2H), 2.38 – 2.31 (m, 1H), 1.64 (d, *J* = 3.0 Hz, 2H), 1.50 (d, *J* = 12.0 Hz, 2H), 1.33 (dd, *J* = 20.0, 6.8 Hz, 4H), 1.00 (s, 3H), 0.95 (s, 3H).

Compound 410

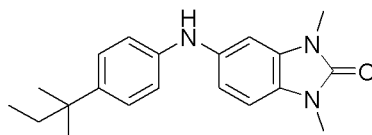
N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)isoindolin-5-amine



To a solution of 2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)aniline (72 mg, 0.278 mmol) and 5-bromoisoindoline (50 mg, 0.253 mmol) in 1,4-dioxane (5 mL) was added BrettPhos Pd G3 (23 mg, 0.025 mmol), BrettPhos (27 mg, 0.051 mmol) and Cs₂CO₃ (247 mg, 0.759 mmol), then the mixture was stirred at 110°C for 16 h. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by TLC (MeOH/DCM = 1/5) to give the desired product as a yellow solid (14.2 mg, 14.9%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.97 (t, *J* = 8.0 Hz, 2H), 6.84 (s, 1H), 6.75 (d, *J* = 9.2 Hz, 1H), 6.51 (d, *J* = 6.4 Hz, 2H), 3.92 (d, *J* = 6.0 Hz, 3H), 3.68 (d, *J* = 12.4 Hz, 2H), 2.66 (q, *J* = 12.4 Hz, 3H), 2.44 (d, *J* = 10.0 Hz, 1H), 2.12 (s, 3H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.56 (q, *J* = 12.4 Hz, 2H). Mass (m/z): 376.3 [M+H]⁺.

Compound 411

1,3-dimethyl-5-((4-(tert-pentyl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one

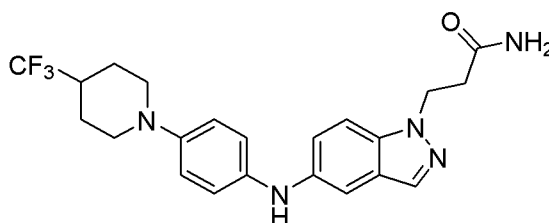


To a solution of 5-bromo-1,3-dimethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one (134 mg, 0.558 mmol) and 4-(tert-pentyl)aniline (100 mg, 0.613mmol) in dioxane (5 mL) was added $\text{Pd}_2(\text{dba})_3$ (25.5 mg, 0.028 mmol), X-phos (26.6 mg, 0.0558 mmol) and Cs_2CO_3 (364 mg, 1.12mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as a white solid (20.3 mg, 24.0%). ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.82 (s, 1H), 7.13 (d, J = 8.6 Hz, 2H), 6.99 (d, J = 8.3 Hz, 1H), 6.92 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 2.0 Hz, 1H), 6.77 (dd, J = 8.3, 2.0 Hz, 1H), 3.28 (d, J = 4.9 Hz, 6H), 1.55 (t, J = 7.4 Hz, 2H), 1.20 (s, 6H), 0.64 (t, J = 7.4 Hz, 3H). Mass (m/z): 324.2 $[\text{M}+\text{H}]^+$

15

Compound 412

3-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indazol-1-yl)propanamide



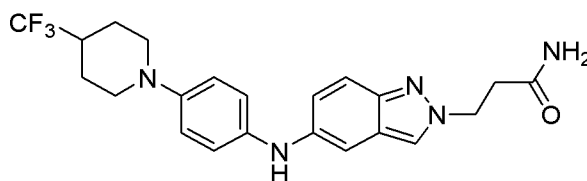
The title compound **412** (37.7 mg) was prepared in a total yield of 36.5% as a purple powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (70 mg, 0.29 mmol), 3-(5-bromo-1H-indazol-1-yl)propanamide (63 mg, 0.24 mmol), $\text{Pd}_2(\text{dba})_3$ (2.3 mg, 2.5 μmol), X-Phos (6.0 mg, 12.5 μmol), and Cs_2CO_3 (122 mg, 0.38 mmol) according to the procedure for compound 1. ^1H NMR (400 MHz, Methanol- d_4) δ 7.81 (s, 1H), 7.55 (s, 2H), 7.32 – 6.68 (m, 7H), 4.63 (t, J = 6.8 Hz, 2H), 3.75 – 3.48 (m, 2H), 2.79 (t, J = 6.8 Hz, 2H), 2.74 – 2.47 (m, 2H), 2.35 – 2.22 (m, 1H), 2.04 – 1.88 (m, 2H), 1.80 –

25

1.64 (m, 2H). Mass (m/z): 432.1 [M+H]⁺.

Compound 413

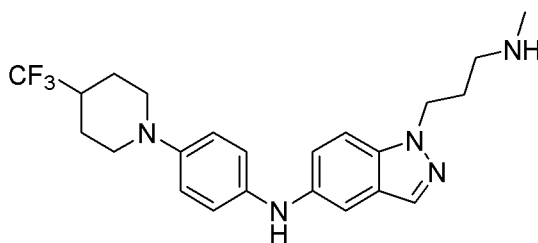
3-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-indazol-2-yl)propanamide



The title compound **413** (16.5 mg) was prepared in a total yield of 16.0% as a purple powder from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (70 mg, 0.29 mmol), 3-(5-bromo-2H-indazol-2-yl)propanamide (63 mg, 0.24 mmol), Pd₂(dba)₃ (2.3 mg, 2.5 μmol), X-Phos (6.0 mg, 12.5 μmol), and Cs₂CO₃ (122 mg, 0.38 mmol) according to the procedure for compound 1. ¹H NMR (400 MHz, Methanol-*d*₄) δ 7.91 (s, 2H), 7.46 (d, *J* = 9.4 Hz, 1H), 7.30 – 6.71 (m, 7H), 4.63 (t, *J* = 6.8 Hz, 2H), 3.75 – 3.48 (m, 2H), 2.89 (t, *J* = 6.8 Hz, 2H), 2.80 – 2.61 (m, 2H), 2.35 – 2.22 (m, 1H), 2.04 – 1.88 (m, 2H), 1.80 – 1.64 (m, 2H). Mass (m/z): 432.1 [M+H]⁺.

Compound 414

1-(3-(methylamino)propyl)-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indazol-5-amine

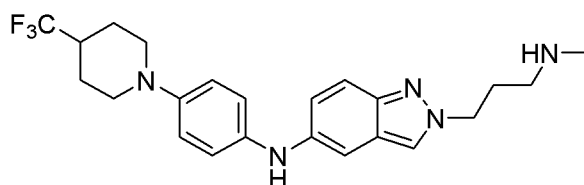


To a solution of tert-butyl (3-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indazol-1-yl)propyl)carbamate (116 mg, 0.22 mol) in THF (10 mL) was added LiAlH₄ (17 mg, 0.45 mol) at 0°C, and the mixture was refluxed for 2 h. After cooling to 0°C, water (17 μL), 10% NaOH (34 μL) and water (51 μL) were added, and the mixture was stirred for 3 min at room temperature. The solid was filtered and the filtered gray cake was washed with THF (10 mL x 2); then the combined filtrates were dried over

Na₂SO₄ and concentrated. The residue was purified by prep-TLC (MeOH/DCM=1/5) to give the desired products as a white solid. (28.5 mg, 29.5%). ¹H NMR (400 MHz, DMSO-*D*₆) δ 8.67 (s, 1H), 7.83 (s, 1H), 7.68 (s, 1H), 7.53 (d, *J* = 8.9 Hz, 1H), 7.19 (s, 1H), 7.08 (dd, *J* = 9.1, 2.0 Hz, 1H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.40 (t, *J* = 6.7 Hz, 2H), 3.56 (d, *J* = 11.7 Hz, 2H), 2.91-2.79 (m, 2H), 2.62 – 2.55 (m, 2H), 2.39 (s, 1H), 2.10 (p, *J* = 6.9 Hz, 2H), 1.85 (d, *J* = 12.5 Hz, 2H), 1.67 – 1.44 (m, 2H). Mass (m/z):432.3 [M+H]⁺.

Compound 415

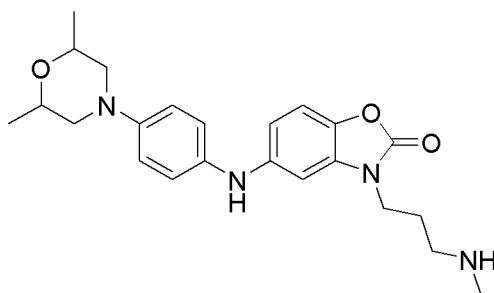
2-(3-(methylamino)propyl)-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-2H-indazol-5-amine



The title compound **415** (129 mg) was prepared in a total yield of 54.6% as a yellow powder from tert-butyl (3-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-indazol-2-yl)propyl)carbamate (176 mg, 0.5mmol) and LiAlH₄ (38 mg, 0.45 mol) according to the procedure for compound **414**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.92 (s, 2H), 8.06 (s, 1H), 7.67 (s, 1H), 7.44 (d, *J* = 9.2 Hz, 1H), 7.05 – 6.88 (m, 5H), 4.42 (t, *J* = 6.7 Hz, 2H), 3.57 (d, *J* = 12.0 Hz, 2H), 2.92– 2.75 (m, 2H), 2.62 – 2.54 (m, 2H), 2.45– 2.32 (m, 1H) 2.27 – 2.14 (m, 2H), 1.92 – 1.80 (m, 2H), 1.62 – 1.47 (m, 2H). Mass (m/z):432.3 [M+H]⁺.

Compound 416

tert-butyl(3-(5-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-oxobenzo[d]oxazol-3(2H)-yl)propyl)(methyl)carbamate

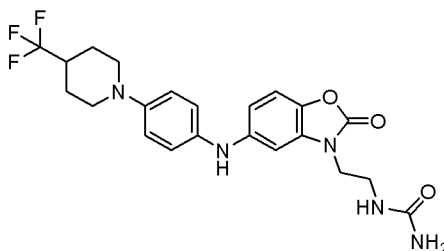


TFA (1 mL) was added to a solution of tert-butyl (3-(5-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-oxobenzo[d]oxazol-3(2H)-yl)propyl)(methyl)carbamate (130 mg, 0.25 mmol) in dichloromethane (5 mL).

- 5 The mixture was stirred at room temperature for 2h. The reaction mixture was concentrated under vacuum. The residue was diluted with a saturated solution of NaHCO₃ (30 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic phases were dried and concentrated. The residue was purified by Prep-HPLC with the following conditions:
- 10 Column: Spherical C18 40-60 μ m, 40 g; Mobile phase A: water (0.5% NH₄HCO₃); Mobile phase B: acetonitrile or ACN; Flow rate: 45 mL/min; Gradient: 30%B-65%B in 20 min; Detector: 254 nm. The fractions containing desired product were collected at 55% B and concentrated under reduced pressure to give the titled compound **416** (51 mg, 48.8%) as
- 15 a grey solid. LC-MS (m/z) 411.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.66 (s, 1H), 7.87 (s, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 7.03 – 6.97 (m, 2H), 6.93 – 6.84 (m, 3H), 6.64 (dd, *J* = 8.6, 2.2 Hz, 1H), 3.84 (t, *J* = 6.7 Hz, 2H), 3.69 (dt, *J* = 12.6, 6.4, 3.7 Hz, 2H), 3.48 – 3.40 (m, 2H), 3.31 (s, 3H), 2.95 – 2.86 (m, 2H), 2.19 (dd, *J* = 11.8, 10.2 Hz, 2H), 1.99 (p, *J* = 6.9 Hz, 2H),
- 20 1.14 (d, *J* = 6.2 Hz, 6H).

Compound 417

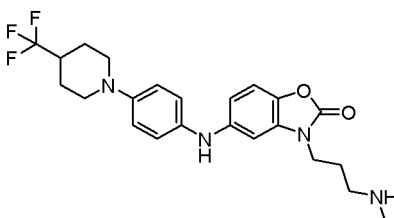
1-(2-(2-oxo-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-3(2H)-yl)ethyl)urea



To a solution of 3-(2-aminoethyl)-5-((4-(4-(trifluoromethyl) piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one (crude) in DMSO (6 mL) was added phenyl carbamate (8 mg, 0.0577 mmol), TEA (7.5 mg, 0.0722 mmol). Then the mixture was stirred at 60°C for 2 hours. The mixture was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as a blue solid (17.2 mg, 77%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.79 (d, J = 11.5 Hz, 1H), 7.08 (d, J = 8.6 Hz, 1H), 6.99 – 6.92 (m, 2H), 6.89 – 6.84 (m, 2H), 6.76 (t, J = 9.0 Hz, 1H), 6.58 (dt, J = 11.3, 5.7 Hz, 1H), 6.17 – 6.03 (m, 1H), 5.41 (d, J = 35.3 Hz, 2H), 3.76 – 3.65 (m, 2H), 3.56 (t, J = 15.9 Hz, 2H), 3.21 (dd, J = 15.1, 9.1 Hz, 2H), 1.85 (d, J = 12.1 Hz, 3H), 1.63 – 1.47 (m, 3H). Mass (m/z): 464.2 [M+H]⁺.

Compound 418

3-(3-(methylamino)propyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one

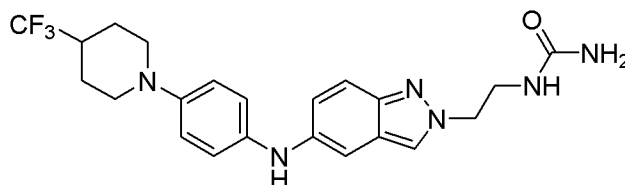


To a solution of tert-butyl methyl(3-(2-oxo-5-((4-(4-(trifluoromethyl) piperidin-1-yl)phenyl)amino)benzo[d]oxazol-3(2H)-yl)propyl)carbamate (crude) in DCM (6 mL) was added TFA (2 mL). The mixture was stirred at r.t. for 0.5 hour. Then the mixture was concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as a purple solid (13.9 mg, 12.6%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.87 (s, 1H), 7.11 (d, J = 8.6 Hz, 1H), 6.96 (d, J = 9.0 Hz, 2H), 6.89 – 6.80 (m, 3H),

6.62 (dd, $J = 8.7, 2.2$ Hz, 1H), 3.81 (t, $J = 6.8$ Hz, 2H), 3.69 – 3.51 (m, 2H), 2.94 – 2.77 (m, 2H), 2.76 – 2.56 (m, 3H), 2.43 (s, 3H), 2.06 – 1.73 (m, 4H), 1.54 (qd, $J = 12.4, 4.0$ Hz, 2H). Mass (m/z): 449.2 $[M+H]^+$.

Compound 419

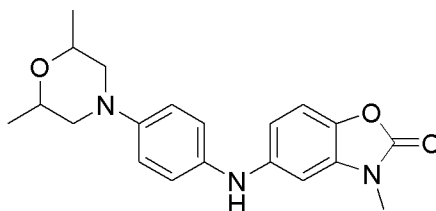
5 *1-(2-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-indazol-2-yl)ethyl)urea*



To a solution of 2-(2-aminoethyl)-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-2H-indazol-5-amine (66 mg, 0.15 mmol) and TEA (45 mg, 0.45 mmol) in DMSO (1 mL) was added phenyl carbamate (21 mg, 0.15 mmol). Then the mixture was stirred for 1 hour at 60°C. After cooling to r.t., 10 mL of water was added. The resulting solution was extracted with 3x10 mL of ethyl acetate. The organic layers were combined, washed with water (3x15 mL), dried and concentrated under vacuum. The residue was purified by prep-TLC (MeOH/DCM=1/10) to afford the desired product as a yellow solid (10.0 mg, 15.0 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.96 (d, $J = 1.0$ Hz, 1H), 7.61 (s, 1H), 7.47 – 7.40 (m, 1H), 7.05 – 7.02 (m, 1H), 6.97 – 6.93 (m, 2H), 6.88 – 6.84 (m, 1H), 5.96 (t, $J = 5.9$ Hz, 1H), 5.48 (s, 2H), 4.30 (t, $J = 6.0$ Hz, 2H), 3.57 (d, $J = 12.3$ Hz, 2H), 3.45 (q, $J = 6.0$ Hz, 2H), 2.63 – 2.56 (m, 2H), 2.44 – 2.33 (m, 1H), 1.88 – 1.80 (m, 2H), 1.62 – 1.47 (m, 1H). Mass (m/z): 447.2 $[M+H]^+$.

Compound 420

5-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

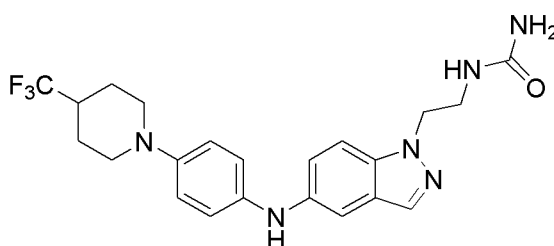


The titled compound **420** (62.3 mg, 30.9%) was obtained as an off-white

solid according to the procedure outlined for compound **1**. LC-MS (m/z) 354.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 7.83 (s, 1H), 7.12 (d, J = 8.6 Hz, 1H), 7.04 – 6.96 (m, 2H), 6.94 – 6.84 (m, 2H), 6.74 (d, J = 2.3 Hz, 1H), 6.62 (dd, J = 8.6, 2.3 Hz, 1H), 3.69 (dq, J = 12.4, 6.2, 2.2 Hz, 2H),
 5 3.45 (dt, J = 10.8, 2.0 Hz, 2H), 3.26 (s, 3H), 2.19 (dd, J = 11.8, 10.2 Hz, 2H), 1.14 (d, J = 6.2 Hz, 6H).

Compound 421

1-(2-(5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indazol-1-yl)ethyl)urea

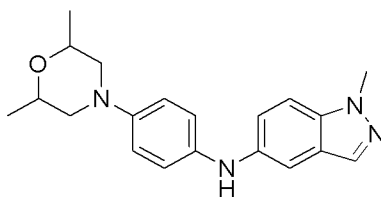


10

The title compound **421** (19.9 mg) was prepared in a total yield of 29.9% as a light yellow powder from 1-(2-aminoethyl)-N-(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indazol-5-amine (66 mg, 0.15 mmol), TEA (48 mg, 0.45 mmol) and phenyl carbamate (21 mg, 0.15 mmol) according to
 15 the procedure for compound **1**. ^1H NMR (400 MHz, Methanol- d_4) δ 7.84 (s, 1H), 7.50 - 6.65 (m, 8H), 4.44 (t, J = 6.0 Hz, 2H), 3.75 – 3.52 (m, 4H), 2.78 – 2.53 (m, 2H), 2.34 – 2.20 (m, 2H), 2.05 – 1.92 (m, 2H), 1.82 – 1.66 (m, 2H). Mass (m/z):447.3 $[M+H]^+$.

Compound 422

20 *N-(4-(2,6-dimethylmorpholino)phenyl)-1-methyl-1H-indazol-5-amine*

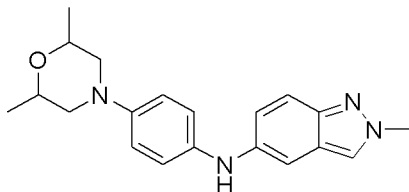


The titled compound **422** (89.6 mg, 30.9%) as a gray solid was prepared according to the procedure outlined for compound **1**. LC-MS (m/z) 337.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 8.07 (s, 2H), 7.51 (s, 1H), 7.18
 25 (s, 3H), 7.02 (s, 3H), 4.10 (s, 3H), 3.84 (s, 2H), 3.48 (s, 2H), 2.75-2.60 (m,

2H), 1.17 (d, $J = 6.2$ Hz, 6H).

Compound 423

N-(4-(2,6-dimethylmorpholino)phenyl)-2-methyl-2H-indazol-5-amine

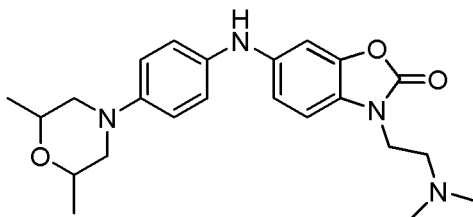


- 5 The titled compound **423** (68.1 mg, 30.9%) as a light yellow solid was prepared according to the procedure outlined for compound **1**. LC-MS (m/z) 337.2 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 8.09 (s, 2H), 7.50 (s, 1H), 7.20 (s, 3H), 7.02 (s, 3H), 4.05 (s, 3H), 3.81 (s, 2H), 3.45 (s, 2H), 2.74-2.60 (m, 2H), 1.17 (d, $J = 6.2$ Hz, 6H).

10

Compound 424

3-(2-(dimethylamino)ethyl)-6-((4-(2,6-dimethylmorpholino)phenyl)amino)benzo[d]oxazol-2(3H)-one

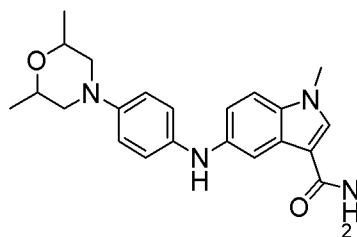


- To a solution of 5-bromo-3-(2-(dimethylamino)ethyl)benzo[d]oxazol-2(3H)-one (96.5 mg, 0.339 mmol) and 4-(2,6-dimethylmorpholino)aniline (70 mg, 0.339 mmol) in dioxane (5 mL) was added $Pd_2(dba)_3$ (15.6 mg, 0.017 mmol), X-phos (16.2 mg, 0.0339 mmol) and Cs_2CO_3 (166.2 mg, 0.51 mmol) under nitrogen atmosphere. Then the mixture was stirred at 100 °C overnight. The mixture was extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as a pink solid (35.2 mg, 25.3%). ^1H NMR (400 MHz, DMSO- d_6) δ 7.81 (s, 1H), 6.99 (dd, $J = 15.6, 8.9$ Hz, 3H), 6.88 (d, $J = 9.0$ Hz, 2H), 6.61 (dd, $J = 8.7, 2.4$ Hz, 1H), 6.53 (d, $J = 2.4$ Hz, 1H), 5.76 (s, 1H), 4.54 (s, 2H), 3.93 (t, $J = 6.9$ Hz, 2H), 3.75 – 3.62 (m, 3H), 3.45 (d, $J = 10.6$ Hz, 2H), 2.39 (t, $J = 6.9$ Hz, 2H), 2.23 – 2.12 (m, 7H),
- 15
- 20
- 25

2.06 (s, 1H), 1.15 (t, $J = 5.7$ Hz, 6H). Mass (m/z): 411.2 $[M+H]^+$.

Compound 425

5-((4-(2,6-dimethylmorpholino)phenyl)amino)-1-methyl-1H-indole-3-carboxamide



5

To a solution of 5-((4-(2,6-dimethylmorpholino)phenyl)amino)-1-methyl-1H-indole-3-carboxylic acid (120 mg, 0.317 mmol) in DMF (5 mL) was added HATU (301 mg, 0.793 mmol), NH_4Cl (33.9 mg, 0.633 mmol) and TEA (128 mg, 1.27 mmol). The mixture was stirred at 80°C for 2 hours.

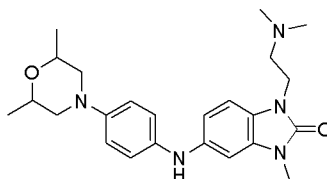
10 Then the mixture was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na_2SO_4 and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as green solid (9.2 mg, 7.7%). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.92 – 7.76 (m, 2H), 7.57 (s, 1H), 7.32 (d, $J = 8.8$ Hz, 1H), 6.97 – 6.88 (m, 3H), 6.84 (d, $J = 9.0$ Hz, 2H), 3.75 (s, 3H), 3.72 – 3.63 (m, 2H), 3.45 – 3.36 (m, 2H), 2.17 (t, $J = 11.0$ Hz, 2H), 1.14 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 379.2 $[M+H]^+$.

15

Compound 426

1-(2-(dimethylamino)ethyl)-5-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one

20



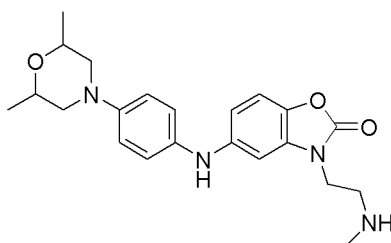
The titled compound **426** (16.7 mg, 8%) as a purple solid was prepared from 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.50 mmol), 5-bromo-1-(2-(dimethylamino)ethyl)-3-methyl-1H-benzo[d]imidazol-2(3H)-one (150 mg, 0.51 mmol), 1,4-dioxane (2 mL), $\text{Pd}_2(\text{dba})_3$ (46 mg, 0.05

25

mmol), Xphos (48 mg, 0.10 mmol) and Cs_2CO_3 (329 mg, 1.01 mmol) according to the procedure outlined for compound 1. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.61 (s, 2H), 7.00 (d, $J = 8.3$ Hz, 2H), 6.98 – 6.92 (m, 4H), 6.89 – 6.81 (m, 4H), 6.73 (d, $J = 2.1$ Hz, 2H), 6.66 (dd, $J = 8.4, 2.1$ Hz, 2H), 3.85 (t, $J = 6.6$ Hz, 4H), 3.75 – 3.63 (m, 4H), 3.45 – 3.37 (m, 4H), 3.24 (s, 6H), 2.48 (s, 1H), 2.20 (s, 1H), 2.17 (s, 14H), 2.15 (s, 1H), 1.14 (d, $J = 6.2$ Hz, 12H). Mass (m/z): 424.4 $[\text{M}+\text{H}]^+$.

Compound 427

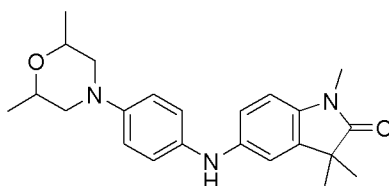
5-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-(2-(methylamino)ethyl)benzo[d]oxazol-2(3H)-one



To a solution of tert-butyl (2-(5-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-oxobenzo[d]oxazol-3(2H)-yl)ethyl)(methyl)carbamate (crude) in DCM (6 mL) was added TFA (2 mL). The mixture was stirred at r.t. for 0.5 hour. Then the mixture was concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as gray solid (7.4 mg, 4.8%). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.57 (s, 1H), 6.97 – 6.87 (m, 4H), 6.86 – 6.75 (m, 3H), 6.58 (s, 1H), 3.77 – 3.60 (m, 7H), 3.39 (dd, $J = 18.6, 9.6$ Hz, 3H), 2.52 (d, $J = 2.8$ Hz, 2H), 2.20 – 2.10 (m, 2H), 1.13 (d, $J = 6.2$ Hz, 6H). Mass (m/z): 397.2 $[\text{M}+\text{H}]^+$.

Compound 428

5-((4-(2,6-dimethylmorpholino)phenyl)amino)-1,3,3-trimethylindolin-2-one

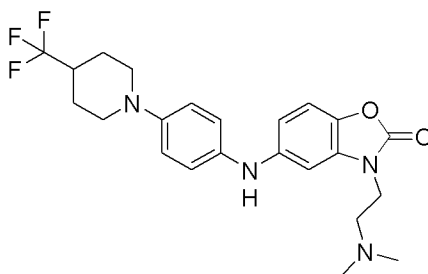


To a solution of 5-bromo-1,3,3-trimethylindolin-2-one (135 mg, 0.53

mmol) and 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.49 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (44 mg, 0.05 mmol), Xphos (46 mg, 0.09 mmol) and Cs_2CO_3 (317 mg, 0.97 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was
 5 purified by prep HPLC to give 5-((4-(2,6-dimethylmorpholino)phenyl)amino)-1,3,3-trimethylindolin-2-one (71 mg, 38%) as a light purple solid. Mass (m/z): 380.4 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.57 (s, 1H), 6.95 – 6.91 (m, 1H), 6.89 – 6.85 (m, 2H), 6.83 – 6.79 (m, 4H), 3.65 (s, 2H), 3.41 – 3.34 (m, 2H), 2.16 – 2.11 (m, 2H), 1.20 (s, 6H), 1.10 (d, $J = 6.2$
 10 Hz, 6H).

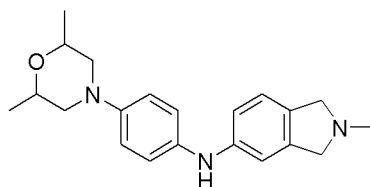
Compound 429

3-(2-(dimethylamino)ethyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one



To a solution of 5-bromo-3-(2-(dimethylamino)ethyl)benzo[d]oxazol-2(3H)-one (70 mg, 0.25 mmol) and 5-bromo-2-methylisoindoline (66 mg, 0.27 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (22 mg, 0.02 mmol), Xphos (23 mg, 0.04 mmol) and Cs_2CO_3 (161 mg, 0.50 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h and
 20 the mixture was purified by flash chromatography to give 3-(2-(dimethylamino)ethyl)-5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one (25 mg, 22%) as a grey solid. ^1H NMR (400 MHz, DMSO) δ 7.85 (s, 1H), 7.12 (d, $J = 8.6$ Hz, 1H), 7.02 – 6.94 (m, 2H), 6.94 – 6.86 (m, 2H), 6.83 (d, $J = 2.2$ Hz, 1H), 6.63 (dd, $J = 8.6, 2.3$
 25 Hz, 1H), 3.83 (t, $J = 6.2$ Hz, 2H), 3.62 (d, $J = 12.0$ Hz, 2H), 2.68 – 2.57 (m, 2H), 2.55 – 2.52 (m, 2H), 2.47 – 2.43 (m, 1H), 2.17 (s, 6H), 1.93 – 1.83 (m, 2H), 1.64 – 1.50 (m, 2H). Mass (m/z): 449.4 $[\text{M}+\text{H}]^+$.

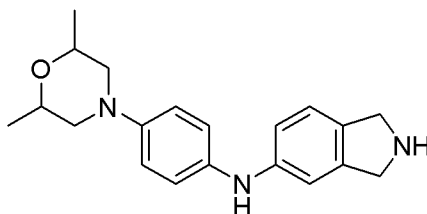
Compound 430

N-(4-(2,6-dimethylmorpholino)phenyl)-2-methylisoindolin-5-amine

To a solution of 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.48 mmol) and 5-bromo-2-methylisoindoline (113 mg, 0.53 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (44 mg, 0.05 mmol), Xphos (46 mg, 0.10 mmol) and Cs₂CO₃ (316 mg, 0.97 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12 h and the mixture was purified by flash chromatography to give *N*-(4-(2,6-dimethylmorpholino)phenyl)-2-methylisoindolin-5-amine (32 mg, 19%) as a light blue solid. ¹H NMR (400 MHz, DMSO) δ 8.04 (s, 1H), 7.26 – 7.09 (m, 1H), 7.09 – 6.98 (m, 2H), 6.98 – 6.75 (m, 3H), 4.65 – 4.61 (m, 2H), 4.35 – 4.26 (m, 2H), 3.74 – 3.69 (m, 2H), 2.98 – 2.93 (m, 3H), 2.24 – 2.20 (m, 2H), 1.15 (d, *J* = 6.2 Hz, 6H). LC-MS (*m/z*): 338.2 [M+H]⁺.

Compound 431

N-(4-(2,6-dimethylmorpholino)phenyl)isoindolin-5-amine

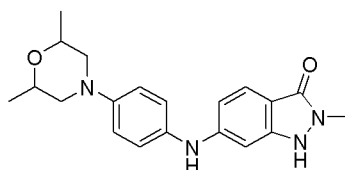


To a solution of 5-bromoisoindoline (105 mg, 0.53 mmol) and 4-(2,6-dimethylmorpholino)aniline (100 mg, 0.48 mmol) in 1,4-dioxane (2 mL) was added Brettphos Pd G3 (44 mg, 0.04 mmol), Brettphos (52 mg, 0.10 mmol) and Cs₂CO₃ (316 mg, 0.97 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by prep TLC then purified by flash chromatography to give *N*-(4-(2,6-dimethylmorpholino)phenyl)isoindolin-5-amine (86 mg, 54%) as a light yellow solid. Mass (*m/z*): 324.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.70 (s, 1H), 7.08 – 6.99 (m, 1H), 6.98 – 6.90 (m, 2H), 6.88 – 6.81 (m, 2H), 6.81 – 6.70 (m, 2H), 4.43 (d, *J* = 7.7 Hz, 1H), 4.01 (d, *J* = 5.4

Hz, 3H), 3.71 – 3.59 (m, 2H), 3.44 – 3.35 (m, 2H), 2.19 – 2.09 (m, 2H), 1.10 (d, $J = 6.3$ Hz, 6H).

Compound 432

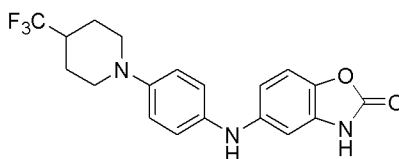
6-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-methyl-1H-indazol-3(2H)-one



To a solution of tert-butyl 6-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-methyl-3-oxo-2,3-dihydro-1H-indazole-1-carboxylate (100 mg, 0.22 mmol) in DCM (3 mL) was added 2,2,2-trifluoroacetic acid (1 mL). The mixture was stirred at r.t. for 1h, the mixture was concentrated and purified by flash chromatography to give 6-((4-(2,6-dimethylmorpholino)phenyl)amino)-2-methyl-1H-indazol-3(2H)-one (32 mg, 41%) as a white solid. Mass (m/z): 353.4 $[M+H]^+$. ^1H NMR (400 MHz, DMSO- d_6) δ 9.63 (s, 1H), 8.20 (s, 1H), 7.32 (d, $J = 8.6$ Hz, 1H), 7.07 – 6.99 (m, 2H), 6.94 – 6.86 (m, 2H), 6.57 (dd, $J = 8.6, 1.9$ Hz, 1H), 6.46 (d, $J = 1.8$ Hz, 1H), 3.72 – 3.60 (m, 2H), 3.51 – 3.43 (m, 2H), 3.18 (s, 3H), 2.23 – 2.13 (m, 2H), 1.12 (d, $J = 6.2$ Hz, 6H).

Compound 433

5-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one



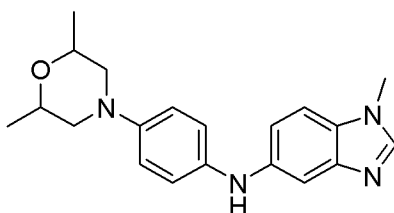
The title compound **433** (3.8 mg) was prepared in a total yield of 4.3 % as a white solid from 4-(4-(trifluoromethyl)piperidin-1-yl)aniline (64 mg, 0.259 mmol), 5-bromobenzo[d]oxazol-2(3H)-one (50 mg, 0.236 mmol), Pd₂(dba)₃ (2 mg, 0.002 mmol), X-phos (6 mg, 0.01 mmol), Cs₂CO₃ (115 mg, 0.354 mmol) and 1,4-dioxane (5 mL) according to the procedure for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.24 (s, 1H), 6.88 – 6.78 (m,

3H), 6.65 (d, $J = 8.0$ Hz, 1H), 6.45 (d, $J = 2.4$ Hz, 1H), 6.25 (dd, $J = 8.0$, 2.0 Hz, 1H), 3.53 (d, $J = 12.0$ Hz, 2H), 2.61 – 2.54 (m, 2H), 2.38 (dt, $J = 8.8$, 4.8 Hz, 1H), 1.87 (d, $J = 12.0$ Hz, 2H), 1.62 – 1.54 (m, 2H). Mass (m/z): 378.3 $[M+H]^+$.

5

Compound 434

N-(4-(2,6-dimethylmorpholino)phenyl)-1-methyl-1H-benzo[d]imidazol-5-amine

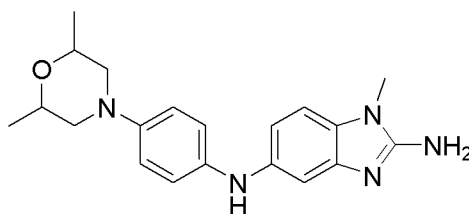


A mixture solution of 4-(2,6-dimethylmorpholino)aniline (0.2 g, 0.97 mmol), 5-bromo-1-methyl-1H-benzo[d]imidazole (0.22 g, 1.07 mmol), Pd₂(dba)₃ (88 mg, 0.1 mmol), Ruphos (89 mg, 0.2 mmol), Cs₂CO₃ (0.95 g, 0.3 mmol) and 1,4-dioxane (10 mL) was stirred at 100 °C under N₂ atmosphere for 12 hrs. The mixture was concentrated and the residue was purified by prep-HPLC to give **434** as a yellow solid (0.11 g, 34.0%). Mass (m/z): 336.8 $[M+H]^+$. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.98 (s, 1H), 7.60 (s, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 7.15 (d, $J = 2.0$ Hz, 1H), 6.94 – 6.90 (m, 3H), 6.86 – 6.78 (m, 2H), 3.73 (s, 3H), 3.69 – 3.62 (m, 2H), 3.37 (d, $J = 10.4$ Hz, 2H), 2.14 (dd, $J = 11.6$, 10.4 Hz, 2H), 1.10 (d, $J = 6.0$ Hz, 6H).

20

Compound 435

N-(4-(2,6-dimethylmorpholino)phenyl)-1-methyl-1H-benzo[d]imidazol-5-amine

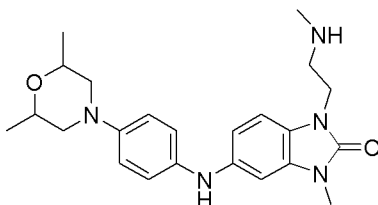


A mixture solution of tert-butyl (5-bromo-1-methyl-1H-benzo[d]imidazol-2-yl)(tert-butoxycarbonyl)carbamate (0.26 g, 0.61 mmol), 4-(2,6-dimethylmorpholino)aniline (0.25 g, 1.22 mmol), Pd₂(dba)₃ (56 mg, 0.06 mmol), Ruphos (57 mg, 0.12 mmol), Cs₂CO₃ (0.6 g, 1.83 mmol) and

dioxane (10 mL) was stirred at 100°C under N₂ atmosphere for 12 hrs. The mixture was concentrated and the residue was purified by prep-HPLC to give compound **435** as a yellow solid (18.3 mg, 8.5%). Mass (m/z): 351.8 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.33 (s, 1H), 7.06 – 6.72 (m, 6H), 6.59 (s, 1H), 6.26 (s, 2H), 3.69 (s, 2H), 3.44 (s, 5H), 2.17 (d, *J* = 10.4 Hz, 2H), 1.14 (s, 6H).

Compound 436

5-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-methyl-1-(2-(methylamino)ethyl)-1H-benzo[d]imidazol-2(3H)-one



10

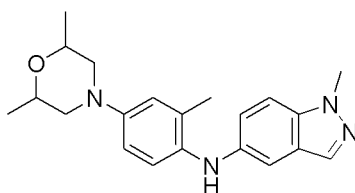
To a solution of tert-butyl (2-(5-((4-(2,6-dimethylmorpholino) phenyl) amino)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)ethyl) (methyl)carbamate (100 mg, 0.19 mmol) in DCM (3 mL) was added 2,2,2-trifluoroacetic acid (1 mL). The mixture was stirred at r.t. for 1h, the mixture was concentrated and purified by prep HPLC to give 5-((4-(2,6-dimethylmorpholino)phenyl)amino)-3-methyl-1-(2-(methylamino)ethyl)-1H-benzo[d]imidazol-2(3H)-one (23 mg, 28%) as a purple solid. Mass (m/z): 410.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.61 (s, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 6.98 – 6.91 (m, 2H), 6.89 – 6.81 (m, 2H), 6.73 (d, *J* = 2.1 Hz, 1H), 6.66 (dd, *J* = 8.3, 2.1 Hz, 1H), 3.84 (t, *J* = 6.4 Hz, 2H), 3.75 – 3.63 (m, 2H), 3.45 – 3.37 (m, 2H), 3.24 (s, 3H), 2.75 (t, *J* = 6.5 Hz, 2H), 2.29 (s, 3H), 2.22 – 2.12 (m, 2H), 1.14 (d, *J* = 6.2 Hz, 6H).

20

Compound 437

N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-1-methyl-1H-indazol-5-amine

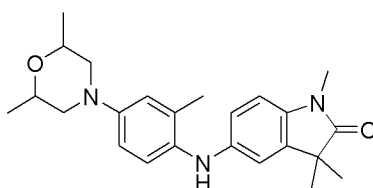
25



To a solution of 5-bromo-1-methyl-1H-indazole (105 mg, 0.5 mmol) and 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (41 mg, 0.04 mmol), Xphos (43 mg, 0.09 mmol) and Cs₂CO₃ (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by flash chromatography to give N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-1-methyl-1H-indazol-5-amine (15 mg, 9%) as a light brown solid. Mass (m/z): 351.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.73 (d, *J* = 1.0 Hz, 1H), 7.44 (d, *J* = 8.9 Hz, 1H), 7.05 – 6.98 (m, 2H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.77 – 6.70 (m, 2H), 3.96 (s, 3H), 3.75 – 3.63 (m, 2H), 3.52 – 3.44 (m, 2H), 2.25 – 2.16 (m, 2H), 2.14 (s, 3H), 1.15 (d, *J* = 6.2 Hz, 6H).

Compound 438

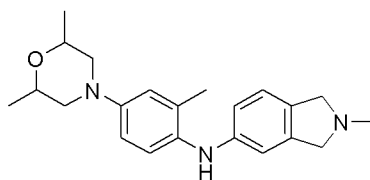
5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-1,3,3-trimethylindolin-2-one



To a solution of 5-bromo-1,3,3-trimethylindolin-2-one (126 mg, 0.5 mmol) and 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (41 mg, 0.04 mmol), Xphos (43 mg, 0.09 mmol) and Cs₂CO₃ (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for 12h, the mixture was purified by flash chromatography to give 5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-1,3,3-trimethylindolin-2-one (48 mg, 26.8%) as a light pink solid. Mass (m/z): 395.4 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.99 – 6.92 (m, 2H), 6.84 – 6.75 (m, 3H), 6.71 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.56 (dd, *J* = 8.3, 2.2 Hz, 1H), 3.74 – 3.62 (m, 2H), 3.52 – 3.43 (m, 2H), 3.07 (s, 3H), 2.24 – 2.15 (m, 2H), 2.13 (s, 3H), 1.21 (s, 6H), 1.14 (d, *J* = 6.2 Hz, 6H).

Compound 439

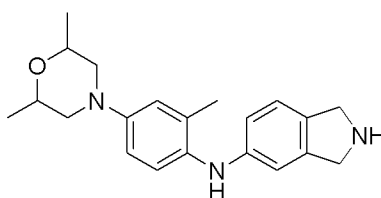
N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-2-methylisoindolin-5-amine



To a solution of 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) and 5-bromo-2-methylisoindoline (86 mg, 0.40 mmol) in 1,4-dioxane (2 mL) was added Pd₂(dba)₃ (41 mg, 0.05 mmol), Xphos (43 mg, 0.09 mmol) and Cs₂CO₃ (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by flash chromatography to give *N*-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-2-methylisoindolin-5-amine (15 mg, 9%) as a grey solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.50 (s, 1H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.90 (s, 1H), 6.81 (s, 1H), 6.64 – 6.58 (m, 1H), 6.53 (s, 1H), 4.63 – 4.55 (m, 2H), 4.31 – 4.21 (m, 2H), 3.73 – 3.66 (m, 2H), 3.54 – 3.46 (m, 2H), 2.93 (d, *J* = 4.8 Hz, 3H), 2.28 – 2.24 (m, 2H), 2.10 (s, 3H), 1.14 (d, *J* = 6.2 Hz, 6H).

Compound 440

N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)isoindolin-5-amine

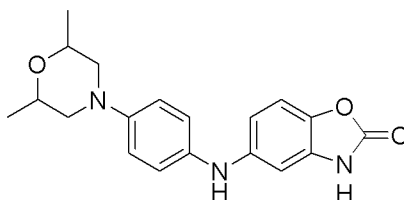


To a solution of 5-bromoisoindoline (99 mg, 0.50 mmol) and 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) in 1,4-dioxane (2 mL) was added Brettphos Pd G3 (41 mg, 0.05 mmol), Brettphos (49 mg, 0.09 mmol) and Cs₂CO₃ (296 mg, 0.91 mmol) under a nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC then purified by flash chromatography to give *N*-(4-(2,6-dimethylmorpholino)-2-methylphenyl)isoindolin-5-amine (71 mg, 48%) as a grey solid. Mass (m/z): 338.4 [M+H]⁺. ¹H NMR

(400 MHz, DMSO) δ 9.64 (s, 1H), 7.45 (s, 1H), 7.08 (d, $J = 8.3$ Hz, 1H), 6.97 (d, $J = 8.5$ Hz, 1H), 6.86 (s, 1H), 6.77 (s, 1H), 6.61 (d, $J = 8.3$ Hz, 1H), 6.51 (s, 1H), 4.31 (d, $J = 5.6$ Hz, 4H), 3.70 – 3.66 (m, 2H), 3.50 (d, $J = 11.6$ Hz, 2H), 2.24 – 2.19 (m, 2H), 2.08 (d, $J = 14.6$ Hz, 3H), 1.13 (d, $J = 6.2$ Hz, 6H).

Compound 441

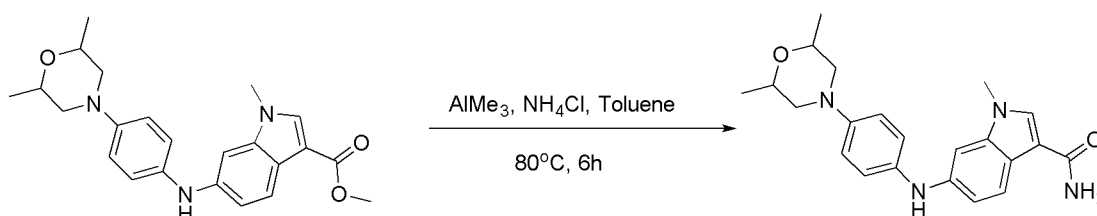
5-((4-(2,6-dimethylmorpholino)phenyl)amino)benzo[d]oxazol-2(3H)-one



To a solution of 5-bromobenzo[d]oxazol-2(3H)-one (200 mg, 0.93 mmol) and 4-(2,6-dimethylmorpholino)aniline (193 mg, 0.93 mmol) in t-BuOH (5 mL) was added $\text{Pd}_2(\text{dba})_3$ (42 mg, 0.05 mmol), Brettphos (50.1 mg, 0.09 mmol) and Cs_2CO_3 (609 mg, 1.87 mmol) under nitrogen atmosphere. The mixture was stirred at 100°C for overnight. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3x 50 mL). The combined organic phases were dried and concentrated. The residue was purified by Prep-TLC (Petroleum ether: Ethyl acetate=1:5) and further purified by Prep-HPLC with the following conditions: Column: Spherical C18 40-60 μm , 40 g; Mobile phase A: water (0.5% NH_4HCO_3); Mobile phase B: acetonitrile or ACN; Flow rate: 50 mL/min; Gradient: 20%B-65%B in 20 min; Detector: 254 nm. The fractions containing desired product were collected at 60% B and concentrated under reduced pressure to give the titled compound **441** (34.2 mg, 10.8%) as a white solid. LC-MS (m/z) 340.2 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 11.31 (s, 1H), 7.74 (s, 1H), 7.06 (d, $J = 8.5$ Hz, 1H), 7.01 – 6.93 (m, 2H), 6.92 – 6.84 (m, 2H), 6.63 – 6.53 (m, 2H), 3.69 (dq, $J = 12.5, 6.1, 2.2$ Hz, 2H), 3.44 (dt, $J = 10.7, 2.0$ Hz, 2H), 2.19 (dd, $J = 11.8, 10.2$ Hz, 2H), 1.14 (d, $J = 6.2$ Hz, 6H).

Compound 442

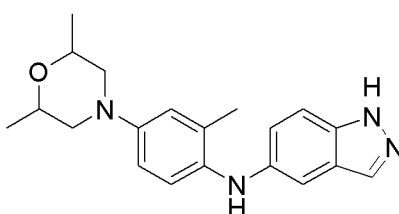
6-((4-(2,6-dimethylmorpholino)phenyl)amino)-1-methyl-1H-

indole-3-carboxamide

To a suspension of NH₄Cl in toluene at 0°C was treated with AlMe₃, and the mixture was stirred at room temperature for 10 min. Methyl 6-((4-(2,6-dimethylmorpholino)phenyl)amino)-1-methyl-1H-indole-3-carboxylate (85 mg, 0.22 mmol) in toluene (5 mL) was added to the above mixture. The mixture was heated to 80°C and stirred for 6h. The reaction mixture was cooled and quenched with water (10 mL) and extracted with ethyl acetate (3x 20 mL). The combined organic phases were dried and concentrated. The residue was purified by Prep-TLC (Petroleum ether: Ethyl acetate=1:10) to give the titled compound **442** (44.4 mg, 54.3%) as a white solid. LC-MS (m/z) 379.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.04-7.6 (m, 3H), 7.75-6.52 (m, 8H), 3.74 (s, 3H), 3.69 (dq, *J* = 12.5, 6.1, 2.2 Hz, 2H), 3.44 (dt, *J* = 10.7, 2.0 Hz, 2H), 2.19 (dd, *J* = 11.8, 10.2 Hz, 2H), 1.14 (d, *J* = 6.2 Hz, 6H).

Compound 443

N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-1H-indazol-5-amine

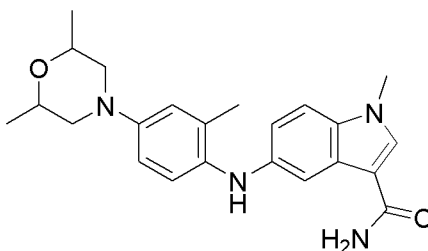


A mixture of tert-butyl 5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-1H-indazole-1-carboxylate (110 mg, 0.25 mmol) in HCl (4M in dioxane, 5 mL) was stirred at room temperature for 2h. The reaction mixture was concentrated under vacuum. The residue was diluted with a saturated solution of NaHCO₃ (30 mL) and extracted with dichloromethane (3x 50 mL). The combined organic phases were dried and concentrated. The residue was purified by Prep-HPLC with the following conditions: Column: Spherical C18 40-60 μm, 40 g; Mobile phase A: water (0.5%

NH₄HCO₃); Mobile phase B: acetonitrile or ACN; Flow rate: 45 mL/min; Gradient: 20%B-65%B in 20 min; Detector: 254 nm. The fractions containing desired product were collected at 45% B and concentrated under reduced pressure to give the titled compound **443** (11.7 mg, 13.8%) as a white solid. LC-MS (m/z) 337.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.31 (s, 1H), 7.74 (s, 1H), 7.06 (d, *J* = 8.5 Hz, 1H), 7.01 – 6.93 (m, 2H), 6.92 – 6.84 (m, 2H), 6.63 – 6.53 (m, 2H), 3.83 – 3.61 (m, 2H), 3.44 (dt, *J* = 10.7, 2.0 Hz, 2H), 3.33–3.29 (m, 2H), 2.19 (s, 3H), 1.14 (d, *J* = 6.2 Hz, 6H).

Compound 444

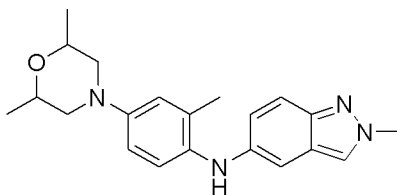
5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-1-methyl-1H-indole-3-carboxamide



To a solution of 5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-1-methyl-1H-indole-3-carboxylic acid (50 mg, 0.127 mmol) in DMF (5 mL) was added HATU (58 mg, 0.152 mmol), NH₄Cl (8.1 mg, 0.152 mmol) and TEA (19.2 mg, 0.191 mmol). The mixture was stirred at 80°C for 2 hours. Then the mixture was diluted with water and extracted by EA (25 mL x 3). The combined organic layers were washed with brine (15 mL x 3), dried over Na₂SO₄ and concentrated to give the crude product, which was purified by pre-HPLC to give the desired product as pink solid (3 mg, 6.1%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.83 (s, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 6.89 – 6.64 (m, 4H), 3.83 – 3.60 (m, 5H), 3.46 (d, *J* = 10.6 Hz, 2H), 2.25 – 2.08 (m, 4H), 1.14 (d, *J* = 6.2 Hz, 6H). Mass (m/z): 393.2 [M+H]⁺.

Compound 445

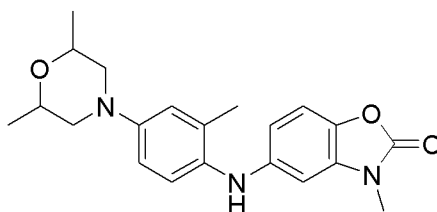
N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-2-methyl-2H-indazol-5-amine



To a solution of 5-bromo-2-methyl-2H-indazole (105 mg, 0.5 mmol) and 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (41 mg, 0.04 mmol), Xphos (43 mg, 0.09 mmol) and Cs_2CO_3 (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by flash chromatography to give N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-2-methyl-2H-indazol-5-amine (24.5 mg, 15%) as a grey solid. Mass (m/z): 351.4 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.90 (d, $J = 0.9$ Hz, 1H), 7.41 (d, $J = 9.1$ Hz, 1H), 7.02 – 6.96 (m, 2H), 6.93 (dd, $J = 9.2, 2.2$ Hz, 1H), 6.84 (d, $J = 2.8$ Hz, 1H), 6.74 (dd, $J = 8.6, 2.9$ Hz, 1H), 6.50 (d, $J = 2.0$ Hz, 1H), 4.04 (s, 3H), 3.75 – 3.63 (m, 2H), 3.53 – 3.45 (m, 2H), 2.26 – 2.16 (m, 2H), 2.14 (s, 3H), 1.15 (d, $J = 6.2$ Hz, 6H).

Compound 446

5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one

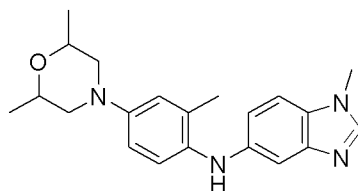


To a solution of 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) and 5-bromo-3-methylbenzo[d]oxazol-2(3H)-one (113 mg, 0.5 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (41 mg, 0.05 mmol), Xphos (43 mg, 0.09 mmol) and Cs_2CO_3 (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by prep TLC to give 5-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-3-methylbenzo[d]oxazol-2(3H)-one (69 mg, 41%) as a light blue solid. Mass (m/z): 368.4 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.26 (s, 1H), 7.03 (dd, $J = 16.8, 8.6$ Hz, 2H), 6.85 (d, $J = 2.8$

Hz, 1H), 6.75 (dd, $J = 8.6, 2.9$ Hz, 1H), 6.44 (d, $J = 2.2$ Hz, 1H), 6.35 (dd, $J = 8.6, 2.3$ Hz, 1H), 3.74 – 3.62 (m, 2H), 3.55 – 3.47 (m, 2H), 3.22 (s, 3H), 2.26 – 2.16 (m, 2H), 2.14 (s, 3H), 1.15 (d, $J = 6.2$ Hz, 6H).

Compound 447

5 *N*-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-1-methyl-1H-benzo[d]imidazol-5-amine

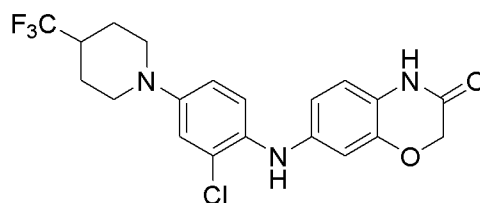


To a solution of 5-bromo-1-methyl-1H-benzo[d]imidazole (105 mg, 0.5 mmol) and 4-(2,6-dimethylmorpholino)-2-methylaniline (100 mg, 0.45 mmol) in 1,4-dioxane (2 mL) was added $\text{Pd}_2(\text{dba})_3$ (41 mg, 0.04 mmol), Xphos (43 mg, 0.09 mmol) and Cs_2CO_3 (296 mg, 0.91 mmol) under nitrogen atmosphere. The mixture was stirred at 100 °C for 12h, the mixture was purified by flash chromatography to give *N*-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-1-methyl-1H-benzo[d]imidazol-5-amine (45 mg, 28%) as a pink solid. Mass (m/z): 351.4 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, DMSO) δ 7.96 (s, 1H), 7.32 (d, $J = 9.1$ Hz, 1H), 6.98 (d, $J = 8.6$ Hz, 1H), 6.94 (s, 1H), 6.86 – 6.78 (m, 3H), 6.72 (dd, $J = 8.7, 2.9$ Hz, 1H), 3.75 (s, 3H), 3.73 – 3.63 (m, 2H), 3.52 – 3.44 (m, 2H), 2.25 – 2.16 (m, 2H), 2.15 (s, 3H), 1.15 (d, $J = 6.2$ Hz, 6H).

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Compound 448

7-(*{2-chloro-4-[4-(trifluoromethyl)piperidin-1-yl]phenyl}*amino)-2,4-dihydro-1,4-benzoxazin-3-one



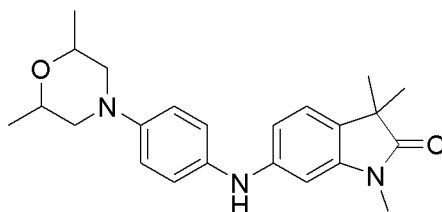
The titled compound **448** (6.8 mg, 4.38%) as a light-yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR

(400 MHz, DMSO- d_6) δ 10.45 (s, 1H), 7.34 – 7.27 (m, 1H), 7.26 -7.00 (m, 2H), 6.91 (s, 1H), 6.69 (s, 1H), 6.41 (s, 2H), 4.47 (s, 2H), 3.80 – 3.66 (m, 2H), 3.51 (br, 1H), 2.76 - 2.62 (m, 2H), 1.86 (s, 2H), 1.56 (s, 2H). Mass (m/z): 425.9 [M+H]⁺.

5

Compound 449

6-((4-(2,6-dimethylmorpholino)phenyl)amino)-1,3,3-trimethylindolin-2-one

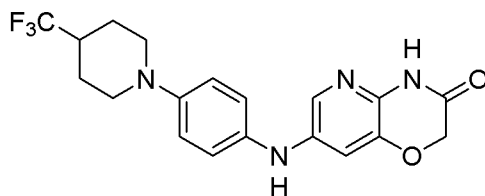


The titled compound **449** (3.8 mg, 2.06%) as a light-brown solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO- d_6) δ 7.86 (s, 1H), 7.06 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 9.2 Hz, 2H), 6.56 - 6.49 (m, 2H), 3.72 - 3.64 (m, 2H), 3.45 (d, J = 10.4 Hz, 2H), 3.05 (s, 3H), 2.22 - 2.15 (m, 2H), 1.22 (s, 6H), 1.14 (d, J = 6.4 Hz, 6H). Mass (m/z): 380.0 [M+H]⁺.

15

Compound 450

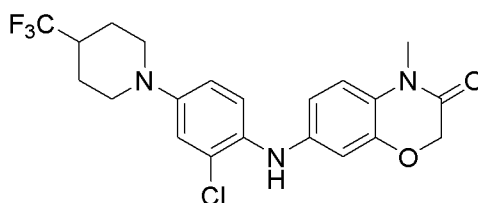
7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one



The titled compound **450** (3.5 mg, 2.15%) as a light-purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO- d_6) δ 7.85 (s, 1H), 7.59 (d, J = 2.4 Hz, 1H), 7.00 - 6.87 (m, 5H), 4.57 (s, 2H), 3.62 (d, J = 12.4 Hz, 2H), 2.62 (t, J = 11.2 Hz, 2H), 2.45 - 2.39 (m, 1H), 1.88 (d, J = 12.8 Hz, 2H), 1.61 - 1.53 (m, 2H). Mass (m/z): 392.9 [M+H]⁺.

Compound 451

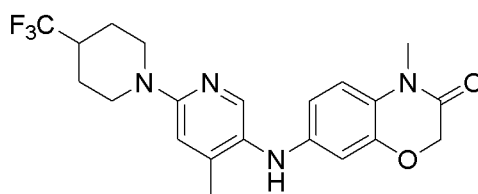
7-((2-chloro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



- 5 The titled compound **451** (19.4 mg, 12.1%) as a light-purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.45 (s, 1H), 7.14 (d, J = 8.8 Hz, 1H), 7.04 (d, J = 2.8 Hz, 1H), 6.97 - 6.89 (m, 2H), 6.48 (dd, J = 8.8, 2.4 Hz, 1H), 6.42 (d, J = 2.4 Hz, 1H), 4.56 (s, 2H), 3.73 (d, J = 12.0 Hz, 2H), 3.22 (s, 3H), 2.69
10 (dd, J = 12.4, 10.4 Hz, 2H), 1.88 (d, J = 12.4 Hz, 2H), 1.54 (dt, J = 12.4, 8.8 Hz, 2H). Mass (m/z): 439.9 $[\text{M}+\text{H}]^+$.

Compound 452

4-methyl-7-((4-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

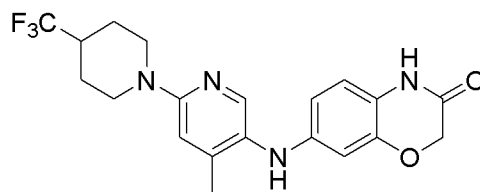


15

- The titled compound **452** (54.9 mg, 32.20%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.87 (s, 1H), 7.29 (s, 1H), 6.91 (d, J = 8.8 Hz, 1H), 6.82 (s, 1H), 6.24 (dd, J = 8.8, 2.4 Hz, 1H), 6.18 (d, J = 2.4 Hz, 1H), 4.54 (s, 2H),
20 4.35 (d, J = 13.2 Hz, 2H), 3.20 (s, 3H), 2.80 (t, J = 12.0 Hz, 2H), 2.66 - 2.54 (m, 1H), 2.09 (s, 3H), 1.85 (d, J = 11.2 Hz, 2H), 1.46 - 1.21 (m, 2H). Mass (m/z): 421.0 $[\text{M}+\text{H}]^+$.

Compound 453

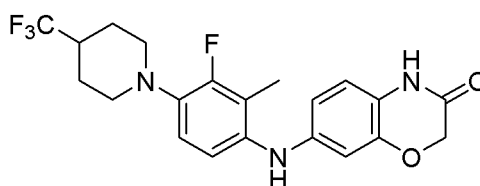
7-((4-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

-2H-benzo[b][1,4]oxazin-3(4H)-one

The titled compound **453** (23.5 mg, 14.23%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.38 (s, 1H), 7.85 (s, 1H), 7.16 (s, 1H), 6.80 (s, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.16 (d, *J* = 8.4 Hz, 2H), 4.45 (s, 2H), 4.34 (d, *J* = 12.4 Hz, 2H), 2.79 (t, *J* = 12.4 Hz, 2H), 2.53 (s, 1H), 2.08 (s, 3H), 1.85 (d, *J* = 11.6 Hz, 2H), 1.43 (d, *J* = 11.6 Hz, 2H). Mass (*m/z*): 407.0 [M+H]⁺.

Compound 454

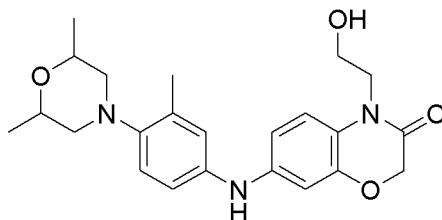
7-((3-fluoro-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **454** (21.4 mg, 13.95%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.46 (s, 1H), 7.31 (s, 1H), 6.91 - 6.78 (m, 2H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.43 - 6.36 (m, 2H), 4.48 (s, 2H), 3.31 (s, 1H), 2.65 (t, *J* = 11.2 Hz, 2H), 2.49 - 2.35 (m, 2H), 2.06 (t, *J* = 6.0 Hz, 3H), 1.89 (d, *J* = 11.6 Hz, 2H), 1.65 - 1.52 (m, 2H). Mass (*m/z*): 424.0 [M+H]⁺.

Compound 455

7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[b][1,4]oxazin-3(4H)-one

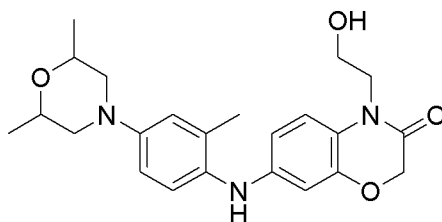


The titled compound **455** (12.1 mg, 29.63%) as a light-purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.90 (s, 1H), 7.10 (d, $J = 8.8$ Hz, 1H), 6.92 (d, $J = 8.4$ Hz, 1H), 6.87 - 6.82 (m, 2H), 6.67 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.59 (d, $J = 2.4$ Hz, 1H), 4.87 (t, $J = 5.6$ Hz, 1H), 4.55 (s, 2H), 3.90 (t, $J = 6.4$ Hz, 2H), 3.75 - 3.68 (m, 2H), 3.56 (q, $J = 6.4$ Hz, 2H), 2.84 (d, $J = 10.8$ Hz, 2H), 2.28 (dd, $J = 11.6, 10.0$ Hz, 2H), 2.21 (s, 3H), 1.10 (d, $J = 6.4$ Hz, 6H). Mass (m/z): 412.0 $[\text{M}+\text{H}]^+$.

10

Compound 456

7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[b][1,4]oxazin-3-one

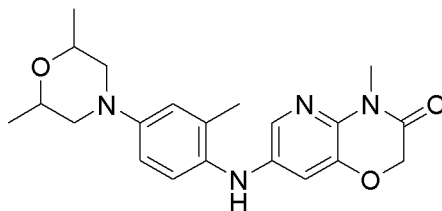


The titled compound **456** (36.0 mg, 57.33%) as a light-purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.17 (s, 1H), 6.96 (dd, $J = 13.6, 8.8$ Hz, 2H), 6.80 (d, $J = 2.8$ Hz, 1H), 6.71 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.30 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.21 (d, $J = 2.4$ Hz, 1H), 6.04 (s, 1H), 4.47 (s, 2H), 3.83 (t, $J = 6.4$ Hz, 2H), 3.67 - 3.60 (m, 2H), 3.53 - 3.45 (m, 4H), 2.20 - 2.14 (m, 2H), 2.08 (s, 3H), 1.11 (d, $J = 6.4$ Hz, 6H). Mass (m/z): 412.0 $[\text{M}+\text{H}]^+$.

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Compound 457

7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-4-methyl-2H-

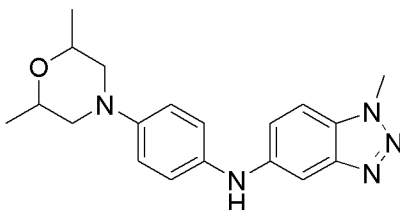
pyrido[3,2-b][1,4]oxazin-3(4H)-one

The titled compound **457** (126 mg, 48.6%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.47 (d, *J* = 2.4 Hz, 1H), 7.38 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 2.8 Hz, 1H), 6.76 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 4.66 (s, 2H), 3.69 - 3.65 (m, 2H), 3.51 (d, *J* = 10.4 Hz, 2H), 3.26 (s, 3H), 2.23 - 2.20 (m, 2H), 2.14 (s, 3H), 1.15 (d, *J* = 6.4 Hz, 6H). Mass (m/z): 383.0 [M+H]⁺.

10

Compound 458

N-(4-(2,6-dimethylmorpholino) phenyl)-1-methyl-1H-benzo[d][1,2,3]triazol-5-amine

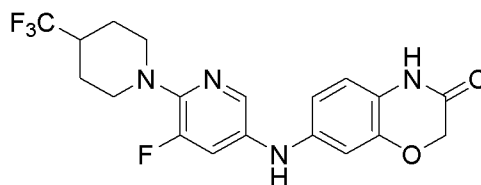


The titled compound **458** (61.8 mg, 34.55%) as a green solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.99 (s, 1H), 7.66 - 7.64 (m, 1H), 7.28 (s, 2H), 7.20 - 7.18 (m, 1H), 7.08-7.05 (d, *J* = 12 Hz, 2H), 6.94 - 6.91 (m, 2H), 4.22 (s, 3H), 3.70 - 3.68 (m, 2H), 3.48-3.46 (m, 2H), 2.24 - 2.21 (m, 2H), 1.16 - 1.14 (m, 6H). Mass (m/z): 338.0 [M+H]⁺.

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Compound 459

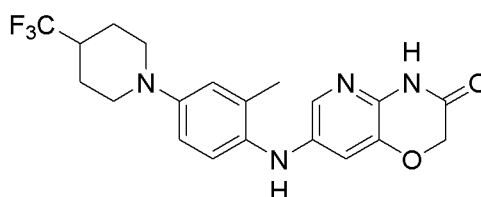
7-((5-fluoro-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **459** (70.6 mg, 45.31%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.53 (s, 1H), 8.06 (s, 1H), 7.81 (d, *J* = 1.6 Hz, 1H), 7.23 (dd, *J* = 14.4, 2.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.62 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.57 (d, *J* = 2.4 Hz, 1H), 4.51 (s, 2H), 3.76 (d, *J* = 12.8 Hz, 2H), 3.34 - 3.33 (m, 1H), 2.80 (t, *J* = 11.6 Hz, 2H), 1.87 (d, *J* = 11.6 Hz, 2H), 1.56 (dd, *J* = 12.8, 3.6 Hz, 2H). Mass (*m/z*): 411.0 [M+H]⁺.

Compound 460

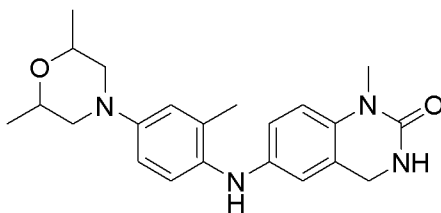
7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one



The titled compound **460** (24.7 mg, 14.51%) as a light-purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.37 (d, *J* = 2.4 Hz, 1H), 7.26 (s, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 4.54 (s, 2H), 3.70 (d, *J* = 12.4 Hz, 2H), 2.65 (dd, *J* = 12.4, 10.4 Hz, 2H), 2.48 - 2.39 (m, 1H), 2.13 (s, 3H), 1.88 (d, *J* = 12.0 Hz, 2H), 1.62 - 1.52 (m, 2H). Mass (*m/z*): 407.0 [M+H]⁺.

Compound 461

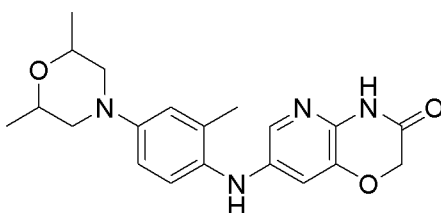
7-((4-(2,6-dimethylmorpholino)-3-methylphenyl)amino)-4-(2-hydroxyethyl)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **461** (3.3 mg, 10.02% yield) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.99 - 6.94 (m, 2H), 6.85 - 6.80 (m, 2H), 6.75 - 6.69 (m, 2H), 6.57 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.50 (d, *J* = 2.4 Hz, 1H), 4.14 (s, 2H), 3.72 - 3.65 (m, 2H), 3.48 (d, *J* = 10.4 Hz, 2H), 3.09 (s, 3H), 2.22 - 2.16 (m, 2H), 2.12 (s, 3H), 1.14 (d, *J* = 6.4 Hz, 6H). Mass (*m/z*): 412.0 [M+H]⁺.

Compound 462

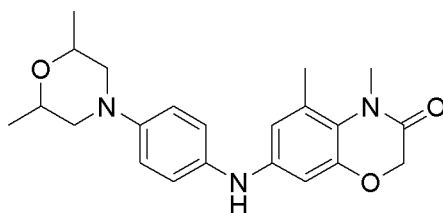
7-((4-(2,6-dimethylmorpholino)-2-methylphenyl)amino)-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one



The titled compound **462** (26.0 mg, 15.33%) as a light purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.37 (d, *J* = 2.4 Hz, 1H), 7.26 (s, 1H), 6.98 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 4.54 (s, 2H), 3.70 (d, *J* = 12.4 Hz, 2H), 2.65 (dd, *J* = 12.4, 10.4 Hz, 2H), 2.48 - 2.39 (m, 1H), 2.13 (s, 3H), 1.88 (d, *J* = 12.0 Hz, 2H), 1.62 - 1.52 (m, 2H). Mass (*m/z*): 369.0 [M+H]⁺.

Compound 463

7-{[4-(2,6-dimethylmorpholin-4-yl)phenyl]amino}-4,5-dimethyl-2H-1,4-benzoxazin-3-one



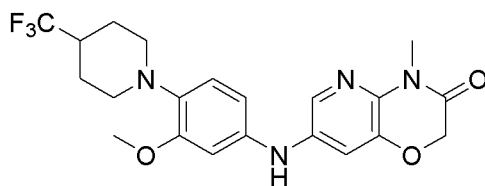
The titled compound **463** (4.0 mg, 1.82%) as a light-yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.79 (s, 1H), 6.93 (dd, $J = 34.4, 8.8$ Hz, 4H), 6.43 (d, $J = 16.8$ Hz, 2H), 4.40 (s, 2H), 3.76 - 3.61 (m, 2H), 3.45 (d, $J = 11.2$ Hz, 2H), 3.26 (s, 3H), 2.29 (s, 3H), 2.19 (t, $J = 11.2$ Hz, 2H), 1.14 (d, $J = 6.4$ Hz, 6H). Mass (m/z): 382.0 $[\text{M}+\text{H}]^+$.

Compound 464

7-({3-methoxy-4-[4-(trifluoromethyl)piperidin-1-yl]phenyl}amino)-4-

10

methyl-2H-pyrido[3,2-b][1,4]oxazin-3-one

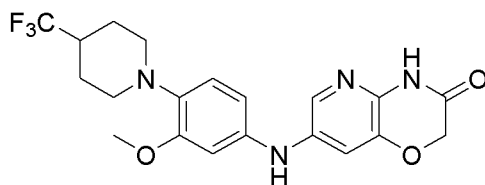


The titled compound **464** (12.5 mg, 7.73%) as a light-yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.09 (s, 1H), 7.78 (d, $J = 2.4$ Hz, 1H), 7.02 (d, $J = 2.4$ Hz, 1H), 6.82 (d, $J = 8.4$ Hz, 1H), 6.65 - 6.56 (m, 2H), 4.70 (s, 2H), 3.75 (s, 3H), 3.29 (s, 4H), 2.59 - 2.51 (m, 3H), 2.43 - 2.32 (m, 1H), 1.86 (d, $J = 11.2$ Hz, 2H), 1.59 (dd, $J = 12.4, 3.6$ Hz, 2H). Mass (m/z): 437.0 $[\text{M}+\text{H}]^+$.

Compound 465

20

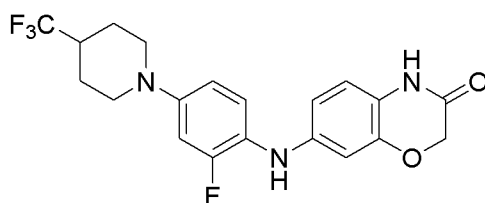
7-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one



The titled compound **465** (7.8 mg, 4.94%) as a light-brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 11.20 - 10.78 (m, 1H), 7.99 (s, 1H), 7.67 (d, J = 2.4 Hz, 1H), 6.99 (d, J = 2.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.65 - 6.49 (m, 2H), 4.58 (s, 2H), 3.74 (s, 3H), 3.30 (s, 2H), 2.54 (d, J = 12.0 Hz, 2H), 2.37 (dd, J = 12.4, 8.8 Hz, 1H), 1.86 (d, J = 11.2 Hz, 2H), 1.59 (qd, J = 12.4, 3.6 Hz, 2H). Mass (m/z): 422.9 $[\text{M}+\text{H}]^+$.

Compound 466

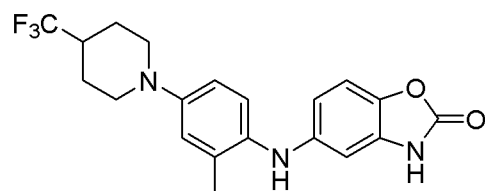
7-((2-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **466** ((4.7 mg, 3.02%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CDCl $_3$) δ 7.71 (s, 1H), 7.16 (s, 1H), 6.73 (s, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.61 (s, 1H), 6.56 (s, 1H), 4.58 (s, 2H), 3.67 (d, J = 10.0 Hz, 2H), 2.74 (s, 2H), 2.19 (s, 1H), 2.01 (s, 2H), 1.82 (s, 2H). Mass (m/z): 410.0 $[\text{M}+\text{H}]^+$.

Compound 467

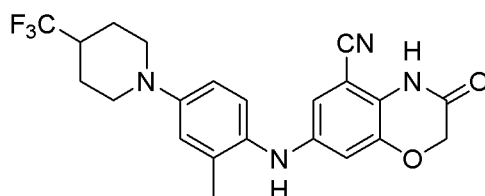
5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)benzo[d]oxazol-2(3H)-one



The titled compound **467** (12.0 mg, 7.9%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CD_3OD) δ 7.02 (d, $J = 8.8$ Hz, 1H), 6.94 (d, $J = 8.8$ Hz, 1H), 6.88 (d, $J = 2.4$ Hz, 1H), 6.78 - 6.80 (m, 1H), 6.50 - 6.32 (m, 2H), 3.66 (d, $J = 12.0$ Hz, 2H), 2.65 - 2.68 (m, 2H), 2.25 - 2.27 (m, 1H), 2.17 (d, $J = 10.0$ Hz, 3H), 1.97 - 2.00 (m, 2H), 1.75 - 1.64 (m, 2H). Mass (m/z): 391.7 $[\text{M}+\text{H}]^+$.

Compound 468

7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazine-5-carbonitrile



10

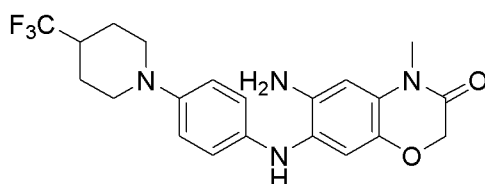
The titled compound **468** (12.0 mg, 7.9%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.69 (s, 1H), 7.55 (s, 1H), 6.99 (d, $J = 8.8$ Hz, 1H), 6.89 (d, $J = 2.8$ Hz, 1H), 6.80 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.53 (d, $J = 2.4$ Hz, 1H), 6.42 (d, $J = 2.4$ Hz, 1H), 4.54 (s, 2H), 3.74 (d, $J = 12.8$ Hz, 2H), 2.67 (dd, $J = 12.4, 10.4$ Hz, 2H), 2.45 (dd, $J = 12.4, 8.8$ Hz, 1H), 2.10 (s, 3H), 1.91 - 1.85 (m, 2H), 1.60 - 1.50 (m, 2H). Mass (m/z): 431.0 $[\text{M}+\text{H}]^+$.

15

Compound 469

6-amino-4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

20

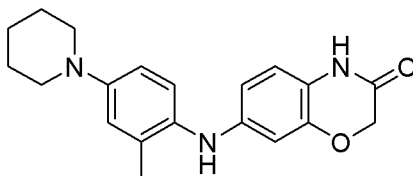


The titled compound **468** (6 mg, 3.6%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 6.92 - 6.78 (m, 3H), 6.71 (d, $J = 6.8$ Hz, 2H), 6.56 (s, 2H),

4.47 (s, 2H), 3.60 - 3.50 (m, 2H), 3.21 (s, 3H), 2.79 - 2.58 (m, 2H), 2.48 - 2.34 (m, 1H), 1.88 (d, $J = 12.4$ Hz, 2H), 1.67 - 1.48 (m, 2H). Mass (m/z): 420.9 $[M+H]^+$.

Compound 470

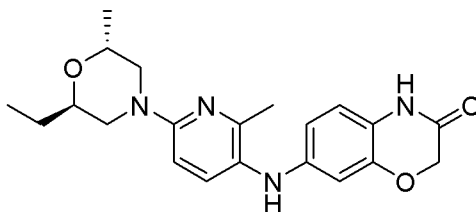
5 7-((2-methyl-4-(piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **470** (32.9 mg, 20.1%) as a blue solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 12.57 (s, 1H), 10.38 (s, 1H), 7.08 - 6.90 (m, 2H), 6.85 - 6.57 (m, 3H), 6.32 - 6.20 (m, 1H), 4.46 (s, 2H), 2.12 (s, 3H), 1.61 (s, 4H), 1.28 - 1.21 (m, 4H), 0.85 (t, $J = 6.4$ Hz, 2H). Mass (m/z): 338.3 $[M+H]^+$.

Compound 471

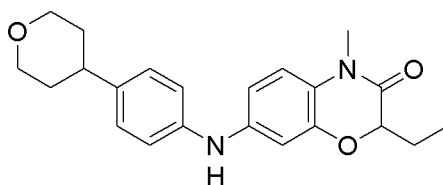
15 7-(((6-((2R,6R)-2-ethyl-6-methylmorpholino)-2-methylpyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **471** (35.0 mg, 48.2%) as a light-yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.33 (d, $J = 8.8$ Hz, 1H), 6.68 (d, $J = 8.4$ Hz, 1H), 6.60 (d, $J = 8.8$ Hz, 1H), 6.28 - 6.18 (m, 2H), 4.47 (s, 2H), 4.09 - 4.01 (m, 1H), 3.87 - 3.75 (m, 1H), 3.70 - 3.61 (m, 1H), 3.53 - 3.44 (m, 1H), 3.39 - 3.33 (m, 1H), 3.14 - 3.04 (m, 1H), 2.28 (s, 3H), 1.81 - 1.69 (m, 1H), 1.63 - 1.52 (m, 1H), 1.25 (d, $J = 6.4$ Hz, 3H), 0.98 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 383.2 $[M+H]^+$.

Compound 472

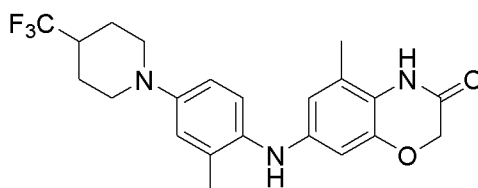
2-ethyl-4-methyl-7-((4-(tetrahydro-2H-pyran-4-yl)phenyl)amino)-2H-

benzo[b][1,4]oxazin-3(4H)-one

The titled compound **472** (46.0 mg, 34%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CD₃OD) δ 7.13 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.74 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 4.49 - 4.39 (m, 1H), 4.03 (d, *J* = 11.2 Hz, 2H), 3.61 - 3.50 (m, 2H), 2.82 - 2.66 (m, 1H), 1.91 - 1.71 (m, 6H), 1.05 (t, *J* = 7.2 Hz, 3H). Mass (m/z): 367.5 [M+H]⁺.

Compound 473

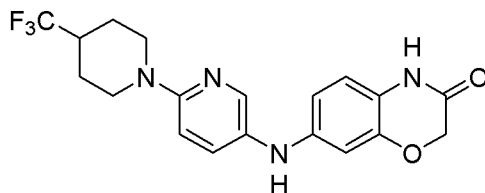
5-methyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **473** (50.8 mg, 34%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.92 (s, 1H), 7.00 (s, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 6.83 (d, *J* = 2.8 Hz, 1H), 6.75 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.15 (s, 1H), 6.10 (s, 1H), 4.39 (s, 2H), 3.68 (d, *J* = 12.0 Hz, 2H), 2.65 (t, *J* = 11.6 Hz, 2H), 2.46 - 2.38 (m, 1H), 2.10 (s, 6H), 1.88 (d, *J* = 11.6 Hz, 2H), 1.63 - 1.48 (m, 2H). Mass (m/z): 420.5 [M+H]⁺.

Compound 474

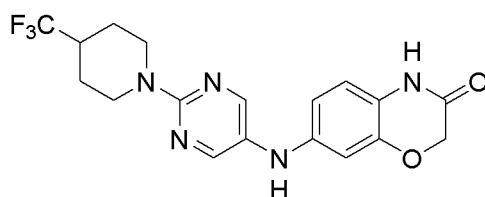
7-((6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **474** (70.3 mg, 43%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.41 (s, 1H), 7.93 (d, $J = 2.8$ Hz, 1H), 7.61 (s, 1H), 7.34 (dd, $J = 9.2, 2.8$ Hz, 1H), 6.84 (d, $J = 9.2$ Hz, 1H), 6.70 (d, $J = 8.4$ Hz, 1H), 6.49 - 6.39 (m, 2H), 4.47 (s, 2H), 4.27 (d, $J = 13.2$ Hz, 2H), 2.76 (t, $J = 12.4$ Hz, 2H), 2.61 - 2.54 (m, 1H), 1.85 (d, $J = 12.8$ Hz, 2H), 1.52 - 1.37 (m, 2H). Mass (m/z): 393.4 $[\text{M}+\text{H}]^+$.

Compound 475

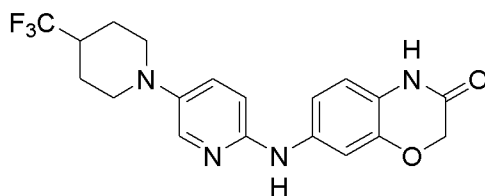
7-((2-(4-(trifluoromethyl)piperidin-1-yl)pyrimidin-5-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **475** (58.5 mg, 36%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.42 (s, 1H), 8.22 (s, 2H), 7.57 (s, 1H), 6.70 (d, $J = 8.4$ Hz, 1H), 6.44 - 6.35 (m, 2H), 4.72 - 4.64 (m, 2H), 4.47 (s, 2H), 2.94 - 2.82 (m, 2H), 2.59 - 2.55 (m, 1H), 1.87 (d, $J = 12.0$ Hz, 2H), 1.46 - 1.31 (m, 2H). Mass (m/z): 394.4 $[\text{M}+\text{H}]^+$.

Compound 476

7-((2-(4-(trifluoromethyl)piperidin-1-yl)pyrimidin-5-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



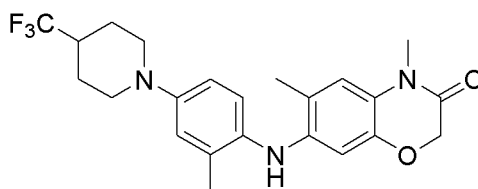
The titled compound **476** (10.5 mg, 6%) as an off-white solid was prepared

according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.42 (s, 1H), 8.22 (s, 2H), 7.57 (s, 1H), 6.70 (d, $J = 8.4$ Hz, 1H), 6.44 - 6.35 (m, 2H), 4.72 - 4.64 (m, 2H), 4.47 (s, 2H), 2.94 - 2.82 (m, 2H), 2.59 - 2.55 (m, 1H), 1.87 (d, $J = 12.0$ Hz, 2H), 1.46 - 1.31 (m, 2H).

5 Mass (m/z): 393.4 $[\text{M}+\text{H}]^+$.

Compound 477

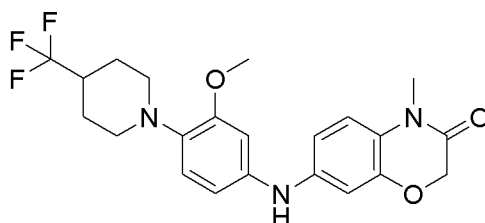
4,6-dimethyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



10 The titled compound **477** (67.7 mg, 44.7%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 6.92 - 6.84 (m, 2H), 6.84 - 6.72 (m, 2H), 6.44 (s, 1H), 5.93 (s, 1H), 4.46 (s, 2H), 3.70 (d, $J = 12.4$ Hz, 2H), 3.22 (s, 3H), 2.66 (t, $J = 12.0$ Hz, 2H), 2.47 - 2.38 (m, 2H) 2.17 (s, 3H), 2.08 (s, 3H), 1.88 (d, $J = 13.2$ Hz, 2H), 1.64 - 1.49 (m, 2H). Mass (m/z): 434.5 $[\text{M}+\text{H}]^+$.

Compound 478

7-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one

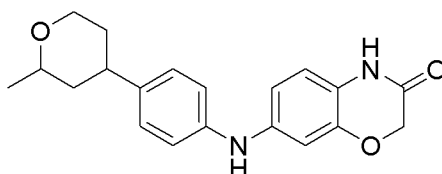


20 The titled compound **478** (23.3 mg, 14.7%) as a gray solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.97 (s, 1H), 7.62 (d, $J = 2.3$ Hz, 1H), 7.04 - 6.95 (m, 2H), 6.69 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.58 (d, $J = 2.4$ Hz, 1H), 4.58 (s, 2H), 3.85 - 3.78 (m, 2H), 3.77 (s, 3H), 3.23 (s, 3H), 2.66 (d, $J = 24.0$ Hz, 2H), 1.85 (d, $J = 12.0$ Hz, 2H), 1.57 (qd, $J = 12.4, 3.6$ Hz, 2H). Mass (m/z): 436.2

[M+H]⁺.

Compound 479

7-((4-(2-methyltetrahydro-2H-pyran-4-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



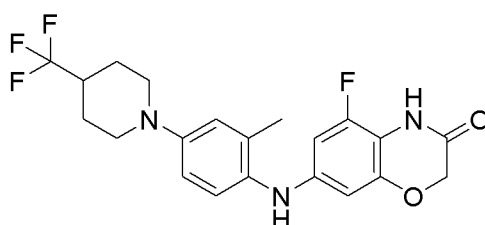
5

The titled compound **479** (26.2 mg, 11.4%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 7.94 (s, 1H), 7.13 - 7.05 (m, 2H), 7.03 - 6.88 (m, 2H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.69 - 6.55 (m, 2H), 4.50 (s, 2H), 4.03 - 3.85 (m, 1H), 3.54 - 3.41 (m, 2H), 2.66 (dd, *J* = 24.0, 3.6 Hz, 1H), 1.82 - 1.45 (m, 3H), 1.25 (td, *J* = 12.4, 10.8 Hz, 1H), 1.12 (d, *J* = 6.0 Hz, 3H). Mass (m/z): 339.2 [M+H]⁺.

10

Compound 480

5-fluoro-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



15

The titled compound **480** (25 mg, 5.9%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.50 (s, 1H), 7.34 (s, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.78 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.06 (d, *J* = 11.2 Hz, 2H), 4.48 (s, 2H), 3.72 (d, *J* = 12.4 Hz, 2H), 2.67 (t, *J* = 12.0 Hz, 3H), 2.51-2.49 (m, 1H), 2.10 (s, 3H), 1.88 (d, *J* = 12.0 Hz, 2H), 1.56 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass(m/z): 424.2 [M+H]⁺.

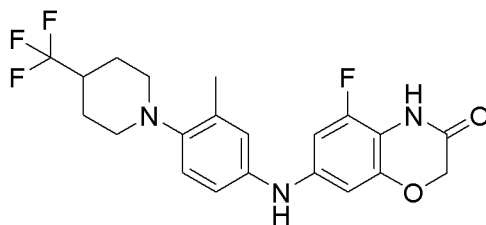
20

Compound 481

5-fluoro-7-((3-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

25

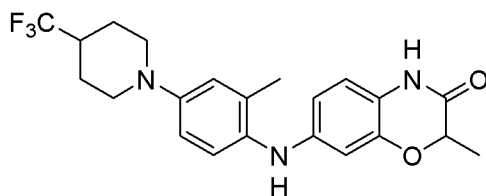
amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **481** (34.7 mg, 8.2%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.60 (s, 1H), 7.98 (s, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 7.2 Hz, 2H), 6.44 (d, *J* = 12.4 Hz, 1H), 6.38 (s, 1H), 4.53 (s, 2H), 3.05 (d, *J* = 11.6 Hz, 2H), 2.63 (d, *J* = 11.6 Hz, 2H), 2.51 - 2.49 (m, 1H), 2.20 (s, 3H), 1.97 - 1.80 (m, 2H), 1.60 (qd, *J* = 12.4, 4.0 Hz, 2H). Mass(*m/z*): 424.2 [M+H]⁺.

Compound 482

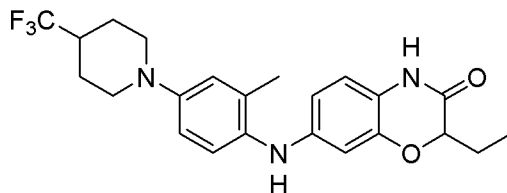
2-methyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **482** (27.2 mg, 13.1%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.29 (s, 1H), 7.05 (s, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.75 (dd, *J* = 8.0, 2.8 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.29 (d, *J* = 8.4 Hz, 1H), 6.23 (s, 1H), 4.52 (q, *J* = 6.8 Hz, 1H), 3.68 (d, *J* = 12.0 Hz, 2H), 2.65 (t, *J* = 12.0 Hz, 2H), 2.47 - 2.37 (m, 1H), 2.11 (s, 3H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.61 - 1.51 (m, 2H), 1.36 (d, *J* = 6.8 Hz, 3H). Mass (*m/z*): 420.2 [M+H]⁺.

Compound 483

2-ethyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

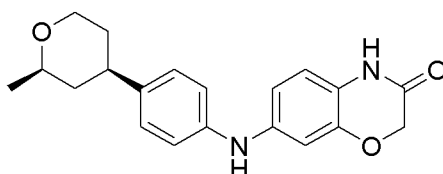


The titled compound **483** (12 mg, 5.9 %) as a white solid was prepared according to the procedure outlined for **1**. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 10.29 (s, 1H), 7.05 (s, 1H), 6.97 (d, $J = 8.8$ Hz, 1H), 6.85 (d, $J = 2.8$ Hz, 1H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.66 (d, $J = 8.4$ Hz, 1H), 6.29 (d, $J = 8.4$ Hz, 1H), 6.23 (s, 1H), 4.36 (q, $J = 8.0$ Hz, 1H), 3.68 (d, $J = 12.0$ Hz, 2H), 2.63 (t, $J = 12.4$ Hz, 2H), 2.47 - 2.37 (m, 1H), 2.11 (s, 3H), 1.88 (d, $J = 12.8$ Hz, 2H), 1.78 - 1.67 (m, 2H), 1.61 - 1.50 (m, 2H), 0.95 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 434.2 $[\text{M}+\text{H}]^+$.

10

Compound 484

7-((4-((2R,4R)-2-methyltetrahydro-2H-pyran-4-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

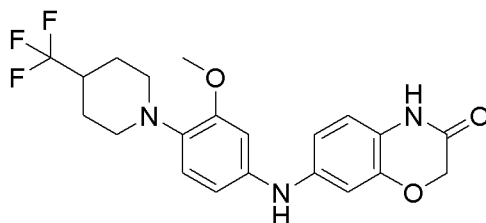


[0001] The titled compound **484** (26.2 mg, 11.4%) as a white solid was prepared according to the procedure outlined for **1**. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 10.50 (s, 1H), 7.94 (s, 1H), 7.13 - 7.05 (m, 2H), 7.03 - 6.88 (m, 2H), 6.75 (d, $J = 8.4$ Hz, 1H), 6.69 - 6.55 (m, 2H), 4.50 (s, 2H), 4.03 - 3.85 (m, 1H), 3.54 - 3.41 (m, 2H), 2.66 (dd, $J = 24.0, 3.6$ Hz, 1H), 1.82 - 1.45 (m, 3H), 1.25 (td, $J = 12.8, 10.8$ Hz, 1H), 1.12 (d, $J = 6.0$ Hz, 3H). Mass (m/z): 339.2 $[\text{M}+\text{H}]^+$.

20

Compound 485

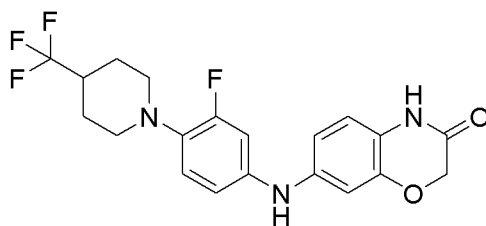
7-((3-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **485** (32 mg, 20.7%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.46 (s, 1H), 7.81 (s, 1H), 6.76 (dd, $J = 19.6, 8.4$ Hz, 2H), 6.66 - 6.49 (m, 4H), 4.49 (s, 2H), 3.73 (s, 3H), 3.28 (s, 2H), 2.55-2.53 (m, 2H), 2.51-2.49 (m, 1H), 1.85 (d, $J = 12.8$ Hz, 2H), 1.59 (qd, $J = 12.0, 40$ Hz, 2H). Mass (m/z): 424.4 $[\text{M}+\text{H}]^+$.

Compound 486

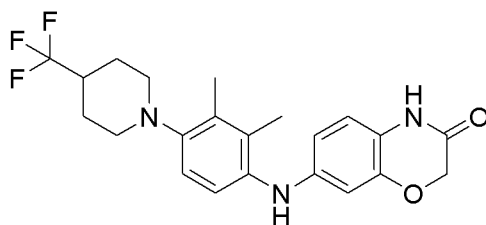
7-((3-fluoro-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **486** (18.1 mg, 11.6%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.52 (s, 1H), 8.00 (s, 1H), 6.94 (t, $J = 9.2$ Hz, 1H), 6.82 - 6.70 (m, 3H), 6.68 - 6.55 (m, 2H), 4.51 (s, 2H), 3.27 (d, $J = 12.0$ Hz, 2H), 2.71 - 2.60 (m, 2H), 2.44 - 2.36 (m, 1H), 1.88 (d, $J = 12.4$ Hz, 2H), 1.70 - 1.51 (m, 2H). Mass (m/z): 410.4 $[\text{M}+\text{H}]^+$.

Compound 487

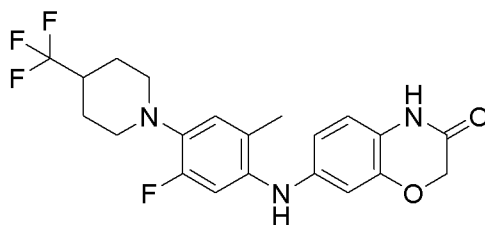
7-((2,3-dimethyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **487** (10 mg, 6.5%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 7.21 (s, 1H), 6.98 - 6.81 (m, 2H), 6.66 (d, J = 8.4 Hz, 1H), 6.33 - 6.16 (m, 2H), 4.44 (s, 2H), 3.03 (d, J = 11.6 Hz, 2H), 2.63 (d, J = 11.6 Hz, 3H), 2.19 (s, 3H), 2.05 (s, 3H), 1.89 (d, J = 12.4 Hz, 2H), 1.64 (tt, J = 14.8, 8.0 Hz, 2H). Mass(m/z): 420.2 $[\text{M}+\text{H}]^+$.

Compound 488

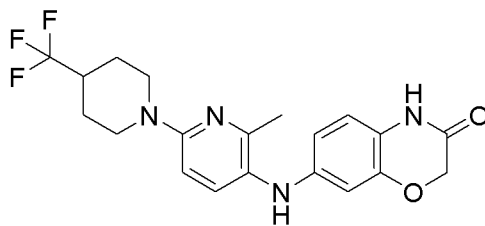
7-((5-fluoro-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **488** (24 mg, 15.7%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.47 (s, 1H), 7.22 (s, 1H), 6.94 - 6.68 (m, 3H), 6.53 - 6.35 (m, 2H), 4.49 (s, 2H), 3.29 (d, J = 11.6 Hz, 2H), 2.74 - 2.59 (m, 2H), 2.42 - 2.39 (m, 1H), 2.11 (s, 3H), 1.89 (d, J = 12.4 Hz, 2H), 1.60 (q, J = 12.4, 11.6 Hz, 2H). Mass(m/z): 424.2 $[\text{M}+\text{H}]^+$.

Compound 489

7-((2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one

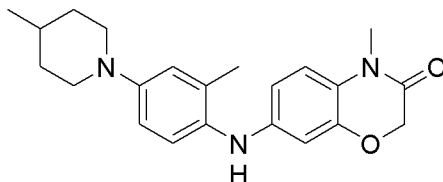


The titled compound **489** (26.7 mg, 17%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 7.28 (d, J = 8.8 Hz, 1H), 7.13 (s, 1H), 6.67 (t, J = 9.6 Hz, 2H), 6.19 (d, J = 9.6 Hz, 2H), 4.45 (s, 2H), 4.34 (d, J = 13.2

Hz, 2H), 2.76 (t, $J = 12.8$ Hz, 2H), 2.42 - 2.39 (m, 1H), 2.21 (s, 3H), 1.86 (d, $J = 12.8$ Hz, 2H), 1.43 (qd, $J = 12.4, 3.6$ Hz, 2H). Mass(m/z): 407.2 $[M+H]^+$.

Compound 490

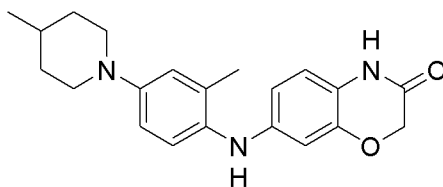
5 4-methyl-7-((2-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **490** (32.9 mg, 18.35%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.18 (s, 1H), 6.96 (d, $J = 8.8$ Hz, 1H), 6.90 (d, $J = 8.8$ Hz, 1H), 6.82 (d, $J = 2.8$ Hz, 1H), 6.73 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.33 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.25 (d, $J = 2.4$ Hz, 1H), 4.53 (s, 2H), 3.57 (d, $J = 12.4$ Hz, 2H), 3.20 (s, 3H), 2.58 (t, $J = 11.2$ Hz, 2H), 2.09 (d, $J = 11.2$ Hz, 3H), 1.68 (d, $J = 11.6$ Hz, 2H), 1.53 - 1.37 (m, 1H), 1.23 (qd, $J = 12.4, 4.0$ Hz, 2H), 0.94 (d, $J = 6.8$ Hz, 3H). Mass(m/z): 365.9 $[M+H]^+$.

Compound 491

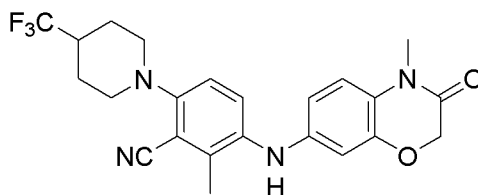
7-((2-methyl-4-(4-methylpiperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



20 The titled compound **491** (7.8 mg, 4.52%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CDCl_3) δ 7.95 (s, 1H), 7.05 (d, $J = 8.0$ Hz, 1H), 6.81 (d, $J = 20.0$ Hz, 2H), 6.61 (d, $J = 8.0$ Hz, 1H), 6.36 (s, 2H), 5.12 (s, 1H), 4.55 (s, 2H), 3.60 (d, $J = 11.2$ Hz, 2H), 2.67 (s, 2H), 2.19 (s, 3H), 1.75 (d, $J = 12.4$ Hz, 2H), 1.58 (s, 1H), 1.36 (d, $J = 11.2$ Hz, 2H), 0.99 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 352.1 $[M+H]^+$.

Compound 492

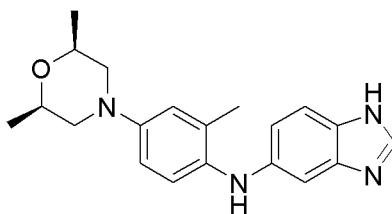
2-methyl-3-((4-methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)amino)-6-(4-(trifluoromethyl)piperidin-1-yl)benzonitrile



- 5 The titled compound **492** (74.9 mg, 59.73%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CDCl₃) δ 7.31 - 7.26 (m, 1H), 6.94 - 6.86 (m, 1H), 6.83 (d, *J* = 8.6 Hz, 1H), 6.46 (dd, *J* = 11.8, 2.9 Hz, 2H), 4.57 (s, 2H), 3.55 (d, *J* = 11.8 Hz, 2H), 3.32 (s, 3H), 2.75 (d, *J* = 11.4 Hz, 2H), 2.42 (s, 3H), 2.23 - 2.09 (m, 1H),
10 2.04 - 1.86 (m, 4H). Mass (m/z): 444.8 [M+H]⁺.

Compound 493

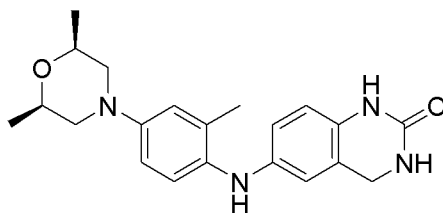
N-(4-((2R,6S)-2,6-dimethylmorpholino)-2-methylphenyl)-1H-benzo[d]imidazol-5-amine



- 15 The titled compound **493** (35.6 mg, 56%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.95 (s, 1H), 7.94 (s, 1H), 7.36 (d, *J* = 8.8 Hz, 1H), 7.06 - 6.99 (m, 2H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.77 - 6.70 (m, 2H), 6.67 (s, 1H), 3.69 (m, 2H), 3.49 (d, *J* = 10.4 Hz, 2H), 2.25 - 2.17 (m, 2H), 2.15 (s, 3H),
20 1.15 (d, *J* = 6.4 Hz, 6H). Mass (m/z): 337 [M+H]⁺.

Compound 494

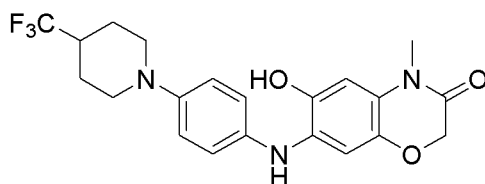
6-((4-((2R,6S)-2,6-dimethylmorpholino)-2-methylphenyl)amino)-3,4-dihydroquinazolin-2(1H)-one



The titled compound **494** (4.2 mg, 1.72%) as a light-yellow solid was prepared according to the procedure outlined for compound **461**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.69 (s, 1H), 6.92 (d, $J = 8.8$ Hz, 1H), 6.84 (s, 1H), 6.79 (d, $J = 2.8$ Hz, 1H), 6.70 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.57 (d, $J = 8.4$ Hz, 2H), 6.50 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.44 (s, 1H), 4.18 (s, 2H), 3.71 - 3.64 (m, 2H), 3.46 (d, $J = 10.4$ Hz, 2H), 2.21 - 2.15 (m, 2H), 2.11 (s, 3H), 1.14 (d, $J = 6.2$ Hz, 6H). Mass(m/z): 366.9 $[\text{M}+\text{H}]^+$.

Compound 495

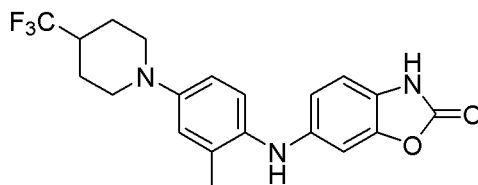
10 6-hydroxy-4-methyl-7-({4-[4-(trifluoromethyl)piperidin-1-yl]phenyl}
amino)-2H-1,4-benzoxazin-3-one



The titled compound **495** (15 mg, 7.6%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.44 (s, 1H), 7.72 (s, 1H), 7.39 (s, 2H), 6.93 (d, $J = 7.6$ Hz, 2H), 6.73 (d, $J = 33.2$ Hz, 2H), 4.55 (s, 2H), 3.63 (s, 4H), 3.23 (s, 3H), 2.76 (d, $J = 23.6$ Hz, 1H), 2.12 (s, 2H), 1.94 (d, $J = 18.0$ Hz, 2H). Mass (m/z): 421.8 $[\text{M}+\text{H}]^+$.

Compound 496

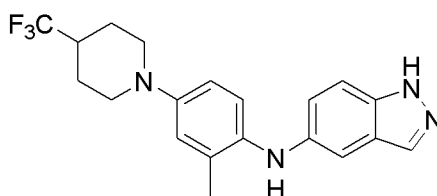
20 6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
benzo[d]oxazol-2(3H)-one



The titled compound **496** (15 mg, 4.9%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CD_3OD) δ 7.03 (d, $J = 8.8$ Hz, 1H), 6.91 (d, $J = 2.4$ Hz, 1H), 6.82 - 6.84 (m, 2H), 6.60 - 6.52 (m, 2H), 3.68 (d, $J = 12.4$ Hz, 2H), 2.67 - 2.69 (m, 2H),
 5 2.34 - 2.23 (m, 1H), 2.17 (d, $J = 5.2$ Hz, 3H), 2.03 - 1.94 (m, 2H), 1.77 - 1.66 (m, 2H). Mass(m/z): 392.2 $[\text{M}+\text{H}]^+$.

Compound 497

N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indazol-5-amine



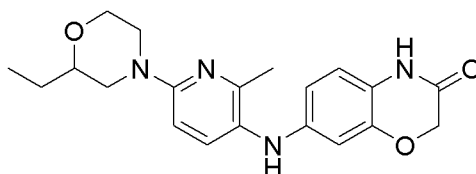
10

The titled compound **497** (41.8 mg, 46.22%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CD_3OD) δ 7.79 (s, 1H), 7.40 (d, $J = 8.9$ Hz, 1H), 7.10 (dd, $J = 8.8, 2.0$ Hz, 1H), 7.05 (d, $J = 8.8$ Hz, 1H), 6.93 (s, 2H), 6.83 (s, 1H), 3.67
 15 (d, $J = 12.4$ Hz, 2H), 2.74 - 2.63 (m, 2H), 2.38 - 2.24 (m, 1H), 2.23 (s, 3H), 1.99 (d, $J = 12.8$ Hz, 2H), 1.75 (qd, $J = 12.8, 4.0$ Hz, 2H). Mass (m/z): 374.7 $[\text{M}+\text{H}]^+$.

Compound 498

7-((6-(2-ethylmorpholino)-2-methylpyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

20

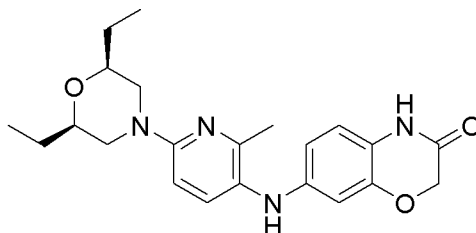


The titled compound **498** (36.9 mg, 51.3%) as a light-yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.36 (s, 1H), 7.29 (d, $J = 8.4$ Hz, 1H), 7.13 (s, 1H), 6.65 (d, $J = 8.4$ Hz, 2H), 6.26 - 6.11 (m, 2H), 4.45 (s, 2H), 4.04 (d, $J = 12.4$ Hz, 1H), 3.99 - 3.89 (m, 2H), 3.60 - 3.47 (m, 1H), 3.42 - 3.33 (m, 1H),
 25

2.80 - 2.66 (m, 1H), 2.43 (t, $J = 11.6$ Hz, 1H), 2.22 (s, 3H), 1.56 - 1.46 (m, 2H), 0.94 (t, $J = 8.4, 6.4$ Hz, 3H). Mass (m/z): 369.2 $[M+H]^+$.

Compound 499

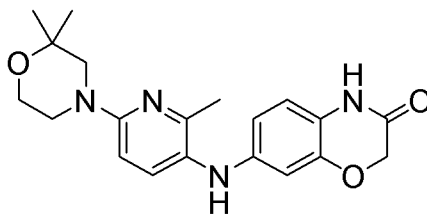
7-((6-((2*S*,6*R*)-2,6-diethylmorpholino)-2-methylpyridin-3-yl)
amino)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one



The titled compound **499** (34.5 mg, 50.6%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.36 (s, 1H), 7.28 (d, $J = 8.8$ Hz, 1H), 7.12 (s, 1H), 6.66 (d, $J = 8.0$ Hz, 2H), 6.23 - 6.11 (m, 2H), 4.44 (s, 2H), 4.06 (d, $J = 12.4$ Hz, 2H), 3.43 - 3.34 (m, 2H), 2.34 (t, $J = 11.2$ Hz, 2H), 2.21 (s, 3H), 1.58 - 1.45 (m, 4H), 0.96 (t, $J = 6.4$ Hz, 6H). Mass (m/z): 397.3 $[M+H]^+$.

Compound 500

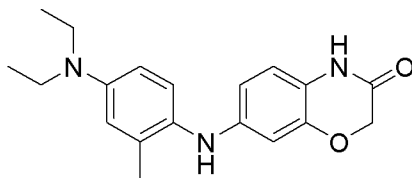
7-((6-(2,2-dimethylmorpholino)-2-methylpyridin-3-yl)amino)-
2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one



The titled compound **500** (5.9 mg, 3.54%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.31 (s, 1H), 7.23 (d, $J = 8.8$ Hz, 1H), 7.07 (s, 1H), 6.60 (d, $J = 8.4$ Hz, 2H), 6.13 (d, $J = 8.8$ Hz, 2H), 4.39 (s, 2H), 3.66 (t, $J = 5.2$ Hz, 2H), 3.18 (s, 2H), 2.15 (s, 3H), 1.15 (s, 6H). Mass (m/z): 369.6 $[M+H]^+$.

Compound 501

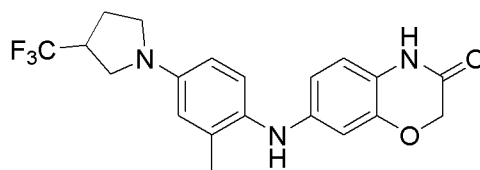
7-((4-(diethylamino)-2-methylphenyl)amino)-2*H*-
benzo[*b*][1,4]oxazin-3(4*H*)-one



The titled compound **501** (33.4 mg, 22.04%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.32 (s, 1H), 6.96 (s, 1H), 6.89 (d, $J = 8.8$ Hz, 1H), 6.62 (d, $J = 8.8$ Hz, 1H), 6.54 (d, $J = 3.2$ Hz, 1H), 6.48 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.18 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.14 (d, $J = 2.4$ Hz, 1H), 4.42 (d, $J = 2.0$ Hz, 2H), 3.27 (t, $J = 7.2$ Hz, 4H), 2.08 (s, 3H), 1.07 (t, $J = 7.2$ Hz, 6H). Mass (m/z): 326.3 $[\text{M}+\text{H}]^+$.

Compound 502

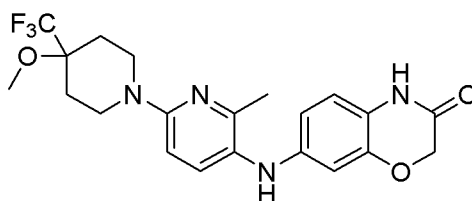
7-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **502** (3.9 mg, 4.35%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.33 (s, 1H), 7.03 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 6.62 (d, $J = 8.5$ Hz, 1H), 6.52 (s, 1H), 6.44 (d, $J = 8.3$ Hz, 1H), 6.18 (d, $J = 8.5$ Hz, 1H), 6.14 (s, 1H), 4.43 (s, 2H), 3.49 (t, $J = 8.5$ Hz, 1H), 3.26 (d, $J = 8.0$ Hz, 4H), 2.25 (d, $J = 6.3$ Hz, 1H), 2.10 (s, 4H). Mass(m/z): 437.7 $[\text{M}+\text{H}]^+$. Mass (m/z): 392.7 $[\text{M}+\text{H}]^+$.

Compound 503

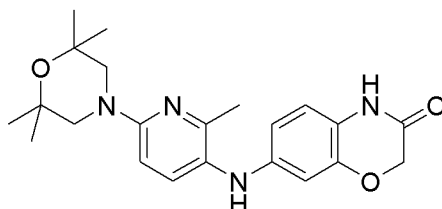
7-(((6-(4-methoxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylpyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **503** (10.7 mg, 12.78%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.37 (s, 1H), 7.29 (d, *J* = 8.7 Hz, 1H), 7.13 (s, 1H), 6.70 (d, *J* = 8.7 Hz, 1H), 6.66 (d, *J* = 8.2 Hz, 1H), 6.19 (d, *J* = 10.7 Hz, 2H), 4.45 (s, 2H), 4.18 (d, *J* = 13.1 Hz, 2H), 3.41 (s, 3H), 2.89 (t, *J* = 12.8 Hz, 2H), 2.22 (s, 3H), 1.98 (d, *J* = 13.7 Hz, 2H), 1.70 (td, *J* = 13.3, 4.5 Hz, 2H). Mass (m/z): 437.7 [M+H]⁺.

Compound 504

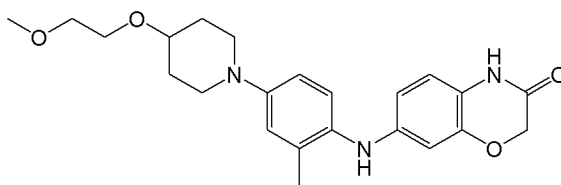
7-((2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **504** (18.9 mg, 15.5%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.38 (s, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.12 (s, 1H), 6.65 (t, *J* = 8.0 Hz, 2H), 6.18 (d, *J* = 10.0 Hz, 2H), 4.44 (s, 2H), 2.20 (s, 3H), 1.19 (s, 12H). Mass (m/z): 397.3 [M+H]⁺.

Compound 505

7-((2-methyl-6-(4-(trifluoromethyl)piperidin-1-yl)pyridin-3-yl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one

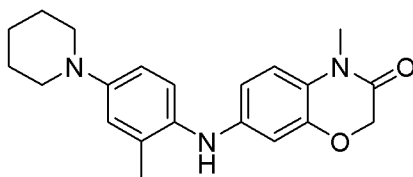


The titled compound **505** (9.2 mg, 9.4%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.39 (s, 1H), 7.09 (s, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.81 (s, 1H), 6.75 - 6.63 m, 3H), 6.29 - 6.21 (m, 2H), 4.44 (s, 2H), 3.56 (t, *J* = 5.2 Hz, 2H), 3.44 (t, *J* = 4.8 Hz, 4H), 3.40 (s, 1H), 3.25 (s, 3H), 2.79 (t, *J* = 11.2 Hz, 2H), 2.10 (s, 3H), 1.94 - 1.89 (m, 2H), 1.45 - 1.53 (q, *J* = 6.6, 3.6

Hz, 2H). Mass (m/z): 412.2 [M+H]⁺.

Compound 506

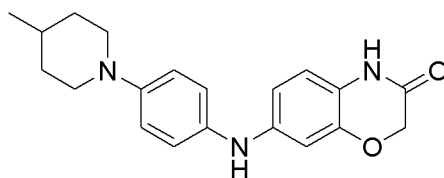
4-methyl-7-((2-methyl-4-(piperidin-1-yl)phenyl)amino)-2H-
benzo[b][1,4]oxazin-3(4H)-one
5 benzo[b][1,4]oxazin-3(4H)-one



The titled compound **506** (46.7 mg, 31.5%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CD₃OD) δ 7.03 (d, *J* = 8.8 Hz, 1H), 6.94 - 6.87 (m, 2H), 6.82 (d, *J* = 8.8 Hz, 1H), 6.40 (d, *J* = 8.8 Hz, 1H), 6.30 (s, 1H), 4.50 (s, 2H), 3.30 (s, 3H), 3.11 - 3.04 (m, 4H), 2.16 (s, 3H), 1.78 - 1.68 (m, 4H), 1.63 - 1.54 (m, 3H). Mass (m/z): 352.5 [M+H]⁺.

Compound 507

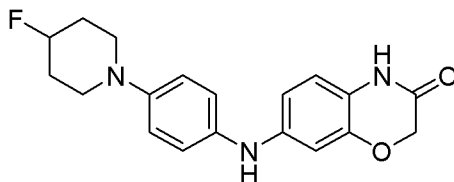
7-((4-(4-methylpiperidin-1-yl)phenyl)amino)-2H-
15 benzo[b][1,4]oxazin-3(4H)-one



The titled compound **507** (34.1 mg, 19.5%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.43 (s, 1H), 7.65 (s, 1H), 6.95 - 6.81 (m, 4H), 6.70 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.55 - 6.46 (m, 2H), 4.47 (s, 2H), 3.53 - 3.45 (m, 2H), 2.59 - 2.52 (m, 2H), 1.68 (d, *J* = 12.8 Hz, 2H), 1.49 - 1.39 (m, 1H), 1.32 - 1.17 (m, 2H), 0.97 - 0.90 (m, 3H). Mass (m/z): 337.5 [M+H]⁺.

Compound 508

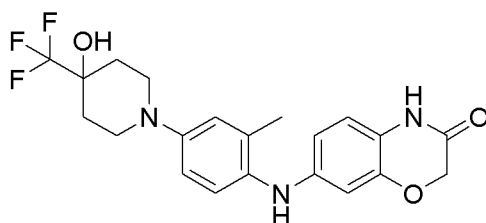
7-((4-(4-fluoropiperidin-1-yl)phenyl)amino)-2H-
25 benzo[b][1,4]oxazin-3(4H)-one



The titled compound **508** (42.5 mg, 24%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CD_3OD) δ 7.02 - 6.91 (m, 4H), 6.75 - 6.68 (m, 1H), 6.60 - 6.53 (m, 2H), 4.83 - 4.60 (m, 1H), 4.49 (s, 2H), 3.27 - 3.20 (m, 2H), 3.06 - 3.01 (m, 2H), 2.08 - 1.96 (m, 2H), 1.96 - 1.89 (m, 2H). Mass(m/z): 342.5 $[\text{M}+\text{H}]^+$.

Compound 509

7-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



10

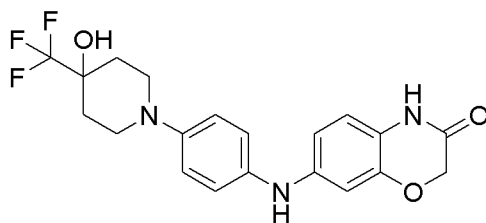
The titled compound **509** (38 mg, 23.5%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, CD_3OD) δ 7.03 (d, $J = 8.8$ Hz, 1H), 6.91 (s, 1H), 6.83 (d, $J = 8.8$ Hz, 1H), 6.67 (d, $J = 8.4$ Hz, 1H), 6.33 (d, $J = 8.8$ Hz, 1H), 6.29 (s, 1H), 4.47 (s, 2H), 3.49 (d, $J = 12.0$ Hz, 2H), 2.98 (t, $J = 12.4$ Hz, 2H), 2.17 (s, 3H), 2.02 - 1.90 (m, 2H), 1.81 (d, $J = 13.2$ Hz, 2H). Mass(m/z): 422.5 $[\text{M}+\text{H}]^+$.

15

Compound 510

7-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

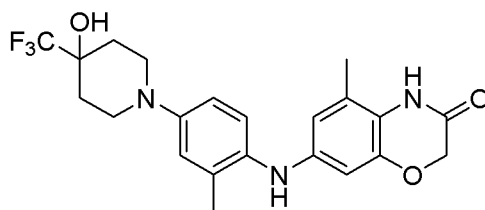
20



The titled compound **510** (56.7 mg, 36%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CD₃OD) δ 7.00 - 6.96 (m, 4H), 6.75 - 6.69 (m, 1H), 6.60 - 6.56 (m, 2H), 4.49 (s, 2H), 3.45 - 3.38 (m, 2H), 2.98 - 2.94 (m, 2H), 2.05 - 1.91 (m, 2H), 1.86 - 1.78 (m, 2H). Mass (m/z): 408.5 [M+H]⁺.

Compound 511

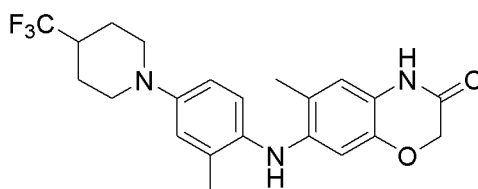
7-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-5-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **511** (50.4 mg, 30%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.94 (s, 1H), 7.01 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.85 (s, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.15 (s, 1H), 6.09 (s, 1H), 5.94 (s, 1H), 4.40 (s, 2H), 3.52 (d, *J* = 12.0 Hz, 2H), 2.89 (t, *J* = 12.0 Hz, 2H), 2.10 (s, 6H), 1.88 - 1.63 (m, 4H). Mass(m/z): 437.5 [M+H]⁺.

Compound 512

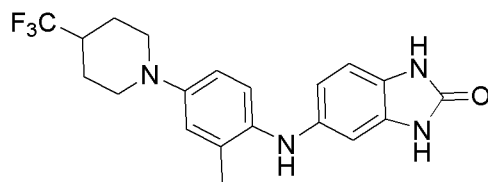
6-methyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **512** (4.6 mg, 2.8%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CDCl₃) δ 7.01 - 6.64 (m, 3H), 6.53 (s, 1H), 6.17 (s, 1H), 4.36 (s, 2H), 3.64 - 3.51 (m, 2H), 3.29 - 3.21 (m, 1H), 2.71 - 2.49 (m, 2H), 2.08 (s, 6H), 1.99 - 1.85 (m, 2H), 1.81 - 1.62 (m, 2H). Mass(m/z): 420.5 [M+H]⁺.

Compound 513

5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3-

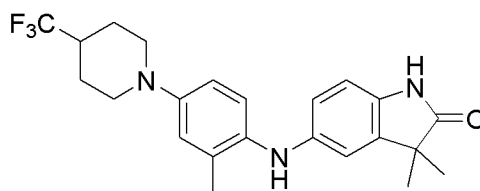
dihydro-2H-benzo[d]imidazol-2-one

The titled compound **513** (3.6 mg, 0.48%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.21 (s, 2H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.83 (d, *J* = 3.6 Hz, 2H), 6.75 - 6.67 (m, 2H), 6.36 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.31 (d, *J* = 2.0 Hz, 1H), 3.65 (d, *J* = 12.0 Hz, 2H), 2.63 (dd, *J* = 12.0, 10.4 Hz, 2H), 2.44 (dd, *J* = 8.8, 3.6 Hz, 1H), 2.12 (s, 3H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.56 (m, *J* = 12.4, 8.4 Hz, 2H). Mass(*m/z*): 390.8 [M+H]⁺.

10

Compound 514

3,3-dimethyl-5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)indolin-2-one

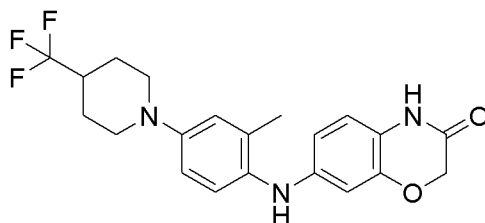


The titled compound **514** (4.8 mg, 0.99%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.03 (s, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.87 (s, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.76 - 6.69 (m, 2H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.52 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.64 (d, *J* = 12.4 Hz, 2H), 2.62 (dd, *J* = 12.0, 10.0 Hz, 2H), 2.43 (d, *J* = 8.8 Hz, 1H), 2.12 (s, 3H), 1.88 (d, *J* = 12.8 Hz, 2H), 1.61 - 1.51 (m, 2H), 1.20 (s, 6H). Mass (*m/z*): 417.8 [M+H]⁺.

20

Compound 515

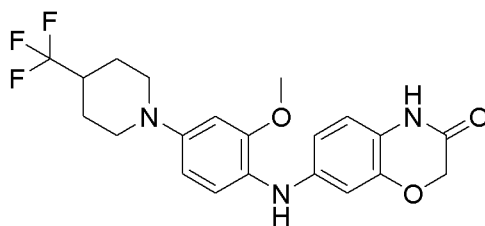
7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **515** (14.4 mg, 9.2%) as a blue solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.44 (s, 1H), 7.11 - 6.91 (m, 2H), 6.87 - 6.64 (m, 3H), 6.36
 5 - 6.15 (m, 2H), 4.41 (d, *J* = 2.4 Hz, 2H), 3.68 (d, *J* = 12.0 Hz, 2H), 2.64 (s, 2H), 2.42 - 2.39 (m, 1H), 2.11 (s, 3H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.56 (q, *J* = 12.8 Hz, 2H). Mass (m/z): 406.2 [M+H]⁺.

Compound 516

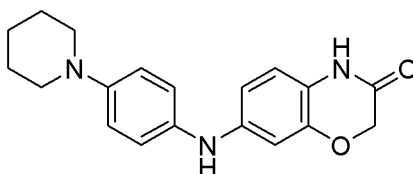
7-((2-methoxy-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-
 10 benzo[b][1,4]oxazin-3(4H)-one



The titled compound **516** (26.3 mg, 17%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.39 (s, 1H), 7.05 - 6.89 (m, 2H), 6.65 (d, *J* = 9.2 Hz, 2H),
 15 6.44 (dd, *J* = 15.2, 6.4 Hz, 3H), 4.45 (d, *J* = 2.4 Hz, 2H), 3.76 (d, *J* = 2.4 Hz, 3H), 3.70 (d, *J* = 12.4 Hz, 2H), 2.67 (d, *J* = 9.2 Hz, 2H), 2.51-2.49 (m, 1H), 1.89 (d, *J* = 12.4 Hz, 2H), 1.58 (q, *J* = 11.6, 11.2 Hz, 2H). Mass (m/z): 424.4 [M+H]⁺.

Compound 517

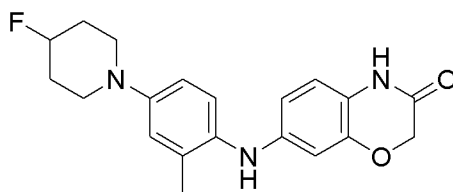
7-(4-(piperidin-1-yl)phenylamino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **517** (48.5 mg, 22.8%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.43 (s, 1H), 6.93 - 6.91 (m, 2H), 6.86-6.84 (m, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.53-6.49 (m, 2H), 4.74 (s, 2H), 3.02 - 2.96 (m, 4H),
 5 1.65 - 1.58 (m, 4H), 1.53 - 1.45 (m, 2H). Mass (m/z): 324.1 [M+H]⁺.

Compound 518

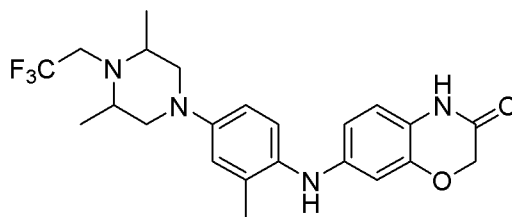
7-((4-(4-fluoropiperidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



10 The titled compound **518** (55.4 mg, 23.7%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.37 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.84 (s, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.28 - 6.24 (m, 2H), 4.91 - 4.71 (m, 1H), 4.44 (s, 2H), 3.31 - 3.22 (m, 2H), 3.08 - 2.98
 15 (m, 2H), 2.11 (s, 3H), 2.04 - 1.89 (m, 2H), 1.85 - 1.72 (m, 2H). Mass (m/z): 356.1 [M+H]⁺.

Compound 519

7-((4-(3,5-dimethyl-4-(2,2,2-trifluoroethyl)piperazin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

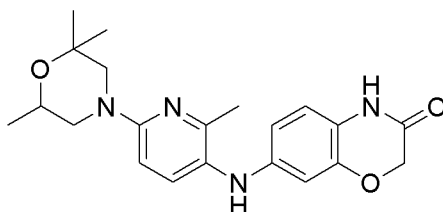


20 The titled compound **519** (12.4 mg, 10.5%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.37 (s, 1H), 7.07 (s, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.81 (s, 1H), 6.73 (d, *J* = 8.8 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.31 - 6.17 (m, 2H), 4.44 (s, 2H), 3.47 (d, *J* = 11.6 Hz, 2H), 3.38 (t, *J* = 10.4
 25 Hz, 2H), 2.82 (t, *J* = 8.4 Hz, 2H), 2.33 (t, *J* = 11.2 Hz, 2H), 2.11 (s, 3H),

1.10 (d, $J = 6.4$ Hz, 6H). Mass (m/z): 449.2 $[M+H]^+$.

Compound 520

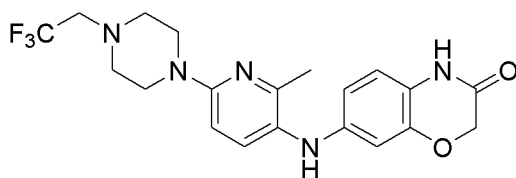
7-((2-methyl-6-(2,2,6-trimethylmorpholino)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **520** (12.4 mg, 10.5%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.36 (s, 1H), 7.27 (d, $J = 8.8$ Hz, 1H), 7.11 (s, 1H), 6.66 (d, $J = 2.0$ Hz, 1H), 6.65 - 6.62 (m, 1H), 6.20 - 6.14 (m, 2H), 4.44 (s, 2H), 4.13 (d, $J = 12.0$ Hz, 1H), 3.93 (d, $J = 12.4$ Hz, 1H), 3.89 - 3.80 (m, 1H), 2.48 - 2.43 (m, 1H), 2.32 - 2.23 (m, 1H), 2.20 (s, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.09 (d, $J = 6.0$ Hz, 3H). Mass (m/z): 383.1 $[M+H]^+$.

Compound 521

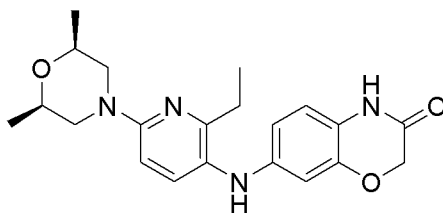
7-((2-methyl-6-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)pyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **521** (28.1 mg, 18.3%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.36 (s, 1H), 7.28 (d, $J = 8.8$ Hz, 1H), 7.13 (s, 1H), 6.65 (dd, $J = 8.4, 5.6$ Hz, 2H), 6.24 - 6.11 (m, 2H), 4.44 (s, 2H), 3.43 (t, $J = 5.2$ Hz, 4H), 3.22 (q, $J = 10.4$ Hz, 2H), 2.70 (t, $J = 5.2$ Hz, 4H), 2.21 (s, 3H). Mass (m/z): 422.3 $[M+H]^+$.

Compound 522

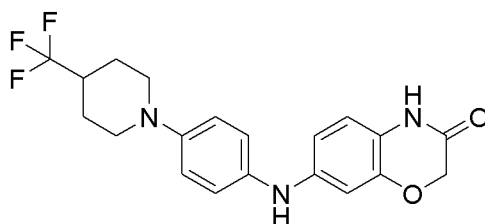
7-((6-((2S,6R)-2,6-dimethylmorpholino)-2-ethylpyridin-3-yl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **522** (35.3 mg, 45.6%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.36 (s, 1H), 7.28 (dd, J = 8.8, 2.4 Hz, 1H), 7.10 (s, 1H),
 5 6.70 - 6.57 (m, 2H), 6.21 - 6.09 (m, 2H), 4.49 - 4.40 (m, 2H), 4.08 (d, J = 12.4 Hz, 2H), 3.68 - 3.51 (m, 2H), 2.61 - 2.53 (m, 2H), 2.33 (t, J = 11.6 Hz, 2H), 1.20 - 1.07 (m, 9H). Mass (m/z): 383.3 $[\text{M}+\text{H}]^+$.

Compound 523

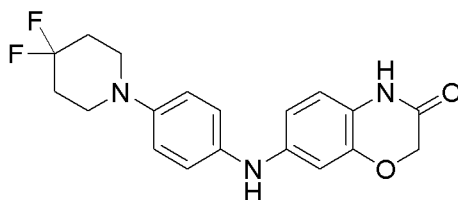
7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-
 10 benzo[b][1,4]oxazin-3(4H)-one



The titled compound **523** (29 mg, 18.1%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.51 (s, 1H), 7.66 (s, 1H), 7.00 - 6.84 (m, 4H), 6.77 (d, J =
 15 8.8 Hz, 1H), 6.58 (d, J = 3.6 Hz, 1H), 6.48 (d, J = 8.8 Hz, 1H), 4.45 (d, J = 2.4 Hz, 2H), 3.60 (d, J = 12.0 Hz, 2H), 2.61 (s, 3H), 1.88 (d, J = 12.4 Hz, 2H), 1.57 (q, J = 12.8 Hz, 2H). Mass (m/z): 392.2 $[\text{M}+\text{H}]^+$.

Compound 524

7-((4-(4,4-difluoropiperidin-1-yl)phenyl)amino)-2H-
 20 benzo[b][1,4]oxazin-3(4H)-one



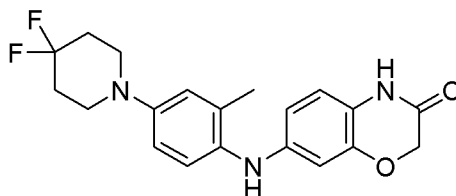
The titled compound **524** (11.7 mg, 6.9%) as a pink solid was prepared

according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.45 (s, 1H), 7.73 (s, 1H), 6.93 (s, 3H), 6.71 (d, J = 8.4 Hz, 1H), 6.54 (d, J = 16.0 Hz, 2H), 4.48 (d, J = 2.4 Hz, 2H), 3.18 (d, J = 6.0 Hz, 4H), 2.06 (p, J = 8.8 Hz, 4H). Mass (m/z): 360.1 $[\text{M}+\text{H}]^+$.

5

Compound 525

7-((4-(4,4-difluoropiperidin-1-yl)-2-methylphenyl)amino)
-2H-benzo[b][1,4]oxazin-3(4H)-one

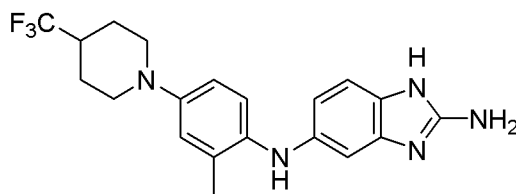


The titled compound **525** (14.4 mg, 8.7%) as pink oil was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 7.09 (s, 1H), 6.97 (dd, J = 8.8, 2.4 Hz, 1H), 6.88 (s, 1H), 6.78 (d, J = 8.8 Hz, 1H), 6.66 (dd, J = 8.4, 2.4 Hz, 1H), 6.36 - 6.19 (m, 2H), 4.45 (d, J = 2.4 Hz, 2H), 3.26 - 3.24 (m, 4H), 2.11 (d, J = 2.4 Hz, 3H), 2.04 (dq, J = 12.8, 6.8, 5.2 Hz, 4H). Mass (m/z): 374.2 $[\text{M}+\text{H}]^+$

15

Compound 526

N5-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)
-1H-benzo[d]imidazole-2,5-diamine

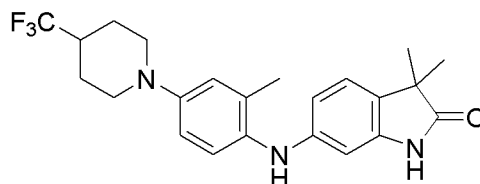


The titled compound **526** (21.1 mg 91.8%) as a black solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.52 (s, 1H), 6.91 - 6.89 (m, 2H), 6.80 (d, J = 2.4, 1H), 6.69 - 6.67 (m, 1H), 6.58 (d, J = 1.6, 2H), 6.44 (s, 1H), 5.92 (s, 2H), 3.60 (d, J = 12.0, 2H), 2.60 (t, J = 12.0, 2H), 2.42 - 2.37 (m, 1H), 2.15 (d, J = 4.4, 3H), 1.87 (d, J = 12.0, 2H), 1.62 - 1.51 (m, 2H). Mass (m/z): 389.7 $[\text{M}+\text{H}]^+$.

25

Compound 527

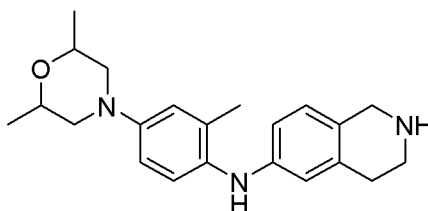
3,3-dimethyl-6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)indolin-2-one



The titled compound **527** (15.3 mg, 4.73%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.03 (s, 1H), 7.19 (s, 1H), 6.98 (dd, *J* = 23.6, 8.4 Hz, 2H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.24 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.16 (d, *J* = 2.0 Hz, 1H), 3.70 (d, *J* = 12.4 Hz, 2H), 2.65 (dd, *J* = 12.0, 10.4 Hz, 2H), 2.47 - 2.40 (m, 1H), 2.13 (s, 3H), 1.89 (d, *J* = 12.0 Hz, 2H), 1.56 (m, *J* = 12.4, 8.8 Hz, 2H), 1.18 (s, 6H). Mass (m/z): 417.7 [M+H]⁺.

Compound 528

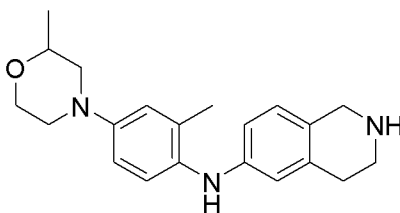
N-(4-(2,6-dimethylmorpholino)-2-methylphenyl)-1,2,3,4-tetrahydroisoquinolin-6-amine



The titled compound **528** (25.1 mg, 15.7%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.00 - 6.91 (m, 2H), 6.81 (s, 1H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.43 (d, *J* = 8.4 Hz, 1H), 6.33 (s, 1H), 3.72 - 3.62 (m, 4H), 3.48 (d, *J* = 11.6 Hz, 2H), 3.33 - 3.32 (m, 2H), 2.86 (s, 2H), 2.19 (t, *J* = 11.2 Hz, 2H), 2.11 (s, 3H), 1.17 - 1.11 (m, 6H). Mass (m/z): 352.5 [M+H]⁺.

Compound 529

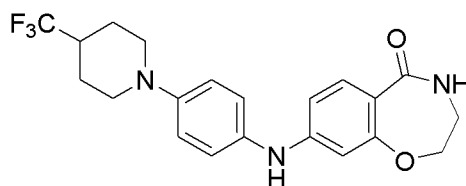
N-(2-methyl-4-(2-methylmorpholino)phenyl)-1,2,3,4-tetrahydroisoquinolin-6-amine



The titled compound **529** (15 mg, 9.7%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 6.99 - 6.92 (m, 2H), 6.81 (s, 1H), 6.73 (d, J = 8.4 Hz, 2H), 6.44 (d, J = 8.4 Hz, 1H), 6.34 (s, 1H), 3.89 (d, J = 11.2 Hz, 1H), 3.70 (s, 2H), 3.68 - 3.56 (m, 2H), 3.49 (d, J = 11.6 Hz, 1H), 3.39 (d, J = 12.0 Hz, 1H), 2.90 - 2.83 (m, 2H), 2.70 - 2.58 (m, 2H), 2.35 - 2.23 (m, 2H), 2.11 (s, 3H), 1.14 (d, J = 6.4 Hz, 3H). Mass (m/z): 338.5 $[\text{M}+\text{H}]^+$.

Compound 530

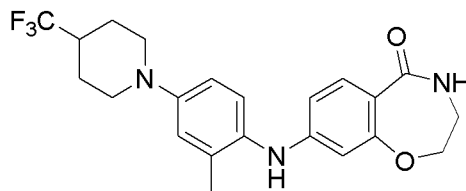
8-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **530** (26.7 mg, 17%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.25 (s, 1H), 7.96 - 7.89 (m, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.07 - 7.00 (m, 2H), 6.98 - 6.91 (m, 2H), 6.57 (d, J = 8.8 Hz, 1H), 6.35 (s, 1H), 4.21 (d, J = 4.8 Hz, 2H), 3.69 (d, J = 12.0 Hz, 2H), 3.33 (d, J = 2.0 Hz, 2H), 2.66 (t, J = 12.0 Hz, 2H), 2.47 - 2.36 (m, 1H), 1.88 (d, J = 12.4 Hz, 2H), 1.64 - 1.49 (m, 2H). Mass(m/z): 406.5 $[\text{M}+\text{H}]^+$.

Compound 531

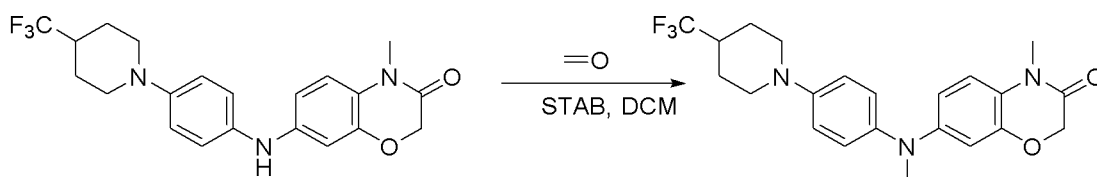
8-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydrobenzo[f][1,4]oxazepin-5(2H)-one



The titled compound **531** (18 mg, 10%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.86 (s, 1H), 7.76 (s, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.88 (s, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.34 (d, *J* = 8.8 Hz, 1H), 6.00 (s, 1H), 4.18 (d, *J* = 5.2 Hz, 2H), 3.75 (d, *J* = 12.0 Hz, 2H), 3.28 (s, 2H), 2.73 - 2.62 (m, 2H), 2.41 - 2.37 (m, 1H), 2.11 (s, 3H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.63 - 1.49 (m, 2H). Mass(*m/z*): 420.5 [M+H]⁺.

Compound 532

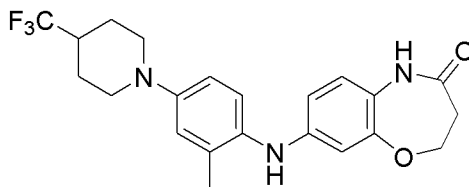
10 *4-methyl-7-(methyl(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one*



To a solution of 4-methyl-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (100 mg, 0.24 mmol) in DCM (2 mL) was added formaldehyde (15 mg, 0.49 mmol) and sodium triacetoxyhydroborate (104 mg, 0.49 mmol). The mixture was stirred for 2 hs and concentrated under vacuum. The residue was purified by C18 column to give 4-methyl-7-(methyl(4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one (22.5 mg, 21.7%) as an off-white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.03 - 6.92 (m, 5H), 6.43 (d, *J* = 8.8 Hz, 1H), 6.37 (s, 1H), 4.56 (s, 2H), 3.73 (d, *J* = 12.4 Hz, 2H), 3.22 (s, 3H), 3.15 (s, 3H), 2.74 - 2.63 (m, 2H), 2.45 - 2.40 (m, 1H), 1.89 (d, *J* = 12.8 Hz, 2H), 1.63 - 1.49 (m, 2H). Mass (*m/z*): 420.5 [M+H]⁺.

Compound 533

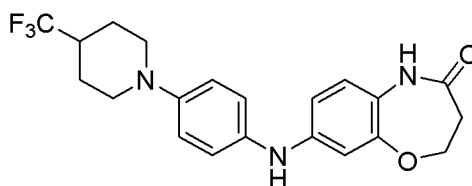
25 *5-(4-methoxybenzyl)-8-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one*



The titled compound **533** (7.5 mg, 19%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.34 (s, 1H), 7.17 (s, 1H), 6.98 (d, $J = 9.2$ Hz, 1H), 6.85 (s, 1H), 6.82 - 6.72 (m, 2H), 6.36 (d, $J = 8.8$ Hz, 1H), 6.26 (s, 1H), 4.35 - 4.28 (m, 2H), 3.69 (d, $J = 12.4$ Hz, 2H), 2.67 - 2.63 (m, 2H), 2.44 - 2.37 (m, 1H), 2.11 (s, 3H), 1.88 (d, $J = 12.8$ Hz, 2H), 1.63 - 1.49 (m, 2H). Mass (m/z): 420.5 $[\text{M}+\text{H}]^+$.

Compound 534

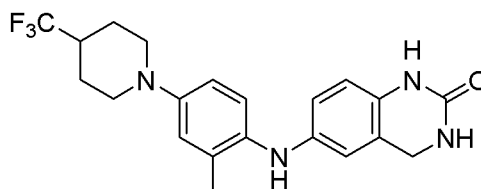
8-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **534** (8.8 mg, 22%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.41 (s, 1H), 7.78 (s, 1H), 6.96 (d, $J = 8.4$ Hz, 2H), 6.90 (d, $J = 8.4$ Hz, 2H), 6.84 (d, $J = 8.6$ Hz, 1H), 6.60 (d, $J = 8.7$ Hz, 1H), 6.55 (s, 1H), 4.34 (t, $J = 6.2$ Hz, 2H), 3.62 (d, $J = 12.1$ Hz, 2H), 2.68 - 2.58 (m, 4H), 2.43 - 2.36 (m, 1H), 1.88 (d, $J = 12.7$ Hz, 2H), 1.66 - 1.49 (m, 2H). Mass(m/z): 406.5 $[\text{M}+\text{H}]^+$.

Compound 535

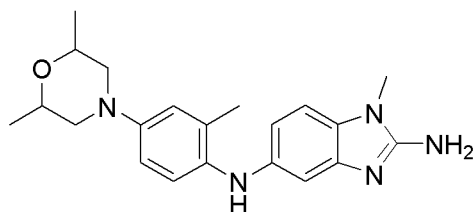
6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydroquinazolin-2(1H)-one



The titled compound **535** (22.0 mg, 15.28%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.70 (s, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.86 - 6.77 (m, 2H), 6.71 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 2H), 6.52 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 4.19 (s, 2H), 3.64 (d, *J* = 12.4 Hz, 2H), 2.68 - 2.57 (m, 2H), 2.45 - 2.36 (m, 1H), 2.11 (s, 3H), 1.87 (d, *J* = 12.0 Hz, 2H), 1.61 - 1.50 (m, 2H). Mass(m/z): 404.8 [M+H]⁺.

Compound 536

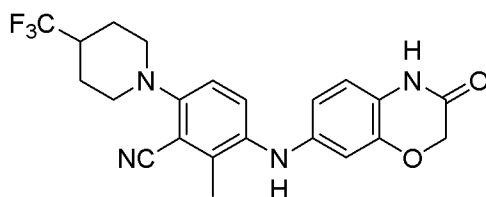
10 5-*N*-[4-(2,6-dimethylmorpholin-4-yl)-2-methylphenyl]-1-methyl-1,3-benzodiazole-2,5-diamine



The titled compound **536** (2.6 mg, 0.66%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.91 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 2.4 Hz, 1H), 6.71 - 6.60 (m, 2H), 6.56 (d, *J* = 1.2 Hz, 1H), 6.44 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.36 (s, 2H), 3.73 - 3.63 (m, 2H), 3.43 (d, *J* = 10.0 Hz, 5H), 2.22 - 2.10 (m, 5H), 1.14 (d, *J* = 6.4 Hz, 6H). Mass (m/z): 366.0 [M+H]⁺.

Compound 537

20 2-methyl-3-((3-oxo-3,4-dihydro-2H-benzo[*b*][1,4]oxazin-7-yl)amino)-6-(4-(trifluoromethyl)piperidin-1-yl)benzonitrile

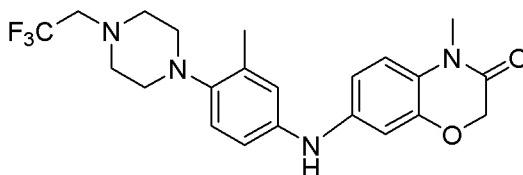


The titled compound **537** (29.3 mg, 17.03%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CDCl₃) δ 8.17 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.42 (dd, *J* = 11.6, 3.2 Hz, 2H), 4.57 (s, 2H), 3.54 (d, *J* =

12.0 Hz, 2H), 2.78 (t, $J = 11.2$ Hz, 2H), 2.41 (s, 3H), 2.15 (ddd, $J = 12.0$, 8.0, 4.0 Hz, 1H), 2.04 - 1.86 (m, 4H). Mass (m/z): 430.8 [M+H]⁺.

Compound 538

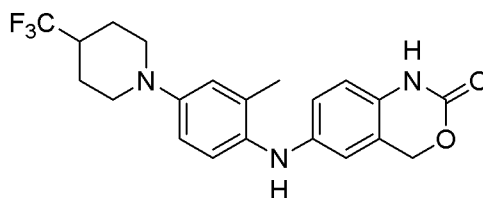
4-methyl-7-((3-methyl-4-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **538** (10.0 mg, 12.34%) as a pink solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CDCl₃) δ 7.17 (s, 1H), 6.94 (d, $J = 8.8$ Hz, 1H), 6.87 (d, $J = 8.8$ Hz, 1H), 6.80 (d, $J = 2.8$ Hz, 1H), 6.70 (dd, $J = 8.8$, 2.8 Hz, 1H), 6.31 (dd, $J = 8.8$, 2.4 Hz, 1H), 6.23 (d, $J = 2.4$ Hz, 1H), 4.49 (s, 2H), 3.25 - 3.18 (m, 2H), 3.16 (s, 3H), 3.08 - 3.01 (m, 4H), 2.75 - 2.68 (m, 4H), 2.08 (s, 3H). Mass (m/z): 434.9 [M+H]⁺.

Compound 539

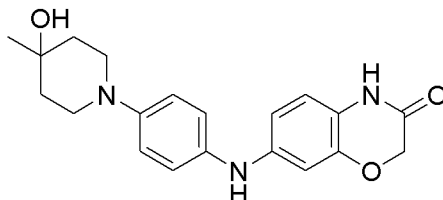
6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one



The titled compound **539** (5 mg, 3.2%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹ NMR (400 MHz, DMSO-*d*₆) δ 9.78 (s, 1H), 7.03 (s, 1H), 6.91 (d, $J = 8.8$ Hz, 1H), 6.80 (d, $J = 2.8$ Hz, 1H), 6.70 (dd, $J = 8.8$, 2.8 Hz, 1H), 6.64 (d, $J = 8.8$ Hz, 1H), 6.56 (dd, $J = 8.8$, 2.4 Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 5.10 (s, 2H), 3.64 (d, $J = 12.4$ Hz, 2H), 2.60 (td, $J = 12.4$, 2.0 Hz, 2H), 2.08 (s, 3H), 1.84 (d, $J = 11.6$ Hz, 2H), 1.52 (dd, $J = 12.4$, 3.6 Hz, 2H), 1.20 (s, 1H). Mass(m/z): 405.9 [M+H]⁺.

Compound 540

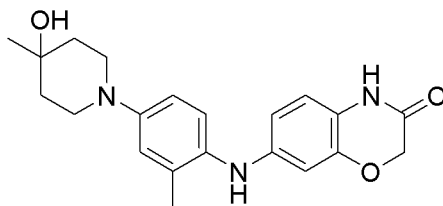
7-((4-(4-hydroxy-4-methylpiperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **540** (46.8 mg, 30.2%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.43 (s, 1H), 7.66 (s, 1H), 7.11 - 6.31 (m, 7H), 4.47 (d, *J* = 2.4 Hz, 2H), 4.26 (s, 1H), 3.28 - 2.75 (m, 4H), 1.57 (s, 4H), 1.15 (s, 3H). Mass (m/z): 354.1 [M+H]⁺.

Compound 541

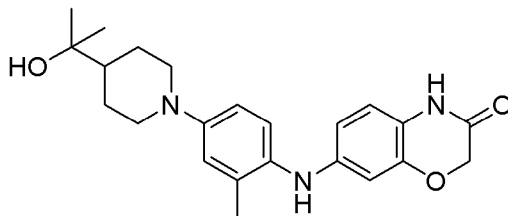
7-((4-(4-hydroxy-4-methylpiperidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **541** (17.6 mg, 10.9%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.37 (s, 1H), 7.26 - 6.46 (m, 5H), 6.43 - 5.99 (m, 2H), 4.44 (s, 2H), 4.26 (s, 1H), 3.12 (m, 4H), 2.10 (s, 3H), 1.56 (s, 4H), 1.15 (s, 3H). Mass(m/z): 368.1 [M+H]⁺.

Compound 542

7-((4-(4-(2-hydroxypropan-2-yl)piperidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



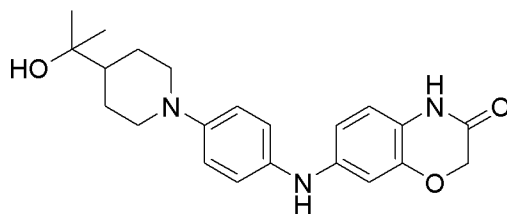
The titled compound **542** (23.8 mg, 15.0%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz,

DMSO- d_6) δ 10.37 (s, 1H), 7.06 (s, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.81 (s, 1H), 6.72 (d, J = 8.8 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 6.29 - 6.20 (m, 2H), 4.44 (s, 2H), 4.13 (s, 1H), 3.66 (d, J = 11.6 Hz, 2H), 2.53 (m, 2H), 2.10 (s, 3H), 1.77 (d, J = 11.2 Hz, 2H), 1.44 - 1.21 (m, 3H), 1.06 (s, 6H).

5 Mass (m/z): 396.2 [M+H]⁺.

Compound 543

7-((4-(4-(2-hydroxypropan-2-yl)piperidin-1-yl)phenyl)amino)-
-2H-benzo[b][1,4]oxazin-3(4H)-one

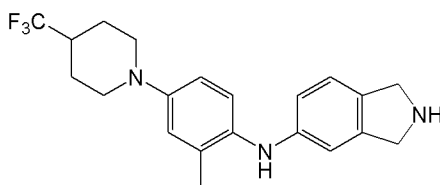


10 The titled compound **543** (43.5 mg, 26.8%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO- d_6) δ 10.45 (s, 1H), 7.92 - 7.43 (m, 1H), 7.18 - 6.18 (m, 7H), 4.48 (s, 2H), 4.13 (s, 1H), 3.59 (s, 2H), 2.45-2.22 (m, 2H), 1.95 - 1.56 (m, 2H), 1.43 - 1.22 (m, 3H), 1.06 (s, 6H). Mass(m/z): 382.2 [M+H]⁺.

15

Compound 544

N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)isoindolin-
-5-amine

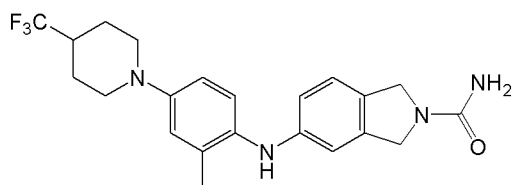


20 The titled compound **544** (14.2 mg, 13.2%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO- d_6) δ 6.97 (t, J = 8.0 Hz, 2H), 6.84 (s, 1H), 6.75 (d, J = 9.2 Hz, 1H), 6.51 (d, J = 6.4 Hz, 2H), 3.92 (d, J = 6.0 Hz, 3H), 3.68 (d, J = 12.4 Hz, 2H), 2.66 (q, J = 12.4 Hz, 3H), 2.44 (d, J = 10.0 Hz, 1H), 2.12 (s, 3H), 1.88 (d, J = 12.4 Hz, 2H), 1.56 (q, J = 12.4 Hz, 2H). Mass (m/z): 376.3 [M+H]⁺.

25

Compound 545

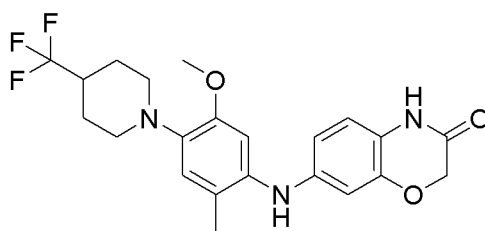
5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)

isoindoline-2-carboxamide

The titled compound **545** (22.1 mg, 18.7%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.24 (s, 1H), 7.01 (t, *J* = 8.0 Hz, 2H), 6.86 (s, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.52 (s, 1H), 5.87 (s, 2H), 4.42 (s, 4H), 3.70 (d, *J* = 12.4 Hz, 2H), 2.66 (t, *J* = 12.0 Hz, 2H), 2.44 (s, 1H), 2.12 (s, 3H), 1.88 (d, *J* = 12.8 Hz, 2H), 1.56 (q, *J* = 12.4 Hz, 2H). Mass (*m/z*): 419.3 [M+H]⁺.

Compound 546

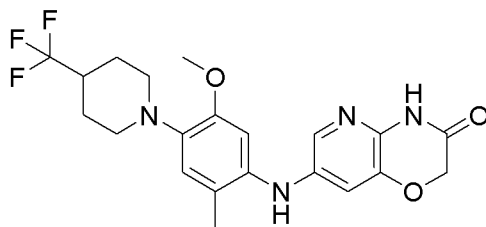
7-((5-methoxy-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **546** (25.6 mg, 21.2%) as a pink solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.41 (s, 1H), 7.18 (s, 1H), 6.70 (d, *J* = 23.2 Hz, 3H), 6.42 - 6.29 (m, 2H), 4.46 (d, *J* = 2.4 Hz, 2H), 3.68 (d, *J* = 2.4 Hz, 3H), 3.38 (s, 2H), 2.60 - 2.55 (m, 3H), 2.06 (d, *J* = 2.4 Hz, 3H), 1.87 (d, *J* = 12.4 Hz, 2H), 1.61 (dd, *J* = 14.0, 10.4 Hz, 2H). Mass (*m/z*): 436.2 [M+H]⁺.

Compound 547

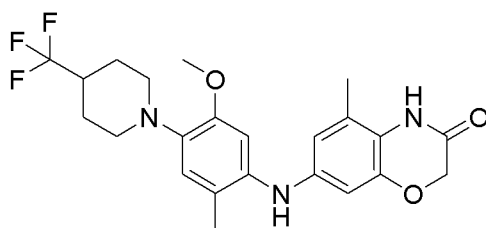
7-((5-methoxy-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-pyrido[3,2-*b*][1,4]oxazin-3(4H)-one



The titled compound **547** (18.3 mg, 15.1%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.91 (s, 1H), 7.45 (s, 1H), 7.34 (s, 1H), 6.75 (s, 1H), 6.72 - 6.60 (m, 2H), 4.55 (d, $J = 2.4$ Hz, 2H), 3.69 (d, $J = 2.4$ Hz, 3H), 3.37 (d, $J = 13.6$ Hz, 2H), 2.58 - 2.55 (m, 2H), 2.43 - 2.39 (m, 1H), 2.08 (d, $J = 2.4$ Hz, 3H), 1.87 (d, $J = 12.4$ Hz, 2H), 1.59 (q, $J = 12.4$ Hz, 2H). Mass (m/z): 437.2 $[\text{M}+\text{H}]^+$.

Compound 548

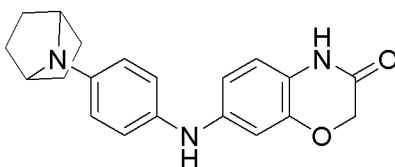
7-((5-methoxy-2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-5-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **548** (24 mg, 19.2%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.97 (s, 1H), 7.13 (s, 1H), 6.70 (d, $J = 23.6$ Hz, 2H), 6.20 (d, $J = 24.4$ Hz, 2H), 4.41 (s, 2H), 3.68 (d, $J = 2.4$ Hz, 3H), 3.37 (d, $J = 10.0$ Hz, 2H), 2.58 - 2.55 (m, 2H), 2.43 - 2.39 (m, 1H), 2.12 (s, 3H), 2.05 (s, 3H), 1.87 (d, $J = 12.4$ Hz, 2H), 1.59 (q, $J = 12.4$ Hz, 2H). Mass (m/z): 450.2 $[\text{M}+\text{H}]^+$.

Compound 549

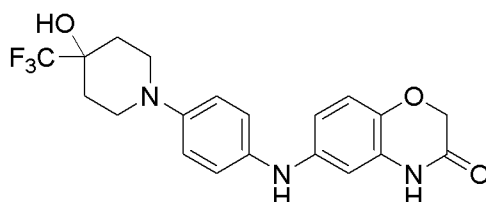
7-((4-(7-azabicyclo[2.2.1]heptan-7-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **549** (6.8mg, 4.8%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.42 (s, 1H), 7.59 (s, 1H), 6.95 - 6.77 (m, 4H), 6.69 (d, J = 8.4 Hz, 1H), 6.55 - 6.40 (m, 2H), 4.47 (d, J = 2.8 Hz, 2H), 4.13 (s, 2H), 1.64 (d, J = 7.6 Hz, 4H), 1.37 (d, J = 7.6 Hz, 4H). Mass (m/z): 336.2 $[\text{M}+\text{H}]^+$.

Compound 550

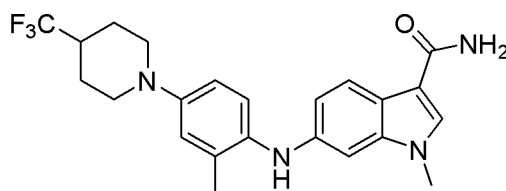
6-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **550** (17.3 mg, 19.4%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.44 (s, 1H), 7.03 (s, 1H), 7.00 - 6.90 (m, 1H), 6.85 (s, 1H), 6.80 - 6.65 (m, 2H), 6.34 - 6.18 (m, 2H), 5.94 (s, 1H), 4.41 (d, J = 2.4 Hz, 2H), 3.51 (d, J = 12.0 Hz, 2H), 2.88 (t, J = 12.0 Hz, 2H), 2.11 (d, J = 2.4 Hz, 3H), 1.89 - 1.63 (m, 4H). Mass (m/z): 408.2 $[\text{M}+\text{H}]^+$.

Compound 551

1-methyl-6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indole-3-carboxamide



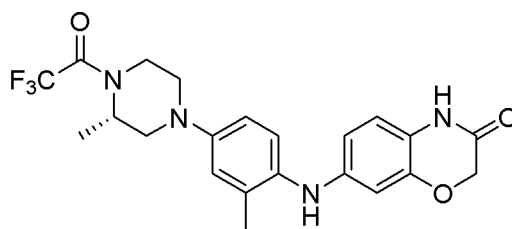
The titled compound **551** (18 mg, 10.8%) as a black solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.86 (d, J = 8.8 Hz, 1H), 7.71 (s, 1H), 7.10 - 7.05 (m, 2H),

6.86 (d, $J = 2.8$ Hz, 1H), 6.77 - 6.74 (m, 1H), 6.71 - 6.68 (m, 1H), 6.60 (d, $J = 1.6$ Hz, 1H), 3.69 (d, $J = 12.4$ Hz, 2H), 3.61 (s, 3H), 3.31 (m, 1H), 2.63 (d, $J = 10.4$ Hz, 2H), 2.16 (s, 3H), 1.89 (d, $J = 12.4$ Hz, 2H), 1.57 (dd, $J = 12.4, 4.0$ Hz, 2H). Mass (m/z): 430.8 $[M+H]^+$.

5

Compound 552

(S)-7-((2-methyl-4-(3-methyl-4-(2,2,2-trifluoroacetyl)piperazin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

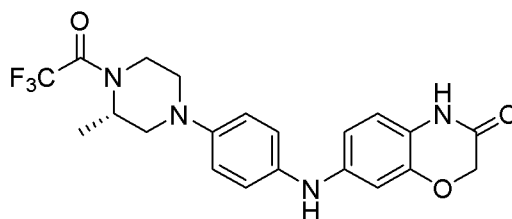


The titled compound **552** (8 mg, 5%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 7.11 (s, 1H), 6.99 (d, $J = 8.8$ Hz, 1H), 6.84 (s, 1H), 6.78 - 6.71 (m, 1H), 6.66 (d, $J = 8.4$ Hz, 1H), 6.32 - 6.24 (m, 2H), 4.63 - 4.58 (m, 1H), 4.45 (s, 2H), 4.28 - 4.20 (m, 1H), 3.79 (d, $J = 13.6$ Hz, 1H), 3.68 - 3.53 (m, 2H), 3.53 - 3.47 (m, 1H), 2.93 - 2.77 (m, 1H), 2.12 (s, 3H), 1.49 - 1.30 (m, 3H). Mass (m/z): 449.5 $[M+H]^+$.

15

Compound 553

(S)-7-((4-(3-methyl-4-(2,2,2-trifluoroacetyl)piperazin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

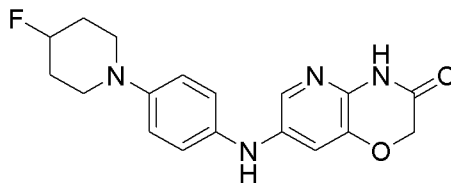


The titled compound **553** (24.4 mg, 16.9%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.45 (s, 1H), 7.75 (s, 1H), 6.98 - 6.92 (m, 2H), 6.88 (d, $J = 8.4$ Hz, 2H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.58 - 6.49 (m, 2H), 4.63 - 4.58 (m, 1H), 4.48 (s, 2H), 4.28 - 4.20 (m, 1H), 3.82 - 3.75 (m, 1H), 3.67 - 3.40 (m, 3H), 2.84 - 2.77 (m, 1H), 1.53 - 1.30 (m, 3H). Mass (m/z): 435.5 $[M+H]^+$.

25

Compound 554

7-((4-(4-fluoropiperidin-1-yl)phenyl)amino)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one

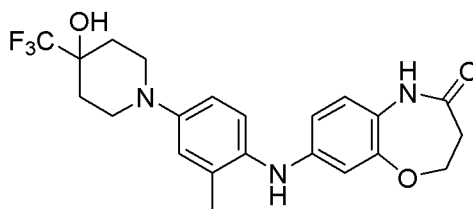


- 5 The titled compound **554** (23.9 mg, 13.5%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.98 (s, 1H), 7.86 (s, 1H), 7.60 (s, 1H), 6.96 - 6.88 (m, 5H), 4.97 - 4.68 (m, 1H), 4.57 (s, 2H), 3.26 - 3.22 (m, 2H), 3.04 - 3.00 (m, 2H), 2.06 - 1.90 (m, 2H), 1.86 - 1.78 (m, 2H). Mass (m/z): 343.5 [M+H]⁺.

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Compound 555

8-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5H)-one

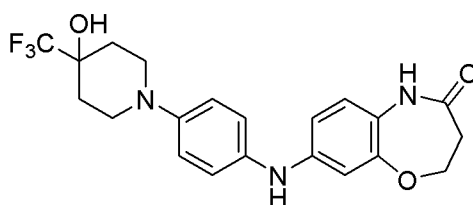


- 15 The titled compound **555** (16.6 mg, 42%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.33 (s, 1H), 7.17 (s, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.86 (s, 1H), 6.79 (d, *J* = 7.6 Hz, 2H), 6.36 (d, *J* = 8.8 Hz, 1H), 6.26 (s, 1H), 5.94 (s, 1H), 4.32 (t, *J* = 6.4 Hz, 2H), 3.53 (d, *J* = 12.0 Hz, 2H), 2.89 (t, *J* = 12.0 Hz, 2H), 2.11 (s, 3H), 1.84 - 1.68 (m, 4H). Mass (m/z): 436.5 [M+H]⁺.

20

Compound 556

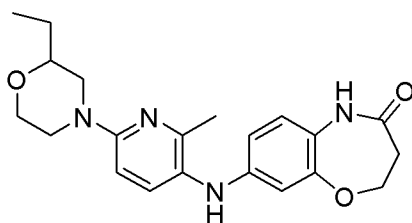
8-((4-(4-hydroxy-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5H)-one



The titled compound **556** (11.7 mg, 30%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.41 (s, 1H), 7.77 (s, 1H), 6.96 (d, $J = 8.4$ Hz, 2H), 6.91 (d, $J = 8.4$ Hz, 2H), 6.84 (d, $J = 8.4$ Hz, 1H), 6.63 - 6.52 (m, 2H), 5.93 (s, 1H),
 5 4.34 (t, $J = 6.4$ Hz, 2H), 3.45 (d, $J = 12.0$ Hz, 2H), 2.87 (t, $J = 12.0$ Hz, 2H), 2.62 - 2.58 (m, 2H), 1.89 - 1.70 (m, 4H). Mass (m/z): 422.5 $[\text{M}+\text{H}]^+$.

Compound 557

8-((6-(2-ethylmorpholino)-2-methylpyridin-3-yl)amino)-2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5*H*)-one

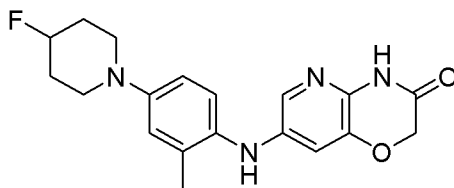


10

The titled compound **557** (10 mg, 24%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.34 (s, 1H), 7.32 (d, $J = 8.8$ Hz, 1H), 7.25 (s, 1H), 6.79 (d, $J = 8.8$ Hz, 1H), 6.67 (d, $J = 8.8$ Hz, 1H), 6.29 (d, $J = 8.8$ Hz, 1H), 6.18 (s,
 15 1H), 4.32 (t, $J = 5.2$ Hz, 2H), 4.05 (d, $J = 12.4$ Hz, 1H), 3.95 (t, $J = 10.8$ Hz, 2H), 3.54 (t, $J = 11.6$ Hz, 1H), 2.76 - 2.72 (m, 1H), 2.62 - 2.58 (m, 1H), 2.48 - 2.37 (m, 3H), 2.22 (s, 3H), 1.50 (p, $J = 8.0$ Hz, 2H), 0.95 (t, $J = 7.6$ Hz, 3H). Mass (m/z): 383.5 $[\text{M}+\text{H}]^+$.

Compound 558

20 7-(4-(4-fluoropiperidin-1-yl)-2-methylphenylamino)-2H-pyrido[3,2-*b*][1,4]oxazin-3(4*H*)-one

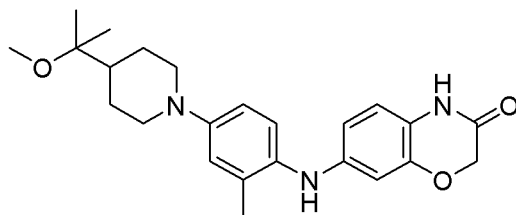


The titled compound **558** (11 mg, 6.47%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.89 (s, 1H), 7.37 (s, 1H), 7.26 (s, 1H), 6.97 (d, $J = 8.8$ Hz,
 25 1H), 6.87 (s, 1H), 6.77 (d, $J = 8.8$ Hz, 1H), 6.60 (s, 1H), 4.95 - 4.78 (m,

1H), 4.54 (s, 2H), 3.29 - 3.27 (m, 2H), 3.11 - 2.98 (m, 2H), 2.13 (s, 3H), 2.05 - 1.88 (m, 2H), 1.85 - 1.70 (m, 2H). Mass (m/z): 357.1 [M+H]⁺.

Compound 559

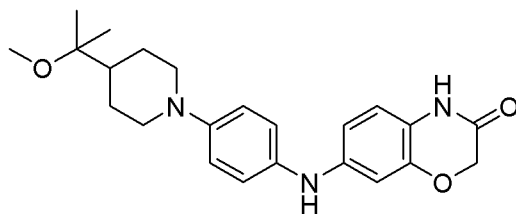
7-((4-(4-(2-methoxypropan-2-yl)piperidin-1-yl)-2-methylphenyl)
amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **559** (37.8 mg, 24.2%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ10.37 (s, 1H), 7.05 (s, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.80 (s, 1H), 6.72 (d, *J* = 8.8 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.29 - 6.20 (m, 2H), 4.44 (s, 2H), 3.65 (d, *J* = 11.6 Hz, 2H), 3.10 (s, 3H), 2.10 (s, 3H), 1.69 (d, *J* = 12.4 Hz, 2H), 1.55 - 1.44 (m, 1H), 1.41 - 1.27 (m, 2H), 1.06 (s, 6H). Mass (m/z): 410.2 [M+H]⁺.

Compound 560

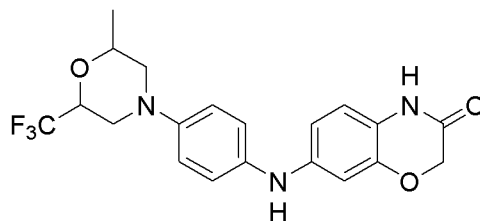
7-((4-(4-(2-methoxypropan-2-yl)piperidin-1-yl)phenyl)amino)-
2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **560** (13 mg, 8.2%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ10.44 (s, 1H), 7.66 (s, 1H), 6.95 - 6.88 (m, 2H), 6.85 (d, *J* = 7.2 Hz, 2H), 6.73 - 6.67 (m, 1H), 6.55 - 6.47 (m, 2H), 4.47 (d, *J* = 2.4 Hz, 2H), 3.58 (d, *J* = 11.6 Hz, 2H), 3.09 (d, *J* = 2.4 Hz, 3H), 2.48 - 2.42 (m, 2H), 1.69 (d, *J* = 12.4 Hz, 2H), 1.54 - 1.44 (m, 1H), 1.35 (q, *J* = 12.4 Hz, 2H), 1.10 (s, 6H). Mass (m/z): 396.2 [M+H]⁺.

Compound 561

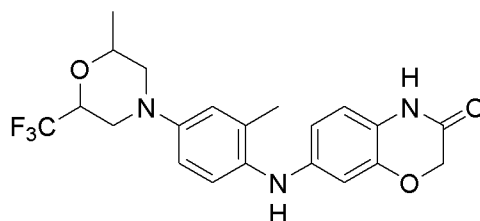
7-((4-(2-methyl-6-(trifluoromethyl)morpholino)phenyl)amino)-2H-

benzo[b][1,4]oxazin-3(4H)-one

The titled compound **561** (44 mg, 16.4 %) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.46 (s, 1H), 7.76 (s, 1H), 6.96 - 6.86 (m, 4H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.57 - 6.46 (m, 2H), 4.48 (s, 2H), 4.29 (d, *J* = 68.4 Hz, 1H), 3.87 (s, 1H), 3.58 - 3.46 (m, 1H), 3.23 - 3.06 (m, 2H), 2.82 - 2.75 (m, 1H), 1.24 (dd, *J* = 23.2, 6.4 Hz, 3H). Mass (*m/z*): 408.2 [M+H]⁺.

Compound 562

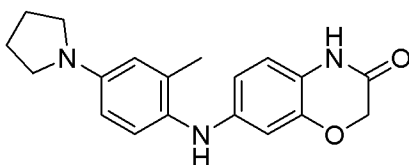
7-((2-methyl-4-(2-methyl-6-(trifluoromethyl)morpholino)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **562** (40 mg, 14.4 %) as a light-yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.38 (s, 1H), 7.11 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 19.6 Hz, 1H), 6.82 - 6.72 (m, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.32 - 6.22 (m, 2H), 4.48 (s, 2H), 4.29 (d, *J* = 68.4 Hz, 1H), 3.87 (s, 1H), 3.58 - 3.46 (m, 1H), 3.23 - 3.06 (m, 2H), 2.82 - 2.75 (m, 1H), 2.12 (s, 3H), 1.24 (dd, *J* = 23.2, 6.4 Hz, 3H). Mass (*m/z*): 422.2 [M+H]⁺.

Compound 563

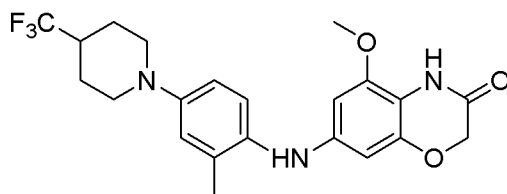
7-((2-methyl-4-(pyrrolidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **563** (14.8 mg, 13.7%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.31 (s, 1H), 6.98 (s, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 6.61 (d, $J = 8.4$ Hz, 1H), 6.42 (d, $J = 2.8$ Hz, 1H), 6.36 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.15 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.11 (d, $J = 2.4$ Hz, 1H), 4.42 (s, 2H), 3.19 (q, $J = 6.0, 4.8$ Hz, 4H), 2.08 (s, 3H), 1.98 - 1.88 (m, 4H). Mass (m/z): 324.2 $[\text{M}+\text{H}]^+$.

Compound 564

10 *5-methoxy-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one*

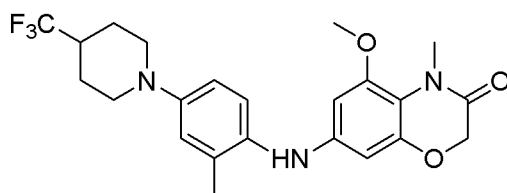


The titled compound **564** (10.2 mg, 5.99%) as a light purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.80 (s, 1H), 7.14 (s, 1H), 7.00 (d, $J = 8.8$ Hz, 1H), 6.84 (d, $J = 2.8$ Hz, 1H), 6.76 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.10 (d, $J = 2.0$ Hz, 1H), 5.82 (d, $J = 2.0$ Hz, 1H), 4.39 (s, 2H), 3.77 - 3.63 (m, 5H), 2.65 (dd, $J = 12.4, 10.0$ Hz, 2H), 2.45 (dd, $J = 12.0, 3.6$ Hz, 1H), 2.12 (s, 3H), 1.88 (d, $J = 12.4$ Hz, 2H), 1.62 - 1.50 (m, 2H). Mass (m/z): 435.8 $[\text{M}+\text{H}]^+$.

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Compound 565

5-methoxy-4-methyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

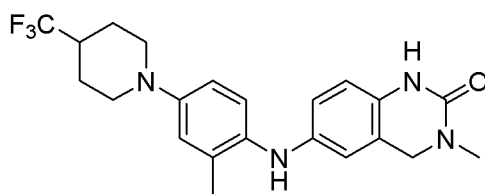


The titled compound **565** (3.7 mg, 2.04%) as a dark purple solid was

prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.33 (s, 1H), 7.02 (d, $J = 8.8$ Hz, 1H), 6.86 (d, $J = 2.8$ Hz, 1H), 6.77 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.17 (d, $J = 2.4$ Hz, 1H), 5.85 (d, $J = 2.4$ Hz, 1H), 4.38 (s, 2H), 3.71 (d, $J = 14.4$ Hz, 5H), 3.25 (s, 3H), 2.70 - 2.60 (m, 2H), 2.47 - 2.40 (m, 1H), 2.13 (s, 3H), 1.88 (d, $J = 12.0$ Hz, 2H), 1.60 - 1.50 (m, 2H). Mass (m/z): 449.8 $[\text{M}+\text{H}]^+$.

Compound 566

3-methyl-6-({2-methyl-4-[4-(trifluoromethyl)piperidin-1-yl]phenyl} amino)-1,4-dihydroquinazolin-2-one



10

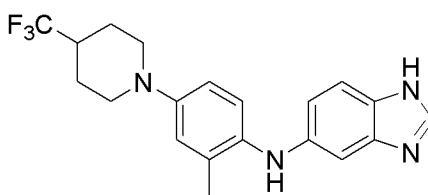
The titled compound **566** (14.3 mg, 7%) as a light yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.88 (s, 1H), 6.92 (d, $J = 8.8$ Hz, 1H), 6.87 (s, 1H), 6.82 (d, $J = 2.4$ Hz, 1H), 6.71 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.55 (dt, $J = 8.4, 5.2$ Hz, 2H), 6.45 (s, 1H), 4.26 (s, 2H), 3.65 (d, $J = 12.4$ Hz, 2H), 2.81 (s, 3H), 2.62 (t, $J = 11.2$ Hz, 2H), 2.47 - 2.37 (m, 1H), 2.11 (s, 3H), 1.87 (d, $J = 11.6$ Hz, 2H), 1.56 (tt, $J = 12.4, 6.4$ Hz, 2H). Mass (m/z): 418.9 $[\text{M}+\text{H}]^+$.

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Compound 567

tert-butyl 6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl) phenyl)amino)-3H-imidazo[4,5-b] pyridine-3-carboxylate

20



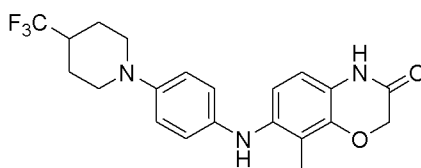
The titled compound **567** (32.1 mg, 40%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.38 (s, 1H), 7.44 (d, $J = 8.8$ Hz, 1H), 7.28 (s, 1H), 7.03 (d, $J = 8.4$ Hz, 1H), 6.89 (s, 1H), 6.81 (dd, $J = 14.0, 9.2$ Hz, 1H), 6.69 (s, 1H), 3.71 (d, $J = 11.6$ Hz, 2H), 2.67 (t, $J = 11.6$ Hz, 2H), 2.50 - 2.33 (m, 1H),

25

2.15 (s, 3H), 1.89 (d, $J = 12.0$ Hz, 2H), 1.58 (dd, $J = 12.4, 2.8$ Hz, 2H).
Mass (m/z): 375 $[M+H]^+$.

Compound 568

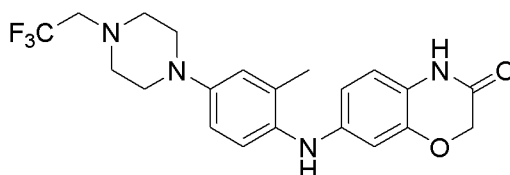
8-methyl-7-((4-(4-(trifluoromethyl) piperidin-1-yl)phenyl)
amino)-2H-benzo[b][1,4] oxazin-3(4H)-one



The titled compound **568** (38.9 mg, 22.66%) as a dark purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.48 (s, 1H), 6.99 (s, 1H), 6.74 (m, 6H), 4.54 (s, 2H), 3.55 (d, $J = 11.2$ Hz, 2H), 2.60 (m, 2H), 2.40 (s, 1H), 2.05 (d, $J = 20.4$ Hz, 3H), 1.87 (d, $J = 10.4$ Hz, 2H), 1.57 (d, $J = 10.4$ Hz, 2H). Mass (m/z): 406 $[M+H]^+$.

Compound 569

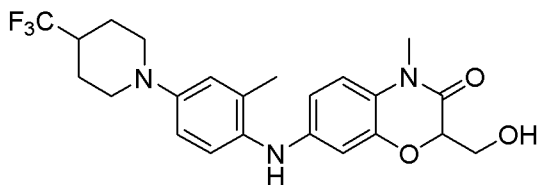
7-((2-methyl-4-(4-(2,2,2-trifluoroethyl) piperazin-1-yl)phenyl)
amino)-2H-benzo[b][1,4] oxazin-3(4H)-one



The titled compound **569** (69.2 mg, 29%) as a purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 7.08 (s, 1H), 6.96 (d, $J = 8.8$ Hz, 1H), 6.81 (d, $J = 2.4$ Hz, 1H), 6.72 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 6.31 - 6.21 (m, 2H), 4.45 (s, 2H), 3.23 (q, $J = 10.0$ Hz, 2H), 3.12 - 3.03 (m, 4H), 2.78 - 2.72 (m, 4H), 2.11 (s, 3H). Mass (m/z): 421 $[M+H]^+$.

Compound 570

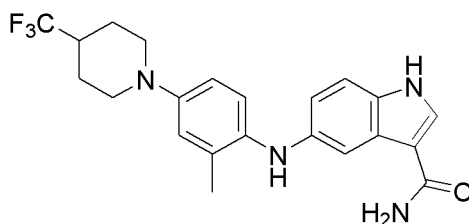
2-(hydroxymethyl)-4-methyl-7-((2-methyl-4-(4-(trifluoromethyl) piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **570** (2.1 mg, 3.44%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.16 - 7.13 (m, 1H), 6.97 - 6.94 (m, 1H), 6.84 - 6.81 (m, 2H), 6.75 - 6.71 (m, 1H), 6.31 - 6.27 (m, 1H), 6.23 - 6.22 (m, 1H), 5.01 - 4.93 (m, 1H), 4.53 - 4.50 (m, 1H), 3.72 - 3.63 (m, 4H), 3.15 (s, 3H), 2.65 - 2.58 (m, 2H), 2.44 - 2.37 (m, 1H), 2.08 (s, 3H), 1.84 (d, $J = 11.6$ Hz, 2H), 1.57 - 1.48 (m, 2H). Mass (m/z): 449.8 $[\text{M}+\text{H}]^+$.

Compound 571

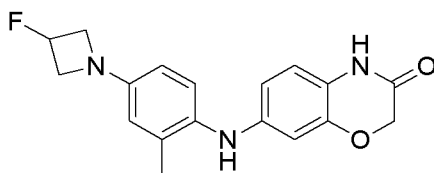
5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1H-indole-3-carboxamide



The titled compound **571** (18 mg, 10.8%) as a black solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 11.20 (d, $J = 2.4$ Hz, 1H), 7.85 (d, $J = 3.2$ Hz, 1H), 7.53 (d, $J = 2.0$ Hz, 1H), 7.17 (d, $J = 8.8$ Hz, 1H), 6.91 (d, $J = 8.8$ Hz, 1H), 6.80 - 6.76 (m, 2H), 6.71 - 6.64 (m, 2H), 3.60 (d, $J = 12.0$ Hz, 2H), 2.65 - 2.54 (m, 2H), 2.38 (dd, $J = 8.0, 3.6$ Hz, 1H), 2.12 (s, 3H), 1.84 (d, $J = 12.0$ Hz, 2H), 1.54 (dd, $J = 12.4, 3.6$ Hz, 2H). Mass (m/z): 416.7 $[\text{M}+\text{H}]^+$.

Compound 572

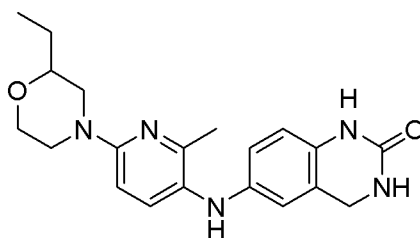
7-(4-(3-fluoroazetidin-1-yl)-2-methylphenylamino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **572** (23.5 mg, 17.0%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.36 (s, 1H), 7.05 (s, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.38 (s, 1H), 6.31 (d, *J* = 8.8 Hz, 1H), 6.25 - 6.11 (m, 2H),
 5 5.58 - 5.34 (m, 1H), 4.44 (s, 2H), 4.19 - 4.05 (m, 2H), 3.88 - 3.75 (m, 2H), 2.09 (s, 3H). Mass (m/z): 328.2 [M+H]⁺.

Compound 573

6-{[6-(2-ethylmorpholin-4-yl)-2-methylpyridin-3-yl]amino}-3,4-dihydro-1H-quinazolin-2-one



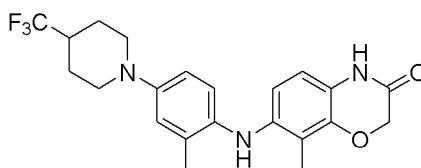
10

The titled compound **573** (26.6 mg, 5.05%) as a light-yellow solid was prepared according to the procedure outlined for compound **461**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.68 (s, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 6.93 (s, 1H), 6.63 (d, *J* = 8.8 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 2H), 6.44 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.35 (d, *J* = 1.6 Hz, 1H), 4.18 (s, 2H), 4.02 (d, *J* = 12.0 Hz, 1H), 3.93
 15 (d, *J* = 10.8 Hz, 2H), 3.54 (dd, *J* = 11.6, 9.2 Hz, 1H), 3.37 (s, 1H), 2.76 - 2.67 (m, 1H), 2.40 (dd, *J* = 12.4, 10.4 Hz, 1H), 2.22 (s, 3H), 1.49 (dd, *J* = 14.4, 7.2 Hz, 2H), 0.95 (t, *J* = 7.6 Hz, 3H). Mass(m/z): 367.9 [M+H]⁺.

Compound 574

8-methyl-7-((2-methyl-4-(4-(trifluoromethyl) piperidin-1-yl) phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

20



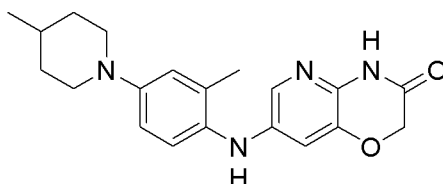
The titled compound **574** (20.0 mg, 10.4%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.16 - 7.13 (m, 1H), 6.97 - 6.94 (m, 1H), 6.84 - 6.81 (m, 2H),
 25

6.75 - 6.71 (m, 1H), 6.31 - 6.27 (m, 1H), 6.23 - 6.22 (m, 1H), 5.01 - 4.93 (m, 1H), 4.53 - 4.50 (m, 1H), 3.72 - 3.63 (m, 4H), 3.15 (s, 3H), 2.63 (m, 2H), 2.44 - 2.37 (m, 1H), 2.08 (s, 3H), 1.84 (d, $J = 11.6$ Hz, 2H), 1.57 - 1.48 (m, 2H). Mass (m/z): 420 $[M+H]^+$.

5

Compound 575

7-((2-methyl-4-(4-methylpiperidin-1-yl) phenyl) amino)-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one

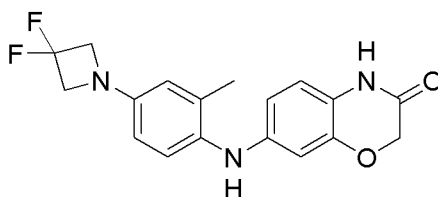


The titled compound **575** (31.2 mg, 33.80%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.85 (s, 1H), 7.32 (d, $J = 2.4$ Hz, 1H), 7.20 (s, 1H), 6.91 (d, $J = 8.8$ Hz, 1H), 6.79 (d, $J = 2.8$ Hz, 1H), 6.69 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.54 (d, $J = 2.4$ Hz, 1H), 4.50 (s, 2H), 3.54 (d, $J = 12.4$ Hz, 2H), 2.54 (d, $J = 2.4$ Hz, 2H), 2.08 (s, 3H), 1.64 (d, $J = 12.4$ Hz, 2H), 1.45 - 1.39 (m, 1H), 1.19 (dd, $J = 12.0, 3.6$ Hz, 2H), 0.90 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 353 $[M+H]^+$.

15

Compound 576

7-((4-(3,3-difluoroazetidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



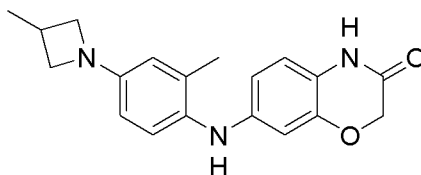
20

The titled compound **576** (4.6 mg, 1.45%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.37 (s, 1H), 7.10 (s, 1H), 6.98 (d, $J = 8.4$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 6.38 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.26 - 6.18 (m, 2H), 4.44 (s, 2H), 4.21 (t, $J = 12.4$ Hz, 4H), 2.10 (s, 3H). Mass(m/z): 345.8 $[M+H]^+$.

25

Compound 577

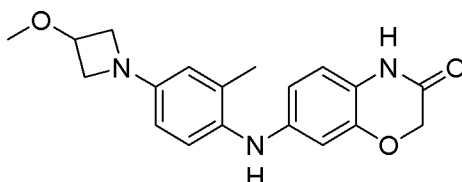
7-((2-methyl-4-(3-methylazetidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



- 5 The titled compound **577** (3.3 mg, 1.15%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.34 (s, 1H), 7.01 (s, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.28 (d, *J* = 2.4 Hz, 1H), 6.23 - 6.16 (m, 2H), 6.13 (d, *J* = 2.4 Hz, 1H), 4.43 (s, 2H), 3.90 (t, *J* = 7.2 Hz, 2H), 3.31 (d, *J* = 6.8 Hz, 1H),
 10 2.74 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.06 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 3H). Mass(*m/z*): 323.9 [M+H]⁺.

Compound 578

7-((4-(3-methoxyazetidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



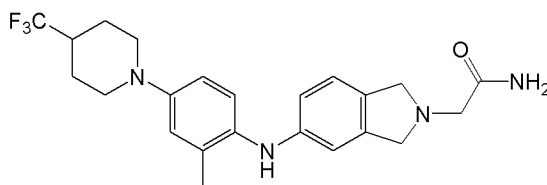
15

- The titled compound **578** (2.1 mg, 1.07%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.34 (s, 1H), 7.03 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.33 (d, *J* = 2.4 Hz, 1H), 6.26 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.21
 20 - 6.12 (m, 2H), 4.43 (s, 2H), 4.31 - 4.26 (m, 1H), 4.05 - 3.96 (m, 2H), 3.53 (dd, *J* = 8.4, 4.4 Hz, 2H), 3.23 (s, 3H), 2.07 (s, 3H). Mass (*m/z*): 339.8 [M+H]⁺.

Compound 579

2-(5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)isoindolin-2-yl)acetamide

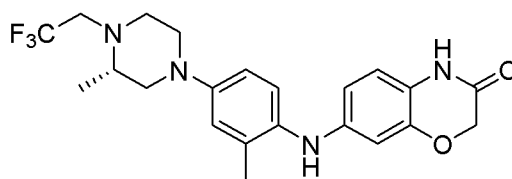
25



The titled compound **579** (2.3 mg, 3.5%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.28 (s, 1H), 7.09 (d, $J = 7.6$ Hz, 2H), 6.96 (t, $J = 9.2$ Hz, 2H), 6.84 (s, 1H), 6.75 (d, $J = 8.8$ Hz, 1H), 6.51 (d, $J = 5.6$ Hz, 2H), 3.83 (s, 4H), 3.69 (d, $J = 12.4$ Hz, 2H), 3.22 (s, 2H), 2.71 - 2.63 (m, 3H), 2.11 (s, 3H), 1.88 (d, $J = 12.4$ Hz, 2H), 1.56 (d, $J = 12.4$ Hz, 2H). Mass (m/z): 433.2 $[\text{M}+\text{H}]^+$.

Compound 580

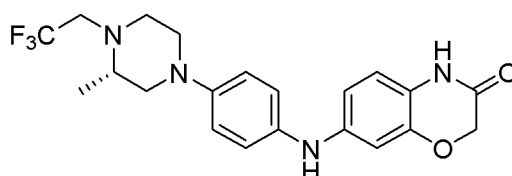
(S)-7-((2-methyl-4-(3-methyl-4-(2,2,2-trifluoroethyl)piperazin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **580** (23.7 mg, 15%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.37 (s, 1H), 7.07 (s, 1H), 6.95 (d, $J = 8.4$ Hz, 1H), 6.81 (s, 1H), 6.72 (d, $J = 8.8$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 6.30 - 6.21 (m, 2H), 4.44 (s, 2H), 3.49 - 3.34 (m, 2H), 3.20 - 3.06 (m, 1H), 3.03 - 2.95 (m, 1H), 2.80 - 2.68 (m, 3H), 2.48 - 2.42 (m, 2H), 2.11 (s, 3H), 1.12 - 1.06 (m, 3H). Mass (m/z): 435.5 $[\text{M}+\text{H}]^+$.

Compound 581

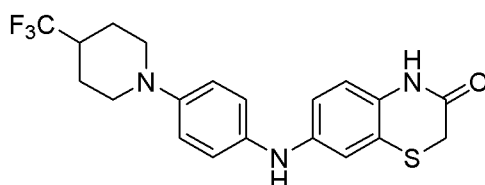
(S)-7-((4-(3-methyl-4-(2,2,2-trifluoroethyl)piperazin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **581** (42.7 mg, 22.7%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.44 (s, 1H), 7.68 (s, 1H), 6.93 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 1H), 6.56 - 6.47 (m, 2H), 4.47 (s, 2H), 3.50 - 3.37 (m, 1H), 3.31 - 3.21 (m, 2H), 3.17 - 3.06 (m, 1H), 3.02 - 2.95 (m, 1H), 2.77 - 2.71 (m, 3H), 2.48 - 2.41 (m, 2H), 1.11 - 1.05 (m, 3H). Mass (m/z): 421.5 $[\text{M}+\text{H}]^+$.

Compound 582

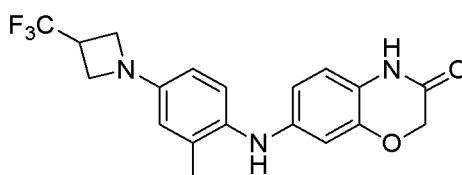
7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]thiazin-3(4H)-one



The titled compound **582** (21.6 mg, 12.9%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.29 (s, 1H), 7.74 (s, 1H), 6.97 - 6.86 (m, 4H), 6.84 - 6.78 (m, 2H), 6.78 - 6.72 (m, 1H), 3.62 (d, J = 12.0 Hz, 2H), 3.39 (s, 2H), 2.64 - 2.57 (m, 2H), 2.44 - 2.37 (m, 1H), 1.88 (d, J = 12.8 Hz, 2H), 1.65 - 1.49 (m, 2H). Mass (m/z): 408.5 $[\text{M}+\text{H}]^+$.

Compound 583

7-((2-methyl-4-(3-(trifluoromethyl)azetidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

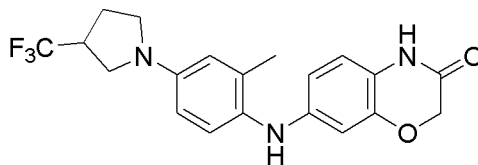


The titled compound **583** (19.1 mg, 11.6%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.35 (s, 1H), 7.06 (s, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.63 (d, J = 8.4 Hz, 1H), 6.38 (s, 1H), 6.31 (d, J = 8.8 Hz, 1H), 6.24 - 6.14 (m, 2H), 4.44 (s, 2H), 4.00 (t, J = 8.4 Hz, 2H), 3.80 (t, J = 6.8 Hz, 2H), 3.70 - 3.66

(m, 1H), 2.09 (s, 3H). Mass (m/z): 378.5 [M+H]⁺.

Compound 584

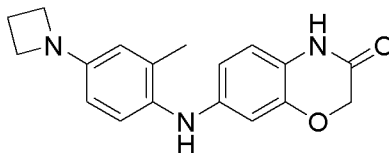
6-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **584** (6.8 mg, 6.1%) as brown oil was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.40 (s, 1H), 7.07 - 6.89 (m, 2H), 6.69 (d, *J* = 8.8 Hz, 1H), 6.52 (s, 1H), 6.44 (d, *J* = 8.4 Hz, 1H), 6.25 - 6.08 (m, 2H), 4.39 (s, 2H), 3.47 (d, *J* = 9.2 Hz, 1H), 3.26 (d, *J* = 8.5 Hz, 2H), 2.15 - 2.0 (m, 4H), 1.23 (s, 2H). Mass(m/z): 392.4 [M+H]⁺.

Compound 585

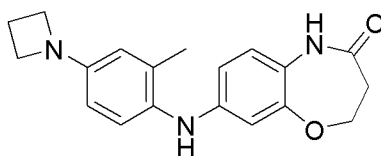
7-((4-(azetidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **585** (22.6 mg, 14.8%) as pink oil was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.34 (s, 1H), 7.01 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.29 (s, 1H), 6.26 - 6.06 (m, 3H), 4.43 (d, *J* = 2.8 Hz, 2H), 3.75 (t, *J* = 7.6 Hz, 4H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.07 (s, 3H). Mass(m/z): 310.2 [M+H]⁺.

Compound 586

8-((4-(azetidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one

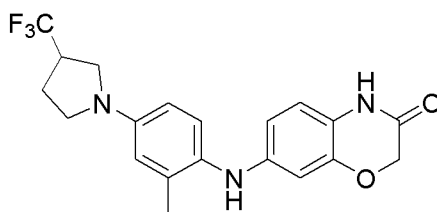


The titled compound **586** (19.3 mg, 58.5%) as pink oil was prepared

according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.30 (s, 1H), 7.11 (d, J = 2.8 Hz, 1H), 6.92 (dd, J = 8.4, 2.4 Hz, 1H), 6.76 (dd, J = 8.8, 2.4 Hz, 1H), 6.35 - 6.19 (m, 3H), 6.16 (s, 1H), 4.31 (q, J = 5.2 Hz, 2H), 3.83 - 3.67 (m, 4H), 2.56 (s, 2H), 2.27 (t, J = 7.6 Hz, 2H), 2.07 (d, J = 2.8 Hz, 3H). Mass(m/z): 324.2 $[\text{M}+\text{H}]^+$.

Compound 587

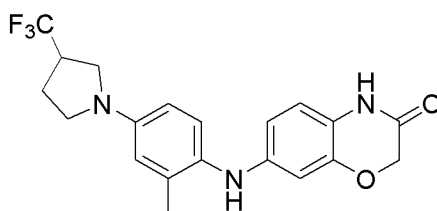
7-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **587** (33.5 mg, 6.9%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.34 (s, 1H), 7.03 (s, 1H), 6.97 - 6.90 (m, 1H), 6.66 - 6.59 (m, 1H), 6.52 (s, 1H), 6.44 (d, J = 8.8 Hz, 1H), 6.21 - 6.12 (m, 2H), 4.43 (s, 2H), 3.53 - 3.44 (m, 1H), 3.40 - 3.35 (m, 2H), 3.32 - 3.23 (m, 2H), 2.30 - 2.25 (m, 1H), 2.14 - 2.01 (m, 4H). Mass (m/z): 392.4 $[\text{M}+\text{H}]^+$.

Compound 588

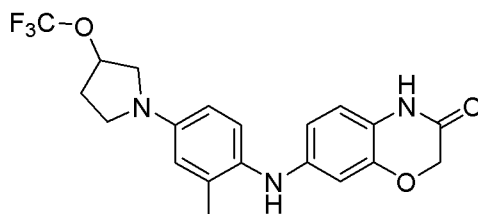
7-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one



The titled compound **588** (24.4 mg, 5%) as a purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.34 (s, 1H), 7.03 (s, 1H), 6.97 - 6.90 (m, 1H), 6.66 - 6.59 (m, 1H), 6.52 (s, 1H), 6.44 (d, J = 8.8 Hz, 1H), 6.21 - 6.12 (m, 2H), 4.43 (s, 2H), 3.53 - 3.44 (m, 1H), 3.40 - 3.35 (m, 2H), 3.32 - 3.23 (m, 1H), 2.28 (d, J = 12.0 Hz, 1H), 2.16 - 2.01 (m, 4H). Mass (m/z): 392.4 $[\text{M}+\text{H}]^+$.

Compound 589

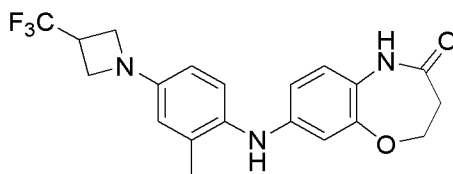
7-((2-methyl-4-(3-(trifluoromethoxy)pyrrolidin-1-yl)phenyl)amino)-
-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **589** (8.7 mg, 5.5%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.33 (s, 1H), 7.03 (s, 1H), 6.97 - 6.90 (m, 1H), 6.66 - 6.58 (m, 1H), 6.48 (s, 1H), 6.41 (d, *J* = 8.8 Hz, 1H), 6.20 - 6.11 (m, 2H), 5.22 (s, 1H), 4.43 (s, 2H), 3.62 - 3.54 (m, 1H), 3.44 - 3.34 (m, 2H), 2.43 - 2.27 (m, 2H), 2.26 - 2.16 (m, 1H), 2.10 (s, 3H). Mass (*m/z*): 408.5 [M+H]⁺.

Compound 590

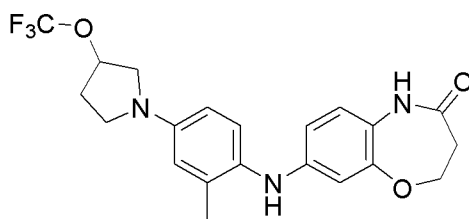
5-(4-methoxybenzyl)-8-((2-methyl-4-(3-(trifluoromethyl)azetidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **590** (11 mg, 28%) as a purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.31 (s, 1H), 7.15 (s, 1H), 7.00 - 6.93 (m, 1H), 6.80 - 6.73 (m, 1H), 6.39 (s, 1H), 6.35 - 6.26 (m, 2H), 6.18 (s, 1H), 4.35 - 4.27 (m, 2H), 4.05 - 3.96 (m, 2H), 3.86 - 3.75 (m, 2H), 3.71 - 3.66 (m, 1H), 2.62 - 2.54 (m, 2H), 2.09 (s, 3H). Mass (*m/z*): 392.5 [M+H]⁺.

Compound 591

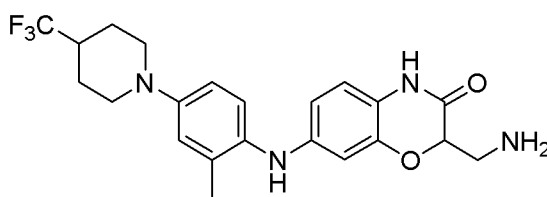
8-((2-methyl-4-(3-(trifluoromethoxy)pyrrolidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **591** (3.1 mg, 7.9%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, CD₃OD) δ 6.99 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 6.33 (d, *J* = 8.4 Hz, 1H), 6.24 (s, 1H), 5.12 (s, 1H), 4.41 (s, 2H), 3.64 - 3.60 (m, 1H), 3.47 - 3.40 (m, 3H), 2.69 - 2.61 (m, 2H), 2.33 - 2.29 (m, 2H), 2.16 (s, 3H). Mass (m/z): 422.5 [M+H]⁺.

Compound 592

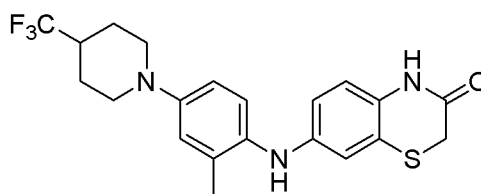
2-(aminomethyl)-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **592** (10.9 mg, 26.8%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.35 (s, 1H), 7.07 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.84 (s, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.27 (d, *J* = 11.2 Hz, 2H), 4.38 - 4.33 (m, 1H), 3.68 (d, *J* = 12.0 Hz, 2H), 2.90 (s, 2H), 2.66 - 2.59 (m, 2H), 2.44 - 2.36 (m, 1H), 2.11 (s, 3H), 1.88 (d, *J* = 12.8 Hz, 2H), 1.63 - 1.49 (m, 2H). Mass (m/z): 435.5 [M+H]⁺.

Compound 593

7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]thiazin-3(4H)-one

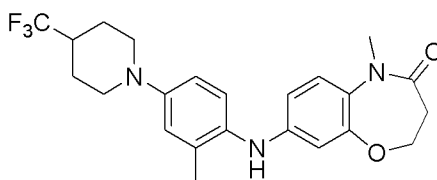


The titled compound **593** (28.7 mg, 15%) as a white solid was prepared

according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.22 (s, 1H), 7.14 (s, 1H), 6.99 - 6.92 (m, 1H), 6.85 (s, 1H), 6.79 - 6.71 (m, 2H), 6.55 - 6.47 (m, 2H), 3.69 (d, J = 12.0 Hz, 2H), 3.37 (s, 2H), 2.63 (d, J = 12.4 Hz, 2H), 2.48 - 2.36 (m, 1H), 2.11 (d, J = 2.8 Hz, 3H), 1.88 (d, J = 12.4 Hz, 2H), 1.63 - 1.49 (m, 2H). Mass (m/z): 422.5 $[\text{M}+\text{H}]^+$.

Compound 594

5-methyl-8-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



10

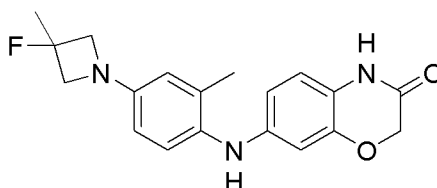
The titled compound **594** (25.8 mg, 18%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.39 (s, 1H), 7.09 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.87 (s, 1H), 6.78 (d, J = 8.4 Hz, 1H), 6.49 (d, J = 8.4 Hz, 1H), 6.32 (s, 1H), 4.41 - 4.34 (m, 2H), 3.72 (d, J = 12.0 Hz, 2H), 3.33 (s, 3H), 2.72 - 2.61 (m, 2H), 2.46 - 2.38 (m, 1H), 2.13 (s, 3H), 1.88 (d, J = 12.8 Hz, 2H), 1.63 - 1.49 (m, 2H). Mass (m/z): 434.5 $[\text{M}+\text{H}]^+$.

15

Compound 595

7-((4-(3-fluoro-3-methylazetidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

20



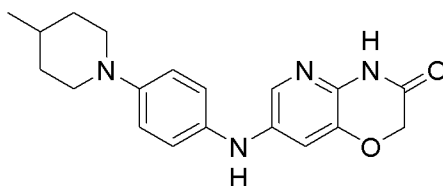
The titled compound **595** (37.7 mg, 13%) as a purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.35 (s, 1H), 7.05 (s, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.63 (d, J = 8.4 Hz, 1H), 6.37 (d, J = 2.4 Hz, 1H), 6.30 (dd, J = 8.4, 2.8 Hz, 1H), 6.21 (dd, J = 8.4, 2.4 Hz, 1H), 6.16 (d, J = 2.4 Hz, 1H), 4.44 (s, 2H), 3.86

25

(d, $J = 19.2$ Hz, 4H), 2.08 (s, 3H), 1.62 (d, $J = 22.4$ Hz, 3H). Mass (m/z): 342 $[M+H]^+$.

Compound 596

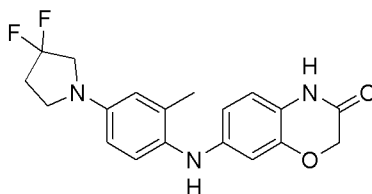
7-((4-(4-methylpiperidin-1-yl)phenyl)amino)
-2H-pyrido[3,2-b][1,4]oxazin-3(4H)-one



The titled compound **596** (22.5 mg, 15.19%) as a green solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.93 (s, 1H), 7.77 (s, 1H), 7.54 (d, $J = 2.4$ Hz, 1H), 6.90 (d, $J = 8.8$ Hz, 2H), 6.86 - 6.83 (m, 3H), 4.53 (s, 2H), 3.47 (d, $J = 12.4$ Hz, 2H), 2.58 - 2.48 (m, 2H), 1.65 (d, $J = 12.8$ Hz, 2H), 1.45 - 1.38 (m, 1H), 1.20 (dd, $J = 11.6, 3.2$ Hz, 2H), 0.90 (d, $J = 6.4$ Hz, 3H). Mass (m/z): 339 $[M+H]^+$.

Compound 597

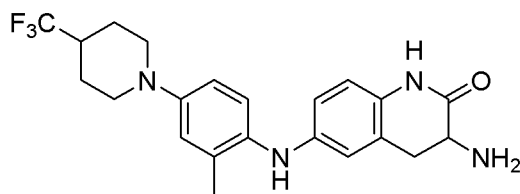
7-((4-(3,3-difluoropyrrolidin-1-yl)-2-methylphenyl)amino)
-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **597** (53.4 mg, 24.23%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.35 (s, 1H), 7.06 (s, 1H), 6.96 (d, $J = 8.4$ Hz, 1H), 6.63 (d, $J = 8.4$ Hz, 1H), 6.53 (d, $J = 2.4$ Hz, 1H), 6.45 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.22 - 6.15 (m, 2H), 4.43 (s, 2H), 3.65 (t, $J = 13.6$ Hz, 2H), 3.43 (t, $J = 7.2$ Hz, 2H), 2.54 (d, $J = 7.6$ Hz, 1H), 2.48 (s, 1H), 2.11 (s, 3H). Mass (m/z): 360 $[M+H]^+$.

Compound 598

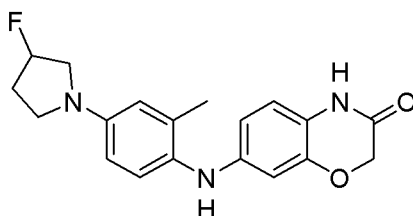
3-amino-6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)

-3,4-dihydroquinolin-2(1H)-one

The titled compound **598** (4.3 mg, 8.56%) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.13 (s, 1H), 6.99 (s, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.80 (d, *J* = 2.8 Hz, 1H), 6.70 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.53 - 6.47 (m, 2H), 5.96 (s, 1H), 3.73 (dd, *J* = 13.6, 6.6 Hz, 1H), 3.64 (d, *J* = 12.4 Hz, 2H), 2.88 - 2.72 (m, 2H), 2.64 - 2.57 (m, 2H), 2.45 - 2.35 (m, 1H), 2.08 (s, 3H), 1.84 (d, *J* = 12.4 Hz, 2H), 1.60 - 1.45 (m, 2H). Mass (m/z): 418.8 [M+H]⁺.

Compound 599

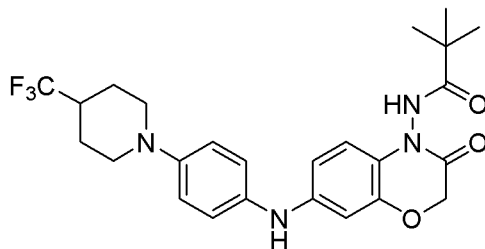
7-{[4-(3-fluoropyrrolidin-1-yl)-2-methylphenyl]amino}-2,4-dihydro-1,4-benzoxazin-3-one



The titled compound **599** (7 mg, 3.89 %) as a white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.33 (s, 1H), 7.02 (s, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 2.4 Hz, 1H), 6.39 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.21 - 6.10 (m, 2H), 4.43 (s, 2H), 3.49 (m, 3H), 3.29 (d, *J* = 9.2 Hz, 2H), 2.29 - 2.13 (m, 2H), 2.08 (d, *J* = 8.0 Hz, 3H). Mass (m/z): 341.9 [M+H]⁺.

Compound 600

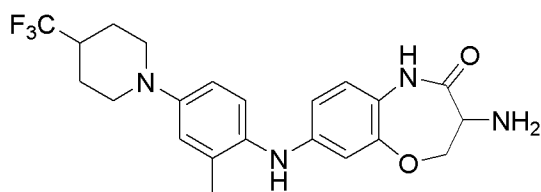
N-(3-oxo-7-((4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)pivalamide



The titled compound **600** (9.6 mg, 4.3%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.19 (d, J = 2.8 Hz, 1H), 7.83 (s, 1H), 6.96 (d, J = 9.6 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 9.2 Hz, 1H), 6.63 - 6.52 (m, 2H), 4.77 - 4.65 (m, 2H), 3.62 (d, J = 12.0 Hz, 2H), 2.62 (s, 2H), 2.46 - 2.38 (m, 1H), 1.88 (d, J = 12.8 Hz, 2H), 1.57 (q, J = 12.8 Hz, 2H), 1.23 (d, J = 3.2 Hz, 9H). Mass (m/z): 491.2 $[\text{M}+\text{H}]^+$.

Compound 601

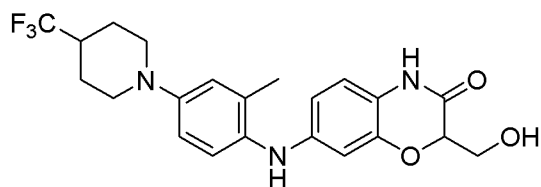
10 *(S)-8-(4-(4-(trifluoromethyl)piperidin-1-yl)-2-methylphenylamino)-3-amino-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one*



The titled compound **601** (19.5 mg, 39.8%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.48 (s, 1H), 7.24 (s, 1H), 6.99 (d, J = 8.8, 1H), 6.85 (s, 1H), 6.82 - 6.73 (m, 2H), 6.39 (d, J = 8.8 Hz, 1H), 6.31 (s, 1H), 4.24 - 4.15 (m, 1H), 3.92 (t, J = 10.8 Hz, 1H), 3.70 (d, J = 12.4 Hz, 2H), 3.58 (t, J = 9.2 Hz, 1H), 2.65 (t, J = 12.4 Hz, 3H), 2.48 - 2.39 (m, 2H), 2.11 (s, 3H), 1.88 (d, J = 12.8 Hz, 2H), 1.72 (s, 2H), 1.64-1.48 (m, 2H). Mass(m/z): 435.2 $[\text{M}+\text{H}]^+$.

Compound 602

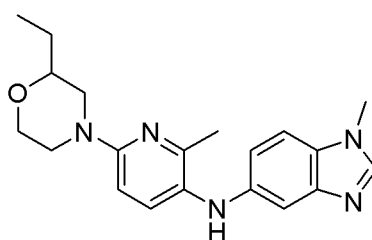
2-(hydroxymethyl)-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **602** (2.7 mg, 1.54%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.35 (s, 1H), 7.05 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 6.75 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.24 (dt, *J* = 6.8, 2.4 Hz, 2H), 5.01 (t, *J* = 5.6 Hz, 1H), 4.49 (dd, *J* = 5.2, 3.2 Hz, 1H), 3.79 - 3.64 (m, 4H), 2.64 (td, *J* = 12.0, 2.0 Hz, 2H), 2.47 - 2.40 (m, 1H), 2.11 (s, 3H), 1.88 (d, *J* = 11.2 Hz, 2H), 1.61 - 1.50 (m, 2H). Mass(*m/z*): 435.8 [M+H]⁺.

Compound 603

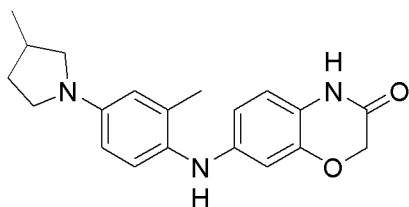
N-[6-(2-ethylmorpholin-4-yl)-2-methylpyridin-3-yl]-1-methyl-1,3-benzodiazol-5-amine



The titled compound **603** (8.7 mg, 4.22%) as a light brown was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.31 (s, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.25 (s, 1H), 6.82 (dd, *J* = 8.8, 1.6 Hz, 1H), 6.68 (dd, *J* = 5.2, 3.2 Hz, 2H), 4.05 (d, *J* = 12.4 Hz, 1H), 4.00 - 3.91 (m, 2H), 3.81 (s, 3H), 3.55 (td, *J* = 11.6, 2.4 Hz, 1H), 3.40 - 3.32 (m, 1H), 2.75 (d, *J* = 3.2 Hz, 1H), 2.44 (dd, *J* = 12.4, 10.4 Hz, 1H), 2.24 (s, 3H), 1.57 - 1.41 (m, 2H), 0.95 (t, *J* = 7.6 Hz, 3H). Mass(*m/z*): 351.9 [M+H]⁺.

Compound 604

7-((2-methyl-4-(3-methylpyrrolidin-1-yl)phenyl)amino)-2H-benzo[*b*][1,4]oxazin-3(4H)-one

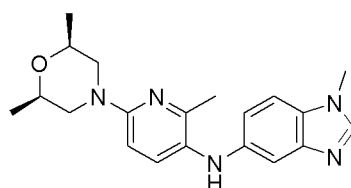


The titled compound **604** (19.0 mg, 10.35%) as a dark blue solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.38 (s, 1H), 6.94 (s, 1H), 6.89 (d, $J = 8.4$ Hz, 1H), 6.67 (d, $J = 8.4$ Hz, 1H), 6.39 (d, $J = 2.4$ Hz, 1H), 6.33 (dd, $J = 8.4$, 2.8 Hz, 1H), 6.15 (d, $J = 2.4$ Hz, 1H), 6.11 (dd, $J = 8.8$, 2.4 Hz, 1H), 4.38 (s, 2H), 3.38 (d, $J = 8.8$ Hz, 2H), 3.28 - 3.20 (m, 2H), 2.80 - 2.73 (m, 1H), 2.38 - 2.30 (m, 1H), 2.08 (s, 3H), 1.57 (dd, $J = 12.0$, 8.4 Hz, 1H), 1.08 (d, $J = 6.8$ Hz, 3H). Mass(m/z): 338 $[\text{M}+\text{H}]^+$.

10

Compound 605

N-(6-((2*S*,6*R*)-2,6-dimethylmorpholino)-2-methylpyridin-3-yl)-1-methyl-1*H*-benzo[*d*]imidazol-5-amine

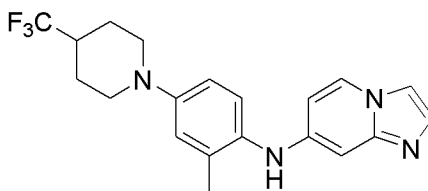


The titled compound **605** (81.3 mg, 51.03%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.93 (s, 1H), 7.29 (d, $J = 8.6$ Hz, 2H), 6.98 (s, 1H), 6.73 - 6.70 (m, 1H), 6.68 (d, $J = 1.8$ Hz, 1H), 6.62 (d, $J = 8.8$ Hz, 1H), 4.01 (dd, $J = 12.7$, 1.9 Hz, 2H), 3.72 (s, 3H), 3.64 - 3.56 (m, 2H), 2.28 (dd, $J = 12.6$, 10.5 Hz, 2H), 2.22 (s, 3H), 1.14 (s, 3H), 1.12 (s, 3H). Mass(m/z): 352 $[\text{M}+\text{H}]^+$.

20

Compound 606

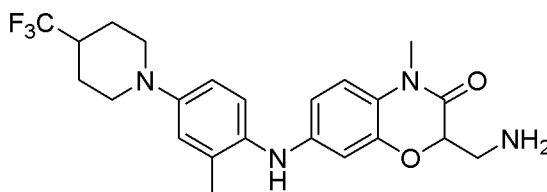
N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)imidazo[1,2-*a*]pyridin-7-amine



The titled compound **606** (13.4 mg, 11%) as a brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.22 (d, $J = 7.2$ Hz, 1H), 7.67 (s, 1H), 7.56 (s, 1H), 7.19 (s, 1H), 7.06 (d, $J = 8.4$ Hz, 1H), 6.92 (s, 1H), 6.83 (d, $J = 8.8$ Hz, 1H), 6.52 (d, $J = 7.2$ Hz, 1H), 6.09 (s, 1H), 3.76 (d, $J = 12.4$ Hz, 2H), 2.72 - 2.68 (m, 1H), 2.47 - 2.38 (m, 1H), 2.14 (s, 3H), 1.89 (d, $J = 12.8$ Hz, 2H), 1.64 - 1.50 (m, 2H). Mass (m/z): 375.5 $[\text{M}+\text{H}]^+$.

Compound 607

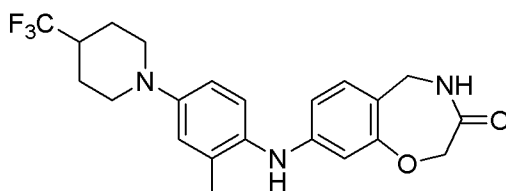
2-(aminomethyl)-4-methyl-7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **607** (4.6 mg, 11%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.20 (s, 1H), 6.99 (d, $J = 9.2$ Hz, 1H), 6.92 - 6.83 (m, 2H), 6.77 (d, $J = 8.8$ Hz, 1H), 6.35 (d, $J = 8.8$ Hz, 1H), 6.29 (s, 1H), 4.43 - 4.37 (m, 1H), 3.70 (d, $J = 12.0$ Hz, 2H), 3.19 (s, 3H), 2.92 - 2.88 (m, 1H), 2.64 - 2.56 (m, 2H), 2.43 - 2.35 (m, 1H), 2.12 (s, 3H), 1.88 (d, $J = 12.8$ Hz, 2H), 1.63 - 1.49 (m, 2H). Mass (m/z): 449.5 $[\text{M}+\text{H}]^+$.

Compound 608

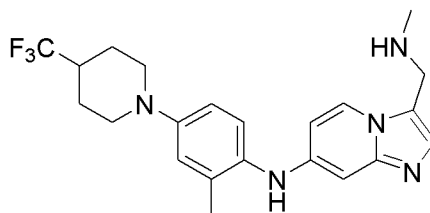
8-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one



The titled compound **608** (12.5 mg, 32%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.26 (s, 1H), 7.35 (s, 1H), 7.03 - 6.92 (m, 2H), 6.86 (s, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 6.23 (s, 1H), 4.44 (s, 2H), 4.11 (s, 2H), 3.71 (d, *J* = 12.0 Hz, 2H), 2.71 - 2.61 (m, 2H), 2.47 - 2.38 (m, 1H), 2.11 (s, 3H), 1.88 (d, *J* = 12.8 Hz, 2H), 1.63 - 1.48 (m, 2H). Mass (m/z): 420.5 [M+H]⁺.

Compound 609

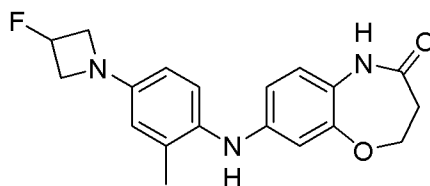
N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-3-((methylamino)methyl)imidazo[1,2-*a*]pyridin-7-amine



The titled compound **609** (16 mg, 24%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.13 (d, *J* = 7.6 Hz, 1H), 7.68 - 7.61 (m, 1H), 7.09 - 7.02 (m, 2H), 6.91 (s, 1H), 6.83 (d, *J* = 8.8 Hz, 1H), 6.55 (d, *J* = 7.2 Hz, 1H), 6.09 (s, 1H), 3.84 (s, 2H), 3.76 (d, *J* = 12.4 Hz, 2H), 2.72 - 2.67 (m, 2H), 2.36 - 2.29 (m, 1H), 2.24 (s, 3H), 2.14 (s, 3H), 1.89 (d, *J* = 12.4 Hz, 2H), 1.64 - 1.50 (m, 2H). Mass (m/z): 418.5 [M+H]⁺.

Compound 610

8-((4-(3-fluoroazetidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5H)-one

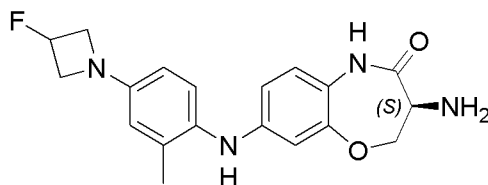


The titled compound **610** (3.3 mg, 10.6%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.31 (s, 1H), 7.15 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 1H), 6.43 - 6.25 (m, 3H), 6.18 (s, 1H), 5.64 - 5.33 (m,

1H), 4.34 - 4.27 (m, 2H), 4.20 - 4.05 (m, 2H), 3.88 - 3.75 (m, 2H), 2.74 - 2.53 (m, 2H), 2.09 (s, 3H). Mass (m/z): 342.1 [M+H]⁺.

Compound 611

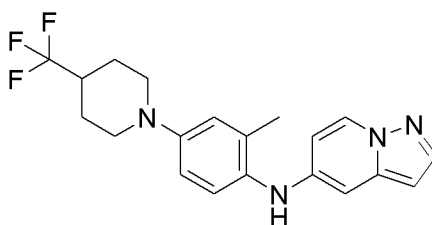
(S)-3-amino-8-((4-(3-fluoroazetidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **611** (4.4 mg, 11.1%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.51 (s, 1H), 7.23 (s, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.43-6.20 (m, 4H), 5.57-5.35 (m, 1H), 4.30 - 4.07 (m, 3H), 4.00 - 3.75 (m, 3H), 3.68-3.60 (m, 1H), 2.81-2.58(m, 2H), 2.09 (s, 3H). Mass (m/z): 357.1 [M+H]⁺.

Compound 612

N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)pyrazolo[1,5-*a*]pyridin-5-amine

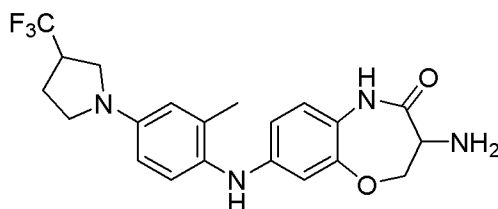


The titled compound **612** (14.5 mg, 12.5%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.35 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 3.8 Hz, 2H), 7.12 - 7.02 (m, 1H), 6.91 (s, 1H), 6.82 (d, *J* = 8.7 Hz, 1H), 6.48 (d, *J* = 7.5 Hz, 1H), 6.19 (s, 1H), 6.04 (s, 1H), 3.76 (d, *J* = 12.2 Hz, 2H), 2.71 (d, *J* = 12.5 Hz, 2H), 2.44 - 2.42 (m, 1H), 2.14 (d, *J* = 2.9 Hz, 3H), 1.89 (d, *J* = 12.6 Hz, 2H), 1.57 (q, *J* = 12.7 Hz, 2H). Mass(m/z): 375.2 [M+H]⁺.

Compound 613

3-amino-8-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)

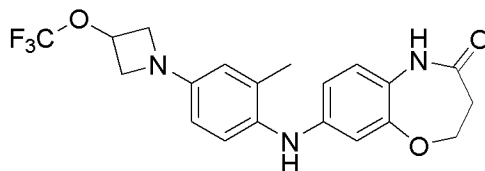
amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **613** (14.6 mg, 44.5%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.44 (s, 1H), 7.20 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.53 (s, 1H), 6.46 (d, *J* = 8.8 Hz, 1H), 6.31 (d, *J* = 8.8 Hz, 1H), 6.22 (s, 1H), 4.18 (t, *J* = 8.8 Hz, 1H), 3.91 (t, *J* = 10.8 Hz, 1H), 3.54 (dt, *J* = 30.8, 8.4 Hz, 2H), 3.28 (t, *J* = 6.8 Hz, 2H), 2.27 (s, 1H), 2.11 (s, 3H), 2.23 - 2.19 (m, 1H), 1.73 (s, 2H). Mass(*m/z*): 421.4 [M+H]⁺.

Compound 614

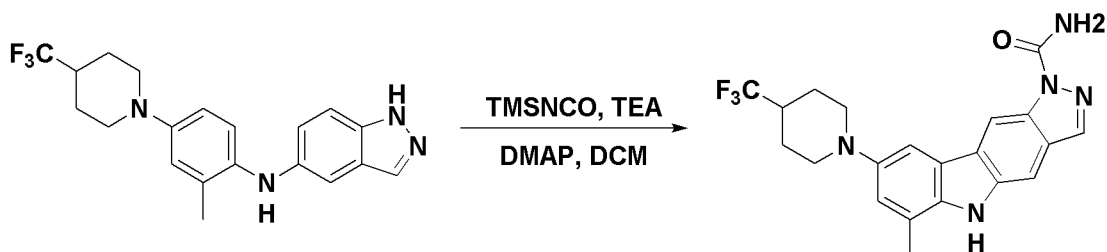
8-((2-methyl-4-(3-(trifluoromethoxy)azetidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **614** (3.0 mg, 9.7%) as a pink solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.31 (s, 1H), 7.16 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.40 (s, 1H), 6.32 (t, *J* = 9.6 Hz, 2H), 6.19 (s, 1H), 5.27 (s, 1H), 4.30 (d, *J* = 7.6 Hz, 2H), 4.18 (d, *J* = 7.6 Hz, 2H), 3.84 (s, 2H), 2.09 (s, 3H). Mass(*m/z*): 408.2 [M+H]⁺.

Compound 615

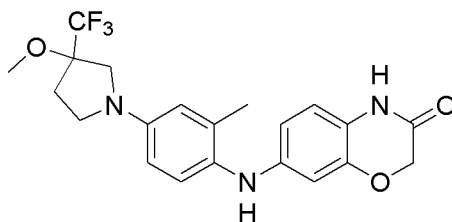
*6-methyl-8-(4-(trifluoromethyl)piperidin-1-yl)pyrazolo[4,3-*b*]carbazole-1(5H)-carboxamide*



To a solution of N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)-1H-indazol-5-amine (200 mg, 0.53 mmol) in DCM (5 mL) was added TEA (108 mg, 1.06 mmol), DMAP (65 mg, 0.53 mmol) and TMSNCO (61 mg, 0.53 mmol) at room temperature. The reaction mixture was heated to 25°C for 8 h under nitrogen atmosphere. After the reaction was completed, the filtrate was concentrated. The residue was purified by silica gel flash column chromatography (PE/EtOAc=10/1) to afford 6-methyl-8-(4-(trifluoromethyl)piperidin-1-yl)pyrazolo[4,3-b]carbazole-1(5H)-carboxamide (10.6 mg, 4.8% yield) as a yellow solid. ¹H NMR (400 MHz, CD₃OD) δ 8.12 (s, 1H), 7.53 - 7.48 (m, 3H), 7.23(d, *J* = 7.6 Hz, 1H), 6.79 (s, 1H), 3.92 - 3.87 (m, 2H), 3.51 - 3.40 (m, 1H), 2.70 - 2.54 (m, 1H), 2.32 - 2.12 (m, 5H), 1.26 - 1.21 (m, 2H). Mass(m/z): 415.7 [M+H]⁺.

Compound 616

7-((4-(3-methoxy-3-(trifluoromethyl)pyrrolidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

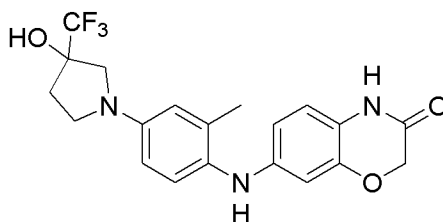


The titled compound **616** (5.2 mg, 2.51%) as a light purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.36 (s, 1H), 7.06 (s, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.54 (d, *J* = 2.8 Hz, 1H), 6.46 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.22 - 6.12 (m, 2H), 4.43 (s, 2H), 3.57 (d, *J* = 11.6 Hz, 1H), 3.49 (d, *J* = 11.2 Hz, 1H), 3.45 - 3.36 (m, 5H), 2.43 - 2.35 (m, 1H), 2.31 (dd, *J* = 10.8, 5.2 Hz, 1H), 2.09 (d, *J* = 9.6 Hz, 3H). Mass (m/z): 421.8

[M+H]⁺.

Compound 617

7-((4-(3-hydroxy-3-(trifluoromethyl)pyrrolidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



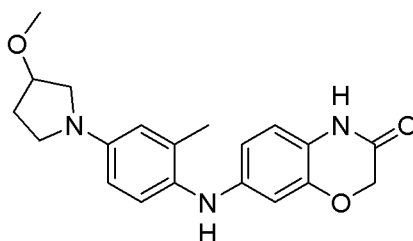
5

The titled compound **617** (44.5 mg, 18.05%) as a dark grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.35 (s, 1H), 7.04 (s, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 2.8 Hz, 1H), 6.44 - 6.37 (m, 2H), 6.20 - 6.12 (m, 2H), 4.43 (s, 2H), 3.59 (d, *J* = 10.8 Hz, 1H), 3.48 - 3.36 (m, 2H), 3.29 (d, *J* = 10.8 Hz, 1H), 2.29 - 2.22 (m, 1H), 2.13 - 2.06 (m, 4H). Mass (m/z): 407.8 [M+H]⁺.

10

Compound 618

7-([4-(3-methoxypyrrolidin-1-yl)-2-methylphenyl]amino)-2,4-dihydro-1,4-benzoxazin-3-one



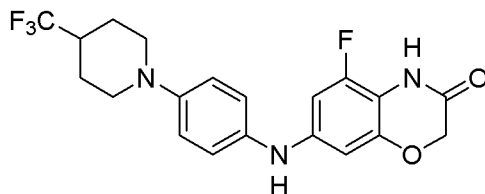
15

The titled compound **618** (3.6 mg, 1.6%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.33 (s, 1H), 7.01 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.43 (d, *J* = 2.4 Hz, 1H), 6.36 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.20 - 6.08 (m, 2H), 4.42 (s, 2H), 3.39 (dd, *J* = 10.8, 5.2 Hz, 2H), 3.26 (s, 3H), 3.22 (dd, *J* = 16.0, 8.8 Hz, 3H), 2.09 (s, 3H), 2.05 (dd, *J* = 10.0, 5.2 Hz, 2H). Mass (m/z): 353.9 [M+H]⁺.

20

Compound 619

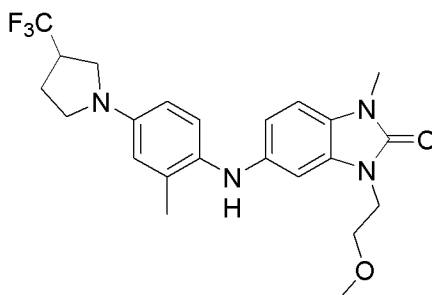
5-fluoro-7-({4-[4-(trifluoromethyl)piperidin-1-yl]phenyl}amino)-2,4-dihydro-1,4-benzoxazin-3-one



The titled compound **619** (5.1 mg, 3.08%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.60 (s, 1H), 7.92 (s, 1H), 6.94 (dd, *J* = 21.2, 9.2 Hz, 4H), 6.43 - 6.23 (m, 2H), 4.51 (s, 2H), 3.65 (d, *J* = 12.4 Hz, 2H), 2.63 (dd, *J* = 12.4, 10.4 Hz, 2H), 2.47 - 2.38 (m, 1H), 1.88 (d, *J* = 12.4 Hz, 2H), 1.64 - 1.49 (m, 2H). Mass (*m/z*): 409.9 [M+H]⁺.

Compound 620

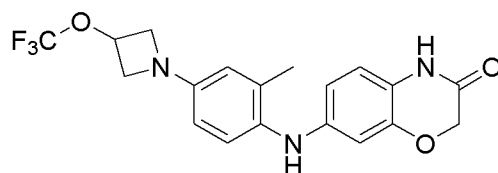
3-(2-methoxyethyl)-1-methyl-5-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)-1,3-dihydro-2H-benzo[d]imidazol-2-one



The titled compound **620** (79.2 mg, 28.7%) as a light purple solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.97 (d, *J* = 8.0 Hz, 1H), 6.91 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.53 (s, 1H), 6.48 (s, 1H), 6.44 (d, *J* = 8.4 Hz, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 3.84 (s, 2H), 3.55 - 3.44 (m, 3H), 3.33 (s, 2H), 3.29 (s, 2H), 3.24 (s, 3H), 3.20 (s, 3H), 2.26 (s, 1H), 2.13 (s, 3H), 2.07 (s, 1H). Mass (*m/z*): 449 [M+H]⁺.

Compound 621

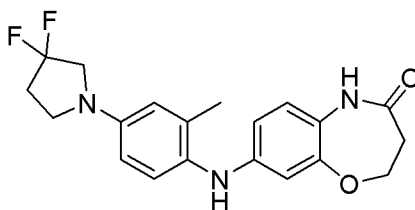
7-((2-methyl-4-(3-(trifluoromethoxy)azetidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **621** (4.6 mg, 5.8%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.35 (s, 1H), 7.06 (s, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.39 (s, 1H), 6.32 (d, J = 8.4 Hz, 1H), 6.25 - 6.11 (m, 2H), 5.27 (s, 1H), 4.43 (d, J = 3.2 Hz, 2H), 4.18 (t, J = 7.6 Hz, 2H), 3.81 (d, J = 8.4 Hz, 2H), 2.09 (d, J = 3.2 Hz, 3H). Mass(m/z): 394.3 $[\text{M}+\text{H}]^+$.

Compound 622

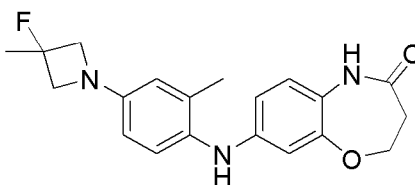
8-((4-(3,3-difluoropyrrolidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **622** (10.1 mg, 26.8%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.30 (s, 1H), 7.16 (s, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 6.53 (s, 1H), 6.46 (d, J = 8.8 Hz, 1H), 6.29 (d, J = 8.8 Hz, 1H), 6.18 (s, 1H), 4.30 (d, J = 7.2 Hz, 2H), 3.65 (t, J = 13.6 Hz, 2H), 3.43 (d, J = 7.6 Hz, 2H), 2.61 - 2.56 (m, 4H), 2.11 (s, 3H). Mass(m/z): 374.4 $[\text{M}+\text{H}]^+$.

Compound 623

8-((2-methyl-4-(3-(trifluoromethoxy)azetidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one

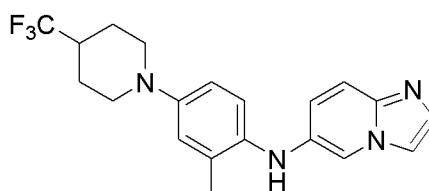


The titled compound **623** (4.8mg, 16.1%) as a red solid was prepared

according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.31 (s, 1H), 7.14 (s, 1H), 6.95 (d, J = 9.6 Hz, 1H), 6.83 - 6.71 (m, 1H), 6.38 (s, 1H), 6.31 (d, J = 7.2 Hz, 2H), 6.18 (s, 1H), 4.31 (q, J = 5.2 Hz, 2H), 3.87 (dd, J = 19.2, 3.2 Hz, 4H), 2.09 (d, J = 3.2 Hz, 3H),
 5 1.72 - 1.52 (m, 3H). Mass(m/z): 356.4 $[\text{M}+\text{H}]^+$.

Compound 624

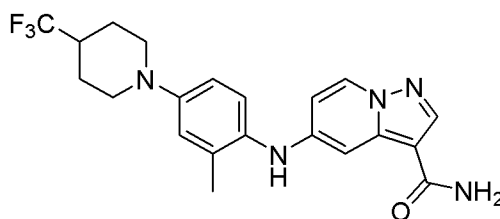
N-(2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)
 imidazo[1,2-*a*]pyridin-6-amine



10 The titled compound **624** (18.8 mg, 15%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.75 (s, 1H), 7.58 (d, J = 2.0 Hz, 1H), 7.44 - 7.34 (m, 2H), 7.03 (s, 1H), 7.02 - 6.94 (m, 2H), 6.88 (d, J = 2.8 Hz, 1H), 6.81 - 6.74 (m, 1H), 3.70 (d, J = 12.4 Hz, 2H), 2.71 - 2.60 (m, 2H), 2.48 - 2.43 (m, 1H),
 15 2.17 (s, 3H), 1.93 - 1.84 (m, 2H), 1.64 - 1.49 (m, 2H). Mass (m/z): 375.5 $[\text{M}+\text{H}]^+$.

Compound 625

5-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)
 pyrazolo[1,5-*a*]pyridine-3-carboxamide

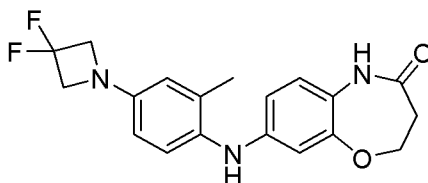


20 The titled compound **625** (16.1 mg, 34%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.39 (d, J = 7.6 Hz, 1H), 8.24 (s, 1H), 8.04 (s, 1H), 7.32 - 7.28 (m, 1H), 7.08 (d, J = 8.8 Hz, 1H), 6.94 (dd, J = 11.2, 2.8 Hz, 2H), 6.84 (dd, J = 8.8, 2.8 Hz, 1H), 6.67 - 6.62 (m, 1H), 6.56 (dd, J = 7.6, 2.4 Hz, 1H), 3.79 (d, J = 12.4 Hz, 2H), 2.77 - 2.66 (m, 2H), 2.45 - 2.38 (m,
 25

1H), 2.14 (s, 3H), 1.89 (d, $J = 12.4$ Hz, 2H), 1.65 - 1.50 (m, 2H). Mass (m/z): 420.5 $[M+H]^+$.

Compound 626

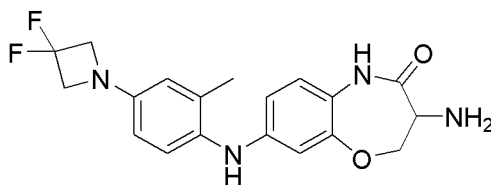
8-((4-(3,3-difluoroazetidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **626** (10.5 mg, 28.1%) as a red solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.33 (s, 1H), 7.19 (s, 1H), 7.00 (d, $J = 8.4$ Hz, 1H), 6.78 (d, $J = 8.4$ Hz, 1H), 6.47 (d, $J = 2.8$ Hz, 1H), 6.39 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.33 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.21 (d, $J = 2.4$ Hz, 1H), 4.31 (t, $J = 6.0$ Hz, 2H), 4.22 (t, $J = 12.4$ Hz, 4H), 2.57 (t, $J = 6.0$ Hz, 2H), 2.11 (s, 3H). Mass(m/z): 360.4 $[M+H]^+$.

Compound 627

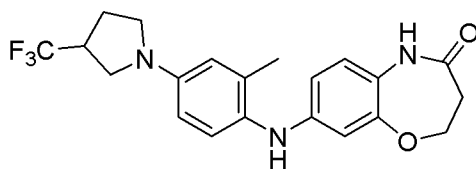
3-amino-8-((4-(3,3-difluoroazetidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **627** (8.1mg, 32.3%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.47 (s, 1H), 7.26 (s, 1H), 7.01 (d, $J = 8.4$ Hz, 1H), 6.77 (d, $J = 8.4$ Hz, 1H), 6.48 (d, $J = 2.8$ Hz, 1H), 6.38 (ddd, $J = 18.0, 8.4, 2.8$ Hz, 2H), 6.27 (d, $J = 2.4$ Hz, 1H), 4.32 - 4.16 (m, 4H), 3.92 (t, $J = 10.8$ Hz, 1H), 3.58 (dd, $J = 11.2, 6.4$ Hz, 1H), 2.11 (s, 3H), 1.79 (s, 1H). Mass(m/z): 375.2 $[M+H]^+$.

Compound 628

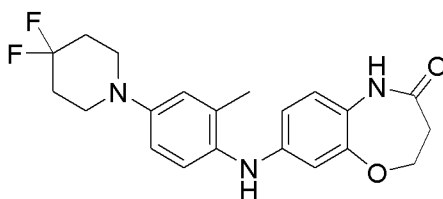
8-((2-methyl-4-(3-(trifluoromethyl)pyrrolidin-1-yl)phenyl)amino)-2,3-

dihydrobenzo[b][1,4]oxazepin-4(5H)-one

The titled compound **628** (22.3 mg, 34.4%) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.30 (s, 1H), 7.13 (s, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.53 (d, *J* = 2.8 Hz, 1H), 6.45 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.28 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.16 (d, *J* = 2.4 Hz, 1H), 4.31 (t, *J* = 6.0 Hz, 2H), 3.50 (t, *J* = 8.8 Hz, 1H), 3.41 - 3.34 (m, 2H), 3.31 - 3.23 (m, 2H), 2.56 (t, *J* = 6.0 Hz, 2H), 2.31 - 2.21 (m, 1H), 2.10 (s, 3H), 2.09 - 2.02 (m, 1H). Mass (m/z): 406.2 [M+H]⁺.

Compound 629

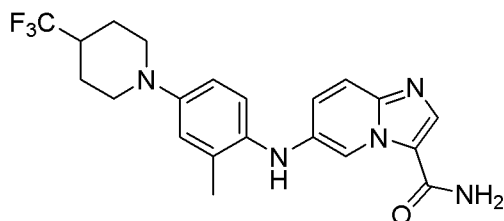
8-((4-(4,4-difluoropiperidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[b][1,4]oxazepin-4(5H)-one



The titled compound **629** (17 mg, 20.6 %) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.34 (s, 1H), 7.19 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 2.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 3.6 Hz, 2H), 6.37 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.27 (d, *J* = 2.4 Hz, 1H), 4.32 (t, *J* = 6.0 Hz, 2H), 3.29 - 3.19 (m, 4H), 2.57 (t, *J* = 6.0 Hz, 2H), 2.12 (s, 3H), 2.10 - 2.00 (m, 4H). Mass (m/z): 388.2 [M+H]⁺.

Compound 630

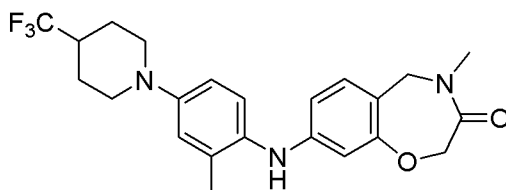
*6-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)imidazo[1,2-*a*]pyridine-3-carboxamide*



The titled compound **630** (10 mg, 21%) as an grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.92 (d, *J* = 2.0 Hz, 1H), 8.32 (s, 1H), 8.03 - 7.83 (m, 1H), 7.66 (d, *J* = 9.6 Hz, 1H), 7.60 (s, 1H), 7.48 - 7.27 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.98 - 6.87 (m, 1H), 6.81 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.74 (d, *J* = 12.4 Hz, 2H), 2.71 (t, *J* = 11.6 Hz, 2H), 2.46 - 2.37 (m, 1H), 2.17 (s, 3H), 1.89 (d, *J* = 11.6 Hz, 2H), 1.67 - 1.48 (m, 2H). Mass (*m/z*): 420.5 [M+H]⁺.

Compound 631

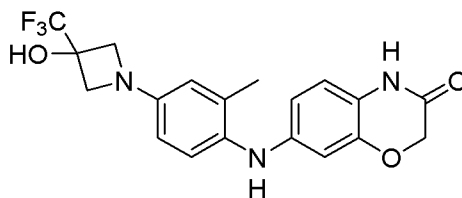
4-methyl-8-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-4,5-dihydrobenzo[f][1,4]oxazepin-3(2H)-one



The titled compound **631** (56 mg, 33%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.33 (s, 1H), 7.01 - 6.90 (m, 2H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.25 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.13 (d, *J* = 2.4 Hz, 1H), 4.61 (s, 2H), 4.45 (s, 2H), 3.71 (d, *J* = 12.0 Hz, 2H), 2.95 (s, 3H), 2.72 - 2.60 (m, 2H), 2.47 - 2.43 (m, 1H), 2.10 (s, 3H), 1.88 (d, *J* = 12.0 Hz, 2H), 1.63 - 1.48 (m, 2H). Mass (*m/z*): 434.5 [M+H]⁺.

Compound 632

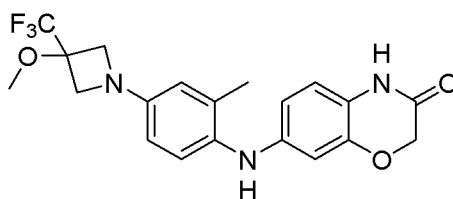
7-({4-[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]-2-methylphenyl}amino)-2,4-dihydro-1,4-benzoxazin-3-one



The titled compound **632** (1.6 mg, 0.64%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.37 (s, 1H), 7.25 (s, 1H), 7.07 (s, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.41 (d, J = 2.4 Hz, 1H), 6.33 (dd, J = 8.4, 2.4 Hz, 1H), 6.21 (dd, J = 8.4, 2.4 Hz, 1H), 6.17 (d, J = 2.0 Hz, 1H), 4.44 (s, 2H), 4.10 (d, J = 8.8 Hz, 2H), 3.76 (d, J = 8.8 Hz, 2H), 2.09 (s, 3H). Mass (m/z): 393.8 $[\text{M}+\text{H}]^+$.

Compound 633

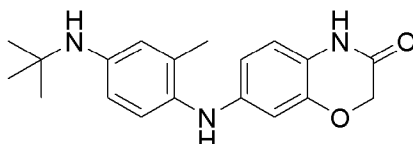
10 7-((4-[3-methoxy-3-(trifluoromethyl)azetidin-1-yl]-2-methylphenyl}
amino)-2,4-dihydro-1,4-benzoxazin-3-one



The titled compound **633** (4.0 mg, 1.82%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.36 (s, 1H), 7.08 (s, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.43 (d, J = 2.4 Hz, 1H), 6.36 (dd, J = 8.4, 2.4 Hz, 1H), 6.24 - 6.16 (m, 2H), 4.44 (s, 2H), 4.05 - 3.98 (m, 4H), 3.47 (s, 3H), 2.10 (s, 3H). Mass (m/z): 407.8 $[\text{M}+\text{H}]^+$.

Compound 634

20 7-((4-(*tert*-butylamino)-2-methylphenyl)amino)-2H-benzo[*b*][1,4]
oxazin-3(4H)-one



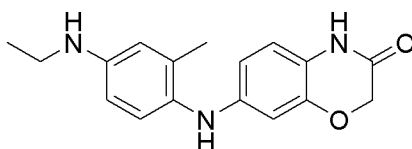
The titled compound **634** (15.4 mg, 10.8%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz,

DMSO- d_6) δ 10.29 (s, 1H), 6.92 (s, 1H), 6.81 (d, $J = 8.4$ Hz, 1H), 6.65 - 6.59 (m, 2H), 6.55 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.20 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.15 (d, $J = 2.4$ Hz, 1H), 4.66 (s, 1H), 4.43 (s, 2H), 2.04 (s, 3H), 1.26 (s, 9H). Mass (m/z): 326.2 $[M+H]^+$.

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Compound 635

7-((4-(ethylamino)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

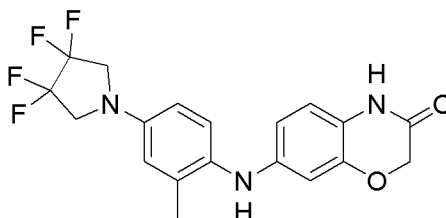


The titled compound **635** (20.4 mg, 15.6 %) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.28 (s, 1H), 6.90 (s, 1H), 6.82 (d, $J = 8.4$ Hz, 1H), 6.61 (d, $J = 8.4$ Hz, 1H), 6.44 (d, $J = 2.4$ Hz, 1H), 6.37 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.20 - 6.04 (m, 2H), 5.24 (s, 1H), 4.42 (s, 2H), 3.00 (q, $J = 7.2$ Hz, 2H), 2.03 (s, 3H), 1.15 (t, $J = 7.2$ Hz, 3H). Mass (m/z): 298.2 $[M+H]^+$.

15

Compound 636

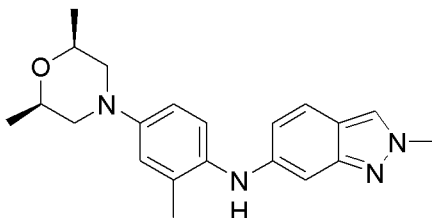
7-((2-methyl-4-(3,3,4,4-tetrafluoropyrrolidin-1-yl)phenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



The titled compound **636** (16.3 mg, 15.1%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.37 (s, 1H), 7.12 (s, 1H), 7.00 (d, $J = 8.8$ Hz, 1H), 6.70 - 6.61 (m, 2H), 6.56-6.50 (m, 1H), 6.27 - 6.17 (m, 2H), 4.44 (s, 2H), 4.03-3.88 (m, 4H), 2.12 (s, 3H). Mass(m/z): 396.2 $[M+H]^+$.

Compound 637

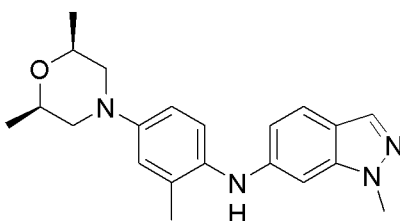
25 *N*-(4-((2*S*,6*R*)-2,6-dimethylmorpholino)-2-methylphenyl)-2-methyl-2H-indazol-6-amine



The titled compound **637** (78.8 mg, 50.0%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 8.04 (s, 1H), 7.43 (d, J = 8.8 Hz, 1H), 7.18 (s, 1H), 7.04 (d, J = 8.8 Hz, 1H), 6.86 (d, J = 2.8 Hz, 1H), 6.79-6.75 (m, 1H), 6.72-6.68 (m, 1H), 6.36 - 6.31 (m, 1H), 3.99 (s, 3H), 3.74-3.64 (m, 2H), 3.55-3.50 (m, 2H), 2.27-2.19 (m, 2H), 2.15 (s, 3H), 1.15 (d, J = 6.4 Hz, 6H). Mass(m/z): 351.1 $[\text{M}+\text{H}]^+$.

Compound 638

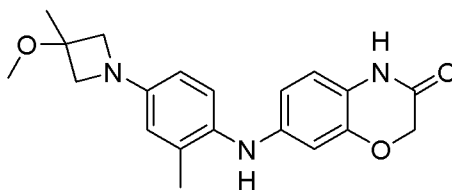
10 *N*-(4-((2*S*,6*R*)-2,6-dimethylmorpholino)-2-methylphenyl)-1-methyl-1*H*-indazol-6-amine



The titled compound **638** (78.5 mg, 49.8%) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.74 (s, 1H), 7.53 - 7.37 (m, 2H), 7.10 (d, J = 8.8 Hz, 1H), 6.88 (d, J = 2.8 Hz, 1H), 6.83 - 6.76 (m, 1H), 6.71 - 6.64 (m, 1H), 6.37 (s, 1H), 3.77 (s, 3H), 3.73 - 3.63 (m, 2H), 3.60 - 3.50 (m, 2H), 2.28 - 2.20 (m, 2H), 2.16 (s, 3H), 1.16 (d, J = 6.4 Hz, 6H). Mass(m/z): 351.2 $[\text{M}+\text{H}]^+$.

Compound 639

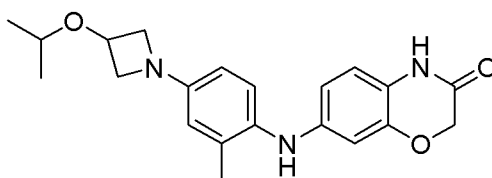
20 7-((4-(3-methoxy-3-methylazetidin-1-yl)-2-methylphenyl)amino)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one



The titled compound **639** (10.2 mg, 5.65%) as a purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.34 (s, 1H), 7.03 (s, 1H), 6.93 (s, 1H), 6.64 (s, 1H), 6.26-6.28 (s, 1H), 6.19- 6.20 (s, 1H), 6.17- 6.18 (s, 1H), 6.14- 6.15 (s, 1H), 4.43 (m, 2H), 3.62- 3.65 (m, 4H), 3.18 (m, 3H), 2.07 (m, 3H), 1.47 (m, 3H). Mass(m/z): 354. 2 $[\text{M}+\text{H}]^+$.

Compound 640

7-((4-(3-isopropoxyazetidin-1-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one



10

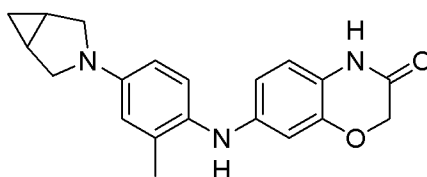
The titled compound **640** (7.1 mg, 2.88%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.34 (s, 1H), 7.02 (s, 1H), 6.91 (d, $J = 8.4$ Hz, 1H), 6.63 (d, $J = 8.4$ Hz, 1H), 6.33 - 6.32 (m, 1H), 6.27 - 6.24 (m, 1H), 6.20 - 6.17 (m, 1H), 6.15 - 6.14 (m, 1H), 4.52 - 4.37 (m, 3H), 4.06 (t, $J = 7.2$ Hz, 2H), 3.66 - 3.60 (m, 1H), 3.48 - 3.45 (m, 2H), 2.07 (s, 3H), 1.10 (d, $J = 6.0$ Hz, 6H). Mass (m/z): 368.2 $[\text{M}+\text{H}]^+$.

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Compound 641

7-((4-(3-azabicyclo[3.1.0]hexan-3-yl)-2-methylphenyl)amino)-2H-benzo[b][1,4]oxazin-3(4H)-one

20



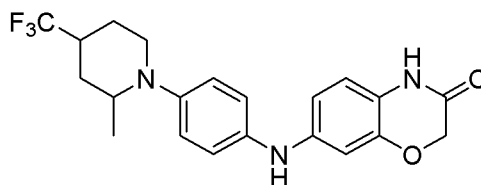
The titled compound **641** (5 mg, 2%) as a white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.34 (s, 1H), 7.01 (s, 1H), 6.89 (d, $J = 8.4$ Hz, 1H), 6.63 (d, $J = 8.4$ Hz, 1H), 6.38 (s, 2H), 6.18 - 6.11 (m, 2H), 4.42 (s, 2H), 3.46 (d, $J = 9.2$ Hz, 2H), 3.11 (d, $J = 8.4$ Hz, 2H), 2.07 (s, 3H), 1.68 - 1.63 (m, 2H),

25

0.68 (td, $J = 7.6, 4.0$ Hz, 1H), 0.27 (d, $J = 4.0$ Hz, 1H). Mass (m/z): 336.2 $[M+H]^+$.

Compound 642

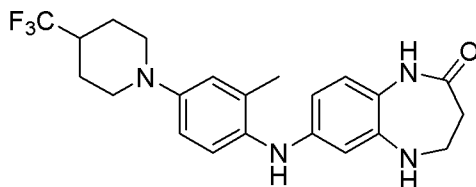
7-((4-(2-methyl-4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2H-
benzo[b][1,4]oxazin-3(4H)-one



The titled compound **642** (6.5 mg, 8.3%) as a purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.50 (s, 1H), 7.93 (s, 1H), 7.06 - 6.87 (m, 4H), 6.76 (d, $J = 8.4$ Hz, 1H), 6.69 - 6.52 (m, 2H), 4.50 (s, 2H), 3.02 (d, $J = 11.6$ Hz, 1H), 2.84 (t, $J = 7.6$ Hz, 1H), 2.78 - 2.68 (m, 1H), 1.96 - 1.76 (m, 2H), 1.56 (tt, $J = 12.6, 6.4$ Hz, 1H), 1.35 - 1.12 (m, 2H), 0.84 (d, $J = 6.0$ Hz, 3H). Mass(m/z): 406.2 $[M+H]^+$.

Compound 643

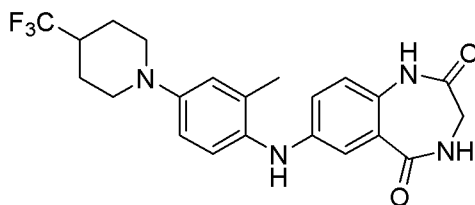
7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,3,4,5-tetrahydro-2H-benzo[b][1,4]diazepin-2-one



The titled compound **643** (2.5mg, 12.3%) as a blue solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 6.90 - 6.77 (m, 2H), 6.67 (dd, $J = 8.8, 3.2$ Hz, 1H), 6.61 (d, $J = 8.0$ Hz, 2H), 6.56 - 6.44 (m, 2H), 4.87 (s, 2H), 3.65 - 3.53 (m, 3H), 2.97 (t, $J = 4.4$ Hz, 2H), 2.61 - 2.59 (m, 2H), 2.12 (s, 3H), 1.87 (d, $J = 12.4$ Hz, 2H), 1.61 - 1.51 (m, 2H). Mass(m/z): 419.2 $[M+H]^+$.

Compound 644

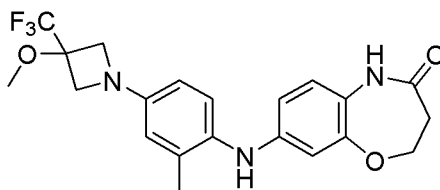
7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-3,4-dihydro-1H-benzo[e][1,4]diazepine-2,5-dione



The titled compound **644** (12.3 mg, 14.7%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.12 (s, 1H), 8.48 (t, $J = 5.6$ Hz, 1H), 7.40 (s, 2H), 7.27 (s, 2H), 7.15 (s, 2H), 6.97 (d, $J = 8.4$ Hz, 1H), 3.65 (s, 2H), 3.56 (d, $J = 5.6$ Hz, 4H), 2.21 (s, 3H), 2.00 (d, $J = 11.2$ Hz, 2H). Mass(m/z): 433.2 $[\text{M}+\text{H}]^+$.

Compound 645

8-[4-[3-methoxy-3-(trifluoromethyl)azetidin-1-yl]-2-methyl-anilino]-3,5-dihydro-2H-1,5-benzoxazepin-4-one



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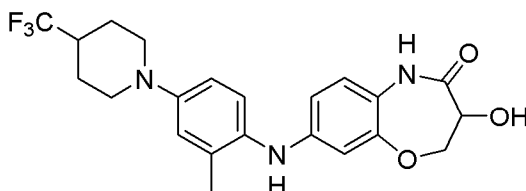
The titled compound **645** (52 mg, 82%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.32 (s, 1H), 7.17 (s, 1H), 6.98 (d, $J = 8.4$ Hz, 1H), 6.78 (d, $J = 8.4$ Hz, 1H), 6.44 (d, $J = 2.8$ Hz, 1H), 6.37 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.31 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.20 (d, $J = 2.4$ Hz, 1H), 4.31 (t, $J = 6.0$ Hz, 2H), 4.07 - 3.97 (m, 4H), 3.48 (s, 3H), 2.60 - 2.53 (m, 2H), 2.10 (s, 3H). Mass (m/z): 422.4 $[\text{M}+\text{H}]^+$.

15

Compound 646

3-hydroxy-8-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5H)-one

20

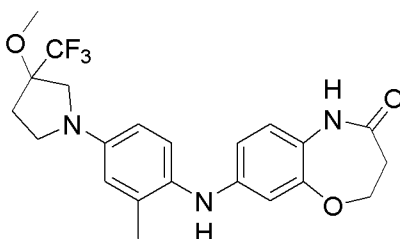


The titled compound **646** (5.6 mg, 13.12 %) as a grey solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz,

DMSO-*d*₆) δ 10.35 (s, 1H), 7.05 (s, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 2.8 Hz, 1H), 6.78 - 6.72 (m, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.29 - 6.20 (m, 2H), 5.00 (t, *J* = 5.6 Hz, 1H), 4.51 - 4.47 (m, 1H), 3.81 - 3.64 (m, 4H), 2.70 - 2.60 (m, 2H), 2.47 - 2.38 (m, 1H), 2.11 (s, 3H), 1.92 - 1.83 (m, 2H), 1.64 - 1.48 (m, 2H). Mass(*m/z*): 436.2 [M+H]⁺.

Compound 647

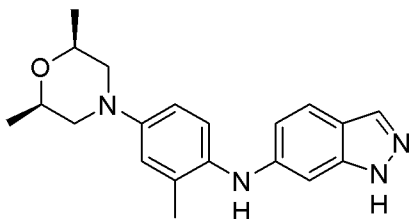
8-((4-(3-methoxy-3-(trifluoromethyl)pyrrolidin-1-yl)-2-methylphenyl)amino)-2,3-dihydrobenzo[*b*][1,4]oxazepin-4(5*H*)-one



The titled compound **647** (20 mg, 35.52 %) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.30 (s, 1H), 7.14 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.55 (d, *J* = 2.8 Hz, 1H), 6.50-6.44 (m, 1H), 6.31-6.26 (m, 1H), 6.17 (d, *J* = 2.4 Hz, 1H), 4.31 (t, *J* = 6.0 Hz, 2H), 3.58 (d, *J* = 11.6 Hz, 1H), 3.50 (d, *J* = 11.6 Hz, 1H), 3.46-3.38 (m, 3H), 3.33 (s, 3H), 2.56 (t, *J* = 6.0 Hz, 2H), 2.46-2.36 (m, 1H), 2.35-2.24 (m, 1H), 2.11 (s, 3H). Mass(*m/z*): 436.1 [M+H]⁺.

Compound 648

N-(2-methyl-4-((2*S*,6*R*)-2,6-dimethylmorpholino)phenyl)-1*H*-indazol-6-amine



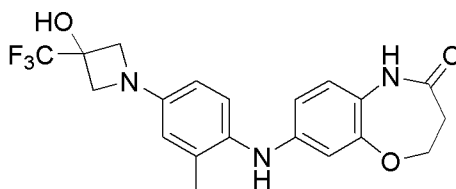
The titled compound **648** (48.5 mg, 60.42 %) as a grey solid was prepared according to the procedure outlined for compound **1**. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.28 (s, 1H), 7.76 (s, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.39 (s,

1H), 7.06 (d, $J = 8.8$ Hz, 1H), 6.88 (d, $J = 2.8$ Hz, 1H), 6.81 - 6.75 (m, 1H), 6.70-6.63 (m, 1H), 6.36 - 6.31 (m, 1H), 3.76 - 3.63 (m, 2H), 3.57 - 3.49 (m, 2H), 2.28 - 2.20 (m, 2H), 2.14 (s, 3H), 1.16 (d, $J = 6.4$ Hz, 6H). Mass(m/z): 337.1 $[M+H]^+$.

5

Compound 649

8-[4-[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]-2-methyl-anilino]-3,5-dihydro-2H-1,5-benzoxazepin-4-one

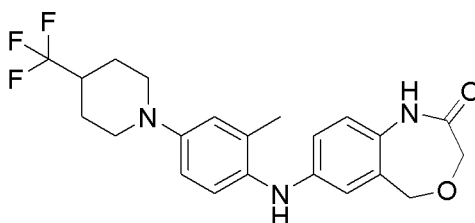


The titled compound **649** (3.9 mg, 9.80%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.31 (s, 1H), 7.23 (s, 1H), 7.15 (s, 1H), 6.97 (d, $J = 8.4$ Hz, 1H), 6.77 (d, $J = 8.4$ Hz, 1H), 6.41 (d, $J = 2.8$ Hz, 1H), 6.38 - 6.26 (m, 2H), 6.18 (d, $J = 2.4$ Hz, 1H), 4.35 - 4.27 (m, 2H), 4.10 (d, $J = 8.8$ Hz, 2H), 3.77 (d, $J = 8.8$ Hz, 2H), 2.60 - 2.52 (m, 2H), 2.09 (s, 3H). Mass (m/z): 408.4 $[M+H]^+$.

15

Compound 650

7-((2-methyl-4-(4-(trifluoromethyl)piperidin-1-yl)phenyl)amino)-1,5-dihydrobenzo[e][1,4]oxazepin-2(3H)-one



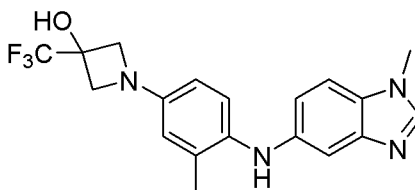
The titled compound **650** (7.2 mg, 39%) as a brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 9.90 (s, 1H), 7.11 (s, 1H), 6.93 (dd, $J = 24.8, 8.4$ Hz, 2H), 6.84 (d, $J = 2.8$ Hz, 1H), 6.74 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.57 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.47 (d, $J = 2.8$ Hz, 1H), 4.54 (s, 2H), 4.31 (s, 2H), 3.68 (d, $J = 12.0$ Hz, 2H), 2.71 - 2.63 (m, 2H), 2.43 - 2.41 (m, 1H), 2.11 (s, 3H),

25

1.88 (d, $J = 12.0$ Hz, 2H), 1.57 (tt, $J = 12.8, 6.4$ Hz, 2H). Mass(m/z): 420.2 $[M+H]^+$.

Compound 651

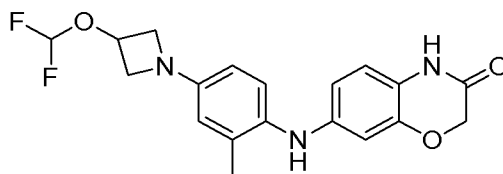
5 *1-[3-methyl-4-[(1-methylbenzimidazol-5-yl)amino]phenyl]-3-(trifluoromethyl)azetidin-3-ol*



The titled compound **651** (51 mg, 32%) as a yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 7.94 (s, 1H), 7.30 (d, $J = 8.8$ Hz, 1H), 7.22 (s, 1H), 6.98 (d, $J = 8.4$ Hz, 1H), 6.91 (s, 1H), 6.76 (dd, $J = 8.8, 2.0$ Hz, 1H), 6.72 (d, $J = 2.0$ Hz, 1H), 6.42 (d, $J = 2.8$ Hz, 1H), 6.34 (dd, $J = 8.4, 2.8$ Hz, 1H), 4.10 (d, $J = 8.8$ Hz, 2H), 3.77 (d, $J = 8.8$ Hz, 2H), 3.74 (s, 3H), 2.12 (s, 3H). Mass (m/z): 377.5 $[M+H]^+$.

Compound 652

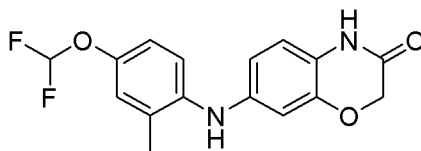
15 *7-[4-[3-(difluoromethoxy)azetidin-1-yl]-2-methyl-anilino]-4H-1,4-benzoxazin-3-one*



The titled compound **652** (23 mg, 14%) as a purple solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.34 (s, 1H), 7.04 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 6.77 (t, $J = 75.2$ Hz, 1H), 6.63 (d, $J = 8.4$ Hz, 1H), 6.37 (d, $J = 2.8$ Hz, 1H), 6.29 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.20 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.16 (d, $J = 2.4$ Hz, 1H), 5.09 - 4.99 (m, 1H), 4.43 (s, 2H), 4.17 - 4.09 (m, 2H), 3.74 - 3.66 (m, 2H), 2.08 (s, 3H). Mass (m/z): 376.4 $[M+H]^+$.

25 *Compound 653*

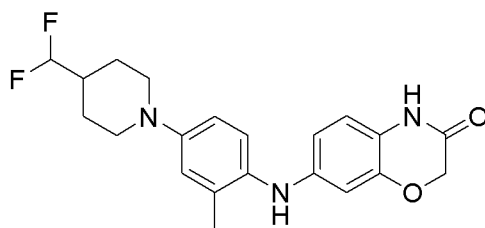
7-[4-(difluoromethoxy)-2-methyl-anilino]-4H-1,4-benzoxazin-3-one



The titled compound **653** (9.0 mg, 9%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.48 (s, 1H), 7.27 (s, 1H), 7.09 (d, $J = 2.0$ Hz, 1H), 7.07 (t, $J = 76$ Hz, 1H), 7.02 (d, $J = 2.8$ Hz, 1H), 6.95 - 6.88 (m, 1H), 6.73 (d, $J = 8.4$ Hz, 1H), 6.51 - 6.42 (m, 2H), 4.49 (s, 2H), 2.18 (s, 3H). Mass (m/z): 321.4 $[\text{M}+\text{H}]^+$.

Compound 654

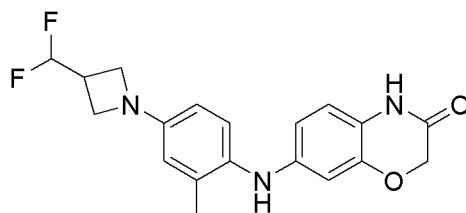
7-[4-[4-(difluoromethyl)-1-piperidyl]-2-methyl-anilino]
-4H-1,4-benzoxazin-3-one



The titled compound **654** (25 mg, 18%) as a brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.35 (s, 1H), 7.05 (s, 1H), 6.95 (d, $J = 8.8$ Hz, 1H), 6.82 (d, $J = 2.8$ Hz, 1H), 6.74 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 6.27 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.23 (d, $J = 2.4$ Hz, 1H), 5.95 (td, $J = 56.8, 4.4$ Hz, 1H), 4.44 (s, 2H), 3.65 (d, $J = 12.0$ Hz, 2H), 2.66 - 2.56 (m, 2H), 2.10 (s, 3H), 2.02 - 1.85 (m, 1H), 1.79 - 1.71 (m, 2H), 1.54 - 1.39 (m, 2H). Mass (m/z): 388.5 $[\text{M}+\text{H}]^+$.

Compound 655

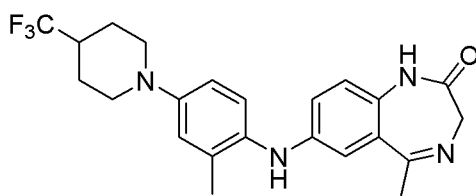
7-[4-[3-(difluoromethyl)azetidin-1-yl]-2-methyl-anilino]
-4H-1,4-benzoxazin-3-one



The titled compound **655** (21 mg, 14%) as an off-white solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.33 (s, 1H), 7.03 (s, 1H), 6.93 (d, $J = 8.4$ Hz, 1H), 6.63 (d, $J = 8.4$ Hz, 1H), 6.51 - 6.20 (m, 3H), 6.19 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.15 (d, $J = 2.4$ Hz, 1H), 4.43 (s, 2H), 3.88 (t, $J = 8.0$ Hz, 2H), 3.71 (dd, $J = 7.6, 5.6$ Hz, 2H), 3.24 - 3.11 (m, 1H), 2.08 (s, 3H). Mass (m/z): 360.5 $[\text{M}+\text{H}]^+$.

Compound 656

5-methyl-7-[2-methyl-4-[4-(trifluoromethyl)-1-piperidyl]anilino]-1,3-dihydro-1,4-benzodiazepin-2-one



10

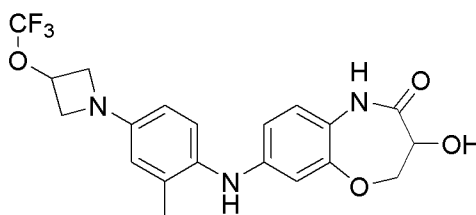
The titled compound **656** (15 mg, 9%) as a light yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.01 (s, 1H), 7.34 (s, 1H), 7.02 (d, $J = 8.8$ Hz, 1H), 6.91 (d, $J = 8.8$ Hz, 1H), 6.88 - 6.84 (m, 2H), 6.81 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.77 (dd, $J = 8.8, 2.8$ Hz, 1H), 3.83 (s, 2H), 3.70 (d, $J = 12.4$ Hz, 2H), 2.71 - 2.60 (m, 2H), 2.47 - 2.40 (m, 1H), 2.27 (s, 3H), 2.14 (s, 3H), 1.93 - 1.84 (m, 2H), 1.64 - 1.49 (m, 2H). Mass (m/z): 431.5 $[\text{M}+\text{H}]^+$.

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Compound 657

3-hydroxy-8-[2-methyl-4-[3-(trifluoromethoxy)azetidin-1-yl]anilino]-3,5-dihydro-2H-1,5-benzoxazepin-4-one

20



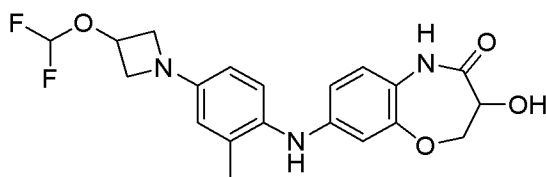
The titled compound **657** (2.3 mg, 5%) as a light yellow solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.32 (s, 1H), 7.02 (s, 1H), 6.95 (d, $J = 8.4$ Hz, 1H), 6.59 (d, $J = 8.4$ Hz, 1H), 6.39 (d, $J = 2.8$ Hz, 1H), 6.32 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.22 - 6.13 (m, 2H), 5.30 - 5.23 (m, 1H), 4.98 (t, $J = 5.6$ Hz, 1H), 4.48 (dd, $J =$

25

5.2, 3.2 Hz, 1H), 4.19 (dd, $J = 8.8, 6.4$ Hz, 2H), 3.82 (dd, $J = 8.8, 4.0$ Hz, 2H), 3.79 - 3.65 (m, 2H), 2.09 (s, 3H). Mass (m/z): 424.5 $[M+H]^+$.

Compound 658

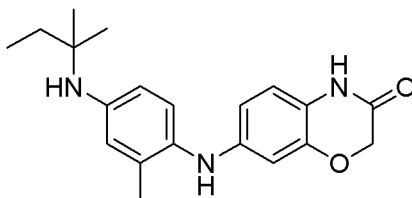
8-[4-[3-(difluoromethoxy)azetidin-1-yl]-2-methyl-anilino]-3-hydroxy
-3,5-dihydro-2H-1,5-benzoxazepin-4-one



The titled compound **658** (6.8 mg, 10%) as a pink solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.32 (s, 1H), 7.01 (s, 1H), 6.94 (d, $J = 8.4$ Hz, 1H), 6.78 (t, $J = 74.8$ Hz, 1H), 6.61 - 6.57 (m, 1H), 6.37 (d, $J = 2.8$ Hz, 1H), 6.30 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.18 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.15 (d, $J = 2.4$ Hz, 1H), 5.09 - 4.95 (m, 2H), 4.51 - 4.44 (m, 1H), 4.17 - 4.09 (m, 2H), 3.80 - 3.65 (m, 4H), 2.09 (s, 3H). Mass (m/z): 406.5 $[M+H]^+$.

Compound 659

7-[4-(1,1-dimethylpropylamino)-2-methyl-anilino]-4H-1,4-benzoxazin-3-one



The titled compound **659** (14 mg, 7%) as a light brown solid was prepared according to the procedure outlined for compound **1**. ^1H NMR (400 MHz, DMSO- d_6) δ 10.32 (s, 1H), 6.93 (s, 1H), 6.80 (d, $J = 8.4$ Hz, 1H), 6.66 - 6.57 (m, 2H), 6.53 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.19 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.14 (d, $J = 2.4$ Hz, 1H), 4.66 (s, 1H), 4.43 (s, 2H), 2.03 (s, 3H), 1.60 (q, $J = 7.2$ Hz, 2H), 1.20 (s, 6H), 0.82 (t, $J = 7.4$ Hz, 3H). Mass (m/z): 340.5 $[M+H]^+$.

Example 2. Determination of EC50 values in HT-1080 cell viability assay

HT-1080 (ATCC, CCL-121) cells (6000 in 100 μ l) were seeded in 96-well plates (Corning) and cultured in a 37°C incubator with a humidified atmosphere of 5% CO₂ for overnight. Cells were then treated with ferroptosis inducer RSL3 (TargetMol) and a 3-fold, 10-point serial dilution series of compounds with 1.1 μ M as the highest concentration, for 20 hours. Cell viability was assessed using the Cell Titer-Glo Kit (Promega). The luminescence intensity was measured with a microplate reader (Envision, PerkinElmer), and cell viability was calculated by normalizing the data to untreated controls. The EC₅₀ values of the compounds (e.g., Compounds 1-659) were calculated in GraphPad Prism (GraphPad Software, Inc., San Diego, CA, USA). The curves were fitted using a non-linear regression model with a sigmoidal dose response.

Ferroptosis inhibitory activity of compounds 1-447 is summarized in Table 2. In Table 2, activity is provided as follows: +++ = 0.1 nM $\leq$ EC₅₀ < 100 nM; ++ = 100 nM $\leq$ EC₅₀ < 1000 nM; + = 1000 nM $\leq$ EC₅₀ < 10000 nM.

Table 2. EC₅₀ Values of Compounds 1 to 447

Cmpd No.	EC₅₀ (nM)	Cmpd No.	EC₅₀ (nM)	Cmpd No.	EC₅₀ (nM)
1	+++	153	+++	305	++
2	+++	154	+++	306	++
3	+++	155	+++	307	++
4	+++	156	+++	308	+++
5	+++	157	+++	309	+++
6	+++	158	+++	310	+++
7	+++	159	+++	311	+++
8	+++	160	+++	312	+++
9	+++	161	+++	313	+++
10	+++	162	+++	314	+++
11	+++	163	+++	315	+++
12	+++	164	+++	316	+++
13	+++	165	+++	317	+++
14	+++	166	+++	318	+++
15	+++	167	+++	319	+++

16	+++	168	+++	320	+++
17	+++	169	+++	321	+++
18	+++	170	+++	322	+++
19	+++	171	+++	323	+++
20	+++	172	+++	324	+++
21	+++	173	+++	325	+++
22	+++	174	+++	326	+++
23	+++	175	+++	327	+++
24	+++	176	+++	328	+++
25	+++	177	+++	329	+++
26	+++	178	+++	330	+++
27	+++	179	+++	331	++
28	+++	180	+++	332	+++
29	+++	181	+++	333	+++
30	+++	182	+++	334	+++
31	+++	183	+++	335	+++
32	+++	184	+++	336	+++
33	+++	185	+++	337	+++
34	++	186	+++	338	+++
35	+++	187	+++	339	+++
36	+++	188	++	340	+++
37	+++	189	+++	341	+++
38	+++	190	+++	342	++
39	++	191	+++	343	+++
40	+++	192	+++	344	+++
41	+++	193	+++	345	+++
42	+++	194	+++	346	++
43	+++	195	+++	347	+++
44	+++	196	+++	348	+++
45	+++	197	+++	349	+++
46	+++	198	+++	350	+++
47	+++	199	+++	351	+++
48	+++	200	+++	352	+++
49	+++	201	+++	353	+++
50	+++	202	+++	354	+++
51	+++	203	+++	355	+++
52	+++	204	+++	356	+++
53	+++	205	+++	357	+++
54	+++	206	+++	358	+++

55	+++	207	+++	359	+++
56	+++	208	+++	360	+++
57	+++	209	+++	361	++
58	+++	210	+++	362	+++
59	+++	211	+++	363	+++
60	+++	212	+++	364	+++
61	+++	213	+++	365	+++
62	+++	214	+++	366	+++
63	+++	215	+++	367	+++
64	+++	216	+++	368	+++
65	+++	217	+++	369	++
66	+++	218	+++	370	+++
67	+++	219	+++	371	+++
68	+++	220	+++	372	+++
69	+++	221	+++	373	+++
70	+++	222	+++	374	+++
71	+++	223	+++	375	+++
72	+++	224	+++	376	+++
73	+++	225	+++	377	+++
74	+++	226	+++	378	+++
75	+++	227	+++	379	+++
76	+++	228	+++	380	+++
77	+++	229	+++	381	+++
78	+++	230	+++	382	+++
79	+++	231	+++	383	+++
80	+++	232	+++	384	+++
81	+++	233	++	385	+++
82	+++	234	+++	386	+++
83	+++	235	+++	387	+++
84	+++	236	+++	388	+++
85	+++	237	+++	389	+++
86	+++	238	+	390	+++
87	+++	239	+++	391	+++
88	+++	240	+++	392	+++
89	+++	241	+++	393	+++
90	+++	242	+++	394	+++
91	+++	243	+++	395	+++
92	+++	244	+++	396	+++
93	+++	245	+++	397	+++

94	+++	246	+++	398	+++
95	+++	247	+++	399	+++
96	+++	248	+++	400	+++
97	+++	249	+++	401	+++
98	+++	250	+++	402	+++
99	+++	251	+++	403	+++
100	+++	252	+++	404	+++
101	++	253	+++	405	+++
102	+++	254	+++	406	+++
103	++	255	+++	407	+++
104	+++	256	+++	408	+++
105	+++	257	+++	409	+++
106	+++	258	+++	410	+++
107	+++	259	+++	411	+++
108	+++	260	+++	412	+++
109	+++	261	+++	413	+++
110	+++	262	+++	414	+++
111	+++	263	+++	415	+++
112	+++	264	+++	416	+++
113	+++	265	+++	417	+++
114	+++	266	+++	418	+++
115	+++	267	+++	419	+++
116	+++	268	+++	420	+++
117	+++	269	+++	421	+++
118	+++	270	+++	422	+++
119	+++	271	+++	423	+++
120	+++	272	+++	424	+++
121	+++	273	+++	425	+++
122	+++	274	+++	426	+++
123	+++	275	+++	427	+++
124	+++	276	+++	428	+++
125	+++	277	+++	429	+++
126	+++	278	+++	430	+++
127	+++	279	+++	431	+++
128	+++	280	+++	432	+++
129	+++	281	+++	433	+++
130	+++	282	+++	434	+++
131	+++	283	+++	435	+++
132	+++	284	+++	436	+++

133	+++	285	+++	437	+++
134	+++	286	+++	438	+++
135	+++	287	+++	439	+++
136	+++	288	+++	440	+++
137	+++	289	+++	441	+++
138	+++	290	+++	442	+++
139	+++	291	+++	443	+++
140	+++	292	+	444	+++
141	+++	293	+++	445	+++
142	+++	294	+++	446	+++
143	+++	295	+	447	+++
144	+++	296	+++		
145	+++	297	+++		
146	+++	298	+++		
147	+++	299	+++		
148	+++	300	+++		
149	+++	301	+++		
150	+++	302	+++		
151	+++	303	+++		
152	++	304	+++		

Ferroptosis inhibitory activity of compounds 448-659 is summarized in Table 3. In Table 3, activity is provided as follows: +++ = $0.1 \text{ nM} \leq \text{EC}_{50} < 100 \text{ nM}$; ++ = $100 \text{ nM} \leq \text{EC}_{50} < 1000 \text{ nM}$; + = $1000 \text{ nM} \leq \text{EC}_{50} < 10000 \text{ nM}$.

Table 3. EC₅₀ Values of Compounds 448 to 659

Cmpd No.	EC₅₀ (nM)	Cmpd No.	EC₅₀ (nM)	Cmpd No.	EC₅₀ (nM)
448	+++	522	+++	596	+++
449	+++	523	+++	597	+++
450	+++	524	+++	598	+++
451	+++	525	+++	599	+++
452	+++	526	+++	600	+++
453	+++	527	+++	601	+++
454	+++	528	+++	602	+++
455	+++	529	+++	603	+++

456	+++	530	+++	604	+++
457	+++	531	+++	605	+++
458	+++	532	++	606	++
459	+++	533	+++	607	+++
460	+++	534	+++	608	+++
461	+++	535	+++	609	+++
462	+++	536	+++	610	+++
463	+++	537	+++	611	+++
464	+++	538	+++	612	+++
465	+++	539	+++	613	+++
466	+++	540	++	614	+++
467	+++	541	++	615	+
468	+++	542	+++	616	+++
469	+++	543	+++	617	+++
470	+++	544	+++	618	+++
471	+++	545	+++	619	+++
472	+++	546	+++	620	+++
473	+++	547	+++	621	+++
474	+++	548	+++	622	+++
475	+++	549	+++	623	+++
476	+++	550	+++	624	+++
477	+++	551	+++	625	+++
478	+++	552	+++	626	+++
479	+++	553	+++	627	+++
480	+++	554	+++	628	+++
481	+++	555	+++	629	+++
482	+++	556	+++	630	+++
483	+++	557	+++	631	+++
484	+++	558	+++	632	+++
485	+++	559	+++	633	+++
486	+++	560	+++	634	+++
487	+++	561	+++	635	+++
488	+++	562	+++	636	+++
489	+++	563	+++	637	+++
490	+++	564	+++	638	+++
491	+++	565	+++	639	+++
492	+++	566	+++	640	+++
493	+++	567	+++	641	+++
494	+++	568	+++	642	+++

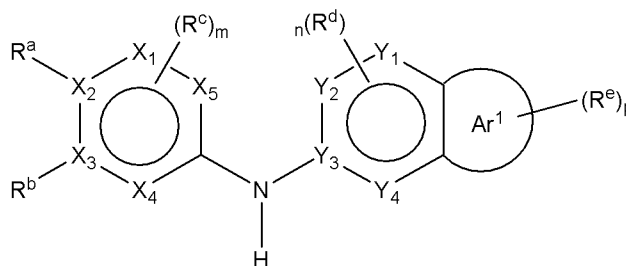
495	+++	569	+++	643	+++
496	+++	570	+++	644	+++
497	+++	571	+++	645	+++
498	+++	572	+++	646	+++
499	+++	573	+++	647	+++
500	+++	574	+++	648	+++
501	+++	575	+++	649	+++
502	+++	576	+++	650	+++
503	+++	577	+++	651	+++
504	+++	578	+++	652	+++
505	+++	579	+++	653	+++
506	+++	580	+++	654	+++
507	+++	581	+++	655	+++
508	+++	582	+++	656	+++
509	+++	583	+++	657	+++
510	+++	584	+++	658	+++
511	+++	585	+++	659	+++
512	+++	586	+++		
513	+++	587	+++		
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515	+++	589	+++		
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517	+++	591	+++		
518	+++	592	+++		
519	+++	593	+++		
520	+++	594	+++		
521	+++	595	+++		

All publications, including but not limited to disclosures and disclosure applications, cited in this specification are herein incorporated by reference as though fully set forth. If certain content of a publication cited herein contradicts or is inconsistent with the present disclosure, the present disclosure controls.

One skilled in the art will readily recognize from the disclosure and claims that various changes, modifications, and variations can be made therein without departing from the spirit and scope of the disclosure as defined in the following claims.

CLAIMS

1. A compound of the following structural Formula I:



Formula I

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:

Ar¹ is aryl, cycloalkyl, heteroaryl, or 5- to 7-membered heterocyclyl;

X₁ is C, N, or S;

X₂, X₃, X₅, Y₁, Y₂, Y₃, and Y₄ are each independently C or N;

X₄ is C or N, but when X₁ is S, X₄ is nothing;

R^a is selected from H, halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^b is selected from H, halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^a and R^b may join together to form an optionally substituted 3- to 10-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring;

R^c, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, and optionally substituted alkyl;

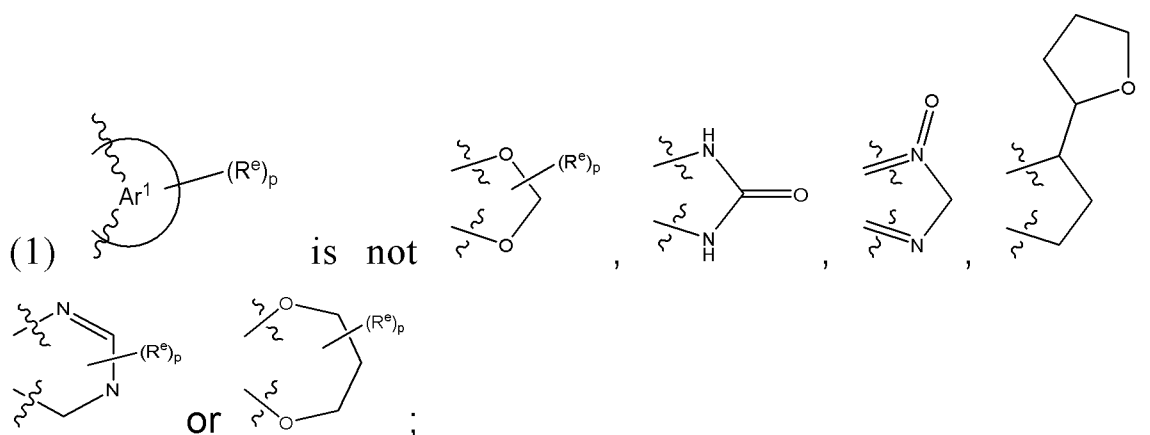
R^d, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, and optionally substituted alkyl;

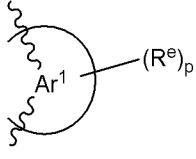
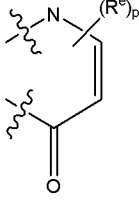
R^e, for each occurrence, is independently selected from halogen, CN, optionally substituted heteroatom, optionally substituted alkyl,

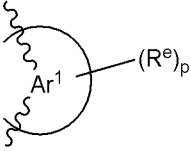
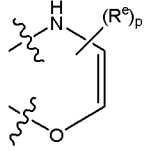
optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl; and

5 m, n, and p are each an integer independently selected from 0, 1, 2, and 3;

provided that:



10 (2) when  is , R^e is not $-C(=O)OH$ or $-C(=O)O(C_1-C_3 \text{ alkyl})$;

(3) when  is , R^a is not OH; and

(4) when Ar^1 is a 5- to 6-membered cycloalkyl, 5- to 6-membered heteroaryl, or 5- to 7-membered heterocyclyl, (i) R^a is selected from optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, and optionally substituted heteroaryl, (ii) R^a is selected from H, halogen, CN, optionally substituted heteroatom, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, provided that p is an integer selected from 1, 2, and 3 and that at least one of the R^e is =O, or (iii) R^a and R^b join together to form an optionally substituted 3- to 10-membered

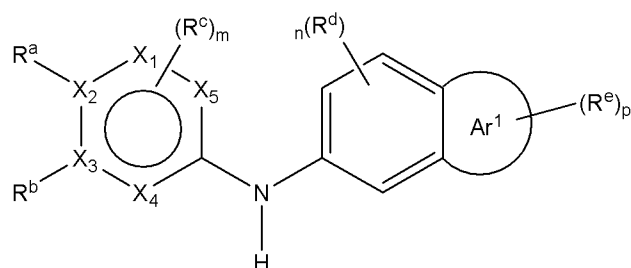
15

20

carbocyclic, heterocyclic, aromatic, or heteroaromatic ring, provided that p is an integer selected from 1, 2, and 3 and that at least one of the R^e is =O.

2. The compound, tautomer, solvate, stereoisomer, or
5 pharmaceutically acceptable salt of claim 1, wherein Ar¹ is 5- to 6-membered heteroaryl or 5- to 7-membered heterocyclyl.

3. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula IIa:

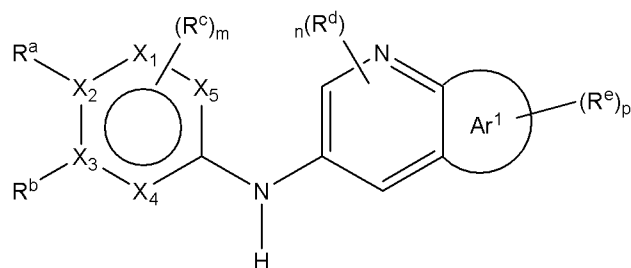


10

Formula IIa

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

4. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula IIb:

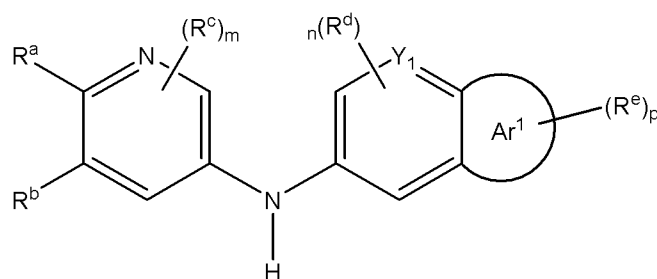


15

Formula IIb

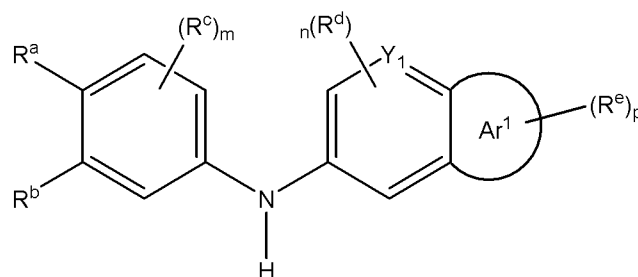
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

5. The compound of any one of claims 1 and 2, wherein the compound
20 has the following structural Formula IIIa:

**Formula IIIa**

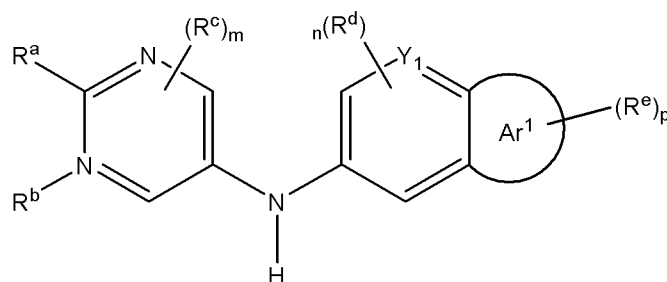
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

- 5 **6.** The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula IIIb:

**Formula IIIb**

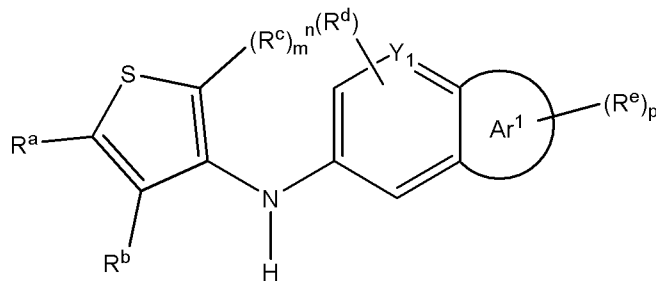
10 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

- 7.** The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula IIIc:

**Formula IIIc**

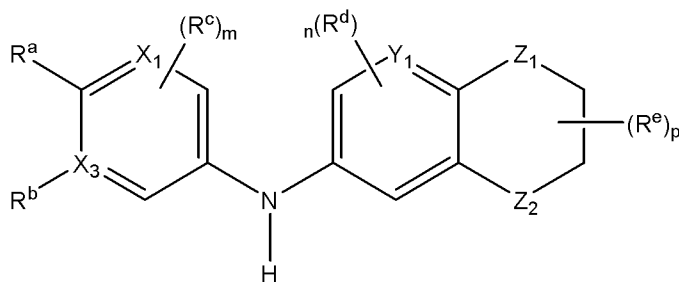
15 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

- 8.** The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula IIId:

**Formula IIIId**

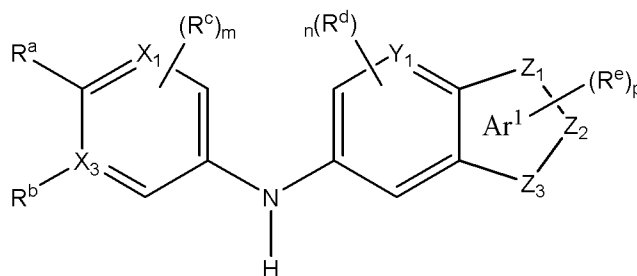
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

- 5 **9.** The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula IVa:

**Formula IVa**

- a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein
 10 X_1 and X_3 are each independently C or N; and Z_1 and Z_2 are each independently N or O.

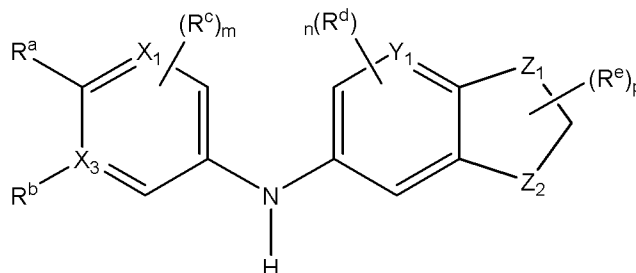
- 10.** The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula IVb:

**Formula IVb**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein

X_1 and X_3 are each independently C or N; Ar^1 is aromatic or non-aromatic; and Z_1 , Z_2 , and Z_3 are each independently N or C.

11. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula IVc:

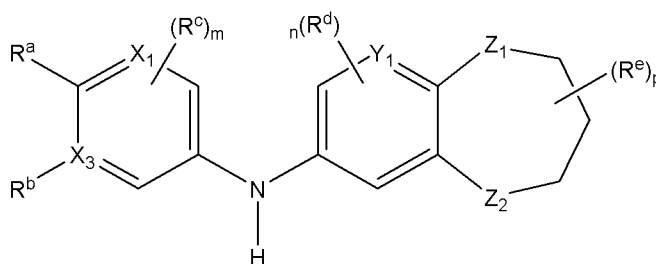


5

Formula IVc

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein X_1 and X_3 are each independently C or N; and Z_1 and Z_2 are each
10 independently O or N.

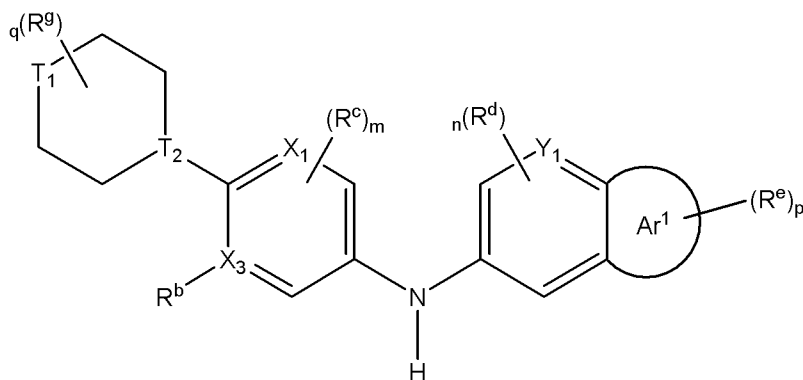
12. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula IVd:



Formula IVd

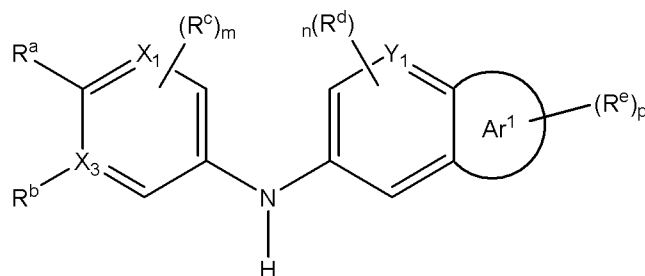
15 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein X_1 and X_3 are each independently C or N; and Z_1 and Z_2 are each independently O or N.

13. The compound of any one of claims 1 and 2, wherein the
20 compound has the following structural Formula Va:

**Formula Va**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein
 5 X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each
 10 occurrence, are each optionally substituted with 1 to 3 groups of halogen.

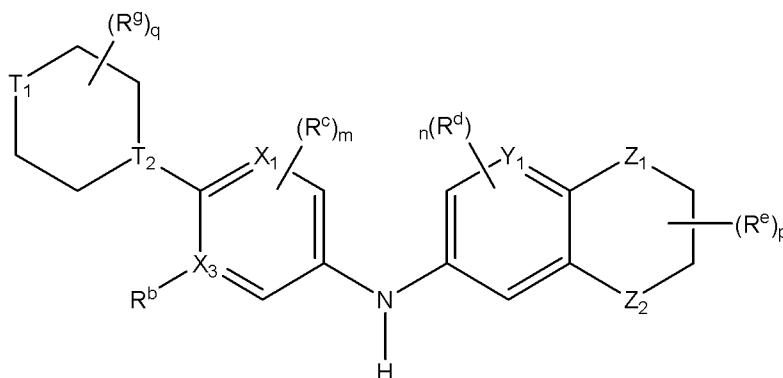
14. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula Vb:

**Formula Vb**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein
 15 X_1 and X_3 are each independently N or C; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^a , R^b , and R^c , for each occurrence, are each optionally substituted with 1 to 3
 20

groups of halogen.

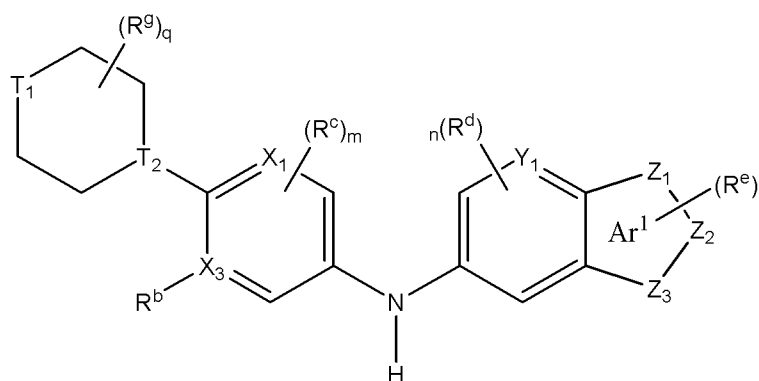
15. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula VIa:



Formula VIa

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is independently selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; Z_1 and Z_2 are each independently N or O.

16. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula VIb:

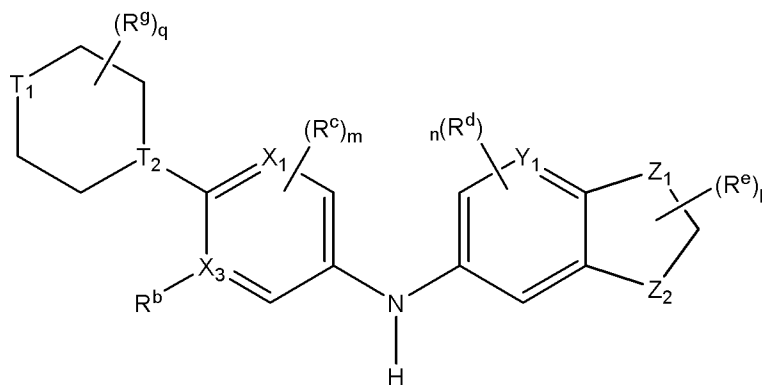


Formula VIb

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein

X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is independently selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; Ar^1 is aromatic or non-aromatic; and Z_1 , Z_2 , and Z_3 are each independently N or C.

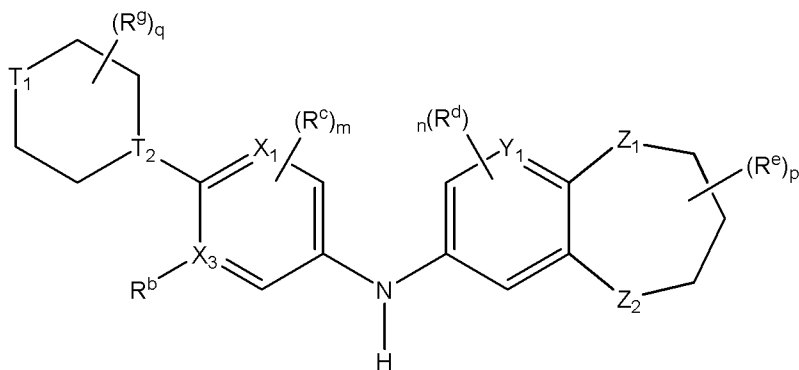
17. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula VIc:



Formula VIc

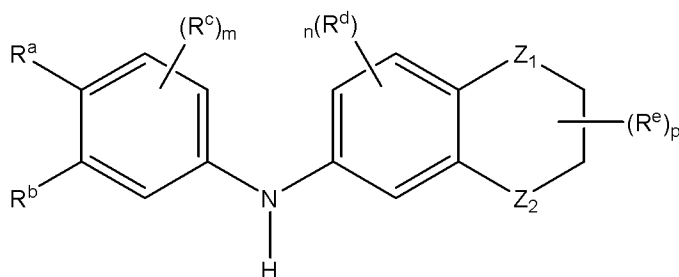
a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is independently selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen; and Z_1 and Z_2 are each independently O or N.

18. The compound of any one of claims 1 and 2, wherein the compound has the following structural Formula VId:

**Formula VIId**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein
 5 X_1 and X_3 are each independently N or C; T_1 is C or O; T_2 is C or N; R^g , for each occurrence, is independently selected from CF_3 , $-CH_3$, $-OCH_3$, and $-CH_2CH_3$; q is 0, 1, or 2; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^b and R^c , for each
 10 occurrence, are each optionally substituted with 1 to 3 groups of halogen; and Z_1 and Z_2 are each independently O or N.

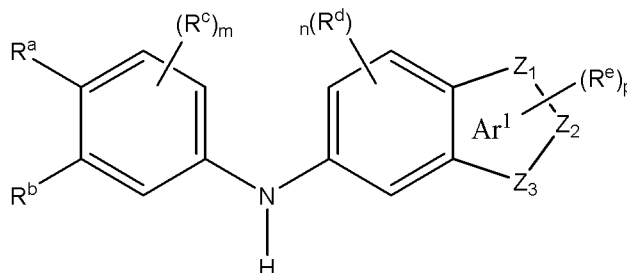
19. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula VIIa:

**Formula VIIa**

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein
 Z_1 and Z_2 are each independently N or O; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^a , R^b ,
 20

and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen.

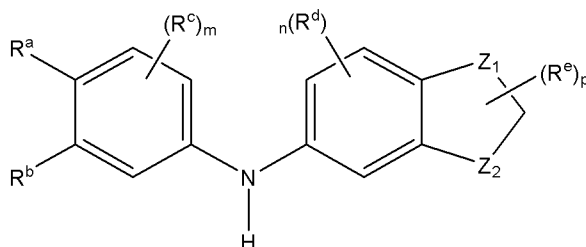
20. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula VIIb:



Formula VIIb

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein Ar^1 is aromatic or non-aromatic; Z_1 , Z_2 , and Z_3 are each independently N or C; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; wherein the C_1 to C_3 alkoxy and C_1 to C_3 alkyl of R^a , R^b , and R^c , for each occurrence, are each optionally substituted with 1 to 3 groups of halogen.

21. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula VIIc:

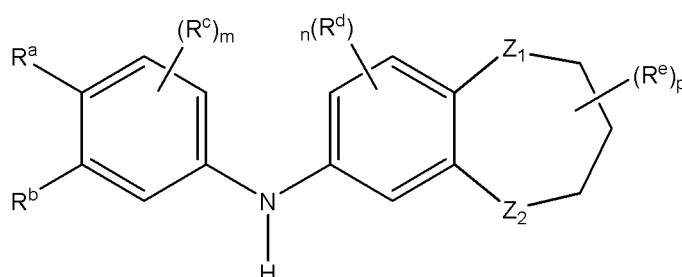


Formula VIIc

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein Z_1 and Z_2 are each independently O or N; R^a is selected from C_1 to C_3 alkoxy and C_1 to C_3 alkyl; R^b is selected from H, halogen, C_1 to C_3 alkoxy, and C_1 to C_3 alkyl; and R^c is selected from halogen, C_1 to C_3 alkoxy, and

C₁ to C₃ alkyl; wherein the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^a, R^b, and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen.

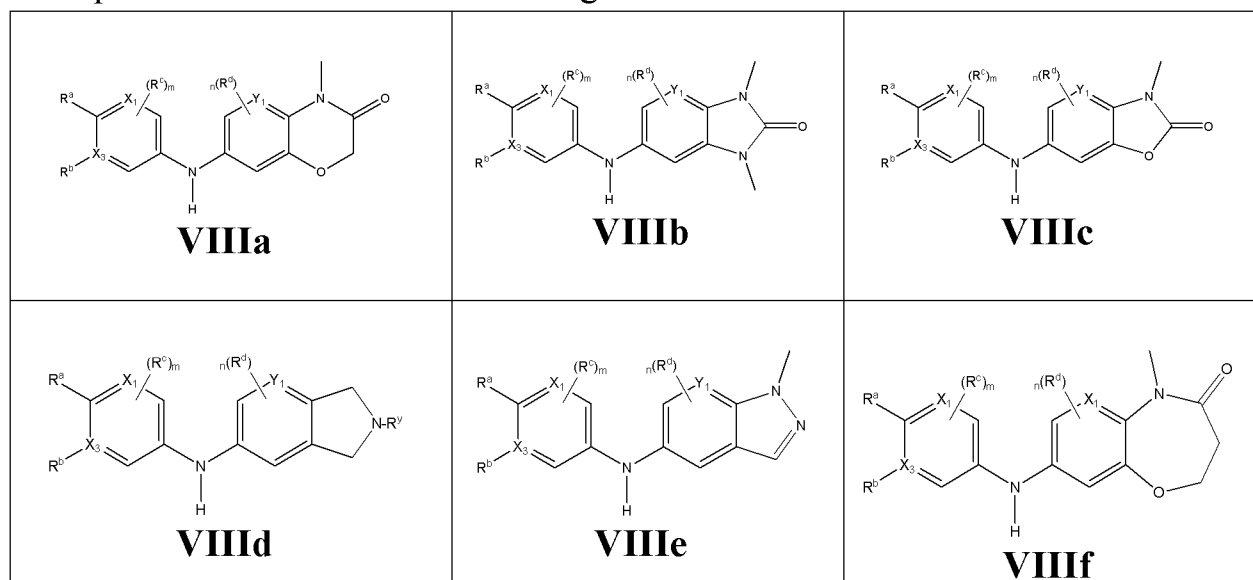
22. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formula VIId:

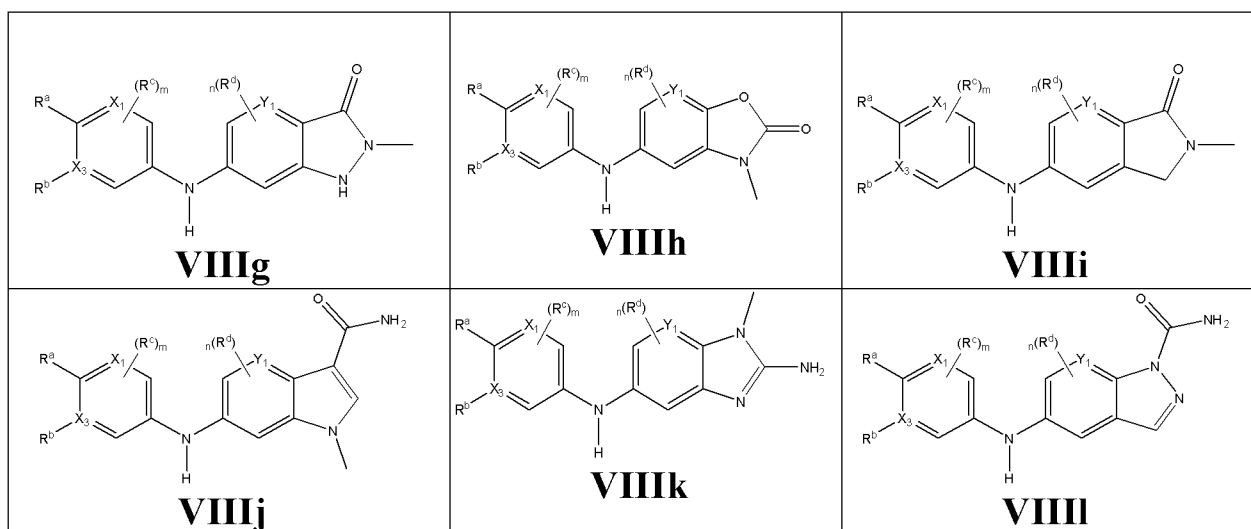


Formula VIId

a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein Z₁ and Z₂ are each independently O or N; R^a is selected from C₁ to C₃ alkoxy and C₁ to C₃ alkyl; R^b is selected from H, halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; and R^c is selected from halogen, C₁ to C₃ alkoxy, and C₁ to C₃ alkyl; wherein the C₁ to C₃ alkoxy and C₁ to C₃ alkyl of R^a, R^b, and R^c, for each occurrence, are each optionally substituted with 1 to 3 groups of halogen.

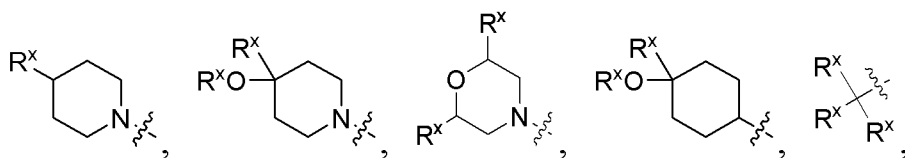
23. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formulae VIIla-VIIIf:





a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:
 X_1 and X_3 are each independently C or N;

R^a is selected from



5 -OR^x, and -CH₂R^x, wherein R^x, for each occurrence, is independently selected from CF₃, -CH₃, and -CH₂CH₃;

R^b is selected from H, halogen, C₁ to C₂ alkyl, and C₁ to C₂ alkoxy;

R^c is selected from halogen, C₁ to C₂ alkyl, and C₁ to C₂ alkoxy;

R^d is selected from halogen, C₁ to C₂ alkyl, and C₁ to C₂ alkoxy;

10 R^y is selected from H and C₁ to C₂ alkyl;

m is 0, 1, or 2; and

n is 0 or 1.

24. The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12, R^a is selected
 15 from hydrogen, halogen, cyano, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, 3- to 10- membered heterocyclyl, phenyl, 5- to 7- membered heteroaryl, -C(=O)R^s, -C(=O)OR^s, -NR^pR^q, -OR^s, wherein

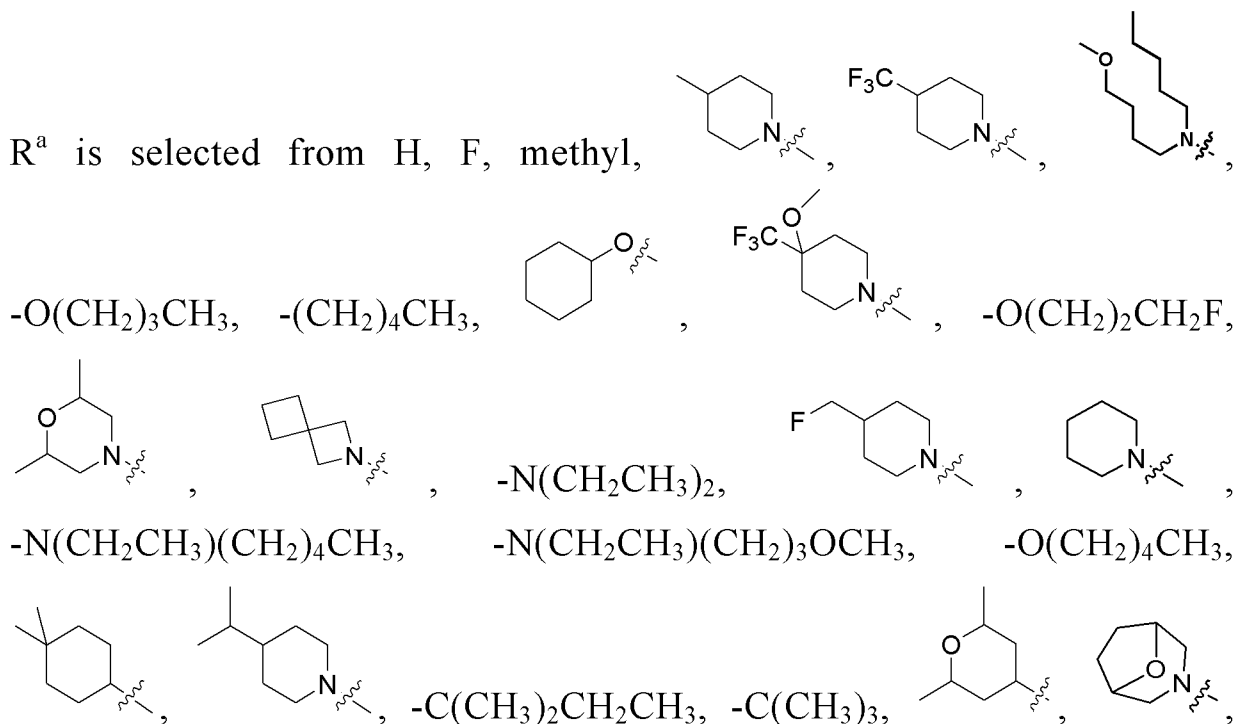
the C₃-C₁₀ cycloalkyl, 3- to 10- membered heterocyclyl, phenyl, and
 5- to 7- membered heteroaryl of R^a are each optionally substituted with 1-3
 20 groups selected from halogen, OR^s, and C₁-C₁₀ alkyl optionally substituted with 1 to 3 groups of halogen;

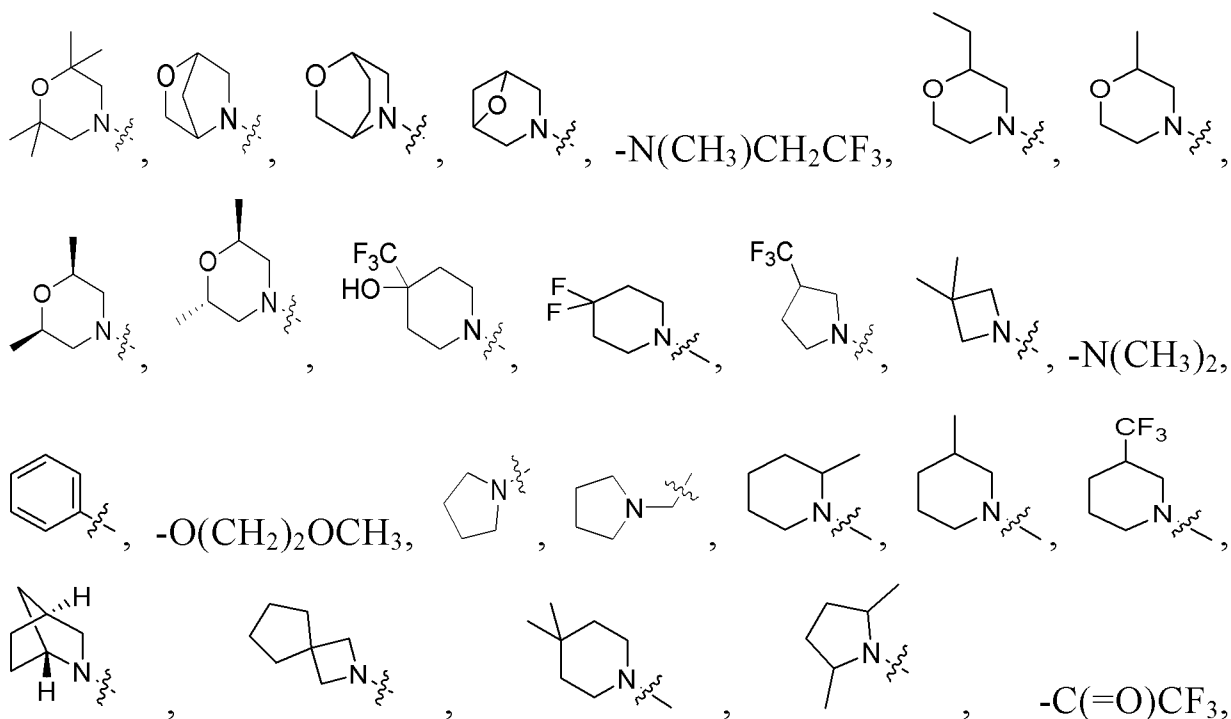
the C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, and C₂-C₁₀ alkynyl of R^a are each optionally substituted with 1 to 3 groups selected from halogen, 3- to 10-membered heterocyclyl, and -OR^s;

R^p and R^q, for each occurrence, are independently selected from hydrogen, C₃-C₁₀ cycloalkyl, and C₁-C₁₀ alkyl, wherein the C₃-C₁₀ cycloalkyl and C₁-C₁₀ alkyl of R^p and R^q are each optionally substituted with 1 to 3 groups selected from halogen, -OR^s and -C(=O)OR^s;

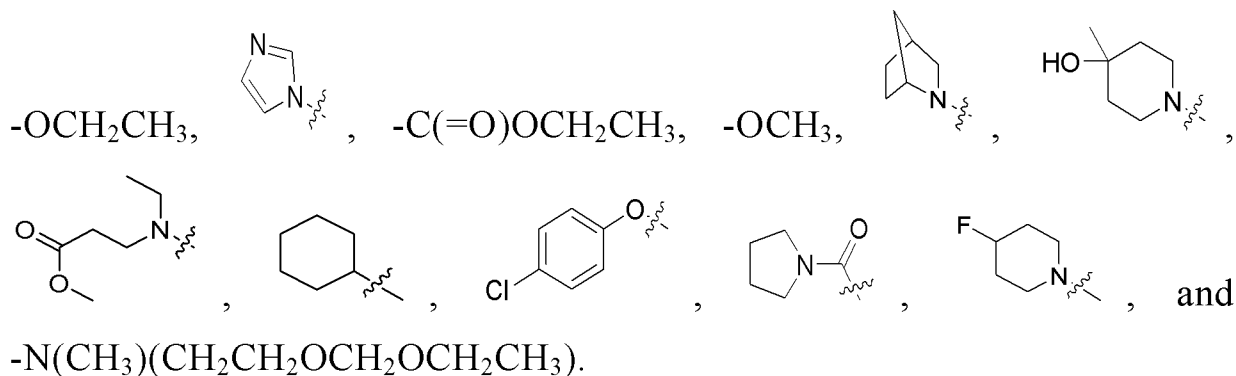
R^s, for each occurrence, is selected from H, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 5- to 6-membered aryl, and C₁-C₁₀ alkyl optionally substituted with 1 to 3 groups selected from halogen, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, and C₁-C₆ alkoxy, wherein the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of R^s and the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of the C₁-C₁₀ alkyl of R^s are each optionally substituted with 1 to 3 groups of C₁-C₆ alkyl optionally substituted with halogen, and the C₁-C₆ alkoxy of the C₁-C₁₀ alkyl of R^s is optionally substituted with 1 to 3 groups of halogen.

25. The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12 and 24, wherein

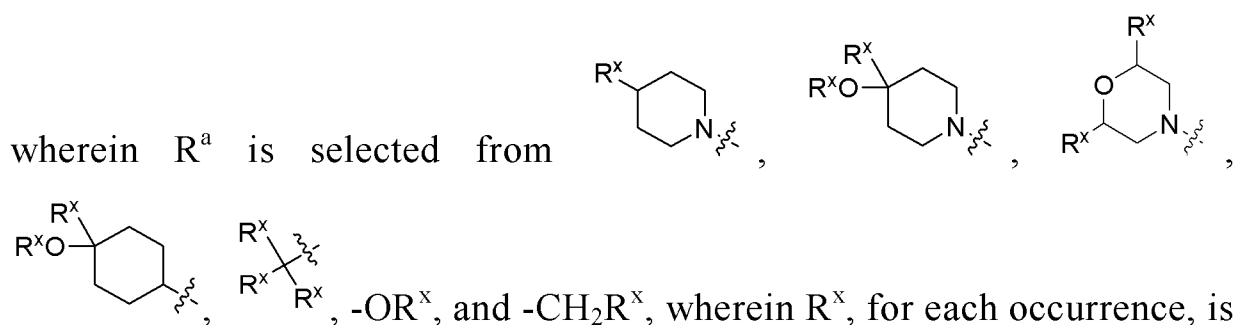




5 -N(CH₂CH₃)(CH₂)₄CH₃, -N(CH₂CH₃)(CH₂)₃OCH₃, $\text{---}\text{C}\equiv\text{CH}$; -O(CH₂)₄CH₃,



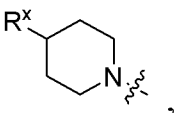
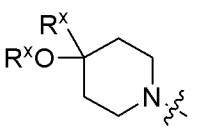
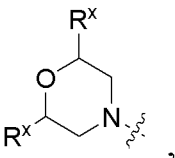
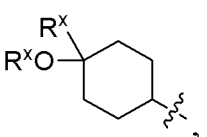
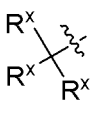
26. The compound, tautomer, solvate, stereoisomer, or
10 pharmaceutically acceptable salt of any one of claims 1-12 and 24-25,



independently selected from C₁ to C₂ alkyl optionally substituted with 1 to 3 groups of halogen.

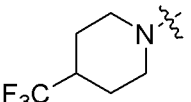
27. The compound, tautomer, solvate, stereoisomer, or

pharmaceutically acceptable salt of any one of claims 1-12 and 24-26,

wherein R^a is selected from , , , , , $-OR^x$, and $-CH_2R^x$, wherein R^x , for each occurrence, is independently selected from CF_3 , $-CH_3$, and $-CH_2CH_3$.

5 **28.** The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12, wherein R^b is selected from is H, halogen, C_1 to C_6 alkyl, $-NR^pR^q$, CN, C_1 - C_6 alkoxy, and 5- to 6- membered heterocyclyl optionally substituted with C_1 - C_3 alkyl optionally substituted with 1 to 3 groups selected from halogen, wherein R^p and R^q are each selected from C_1 to C_6 alkyl, and wherein the C_1 - C_6 alkyl and C_1 - C_6 alkoxy of R^b and the C_1 - C_6 alkyl of R^p and R^q are each optionally substituted with 1 to 3 groups selected from halogen.

15 **29.** The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12 and 28, wherein R^b is H, methyl, $-NHCH_3$, $-N(CH_3)_2$, $-O(CH_2)_2CH_3$, F, $-OCH_3$, $-CF_3$, Cl,

$-N(CH_3)_2$, and .

30. The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12 and 28-29, wherein R^b is selected from halogen, C_1 - C_2 alkyl, and C_1 - C_2 alkoxy.

20 **31.** The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12 and 28-30, wherein R^b is selected from F, methyl, and $-OCH_3$.

32. The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of claims 1-12, wherein R^c , for each occurrence, is independently selected from is halogen, C_1 - C_6 alkyl, $-NR^pR^q$, CN, and C_1 - C_6 alkoxy, wherein R^p and R^q are each selected from

C₁ to C₆ alkyl, and wherein the C₁-C₆ alkyl and C₁-C₆ alkoxy of R^c and the C₁-C₆ alkyl of R^p and R^q are each optionally substituted with 1 to 3 groups selected from halogen.

33. The compound, tautomer, solvate, stereoisomer, or
5 pharmaceutically acceptable salt of any one of claims 1-12 and 32, wherein R^c is selected from methyl, F, -OCH₃, Cl, -N(CH₃)₂, and CN.

34. The compound, tautomer, solvate, stereoisomer, or
pharmaceutically acceptable salt of any one of claims 1-12 and 32-33,
wherein R^c is selected from halogen, C₁-C₂ alkyl, and C₁-C₂ alkoxy.

10 35. The compound, tautomer, solvate, stereoisomer, or
pharmaceutically acceptable salt of any one of claims 1-12 and 32-34,
wherein R^c is selected from F, methyl, and -OCH₃.

36. The compound, tautomer, solvate, stereoisomer, or
pharmaceutically acceptable salt of any one of claims 1-35, wherein R^d, for
15 each occurrence, is independently selected from halogen, C₁-C₆ alkyl, NO₂,
CN, and C₁-C₆ alkoxy, wherein the C₁-C₆ alkyl and C₁-C₆ alkoxy of R^d are
each optionally substituted with 1 to 3 groups selected from halogen.

37. The compound, tautomer, solvate, stereoisomer, or
pharmaceutically acceptable salt of any one of claims 1-36, wherein R^d is
20 selected from F, methyl, Cl, NO₂, and -OCH₃.

38. The compound, tautomer, solvate, stereoisomer, or
pharmaceutically acceptable salt of any one of claims 1-37, wherein R^d is
selected from halogen, C₁-C₂ alkyl, and C₁-C₂ alkoxy.

39. The compound, tautomer, solvate, stereoisomer, or
25 pharmaceutically acceptable salt any one of claims 1-38, wherein R^d is
selected from F, methyl, and -OCH₃.

40. The compound, tautomer, solvate, stereoisomer, or
pharmaceutically acceptable salt of any one of claims 1-22 and 24-39,
wherein R^e, for each occurrence, is independently selected from halogen,
30 cyano, C₁-C₁₀ alkyl, phenyl, 5- to 7-membered heteroaryl, 3- to
10-membered heterocyclyl, C₃-C₁₀ cycloalkyl, -C(=O)R^s, C₂-C₁₀ alkenyl,
=O, =NR^p; -C(=O)OR^s, -C(=O)NR^pR^q, -NR^pR^q, and -NR^pC(=O)R^s,

wherein

the C₁-C₁₀ alkyl and C₂-C₁₀ alkenyl of R^e are each optionally substituted with 1 to 3 groups selected from 5- to 7-membered heteroaryl, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, -OR^s, -C(=O)NR^pR^q,
 5 -NR^pC(=O)NR^qR^r, and -NR^pR^q;

the 3- to 10-membered heterocyclyl and C₃-C₁₀ cycloalkyl of R^e and the 3- to 10-membered heterocyclyl and C₃-C₁₀ cycloalkyl of the C₁-C₁₀ alkyl and C₂-C₁₀ alkenyl of R^e, are each optionally substituted with 1 to 3 groups selected from =O and C₁-C₆ alkyl optionally substituted with 1 to 3
 10 groups selected from halogen and -OR^s;

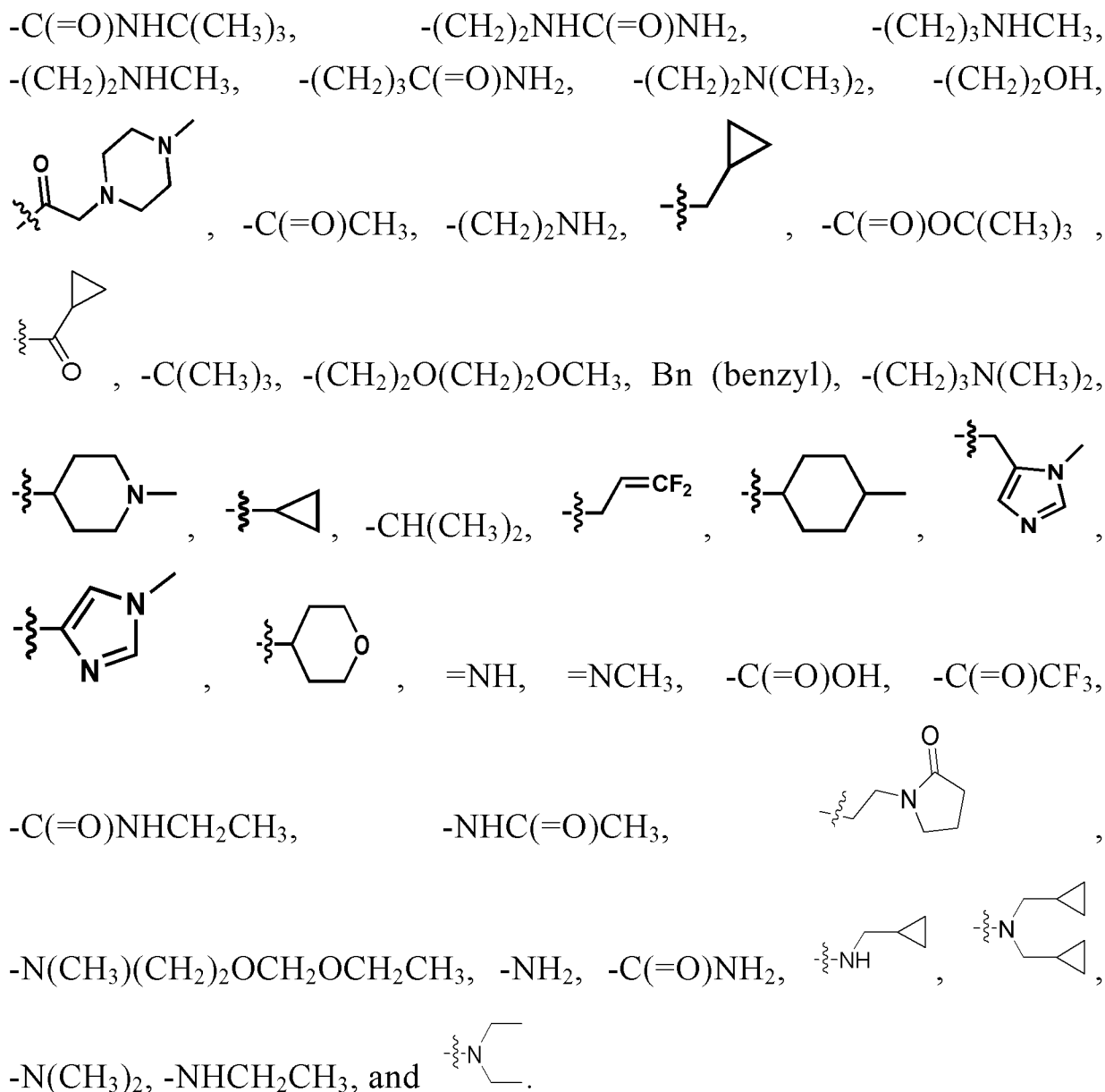
the phenyl and 5- to 7-membered heteroaryl of R^e and the 5- to 7-membered heteroaryl of the C₁-C₁₀ alkyl and C₂-C₁₀ alkenyl of R^e are each optionally substituted with 1 to 3 groups selected from C₁-C₆ alkyl optionally substituted with 1 to 3 groups selected from halogen and -OR^s;

15 R^p, R^q, and R^r, for each occurrence, are independently selected from hydrogen, C₃-C₁₀ cycloalkyl, and C₁-C₁₀ alkyl, wherein the C₃-C₁₀ cycloalkyl and C₁-C₁₀ alkyl of R^p, R^q, and R^r are each optionally substituted with 1 to 3 groups selected from halogen, -OR^s and -C(=O)OR^s;

R^s, for each occurrence, is independently selected from H, C₃-C₁₀
 20 cycloalkyl, 3- to 10- membered heterocyclyl, and C₁-C₁₀ alkyl optionally substituted with 1 to 3 groups selected from halogen, C₃-C₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, and C₁-C₆ alkoxy, wherein

the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of R^s and the C₃-C₁₀ cycloalkyl and 3- to 10-membered heterocyclyl of the
 25 C₁-C₁₀ alkyl of R^s are each optionally substituted with 1 to 3 groups of C₁-C₆ alkyl optionally substituted by halogen, and the C₁-C₆ alkoxy of the C₁-C₁₀ alkyl of R^s is optionally substituted with 1 to 3 groups of halogen.

41. The compound, tautomer, solvate, stereoisomer, or
 30 pharmaceutically acceptable salt of any one of 1-22 and 24-40, wherein R^e, for each occurrence, is selected from methyl, ethyl, =O, -(CH₂)₃OCH₃, -(CH₂)₂OCH₃, -CH₂C(=O)NH₂, -(CH₂)₂C(=O)NH₂, -C(=O)C(CH₃)₃,



10 **42.** The compound, tautomer, solvate, stereoisomer, or
 pharmaceutically acceptable salt of any one of 1-22 and 24-41, wherein R^e
 is selected from $=\text{O}$, $-\text{C}(=\text{O})\text{NR}^p\text{R}^q$, and $\text{C}_1\text{-C}_6$ alkyl, wherein the $\text{C}_1\text{-C}_6$
 alkyl is optionally substituted with 1 to 3 groups selected from $\text{C}_1\text{-C}_3$
 alkoxy, $-\text{C}(=\text{O})\text{NR}^p\text{R}^q$, and $-\text{NR}^p\text{R}^q$, wherein R^p and R^q are each selected
 15 from H and $\text{C}_1\text{-C}_3$ alkyl.

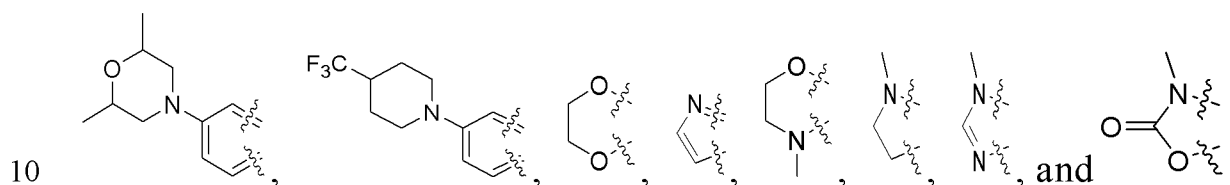
43. The compound, tautomer, solvate, stereoisomer, or
 pharmaceutically acceptable salt of any one of 1-22 and 24-42, wherein R^e
 is selected from $\text{C}_1\text{-C}_2$ alkyl, $=\text{O}$, and $-\text{C}(=\text{O})\text{NH}_2$.

20 **44.** The compound, tautomer, solvate, stereoisomer, or
 pharmaceutically acceptable salt of any one of 1-12 and 32-43, wherein R^a

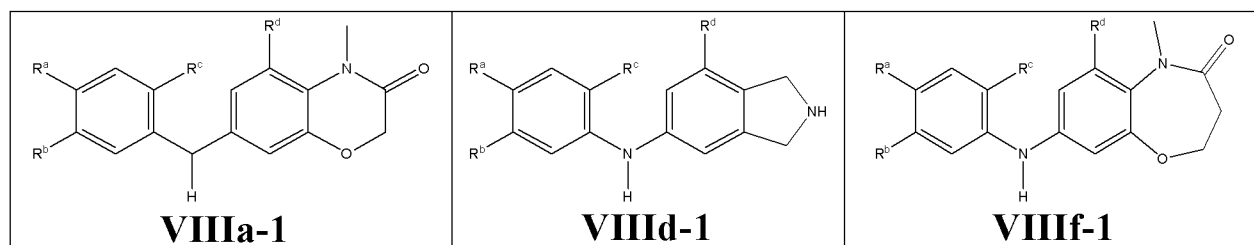
and R^b join to form a 5- to 6-membered carbocyclic, heterocyclic, aromatic, or heteroaromatic ring optionally substituted with 1 to 3 groups selected from =O, C_1 - C_6 alkyl, and 5- to 7-membered heterocyclyl, wherein the C_1 - C_6 alkyl is optionally substituted with 1 to 3 groups of halogen, and the 5- to 7-membered heterocyclyl is optionally substituted with 1 to 3 groups of C_1 - C_3 alkyl optionally substituted with 1 to 3 groups of halogen.

45. The compound, tautomer, solvate, stereoisomer, or pharmaceutically acceptable salt of any one of 1-12 and 32-44, wherein R^a

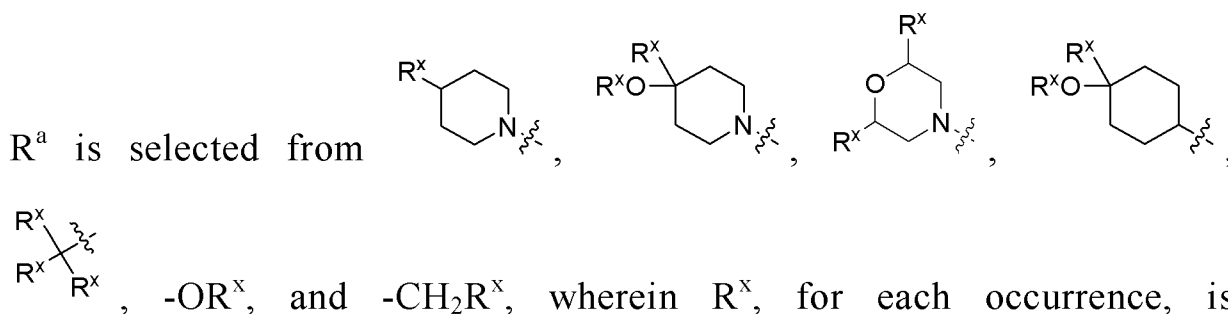
and R^b join to form a structure selected from:



46. The compound of any one of claims 1 and 2, wherein the compound has one of the following structural Formulae VIIId-1, VIIIf-1, and VIIIf-1:



15 a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing, wherein:

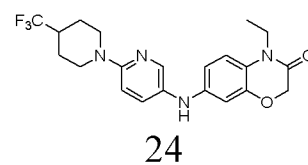
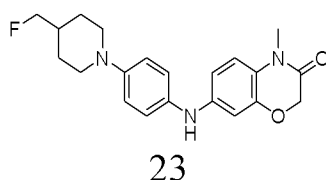
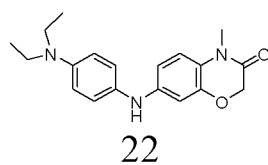
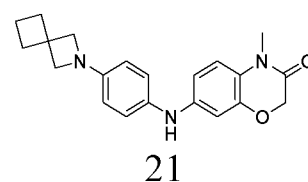
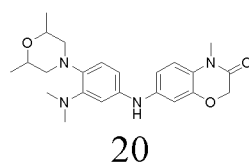
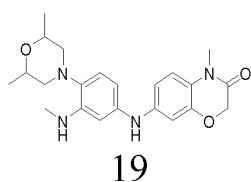
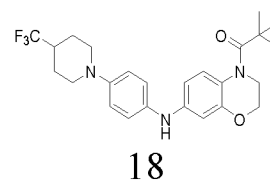
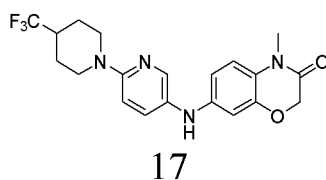
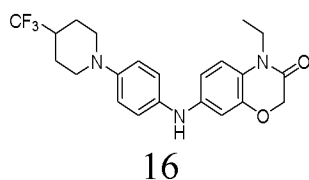
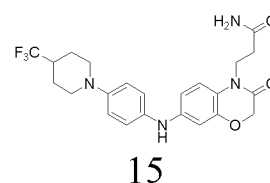
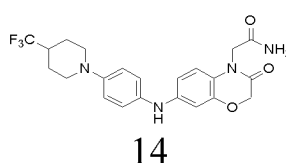
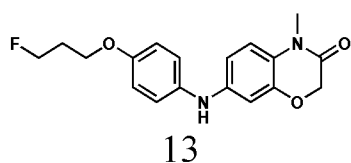
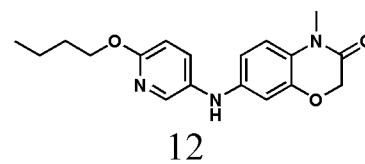
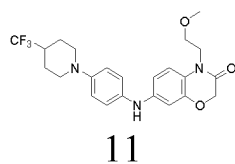
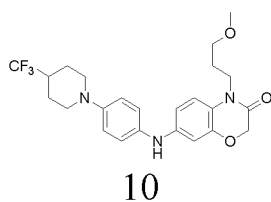
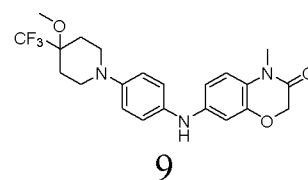
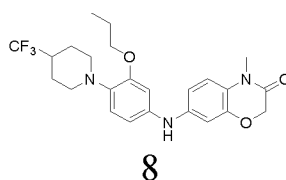
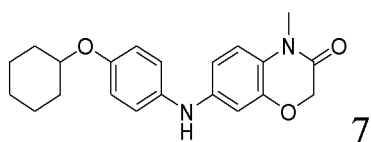
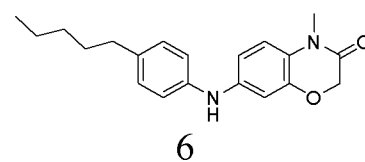
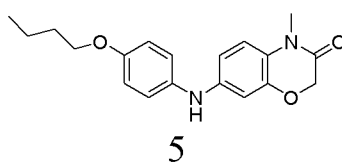
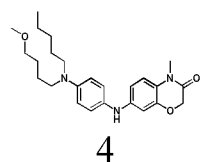
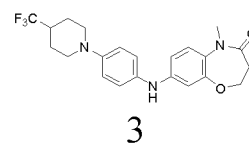
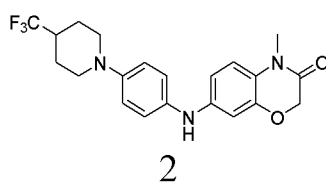
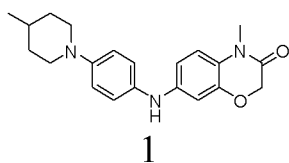


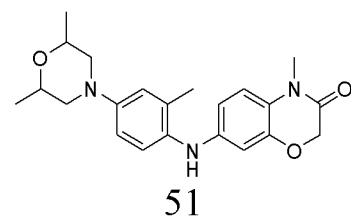
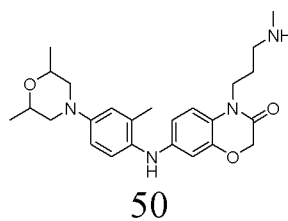
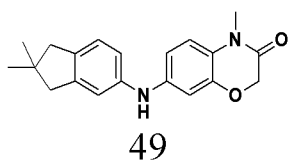
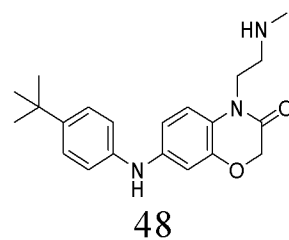
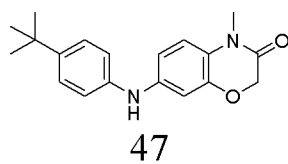
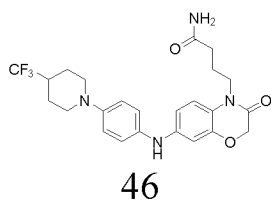
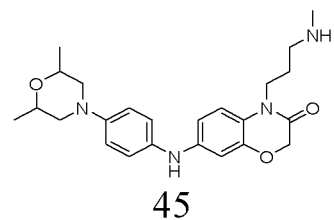
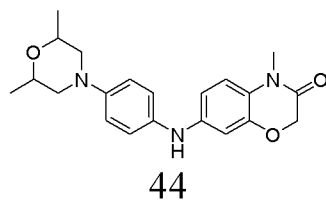
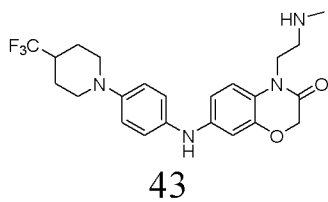
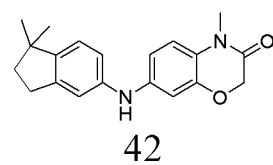
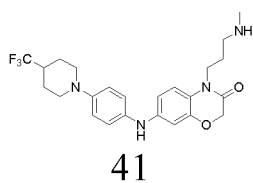
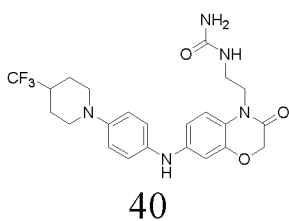
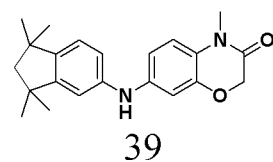
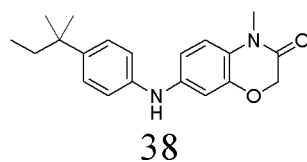
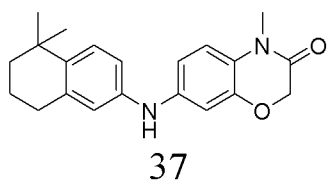
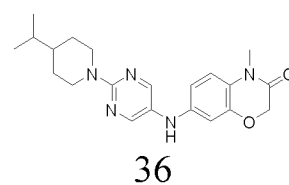
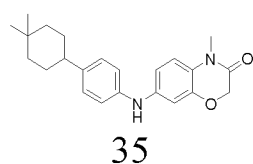
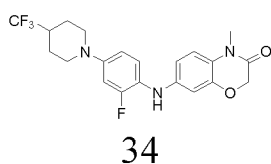
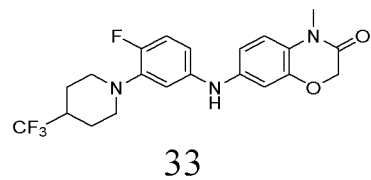
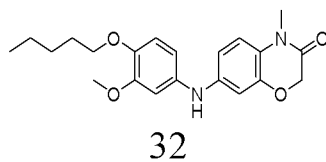
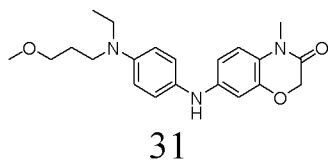
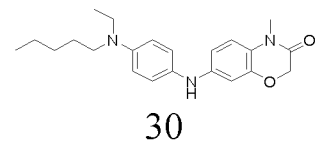
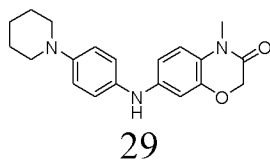
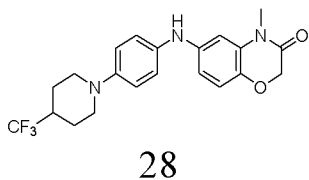
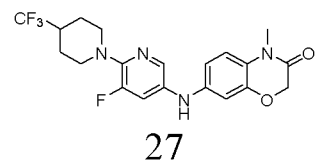
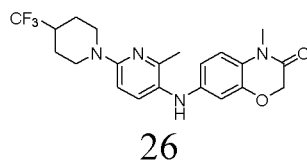
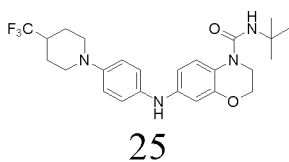
independently selected from CF_3 and C_1 to C_2 alkyl;

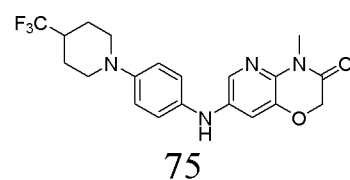
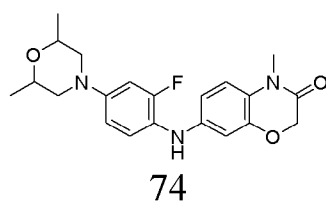
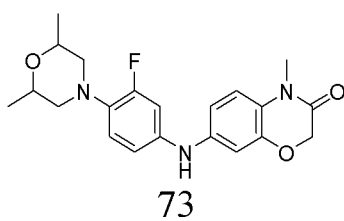
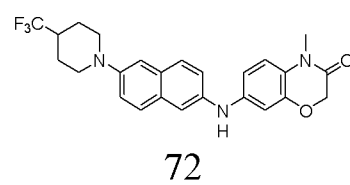
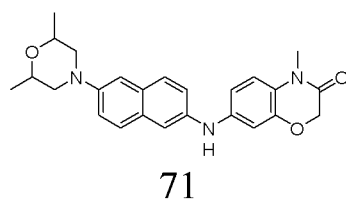
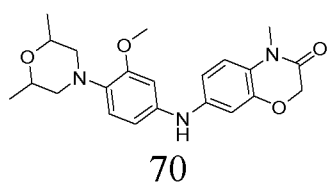
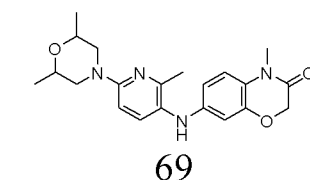
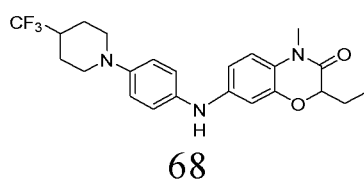
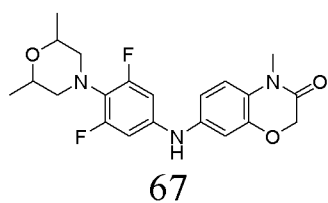
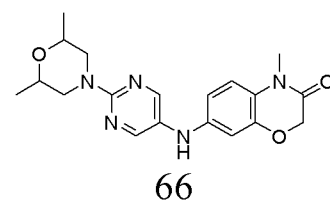
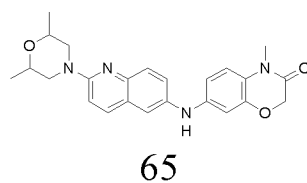
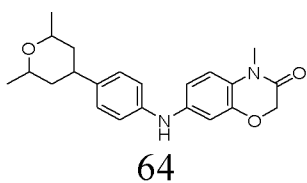
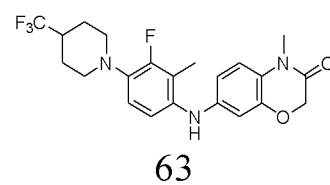
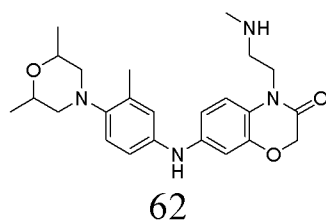
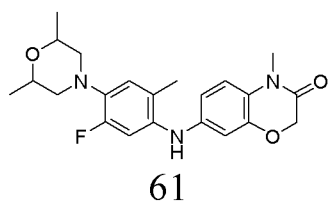
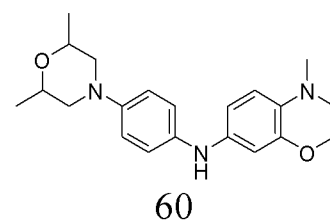
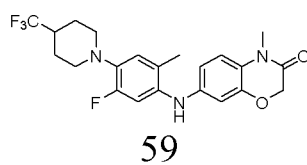
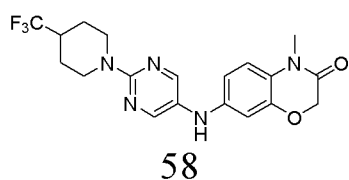
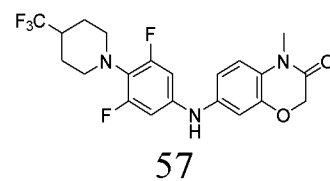
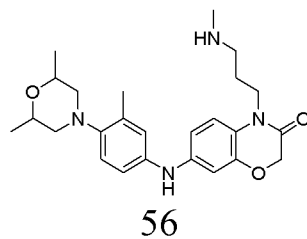
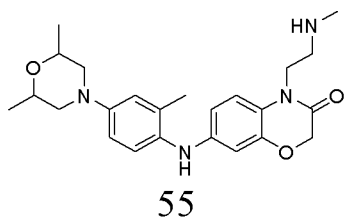
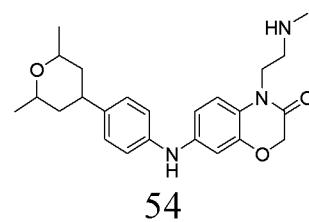
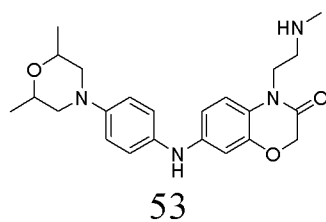
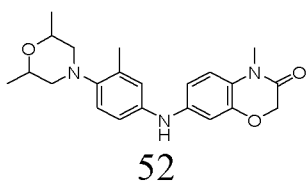
R^b is selected from H, halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy;

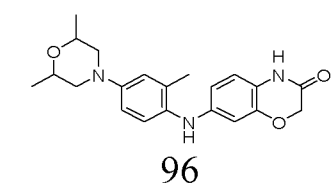
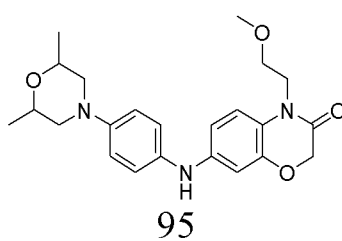
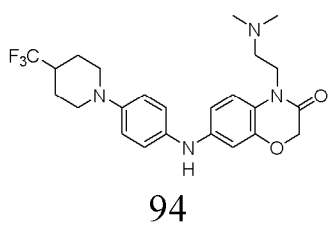
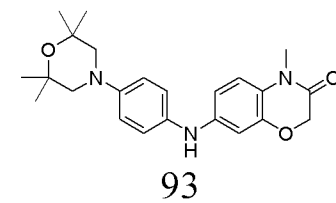
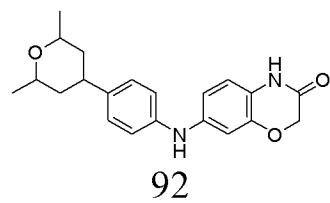
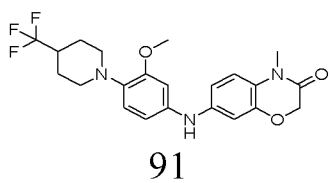
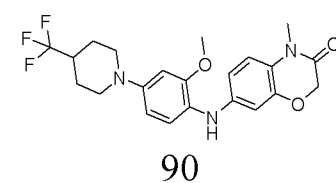
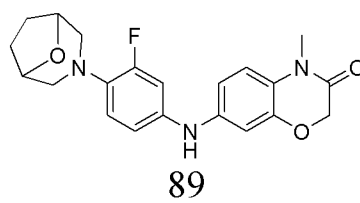
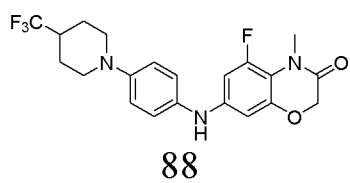
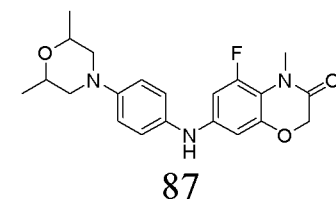
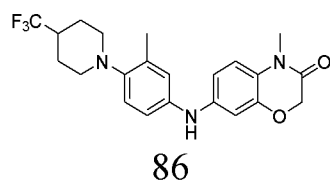
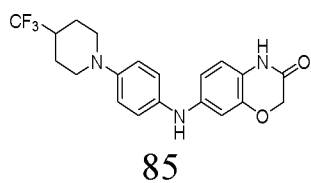
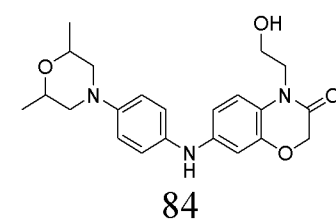
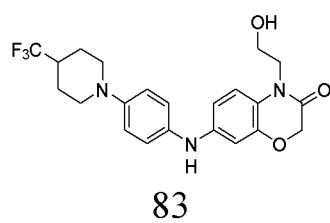
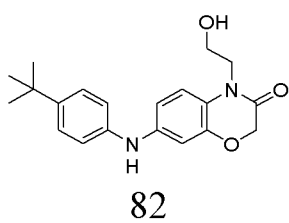
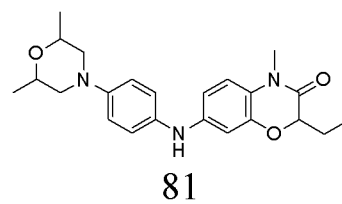
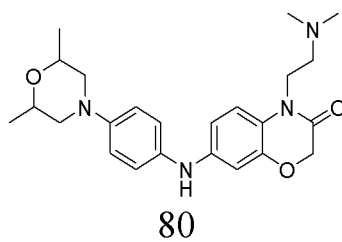
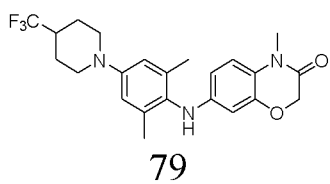
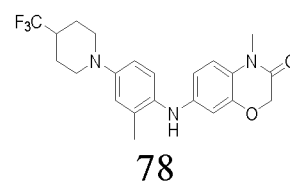
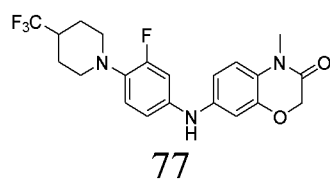
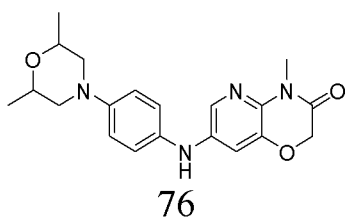
R^c is selected from halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy; and R^d is selected from halogen, C_1 to C_2 alkyl, and C_1 to C_2 alkoxy.

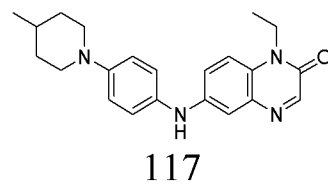
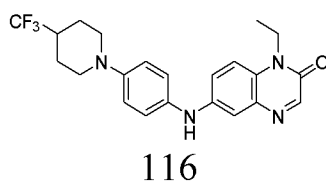
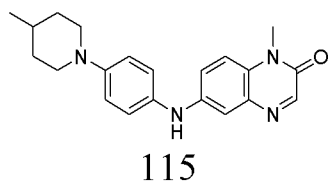
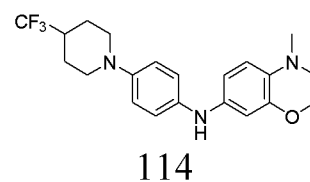
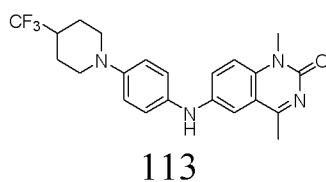
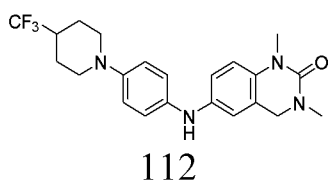
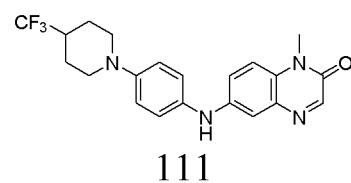
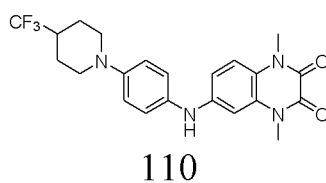
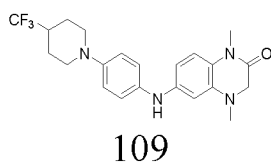
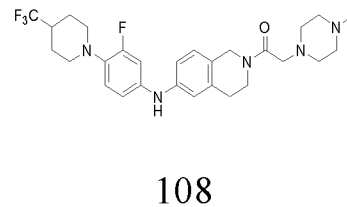
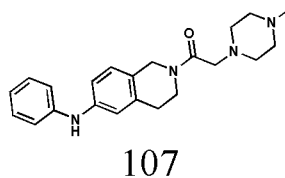
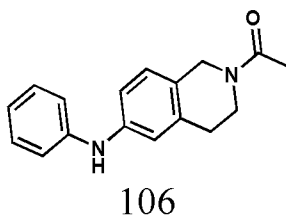
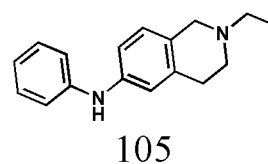
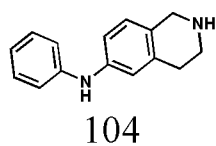
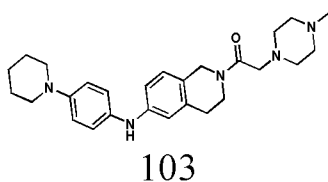
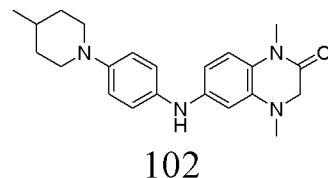
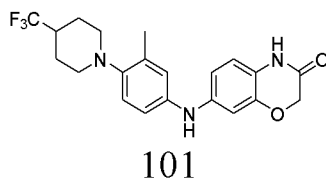
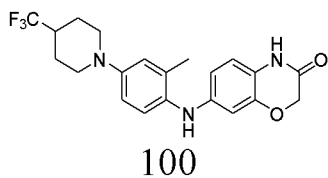
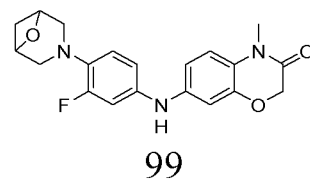
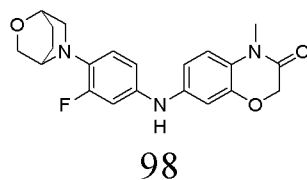
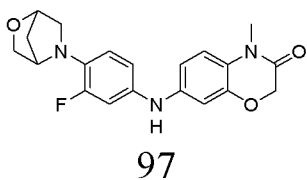
47. The compound according to claim 1, wherein the compound is selected from:

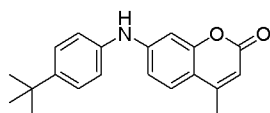




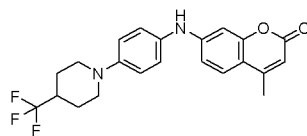




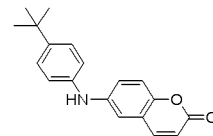




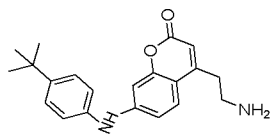
118



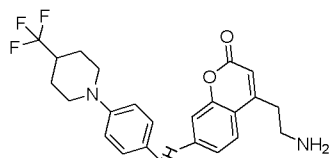
119



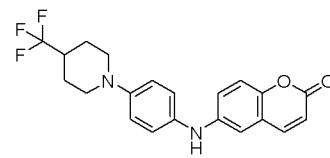
120



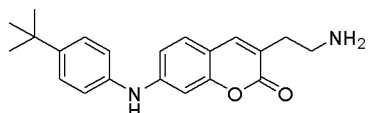
121



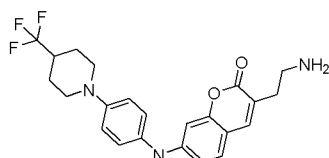
122



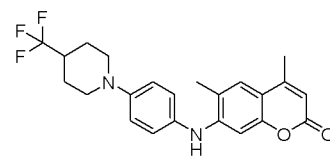
123



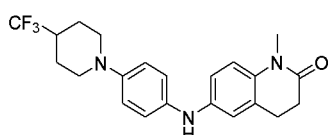
124



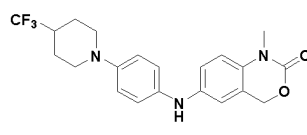
125



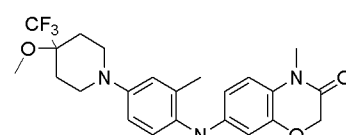
126



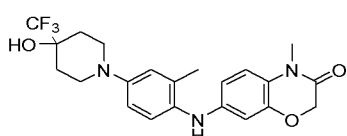
127



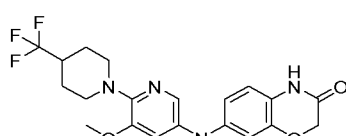
128



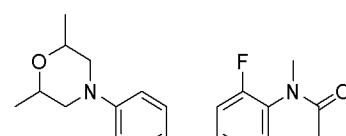
129



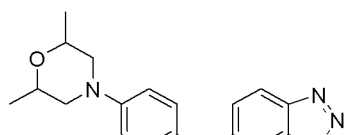
130



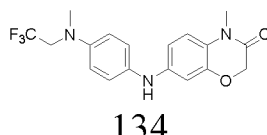
131



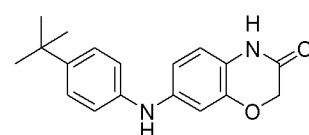
132



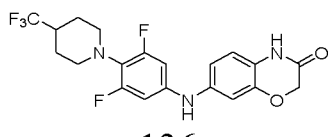
133



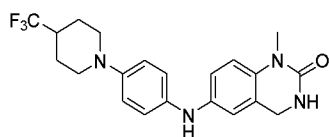
134



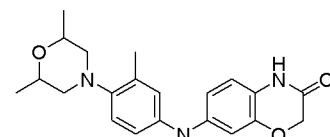
135



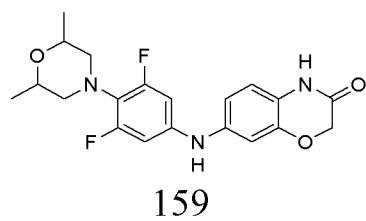
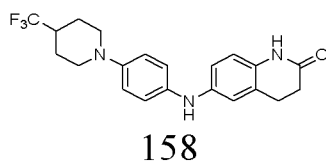
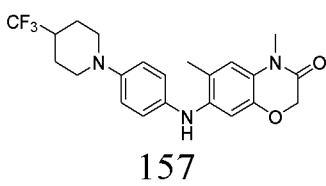
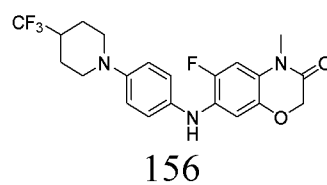
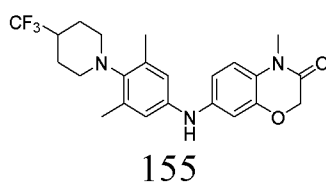
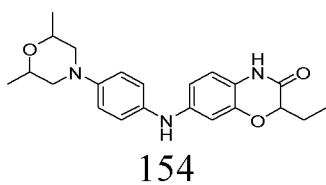
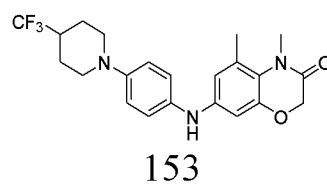
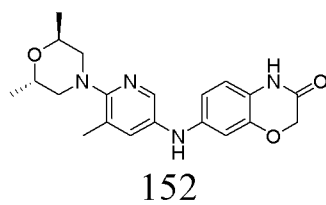
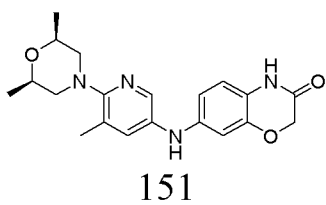
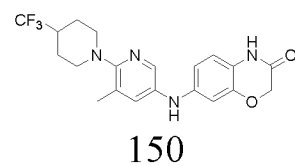
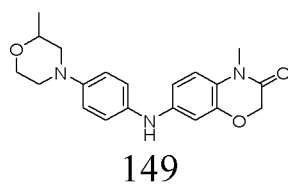
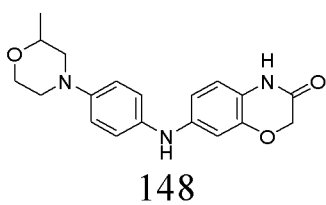
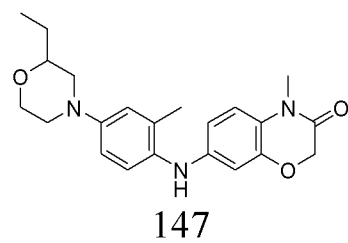
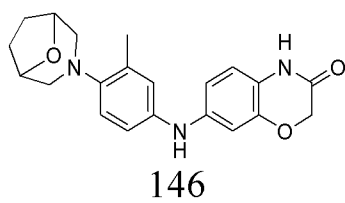
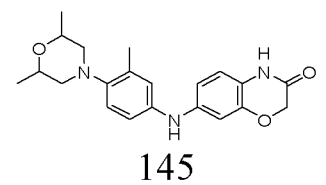
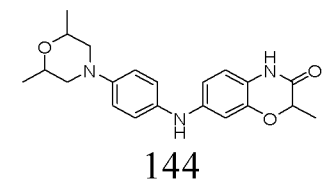
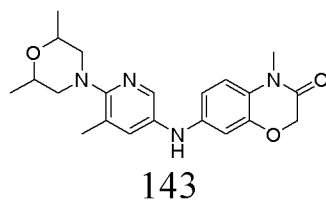
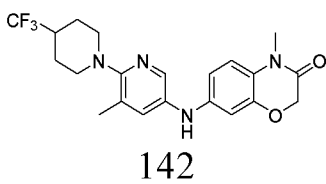
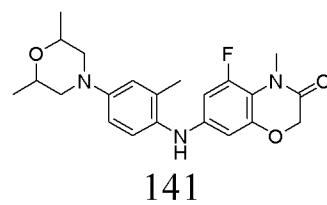
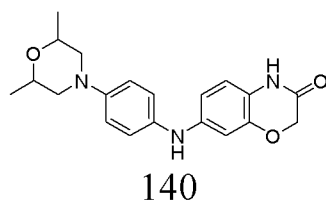
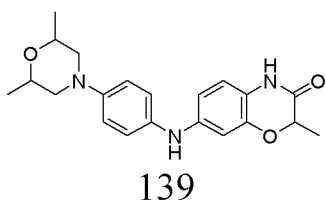
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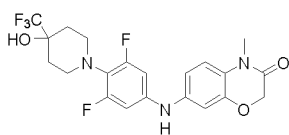


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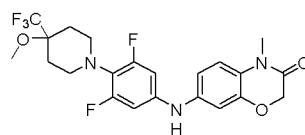


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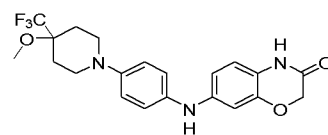




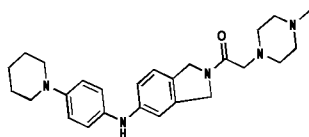
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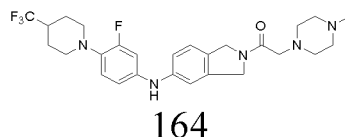
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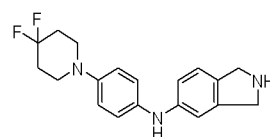
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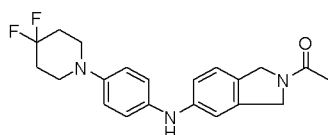
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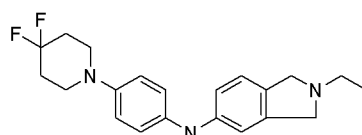
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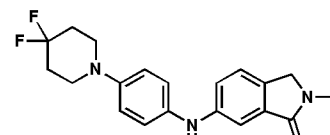
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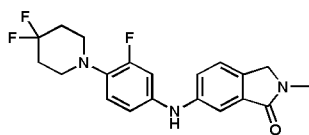
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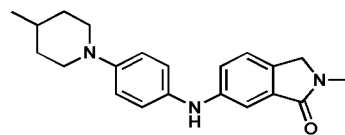
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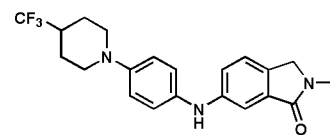
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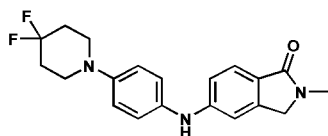
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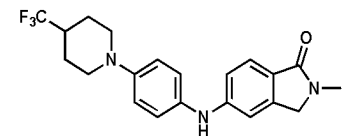
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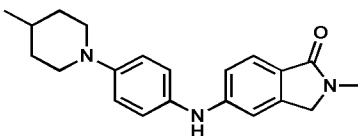
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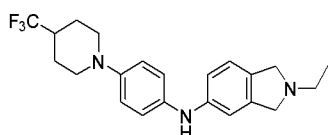
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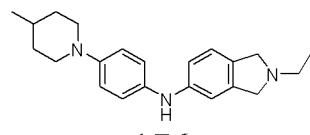
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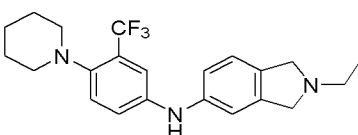
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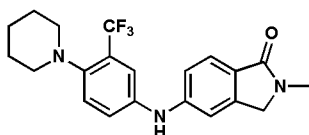
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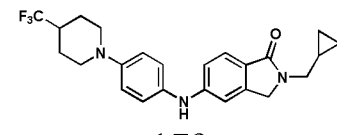
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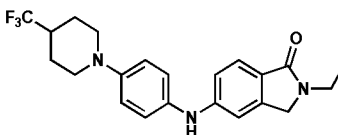
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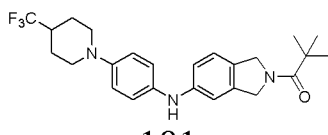
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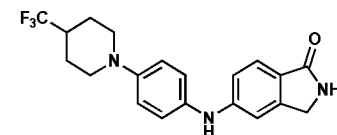
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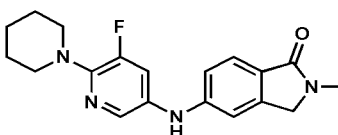
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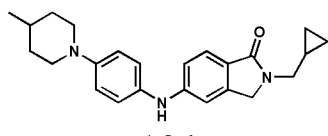
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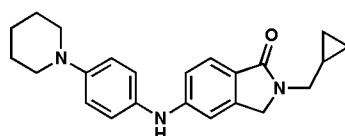
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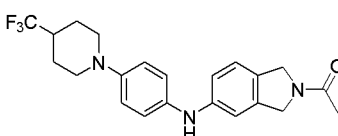
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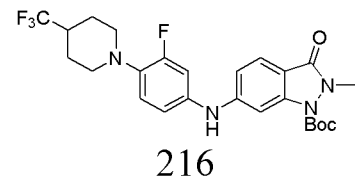
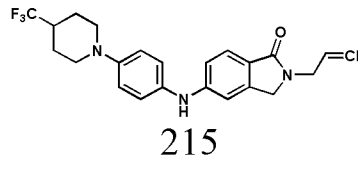
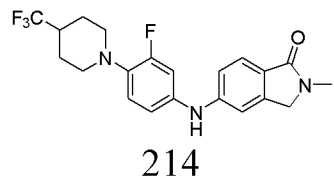
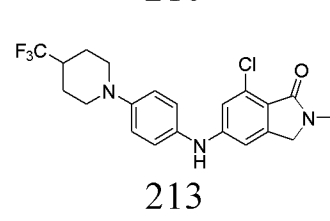
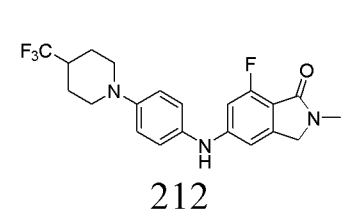
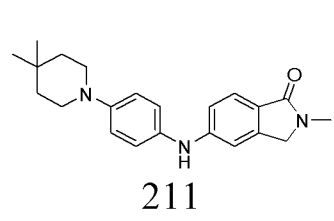
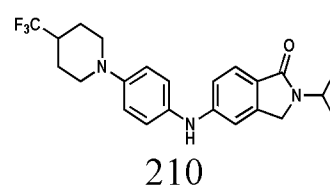
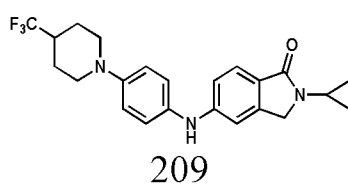
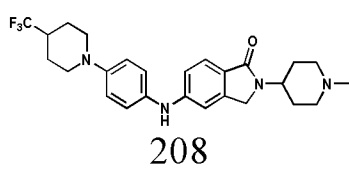
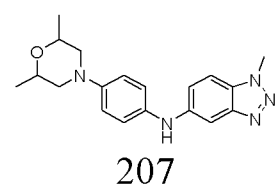
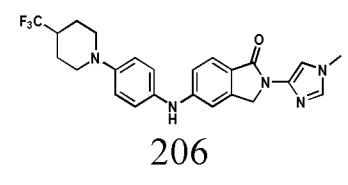
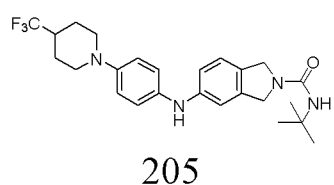
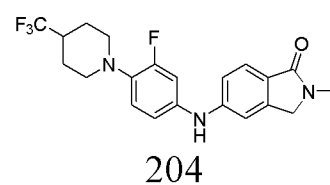
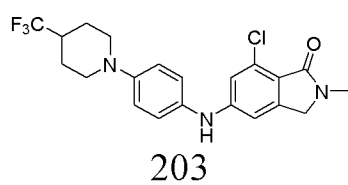
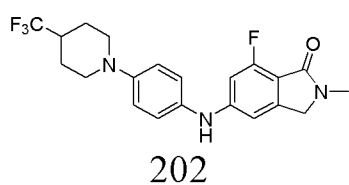
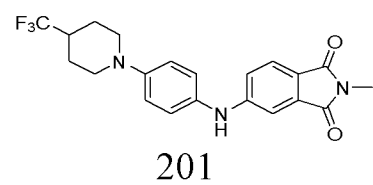
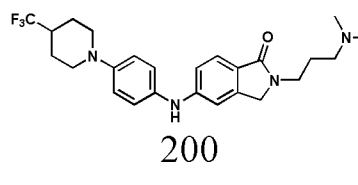
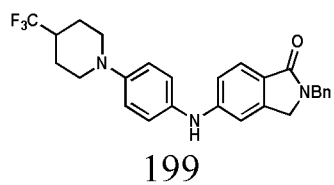
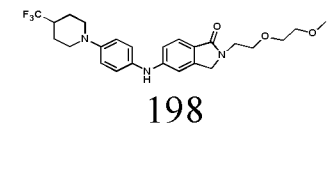
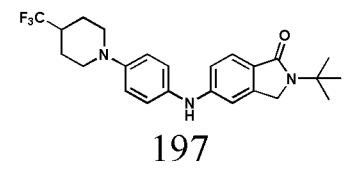
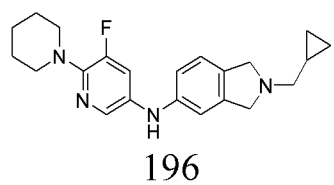
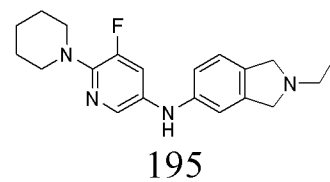
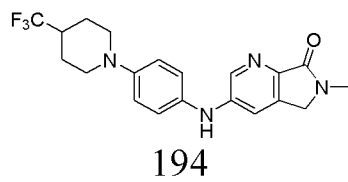
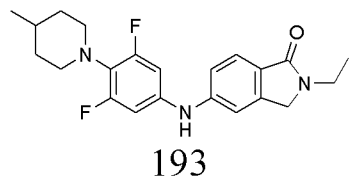
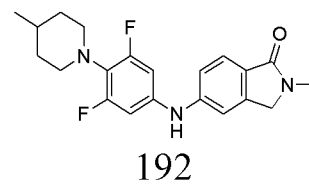
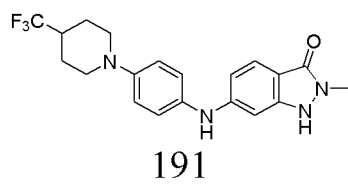
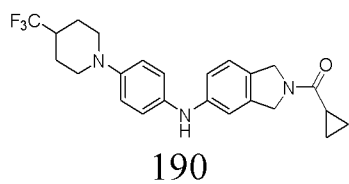
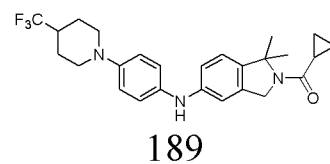
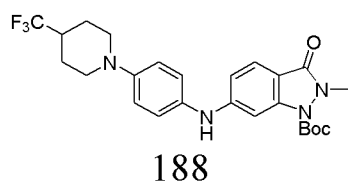
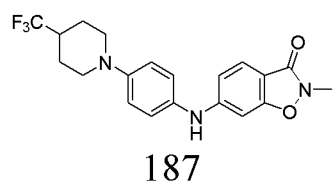
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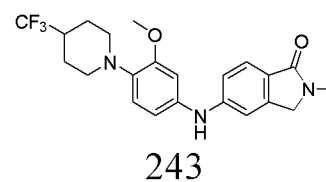
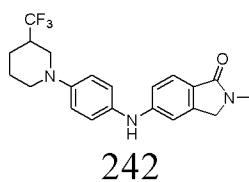
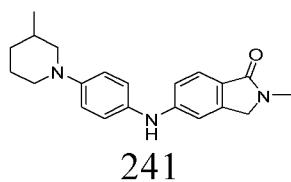
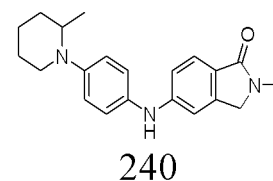
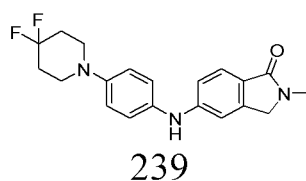
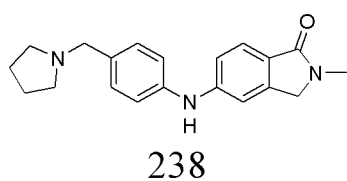
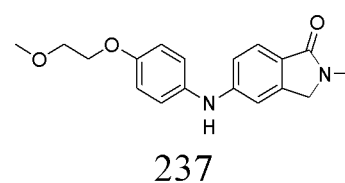
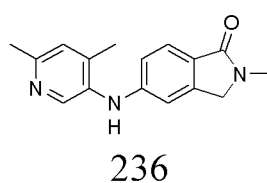
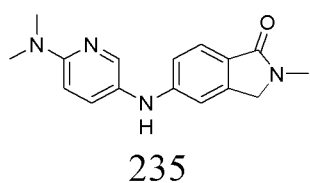
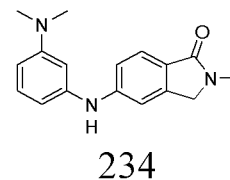
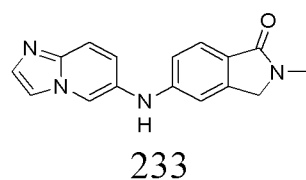
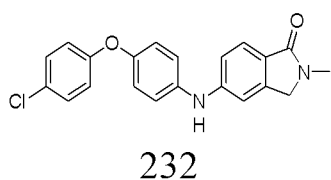
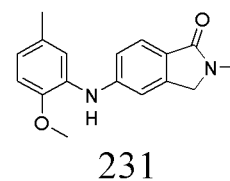
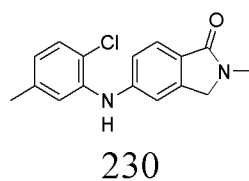
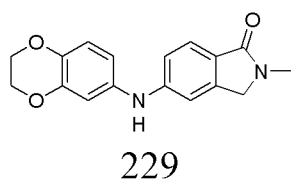
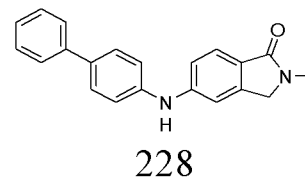
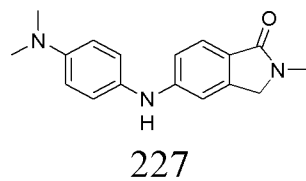
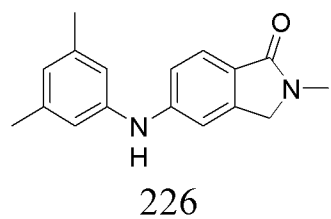
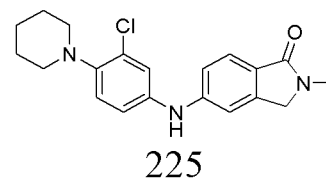
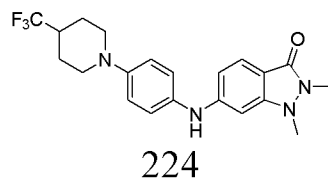
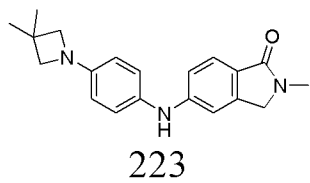
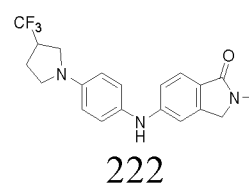
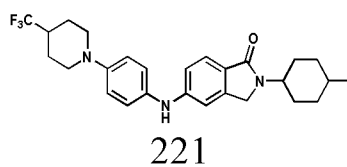
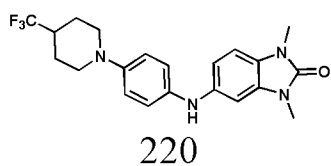
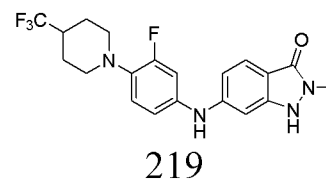
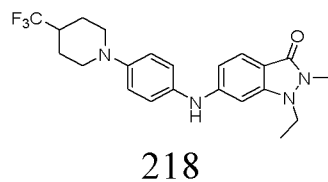
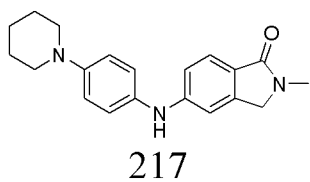


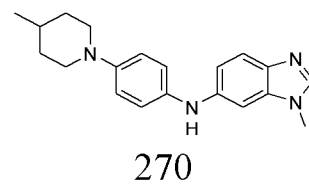
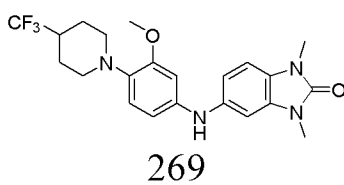
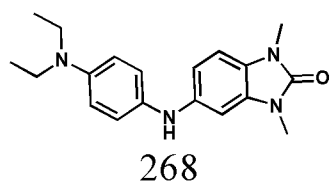
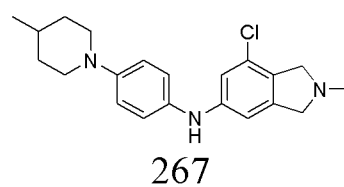
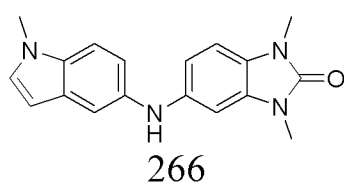
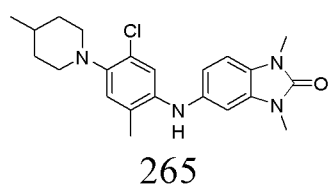
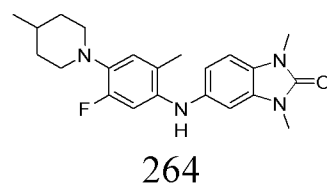
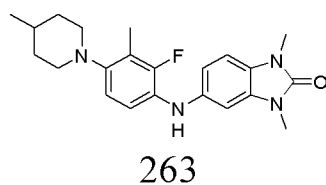
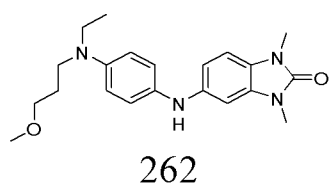
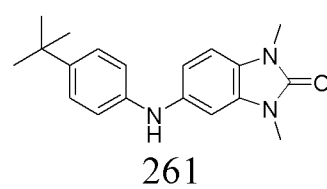
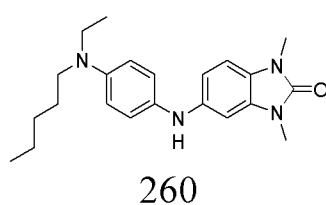
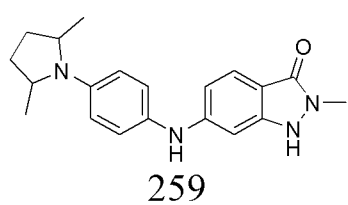
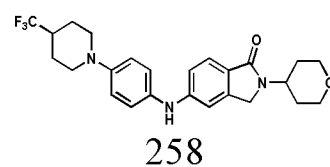
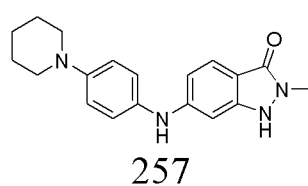
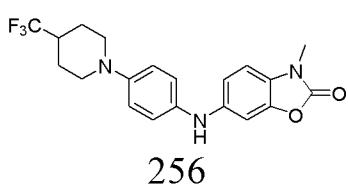
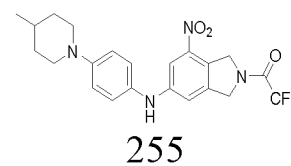
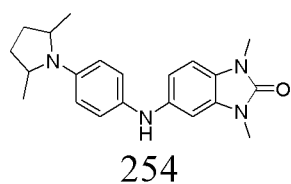
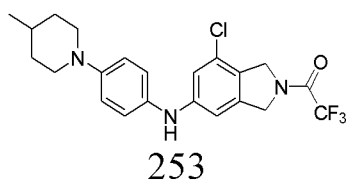
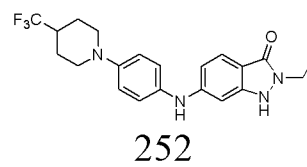
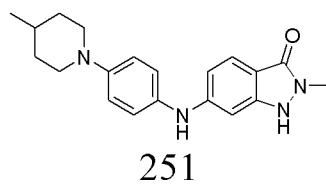
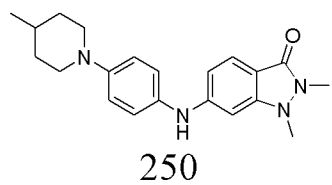
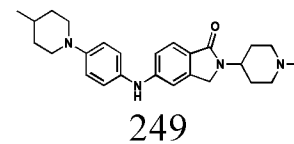
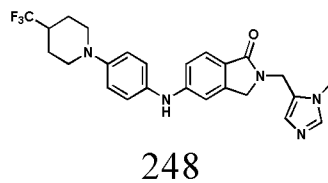
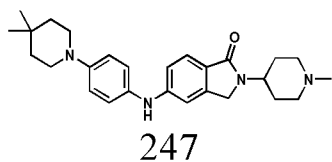
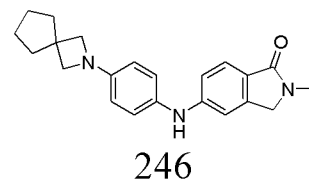
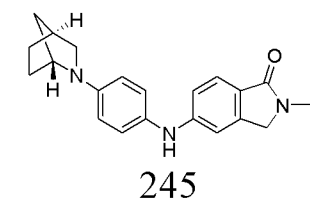
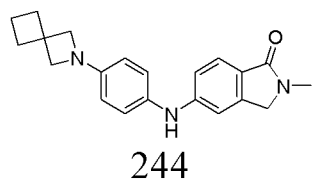
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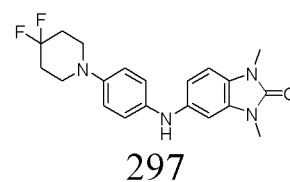
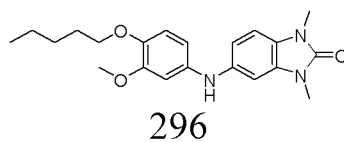
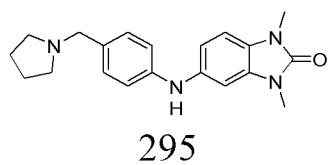
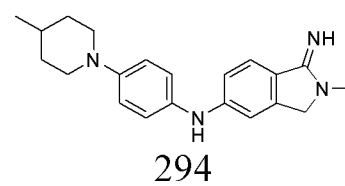
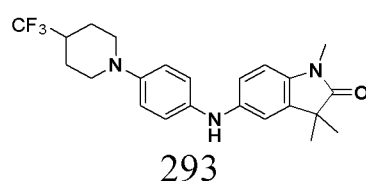
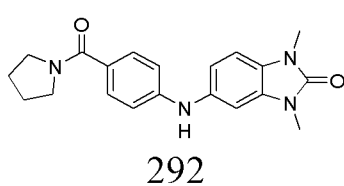
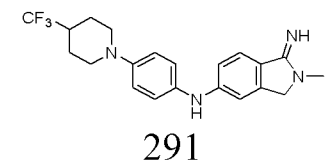
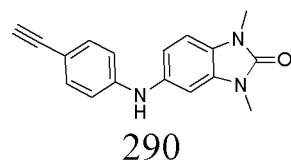
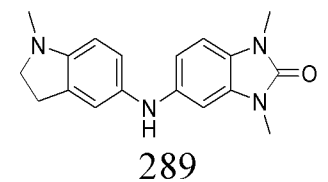
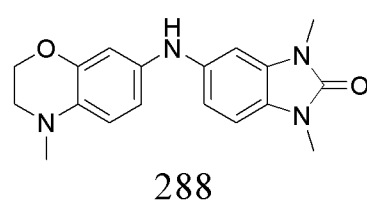
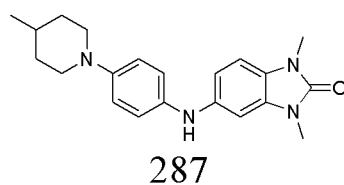
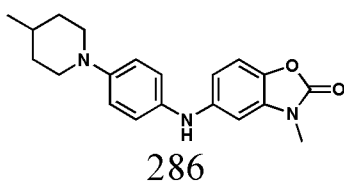
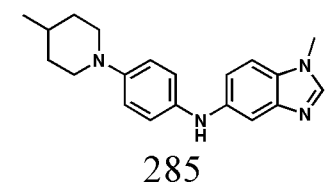
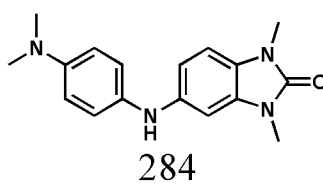
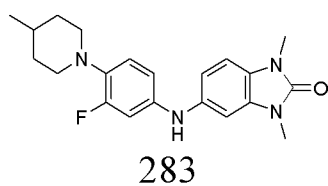
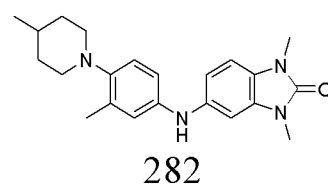
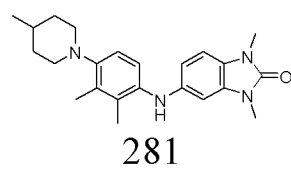
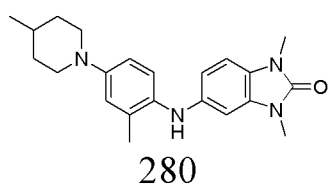
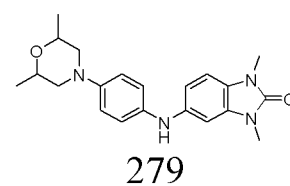
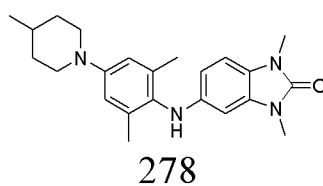
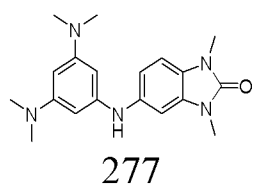
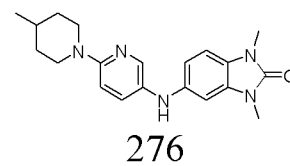
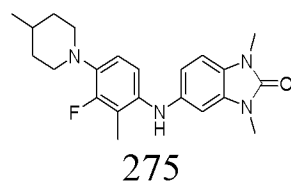
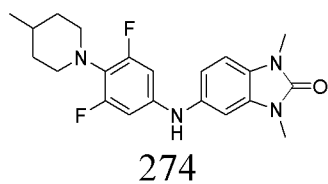
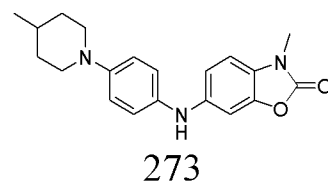
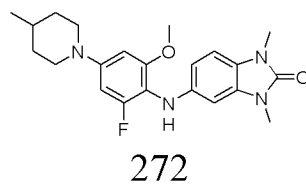
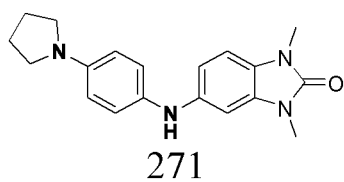


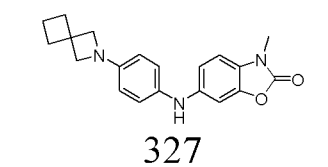
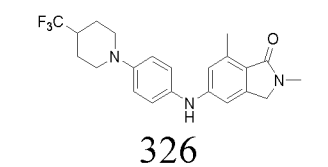
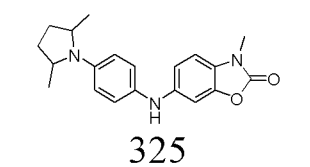
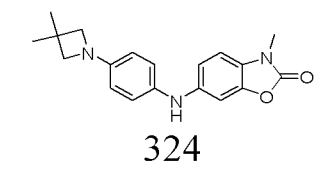
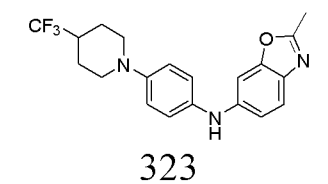
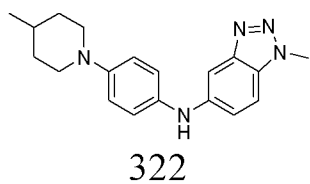
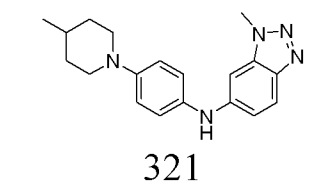
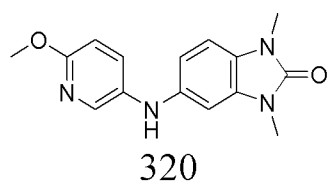
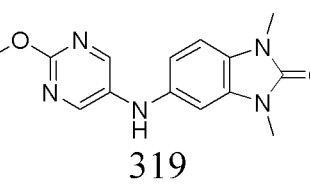
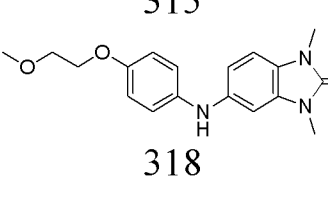
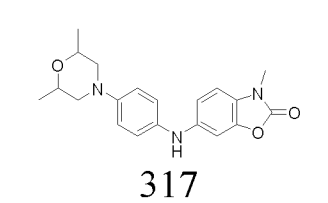
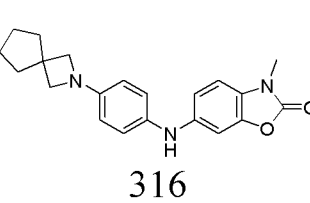
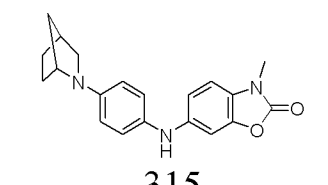
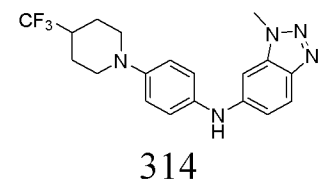
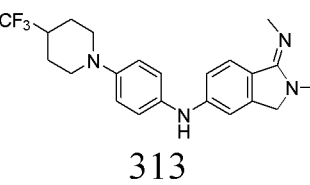
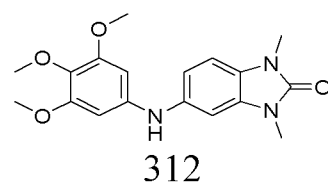
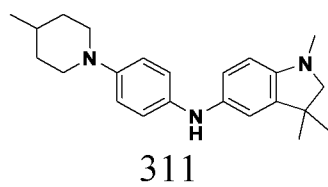
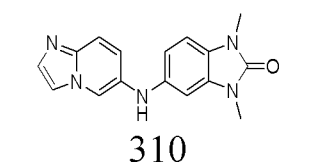
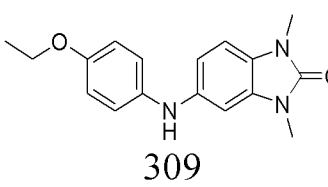
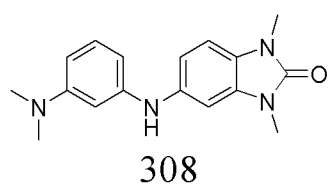
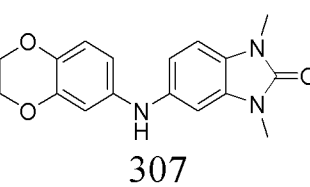
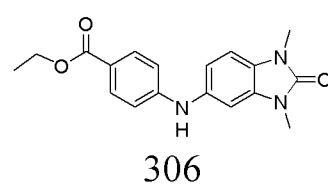
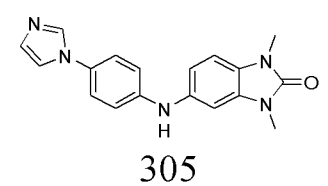
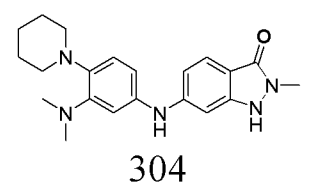
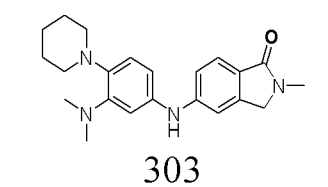
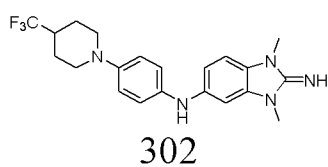
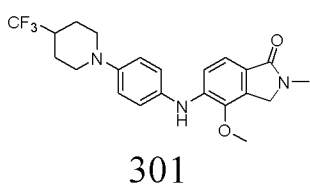
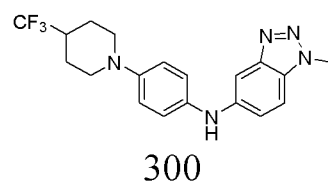
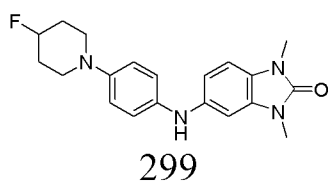
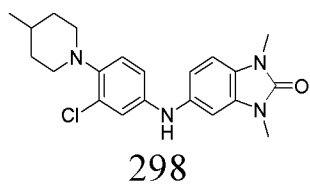
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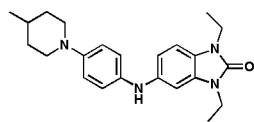




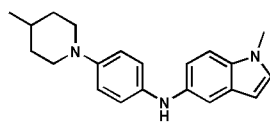




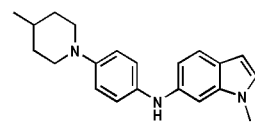




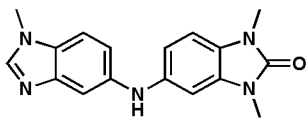
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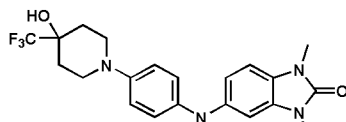
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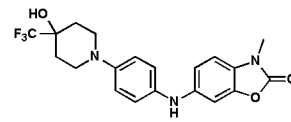
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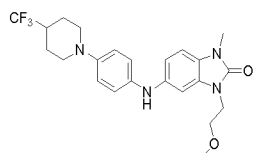
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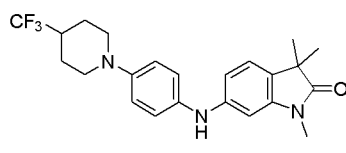
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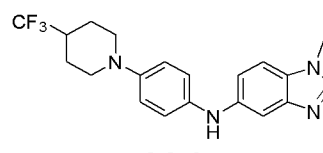
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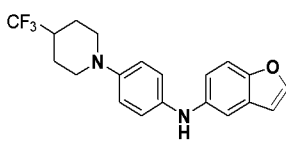
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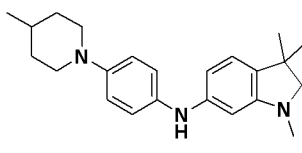
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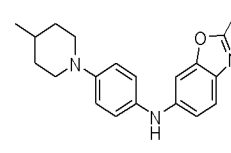
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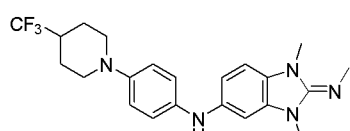
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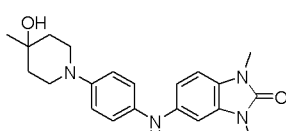
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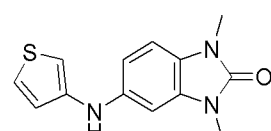
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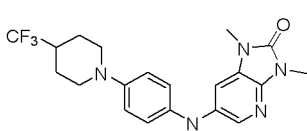
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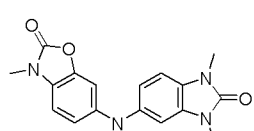
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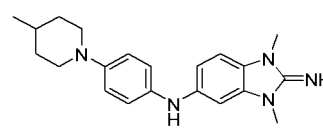
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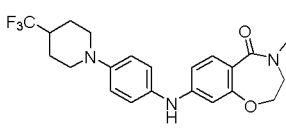
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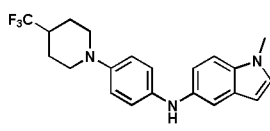
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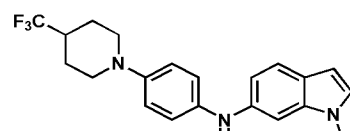
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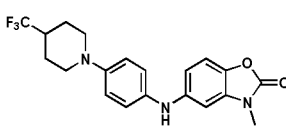
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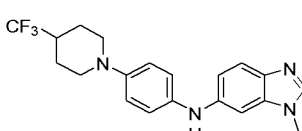
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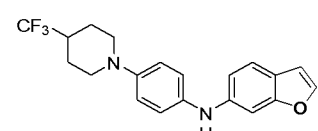
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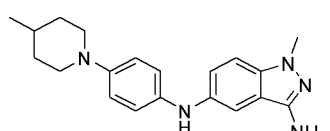
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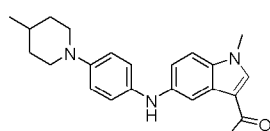
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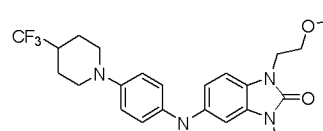
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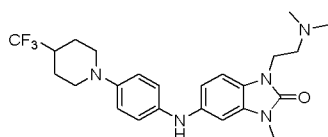
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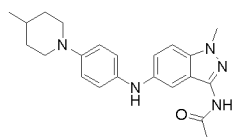
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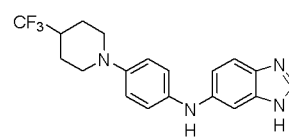
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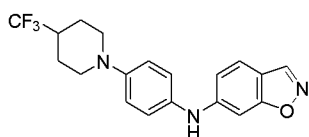
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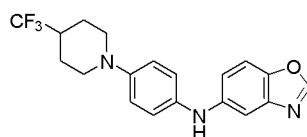
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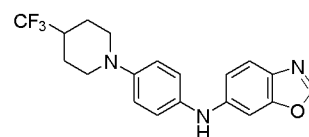
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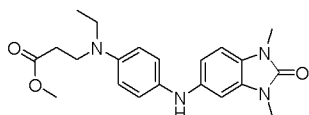
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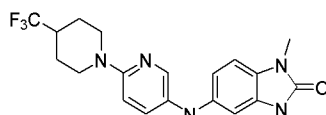
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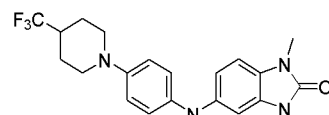
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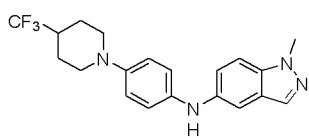
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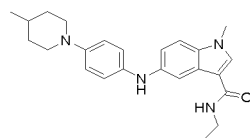
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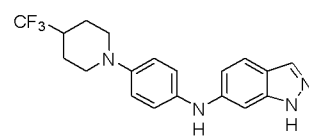
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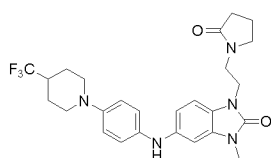
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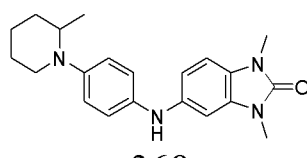
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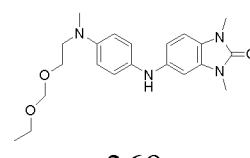
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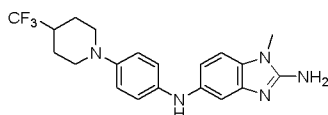
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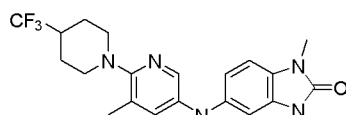
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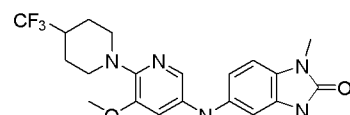
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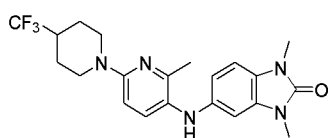
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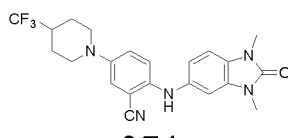
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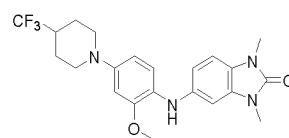
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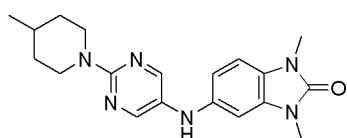
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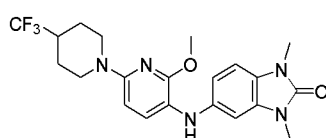
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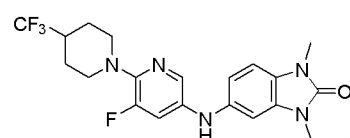
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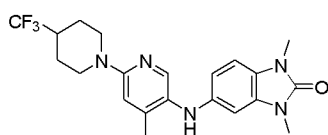
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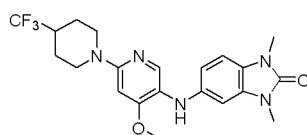
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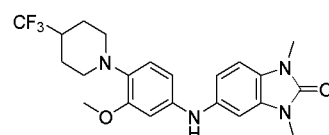
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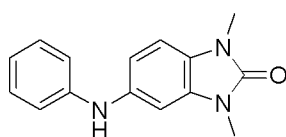
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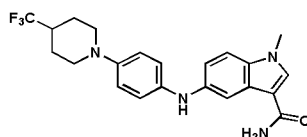
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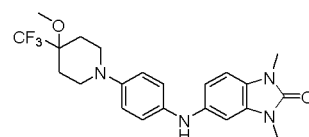
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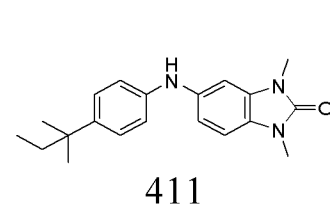
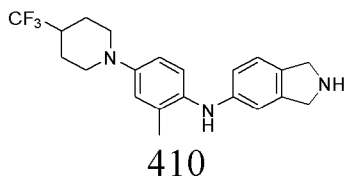
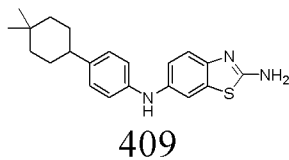
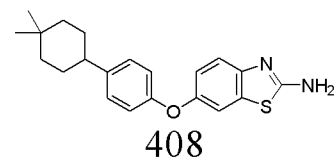
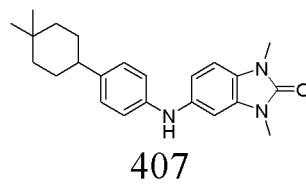
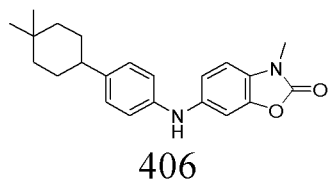
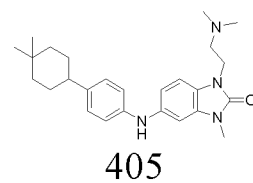
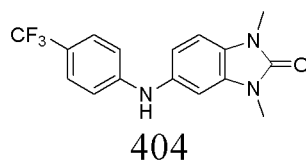
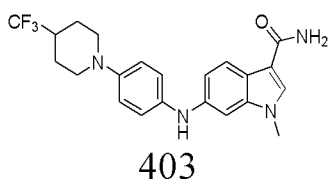
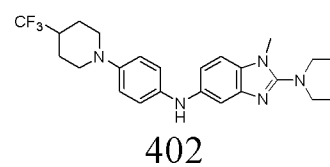
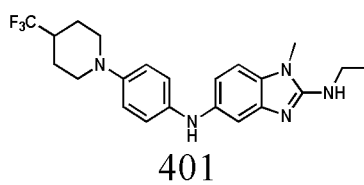
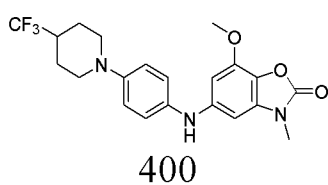
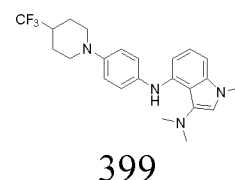
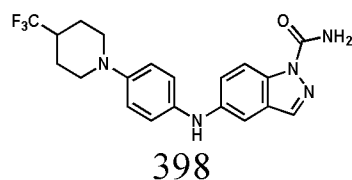
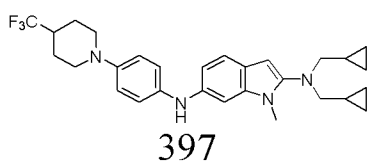
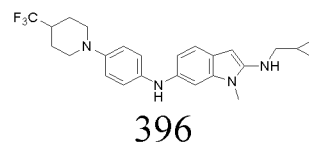
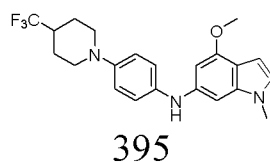
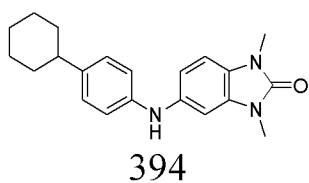
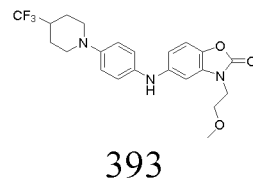
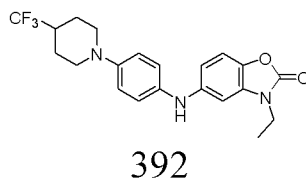
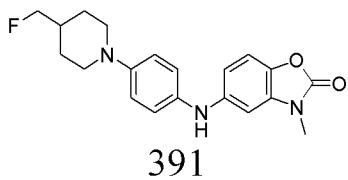
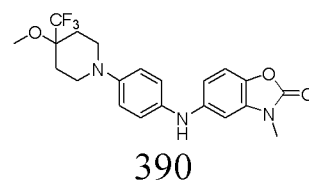
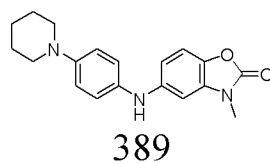
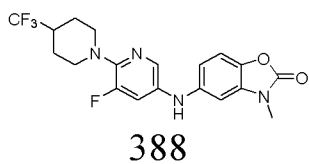
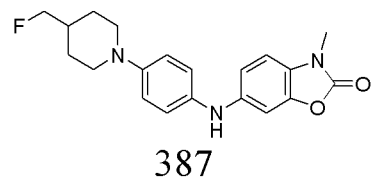
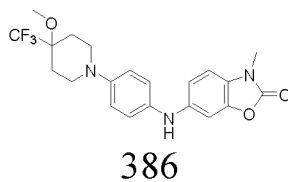
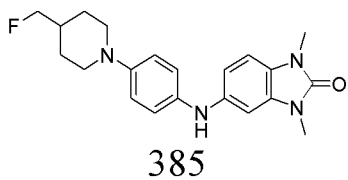
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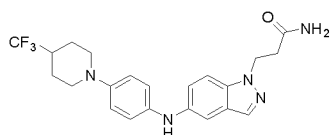


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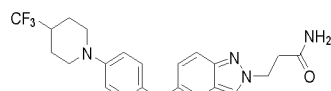


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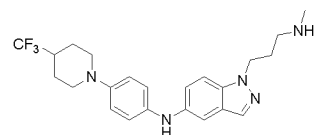




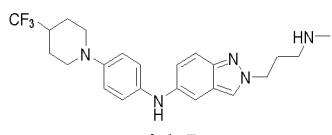
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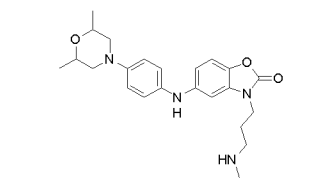
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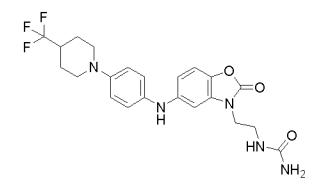
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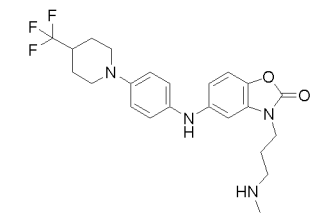
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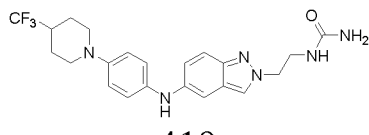
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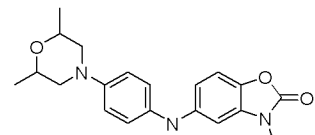
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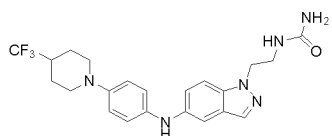
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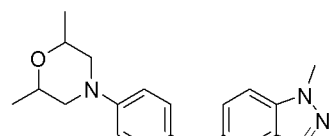
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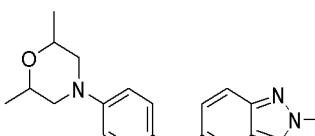
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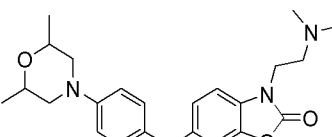
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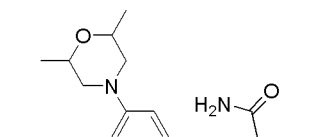
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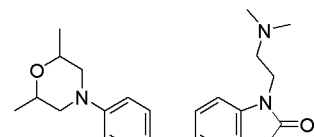
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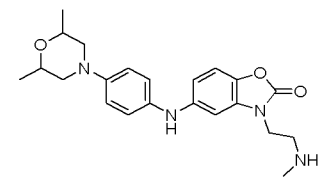
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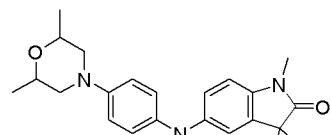
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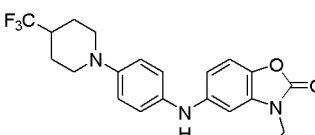
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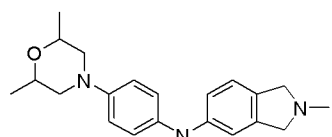
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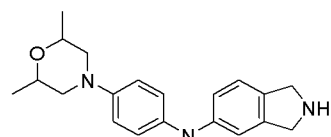
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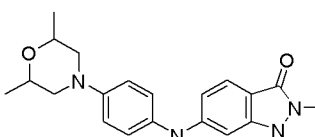
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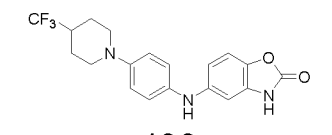
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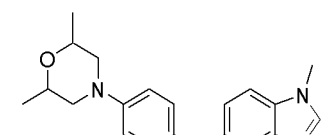
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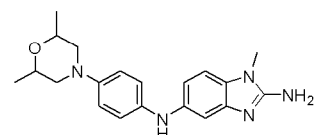
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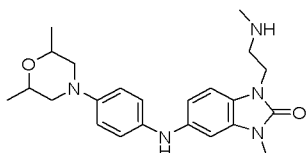
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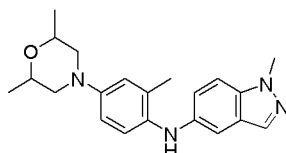
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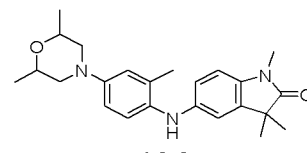
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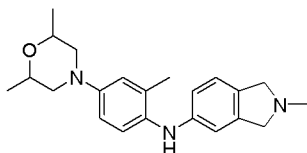
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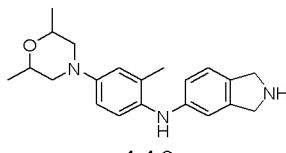
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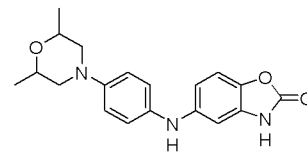
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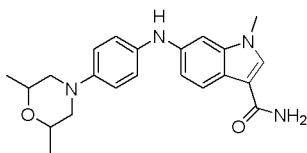
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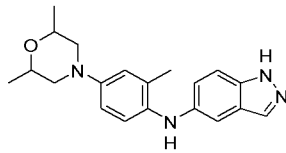
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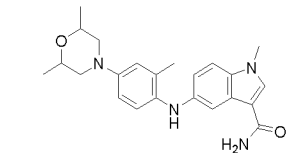
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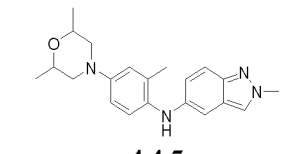
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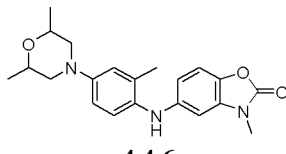
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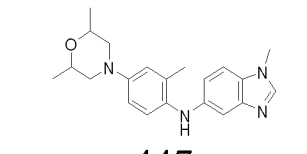
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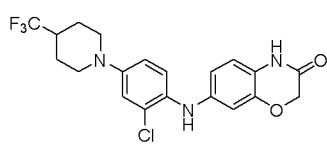
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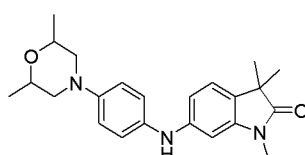
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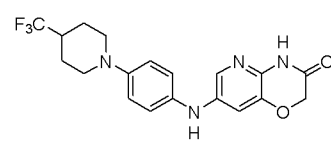
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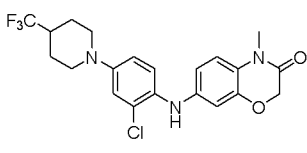
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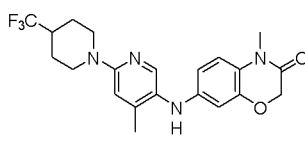
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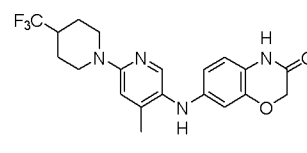
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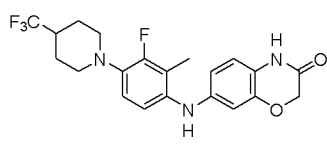
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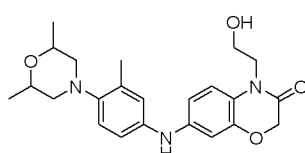
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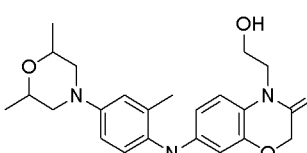
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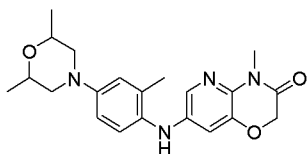
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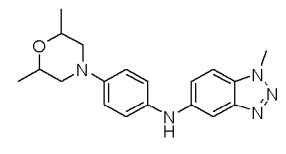
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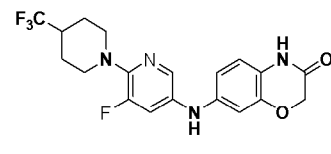
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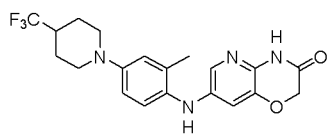
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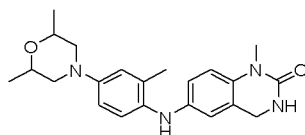
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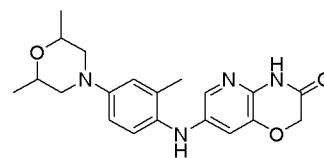
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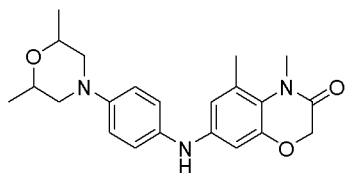
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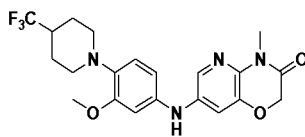
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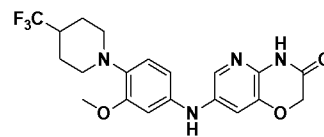
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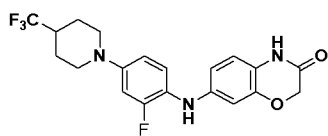
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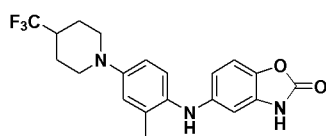
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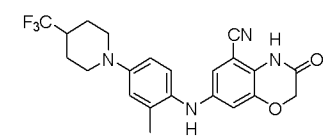
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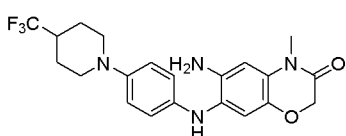
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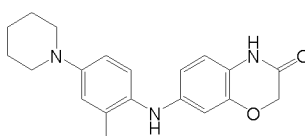
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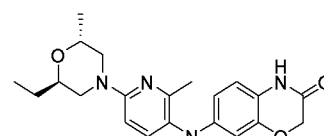
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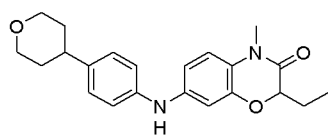
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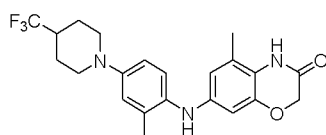
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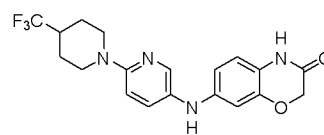
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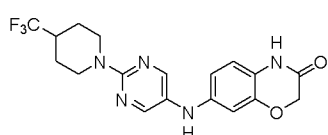
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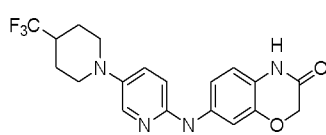
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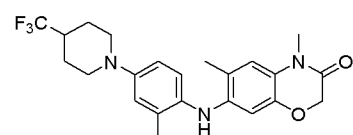
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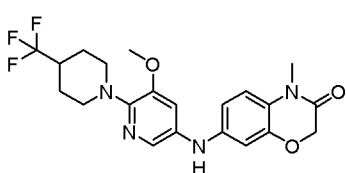
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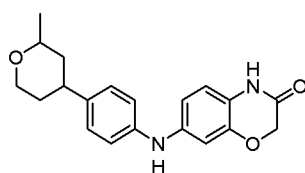
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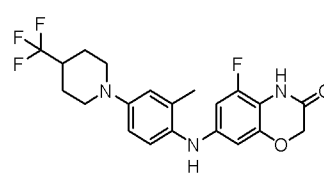
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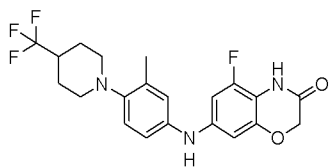
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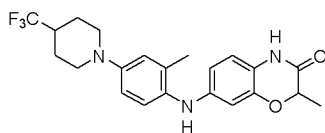
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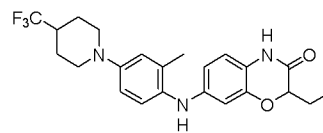
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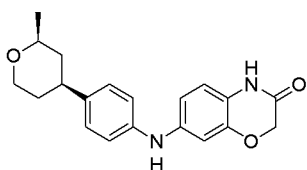
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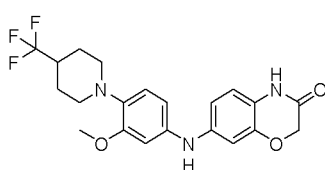
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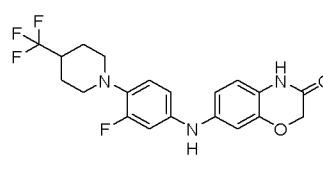
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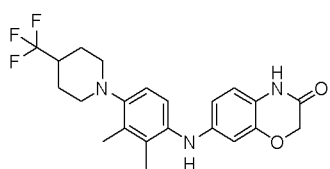
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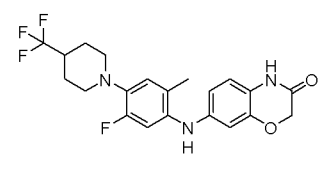
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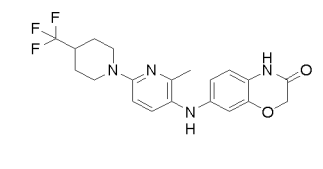
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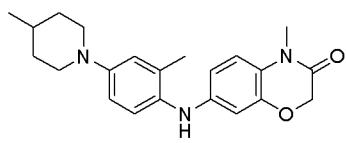
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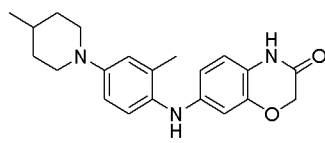
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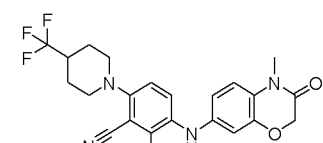
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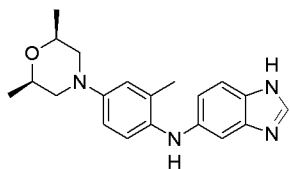
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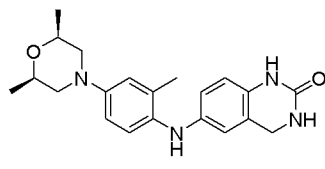
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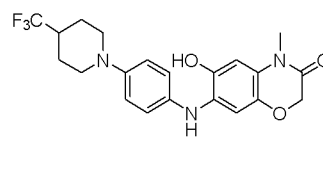
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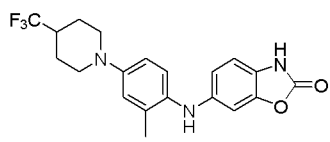
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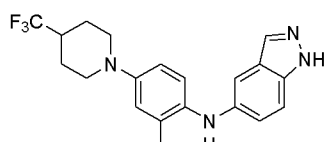
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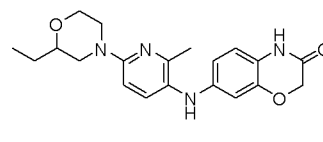
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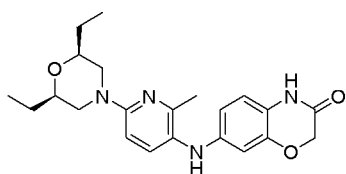
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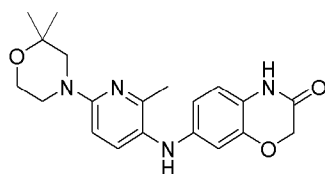
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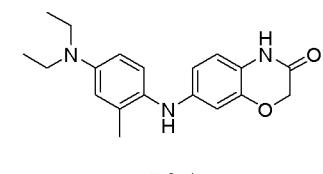
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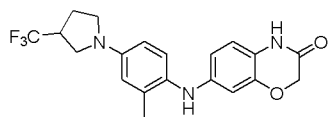
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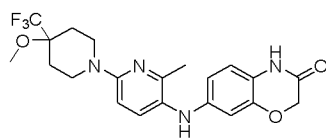
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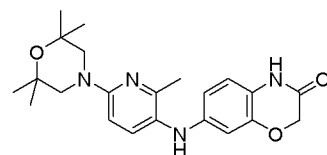
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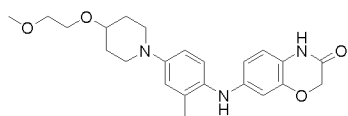
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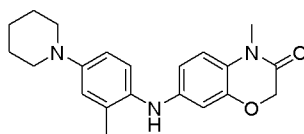
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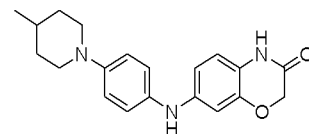
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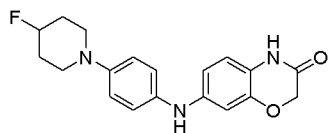
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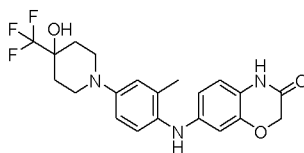
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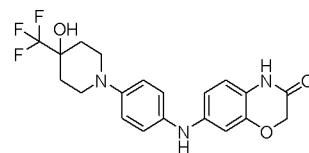
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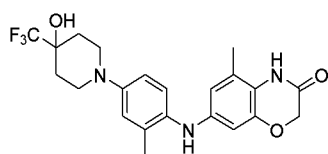
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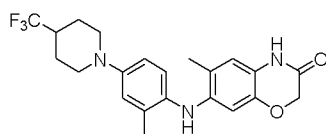
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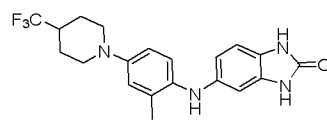
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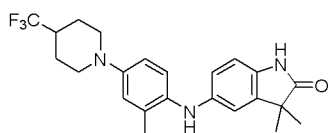
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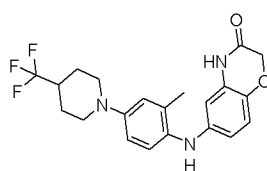
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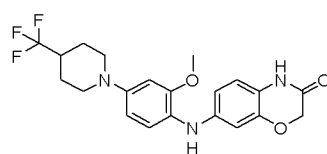
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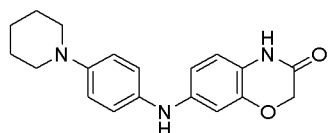
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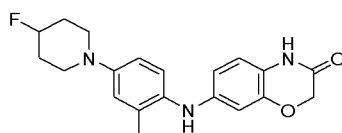
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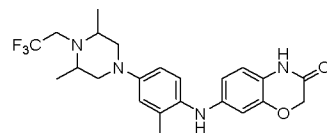
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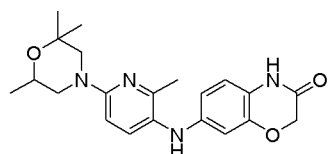
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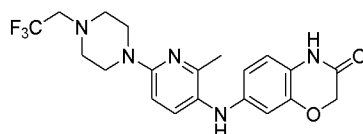
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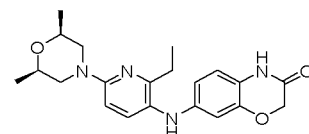
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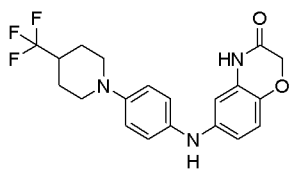
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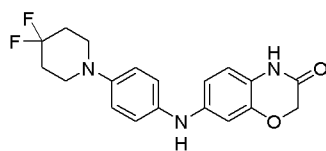
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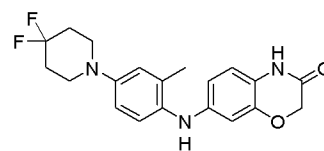
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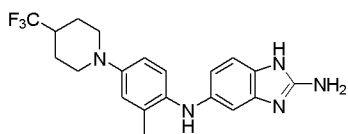
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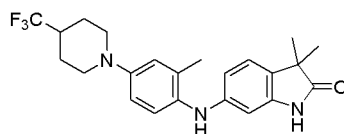
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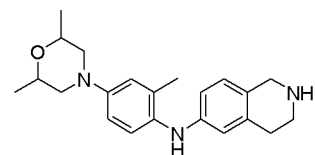
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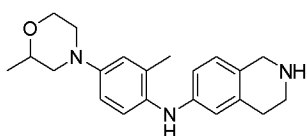
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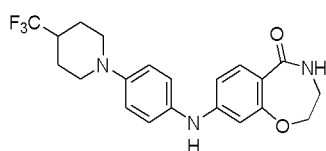
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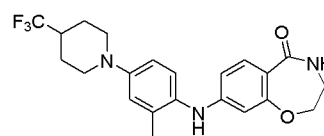
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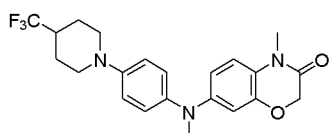
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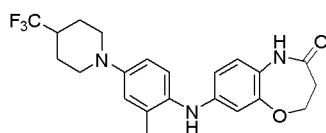
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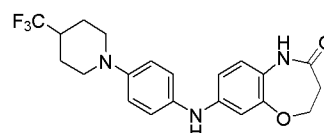
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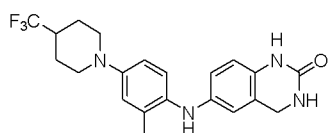
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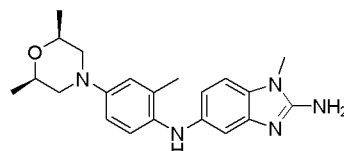
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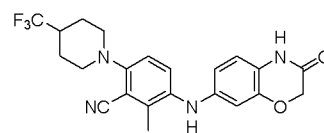
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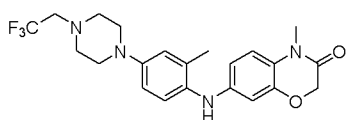
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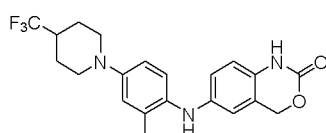
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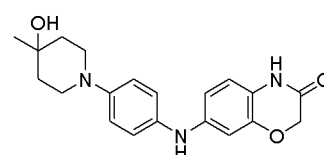
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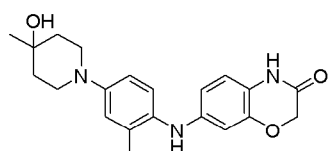
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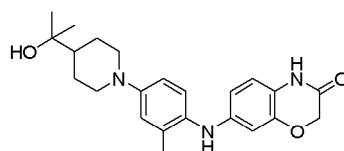
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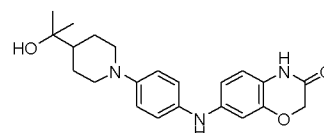
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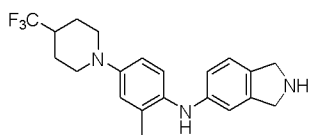
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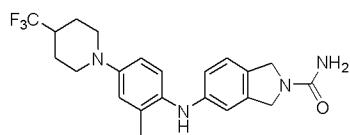
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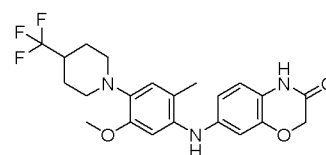
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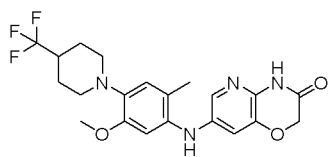
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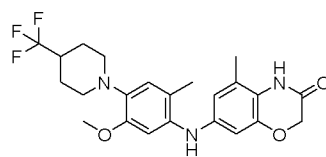
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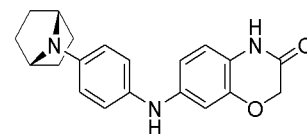
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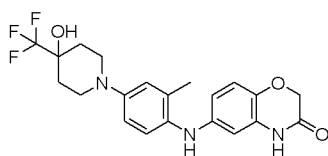
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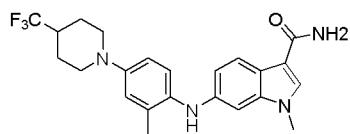
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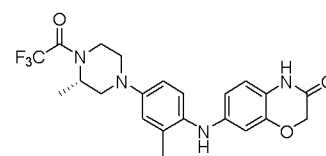
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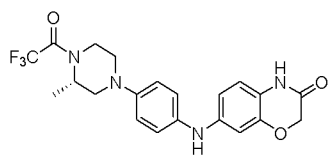
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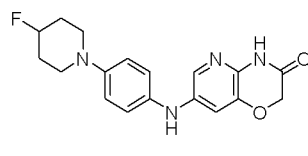
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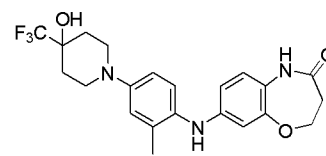
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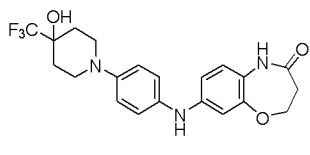
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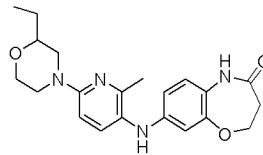
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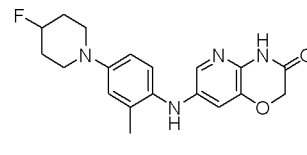
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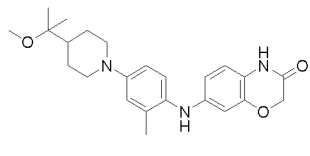
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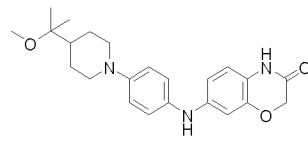
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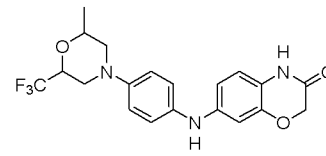
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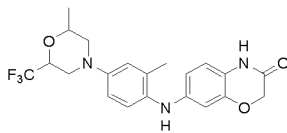
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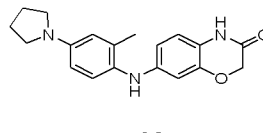
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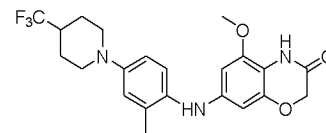
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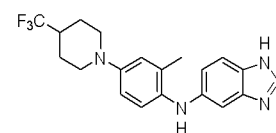
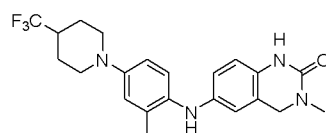
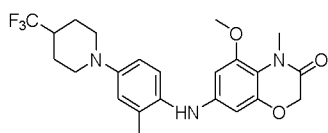
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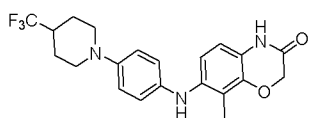
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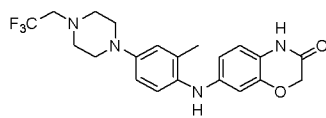
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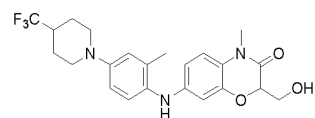
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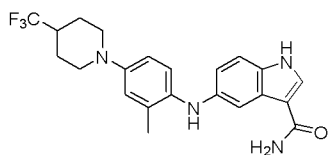
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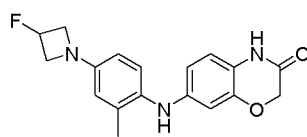
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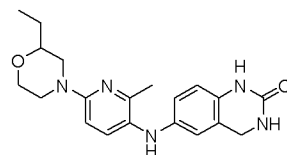
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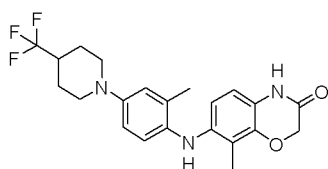
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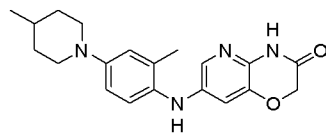
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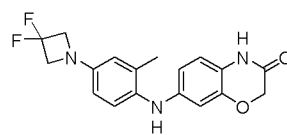
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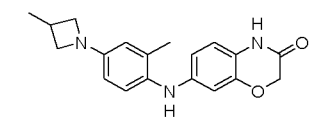
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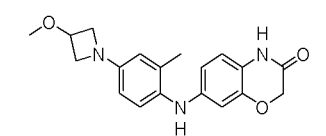
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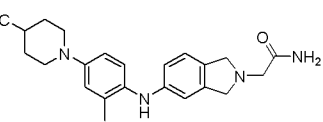
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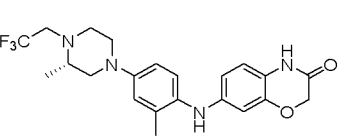
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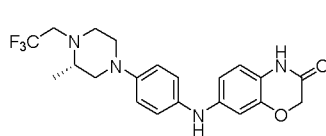
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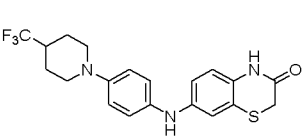
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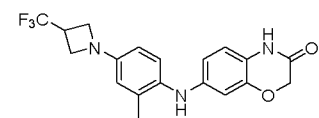
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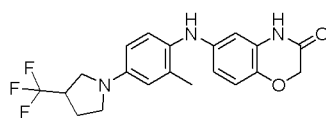
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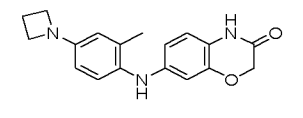
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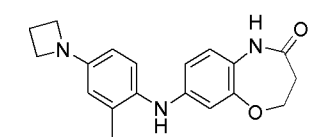
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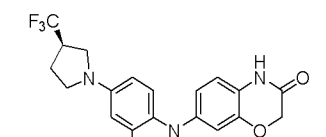
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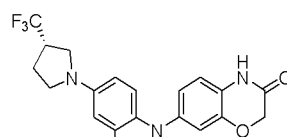
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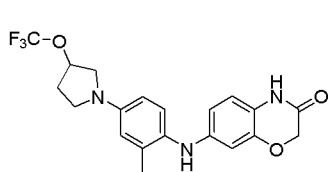
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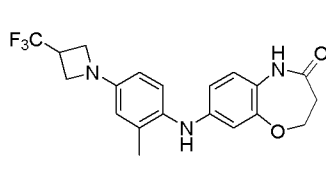
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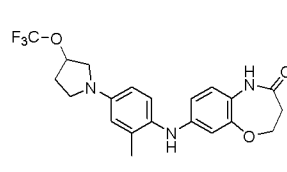
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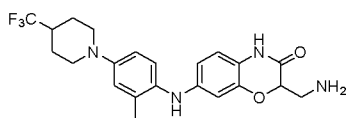
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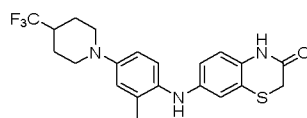
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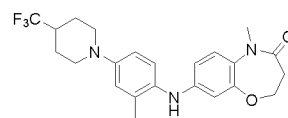
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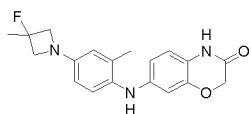
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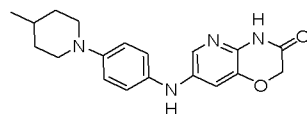
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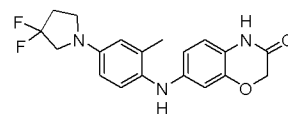
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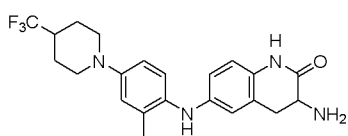
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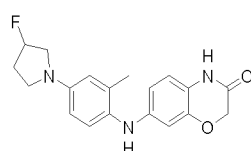
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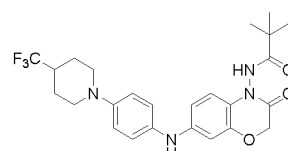
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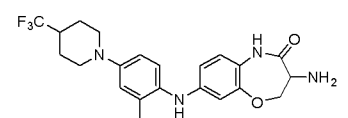
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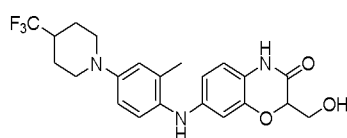
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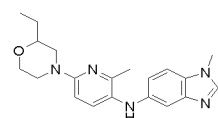
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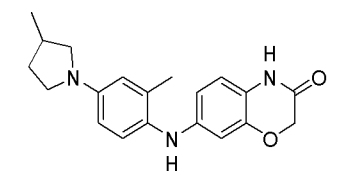
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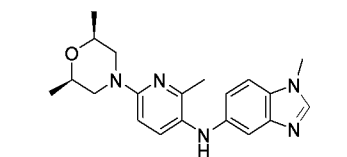
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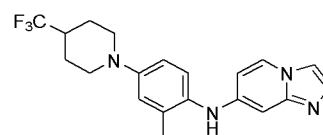
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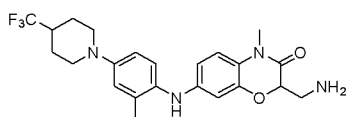
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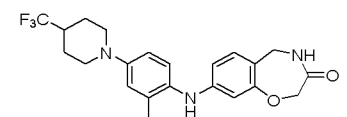
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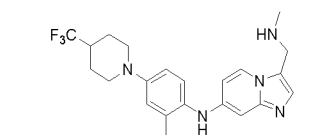
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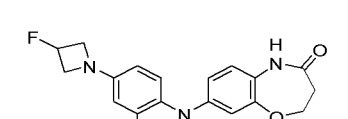
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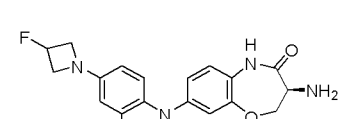
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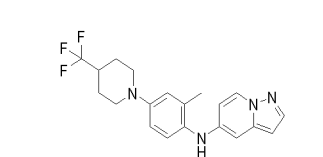
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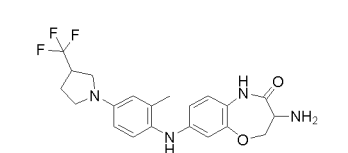
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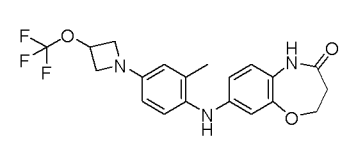
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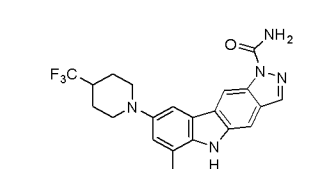
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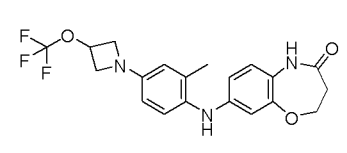
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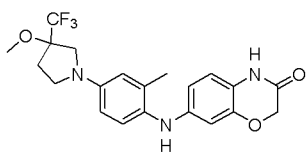
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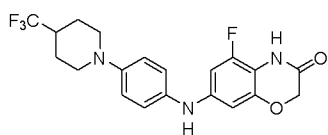
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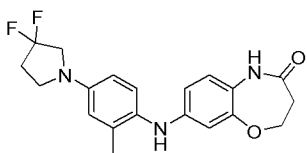
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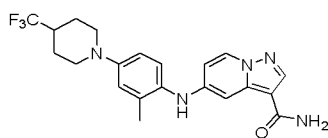
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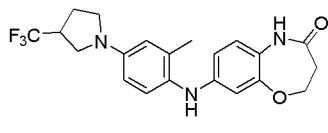
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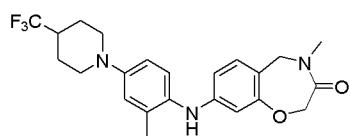
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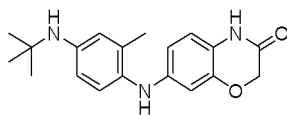
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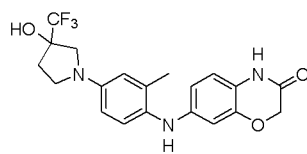
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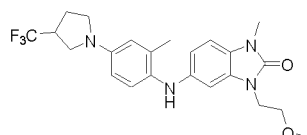
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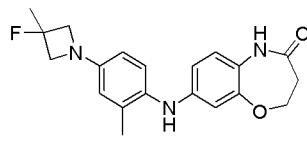
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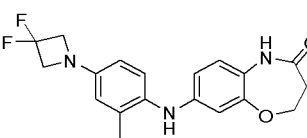
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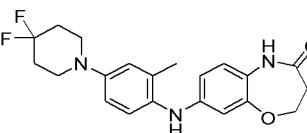
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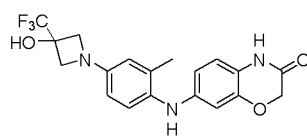
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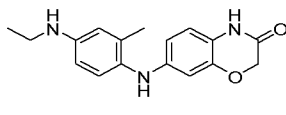
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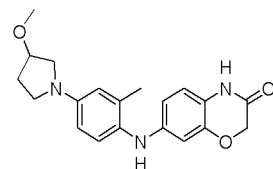


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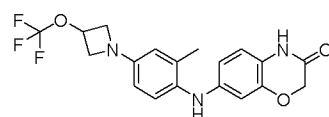


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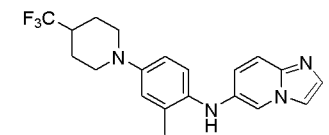
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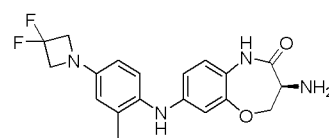
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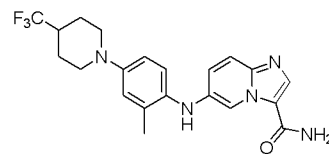
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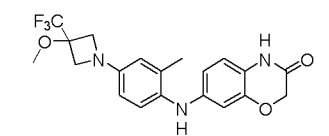
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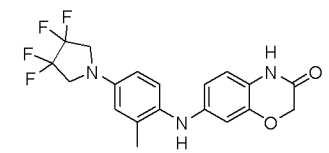
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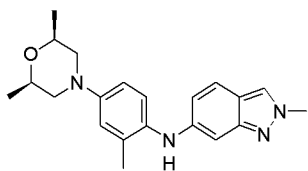
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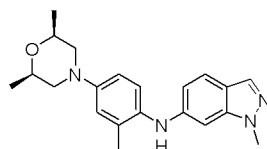
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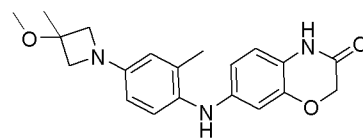
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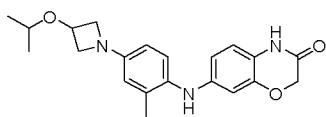
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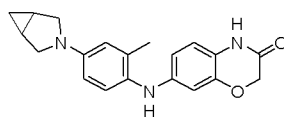
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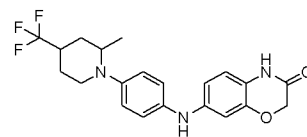
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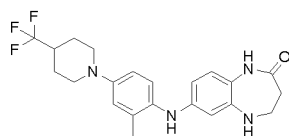
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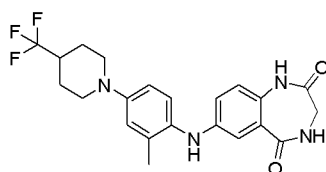
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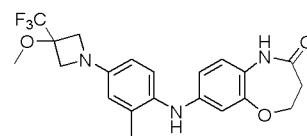
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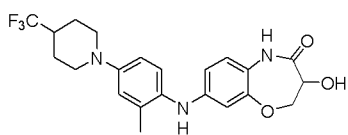
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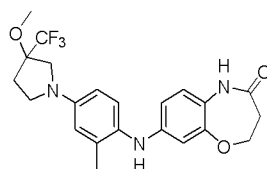
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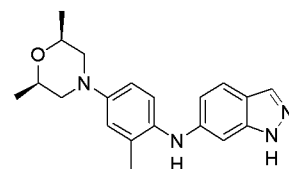
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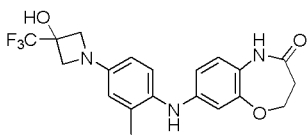
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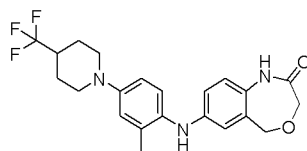
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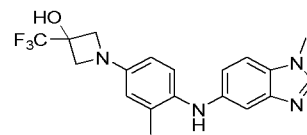
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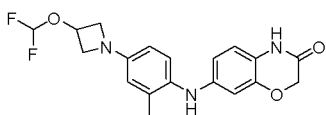
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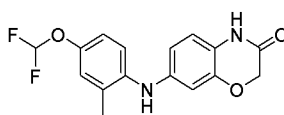
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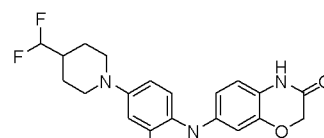
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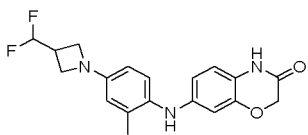
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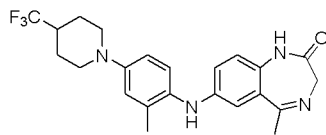
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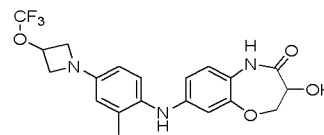
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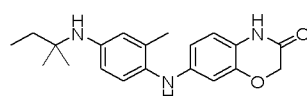
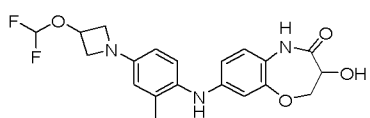
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a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing.

48. A pharmaceutical composition comprising a compound according to any one of claims 1 to 47, a tautomer thereof, a solvate or stereoisomer
5 of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing and at least one pharmaceutically acceptable carrier.

49. A method of treating a disease or condition, comprising administering to a subject in need thereof, a therapeutically effective amount of a compound according to any one of claims 1 to 47, a tautomer
10 thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing or the pharmaceutical composition according to claim 48; wherein the disease or condition is selected from neuropathy, stroke, neurodegenerative disease, Parkinson's Disease, amyotrophic lateral sclerosis (AML), multiple sclerosis,
15 Huntington's Disease, dementia with Lewy bodies, Friedreich's ataxia, hair follicle morphogenesis, diabetes, sepsis, transplant rejection, periventricular leukomalacia, ischemia reperfusion injury, blood coagulation, myocardial infarction, and kidney dysfunction.

50. A method of treating a disease or condition involving ferroptosis,
20 comprising administering to a subject in need thereof, a therapeutically effective amount of a compound according to any one of claims 1 to 47, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing or the pharmaceutical composition according to claim 48.

51. A method of modulating ferroptosis, comprising contacting a
25 subject in need thereof with a compound according to any one of claims 1 to 47, a tautomer thereof, a solvate or stereoisomer of the compound or the tautomer, or a pharmaceutically acceptable salt of the foregoing or the pharmaceutical composition according to claim 48.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2022/104559

A. CLASSIFICATION OF SUBJECT MATTER

C07D 401/12(2006.01)i; C07C 211/55(2006.01)i; A61K 31/136(2006.01)i; A61K 31/395(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D401/-, C07C211/-, A61K31/-

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CNPAT, CNKI, WPI, EPODOC, ISI Web of Knowledge, STN(Registry, Caplus, Marpet): SIRONAX, ferroptosis, benzamide, acetamide, cell w death, iron, search the structures in claims

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 102939282 A (AC IMMUNE S.A.) 20 February 2013 (2013-02-20) abstract, claims 1, 25	1-4, 6, 9-10, 13, 16, 24-25, 28-29, 40-44, 48
X	WO 02085868 A1 (ASTRAZENECA AB et al.) 31 October 2002 (2002-10-31) abstract, examples 14-15	1-3, 6, 9, 14, 19, 24, 26- 29, 40-44, 48
X	WO 2010027002 A1 (SHIONOGI & CO., LTD.) 11 March 2010 (2010-03-11) abstract, pages 136-137 compounds I-312 and I-321	1-2, 4, 6, 9, 13, 15, 24, 28-29, 48
X	WO 2015115673 A1 (ONO PHARMACEUTICAL CO., LTD.) 06 August 2015 (2015-08-06) abstract, examples 37, 42-43, 46, 52, 67, 75, 82, 86, 104, 111, 158- 160, 169, 171, 173, 175, 177	1-4, 6, 9, 11, 24-25, 28- 29, 32-44, 48



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

“A” document defining the general state of the art which is not considered to be of particular relevance

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&” document member of the same patent family

Date of the actual completion of the international search

19 September 2022

Date of mailing of the international search report

10 October 2022

Name and mailing address of the ISA/CN

National Intellectual Property Administration, PRC
6, Xitucheng Rd., Jimen Bridge, Haidian District, Beijing
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Facsimile No. (86-10)62019451

Authorized officer

LI,Bing

Telephone No. 86-(10)-53962156

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2022/104559

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	-. "STN REGISTRY" <i>RN 2552501-69-4, 1921193-48-7, 1921151-34-9, 1916913-48-8, 1685251-49-3, 1477822-78-8, 1384753-63-2, 1347493-30-4, 1082591-46-5, 2552501-63-8, 2552501-58-1, 1982789-79-6, 918330-47-9, 918330-26-4, 918330-25-3, 918330-24-2, 918330-23-1, 953408-42-9, 918506-22-6, 918506-24-8, 918517-77-8, 918518-23-7, 918521-86-5, 918522-02-8, 918522-07-3, 918522-32-4, 1802660-90-7, 1011466-89-9, 1507798-16-4, 1514692-75-1, 1516141-45-9, 1518268-84-2, 2060610-21-9, 1314996-74-1, 1539241-26-3, 09 December 2020 (2020-12-09),</i>	1-3, 5-8, 10, 14, 20, 24, 28-45, 47
A	WO 2020185738 A1 (COLLABORATIVE MEDICINAL DEVELOPMENT, LLC) 17 September 2020 (2020-09-17) abstract, paragraphs[0086]-[0087], [0092]-[0093], claim 2	1-51

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2022/104559

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **49-51**
because they relate to subject matter not required to be searched by this Authority, namely:

[1] Claims 49-51 are directed to the methods for treating diseases, but the report is based on the use of the compounds in the manufacture of medicaments for treating the corresponding diseases.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CN2022/104559

Patent document cited in search report			Publication date (day/month/year)	Patent family member(s)			Publication date (day/month/year)
CN	102939282	A	20 February 2013	BR	112012026249	A2	29 November 2016
				WO	2011128455	A1	20 October 2011
				JP	2013525297	A	20 June 2013
				BR	112016026249	A2	15 August 2017
				CO	6910184	A2	31 March 2014
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				CA	2794808	A1	20 October 2011
				IL	222268	D0	31 December 2012
				US	2016158242	A1	09 June 2016
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				AU	2011239966	A1	25 October 2012
				MX	2012011776	A	17 December 2012
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				EP	2558446	A1	20 February 2013
				ES	2734552	T3	10 December 2019
				KR	20130098154	A	04 September 2013
				ZA	201207613	B	19 December 2018
				NZ	602777	A	25 July 2014
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				JP	2004528335	A	16 September 2004
				EP	1385835	A1	04 February 2004
WO	2010027002	A1	11 March 2010	JP	WO2010027002	A1	02 February 2012
				TW	201011040	A	16 March 2010
				EP	2341052	A1	06 July 2011
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WO	2015115673	A1	06 August 2015	US	2018289718	A1	11 October 2018
				EP	3099672	A1	07 December 2016
				US	2016331757	A1	17 November 2016
				JP	2017504628	A	09 February 2017
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				JP	2022523860	A	26 April 2022
				US	2022144826	A1	12 May 2022
				KR	20210137134	A	17 November 2021
				CA	3133070	A1	17 September 2020
				IL	286180	A	31 October 2021
				CN	113631535	A	09 November 2021
				EP	3938340	A1	19 January 2022