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(54) MODULATORS OF THE SIGMA-2 RECEPTOR AND THEIR METHOD OF USE

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claimer.

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- (63) Continuation of application No. 16/496,073, filed as application No. PCT/US2018/022574 on Mar. 15, 2018, now Pat. No. 10,961,249.
- (60) Provisional application No. 62/474,277, filed on Mar. 21, 2017.
- (51) **Int. Cl.** (2006.01)

(56) References Cited

U.S. PATENT DOCUMENTS

8,148,408	B2	4/2012	Bunnelle et al.
10,961,249	B2 *	3/2021	Blass C07D 203/00
2009/0170824	A1	7/2009	Castro Pineiro et al.
2013/0178458		7/2013	Lindsley et al.
2015/0291539	A1	10/2015	Canney et al.
2016/0016941	A1		Canney et al.
2016/0185785	A1	6/2016	Ioannidis et al.
2016/0303084	A1	10/2016	Chen et al.
2017/0298037	A1	10/2017	Canney et al.
2018/0221365	A1	8/2018	Canney et al.
2019/0367528	A1	12/2019	Canney et al.

FOREIGN PATENT DOCUMENTS

JР	2007-526333 A	9/2007
JP	2010-509402 A	3/2010
JP	2011-519936 A	7/2011

JP	2016-540792 A	12/2016
JP	2019-535825	12/2019
JP	2020-511515	4/2020
WO	WO 2009/137308 A1	11/2009
WO	WO 2014/160592 A2	10/2014
WO	WO 2014/164756 A1	10/2014
WO	WO 2016/040554 A1	3/2016
WO	WO 2016/055394 A1	4/2016
WO	WO 2016/183150 A1	11/2016
WO	WO 2018/093818 A1	5/2018
WO	WO 2018175188	9/2018
WO	WO 2018175190	9/2018
WO	WO 2019217890	11/2019
WO	WO 2021/097116 A1	5/2021
WO	WO 2021/097117 A2	5/2021

2016 540702 4

OTHER PUBLICATIONS

Li, @ 2016 International Society for Neurochemistry, J. Neurochem. (2017) 140, 561-575.*

Bhandare et al., "Modifications to five-substituted 3,3-diethyl-4,5-dihydro-2(3H)-furanones en route to novel muscarinic receptor ligands.", Medicinal Chemistry Research, vol. 20, No. 5, 2011, pp. 558-565, XP055283393.

Bhandare et al., "Bioisosteric Replacement and Related Analogs in the Design, Synthesis and Evaluation of Ligands for Muscarinic Acetylcholine Receptors," Med. Chem. (2014) 10:361-375.

Gao et al., "Homologation as a lead modification approach en route to a series of lactone-based muscarinic ligands", Medicinal Chemistry Research., vol. 23, No. 2, Aug. 22, 2013 (Aug. 22, 2013), pp. 1023-1030, XP055305444, US, ISSN: 1054-2523, DOI: 10.1007/s00044-013-0692-3.

Guo, Lin, and Xuechu Zhen. "Sigma-2 receptor ligands: neurobiological effects." Current medicinal chemistry 22.8 (2015): 989-1003. Hellewell, Susan B., and Wayne D. Bowen. "A sigma-like binding site in rat pheochromocytoma (PC12) cells: decreased affinity for (+)-benzomorphans and lower molecular weight suggest a different sigma receptor form from that of guinea pig brain." Brain research 527.2 (1990): 244-253.

International Preliminary Report on Patentability dated Sep. 24, 2019 for PCT/US2018/022574.

International Search Report dated May 4, 2018 for PCT/US2018/022574.

Izzo, Nicholas J., et al. "Alzheimer's therapeutics targeting amyloid beta 1-42 oligomers I: Abeta 42 oligomer binding to specific neuronal receptors is displaced by drug candidates that improve cognitive deficits." *PloS one* 9.11 (2014).

Izzo, Nicholas J., et al. "Alzheimer's therapeutics targeting amyloid beta 1-42 oligomers II: Sigma-2/PGRMC1 receptors mediate Abeta 42 oligomer binding and synaptotoxicity." *PloS one* 9.11 (2014). Lee Collier, Thomas, Rikki N. Waterhouse, and Michael Kassiou. "Imaging sigma receptors: applications in drug development." *Current pharmaceutical design* 13.1 (2007): 51-72.

(Continued)

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(57) **ABSTRACT**

Pharmaceutical compositions of the invention comprise functionalized lactone derivatives having a disease-modifying action in the treatment of diseases associated with dysregulation of sigma-2 receptor activity.

6 Claims, No Drawings

(56) References Cited

OTHER PUBLICATIONS

Martin, W. R., and C. G. Eades. "Thompson, JA, Huppler, RE and Gilbert." *PE: The effects of morphine-and nalorphine-like drugs in the nondependent and morphine-dependent chronic spinal dog. J. Pharmacol. Exp. Ther* 197 (1976): 517-532.

Matsumoto, Rae R. "σ Receptors: historical perspective and background." *Sigma Receptors*. Springer, Boston, MA, 2007. 1-23. Skuza, Grazyna. "Pharmacology of sigma (σ) receptor ligands from a behavioral perspective." *Current pharmaceutical design* 18.7 (2012): 863-874.

Written Opinion of the International Searching Authority dated May 4, 2018 for PCT/US2018/022574.

Xu, Jinbin, et al. "Identification of the PGRMC1 protein complex as the putative sigma-2 receptor binding site." *Nature communications* 2.1 (2011): 1-7.

^{*} cited by examiner

MODULATORS OF THE SIGMA-2 RECEPTOR AND THEIR METHOD OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation application of U.S. application Ser. No. 16/496,073, filed Sep. 20, 2019, which is a 35 U.S.C. § 371 National Stage Application of International Application No. PCT/US2018/022574, filed Mar. 15, 2018, which claims priority to U.S. Provisional Patent Application No. 62/474,277, filed Mar. 21, 2017, the contents of which are incorporated herein by reference in their entireties.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

This invention was made with government support under grant number HHSN-271-2008-00025-C awarded by the ²⁰ National Institute of Mental Health and grant number 1R41AG052249-01 awarded by the National Institute on Aging. The government has certain rights in the invention.

FIELD OF INVENTION

Embodiments of the invention are directed to novel compounds useful as sigma-2 receptor binders and their method of use. Embodiments are further directed to a novel chemotype useful for the treatment diseases that are associated with dysregulation of sigma-2 receptor activity.

BACKGROUND OF THE INVENTION

The sigma-1 and sigma-2 receptors were first identified in 35 the mid-1970's based on their interaction with radioligands. In 1976, a study of the physiological properties of (±)-SKF-10,047 (N-allylnormetazocine) and it structurally related benzomorphan analogues, morphine and ketazocine, in the chronic spinal dog model identified three receptor sub-types, 40 the μ -opioid receptor, the κ -opioid receptor, and the σ -receptor (sigma receptor) (Martin, W. R.; Eades, C. G.; Thompson, J. A.; Huppler, R. E.; Gilbert, P. E. The effects of morphine- and nalorphine-like drugs in the nondependent and morphine-dependent chronic spinal dog. J. Pharmacol. 45 Exp. Ther. 1976, 197, 517-532). It subsequently determined that (-)-SKF-10,047 binds to the μ-opioid receptor and the κ-opioid receptor, while (+)-SKF-10,047 selectively to the 6-receptor (sigma receptor), although the true function of the 6-receptor remained unknown (Matsumoto, R. R. Sigma 50 Receptors: Historical Perspective and Background. In Sigma Receptors: Chemistry, Cell Biology and Clinical Implications; Matsumoto, R. R., Bowen, W. D., Su, T.-P., Eds.; Springer Science: New York, NY, 2007; pp 1-23. Collier, T. L.; Waterhouse, R. N.; Kassiou, M. Imaging sigma recep- 55 tors: applications in drug development. Curr. Pharm. Des. 2007, 13, 51-72.) The availability of the σ -receptor selective radioligand [³H]o-ditolylguanidine (DTG) facilitated more detailed binding studies of ligand for the σ-receptor, and eventually lead to the identification of two distinct subtypes, 60 the σ_1 -receptor and the σ_2 -receptor (Hellewell, S. B.; Bowen, W. D. A sigma-like binding site in rat pheochromocytoma (PC12) cells: decreased affinity for (+)-benzomorphans and lower molecular weight suggest a different sigma receptor form from that of guinea pig brain. Brain Res. 1990, 65 527, 244-253.) Although the exact structure of the σ_2 -receptor is unknown, recent studies have photoaffinity labeling

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studies have suggested that the σ_2 -receptor is synonymous with the progesterone receptor membrane component-1 (PGRMC1) (Xu, J. et al. Identification of the PGRMC1 protein complex as the putative sigma-2 receptor binding site. Nat. Commun. 2, 380 (2011).

The therapeutic utility of compounds capable of binding to the σ_2 -receptor or modulating activity of the σ_2 -receptor has also been explored. It has recently been discovered, for example, that compounds capable of binding to the σ_2 -receptor can prevent the binding of beta amyloid protein (A3) oligomers to neurons, thereby preventing downstream synaptotoxicity. This aspect of σ_2 -receptor binders provides an opportunity for the application of σ_2 -receptor binders as treatment for Alzheimer's disease, mild cognitive impairments, and memory disorders. It has further been demonstrated that compounds capable of binding to the σ_2 -receptor can displace beta amyloid protein (Aβ) oligomers from neurons, thereby preventing downstream synaptotoxicity. This aspect of σ_2 -receptor binders also provides an opportunity for the application of σ_2 -receptor binders as treatment for Alzheimer's disease, mild cognitive impairments, and memory disorders (Izzo, N. J. et al. Alzheimer's therapeutics targeting amyloid Beta 1-42 oligomers I: abeta 42 oligomer binding to specific neuronal receptors is displaced by drug candidates that improve cognitive deficits. PLoS One 9, e111898 (2014). Izzo, N. J. et al. Alzheimer's Therapeutics Targeting Amyloid Beta 1-42 Oligomers II: Sigma-2/ PGRMC1 Receptors Mediate Abeta 42 Oligomer Binding and Synaptotoxicity. PLoS One 9, e111899 (2014).

Separately, it is has demonstrated that expression of the σ_2 -receptor is elevated in tumor cells as compared with normal cells. Cancer cells in which overexpression of the σ_2 -receptor occurs, but is not limited to, pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer. It has been further discovered that compounds capable of binding to the σ_2 -receptor modulate its activity and induce cancer cell death. As such, the σ_2 -receptor is a viable target for the identification of anti-cancer agents, and compounds capable of binding to the σ_2 -receptor represent an opportunity to develop new anti-cancer agents.

The dysregulation of sigma-2 receptor activity has also been implacted in a number of neuropsychiatric disorders including but not limited to generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia (Guo, L.; Zhen, X. Simga-2 Receptor ligands: Neurobiological effects. Current Medicincal Chemistry, 2015, 22, 8, 989-1003. Skuza, G. Pharmacology of sigma (σ) receptor ligands from a behavioral perspective. Current Pharmaceutical Design, 2012, 18, 7, 863-874.). As such, the σ_2 -receptor is a viable target for the treatment of neuropsychiatric disorders including but not limited to generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessivecompulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia. Compounds that bind to the σ_2 -receptor that are capable of modulating σ₂-receptor represent an opportunity to identify new treatments for a number of neuropsychiatric disorders including but not limited to generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression,

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bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia.

BRIEF SUMMARY OF THE INVENTION

The present invention is directed toward novel sigma-2 receptor binders, compounds of formula (I),

including hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein:

A is selected from a group consisting of

$$N-R^2$$
 and $N-R^3$;

n is 1, 2, or 3;

 R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C_{1-6} linear alkyl, and C_{1-6} branched alkyl, or R^{1a} and R^{1b} may be taken together with the atom to which they are bound to form a ring having from 3 to 7 ring atoms;

 R^2 is selected from a group consisting of a benzene ring that is optionally substituted with 0 to 3 R^4 groups that $_{40}$ are not hydrogen, a 4-pyridine ring that is optionally substituted with 0 to 2 R^5 groups that are not hydrogen, a 3-pyridine ring that is optionally substituted with 0 to 2 R^5 groups that are not hydrogen, and a 2-pyridine ring that is optionally substituted with 0 to 2 R^5 groups that $_{45}$ are not hydrogen;

R³ is selected from a group consisting of a benzene ring that is optionally substituted with 0 to 3 R⁴ groups that are not hydrogen, a 4-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen, 50 a 3-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen, and a 2-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen; are not hydrogen;

R⁴ is at each occurrence independently selected from the 55 group consisting of hydrogen, OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, 60 —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂(C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R⁸, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}; 65 the terms R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} may be used to

designate individual R⁴ groups on a benzene ring;

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 $\rm R^5$ is at each occurrence independently selected from the group consisting of hydrogen, OH, $\rm NO_2$, halogen, CN, $\rm C_{1\text{-}6}$ linear alkyl, $\rm C_{3\text{-}7}$ branched alkyl, $\rm C_{3\text{-}7}$ cycloalkyl, $\rm C_{1\text{-}6}$ linear alkoxy, $\rm C_{3\text{-}7}$ branched alkoxy, $\rm C_{3\text{-}7}$ cycloalkoxy, $\rm C_{1\text{-}6}$ linear haloalkyl, $\rm C_{3\text{-}7}$ branched haloalkyl, $\rm C_{1\text{-}6}$ linear haloalkoxy, heterocyclyl, —S(C $_{1\text{-}6}$ linear alkyl), S(C $_{3\text{-}7}$ branched alkyl), —S(C $_{3\text{-}7}$ cycloalkyl), COR 6 , CO $_2\rm R^7$, CONR $^{8a}\rm R^{8b}$, SO $_2\rm NR^{8a}\rm R^{8b}$, NR $^{9a}\rm R^{9b}$, NR $^{9a}\rm COR^{10}$, NR $^{9a}\rm SO_2\rm R^1$, and NR $^{9a}\rm SO_2\rm NR^{12a}\rm R^{12b}$;

the terms R^{5a} , R^{5b} , R^{5c} , and R^{5d} may be used to designate individual R^{5} groups on a pyridine ring;

R⁶ is at each occurrence independently selected from the group consisting of hydrogen, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, and C₃₋₇ cycloalkyl;

 R^7 is at each occurrence independently selected from the group consisting of C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl;

R^{8a} is at each occurrence independently selected from the group consisting of H, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, and C₃₋₇ cycloalkyl;

 R^{8b} is at each occurrence independently selected from the group consisting of H, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} eycloalkyl;

R^{9a} is at each occurrence independently selected from the group consisting of H, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, and C₃₋₇ cycloalkyl;

R^{9b} is at each occurrence independently selected from the group consisting of H, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, and C₃₋₇ cycloalkyl;

R^{9a} and R^{9b} may be taken together with the atom to which they are bound to form a ring having from 3 to 7 ring atoms optionally containing an oxygen;

 R^{10} is at each occurrence independently selected from the group consisting of H, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl;

 R^{11} is at each occurrence independently selected from the group consisting of C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} eycloalkyl;

 R^{12a} is at each occurrence independently selected from the group consisting of hydrogen, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl; and

 R^{12b} is at each occurrence independently selected from the group consisting of hydrogen, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl.

The present invention further relates to compositions comprising: an effective amount of one or more compounds according to the present invention and an excipient.

The present invention also relates to a method for treating or preventing diseases that involve dysregulation of sigma-2 receptor activity, for example neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, schizophrenia, Alzheimer's disease, mild cognitive impairment, and memory disorders, as well as cancer, for example pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer said method comprising administering to a subject an effective amount of a compound or composition according to the present invention.

The present invention yet further relates to a method for treating or preventing diseases that involve dysregulation of sigma-2 receptor activity, for example neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar

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disorder, anorexia nervosa, bulimia nervosa, substance use disorders, schizophrenia, Alzheimer's disease, mild cognitive impairment, and memory disorders, as well as cancer, for example pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer wherein said method comprises administering to a subject a composition comprising an effective amount of one or more compounds according to the present invention and an excipient.

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The present invention yet further relates to a method for treating or preventing diseases that involve overexpression of the sigma-2 receptor such as cancer, for example pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer said method comprising administering to a subject an effective amount of a compound or composition according to the present invention.

The present invention yet further relates to a method for treating or preventing diseases that involve overexpression of the sigma-2 receptor such as cancer, for example pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer wherein said method comprises administering to a subject a composition comprising an effective amount of one or more compounds according to the present invention and an excipient.

The present invention also relates to a method for treating or preventing disease or conditions associated with dysregulation of sigma-2 receptor activity. Said methods comprise administering to a subject an effective amount of a compound or composition according to the present invention.

The present invention yet further relates to a method for treating or preventing disease or conditions associated with ³⁰ dysregulation of sigma-2 receptor activity, wherein said method comprises administering to a subject a composition comprising an effective amount of one or more compounds according to the present invention and an excipient.

The present invention further relates to a process for ³⁵ preparing the sigma-2 receptor binders modulators of the present invention.

These and other objects, features, and advantages will become apparent to those of ordinary skill in the art from a reading of the following detailed description and the 40 appended claims. All percentages, ratios and proportions herein are by weight, unless otherwise specified. All temperatures are in degrees Celsius (° C.) unless otherwise specified. All documents cited are in relevant part, incorporated herein by reference; the citation of any document is not 45 to be construed as an admission that it is prior art with respect to the present invention.

DETAILED DESCRIPTION OF THE INVENTION

There is evidence that suggests a role for the sigma-2 receptor in a number of disease states including, but not limited to neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, 55 agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders. Sigma-2 receptor activity modulators are likely to have a beneficial effect on patients suffering from these diseases and disorders. The disorders in which Sigma-2 receptor dysregulation plays a role and 65 modulation of Sigma-2 receptor receptor activity by a therapeutic agent may be a viable approach to therapeutic relief

include, but are not limited to, neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders.

There is a long felt need for new Sigma-2 receptor binders and Sigma-2 receptor activity modulators that will provide therapeutic relief from patients suffering from diseases associated with dysregulation of the Sigma-2 receptor. The invention addresses the need to identify novel Sigma-2 receptor binders and Sigma-2 receptor activity modulators capable to treating disease associated with dysregulation of Sigma-2 receptor activity. The present invention addresses the need to develop new therapeutic agents for the treatment and prevention of neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder posttraumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders.

The Sigma-2 receptor binders and Sigma-2 receptor activity modulators of the present invention are capable of treating and preventing diseases associated with dysregulation of the sigma-2 receptor, for example neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders. Without wishing to be limited by theory, it is believed that the Sigma-2 receptor binders and Sigma-2 receptor activity modulators of the present invention can ameliorate, abate, otherwise cause to be controlled, diseases and disorders associated with dysregulation of the sigma-2 receptor. The diseases and disorders include, but are not limited to neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia ner-50 vosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders.

The Sigma-2 receptor binders and Sigma-2 receptor activity modulators of the present invention are also capable of treating and preventing diseases associated with overexpression of the sigma-2 receptor, for example neuropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders. Without wishing to be limited by theory, it is believed that

the Sigma-2 receptor binders and Sigma-2 receptor activity modulators of the present invention can ameliorate, abate, otherwise cause to be controlled, diseases and disorders associated with overexpression of the sigma-2 receptor. The diseases and disorders include, but are not limited to neu- 5 ropsychiatric disorders such as generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive-compulsive disorder post-traumatic stress disorder, depression, bipolar disorder, anorexia nervosa, bulimia nervosa, substance use disorders, and schizophrenia, cancers such as pancreatic cancer, lung cancer, breast cancer, melanoma, prostate cancer, and ovarian cancer, as well as Alzheimer's disease, mild cognitive impairments, and memory disorders.

Throughout the description, where compositions are 15 described as having, including, or comprising specific components, or where processes are described as having, including, or comprising specific process steps, it is contemplated that compositions of the present teachings also consist essentially of, or consist of, the recited components, and that 20 the processes of the present teachings also consist essentially of, or consist of, the recited processing steps.

In the application, where an element or component is said to be included in and/or selected from a list of recited elements or components, it should be understood that the 25 element or component can be any one of the recited elements or components and can be selected from a group consisting of two or more of the recited elements or components.

The use of the singular herein includes the plural (and vice versa) unless specifically stated otherwise. In addition, 30 where the use of the term "about" is before a quantitative value, the present teachings also include the specific quantitative value itself, unless specifically stated otherwise.

It should be understood that the order of steps or order for performing certain actions is immaterial so long as the 35 present teachings remain operable. Moreover, two or more steps or actions can be conducted simultaneously.

As used herein, the term "halogen" shall mean chlorine, bromine, fluorine and iodine.

As used herein, unless otherwise noted, "alkyl" and/or 40 "aliphatic" whether used alone or as part of a substituent group refers to straight and branched carbon chains having 1 to 20 carbon atoms or any number within this range, for example 1 to 6 carbon atoms or 1 to 4 carbon atoms. Designated numbers of carbon atoms (e.g. C_{1-6}) shall refer 45 independently to the number of carbon atoms in an alkyl moiety or to the alkyl portion of a larger alkyl-containing substituent. Non-limiting examples of alkyl groups include methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, isobutyl, tert-butyl, and the like. Alkyl groups can be optionally 50 substituted. Non-limiting examples of substituted alkyl groups include hydroxymethyl, chloromethyl, trifluoromethyl, aminomethyl, 1-chloroethyl, 2-hydroxyethyl, 1,2-difluoroethyl, 3-carboxypropyl, and the like. In substituent groups with multiple alkyl groups such as (C1-6alkyl)2 55 wherein the haloalkyl group is as defined above. Examples amino, the alkyl groups may be the same or different.

As used herein, the terms "alkenyl" and "alkynyl" groups, whether used alone or as part of a substituent group, refer to straight and branched carbon chains having 2 or more carbon atoms, preferably 2 to 20, wherein an alkenyl chain 60 has at least one double bond in the chain and an alkynyl chain has at least one triple bond in the chain. Alkenyl and alkynyl groups can be optionally substituted. Nonlimiting examples of alkenyl groups include ethenyl, 3-propenyl, 1-propenyl (also 2-methylethenyl), isopropenyl (also 65 2-methylethen-2-yl), buten-4-yl, and the like. Nonlimiting examples of substituted alkenyl groups include 2-chloroeth-

enyl (also 2-chlorovinyl), 4-hydroxybuten-1-yl, 7-hydroxy-7-methyloct-4-en-2-yl, 7-hydroxy-7-methyloct-3,5-dien-2yl, and the like. Nonlimiting examples of alkynyl groups include ethynyl, prop-2-ynyl (also propargyl), propyn-1-yl, and 2-methyl-hex-4-yn-1-yl. Nonlimiting examples of substituted alkynyl groups include, 5-hydroxy-5-methylhex-3ynyl, 6-hydroxy-6-methylhept-3-yn-2-yl, 5-hydroxy-5-ethylhept-3-ynyl, and the like.

As used herein, "cycloalkyl," whether used alone or as part of another group, refers to a non-aromatic carboncontaining ring including cyclized alkyl, alkenyl, and alkynyl groups, e.g., having from 3 to 14 ring carbon atoms, preferably from 3 to 7 or 3 to 6 ring carbon atoms, or even 3 to 4 ring carbon atoms, and optionally containing one or more (e.g., 1, 2, or 3) double or triple bond. Cycloalkyl groups can be monocyclic (e.g., cyclohexyl) or polycyclic (e.g., containing fused, bridged, and/or spiro ring systems), wherein the carbon atoms are located inside or outside of the ring system. Any suitable ring position of the cycloalkyl group can be covalently linked to the defined chemical structure. Cycloalkyl rings can be optionally substituted. Nonlimiting examples of cycloalkyl groups include: cyclopropyl, 2-methyl-cyclopropyl, cyclopropenyl, cyclobutyl, 2,3-dihydroxycyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclopentadienyl, cyclohexyl, cyclohexenyl, cycloheptyl, cyclooctanyl, decalinyl, 2,5-dimethylcyclopentyl, 3,5-dichlorocyclohexyl, 4-hydroxycyclohexyl, 3,3,5trimethylcyclohex-1-yl, octahydropentalenyl, octahydro-1H-indenyl, 3a,4,5,6,7,7a-hexahydro-3H-inden-4-yl, decahydroazulenyl; bicyclo[6.2.0]decanyl, decahydronaphthalenyl, and dodecahydro-1H-fluorenyl. The term "cycloalkyl" also includes carbocyclic rings which are bicyclic hydrocarbon rings, non-limiting examples of which include, bicyclo-[2.1.1]hexanyl, bicyclo[2.2.1]heptanyl, [3.1.1]heptanyl, 1,3-dimethyl[2.2.1]heptan-2-yl, bicyclo [2.2.2]octanyl, and bicyclo[3.3.3]undecanyl.

"Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen. Haloalkyl groups include perhaloalkyl groups, wherein all hydrogens of an alkyl group have been replaced with halogens (e.g., —CF₃, —CF₂CF₃). Haloalkyl groups can optionally be substituted with one or more substituents in addition to halogen. Examples of haloalkyl groups include, but are not limited to, fluoromethyl, dichloroethyl, trifluoromethyl, trichloromethyl, pentafluoroethyl, and pentachloroethyl groups.

The term "alkoxy" refers to the group —O-alkyl, wherein the alkyl group is as defined above. Alkoxy groups optionally may be substituted. The term C_3 - C_6 cyclic alkoxy refers to a ring containing 3 to 6 carbon atoms and at least one oxygen atom (e.g., tetrahydrofuran, tetrahydro-2H-pyran). C₃-C₆ cyclic alkoxy groups optionally may be substituted.

The term "haloalkoxy" refers to the group —O-haloalkyl, of haloalkoxy groups include, but are not limited to, fluoromethoxy, difluoromethoxy, trifluoromethoxy, and pentafluoroethoxyl.

The term "aryl," wherein used alone or as part of another group, is defined herein as a an unsaturated, aromatic monocyclic ring of 6 carbon members or to an unsaturated, aromatic polycyclic ring of from 10 to 14 carbon members. Aryl rings can be, for example, phenyl or naphthyl ring each optionally substituted with one or more moieties capable of replacing one or more hydrogen atoms. Non-limiting examples of aryl groups include: phenyl, naphthylen-1-yl, naphthylen-2-yl, 4-fluorophenyl, 2-hydroxyphenyl, 3-methylphenyl, 2-amino-4-fluorophenyl, 2-(N,N-diethylamino) phenyl, 2-cyanophenyl, 2,6-di-tert-butylphenyl, 3-methoxyphenyl, 8-hydroxynaphthylen-2-yl 4,5-dimethoxynaphthylen-1-yl, and 6-cyano-naphthylen-1-yl. Aryl groups also include, for example, phenyl or naphthyl rings fused 5 with one or more saturated or partially saturated carbon rings (e.g., bicyclo[4.2.0]octa-1,3,5-trienyl, indanyl), which can be substituted at one or more carbon atoms of the aromatic and/or saturated or partially saturated rings.

The term "arylalkyl" or "aralkyl" refers to the group 10 -alkyl-aryl, where the alkyl and aryl groups are as defined herein. Aralkyl groups of the present invention are optionally substituted. Examples of arylalkyl groups include, for example, benzyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 2-phenylpropyl, fluorenylmethyl and the like.

The terms "heterocyclic" and/or "heterocycle" and/or "heterocyclyl," whether used alone or as part of another group, are defined herein as one or more ring having from 3 to 20 atoms wherein at least one atom in at least one ring is a heteroatom selected from nitrogen (N), oxygen (O), or 20 sulfur (S), and wherein further the ring that includes the heteroatom is non-aromatic. In heterocycle groups that include 2 or more fused rings, the non-heteroatom bearing ring may be aryl (e.g., indolinyl, tetrahydroquinolinyl, chromanyl). Exemplary heterocycle groups have from 3 to 14 25 ring atoms of which from 1 to 5 are heteroatoms independently selected from nitrogen (N), oxygen (O), or sulfur (S). One or more N or S atoms in a heterocycle group can be oxidized. Heterocycle groups can be optionally substituted.

Non-limiting examples of heterocyclic units having a 30 single ring include: diazirinyl, aziridinyl, urazolyl, azetidinyl, pyrazolidinyl, imidazolidinyl, oxazolidinyl, isoxazolinyl, isoxazolyl, thiazolidinyl, isothiazolyl, isothiazolinyl oxathiazolidinonyl, oxazolidinonyl, hydantoinyl, tetrahydrofuranyl, pyrrolidinyl, morpholinyl, piperazinyl, piperidi- 35 nyl, dihydropyranyl, tetrahydropyranyl, piperidin-2-onyl (valerolactam), 2,3,4,5-tetrahydro-1H-azepinyl, 2,3-dihydro-1H-indole, and 1,2,3,4-tetrahydro-quinoline. Nonlimiting examples of heterocyclic units having 2 or more rings include: hexahydro-1H-pyrrolizinyl, 3a,4,5,6,7,7a-40 hexahydro-1H-benzo[d]imidazolyl, 3a,4,5,6,7,7a-hexahydro-1H-indolyl, 1,2,3,4-tetrahydroquinolinyl, chromanyl, isochromanyl, indolinyl, isoindolinyl, and decahydro-1Hcycloocta[b]pyrrolyl.

The term "heteroaryl," whether used alone or as part of 45 another group, is defined herein as one or more rings having from 5 to 20 atoms wherein at least one atom in at least one ring is a heteroatom chosen from nitrogen (N), oxygen (O), or sulfur (S), and wherein further at least one of the rings that includes a heteroatom is aromatic. In heteroaryl groups that 50 include 2 or more fused rings, the non-heteroatom bearing ring may be a carbocycle (e.g., 6,7-Dihydro-5H-cyclopentapyrimidine) or aryl (e.g., benzofuranyl, benzothiophenyl, indolyl). Exemplary heteroaryl groups have from 5 to 14 ring atoms and contain from 1 to 5 ring heteroatoms inde- 55 pendently selected from nitrogen (N), oxygen (O), or sulfur (S). One or more N or S atoms in a heteroaryl group can be oxidized. Heteroaryl groups can be substituted. Non-limiting examples of heteroaryl rings containing a single ring include: 1,2,3,4-tetrazolyl, [1,2,3]triazolyl, [1,2,4]triazolyl, 60 triazinyl, thiazolyl, 1H-imidazolyl, oxazolyl, furanyl, thiopheneyl, pyrimidinyl, 2-phenylpyrimidinyl, pyridinyl, 3-methylpyridinyl, and 4-dimethylaminopyridinyl. Nonlimiting examples of heteroaryl rings containing 2 or more fused rings include: benzofuranyl, benzothiophenyl, benzo- 65 xazolyl, benzthiazolyl, benztriazolyl, cinnolinyl, naphthyridinyl, phenanthridinyl, 7H-purinyl, 9H-purinyl, 6-amino-

9H-purinyl, 5H-pyrrolo[3,2-d]pyrimidinyl, 7H-pyrrolo[2,3-d]pyrimidinyl, pyrido[2,3-d]pyrimidinyl, 2-phenylbenzo[d] thiazolyl, 1H-indolyl, 4,5,6,7-tetrahydro-1-H-indolyl, quinoxalinyl, 5-methylquinoxalinyl, quinazolinyl, quinolinyl, 8-hydroxy-quinolinyl, 1H-benzo[d]imidazol-2(3H)-onyl, 1H-benzo[d]imidazolyl, and isoquinolinyl.

One non-limiting example of a heteroaryl group as described above is C_1 - C_5 heteroaryl, which has 1 to 5 carbon ring atoms and at least one additional ring atom that is a heteroatom (preferably 1 to 4 additional ring atoms that are heteroatoms) independently selected from nitrogen (N), oxygen (O), or sulfur (S). Examples of C_1 - C_5 heteroaryl include, but are not limited to, triazinyl, thiazol-2-yl, thiazol-4-yl, imidazol-1-yl, 1H-imidazol-2-yl, 1H-imidazol-4-yl, isoxazolin-5-yl, furan-2-yl, furan-3-yl, thiophen-2-yl, thiophen-4-yl, pyrimidin-2-yl, pyrimidin-3-yl, and pyridin-4-yl.

Unless otherwise noted, when two substituents are taken together to form a ring having a specified number of ring atoms (e.g., R² and R³ taken together with the nitrogen (N) to which they are attached to form a ring having from 3 to 7 ring members), the ring can have carbon atoms and optionally one or more (e.g., 1 to 3) additional heteroatoms independently selected from nitrogen (N), oxygen (O), or sulfur (S). The ring can be saturated or partially saturated and can be optionally substituted.

For the purposed of the present invention fused ring units, as well as spirocyclic rings, bicyclic rings and the like, which comprise a single heteroatom will be considered to belong to the cyclic family corresponding to the heteroatom containing ring. For example, 1,2,3,4-tetrahydroquinoline having the formula:

is, for the purposes of the present invention, considered a heterocyclic unit. 6,7-Dihydro-5H-cyclopentapyrimidine having the formula:

is, for the purposes of the present invention, considered a heteroaryl unit. When a fused ring unit contains heteroatoms in both a saturated and an aryl ring, the aryl ring will predominate and determine the type of category to which the ring is assigned. For example, 1,2,3,4-tetrahydro-[1,8]naphthyridine having the formula:

is, for the purposes of the present invention, considered a heteroaryl unit. limitations given above for "alkyl" and "aryl."

Whenever a term or either of their prefix roots appear in a name of a substituent the name is to be interpreted as including those limitations provided herein. For example, whenever the term "alkyl" or "aryl" or either of their prefix roots appear in a name of a substituent (e.g., arylalkyl, alkylamino) the name is to be interpreted as including those

The term "substituted" is used throughout the specification. The term "substituted" is defined herein as a moiety, whether acyclic or cyclic, which has one or more hydrogen atoms replaced by a substituent or several (e.g., 1 to 10) substituents as defined herein below. The substituents are capable of replacing one or two hydrogen atoms of a single moiety at a time. In addition, these substituents can replace 15 two hydrogen atoms on two adjacent carbons to form said substituent, new moiety or unit. For example, a substituted unit that requires a single hydrogen atom replacement includes halogen, hydroxyl, and the like. A two hydrogen atom replacement includes carbonyl, oximino, and the like. 20 A two hydrogen atom replacement from adjacent carbon atoms includes epoxy, and the like. The term "substituted" is used throughout the present specification to indicate that a moiety can have one or more of the hydrogen atoms replaced by a substituent. When a moiety is described as 25 "substituted" any number of the hydrogen atoms may be replaced. For example, difluoromethyl is a substituted C₁ alkyl; trifluoromethyl is a substituted C1 alkyl; 4-hydroxyphenyl is a substituted aromatic ring; (N,N-dimethyl-5amino)octanyl is a substituted C₈ alkyl; 3-guanidinopropyl 30 is a substituted C₃ alkyl; and 2-carboxypyridinyl is a substituted heteroaryl.

The variable groups defined herein, e.g., alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, aryloxy, aryl, heterocycle and heteroaryl groups defined herein, whether used alone or as 35 part of another group, can be optionally substituted. Optionally substituted groups will be so indicated.

The following are non-limiting examples of substituents which can substitute for hydrogen atoms on a moiety: halogen (chlorine (Cl), bromine (Br), fluorine (F) and iodine 40 $(\mathrm{I})), -\!\!-\!\!\mathrm{CN}, -\!\!-\!\!\mathrm{NO}_2, \mathrm{oxo}\,(=\!\!-\!\!\mathrm{O}), -\!\!-\!\!\mathrm{OR}^{13}, -\!\!-\!\!\mathrm{SR}^{13}, -\!\!-\!\!\mathrm{N}(\mathrm{R}^{13})_2,$ $\begin{array}{l} \text{(1)),} \quad \text{C11,} \quad \text{C12,} \quad \text{C13,} \quad \text{C13,}$ cycloalkyl, aryl, heterocycle, or heteroaryl, wherein each of 45 the alkyl, haloalkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, arvl, heterocycle, and heteroarvl groups is optionally substituted with 1-10 (e.g., 1-6 or 1-4) groups selected independently from halogen, —CN, —NO₂, oxo, and R¹³; wherein R¹³, at each occurrence, independently is hydrogen, 50 $\begin{array}{l} -\text{OR}^{14}, \quad -\text{SR}^{14}, \quad -\text{C(O)}\text{R}^{14}, \quad -\text{C(O)}\text{OR}^{14}, \quad -\text{C(O)}\text{N} \\ (\text{R}^{14})_2, \quad -\text{SO}_2\text{R}^{14}, \quad -\text{S(O)}_2\text{OR}^{14}, \quad -\text{N(R}^{14})_2, \quad -\text{NR}^{14}\text{C(O)} \\ \text{R}^{14}, \quad \text{C}_{1\text{-}6} \text{ alkyl}, \quad \text{C}_{1\text{-}6} \text{ haloalkyl}, \quad \text{C}_{2\text{-}8} \text{ alkenyl}, \quad \text{C}_{2\text{-}8} \text{ alkynyl}, \end{array}$ cycloalkyl (e.g., $C_{3.6}$ cycloalkyl), aryl, heterocycle, or heteroaryl, or two R^{13} units taken together with the atom(s) to 55 which they are bound form an optionally substituted carbocycle or heterocycle wherein said carbocycle or heterocycle has 3 to 7 ring atoms; wherein R¹⁴, at each occurrence, independently is hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₂₋₈ alkenyl, C_{2-8} alkynyl, cycloalkyl (e.g., C_{3-6} cycloalkyl), aryl, 60 heterocycle, or heteroaryl, or two R^{14} units taken together with the atom(s) to which they are bound form an optionally substituted carbocycle or heterocycle wherein said carbocycle or heterocycle preferably has 3 to 7 ring atoms.

In some embodiments, the substituents are selected from 65 i) —OR^{1,5}; for example, —OH, —OCH₃, —OCH₂CH₃, —OCH₂CH₃;

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ii) —C(O)R¹⁵; for example, —COCH₃, —COCH₂CH₃, —COCH₂CH₃;

iii) —C(O)OR¹⁵; for example, —CO₂CH₃, —CO₂CH₂CH₃, —CO₂CH₂CH₂CH₃;

iv) $-\text{C(O)N(R}^{15})_2$; for example, $-\text{CONH}_2$, $-\text{CONHCH}_3$, $-\text{CON(CH}_3)_2$;

v) —N(R¹⁵)₂; for example, —NH₂, —NHCH₃, —N(CH₃)₂, —NH(CH₂CH₃);

vi) halogen: —F, —Cl, —Br, and —I;

vii) —CH_eX_g; wherein X is halogen, m is from 0 to 2, e+g=3; for example, —CH₂F, —CHF₂, —CF₃, —CCl₃, or —CBr₃;

viii) $-SO_2R^{15}$; for example, $-SO_2H$; $-SO_2CH_3$; $-SO_2C_6H_5$;

ix) C₁-C₆ linear, branched, or cyclic alkyl;

x) Cyano

xi) Nitro;

xii) $N(R^{15})C(O)R^{15}$;

xiii) Oxo (=O);

xiv) Heterocycle; and

xv) Heteroaryl.

wherein each R^{15} is independently hydrogen, optionally substituted C_1 - C_6 linear or branched alkyl (e.g., optionally substituted C_1 - C_4 linear or branched alkyl), or optionally substituted C_3 - C_6 cycloalkyl (e.g. optionally substituted C_3 - C_6 cycloalkyl); or two R^{15} units can be taken together to form a ring comprising 3-7 ring atoms. In certain aspects, each R^{15} is independently hydrogen, C_1 - C_6 linear or branched alkyl optionally substituted with halogen or C_3 - C_6 cycloalkyl or C_3 - C_6 cycloalkyl.

At various places in the present specification, substituents of compounds are disclosed in groups or in ranges. It is specifically intended that the description include each and every individual subcombination of the members of such groups and ranges. For example, the term " C_{1-6} alkyl" is specifically intended to individually disclose C_1 , C_2 , C_3 , C_4 , C_5 , C_6 , C_1 - C_6 , C_1 - C_5 , C_1 - C_4 , C_1 - C_3 , C_1 - C_2 , C_2 - C_6 , C_2 - C_5 , C_2 - C_4 , C_2 - C_3 , C_3 - C_6 , C_3 - C_5 , C_3 - C_4 , C_4 - C_6 , C_4 - C_6 , and C_5 - C_6 , alkyl.

For the purposes of the present invention the terms "compound," "analog," and "composition of matter" stand equally well for the sigma-2 receptor activity modulators and sigma-2 receptor binders described herein, including all enantiomeric forms, diastereomeric forms, salts, and the like, and the terms "compound," "analog," and "composition of matter" are used interchangeably throughout the present specification.

Compounds described herein can contain an asymmetric atom (also referred as a chiral center), and some of the compounds can contain one or more asymmetric atoms or centers, which can thus give rise to optical isomers (enantiomers) and diastereomers. The present teachings and compounds disclosed herein include such enantiomers and diastereomers, as well as the racemic and resolved, enantiomerically pure R and S stereoisomers, as well as other mixtures of the R and S stereoisomers and pharmaceutically acceptable salts thereof. Optical isomers can be obtained in pure form by standard procedures known to those skilled in the art, which include, but are not limited to, diastereomeric salt formation, kinetic resolution, and asymmetric synthesis. The present teachings also encompass cis and trans isomers of compounds containing alkenyl moieties (e.g., alkenes and imines). It is also understood that the present teachings encompass all possible regioisomers, and mixtures thereof, which can be obtained in pure form by standard separation procedures known to those skilled in the art, and include, but

are not limited to, column chromatography, thin-layer chromatography, and high-performance liquid chromatography.

Pharmaceutically acceptable salts of compounds of the present teachings, which can have an acidic moiety, can be formed using organic and inorganic bases. Both mono and polyanionic salts are contemplated, depending on the number of acidic hydrogens available for deprotonation. Suitable salts formed with bases include metal salts, such as alkali metal or alkaline earth metal salts, for example sodium, potassium, or magnesium salts; ammonia salts and organic amine salts, such as those formed with morpholine, thiomorpholine, piperidine, pyrrolidine, a mono-, di- or tri-lower alkylamine (e.g., ethyl-tert-butyl-, diethyl-, diisopropyl-, triethyl-, tributyl- or dimethylpropylamine), or a mono-, di-, or 15 trihydroxy lower alkylamine (e.g., mono-, di- or triethanolamine). Specific non-limiting examples of inorganic bases include NaHCO₃, Na₂CO₃, KHCO₃, K₂CO₃, Cs₂CO₃, LiOH, NaOH, KOH, NaH₂PO₄, Na₂HPO₄, and Na₃PO₄. Internal salts also can be formed. Similarly, when a com- 20 pound disclosed herein contains a basic moiety, salts can be formed using organic and inorganic acids. For example, salts can be formed from the following acids: acetic, propionic, lactic, benzenesulfonic, benzoic, camphorsulfonic, citric, tartaric, succinic, dichloroacetic, ethenesulfonic, formic, 25 fumaric, gluconic, glutamic, hippuric, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, malonic, mandelic, methanesulfonic, mucic, napthalenesulfonic, nitric, oxalic, pamoic, pantothenic, phosphoric, phthalic, propionic, succinic, sulfuric, tartaric, toluenesulfonic, and camphorsulfonic as well as other known pharmaceutically acceptable acids.

When any variable occurs more than one time in any constituent or in any formula, its definition in each occurrence is independent of its definition at every other occurrence (e.g., in $N(R^9)_2$, each R^9 may be the same or different than the other). Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

The terms "treat" and "treating" and "treatment" as used herein, refer to partially or completely alleviating, inhibiting, ameliorating and/or relieving a condition from which a patient is suspected to suffer.

As used herein, "therapeutically effective" and "effective 45 dose" refer to a substance or an amount that elicits a desirable biological activity or effect.

Except when noted, the terms "subject" or "patient" are used interchangeably and refer to mammals such as human patients and non-human primates, as well as experimental $\,^{50}$ animals such as rabbits, rats, and mice, and other animals. Accordingly, the term "subject" or "patient" as used herein means any mammalian patient or subject to which the compounds of the invention can be administered. In an exemplary embodiment of the present invention, to identify subject patients for treatment according to the methods of the invention, accepted screening methods are employed to determine risk factors associated with a targeted or suspected disease or condition or to determine the status of an existing disease or condition in a subject. These screening methods include, for example, conventional work-ups to determine risk factors that may be associated with the targeted or suspected disease or condition. These and other routine methods allow the clinician to select patients in need of therapy using the methods and compounds of the present invention.

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The Sigma-2 Receptor Binders and Sigma-2 Receptor Activity Modulators

The sigma-2 receptor binders and sigma-2 receptor activity modulators of the present invention include all enantiomeric and diastereomeric forms alts thereof having the formula

The present invention is directed toward novel sigma-2 receptor binders, compounds of formula (I),

$$\begin{array}{c}
R^{1a} \\
 R^{1b}
\end{array}$$
(I)

including hydrates, solvates, pharmaceutically acceptable salts, prodrugs and complexes thereof, wherein:

A is selected from a group consisting of

$$N-R^2$$
 and $N-R^3$;

n is 1, 2, or 3;

 R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C_{1-6} linear alkyl, and C_{1-6} branched alkyl, or R^{1a} and R^{1b} may be taken together with the atom to which they are bound to form a ring having from 3 to 7 ring atoms;

R² is selected from a group consisting of a benzene ring that is optionally substituted with 0 to 3 R⁴ groups that are not hydrogen, a 4-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen, a 3-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen, and a 2-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen;

R³ is selected from a group consisting of a benzene ring that is optionally substituted with 0 to 3 R⁴ groups that are not hydrogen, a 4-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen, a 3-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen, and a 2-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen; are not hydrogen;

 $\rm R^4$ is at each occurrence independently selected from the group consisting of hydrogen, OH, $\rm NO_2$, halogen, CN, $\rm C_{1\text{-}6}$ linear alkyl, $\rm C_{3\text{-}7}$ branched alkyl, $\rm C_{3\text{-}7}$ cycloalkyl, $\rm C_{1\text{-}6}$ linear alkoxy, $\rm C_{3\text{-}7}$ branched alkoxy, $\rm C_{3\text{-}7}$ cycloalkoxy, $\rm C_{1\text{-}6}$ linear haloalkyl, $\rm C_{3\text{-}7}$ branched haloalkyl, $\rm C_{1\text{-}6}$ linear haloalkoxy, heterocyclyl, —S(C_{1\text{-}6} linear alkyl), S(C_{3\text{-}7} branched alkyl), —S(C_{3\text{-}7} cycloalkyl), —SO_2(C_{1\text{-}6} linear alkyl), SO_2(C_{3\text{-}7} cycloalkyl), COR^6, CO_2R^7, CONR^{8a}R^{8b}, SO_2NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{5a}COR^{10}, NR^{9a}SO_2R^{11}, and NR^{9a}SO_2NR^{12a}R^{12b}; the terms $\rm R^{4a}$, $\rm R^{4b}$, $\rm R^{4c}$, $\rm R^{4d}$, and $\rm R^{4e}$ may be used to

designate individual R⁴ groups on a benzene ring;

 $\rm R^5$ is at each occurrence independently selected from the group consisting of hydrogen, OH, NO2, halogen, CN, $\rm C_{1-6}$ linear alkyl, $\rm C_{3-7}$ branched alkyl, $\rm C_{3-7}$ cycloalkyl, $\rm C_{1-6}$ linear alkoxy, $\rm C_{3-7}$ branched alkoxy, $\rm C_{3-7}$ cycloalkoxy, $\rm C_{1-6}$ linear haloalkyl, $\rm C_{3-7}$ branched haloalkyl, $\rm C_{1-6}$ linear haloalkoxy, heterocyclyl, —S(C1-6 linear alkyl), S(C3-7 branched alkyl), —S(C3-7 cycloalkyl), COR6, CO2R7, CONR8aR8b, SO2NR8aR8b, NR9aR9b, NR9aCOR10, NR9aSO2R11, 10 and NR9aSO2NR12aR12b;

the terms R^{5a}, R^{5b}, R^{5c}, and R^{5d} may be used to designate individual R⁵ groups on a pyridine ring;

R⁶ is at each occurrence independently selected from the ¹⁵ group consisting of hydrogen, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, and C₃₋₇ cycloalkyl;

 R^7 is at each occurrence independently selected from the group consisting of C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl;

 R^{8a} is at each occurrence independently selected from the group consisting of H, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl;

 R^{8b} is at each occurrence independently selected from the group consisting of H, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl;

R^{9a} is at each occurrence independently selected from the group consisting of H, C₁₋₆ linear alkyl, C₃₋₇ branched ³⁰ alkyl, and C₃₋₇ cycloalkyl;

 R^{9b} is at each occurrence independently selected from the group consisting of H, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl;

R^{9a} and R^{9b} may be taken together with the atom to which they are bound to form a ring having from 3 to 7 ring atoms optionally containing an oxygen;

R¹⁰ is at each occurrence independently selected from the group consisting of H, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, and C₃₋₇ cycloalkyl;

 $\rm R^{11}$ is at each occurrence independently selected from the group consisting of $\rm C_{1\text{--}6}$ linear alkyl, $\rm C_{3\text{--}7}$ branched alkyl, and $\rm C_{3\text{--}7}$ cycloalkyl;

 $R^{12\alpha}$ is at each occurrence independently selected from the group consisting of hydrogen, C_{1-6} linear alkyl, C_{3-7} branched alkyl, and C_{3-7} cycloalkyl; and

 $\rm R^{12\it b}$ is at each occurrence independently selected from the group consisting of hydrogen, $\rm C_{1-6}$ linear alkyl, $\rm C_{3-7}$ branched alkyl, and $\rm C_{3-7}$ cycloalkyl.

In one embodiment, the present invention includes compounds having formula (II):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes compounds having formula (IIa):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, —S(C₁₋₆ linear alkyl), heterocyclyl, —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IIb):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

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In one embodiment, the present invention includes compounds having formula (IIc):

 R^{1a} R^{5a} R^{5b} R^{5c} R^{5c} R^{5c}

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof ¹⁵ wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IId):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (III):

$$R^{1a}$$
 R^{1b}
 R^{1b}
 R^{1b}
 R^{1b}
 R^{1b}
 R^{1b}
 R^{2}
 R^{1b}
 R^{2}

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes compounds having formula (IIIa):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
R^{4a} \\
R^{4c}
\end{array}$$

$$\begin{array}{c}
R^{4c} \\
R^{4c}
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (ITb):

$$\begin{array}{c} R^{1a} \\ R^{1b} \end{array} \begin{array}{c} O \\ R^{5c} \end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IIIc):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are 20 pounds having formula (IVa): hydrogen and 0 to 2 of R5a, R5b, R5c, and R5d are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched 25 alkoxy, C_{3-7} cycloalkoxy, C_{1-6} linear haloalkyl, C_{3-7} branched haloalkyl, C_{1-6} linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), $-S(C_{3-7} \text{ cycloalkyl}), -SO_2(C_{1-6} \text{ linear alkyl}), SO_2 30$ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO_2R^7 , $CONR^{8a}R^{8b}$, $SO_2NR^{8a}R^{8b}$, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes com- 35 pounds having formula (IId):

$$R^{1a}$$
 R^{1b}
 R^{5a}
 R^{5a}
 R^{5c}
 R^{5c}
 R^{5c}
 R^{5c}
 R^{5c}
 R^{5c}

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R5a, R5b, R5c, and R5d, are hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are $_{55}$ independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C_{3-7} cycloalkyl, C_{1-6} linear alkoxy, C_{3-7} branched alkoxy, C_{3-7} cycloalkoxy, C_{1-6} linear haloalkyl, C_{3-7} 60 branched haloalkyl, C_{1-6} linear haloalkoxy, heterocyclyl, — $S(C_{1-6}$ linear alkyl), $S(C_{3-7}$ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO_2R^7 , $CONR^{8a}R^{8b}$, $SO_2NR^{8a}R^{8b}$, $NR^{9a}R^{9b}$, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IV):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
N \\
R^{2}
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes com-

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
R^{4a} \\
R^{4c}
\end{array}$$

$$\begin{array}{c}
R^{4c} \\
R^{4c}
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, $-S(C_{1-6} \text{ linear alkyl})$, $S(C_{3-7} \text{ branched alkyl})$, $-S(C_{3-7} \text{ cycloalkyl}), -SO_2(C_{1-6} \text{ linear alkyl}), SO_2$ $(C_{3-7} \text{ branched alkyl}), -SO_2(C_{3-7} \text{ cycloalkyl}), COR^6$ CO_2R^7 , $CONR^{8a}R^{8b}$, $SO_2NR^{8a}R^{8b}$, $NR^{9a}R^{9b}$ $NR^{9a}COR^{10}$, $NR^{9a}SO_2R^{11}$, and $NR^{9a}SO_2NR^{12a}R^{12b}$.

In one embodiment, the present invention includes compounds having formula (IVb):

$$\begin{array}{c}
O \\
R^{1a}
\end{array}$$

$$\begin{array}{c}
O \\
R^{5a}
\end{array}$$

$$\begin{array}{c}
R^{5c}
\end{array}$$

$$\begin{array}{c}
R^{5c}
\end{array}$$

$$\begin{array}{c}
R^{5c}
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

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at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IVc):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IVd):

$$\begin{array}{c} O \\ R^{1a} \\ R^{1b} \end{array} \begin{array}{c} O \\ N \\ R^{5a} \\ N \\ R^{5c} \end{array} \begin{array}{c} (Ivd) \\ N \\ R^{5c} \end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, 55 pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of 60 OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), 65 —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶,

CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR^{9b}, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}. In one embodiment, the present invention includes compounds having formula (V):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes com-20 pounds having formula (Va):

35 Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (Vb):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

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at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), CO2⁶, CO2⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (Vc):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (Vd): $_{45}$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are 65 hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of

OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂(C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COg⁶, CO₂R⁷, CONR⁸ar⁸b, SO₂NR⁸ar⁸b, NR⁹ar⁹b, NR⁹a²COR¹⁰, NR⁹aSO₂R¹¹, and NR⁹aSO₂NR¹²ar¹²b.

In one embodiment, the present invention includes compounds having formula (VI):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
O \\
N
\end{array}$$

$$\begin{array}{c}
N
\end{array}$$

$$\begin{array}{c}
R^3
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes compounds having formula (VIa):

$$\mathbb{R}^{1a}$$
 \mathbb{R}^{4e} \mathbb{R}^{4d} \mathbb{R}^{4c} \mathbb{R}^{4c}

(VIa)

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (VIb):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are 5 independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}. 15

In one embodiment, the present invention includes compounds having formula (VIc):

$$R^{1a}$$
 R^{1b}
 R^{5d}
 R^{5c}
 R^{5b}

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (VId):

Including hydrates, solvates, enantiomers, diastereomers, 60 pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched

alkoxy, C_{3-7} cycloalkoxy, C_{1-6} linear haloalkyl, C_{3-7} branched haloalkyl, C_{1-6} linear haloalkoxy, heterocyclyl, —S(C_{1-6} linear alkyl), S(C_{3-7} branched alkyl), —S(C_{3-7} cycloalkyl), —SO₂(C_{1-6} linear alkyl), SO₂(C_{3-7} branched alkyl), —SO₂(C_{3-7} cycloalkyl), COR⁶, CO₂R⁷, CONR⁸ a R⁸ b , SO₂NR⁸ a R⁸ b , NR⁹ a R⁹ b , NR⁹ a COR¹, NR⁹ a SO₂R¹¹, and NR⁹ a SO₂NR¹² a R¹² b .

In one embodiment, the present invention includes compounds having formula (VII):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
N \\
R^{3}
\end{array}$$

(VIc) 20 Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes compounds having formula (VIIa):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (VIIb):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

25

45

55

at least 2 of the group R^{5a} , R^{5b} , R^{5c} , and R^{5d} , are hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (VIIc):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (VIId):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are 60 independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂

 $(C_{3-7} \text{ branched alkyl}), -SO_2(C_{3-7} \text{ cycloalkyl}), COR^6, CO_2R^7, CONR^{8a}R^{8b}, SO_2NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR^{10}, NR^{9a}SO_2R^{11}, and NR^{9a}SO_2NR^{12a}R^{12b}.$

In one embodiment, the present invention includes compounds having formula (VIII):

$$\mathbb{R}^{|a|}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes compounds having formula (VIIIa):

$$\mathbb{R}^{1a}$$
 \mathbb{R}^{1b}
 \mathbb{R}^{4e}
 \mathbb{R}^{4d}
 \mathbb{R}^{4c}
 \mathbb{R}^{4b}

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R⁴ are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (VIIIb):

$$(VIIIb)$$

$$R^{1a}$$

$$R^{1b}$$

$$R^{5c}$$

$$R^{5c}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a} , R^{5b} , R^{5c} , and R^{5d} , are hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are

independently selected from the group consisting of OH, NO $_2$, halogen, CN, C $_{1\text{-}6}$ linear alkyl, C $_{3\text{-}7}$ branched alkyl, C $_{3\text{-}7}$ cycloalkyl, C $_{1\text{-}6}$ linear alkoxy, C $_{3\text{-}7}$ branched alkoxy, C $_{3\text{-}7}$ cycloalkoxy, C $_{1\text{-}6}$ linear haloalkyl, C $_{3\text{-}7}$ branched haloalkyl, C $_{1\text{-}6}$ linear haloalkoxy, heterocyclyl, —S(C $_{1\text{-}6}$ linear alkyl), S(C $_{3\text{-}7}$ branched alkyl), —S(C $_{3\text{-}7}$ cycloalkyl), —SO $_2$ (C $_{1\text{-}6}$ linear alkyl), SO $_2$ (C $_{3\text{-}7}$ branched alkyl), —SO $_2$ (C $_{3\text{-}7}$ cycloalkyl), COP $_3$ 6, COP $_3$ 7, CONR $_3$ 8 $_3$ 8 $_3$ 8, SO $_2$ NR $_3$ 8 $_3$ 8 $_3$ 8, NR $_3$ 9 $_3$ 9 $_3$ 8, NR $_3$ 9 $_3$ 9 $_3$ 8, NR $_3$ 9 $_3$ 9 $_3$ 1, and NR $_3$ 9 $_3$ 2 $_3$ 0, NR $_3$ 1 $_3$ 1 $_3$ 1.

In one embodiment, the present invention includes compounds having formula (VIIIc):

Including hydrates, solvates, enantiomers, diastereomers, ²⁵ pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a} , R^{5b} , R^{5c} , and R^{5d} , are hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}. 40

In one embodiment, the present invention includes compounds having formula (VIIId):

Including hydrates, solvates, enantiomers, diastereomers, 55 pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{5a}, R^{5b}, R^{5c}, and R^{5d}, are hydrogen and 0 to 2 of R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently selected from the group consisting of 60 OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), 65 —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶,

CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}. In one embodiment, the present invention includes compounds having formula (IX):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
N \\
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof.

In one embodiment, the present invention includes com-20 pounds having formula (IXa):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
R^{4a} \\
R^{4c}
\end{array}$$

$$\begin{array}{c}
R^{4c} \\
R^{4d}
\end{array}$$

$$\begin{array}{c}
R^{4c} \\
R^{4d}
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

at least 2 of the group R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are hydrogen and 0 to 3 of R^{4a}, R^{4b}, R^{4c}, R^{4d}, and R^{4e} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), —S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO₂R⁷, CONR^{8a}R^{8b}, SO₂NR^{8a}R^{8b}, NR^{9a}R^{9b}, NR^{9a}COR¹⁰, NR^{9a}SO₂R¹¹, and NR^{9a}SO₂NR^{12a}R^{12b}.

In one embodiment, the present invention includes compounds having formula (IXb):

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof wherein:

20

at least 2 of the group R5a, R5b, R5c, and R5d, are hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are independently selected from the group consisting of OH, NO_2 , halogen, CN, C_{1-6} linear alkyl, C_{3-7} branched alkyl, $\rm C_{3-7}$ cycloalkyl, $\rm C_{1-6}$ linear alkoxy, $\rm C_{3-7}$ branched alkoxy, C_{3-7} cycloalkoxy, C_{1-6} linear haloalkyl, C_{3-7} branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, $-S(C_{1-6} \text{ linear alkyl})$, $S(C_{3-7} \text{ branched alkyl})$, $\begin{array}{l} -S(C_{3-7} \text{ cycloalkyl}), -SO_2(C_{1-6} \text{ linear alkyl}), SO_2\\ (C_{3-7} \text{ branched alkyl}), -SO_2(C_{3-7} \text{ cycloalkyl}), COR^6,\\ CO_2R^7, CONR^{8a}R^{8b}, SO_2NR^{8a}R^{8b}, NR^{9a}R^{9b},\\ NR^{9a}COR^{10}, NR^{9a}SO_2R^{11}, \text{ and } NR^{9a}SO_2NR^{12a}R^{12b}. \end{array}$

In one embodiment, the present invention includes compounds having formula (IXc):

$$\begin{array}{c} R^{1a} \\ R^{1b} \end{array} \begin{array}{c} O \\ N \end{array} \begin{array}{c} R^{5d} \\ R^{5b} \end{array} \begin{array}{c} R^{5c} \\ R^{5b} \end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof

at least 2 of the group R^{5a} , R^{5b} , R^{5c} , and R^{5d} , are hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are independently selected from the group consisting of OH, NO₂, halogen, CN, C₁₋₆ linear alkyl, C₃₋₇ branched alkyl, C₃₋₇ cycloalkyl, C₁₋₆ linear alkoxy, C₃₋₇ branched 35 alkoxy, C_{3-7} cycloalkoxy, C_{1-6} linear haloalkyl, C_{3-7} branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl), $-S(C_{3-7} \text{ cycloalkyl}), -SO_2(C_{1-6} \text{ linear alkyl}), SO_2$ $(C_{3-7} \text{ branched alkyl})$, $-SO_2(C_{3-7} \text{ cycloalkyl})$, COR^6 , CO_2R^7 , $CONR^{8a}R^{8b}$, $SO_2NR^{8a}R^{8b}$, $NR^{9a}R^{9b}$, 40 $NR^{9a}COR^{10}$, $NR^{9a}SO_2R^{11}$, and $NR^{9a}SO_2NR^{12a}R^{12b}$.

In one embodiment, the present invention includes compounds having formula (IXd):

$$\begin{array}{c}
R^{1a} \\
R^{1b}
\end{array}$$

$$\begin{array}{c}
R^{5c} \\
R^{5c}
\end{array}$$

$$\begin{array}{c}
R^{5c} \\
R^{5b}
\end{array}$$

Including hydrates, solvates, enantiomers, diastereomers, pharmaceutically acceptable salts, and complexes thereof

at least 2 of the group R^{5a} , R^{5b} , R^{5c} , and R^{5d} , are 60 hydrogen and 0 to 2 of R^{5a} , R^{5b} , R^{5c} , and R^{5d} are independently selected from the group consisting of OH, NO_2 , halogen, CN, C_{1-6} linear alkyl, C_{3-7} branched alkyl, C_{3-7} cycloalkyl, C_{1-6} linear alkoxy, C_{3-7} branched alkoxy, C₃₋₇ cycloalkoxy, C₁₋₆ linear haloalkyl, C₃₋₇ 65 branched haloalkyl, C₁₋₆ linear haloalkoxy, heterocyclyl, —S(C₁₋₆ linear alkyl), S(C₃₋₇ branched alkyl),

—S(C₃₋₇ cycloalkyl), —SO₂(C₁₋₆ linear alkyl), SO₂ (C₃₋₇ branched alkyl), —SO₂(C₃₋₇ cycloalkyl), COR⁶, CO_2R^7 , $CONR^{8a}R^{8b}$, $SO_2NR^{8a}R^{8b}$, $NR^{9a}R^{9b}$ $NR^{9a}COR^{1}$, $NR^{9a}SO_{2}R^{11}$, and $NR^{9a}SO_{2}NR^{12a}R^{12b}$. In some embodiments A is

$$-\underbrace{\frac{1}{N}}_{N} - R^{2}.$$

In some embodiments A is

In some embodiments n is 1.

In some embodiments n is 2.

In some embodiments n is 3.

In some embodiments R^{1a} is hydrogen.

In some embodiments R^{1a} is C_{1-6} linear alkyl.

In some embodiments R^{1a} is C_{1-6} branched alkyl. In some embodiments R^{1b} is hydrogen.

In some embodiments R^{1b} is C_{1-6} linear alkyl. In some embodiments R^{1b} is C_{1-6} branched alkyl. In some embodiments R^{1a} and R^{1b} are be taken together with the atom to which they are bound to form a ring having from 3 ring atoms.

In some embodiments R^{1a} and R^{1b} are be taken together with the atom to which they are bound to form a ring having from 4 ring atoms.

In some embodiments R^{1a} and R^{1b} are be taken together with the atom to which they are bound to form a ring having from 5 ring atoms.

In some embodiments R^{1a} and R^{1b} are be taken together with the atom to which they are bound to form a ring having from 6 ring atoms.

In some embodiments R^{1a} and R^{1b} are be taken together with the atom to which they are bound to form a ring having 45 from 7 ring atoms.

In some embodiments R² is a benzene ring that is optionally substituted with 0 to 3 R⁴ groups that are not hydrogen.

In some embodiments R^2 is a 4-pyridine ring that is optionally substituted with 0 to 2 R^5 groups that are not 50 hydrogen.

In some embodiments R^2 is a 3-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not

In some embodiments R² is a 2-pyridine ring that is 55 optionally substituted with 0 to 2 R⁵ groups that are not hydrogen.

In some embodiments R³ is a benzene ring that is optionally substituted with 0 to 3 R⁴ groups that are not hydrogen.

In some embodiments R³ is a 4-pyridine ring that is optionally substituted with 0 to 2 R^{5} groups that are not

In some embodiments R³ is a 3-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups, that are not hydrogen

In some embodiments R3 is a 2-pyridine ring that is optionally substituted with 0 to 2 R⁵ groups that are not hydrogen.

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In some embodiments R^{4b} is C_{3-7} branched alkoxy. In some embodiments R^{4b} is C_{3-7} cycloalkoxy. In some embodiments R^{4b} is C_{1-6} linear haloalkyl. In some embodiments R^{4b} is C_{3-7} branched haloalkyl. In some embodiments R^{4b} is C_{3-7} branched haloalkyl. In some embodiments R^{4b} is C_{1-6} linear haloalkoxy.
 In some embodiments R<sup>4</sup> is hydrogen.
 In some embodiments R<sup>4</sup> is OH.
 In some embodiments R^4 is NO_2.
 In some embodiments R<sup>4</sup> is halogen.
 In some embodiments R<sup>4</sup> is CN.
                                                                                                                                     In some embodiments R^b is heterocyclyl.
In some embodiments R^4 is C_{1-6} linear alkyl. In some embodiments R^4 is C_{3-7} branched alkyl. In some embodiments R^4 is C_{3-7} cycloalkyl. In some embodiments R^4 is C_{3-7} cycloalkyl. In some embodiments R^4 is C_{3-7} branched alkoxy. In some embodiments R^4 is C_{3-7} branched alkoxy.
                                                                                                                                     In some embodiments R 4b is —S(C<sub>1-6</sub> linear alkyl).
                                                                                                                                    In some embodiments R<sup>4b</sup> is -S(C_{3-7} branched alkyl). In some embodiments R<sup>4b</sup> is -S(C_{3-7} branched alkyl). In some embodiments R<sup>4b</sup> is -SO_2(C_{1-6} linear alkyl). In some embodiments R<sup>4b</sup> is -SO_2(C_{3-7} branched alkyl). In some embodiments R<sup>4b</sup> is -SO_2(C_{3-7} cycloalkyl).
                                                                                                                         10
 In some embodiments R^4 is C_{3-7} cycloalkoxy.
 In some embodiments R^4 is C_{1-6} linear haloalkyl.
                                                                                                                                    In some embodiments R^{4b} is COR^5.

In some embodiments R^{4b} is CO_2R^7.

In some embodiments R^{4b} is CO_2R^7.

In some embodiments R^{4b} is CONR^{8a}R^{8b}
 In some embodiments R^4 is C_{3-7} branched haloalkyl.
 In some embodiments R^4 is C_{1-6} linear haloalkoxy.
In some embodiments R^4 is heterocyclyl. In some embodiments R^4 is -S(C_{1-6} linear alkyl). In some embodiments R^4 is -S(C_{3-7} branched alkyl). In some embodiments R^4 is -S(C_{3-7} cycloalkyl). In some embodiments R^4 is -S(C_{3-7} cycloalkyl).
                                                                                                                                     In some embodiments R<sup>4b</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>.
                                                                                                                                    In some embodiments R^{4b} is SO_2NR R. In some embodiments R^{4b} is NR^{9a}R^{9b}. In some embodiments R^{4b} is NR^{9a}COR^{10}. In some embodiments R^{4b} is NR^{9a}SO_2R^{11}. In some embodiments R^{4b} is NR^{9a}SO_2NR^{12a}R^{12b}.
In some embodiments R^4 is -SO_2(C_{3-7} branched alkyl). 20 In some embodiments R^4 is -SO_2(C_{3-7} cycloalkyl).
                                                                                                                                     In some embodiments R^{4c} is hydrogen.
                                                                                                                                     In some embodiments R^{4c} is OH.
 In some embodiments R<sup>4</sup> is COR<sup>6</sup>
                                                                                                                                     In some embodiments R^{4c} is NO_2.
 In some embodiments R<sup>4</sup> is CO<sub>2</sub>R<sup>7</sup>
                                                                                                                                     In some embodiments R^{4c} is halogen.
                                                                                                                                    In some embodiments R^{4c} is CN. In some embodiments R^{4c} is CN. In some embodiments R^{4c} is C_{1-6} linear alkyl. In some embodiments R^{4c} is C_{3-7} branched alkyl. In some embodiments R^{4c} is C_{3-7} cycloalkyl. In some embodiments R^{4c} is C_{1-6} linear alkoxy. In some embodiments R^{4c} is C_{3-7} branched alkoxy.
 In some embodiments R<sup>4</sup> is CONR<sup>8a</sup>R<sup>8b</sup>
In some embodiments R<sup>4</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>. In some embodiments R<sup>4</sup> is NR<sup>9a</sup>R<sup>9b</sup>. In some embodiments R<sup>4</sup> is NR<sup>9a</sup>COR<sup>10</sup>.
                                                                                                                         25
In some embodiments R<sup>4</sup> is NR<sup>9a</sup>SO<sub>2</sub>R<sup>11</sup>
 In some embodiments R^4 is NR^{9a}SO_2^2NR^{12a}R^{12b}.
                                                                                                                                    In some embodiments R^{4c} is C_{3-7} branched alkoxy. In some embodiments R^{4c} is C_{3-7} cycloalkoxy. In some embodiments R^{4c} is C_{1-6} linear haloalkyl. In some embodiments R^{4c} is C_{3-7} branched haloalkyl. In some embodiments R^{4c} is C_{1-6} linear haloalkoxy. In some embodiments R^{4c} is heterocyclyl. In some embodiments R^{4c} is -S(C_{1-6} linear alkyl). In some embodiments R^{4c} is -S(C_{3-7} branched alkyl). In some embodiments R^{4c} is -S(C_{3-7} cycloalkyl). In some embodiments R^{4c} is -S(C_{3-7} cycloalkyl). In some embodiments R^{4c} is -S(C_{3-7} branched alkyl).
 In some embodiments R^{4a} is hydrogen.
 In some embodiments R^{4a} is OH.
 In some embodiments R<sup>4a</sup> is NO<sub>2</sub>.
In some embodiments R^{4a} is halogen. In some embodiments R^{4a} is CN.
In some embodiments R^{4a} is C_{1-6} linear alkyl. In some embodiments R^{4a} is C_{3-7} branched alkyl. In some embodiments R^{4a} is C_{3-7} cycloalkyl.
In some embodiments R^{4a} is C_{1-6} linear alkoxy.
In some embodiments R^{4a} is C_{3-7} branched alkoxy.
                                                                                                                                     In some embodiments R^{4c} is -SO_2(C_{3-7} branched alkyl).
In some embodiments R^{4a} is C_{3-7} cycloalkoxy.
                                                                                                                                     In some embodiments R^{4c} is -SO_2(C_{3-7}) cycloalkyl).
 In some embodiments R^{4a} is C_{1-6} linear haloalkyl.
                                                                                                                                     In some embodiments R<sup>4c</sup> is COR<sup>6</sup>
In some embodiments R^{4a} is C_{3-7} branched haloalkyl. In some embodiments R^{4a} is C_{1-6} linear haloalkoxy. In some embodiments R^{4a} is heterocyclyl.
                                                                                                                                    In some embodiments R^{4c} is CO_2R^7.

In some embodiments R^{4c} is CO_2R^7.

In some embodiments R^{4c} is SO_2NR^{8a}R^{8b}.

In some embodiments R^{4c} is SO_2NR^{8a}R^{8b}.

In some embodiments R^{4c} is NR^{9a}R^{9}.
In some embodiments R^{4a} is -S(C_{1-6} linear alkyl).
In some embodiments R^{4a} is -S(C_{3-7} branched alkyl).
                                                                                                                                     In some embodiments R<sup>4c</sup> is NR<sup>9a</sup>COR<sup>10</sup>
In some embodiments R^{4a} is -S(C_{3-7} cycloalkyl).
                                                                                                                                     In some embodiments R<sup>4c</sup> is NR<sup>9a</sup>SO<sub>2</sub>R<sup>11</sup>
 In some embodiments R^{4a} is -SO_2(C_{1-6} linear alkyl).
                                                                                                                                     In some embodiments R^{4c} is NR^{9a}SO_2^2NR^{12a}R^{12b}.
 In some embodiments R^{4a} is -SO_2(C_{3-7}) branched alkyl).
                                                                                                                                     In some embodiments R^{4d} is hydrogen.
                                                                                                                                     In some embodiments R^{4d} is OH.
 In some embodiments R^{4a} is -SO_2(\tilde{C}_{3-7} cycloalkyl).
In some embodiments R^{4a} is COR^{6}.
In some embodiments R^{4a} is CO_{2}R^{7}
                                                                                                                                     In some embodiments R^{4d} is NO_2.
In some embodiments R^{4d} is halogen.
                                                                                                                                    In some embodiments R^{4d} is CN.

In some embodiments R^{4d} is CN.

In some embodiments R^{4d} is C_{1-6} linear alkyl.

In some embodiments R^{4d} is C_{3-7} branched alkyl.

In some embodiments R^{4d} is C_{3-7} cycloalkyl.
 In some embodiments R^{4a} is CONR^{8a}R^{8b}
 In some embodiments R<sup>4a</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>.
 In some embodiments R^{4a} is NR^{5a}R^{9b}.
 In some embodiments R<sup>4a</sup> is NR<sup>9a</sup>COR<sup>10</sup>
                                                                                                                                     In some embodiments R^{4d} is C_{1-6} linear alkoxy.
 In some embodiments R<sup>4a</sup> is NR<sup>9a</sup>SO<sub>2</sub>R<sup>11</sup>
                                                                                                                                     In some embodiments R^{4d} is C_{3-7}^{1-6} branched alkoxy.
 In some embodiments R<sup>4a</sup> is NR<sup>9a</sup>SO<sub>2</sub>NR<sup>12a</sup>R<sup>12b</sup>.
                                                                                                                                     In some embodiments R^{4d} is C_{3-7} cycloalkoxy.
 In some embodiments R<sup>4b</sup> is hydrogen.
                                                                                                                                    In some embodiments R^{4d} is C_{1-6} linear haloalkyl. In some embodiments R^{4d} is C_{3-7} branched haloalkyl. In some embodiments R^{4d} is C_{1-6} linear haloalkoxy. In some embodiments R^{4d} is heterocyclyl.
In some embodiments R^{4b} is OH.
In some embodiments R^{4b} is NO_2.
In some embodiments R^{4b} is halogen.
                                                                                                                         60
 In some embodiments R<sup>4b</sup> is CN.
                                                                                                                                     In some embodiments R^{4d} is -S(C_{1-6} linear alkyl).
 In some embodiments R^{4b} is C_{1-6} linear alkyl.
In some embodiments R^{4b} is C_{3-7} branched alkyl.
                                                                                                                                     In some embodiments R^{4d} is -S(C_{3-7}) branched alkyl).
                                                                                                                                     In some embodiments R^{4d} is -S(C_{3-7} cycloalkyl).
In some embodiments R^{4b} is C_{3-7} cycloalkyl.
In some embodiments R^{4b} is C_{1-6} linear alkoxy.
                                                                                                                                     In some embodiments R^{4d} is -SO_2(C_{1-6} linear alkyl).
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In some embodiments R^{4d} is -SO_2(C_{3-7} branched alkyl).
                                                                                                                                       In some embodiments R^{5a} is hydrogen.
In some embodiments R^{4d} is -SO_2(C_{3-7} \text{ cycloalkyl}).
                                                                                                                                       In some embodiments R^{5a} is OH.
 In some embodiments R<sup>4d</sup> is COR<sup>6</sup>
                                                                                                                                       In some embodiments R^{5a} is NO_2.
 In some embodiments R<sup>4d</sup> is CO<sub>2</sub>R<sup>7</sup>
                                                                                                                                      In some embodiments R^{5a} is halogen.
In some embodiments R<sup>4d</sup> is CO<sub>2</sub>R. In some embodiments R<sup>4d</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>. In some embodiments R<sup>4d</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>. In some embodiments R<sup>4d</sup> is NR<sup>9a</sup>R<sup>9b</sup>. In some embodiments R<sup>4d</sup> is NR<sup>9a</sup>COR<sup>10</sup>.
                                                                                                                                       In some embodiments R^{5a} is CN.
                                                                                                                                     In some embodiments R^{5a} is C_{1-6} linear alkyl. In some embodiments R^{5a} is C_{3-7} branched alkyl. In some embodiments R^{5a} is C_{3-7} cycloalkyl. In some embodiments R^{5a} is C_{3-7} cycloalkyl. In some embodiments R^{5a} is C_{3-6} linear alkoxy. In some embodiments R^{5a} is C_{3-7} branched alkoxy.
 In some embodiments R^{4d} is NR^{9a}SO_2R^{11}
 In some embodiments R<sup>4d</sup> is NR<sup>9a</sup>SO<sub>2</sub>NR<sup>12a</sup>R<sup>12b</sup>.
                                                                                                                          10
                                                                                                                                      In some embodiments R^{5a} is C_{3-7} cycloalkoxy.
 In some embodiments R<sup>4c</sup> is hydrogen.
                                                                                                                                      In some embodiments R^{5a} is C_{1-6} linear haloalkyl. In some embodiments R^{5a} is C_{3-7} branched haloalkyl.
 In some embodiments R^{4c} is OH.
 In some embodiments R<sup>4c</sup> is NO<sub>2</sub>.
                                                                                                                                     In some embodiments R^{5a} is C_{3-7} branched haloalkoxy. In some embodiments R^{5a} is C_{1-6} linear haloalkoxy. In some embodiments R^{5a} is -S(C_{1-6} linear alkyl). In some embodiments R^{5a} is -S(C_{3-7} branched alkyl). In some embodiments R^{5a} is -S(C_{3-7} cycloalkyl). In some embodiments R^{5a} is -SO_2(C_{1-6} linear alkyl). In some embodiments R^{5a} is -SO_2(C_{3-7} branched alkyl).
 In some embodiments R^{4c} is halogen.
In some embodiments R^{4c} is CN.

In some embodiments R^{4c} is C_{1-6} linear alkyl.

In some embodiments R^{4c} is C_{3-7} branched alkyl.

In some embodiments R^{4c} is C_{3-7} cycloalkyl.

In some embodiments R^{4c} is C_{3-7} cycloalkyl.
                                                                                                                                      In some embodiments R^{5a} is -SO_2(C_{3-7} cycloalkyl).
 In some embodiments R^{4c} is C_{3-7} branched alkoxy.
                                                                                                                          20
In some embodiments R^{4c} is C_{3-7} cycloalkoxy.
                                                                                                                                       In some embodiments R<sup>5a</sup> is COR<sup>6</sup>
In some embodiments R^{4c} is C_{1-6} linear haloalkyl.
                                                                                                                                       In some embodiments R<sup>5a</sup> is CO<sub>2</sub>R<sup>7</sup>.
 In some embodiments R^{4c} is C_{3-7} branched haloalkyl.
                                                                                                                                       In some embodiments R<sup>5a</sup> is CONR<sup>8a</sup>R<sup>8b</sup>
In some embodiments R^{4c} is C_{1-6} linear haloalkoxy. In some embodiments R^{4c} is heterocyclyl. In some embodiments R^{4c} is -S(C_{1-6} linear alkyl).
                                                                                                                                      In some embodiments R<sup>5a</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>. In some embodiments R<sup>5a</sup> is NR<sup>9a</sup>R<sup>9</sup>. In some embodiments R<sup>5a</sup> is NR<sup>9a</sup>COR<sup>10</sup>.
In some embodiments R^{4c} is -S(C_{3-7} branched alkyl). In some embodiments R^{4c} is -S(C_{3-7} cycloalkyl).
                                                                                                                                      In some embodiments R^{5a} is NR^{9a}SO_2R^{11}
                                                                                                                                       In some embodiments R<sup>5a</sup> is NR<sup>9a</sup>SO<sub>2</sub>NR<sup>12a</sup>R<sup>12b</sup>.
 In some embodiments R^{4c} is -SO_2(C_{1-6} linear alkyl).
                                                                                                                                       In some embodiments R<sup>5b</sup> is hydrogen.
 In some embodiments R^{4c} is -SO_2(C_{3-7}) branched alkyl). 30
                                                                                                                                       In some embodiments R^{5b} is OH.
 In some embodiments R^{4e} is -SO_2(C_{3-7} cycloalkyl).
                                                                                                                                      In some embodiments R^{5b} is NO_2.
                                                                                                                                     In some embodiments R^{5b} is NO_2.

In some embodiments R^{5b} is halogen.

In some embodiments R^{5b} is CN.

In some embodiments R^{5b} is C_{1-6} linear alkyl.

In some embodiments R^{5b} is C_{3-7} branched alkyl.

In some embodiments R^{5b} is C_{3-7} cycloalkyl.

In some embodiments R^{5b} is C_{1-6} linear alkoxy.

In some embodiments R^{5b} is C_{3-7} branched alkoxy.
In some embodiments R ^{4c} is COR^6.

In some embodiments R^{4c} is CO_2R^7.

In some embodiments R^{4c} is CO_2R^7.

In some embodiments R^{4c} is CONR^{8a}R^{8b}.

In some embodiments R^{4c} is SO_2NR^{8a}R^{8b}.

In some embodiments R^{4a} is NR^{9a}R^{9b}.
                                                                                                                          35
 In some embodiments R<sup>4c</sup> is NR<sup>9a</sup>COR<sup>10</sup>
 In some embodiments R4c is NR9aSO2R11
                                                                                                                                      In some embodiments R^{5b} is C_{3-7} cycloalkoxy.
 In some embodiments R<sup>4c</sup> is NR<sup>9a</sup>SO<sub>2</sub>NR<sup>12a</sup>R<sup>12b</sup>.
                                                                                                                                      In some embodiments R^{5b} is C_{1-6} linear haloalkyl.
 In some embodiments R<sup>5</sup> is hydrogen.
                                                                                                                          40
                                                                                                                                     In some embodiments R^{5b} is C_{1-6} linear haloalkyl. In some embodiments R^{5b} is C_{1-6} linear haloalkoxy. In some embodiments R^{5b} is -S(C_{1-6} linear alkyl). In some embodiments R^{5b} is -S(C_{1-6} linear alkyl). In some embodiments R^{5b} is -S(C_{3-7} branched alkyl). In some embodiments R^{5b} is -S(C_{3-7} cycloalkyl).
 In some embodiments R<sup>5</sup> is OH.
 In some embodiments R^5 is NO_2.
In some embodiments R<sup>5</sup> is halogen.

In some embodiments R<sup>5</sup> is CN.

In some embodiments R<sup>5</sup> is CN.

In some embodiments R<sup>5</sup> is C<sub>1-6</sub> linear alkyl.

In some embodiments R<sup>5</sup> is C<sub>3-7</sub> branched alkyl.
                                                                                                                          45
                                                                                                                                      In some embodiments R^{5b} is -SO_2(C_{1-6} linear alkyl).
                                                                                                                                      In some embodiments R^{5b} is -SO_2(C_{3-7}) branched alkyl).
 In some embodiments R^5 is C_{3-7} cycloalkyl.
 In some embodiments R^5 is C_{1-6} linear alkoxy.
                                                                                                                                       In some embodiments R^{5b} is -SO_2(C_{3-7} cycloalkyl).
In some embodiments R^5 is C_{3-7} branched alkoxy. In some embodiments R^5 is C_{3-7} cycloalkoxy.
                                                                                                                                       In some embodiments R<sup>5b</sup> is COR<sup>6</sup>
                                                                                                                                     In some embodiments R<sup>5b</sup> is COR<sup>7</sup>.

In some embodiments R<sup>5b</sup> is CO<sub>2</sub>R<sup>7</sup>.

In some embodiments R<sup>5b</sup> is CONR<sup>8a</sup>R<sup>8b</sup>.

In some embodiments R<sup>5b</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>.

In some embodiments R<sup>5b</sup> is NR<sup>9a</sup>R<sup>9b</sup>.

In some embodiments R<sup>5b</sup> is NR<sup>9a</sup>COR<sup>10</sup>.

In some embodiments R<sup>5b</sup> is NR<sup>9a</sup>SO<sub>2</sub>R<sup>11</sup>.
 In some embodiments R^5 is C_{1-6} linear haloalkyl.
In some embodiments R^5 is C_{3-7} branched haloalkyl. In some embodiments R^5 is C_{1-6} linear haloalkoxy. In some embodiments R^5 is -S(C_{1-6} linear alkyl). In some embodiments R^5 is -S(C_{3-7} branched alkyl).
In some embodiments R^5 is -S(C_{3-7} cycloalkyl).
                                                                                                                                       In some embodiments R^{5b} is NR^{9a}SO_2NR^{12a}R^{12b}.
 In some embodiments R^5 is -SO_2(C_{1-6} linear alkyl)
                                                                                                                                       In some embodiments R^{5c} is hydrogen.
                                                                                                                                       In some embodiments R^{5c} is OH.
 In some embodiments R^5 is -SO_2(C_{3-7}) branched alkyl).
 In some embodiments R^5 is -SO_2(C_{3-7} cycloalkyl).
                                                                                                                                       In some embodiments R^{5c} is NO_2.
                                                                                                                                      In some embodiments R^{5c} is halogen.
In some embodiments R^{5c} is CN.
In some embodiments R^{5c} is CN.
In some embodiments R^{5c} is C_{1-6} linear alkyl.
In some embodiments R^{5c} is C_{3-7} branched alkyl.
 In some embodiments R<sup>5</sup> is COR<sup>6</sup>
                                                                                                                          60
In some embodiments R^5 is CO_2R^7.
In some embodiments R^5 is CONR^{8a}R^{8b}.
In some embodiments R^5 is SO_2NR^{8a}R^{8b}.
                                                                                                                                       In some embodiments R^{5c} is C_{3-7} cycloalkyl.
 In some embodiments R^5 is NR^{9a}R^{9b}.
                                                                                                                                       In some embodiments R^{5c} is C_{1-6} linear alkoxy.
 In some embodiments R<sup>5</sup> is NR<sup>9a</sup>COR<sup>10</sup>.
                                                                                                                                      In some embodiments R^{5c} is C_{3-7} branched alkoxy.
 In some embodiments R<sup>5</sup> is NR<sup>9a</sup>SO<sub>2</sub>R<sup>11</sup>
 In some embodiments R<sup>5</sup> is NR<sup>9a</sup>SO<sub>2</sub>NR<sup>12a</sup>R<sup>12b</sup>.
                                                                                                                                       In some embodiments R^{5c} is C_{3-7} cycloalkoxy.
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In some embodiments R^{5c} is C_{1-6} linear haloalkyl. In some embodiments R^{5c} is C_{3-7} branched haloalkyl.
 In some embodiments R^{5c} is C_{1-6}^{5c} linear haloalkoxy.
 In some embodiments R^{5c} is -S(C_{1-6} linear alkyl).
In some embodiments R^{5c} is -S(C_{1-6} linear alky1). In some embodiments R^{5c} is -S(C_{3-7} branched alky1). In some embodiments R^{5c} is -S(C_{3-7} cycloalky1). In some embodiments R^{5c} is -SO_2(C_{1-6} linear alky1). In some embodiments R^{5c} is -SO_2(C_{3-7} branched alky1). In some embodiments R^{5c} is -SO_2(C_{3-7} cycloalky1).
 In some embodiments R^{5c} is COR^{6}
 In some embodiments R<sup>5c</sup> is CO<sub>2</sub>R<sup>7</sup>.
 In some embodiments R5c is CONR8aR8b
 In some embodiments R<sup>5c</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>.
In some embodiments R^{5c} is NR^{9a}R^9.

In some embodiments R^{5c} is NR^{9a}COR^{10}.

In some embodiments R^{5c} is NR^{9a}COR^{10}.

In some embodiments R^{5c} is NR^{9a}SO_2R^{11}.

In some embodiments R^{5c} is NR^{9a}SO_2NR^{12a}R^{12b}.

In some embodiments R^{5d} is hydrogen.
 In some embodiments R^{5d} is OH.
 In some embodiments R^{5d} is NO_2.
 In some embodiments R^{5d} is halogen.
 In some embodiments R^{5d} is CN.
 In some embodiments R^{5d} is C_{1-6} linear alkyl.
In some embodiments R^{5d} is C_{3-7} branched alkyl. In some embodiments R^{5d} is C_{3-7} cycloalkyl. In some embodiments R^{5d} is C_{3-7} cycloalkyl. In some embodiments R^{5d} is C_{3-6} linear alkoxy. In some embodiments R^{5d} is C_{3-7} branched alkoxy.
In some embodiments R^{5d} is C_{3-7} cycloalkoxy.
In some embodiments R^{5d} is C_{1-6} linear haloalkyl.
In some embodiments R^{5d} is C_{3-7} branched haloalkyl.
In some embodiments R^{5d} is C_{1-6} linear haloalkoxy.
In some embodiments R^{5d} is C_{1-6} linear haloalkoxy. In some embodiments R^{5d} is -S(C_{1-6} linear alkyl). In some embodiments R^{5d} is -S(C_{3-7} branched alkyl). In some embodiments R^{5d} is -S(C_{3-7} cycloalkyl). In some embodiments R^{5d} is -SO_2(C_{1-6} linear alkyl). In some embodiments R^{5d} is -SO_2(C_{3-7} branched alkyl). In some embodiments R^{5d} is -SO_2(C_{3-7} cycloalkyl). In some embodiments R^{5d} is -SO_2(C_{3-7} cycloalkyl).
 In some embodiments R<sup>5d</sup> is CO<sub>2</sub>R<sup>7</sup>
 In some embodiments R<sup>5d</sup> is CONR<sup>8a</sup>R<sup>8b</sup>
In some embodiments R<sup>5d</sup> is SO<sub>2</sub>NR<sup>8a</sup>R<sup>8b</sup>. In some embodiments R<sup>5d</sup> is NR<sup>9a</sup>R<sup>9b</sup>. In some embodiments R<sup>5d</sup> is NR<sup>9a</sup>COR<sup>10</sup>. In some embodiments R<sup>5d</sup> is NR<sup>9a</sup>SO<sub>2</sub>R<sup>11</sup>.
 In some embodiments R^{5d} is NR^{9a}SO_2NR^{12a}R^{12b}.
 In some embodiments R<sup>6</sup> is hydrogen.
 In some embodiments R^6 is C_{1-6} linear alkyl.
In some embodiments R^6 is C_{3-7} branched alkyl. In some embodiments R^6 is C_{3-7} cycloalkyl. In some embodiments R^7 is C_{3-7} cycloalkyl. In some embodiments R^7 is C_{1-6} linear alkyl.
In some embodiments R^7 is C_{3-7} branched alkyl. In some embodiments R^7 is C_{3-7} cycloalkyl. In some embodiments R^{8\alpha} is hydrogen.
In some embodiments R^{8a} is C_{1-6} linear alkyl. In some embodiments R^{8a} is C_{3-7} branched alkyl. In some embodiments R^{8a} is C_{3-7} cycloalkyl.
 In some embodiments R<sup>8b</sup> is hydrogen.
In some embodiments R^{8b} is C_{1-6} linear alkyl.
 In some embodiments R^{8b} is C_{3-7} branched alkyl.
 In some embodiments R^{8b} is C_{3-7} cycloalkyl.
In some embodiments R^{9a} is hydrogen. In some embodiments R^{9a} is C_{1-6} linear alkyl. In some embodiments R^{9a} is C_{3-7} branched alkyl.
 In some embodiments R^{9a} is C_{3-7} cycloalkyl.
 In some embodiments R^{9b} is hydrogen.
In some embodiments R^{9b} is C_{1-6} linear alkyl. In some embodiments R^{9b} is C_{3-7} branched alkyl.
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In some embodiments R^{9b} is C_{3-7} cycloalkyl. In some embodiments R^{9a} and R^{9b} are be taken together with the atom to which they are bound to form a ring having 3 ring atoms.

In some embodiments R^{9a} and R^{9b} are be taken together with the atom to which they are bound to form a ring having 4 ring atoms.

In some embodiments R^{9a} and R^{9b} are be taken together with the atom to which they are bound to form a ring having

In some embodiments R^{9a} and R^{9b} are be taken together with the atom to which they are bound to form a ring having 6 ring atoms optionally containing an oxygen.

In some embodiments R^{9a} and R^{9b} are be taken together with the atom to which they are bound to form a ring having 7 ring atoms optionally containing an oxygen.

In some embodiments R¹⁰ is hydrogen.

In some embodiments R^{10} is C_{1-6} linear alkyl.

In some embodiments R^{10} is C_{3-7} branched alkyl.

In some embodiments R^{10} is C_{3-7} cycloalkyl.

In some embodiments R¹¹ is hydrogen.

In some embodiments R^{11} is C_{1-6} linear alkyl.

In some embodiments R¹¹ is C₃₋₇ branched alkyl. In some embodiments R¹¹ is C₃₋₇ cycloalkyl.

In some embodiments R^{12a} is hydrogen.

In some embodiments R^{12a} is C_{1-6} linear alkyl.

In some embodiments R^{12a} is C_{3-7}^{1-a} branched alkyl.

In some embodiments R^{12a} is C_{3-7} cycloalkyl.

In some embodiments R^{12b} is hydrogen.

In some embodiments R_{1-6}^{12b} is C_{1-6} linear alkyl.

In some embodiments R^{12b} is C_{3-7} branched alkyl.

In some embodiments R^{12b} is C_{3-7} cycloalkyl.

Examples of compounds of the invention include, but are 35 not limited to:

(R)-3-(2-(6-(pyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl) ethyl)-2-oxaspiro[4.5]decan-1-one:

(S)-3-(2-(6-(pyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl) ethyl)-2-oxaspiro[4.5]decan-1-one

40 (R)-3,3-diethyl-5-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)dihydrofuran-2(3H)-one;

(S)-3,3-diethyl-5-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2yl)ethyl)dihydrofuran-2(3H)-one;

(R)-3-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2oxaspiro[4.5]decan-1-one;

(S)-3-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2oxaspiro[4.5]decan-1-one;

(R)-3,3-diethyl-5-(2-(5-(2-isopropylphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-

(S)-3,3-diethyl-5-(2-(5-(2-isopropylphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-

(R)-3-(2-(5-(3-methylpyridin-4-yl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

(S)-3-(2-(5-(3-methylpyridin-4-yl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

(R)-3-(2-(5-(2-methylpyridin-4-yl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

60 (S)-3-(2-(5-(2-methylpyridin-4-yl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

(R)-3-(2-(5-(2,6-dimethylpyridin-4-yl)hexahydropyrrolo[3, 4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

(S)-3-(2-(5-(2,6-dimethylpyridin-4-yl)hexahydropyrrolo[3, 4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

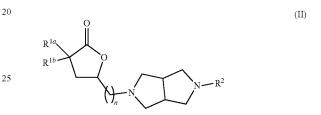
(R)-3-(2-(6-(3-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;

- (S)-3-(2-(6-(3-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;
- (R)-3-(2-(6-(2-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;
- (S)-3-(2-(6-(2-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;
- (R)-3-(2-(6-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro[3.3] heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;
- (S)-3-(2-(6-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro[3.3] heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one;
- (R)-3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- (S)-3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- (R)-3,3-diethyl-5-(2-(5-(m-tolyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- (S)-3,3-diethyl-5-(2-(5-(m-tolyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- (R)-3,3-diethyl-5-(2-(5-(p-tolyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- (S)-3,3-diethyl-5-(2-(5-(p-tolyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- (R)-2-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl)
- hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile; (S)-2-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl)
- hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile; (R)-3-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl)
- hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile;
- (S)-3-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile;
- (R)-4-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile;
- (S)-4-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile;
- (R)-3,3-diethyl-5-(2-(5-(2-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)one:
- (S)-3,3-diethyl-5-(2-(5-(2-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (R)-3,3-diethyl-5-(2-(5-(3-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (S)-3,3-diethyl-5-(2-(5-(3-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (R)-3.3-diethyl-5-(2-(5-(4-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (S)-3,3-diethyl-5-(2-(5-(4-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (R)-3,3-diethyl-5-(2-(5-(2-morpholinophenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (S)-3,3-diethyl-5-(2-(5-(2-morpholinophenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (R)-3,3-diethyl-5-(2-(5-(2-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (S)-3,3-diethyl-5-(2-(5-(2-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (R)-3,3-diethyl-5-(2-(5-(3-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-

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- (S)-3,3-diethyl-5-(2-(5-(3-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- (R)-3,3-diethyl-5-(2-(5-(4-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
 - (S)-3,3-diethyl-5-(2-(5-(4-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-
- $^{10} \ (R) \hbox{-} 3.3 \hbox{-} diethyl \hbox{-} 5 \hbox{-} (2 \hbox{-} (5 \hbox{-} phenylhexahydropyrrolo} [3,4 \hbox{-} c] pyr$ rol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
 - (S)-3,3-diethyl-5-(2-(5-phenylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one;
- or a pharmaceutically acceptable form thereof.

Exemplary embodiments include compounds having the formula (II) or a pharmaceutically acceptable salt form thereof:



wherein non-limiting examples of R1a, R1b, R2 and n are defined herein below in Table 1.

_				TABLE	1
25	Entry	n	R^{1a}	\mathbb{R}^{1b}	R ²
35	1	1	CH ₃	CH_3	Phenyl
	2	2	CH_3	CH_3	Phenyl
	3	3	CH_3	CH_3	Phenyl
	4	1	CH_2CH_3	CH_2CH_3	Phenyl
	5	2	CH ₂ CH ₃	CH ₂ CH ₃	Phenyl
40	6	3	CH_2CH_3	CH_2CH_3	Phenyl
-10	7	1	CH_3	CH_3	4-OH-phenyl
	8	2	CH_3	CH_3	4-OH-phenyl
	10	3	CH ₃	CH ₃	4-OH-phenyl
	11	1	CH_2CH_3	CH ₂ CH ₃	4-OH-phenyl
	12	2	CH_2CH_3	CH_2CH_3	4-OH-phenyl
15	13	3	CH_2CH_3	CH_2CH_3	4-OH-phenyl
45	14	1	CH_3	CH_3	3-OH-phenyl
	15	2	CH_3	CH_3	3-OH-phenyl
	16	3	CH_3	CH_3	3-OH-phenyl
	17	1	CH ₂ CH ₃	CH ₂ CH ₃	3-OH-phenyl
	18	2	CH ₂ CH ₃	CH ₂ CH ₃	3-OH-phenyl
	19	3	CH ₂ CH ₃	CH ₂ CH ₃	3-OH-phenyl
50	20	1	CH_3	CH_3	2-OH-phenyl
	21	2	CH ₃	CH ₃	2-OH-phenyl
	22	3	CH ₃	CH ₃	2-OH-phenyl
	23	1	CH ₂ CH ₃	CH ₂ CH ₃	2-OH-phenyl
	24	2	CH ₂ CH ₃	CH ₂ CH ₃	2-OH-phenyl
	25	3	CH ₂ CH ₃	CH ₂ CH ₃	2-OH-phenyl
55	26	1	CH ₃	CH ₃	4-CH ₃ -Phenyl
	27	2	CH ₃	CH ₃	4-CH ₃ -Phenyl
	28	3	CH ₃	CH ₃	4-CH ₃ -Phenyl
	26	1	CH ₂ CH ₃	CH ₂ CH ₃	4-CH ₃ -Phenyl
	30	2	CH ₂ CH ₃	CH ₂ CH ₃	4-CH ₃ -Phenyl
	31	3	CH ₂ CH ₃	CH ₂ CH ₃	4-CH ₃ -Phenyl
60	32	1	CH ₃	CH ₃	3-CH ₃ -Phenyl
	33	2	CH ₃	CH ₃	3-CH ₃ -Phenyl
	34	3	CH ₃	CH ₃	3-CH ₃ -Phenyl
	35	1	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -Phenyl
	36	2	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -Phenyl
	37	3	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -Phenyl
65	38 39	1 2	CH ₃	CH ₃	2-CH ₃ -Phenyl
00	39 40	3	CH₃ CH₃	CH ₃	2-CH ₃ -Phenyl 2-CH ₃ -Phenyl
	40	3	СП3	СП3	2-CH ₃ -FHEHYI

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Entry	n	$R^{1\alpha}$	R^{1b}	R ²		Entry	n	R^{1a}	R^{1b}	R ²
41	1	CH ₂ CH ₃	CH ₂ CH ₃	2-CH ₃ -Phenyl	- '	119	1	CH ₂ CH ₃	CH ₂ CH ₃	4-Br-Phenyl
42	2	CH ₂ CH ₃	CH ₂ CH ₃	2-CH ₃ -Phenyl	5	120	2	CH ₂ CH ₃	CH ₂ CH ₃	4-Br-Phenyl
43	3	CH ₂ CH ₃	CH ₂ CH ₃	2-CH ₃ -Phenyl		121	3	CH ₂ CH ₃	CH ₂ CH ₃	4-Br-Phenyl
44 45	1 2	CH ₃ CH ₃	CH ₃ CH ₃	4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl		122 123	1 2	CH ₃ CH ₃	CH ₃ CH ₃	4-OCF ₃ -Phenyl 4-OCF ₃ -Phenyl
46	3	CH ₃	CH ₃	4-OCH ₃ -Phenyl		124	3	CH ₃	CH ₃	4-OCF ₃ -Phenyl
47	1	CH_2CH_3	CH ₂ CH ₃	4-OCH ₃ -Phenyl		125	1	CH_2CH_3	CH ₂ CH ₃	4-OCF ₃ -Phenyl
48 49	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl	10	126 127	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-OCF ₃ -Phenyl 4-OCF ₃ -Phenyl
50	1	CH ₃	CH_2CH_3	3-OCH ₃ -Phenyl		128	1	CH_3	CH_2CH_3	3-OCF ₃ -Phenyl
51	2	CH ₃	CH_3	3-OCH ₃ -Phenyl		129	2	CH_3	CH ₃	3-OCF ₃ -Phenyl
52	3	CH ₃	CH ₃ CH ₂ CH ₃	3-OCH Phenyl		130	3	CH ₃ CH ₂ CH ₃	CH ₃	3-OCF Phenyl
53 54	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl		131 132	1 2	CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-OCF ₃ -Phenyl 3-OCF ₃ -Phenyl
55	3	CH ₂ CH ₃	CH ₂ CH ₃	3-OCH ₃ -Phenyl	15	133	3	CH ₂ CH ₃	CH ₂ CH ₃	3-OCF ₃ -Phenyl
56	1	CH ₃	CH ₃	2-OCH ₃ -Phenyl		134	1	CH ₃	CH ₃	2-OCF ₃ -Phenyl
57 58	2	CH₃ CH₃	CH ₃ CH ₃	2-OCH ₃ -Phenyl 2-OCH ₃ -Phenyl		135 136	2	CH₃ CH₃	CH₃ CH₃	2-OCF ₃ -Phenyl 2-OCF ₃ -Phenyl
59	1	CH ₂ CH ₃	CH ₂ CH ₃	2-OCH ₃ -Phenyl		137	1	CH ₂ CH ₃	CH ₂ CH ₃	2-OCF ₃ -Phenyl
60	2	CH_2CH_3	CH ₂ CH ₃	2-OCH ₃ -Phenyl	20	138	2	CH_2CH_3	CH ₂ CH ₃	2-OCF ₃ -Phenyl
61 62	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-OCH ₃ -Phenyl 4-CN-Phenyl	20	139 140	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-OCF ₃ -Phenyl 4-isopropyl-phenyl
63	2	CH ₃	CH ₃	4-CN-Phenyl		141	2	CH ₃	CH ₃	4-isopropyl-phenyl
64	3	CH ₃	CH_3	4-CN-Phenyl		142	3	CH_3	CH ₃	4-isopropyl-phenyl
65	1	CH ₂ CH ₃	CH ₂ CH ₃	4-CN-Phenyl		143	1	CH ₂ CH ₃	CH ₂ CH ₃	4-isopropyl-phenyl
66 67	2 3	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-CN-Phenyl 4-CN-Phenyl	25	144 145	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-isopropyl-phenyl 4-isopropyl-phenyl
68	1	CH ₃	CH ₂ CH ₃	3-CN-Phenyl		146	1	CH ₃	CH ₃	3-isopropyl-phenyl
69	2	CH_3	CH_3	3-CN-Phenyl		147	2	CH_3	CH_3	3-isopropyl-phenyl
70 71	3 1	CH ₃ CH ₂ CH ₃	CH ₃	3-CN-Phenyl 3-CN-Phenyl		148	3 1	CH ₃	CH ₃ CH ₂ CH ₃	3-isopropyl-phenyl
72	2	CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-CN-Phenyl		149 150	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃	3-isopropyl-phenyl 3-isopropyl-phenyl
73	3	CH ₂ CH ₃	CH ₂ CH ₃	3-CN-Phenyl	30	151	3	CH ₂ CH ₃	CH ₂ CH ₃	3-isopropyl-phenyl
74	1	CH ₃	CH_3	2-CN-Phenyl		152	1	CH ₃	CH ₃	2-isopropyl-phenyl
75 76	2	CH ₃ CH ₃	CH ₃ CH ₃	2-CN-Phenyl 2-CN-Phenyl		153 154	2	CH ₃ CH ₃	CH ₃ CH ₃	2-isopropyl-phenyl 2-isopropyl-phenyl
77	1	CH ₂ CH ₃	CH ₂ CH ₃	2-CN-Phenyl		155	1	CH ₂ CH ₃	CH ₂ CH ₃	2-isopropyl-phenyl
78	2	$\mathrm{CH_{2}CH_{3}}$	CH ₂ CH ₃	2-CN-Phenyl		156	2	$\mathrm{CH_{2}CH_{3}}$	CH ₂ CH ₃	2-isopropyl-phenyl
79 80	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-CN-Phenyl 4-F-Phenyl	35	157 158	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-isopropyl-phenyl 4-cyclopropyl-phenyl
81	2	CH ₃	CH ₃	4-F-Phenyl		159	2	CH ₃	CH ₃	4-cyclopropyl-phenyl
82	3	CH_3	CH_3	4-F-Phenyl		160	3	CH_3	CH_3	4-cyclopropyl-phenyl
83	1	CH ₂ CH ₃	CH ₂ CH ₃	4-F-Phenyl		161	1	CH ₂ CH ₃	CH ₂ CH ₃	4-cyclopropyl-phenyl
84 85	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-F-Phenyl 4-F-Phenyl		162 163	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-cyclopropyl-phenyl 4-cyclopropyl-phenyl
86	1	CH ₃	CH_3	3-F-Phenyl	40	164	1	CH ₃	CH ₃	3-cyclopropyl-phenyl
87	2	CH ₃	CH ₃	3-F-Phenyl		165	2	CH ₃	CH ₃	3-cyclopropyl-phenyl
88 89	3 1	CH₃ CH₂CH₃	CH₃ CH₂CH₃	3-F-Phenyl 3-F-Phenyl		166 167	3 1	CH₃ CH₂CH₃	CH ₃ CH ₂ CH ₃	3-cyclopropyl-phenyl 3-cyclopropyl-phenyl
90	2	CH ₂ CH ₃	CH ₂ CH ₃	3-F-Phenyl		168	2	CH ₂ CH ₃	CH ₂ CH ₃	3-cyclopropyl-phenyl
91	3	CH ₂ CH ₃	CH ₂ CH ₃	3-F-Phenyl		169	3	CH ₂ CH ₃	CH ₂ CH ₃	3-cyclopropyl-phenyl
92 93	1 2	CH ₃ CH ₃	CH_3	2-F-Phenyl	45	170 171	1 2	CH ₃	CH ₃	2-cyclopropyl-phenyl
93 94	3	CH ₃	CH ₃ CH ₃	2-F-Phenyl 2-F-Phenyl		171	3	CH ₃ CH ₃	CH ₃ CH ₃	2-cyclopropyl-phenyl 2-cyclopropyl-phenyl
95	1	CH_2CH_3	CH ₂ CH ₃	2-F-Phenyl		173	1	CH ₂ CH ₃	CH ₂ CH ₃	2-cyclopropyl-phenyl
96	2	CH ₂ CH ₃	CH ₂ CH ₃	2-F-Phenyl		174	2	CH ₂ CH ₃	CH ₂ CH ₃	2-cyclopropyl-phenyl
97 98	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-F-Phenyl 4-Cl-Phenyl	50	175 176	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-cyclopropyl-phenyl 4-morpholino-phenyl
99	2	CH ₃	CH ₃	4-Cl-Phenyl	30	177	2	CH ₃	CH ₃	4-morpholino-phenyl
100	3	CH_3	CH_3	4-Cl-Phenyl		178	3	CH ₃	CH ₃	4-morpholino-phenyl
101 102	1	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃	4-Cl-Phenyl 4-Cl-Phenyl		179	1	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-morpholino-phenyl 4-morpholino-phenyl
102	2	CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-Cl-Phenyl		180 181	2	CH_2CH_3 CH_2CH_3	CH ₂ CH ₃	4-morpholino-phenyl
104	1	CH ₃	CH_3	3-Cl-Phenyl	55	182	1	CH ₃	CH ₃	3-morpholino-phenyl
105	2	CH ₃	CH_3	3-Cl-Phenyl		183	2	CH ₃	CH ₃	3-morpholino-phenyl
106 107	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	3-Cl-Phenyl 3-Cl-Phenyl		184 185	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	3-morpholino-phenyl 3-morpholino-phenyl
108	2	CH ₂ CH ₃	CH ₂ CH ₃	3-Cl-Phenyl		186	2	CH ₂ CH ₃	CH ₂ CH ₃	3-morpholino-phenyl
109	3	CH ₂ CH ₃	CH ₂ CH ₃	3-Cl-Phenyl		187	3	CH ₂ CH ₃	CH ₂ CH ₃	3-morpholino-phenyl
110 111	1 2	CH ₃ CH ₃	CH ₃ CH ₃	2-Cl-Phenyl 2-Cl-Phenyl	60	188 189	1 2	CH ₃ CH ₃	CH ₃ CH ₃	2-morpholino-phenyl 2-morpholino-phenyl
111	3	CH ₃	CH ₃	2-Cl-Phenyl		190	3	CH ₃	CH ₃	2-morpholino-phenyl
113	1	CH ₂ CH ₃	CH ₂ CH ₃	2-Cl-Phenyl		191	1	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-phenyl
114	2	CH ₂ CH ₃	CH ₂ CH ₃	2-Cl-Phenyl		192	2	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-phenyl 2-morpholino-phenyl
115 116	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-Cl-Phenyl 4-Br-Phenyl		193 194	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-morpholino-phenyl 2-pyridyl
117	2	CH ₃	CH ₃	4-Br-Phenyl	65	195	2	CH ₃	CH ₃	2-pyridyl
118	3	CH_3	CH_3	4-Br-Phenyl		196	3	CH_3	CH_3	2-pyridyl

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TABLE 2-continued

		TAI	BLE 1-co	ntinued			TABLE	2-continued
Entry	n	R^{1a}	R^{1b}	R ²		Entry	n	R ²
197	1	CH ₂ CH ₃	CH ₂ CH ₃	2-pyridyl		13	1	4-CH ₃ -Phenyl
198	2	CH ₂ CH ₃	CH ₂ CH ₃	2-pyridyl	5	14	2	4-CH ₃ -Phenyl
199 200	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-pyridyl 3-pyridyl		15 16	3 1	4-CH ₃ -Phenyl 3-CH ₃ -Phenyl
200	2	CH ₃	CH ₃	3-pyridyl		17	2	3-CH ₃ -Phenyl
202	3	CH_3	CH_3	3-pyridyl		18	3	3-CH ₃ -Phenyl
203	1	CH_2CH_3	CH ₂ CH ₃	3-pyridyl		19	1	2-CH ₃ -Phenyl
204 205	2	CH ₂ CH ₃	CH ₂ CH ₃	3-pyridyl	10	20 21	2 3	2-CH ₃ -Phenyl
203	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	3-pyridyl 4-pyridyl		22	1	2-CH ₃ -Phenyl 4-OCH ₃ -Phenyl
207	2	CH ₃	CH ₃	4-pyridyl		23	2	4-OCH ₃ -Phenyl
208	3	CH_3	CH_3	4-pyridyl		24	3	4-OCH ₃ -Phenyl
209	1	CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-pyridyl		25 26	1	3-OCH, Phanel
210 211	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-pyridyl 4-pyridyl	15	26 27	2 3	3-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl
212	1	CH ₃	CH ₃	2-CH ₃ -4-pyridyl		28	1	2-OCH ₃ -Phenyl
213	2	CH ₃	CH ₃	2-CH ₃ -4-pyridyl		29	2	2-OCH ₃ -Phenyl
214	3	CH ₃	CH ₃	2-CH ₃ -4-pyridyl		30	3	2-OCH ₃ -Phenyl
215 216	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-CH ₃ -4-pyridyl 2-CH ₃ -4-pyridyl		31 32	1 2	4-CN-Phenyl 4-CN-Phenyl
217	3	CH ₂ CH ₃	CH ₂ CH ₃	2-CH ₃ -4-pyridyl	20	33	3	4-CN-Phenyl
218	1	CH ₃	CH ₃	3-CH ₃ -4-pyridyl		34	1	3-CN-Phenyl
219	2	CH ₃	CH_3	3-CH ₃ -4-pyridyl		35	2	3-CN-Phenyl
220	3	CH ₃	CH ₃	3-CH ₃ -4-pyridyl		36	3	3-CN-Phenyl
221 222	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-CH ₃ -4-pyridyl 3-CH ₃ -4-pyridyl		37 38	1 2	2-CN-Phenyl 2-CN-Phenyl
223	3	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -4-pyridyl	25	39	3	2-CN-Phenyl
224	1	CH ₃	CH_3	3,5-dimethylpyridin-4-yl		40	1	4-F-Phenyl
225	2	CH ₃	CH ₃	3,5-dimethylpyridin-4-yl		41	2	4-F-Phenyl
226 227	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	3,5-dimethylpyridin-4-yl 3,5-dimethylpyridin-4-yl		42 43	3 1	4-F-Phenyl 3-F-Phenyl
228	2	CH ₂ CH ₃	CH ₂ CH ₃	3,5-dimethylpyridin-4-yl		44	2	3-F-Phenyl
229	3	CH ₂ CH ₃	CH ₂ CH ₃	3,5-dimethylpyridin-4-yl	30	45	3	3-F-Phenyl
230	1	CH_3	$\mathrm{CH_3}$	2,6-dimethylpyridin-4-yl		46	1	2-F-Phenyl
231	2	CH ₃	CH_3	2,6-dimethylpyridin-4-yl		47	2 3	2-F-Phenyl
232 233	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2,6-dimethylpyridin-4-yl 2,6-dimethylpyridin-4-yl		48 49	3 1	2-F-Phenyl 4-Cl-Phenyl
234	2	CH ₂ CH ₃	CH ₂ CH ₃	2,6-dimethylpyridin-4-yl		50	2	4-Cl-Phenyl
235	3	CH ₂ CH ₃	CH ₂ CH ₃	2,6-dimethylpyridin-4-yl	35	51	3	4-Cl-Phenyl
						52	1	3-Cl-Phenyl
Exemp	larv.	embodim	ents inclu	de compounds having the		53 54	2 3	3-Cl-Phenyl 3-Cl-Phenyl
				ally acceptable salt form		55	1	2-Cl-Phenyl
thereof:	(21)	or a pha	imaccanc	any acceptable balt form		56	2	2-Cl-Phenyl
uncreon.					40	57	3	2-Cl-Phenyl
					40	58	1	4-Br-Phenyl
				(X)		59 60	2 3	4-Br-Phenyl 4-Br-Phenyl
	Ö			(12)		61	1	4-OCF ₃ -Phenyl
						62	2	4-OCF ₃ -Phenyl
\wedge		\ <u></u>			15	63	3	4-OCF ₃ -Phenyl
<i></i>	1	7			45	64 65	1 2	4-OCF ₃ -Phenyl 4-OCF ₃ -Phenyl
	_		\sim	$N-R^2$		66	3	4-OCF ₃ -Phenyl
		XI_N	` \	N-R		67	1	4-OCF ₃ -Phenyl
		V_n		/		68	2	4-OCF ₃ -Phenyl
					50	69 70	3 1	4-OCF ₃ -Phenyl 4-isopropyl-phenyl
		1::+:		of D ² and n and defined	50	70	2	4-isopropyl-phenyl
				of R ² and n are defined		72	3	4-isopropyl-phenyl
herein be	now	m rabie z	۷.			73	1	3-isopropyl-phenyl
			m, pr p	•		74 75	2 3	3-isopropyl-phenyl
			TABLE	2		75 76	3 1	3-isopropyl-phenyl 2-isopropyl-phenyl
	Entry	n	R ²	_	55	77	2	2-isopropyl-phenyl
	лиц у	11	K			78	3	2-isopropyl-phenyl
	1	1		enyl		79	1	4-cyclopropyl-phenyl
	2	2		enyl		80 81	2 3	4-cyclopropyl-phenyl 4-cyclopropyl-phenyl
	3 4	3 1		enyl OH-phenyl		81 82	3 1	3-cyclopropyl-phenyl
	5	2		OH-phenyl	60	83	2	3-cyclopropyl-phenyl
	6	3	4-0	DH-phenyl		84	3	3-cyclopropyl-phenyl
	7	1		OH-phenyl		85 86	1	2-cyclopropyl-phenyl
	8 9	2 3		OH-phenyl		86 87	2 3	2-cyclopropyl-phenyl 2-cyclopropyl-phenyl
	10	3 1		OH-phenyl OH-phenyl		88	1	4-morpholino-phenyl
	11	2		OH-phenyl	65	89	2	4-morpholino-phenyl
	12	3		OH-phenyl		90	3	4-morpholino-phenyl

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TARLE 3-continued

TABLE 2-cont	tinued			TABLE	3-continued
Entry n R ²			Entry	n	\mathbb{R}^2
91 1 3-m	orpholino-phenyl		25	1	3-OCH ₃ -Phenyl
	orpholino-phenyl	5	26	2	3-OCH ₃ -Phenyl
93 3 3-m	orpholino-phenyl		27	3	3-OCH ₃ -Phenyl
	orpholino-phenyl		28	1	2-OCH ₃ -Phenyl
	orpholino-phenyl		29	2	2-OCH ₃ -Phenyl
	orpholino-phenyl		30	3	2-OCH ₃ -Phenyl
	ridyl	1.0	31 32	1 2	4-CN-Phenyl 4-CN-Phenyl
	ridyl ridyl	10	33	3	4-CN-Phenyl
	ridyl		34	1	3-CN-Phenyl
	ridyl		35	2	3-CN-Phenyl
	ridyl		36	3	3-CN-Phenyl
	ridyl		37	1	2-CN-Phenyl
	ridyl	15	38	2	2-CN-Phenyl
	ridyl		39 40	3	2-CN-Phenyl
	H ₃ -4-pyridyl H ₃ -4-pyridyl		40 41	1 2	4-F-Phenyl 4-F-Phenyl
	H ₃ -4-pyridyl		42	3	4-F-Phenyl
	H ₃ -4-pyridyl		43	1	3-F-Phenyl
	H ₃ -4-pyridyl		44	2	3-F-Phenyl
	H ₃ -4-pyridyl	20	45	3	3-F-Phenyl
	dimethylpyridin-4-yl		46	1	2-F-Phenyl
	dimethylpyridin-4-yl		47	2	2-F-Phenyl
	dimethylpyridin-4-yl		48	3	2-F-Phenyl
	dimethylpyridin-4-yl		49 50	1 2	4-Cl-Phenyl 4-Cl-Phenyl
	dimethylpyridin-4-yl dimethylpyridin-4-yl	25	51	3	4-Cl-Phenyl
	anneary pyriam + yr		52	1	3-Cl-Phenyl
			53	2	3-Cl-Phenyl
Exemplary embodiments include	le compounds having the		54	3	3-Cl-Phenyl
formula (XI) or a pharmaceutica	ally acceptable salt form		55	1	2-Cl-Phenyl
thereof:	•		56	2	2-Cl-Phenyl
		30	57	3	2-Cl-Phenyl
			58 59	1 2	4-Br-Phenyl 4-Br-Phenyl
	(XI)		60	3	4-Br-Phenyl
О	(711)		61	1	4-OCF ₃ -Phenyl
			62	2	4-OCF ₃ -Phenyl
		35	63	3	4-OCF ₃ -Phenyl
\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\		55	64	1	3-OCF ₃ -Phenyl
	<u> </u>		65	2	3-OCF ₃ -Phenyl
$\overline{}$, $/\Upsilon$	$N-R^2$		66	3	3-OCF ₃ -Phenyl
Ŋ - Ŋ, [67 68	1 2	2-OCF ₃ -Phenyl
V_n	~		69	3	2-OCF ₃ -Phenyl 2-OCF ₃ -Phenyl
		40	70	1	4-isopropyl-phenyl
wherein non-limiting examples of	of \mathbb{R}^2 and n are defined		71	2	4-isopropyl-phenyl
herein below in Table 3.	of it and it are defined		72	3	4-isopropyl-phenyl
nerem below in Table 3.			73	1	3-isopropyl-phenyl
			74	2	3-isopropyl-phenyl
TABLE 3	3	45	75 76	3 1	3-isopropyl-phenyl
		73	76 77	2	2-isopropyl-phenyl 2-isopropyl-phenyl
Entry n R ²			78	3	2-isopropyl-phenyl
1 1 Pher	nyl		79	1	4-cyclopropyl-phenyl
2 2 Pher	nyl		80	2	4-cyclopropyl-phenyl
3 Phen			81	3	4-cyclopropyl-phenyl
	H-phenyl	50	82	1	3-cyclopropyl-phenyl
	H-phenyl		83 84	2 3	3-cyclopropyl-phenyl 3-cyclopropyl-phenyl
	H-phenyl H-phenyl		85	1	2-cyclopropyl-phenyl
	H-phenyl		86	2	2-cyclopropyl-phenyl
	H-phenyl		87	3	2-cyclopropyl-phenyl
10 1 2-Ol	H-phenyl	55	88	1	4-morpholino-phenyl
	H-phenyl		89	2	4-morpholino-phenyl
	H-phenyl		90	3	4-morpholino-phenyl
	H ₃ -Phenyl		91 92	1 2	3-morpholino-phenyl 3-morpholino-phenyl
	H ₃ -Phenyl H ₃ -Phenyl		93	3	3-morpholino-phenyl
	H ₃ -Phenyl		94	1	2-morpholino-phenyl
	H ₃ -Phenyl	60	95	2	2-morpholino-phenyl
18 3 3-CI	H ₃ -Phenyl		96	3	2-morpholino-phenyl
19 1 2-CI	H ₃ -Phenyl		97	1	2-pyridyl
	H ₃ -Phenyl		98	2	2-pyridyl
	H ₃ -Phenyl		99 100	3 1	2-pyridyl
	CH ₃ -Phenyl	65	100 101	2	3-pyridyl 3-pyridyl
	CH ₃ -Phenyl CH ₃ -Phenyl	00	102	3	3-pyridyl
	<i>yy</i> -			~	FVV-

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TABLE 4-continued

Entry n R²							
144 2 4-pyris d 38 2 2-(N-Phenyl 106 1 2-(CH)-phenyl 30 3 3 2-(CN-Phenyl 106 1 2-(CH)-phenyl 40 1 4-P-Phenyl	Entry	n	R^2		Entry	n	R^2
144 2 4-pyris d 38 2 2-(N-Phenyl 106 1 2-(CH)-phenyl 30 3 3 2-(CN-Phenyl 106 1 2-(CH)-phenyl 40 1 4-P-Phenyl	103	1	4-pyridyl	_	37	1	2-CN-Phenyl
105 3 4-pyridy 39 3 2-CN-Repy 106 1 2-CH ₂ -4-pyridy 40 1 4-F-Pleny 107 2 2-CH ₂ -4-pyridy 41 2 4-F-Pleny 108 3 2-CH ₂ -4-pyridy 41 2 4-F-Pleny 109 1 3-CH ₂ -4-pyridy 42 3 4-F-Pleny 110 1 3-CH ₂ -4-pyridy 44 2 3 4-F-Pleny 110 1 3-CH ₂ -4-pyridy 46 1 2-F-Pleny 111 3 3-CH ₂ -4-pyridy 47 2 2-F-Pleny 112 1 3-CH ₂ -4-pyridy 47 2 2-F-Pleny 113 2 3-CH ₂ -4-pyridy 47 2 2-F-Pleny 114 3 3-C-H ₂ -Hendy 47 2 2-F-Pleny 115 1 2-C-H ₂ -Hendy 49 1 4-C-Pleny 116 2 2-S-Hendy pyridin-4-y 15 3 3-F-Pleny 116 2 2-S-Hendy pyridin-4-y 15 3 3 4-C-Pleny 117 3 2-S-Hendy pyridin-4-y 15 3 3 4-C-Pleny 16 3 3-C-Pleny 17 3 3-C-Hendy pyridin-4-y 15 3 3 3-C-Pleny 17 3 2-S-Hendy pyridin-4-y 15 3 3 3-C-Pleny 17 3 2-S-Hendy pyridin-4-y 15 3 3 3-C-Pleny 17 3-C-Plen				5			
106 1 2-CH ₃ -4-pyridy 40 1 4-F-Pheny 107 2 2-CH ₃ -4-pyridy 41 2 4-F-Pheny 108 3 2-CH ₃ -4-pyridy 42 3 4-F-Pheny 109 44 1 2 4-F-Pheny 110 44 1 2 4-F-Pheny 111 2 3 3-CH ₃ -4-pyridy 46 1 3 3-F-Pheny 111 2 3 3-GHandaybyrida-dy 47 2 2-F-Pheny 115 2 3-GHandaybyrida-dy 48 3 3-F-Pheny 115 1 2-G-GHANDAYDY 48 3 3-F-Pheny 115 1 2-G-GHANDAYDY 49 1 4-G-Pheny 115 1 2-G-GHANDAYDY 49 1 4-G-Pheny 117 3 2-G-GHANDAYDY 49 1 4-G-Pheny 40 40 40 40 40 40 40							
107 2 2-CH ₃ + 2printy 41 2 4 F-Pheny 106 1 3 CH ₃ + 2printy 42 3 4 F-Pheny 110 1 3 CH ₃ + 2printy 42 3 4 F-Pheny 110 1 3 CH ₃ + 2printy 10 44 2 3 5 F-Pheny 111 2 3 5 CH ₃ + 2printy 10 44 2 3 5 F-Pheny 112 1 3 5 CH ₃ + 2printy 44 1 2 F-Pheny 112 1 3 5 CH ₃ + 2printy 47 2 2 F-Pheny 114 3 3 5 CH ₃ + 2printy 47 2 2 F-Pheny 114 3 3 5 CH ₃ + 2printy 48 3 2 F-Pheny 115 1 2 5 CH ₃ + 2printy 49 1 4 5 F-Pheny 116 2 2 5 CH ₃ + 2printy 49 1 4 5 F-Pheny 116 2 2 5 CH ₃ + 2printy 49 1 4 5 F-Pheny 117 3 2 5 CH ₃ + 2printy 49 1 4 5 F-Pheny 117 3 2 5 CH ₃ + 2printy 49 1 4 5 F-Pheny 4 5 F-P							
108 3 2-CH ₂ -t-pyridy 42 3 4-F-Pieny 10 10 10 10 10 10 10							
110	108	3			42		4-F-Phenyl
111 3 3-CH_st-pyridin 46 1 2-F-Phenyl 113 2 3-5-dimethylpyridin-4-yl 47 2 2-F-Phenyl 114 3 3-5-dimethylpyridin-4-yl 48 3 2-F-Phenyl 114 3 3-5-dimethylpyridin-4-yl 48 3 2-F-Phenyl 115 1 2-5-dimethylpyridin-4-yl 48 3 2-F-Phenyl 116 1 2-5-dimethylpyridin-4-yl 1 4 4 CF-Phenyl 117 3 3-6-dimethylpyridin-4-yl 15 5 3 4 CF-Phenyl 117 3 3-6-dimethylpyridin-4-yl 15 5 3 3 4 CF-Phenyl 117 3 3-6-dimethylpyridin-4-yl 15 5 3 3 4 CF-Phenyl 1 3 3 3 3 3 3 3 3 3 3	109	1	3-CH ₃ -4-pyridyl		43	1	3-F-Phenyl
112	110	2	3-CH ₃ -4-pyridyl	10	44		3-F-Phenyl
113	111	3	3-CH ₃ -4-pyridyl		45		3-F-Phenyl
114 3 3.5.d-methylypridin-4yl 49 1 4-Cl-Phenyl 116 2 2.6-d-methylypridin-4yl 15 50 2 4-Cl-Phenyl 117 3 2.6-d-methylypridin-4yl 15 51 3 4-Cl-Phenyl 117 3 2.6-d-methylypridin-4yl 15 51 3 4-Cl-Phenyl 117 3 2.6-d-methylypridin-4yl 15 51 3 4-Cl-Phenyl 16 51 51 51 51 51 51 51	112				46		2-F-Phenyl
115 1 2,6-dimethylpyridin-4-yl 15 50 2 4-Cl-Phenyl 117 3 2,6-dimethylpyridin-4-yl 15 50 2 4-Cl-Phenyl 117 3 2,6-dimethylpyridin-4-yl 15 51 3 4-Cl-Phenyl 117 3 2,6-dimethylpyridin-4-yl 15 51 3 4-Cl-Phenyl 15 51 3 3-Cl-Phenyl 15 3							
116 2 2.6-dimethylpyridin-4yl 15 50 2 4-Cl-Phenyl 117 3 2.6-dimethylpyridin-4yl 52 1 3-Cl-Phenyl 152 1 3-Cl-Phenyl 153 1 3-Cl-Phenyl 153 1 3-Cl-Phenyl 154 3-Cl-Phenyl 154 3-Cl-Phenyl 154 3-Cl-Phenyl 154 3-Cl-Phenyl 155 3-Cl-Phenyl							
117 3 2.6-dimethylpyridim-4yl 15 51 3 4-Cl-Phenyl							
Exemplary embodiments include compounds having the formula (XII) or a pharmaceutically acceptable salt form				15			
Exemplary embodiments include compounds having the formula (XII) or a pharmaceutically acceptable salt form thereof: 20	117	3	2,6-dimethylpyridin-4-yl				
Exemplary embodiments include compounds having the formula (XII) or a pharmaceutically acceptable salt form thereof:							
Communication Section	г 1 1	1 1 4					
thereof: 20 56 2 2-Cl-Phenyl 58 1 4-Br Phenyl 59 2 4-Br Phenyl 60 3 4-Br Phenyl 61 1 4-OCF, 3-Phenyl 62 2 4-OCF, 3-Phenyl 63 3 4-OCF, 3-Phenyl 64 1 3-OCF, 3-Phenyl 65 2 3-OCF, 3-Phenyl 66 3 3-OCF, 3-Phenyl 67 1 2-OCF, 3-Phenyl 70 1 4-isopropyl-phenyl 70 1 4-isopropyl-phenyl 71 2 4-isopropyl-phenyl 72 3 4-isopropyl-phenyl 73 3 3-isopropyl-phenyl 74 2 3-isopropyl-phenyl 75 2 2-isopropyl-phenyl 76 3 3-isopropyl-phenyl 77 2 2-isopropyl-phenyl 78 3 3-isopropyl-phenyl 79 1 4-isopropyl-phenyl 70 1 4-isopropyl-phenyl 70 1 4-isopropyl-phenyl 71 2 4-isopropyl-phenyl 72 3 3-isopropyl-phenyl 73 3 3-isopropyl-phenyl 74 2 3-isopropyl-phenyl 75 2 2-isopropyl-phenyl 76 3 3-isopropyl-phenyl 77 2 3-isopropyl-phenyl 78 3 3-isopropyl-phenyl 79 1 4-isopropyl-phenyl 80 2 4-isopropyl-phenyl 81 3 4-isopropyl-phenyl 82 4-isopropyl-phenyl 83 2-isopropyl-phenyl 84 1 4-OH-phenyl 85 2 4-isopropyl-phenyl 86 3 4-OH-phenyl 87 3 3-isopropyl-phenyl 88 2 3-OH-phenyl 89 3 3-OH-phenyl 80 3 3-OH-phenyl 80 3 3-OH-phenyl 81 3 4-OH-phenyl 82 4-isopropyl-phenyl 83 3-OH-phenyl 84 4-isopropyl-phenyl 85 4-isopropyl-phenyl 86 2 2-isopropyl-phenyl 87 3 3-isopropyl-phenyl 88 2 3-OH-phenyl 89 3 3-OH-phenyl 80 3 3-OH-phenyl 80 3 3-OH-phenyl 81 3 3-OH-phenyl 82 4-isopropyl-phenyl 83 3-OH-phenyl 84 3 3-isopropyl-phenyl 85 3 3-OH-phenyl 86 3 3-OH-phenyl 87 3 3-OH-phenyl 88 3 3-OH-phenyl 89 3 3-OH-phenyl 90 3 3-OH-phenyl 91 3 3-OH-phenyl 91 3 3-OH-phenyl 92 3 3-OH-phenyl 93 3 3-OH-phenyl 94 4-isopropyl-phenyl 95 4-iso							
(XII) 57 3 2-Cl-Phenyl 58 1 4-Bp-Phenyl 59 2 4-Bp-Phenyl 59 2 4-Bp-Phenyl 59 2 4-Bp-Phenyl 61 1 4-OCF_2-Phenyl 61 1 4-OCF_2-Phenyl 62 2 4-OCF_2-Phenyl 62 2 4-OCF_2-Phenyl 63 3 4-OCF_2-Phenyl 65 2 3-OCF_2-Phenyl 66 3 3-OCF_2-Phenyl 67 1 2-OCF_2-Phenyl 68 2 2-OCF_2-Phenyl 68 2 2-OCF_2-Phenyl 69 3 2-OCF_2-Phenyl 69 3 2-OCF_2-Phenyl 69 3 3-OCF_2-Phenyl 60 3 4-OCF_2-Phenyl		a pharm	aceutically acceptable salt form				
XIII September Septembe	thereof:			20			
(XII) 60 3 4-BP-Phenyl 61 1 4-OCF ₂ -Phenyl 62 2 4-OCF ₂ -Phenyl 62 2 4-OCF ₂ -Phenyl 63 3 4-BP-Phenyl 64 1 3-OCF ₂ -Phenyl 65 2 3-OCF ₂ -Phenyl 66 3 3-OCF ₂ -Phenyl 66 3 3-OCF ₂ -Phenyl 67 1 2-OCF ₂ -Phenyl 68 2 2-OCF ₂ -Phenyl 68 2 2-OCF ₂ -Phenyl 70 1 4-isopropyl-phenyl 80 2 4-OCF ₂ -Phenyl 80 2 4-OCF ₂ -Phenyl 81 3 3-isopropyl-phenyl 81 3 3-isopropyl-phenyl 82 2 2 Phenyl 83 3 3-isopropyl-phenyl 84 1 1 4-OUF-phenyl 85 2 4-OUF-phenyl 86 2 2-OCF ₂ -Phenyl 87 2 2-isopropyl-phenyl 88 3 2-isopropyl-phenyl 89 3 4-OCF ₂ -Phenyl 80 2 4-OCF ₂ -Phenyl 80 2 4-OCF ₂ -Phenyl 81 3 4-OCF ₂ -Phenyl 82 1 3-OCF ₂ -Phenyl 83 2 3-OCF ₂ -Phenyl 84 3 3-OCF ₂ -Phenyl 85 1 2-OCF ₂ -Phenyl 86 2 3-OCF ₂ -Phenyl 87 1 3-OUF-phenyl 88 2 3-OUF-phenyl 89 3 3-OUF-phenyl 80 2 4-OCF ₂ -Phenyl 80 2 4-OCF ₂ -Phenyl 81 3 4-OCF ₂ -Phenyl 82 1 3-OCF ₂ -Phenyl 83 2 3-OCF ₂ -Phenyl 84 3 3-OCF ₂ -Phenyl 85 1 2-OCF ₂ -Phenyl 86 2 2-OCF ₂ -Phenyl 87 1 3-OUF-phenyl 88 2 3-OUF-phenyl 89 3 3-OUF-phenyl 89 3 3-OUF-phenyl 80 2 4-OCF ₂ -Phenyl 80 2 4-OCF ₂ -Phenyl 81 3 3-OCF ₂ -Phenyl 81 3 3-OCF ₂ -Phenyl 82 2 3-OUF-phenyl 83 3 3-OUF-phenyl 84 3 3-OUF-phenyl 85 1 2-OCF ₂ -Phenyl 86 2 2-OCF ₂ -Phenyl 87 3 3-OUF-phenyl 88 1 3-OUF-phenyl 89 2 4-OCF ₂ -Phenyl 89 2 4-OCF ₂ -Phenyl 89 2 2-OCF ₂ -Phenyl 89 3 3-OUF-phenyl 89 3 3-OUF-phenyl 89 2 2-OCF ₂ -Phenyl 89 3 3-OUF-phenyl 89 2 2-OCF ₂ -Phenyl 89 3 3-OUF-phenyl 8				20			
State Care							
Comparison							
25 63 3 4-OCE, Phenyl 4-OCE, Phenyl 3 3-OCE, Phenyl 3 4-OCE, Phenyl 4-OCE,	^		(XII)				
25 63 3 4-OCF ₂ -Phenyl) II						
Company Comp	/ \			2.5			
Section Sect	/ \^	\		25			
## Wherein non-limiting examples of R and n are defined herein below in Table 4. ## TABLE 4 35 75 3 3-isopropyl-phenyl below in Table 4. TABLE 4 35 75 3 3-isopropyl-phenyl below in Table 4. TABLE 4 35 75 3 3-isopropyl-phenyl below in Table 4. TABLE 4 35 75 3 3-isopropyl-phenyl below in Table 4. TABLE 4 35 75 3 3-isopropyl-phenyl below in Table 4. Eatry	$\langle X \rangle$	Ò					
## Wherein non-limiting examples of R and n are defined herein below in Table 4. ## TABLE 4 TABLE 4 35 76 1 2-OCF ₃ -Phenyl	~ /	1	~ ^				
No. Section		1 /	\sim				
wherein non-limiting examples of R and n are defined herein below in Table 4. TABLE 4 TABLE		X1N					
wherein non-limiting examples of R and n are defined herein below in Table 4. TABLE 4 TABLE		$\setminus I_n \setminus$					
wherein non-limiting examples of R and n are defined herein below in Table 4. TABLE 4 TABLE			•	30			
TABLE 4 35 75 3 4							
Table 4.	wherein non-limit	ing exam	ples of R and n are defined herein				
TABLE 4 35 75 3 3-isopropyl-phenyl			1				
Entry n R ²	below in Table 4.						
Entry n R ² 77 2 2-isopropyl-phenyl							
Entry n R2 77 2 2-isopropyl-phenyl		T.	ABLE 4	35			
The first content of the fir							
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31 1 4-CN-Phenyl 109 1 3-CH ₃ -4-pyridyl 32 2 4-CN-Phenyl 110 2 3-CH ₃ -4-pyridyl							
32 2 4-CN-Phenyl 110 2 3-CH ₃ -4-pyridyl							
	33	3	4-CN-Phenyl		111	3	3-CH ₃ -4-pyridyl
34 1 3-CN-Phenyl 112 1 3,5-dimethylpyridin-4-yl				65			
35 2 3-CN-Phenyl 65 113 2 3,5-dimethylpyridin-4-yl				0.5			
36 3 3-CN-Phenyl 114 3 3,5-dimethylpyridin-4-yl	36	3	3-CN-Pnenyl		114	3	3,3-dimethylpyridin-4-yl

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TABLE 5-continued

	TABL	E 4-continued			TABLE	∃ 5-continued
Entry	n	\mathbb{R}^2		Entry	n	\mathbb{R}^2
115	1	2,6-dimethylpyridin-4-yl		48	3	2-F-Phenyl
116	2	2,6-dimethylpyridin-4-yl	5	49	1	4-Cl-Phenyl
117	3	2,6-dimethylpyridin-4-yl		50	2	4-Cl-Phenyl
			_	51	3	4-Cl-Phenyl
				52	1	3-Cl-Phenyl
Exemplary emb	odiment	s include compounds having	the	53	2	3-Cl-Phenyl
		naceutically acceptable salt fo	rm	54	3	3-Cl-Phenyl
eof:	u piuni	incomically acceptable built is	10	55	1	2-Cl-Phenyl
CO1.				56	2	2-Cl-Phenyl
				57	3	2-Cl-Phenyl
				58 59	1 2	4-Br-Phenyl
_		(X	XIII)	60	3	4-Br-Phenyl 4-Br-Phenyl
~ 0				61	1	4-OCF ₃ -Phenyl
			15	62	2	4-OCF ₃ -Phenyl
	\			63	3	4-OCF ₃ -Phenyl
	$\tilde{\gamma}$			64	1	3-OCF ₃ -Phenyl
\sim \setminus	/	~ ^		65	2	3-OCF ₃ -Phenyl
	₹	$N-R^2$		66	3	3-OCF ₃ -Phenyl
	M-1	Ĭ Ĭ Ž		67	1	2-OCF ₃ -Phenyl
	\mathbf{V}_n		20	68	2	2-OCF ₃ -Phenyl
				69	3	2-OCF ₃ -Phenyl
				70	1	4-isopropyl-phenyl
rein non-limit	ting exa	mples of R ² and n are defin	ned	71	2	4-isopropyl-phenyl
in below in Ta				72	3	4-isopropyl-phenyl
an ociow in i	aoic 5.		2.5	73	1	3-isopropyl-phenyl
			25	74	2	3-isopropyl-phenyl
	T	ABLE 5		75	3	3-isopropyl-phenyl
			_	76	1	2-isopropyl-phenyl
Entry	n	R^2		77	2	2-isopropyl-phenyl
		TNI I	_	78	3	2-isopropyl-phenyl
1	1	Phenyl	20	79	1	4-cyclopropyl-phenyl
2	2	Phenyl	30	80	2	4-cyclopropyl-phenyl
3 4	3 1	Phenyl		81	3	4-cyclopropyl-phenyl
5	2	4-OH-phenyl 4-OH-phenyl		82	1	3-cyclopropyl-phenyl
6	3	4-OH-phenyl		83	2	3-cyclopropyl-phenyl
7	1	3-OH-phenyl		84	3	3-cyclopropyl-phenyl
8	2	3-OH-phenyl	2.5	85	1	2-cyclopropyl-phenyl
9	3	3-OH-phenyl	35	86	2	2-cyclopropyl-phenyl
10	1	2-OH-phenyl		87	3	2-cyclopropyl-phenyl
11	2	2-OH-phenyl		88	1	
12	3	2-OH-phenyl		89	2	4-morpholino-phenyl
13	1	4-CH ₃ -Phenyl		90	3	4-morpholino-phenyl 4-morpholino-phenyl
14	2	4-CH ₃ -Phenyl	40	90 91	1	
15	3	4-CH ₃ -Phenyl	40			3-morpholino-phenyl 3-morpholino-phenyl
16	1	3-CH ₃ -Phenyl		92	2	1 1 1
17	2	3-CH ₃ -Phenyl		93 94	3	3-morpholino-phenyl
18	3	3-CH ₃ -Phenyl			1	2-morpholino-phenyl
19	1	2-CH ₃ -Phenyl		95 96	2 3	2-morpholino-phenyl
20	2	2-CH ₃ -Phenyl	45			2-morpholino-phenyl
21	3	2-CH ₃ -Phenyl	7.7	97	1	2-pyridyl
22 23	1 2	4-OCH -Phenyl		98 99	2 3	2-pyridyl
23 24	3	4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl		100		2-pyridyl 3-pyridyl
24 25	1	3-OCH ₃ -Phenyl			1	1.0
26	2	3-OCH ₃ -Phenyl		101	2	3-pyridyl
27	3	3-OCH ₃ -Phenyl	50	102	3	3-pyridyl
28	1	2-OCH ₃ -Phenyl	2.0	103	1	4-pyridyl
29	2	2-OCH ₃ -Phenyl		104	2	4-pyridyl
30	3	2-OCH ₃ -Phenyl		105	3	4-pyridyl
31	1	4-CN-Phenyl		106	1	2-CH3-4-pyridyl
32	2	4-CN-Phenyl		107	2	2-CH3-4-pyridyl
33	3	4-CN-Phenyl	55	108	3	2-CH3-4-pyridyl
34	1	3-CN-Phenyl		109	1	3-CH3-4-pyridyl
35	2	3-CN-Phenyl		110	2	3-CH3-4-pyridyl
36	3	3-CN-Phenyl		111	3	3-CH3-4-pyridyl
37	1	2-CN-Phenyl		112	1	3,5-dimethylpyridin-4-yl
38	2	2-CN-Phenyl		113	2	3,5-dimethylpyridin-4-yl
	3	2-CN-Phenyl	60	114	3	3,5-dimethylpyridin-4-yl
39	1	4-F-Phenyl	0.0	115	1	2,6-dimethylpyridin-4-yl
40	2	4-F-Phenyl		116	2	2,6-dimethylpyridin-4-yl
40 41		4-F-Phenyl		117	3	2,6-dimethylpyridin-4-yl
40 41 42	3					
40 41 42 43	1	3-F-Phenyl				
40 41 42 43 44	1 2	3-F-Phenyl 3-F-Phenyl				
40 41 42 43	1	3-F-Phenyl	65 E	xemplary en	abodiment	s include compounds having

exemplary embodiments include compounds having the formula (VI) or a pharmaceutically acceptable salt form thereof:

 $R^{1\alpha}$

Entry n

(VI)

		O II				Entry	n	R^{1a}	R^{1b}	R ³
R^{I}	a	Ц			_	64	3	CH ₃	CH ₃	4-CN-Phenyl
	_/				5	65	1	CH ₂ CH ₃	CH ₂ CH ₃	4-CN-Phenyl
\mathbb{R}^1	6	\				66	2	CH ₂ CH ₃	CH ₂ CH ₃	4-CN-Phenyl
		igsquare	_ ^	~ 3		67	3	CH ₂ CH ₃	CH ₂ CH ₃	4-CN-Phenyl
			./ 😾	$N-R^3$		68	1	CH ₃	CH ₃	3-CN-Phenyl
		N-	-N /			69	2	CH ₃	CH ₃	3-CN-Phenyl
		` 'n	~			70	3	CH ₃	CH ₃	3-CN-Phenyl
					10	71	1	CH_2CH_3	CH ₂ CH ₃	3-CN-Phenyl
wherei	n ne	on-limiting	examples of	of R ^{1a} , R ^{1b} , R ³ and n are		72	2	CH_2CH_3	CH ₂ CH ₃	3-CN-Phenyl
			in Table 6.	, , , , , , , , , , , , , , , , , , , ,		73	3	CH ₂ CH ₃	CH ₂ CH ₃	3-CN-Phenyl
acimec	1 110	iem below	m rable o.			74	1	CH ₃	CH ₃	2-CN-Phenyl
						75 76	2	CH ₃	CH ₃	2-CN-Phenyl
			TABLE	6		76	3	CH ₃	CH ₃	2-CN-Phenyl 2-CN-Phenyl
		- 1 -	- 12	- 2	15	77 78	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH₂CH₃ CH₂CH₃	2-CN-Phenyl
Entry	n	\mathbb{R}^{1a}	R^{1b}	\mathbb{R}^3		79	3	CH ₂ CH ₃	CH ₂ CH ₃	2-CN-Phenyl
1	1	CH ₃	CH ₃	Phenyl		80	1	CH ₃	CH ₃	4-F-Phenyl
2	2	CH ₃	CH ₃	Phenyl		81	2	CH ₃	CH ₃	4-F-Phenyl
3	3	CH ₃	CH ₃	Phenyl		82	3	CH ₃	CH ₃	4-F-Phenyl
4	1	CH ₂ CH ₃	CH ₂ CH ₃	Phenyl		83	1	CH ₂ CH ₃	CH ₂ CH ₃	4-F-Phenyl
5	2	CH ₂ CH ₃	CH ₂ CH ₃	Phenyl	20	84	2	CH ₂ CH ₃	CH ₂ CH ₃	4-F-Phenyl
6	3	CH ₂ CH ₃	CH ₂ CH ₃	Phenyl		85	3	CH ₂ CH ₃	CH ₂ CH ₃	4-F-Phenyl
7	1	CH_3	CH ₃	4-OH-phenyl		86	1	CH ₃	CH ₃	3-F-Phenyl
8	2	CH ₃	CH ₃	4-OH-phenyl		87	2	CH ₃	CH ₃	3-F-Phenyl
10	3	CH_3	CH_3	4-OH-phenyl		88	3	CH ₃	CH ₃	3-F-Phenyl
11	1	CH_2CH_3	CH_2CH_3	4-OH-phenyl	2.5	89	1	CH ₂ CH ₃	CH ₂ CH ₃	3-F-Phenyl
12	2	CH ₂ CH ₃	CH ₂ CH ₃	4-OH-phenyl	25	90	2	CH ₂ CH ₃	CH ₂ CH ₃	3-F-Phenyl
13	3	CH ₂ CH ₃	CH ₂ CH ₃	4-OH-phenyl		91 92	3 1	CH ₂ CH ₃	CH ₂ CH ₃	3-F-Phenyl 2-F-Phenyl
14	1	CH ₃	CH ₃	3-OH-phenyl		93	2	CH₃ CH₃	CH ₃ CH ₃	2-F-Phenyl
15 16	2	CH ₃	CH ₃	3-OH-phenyl 3-OH-phenyl		94	3	CH ₃	CH ₃	2-F-Phenyl
17	1	CH ₃ CH ₂ CH ₃	CH₃ CH₂CH₃	3-OH-phenyl		95	1	CH ₂ CH ₃	CH ₂ CH ₃	2-F-Phenyl
18	2	CH ₂ CH ₃	CH ₂ CH ₃	3-OH-phenyl	30	96	2	CH ₂ CH ₃	CH ₂ CH ₃	2-F-Phenyl
19	3	CH ₂ CH ₃	CH ₂ CH ₃	3-OH-phenyl	50	97	3	CH ₂ CH ₃	CH ₂ CH ₃	2-F-Phenyl
20	1	CH ₃	CH ₃	2-OH-phenyl		98	1	CH ₃	CH ₃	4-Cl-Phenyl
21	2	CH ₃	CH ₃	2-OH-phenyl		99	2	CH ₃	CH ₃	4-Cl-Phenyl
22	3	CH ₃	CH ₃	2-OH-phenyl		100	3	CH ₃	CH ₃	4-Cl-Phenyl
23	1	CH ₂ CH ₃	CH ₂ CH ₃	2-OH-phenyl		101	1	CH_2CH_3	CH ₂ CH ₃	4-Cl-Phenyl
24	2	CH ₂ CH ₃	CH ₂ CH ₃	2-OH-phenyl	35	102	2	CH_2CH_3	CH ₂ CH ₃	4-Cl-Phenyl
25	3	CH ₂ CH ₃	CH ₂ CH ₃	2-OH-phenyl		103	3	CH_2CH_3	CH ₂ CH ₃	4-Cl-Phenyl
26	1	CH ₃	CH ₃	4-CH ₃ -Phenyl		104	1	CH ₃	CH ₃	3-Cl-Phenyl
27	2	CH ₃	CH ₃	4-CH ₃ -Phenyl		105	2	CH ₃	CH ₃	3-Cl-Phenyl
28	3	CH ₃	CH ₃	4-CH ₃ -Phenyl		106 107	3	CH ₃	CH ₃	3-Cl-Phenyl 3-Cl-Phenyl
26	1	CH ₂ CH ₃	CH ₂ CH ₃	4-CH ₃ -Phenyl		107	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-Cl-Phenyl
30 31	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-CH ₃ -Phenyl 4-CH ₃ -Phenyl	40	109	3	CH ₂ CH ₃	CH ₂ CH ₃	3-Cl-Phenyl
32	1	CH ₂ CH ₃	CH ₃	3-CH ₃ -Phenyl		110	1	CH ₃	CH ₃	2-Cl-Phenyl
33	2	CH ₃	CH ₃	3-CH ₃ -Phenyl		111	2	CH ₃	CH ₃	2-Cl-Phenyl
34	3	CH ₃	CH ₃	3-CH ₃ -Phenyl		112	3	CH ₃	CH ₃	2-Cl-Phenyl
35	1	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -Phenyl		113	1	CH ₂ CH ₃	CH ₂ CH ₃	2-Cl-Phenyl
36	2	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -Phenyl		114	2	CH ₂ CH ₃	CH ₂ CH ₃	2-Cl-Phenyl
37	3	CH ₂ CH ₃	CH ₂ CH ₃	3-CH ₃ -Phenyl	45	115	3	CH₂CH₃	CH ₂ CH ₃	2-Cl-Phenyl
38	1	CH_3	CH_3	2-CH ₃ -Phenyl		116	1	CH ₃	CH ₃	4-Br-Phenyl
39	2	CH ₃	CH ₃	2-CH ₃ -Phenyl		117	2	CH ₃	CH ₃	4-Br-Phenyl
40	3	CH ₃	CH ₃	2-CH ₃ -Phenyl		118	3	CH ₃	CH ₃	4-Br-Phenyl
41	1	CH ₂ CH ₃	CH ₂ CH ₃	2-CH ₃ -Phenyl		119 120	1 2	CH₂CH₃ CH₂CH₃	CH₂CH₃ CH₂CH₃	4-Br-Phenyl 4-Br-Phenyl
42 43	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-CH ₃ -Phenyl 2-CH ₃ -Phenyl	50	120	3	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-Br-Phenyl
43 44	1		CH ₂ CH ₃	4-OCH ₃ -Phenyl	30	122	1	CH ₂ CH ₃	CH ₃	4-OCF ₃ -Phenyl
45	2	CH ₃ CH ₃	CH ₃	4-OCH ₃ -Phenyl		123	2	CH ₃	CH ₃	4-OCF ₃ -Phenyl
46	3	CH ₃	CH ₃	4-OCH ₃ -Phenyl		124	3	CH ₃	CH ₃	4-OCF ₃ -Phenyl
47	1	CH ₂ CH ₃	CH ₂ CH ₃	4-OCH ₃ -Phenyl		125	1	CH ₂ CH ₃	CH ₂ CH ₃	4-OCF ₃ -Phenyl
48	2	CH ₂ CH ₃	CH ₂ CH ₃	4-OCH ₃ -Phenyl		126	2	CH ₂ CH ₃	CH ₂ CH ₃	4-OCF ₃ -Phenyl
49	3	CH ₂ CH ₃	CH ₂ CH ₃	4-OCH ₃ -Phenyl	55	127	3	CH ₂ CH ₃	CH ₂ CH ₃	4-OCF ₃ -Phenyl
50	1	CH ₃	CH ₃	3-OCH ₃ -Phenyl	-	128	1	CH ₃	CH ₃	3-OCF ₃ -Phenyl
51	2	CH ₃	CH ₃	3-OCH ₃ -Phenyl		129	2	CH ₃	CH ₃	3-OCF ₃ -Phenyl
52	3	CH ₃	CH_3	3-OCH ₃ -Phenyl		130	3	CH ₃	CH ₃	3-OCF ₃ -Phenyl
53	1	CH ₂ CH ₃	CH ₂ CH ₃	3-OCH ₃ -Phenyl		131	1	CH ₂ CH ₃	CH ₂ CH ₃	3-OCF ₃ -Phenyl
54	2	CH ₂ CH ₃	CH ₂ CH ₃	3-OCH ₃ -Phenyl		132	2	CH ₂ CH ₃	CH ₂ CH ₃	3-OCF ₃ -Phenyl
55	3	CH ₂ CH ₃	CH ₂ CH ₃	3-OCH ₃ -Phenyl	60	133 134	3 1	CH ₂ CH ₃	CH ₂ CH ₃ CH ₃	3-OCF ₃ -Phenyl 2-OCF ₃ -Phenyl
56	1	CH ₃	CH ₃	2-OCH ₃ -Phenyl		134	2	CH ₃ CH ₃	CH ₃	2-OCF ₃ -Phenyl
57 58	2	CH ₃ CH ₃	CH ₃ CH ₃	2-OCH ₃ -Phenyl 2-OCH ₃ -Phenyl		136	3	CH ₃	CH ₃	2-OCF ₃ -Phenyl
58 59	1	CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2-OCH ₃ -Phenyl		137	1	CH ₂ CH ₃	CH ₂ CH ₃	2-OCF ₃ -Phenyl
60	2	CH ₂ CH ₃	CH ₂ CH ₃	2-OCH ₃ -Phenyl		138	2	CH ₂ CH ₃	CH ₂ CH ₃	2-OCF ₃ -Phenyl
61	3	CH ₂ CH ₃	CH ₂ CH ₃	2-OCH ₃ -Phenyl		139	3	CH ₂ CH ₃	CH ₂ CH ₃	2-OCF ₃ -Phenyl
62	1	CH ₃	CH ₃	4-CN-Phenyl	65	140	1	CH ₃	CH ₃	4-isopropyl-phenyl
63	2	CH ₃	CH ₃	4-CN-Phenyl		141	2	CH ₃	CH ₃	4-isopropyl-phenyl

54 TABLE 6-continued

Postorio		R^{1a}	R^{1b}	R ³	•	D-4		R^{1a}	R^{1b}	R ³
Entry		K***	K**	K*		Entry		K***	K**	K*
142	3	CH_3	CH_3	4-isopropyl-phenyl		220	3	CH ₃	CH ₃	3-CH ₃ -4-pyridyl
143	1	CH2CH3	CH2CH3	4-isopropyl-phenyl	5	221	1	CH_2CH_3	CH ₂ CH ₃	3-CH ₃ -4-pyridyl
144	2	CH2CH3	CH2CH3	4-isopropyl-phenyl		222	2	CH_2CH_3	CH_2CH_3	3-CH ₃ -4-pyridyl
145	3	CH2CH3	CH2CH3	4-isopropyl-phenyl		223	3	CH_2CH_3	CH_2CH_3	3-CH ₃ -4-pyridyl
146	1	CH_3	CH ₃	3-isopropyl-phenyl		224	1	CH_3	CH_3	3,5-dimethylpyridin-4-yl
147	2	CH_3	CH_3	3-isopropyl-phenyl		225	2	CH_3	CH_3	3,5-dimethylpyridin-4-yl
148	3	CH ₃	CH ₃	3-isopropyl-phenyl		226	3	CH ₃	CH ₃	3,5-dimethylpyridin-4-yl
149	1	CH ₂ CH ₃	CH ₂ CH ₃	3-isopropyl-phenyl	10	227	1 2	CH ₂ CH ₃	CH ₂ CH ₃	3,5-dimethylpyridin-4-yl
150	2	CH ₂ CH ₃	CH ₂ CH ₃	3-isopropyl-phenyl		228	2	CH ₂ CH ₃	CH ₂ CH ₃	3,5-dimethylpyridin-4-yl
151 152	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	3-isopropyl-phenyl 2-isopropyl-phenyl		229 230	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	3,5-dimethylpyridin-4-yl 2,6-dimethylpyridin-4-yl
153	2	CH ₃	CH ₃	2-isopropyl-phenyl		230	2	CH ₃	CH ₃	2,6-dimethylpyridin-4-yl
154	3	CH ₃	CH ₃	2-isopropyl-phenyl		232	2	CH ₃	CH ₃	2,6-dimethylpyridin-4-yl
155	1	CH ₂ CH ₃	CH ₂ CH ₃	2-isopropyl-phenyl		233	1	CH ₂ CH ₃	CH ₂ CH ₃	2,6-dimethylpyridin-4-yl
156	2	CH ₂ CH ₃	CH ₂ CH ₃	2-isopropyl-phenyl	15	234	1 2	CH ₂ CH ₃	CH ₂ CH ₃	2,6-dimethylpyridin-4-yl
157	3	CH ₂ CH ₃	CH ₂ CH ₃	2-isopropyl-phenyl		235	3	CH ₂ CH ₃	CH ₂ CH ₃	2,6-dimethylpyridin-4-yl
158	1	CH ₃	CH_3	4-cyclopropyl-phenyl						_
159	2	CH_3	CH ₃	4-cyclopropyl-phenyl		-				
160	3	CH ₃	CH ₃	4-cyclopropyl-phenyl						de compounds having the
161	1	CH ₂ CH ₃	CH ₂ CH ₃	4-cyclopropyl-phenyl	20	formul	la (2	XIV) or a	pharmaceuti	cally acceptable salt form
162	2	CH ₂ CH ₃	CH ₂ CH ₃	4-cyclopropyl-phenyl	20	thereof	f:			
163	3	CH ₂ CH ₃	CH ₂ CH ₃	4-cyclopropyl-phenyl						
164 165	1	CH ₃	CH ₃	3-cyclopropyl-phenyl 3-cyclopropyl-phenyl						
166	2	CH ₃ CH ₃	CH ₃ CH ₃	3-cyclopropyl-phenyl						(XIV)
167	1	CH ₂ CH ₃	CH ₂ CH ₃	3-cyclopropyl-phenyl				0		(AIV)
168	2	CH ₂ CH ₃	CH ₂ CH ₃	3-cyclopropyl-phenyl	25			Ĭ		
169	3	CH ₂ CH ₃	CH ₂ CH ₃	3-cyclopropyl-phenyl		/	\	从		
170	1	CH ₃	CH ₃	2-cyclopropyl-phenyl		/_	\rightarrow	/ \ _o _		
171	2	CH ₃	CH ₃	2-cyclopropyl-phenyl			٦ ١	ιĨ		
172	3	CH ₃	CH ₃	2-cyclopropyl-phenyl				igwedge	\wedge	$\sim R^3$
173	1	CH ₂ CH ₃	CH ₂ CH ₃	2-cyclopropyl-phenyl				X1_	. _N X .	N
174	2	CH ₂ CH ₃	CH ₂ CH ₃	2-cyclopropyl-phenyl	30			(\mathcal{T}_n)	" \	
175	3	CH ₂ CH ₃	CH ₂ CH ₃	2-cyclopropyl-phenyl					•	
176	1	CH_3	CH_3	4-morpholino-phenyl						
177	2	CH ₃	CH ₃	4-morpholino-phenyl		wherei	n n	on-limiting	examples	of R ³ and n are defined
178	3	CH ₃	CH ₃	4-morpholino-phenyl				ow in Tabl		
179	1	CH ₂ CH ₃	CH_2CH_3	4-morpholino-phenyl						
190			CII CII	4 manufacting whomed						
180	2	CH ₂ CH ₃	CH ₂ CH ₃	4-morpholino-phenyl	35				TADLE	7
181	3	CH ₂ CH ₃	CH ₂ CH ₃	4-morpholino-phenyl	35				TABLE	7
181 182	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl	35		Ent			
181 182 183	3 1 2	CH ₂ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl	35		Ent	ry :	TABLE	7 R ³
181 182	3 1 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl	35				n	R ³
181 182 183 184	3 1 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl			1	1	n 1	R ³ Phenyl
181 182 183 184 185 186 187	3 1 2 3 1 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl	35 40			l 2	n	R ³
181 182 183 184 185 186 187 188	3 1 2 3 1 2 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl			1 2	2 :	n 1 2 3 1	R ³ Phenyl Phenyl
181 182 183 184 185 186 187 188	3 1 2 3 1 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl			1 2 3 4	2 3 4 5	1 2 3 1 2	R ³ Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl
181 182 183 184 185 186 187 188 189	3 1 2 3 1 2 3 1 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl			1 2 3 2 5	1	1 2 2 3 1 2 2 3	R ³ Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl 4-OH-phenyl
181 182 183 184 185 186 187 188 189 190	3 1 2 3 1 2 3 1 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl			1 2 3 2 5 6	1 2 2 3 4 4 5 5 5 7	1 2 3 1 2 2 3 1	R ³ Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl 3-OH-phenyl
181 182 183 184 185 186 187 188 189 190 191	3 1 2 3 1 2 3 1 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl	40		1 2 3 2 5 6	1 2 2 3 4 5 5 5 7 7 8 8 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 2 3 1 2 2 3 1 2 2	R ³ Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl 3-OH-phenyl 3-OH-phenyl
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181 182 183 184 185 186 187 188 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217	3 1 2 3 3 1 2 3 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ C	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-pyridyl 2-pyridyl 2-pyridyl 2-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 2-CH ₃ -4-pyridyl	40 45 50 55		11 22 33 4 55 66 77 88 89 10 11 11 12 12 13 14 14 15 15 16 17 17 18 18 19 19 19 19 19 19 19 19 19 19 19 19 19	2 2 3 4 4 5 5 5 5 7 7 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	1 2 2 3 1 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 1 2 3 3 1 1 2 3 3 3 1 1 2 3 3 3 1 1 2 3 3 3 1 1 2 3 3 3 3	R³ Phenyl Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl 3-OH-phenyl 3-OH-phenyl 3-OH-phenyl 3-OH-phenyl 2-OH-phenyl 2-OH-phenyl 2-OH-phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 3-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218	3 1 2 3 1 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ C	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₅ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-pyridyl 2-pyridyl 2-pyridyl 2-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 4-pyridyl 2-CH ₃ -4-pyridyl 2-CH ₃ -4-pyridyl 2-CH ₃ -4-pyridyl 3-CH ₃ -4-pyridyl	40 45 50		11 22 33 4 55 66 77 88 99 10 11 11 12 13 14 14 15 16 16 17 17 18 19 20 21 22 22 23 22 24 26 26 27 28 29 20 20 20 20 20 20 20 20 20 20 20 20 20	2 2 3 4 5 5 5 7 7 8 9 9 9 9 1 1 2 2 3 8 9 9 9 9 1 1 2 2 3 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	1	Phenyl Phenyl Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl 3-OH-phenyl 3-OH-phenyl 3-OH-phenyl 3-OH-phenyl 2-OH-phenyl 2-OH-phenyl 2-OH-phenyl 2-OH-phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 3-CH ₃ -Phenyl 3-CH ₃ -Phenyl 3-CH ₃ -Phenyl 3-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl 4-ON-Phenyl 4-ON-Phenyl 4-CN-Phenyl 4-CN-Phenyl 3-CN-Phenyl
181 182 183 184 185 186 187 188 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217	3 1 2 3 3 1 2 3 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ C	4-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 3-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-morpholino-phenyl 2-pyridyl 2-pyridyl 2-pyridyl 2-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 3-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 4-pyridyl 2-CH ₃ -4-pyridyl	40 45 50 55		11 22 33 4 55 66 77 88 89 10 11 11 12 12 13 14 14 15 15 16 17 17 18 18 19 19 19 19 19 19 19 19 19 19 19 19 19	2 2 3 4 5 5 5 7 7 8 9 9 9 9 1 1 2 2 3 8 9 9 9 9 1 1 2 2 3 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	1 2 2 3 1 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 1 2 3 3 1 1 2 3 3 3 1 1 2 3 3 3 1 1 2 3 3 3 1 1 2 3 3 3 3	R³ Phenyl Phenyl Phenyl Phenyl 4-OH-phenyl 4-OH-phenyl 3-OH-phenyl 3-OH-phenyl 3-OH-phenyl 3-OH-phenyl 2-OH-phenyl 2-OH-phenyl 2-OH-phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 4-CH ₃ -Phenyl 3-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 2-CH ₃ -Phenyl 4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl

n

Entry

 \mathbb{R}^3

			56
		TABLE	7-continued
	Entry	n	R ³
5	114 115 116 117 61 62 63	3 1 2 3 1 2 3	3,5-dimethylpyridin-4-yl 2,6-dimethylpyridin-4-yl 2,6-dimethylpyridin-4-yl 2,6-dimethylpyridin-4-yl
10			
			s include compounds having the acceutically acceptable salt form
15			
20	Ů		$N - R^3$
	wherein non-lin	niting exa	nples of R ³ and n are defined
25	herein below in	Table 8.	
25		Table 8.	ABLE 8
30		Table 8.	ABLE 8

Entry	n	R ³		Entry	n	R ³
36	3	3-CN-Phenyl		114	3	3,5-dimethylpyridin-4-yl
37	1	2-CN-Phenyl	5	115	1	2,6-dimethylpyridin-4-yl
38	2	2-CN-Phenyl		116	2	2,6-dimethylpyridin-4-yl
39	3	2-CN-Phenyl		117	3	2,6-dimethylpyridin-4-yl
40	1	4-F-Phenyl		61	1	
41	2	4-F-Phenyl		62	2	
42	3	4-F-Phenyl	4.0	63	3	
43 44	1 2	3-F-Phenyl 3-F-Phenyl	10			
45	3	3-F-Phenyl		Exemplary er	nbodiment	s include compounds having the
46	1	2-F-Phenyl				aceutically acceptable salt form
47	2	2-F-Phenyl		thereof:	л а рпани	accurreally acceptable sait form
48	3	2-F-Phenyl		mereor:		
49	1	4-Cl-Phenyl	15			
50	2	4-Cl-Phenyl	15			
51	3	4-Cl-Phenyl				(XV)
52	1	3-Cl-Phenyl		0		
53	2	3-Cl-Phenyl		\sim \parallel		
54	3	3-Cl-Phenyl		$\langle \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	_	
55	1	2-Cl-Phenyl	20	\/	ŢĢ	
56 57	2 3	2-Cl-Phenyl 2-Cl-Phenyl		_ /	/ ,	. ^ .
58	1	4-Br-Phenyl			₹. /	$N - R^3$
59	2	4-Br-Phenyl			M-N	/ /
60	3	4-Br-Phenyl			$\langle \gamma_n \rangle$	~
61	1	4-OCF ₃ -Phenyl				
62	2	4-OCF ₃ -Phenyl	25	whorain non lir	niting ava	mples of R ³ and n are defined
63	3	4-OCF ₃ -Phenyl				imples of R and II are defined
64	1	3-OCF ₃ -Phenyl		herein below in	Table 8.	
65	2	3-OCF ₃ -Phenyl				
66	3	3-OCF ₃ -Phenyl			T	ABLE 8
67	1	2-OCF ₃ -Phenyl				
68	2	2-OCF ₃ -Phenyl	30	Entry	n	\mathbb{R}^3
69 70	3 1	2-OCF ₃ -Phenyl 4-isopropyl-phenyl		-	1	DI I
71	2	4-isopropyl-phenyl		1 2	1 2	Phenyl Phenyl
72	3	4-isopropyl-phenyl		3	3	Phenyl
73	1	3-isopropyl-phenyl		4	1	4-OH-phenyl
74	2	3-isopropyl-phenyl	35	5	2	4-OH-phenyl
75	3	3-isopropyl-phenyl	33	6	3	4-OH-phenyl
76	1	2-isopropyl-phenyl		7	1	3-OH-phenyl
77	2	2-isopropyl-phenyl		8	2	3-OH-phenyl
78	3	2-isopropyl-phenyl		9	3	3-OH-phenyl
79	1	4-cyclopropyl-phenyl		10	1	2-OH-phenyl
80	2 3	4-cyclopropyl-phenyl	40	11	2	2-OH-phenyl
81 82	1	4-cyclopropyl-phenyl 3-cyclopropyl-phenyl		12	3	2-OH-phenyl
83	2	3-cyclopropyl-phenyl		13 14	1 2	4-CH ₃ -Phenyl 4-CH ₃ -Phenyl
84	3	3-cyclopropyl-phenyl		15	3	4-CH ₃ -Phenyl
85	1	2-cyclopropyl-phenyl		16	1	3-CH ₃ -Phenyl
86	2	2-cyclopropyl-phenyl		17	2	3-CH ₃ -Phenyl
87	3	2-cyclopropyl-phenyl	45	18	3	3-CH ₃ -Phenyl
88	1	4-morpholino-phenyl		19	1	2-CH ₃ -Phenyl
89	2	4-morpholino-phenyl		20	2	2-CH ₃ -Phenyl
90	3	4-morpholino-phenyl		21	3	2-CH ₃ -Phenyl
91 92	1 2	3-morpholino-phenyl		22	1	4-OCH ₃ -Phenyl
93	3	3-morpholino-phenyl 3-morpholino-phenyl	50	23	2 3	4-OCH ₃ -Phenyl
94	1	2-morpholino-phenyl	50	24 25	1	4-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl
95	2	2-morpholino-phenyl		26	2	3-OCH ₃ -Phenyl
96	3	2-morpholino-phenyl		27	3	3-OCH ₃ -Phenyl
97	1	2-pyridyl		28	1	2-OCH ₃ -Phenyl
98	2	2-pyridyl		29	2	2-OCH ₃ -Phenyl
99	3	2-pyridyl	55	30	3	2-OCH ₃ -Phenyl
100	1	3-pyridyl		31	1	4-CN-Phenyl
101	2	3-pyridyl		32	2	4-CN-Phenyl
102	3	3-pyridyl		33	3	4-CN-Phenyl
103 104	1 2	4-pyridyl 4-pyridyl		34	1	3-CN-Phenyl
104	3	4-pyridyl 4-pyridyl		35 36	2 3	3-CN-Phenyl 3-CN-Phenyl
106	1	2-CH ₃ -4-pyridyl	60	37	1	2-CN-Phenyl
107	2	2-CH ₃ -4-pyridyl		38	2	2-CN-Phenyl
108	3	2-CH ₃ -4-pyridyl		39	3	2-CN-Phenyl
109	1	3-CH ₃ -4-pyridyl		40	1	4-F-Phenyl
110	2	3-CH ₃ -4-pyridyl		41	2	4-F-Phenyl
111	3	3-CH ₃ -4-pyridyl		42	3	4-F-Phenyl
112	1	3,5-dimethylpyridin-4-yl	65	43	1	3-F-Phenyl
113	2	3,5-dimethylpyridin-4-yl		44	2	3-F-Phenyl

TABLE 8-continued

thereof:

Entry	n	\mathbb{R}^3		(O II	(Λ	VI)
45	3	3-F-Phenyl			L		
5 7	1	2-F-Phenyl	5	$\langle X$	` o		
	2 3	2-F-Phenyl 2-F-Phenyl		\sim \backslash	/	. ^	
	3 1	2-r-Pnenyl 4-Cl-Phenyl		_	─(,, /	$N-R^3$	
 	2	4-Cl-Phenyl			()—N		
51	3	4-Cl-Phenyl			\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	~ •	
52	1	3-Cl-Phenyl	10				
53	2	3-Cl-Phenyl		nerein non-li	miting exam	ples of R ³ and n are defin	ied
54	3	3-Cl-Phenyl		rein below in		ipies of it and if are defin	ca
55	1	2-Cl-Phenyl	110.	rem below ii	rable).		
56 57	2 3	2-Cl-Phenyl 2-Cl-Phenyl			TA	DI E A	
58	1	4-Br-Phenyl			1A	BLE 9	
59	2	4-Br-Phenyl	15	Entry	n	\mathbb{R}^3	
50	3	4-Br-Phenyl		Entry	11	K	_
51	1	4-OCF ₃ -Phenyl		1	1	Phenyl	
62	2	4-OCF ₃ -Phenyl		2	2 3	Phenyl	
53	3	4-OCF ₃ -Phenyl		3	3	Phenyl	
64 65	1	3-OCF ₃ -Phenyl	20	4	1	4-OH-phenyl	
66	2 3	3-OCF ₃ -Phenyl 3-OCF ₃ -Phenyl		5 6	2 3	4-OH-phenyl	
7	1	2-OCF ₃ -Phenyl		6 7	3 1	4-OH-phenyl 3-OH-phenyl	
68	2	2-OCF ₃ -Phenyl		8	2	3-OH-phenyl	
69	3	2-OCF ₃ -Phenyl		9	3	3-OH-phenyl	
70	1	4-isopropyl-phenyl		10	1	2-OH-phenyl	
71	2	4-isopropyl-phenyl	25	11	2	2-OH-phenyl	
72 72	3	4-isopropyl-phenyl		12	3	2-OH-phenyl	
73 74	1 2	3-isopropyl-phenyl 3-isopropyl-phenyl		13	1	4-CH ₃ -Phenyl	
75	3	3-isopropyl-phenyl		14 15	2 3	4-CH ₃ -Phenyl 4-CH ₃ -Phenyl	
76	1	2-isopropyl-phenyl		16	1	3-CH ₃ -Phenyl	
77	2	2-isopropyl-phenyl	30	17	2	3-CH ₃ -Phenyl	
78	3	2-isopropyl-phenyl		18	3	3-CH ₃ -Phenyl	
79	1	4-cyclopropyl-phenyl		19	1	2-CH ₃ -Phenyl	
80	2	4-cyclopropyl-phenyl		20	2	2-CH ₃ -Phenyl	
81 82	3 1	4-cyclopropyl-phenyl		21	3	2-CH ₃ -Phenyl	
83	2	3-cyclopropyl-phenyl 3-cyclopropyl-phenyl		22 23	1 2	4-OCH ₃ -Phenyl 4-OCH ₃ -Phenyl	
84	3	3-cyclopropyl-phenyl	35	23 24	3	4-OCH ₃ -Phenyl	
85	1	2-cyclopropyl-phenyl		25	1	3-OCH ₃ -Phenyl	
36	2	2-cyclopropyl-phenyl		26	2	3-OCH ₃ -Phenyl	
7	3	2-cyclopropyl-phenyl		27	3	3-OCH ₃ -Phenyl	
8	1	4-morpholino-phenyl		28	1	2-OCH ₃ -Phenyl	
39	2 3	4-morpholino-phenyl	40	29	2	2-OCH ₃ -Phenyl	
90 91	1	4-morpholino-phenyl 3-morpholino-phenyl		30 31	3 1	2-OCH ₃ -Phenyl 4-CN-Phenyl	
92	2	3-morpholino-phenyl		32	2	4-CN-Phenyl	
93	3	3-morpholino-phenyl		33	3	4-CN-Phenyl	
94	1	2-morpholino-phenyl		34	1	3-CN-Phenyl	
95	2	2-morpholino-phenyl	4.5	35	2	3-CN-Phenyl	
96	3	2-morpholino-phenyl	45	36	3	3-CN-Phenyl	
97	1	2-pyridyl		37	1	2-CN-Phenyl	
98 99	2 3	2-pyridyl 2-pyridyl		38 30	2 3	2-CN-Phenyl	
100	1	2-pyridyl 3-pyridyl		39 40	3 1	2-CN-Phenyl 4-F-Phenyl	
101	2	3-pyridyl		41	2	4-F-Phenyl	
102	2 3	3-pyridyl	50	42	3	4-F-Phenyl	
103	1	4-pyridyl	•	43	1	3-F-Phenyl	
.04	2	4-pyridyl		44	2	3-F-Phenyl	
.05	3	4-pyridyl		45	3	3-F-Phenyl	
06 07	1	2-CH ₃ -4-pyridyl		46 47	1	2-F-Phenyl	
107 108	2 3	2-CH ₃ -4-pyridyl 2-CH ₃ -4-pyridyl		47 48	2 3	2-F-Phenyl 2-F-Phenyl	
108	1	3-CH ₃ -4-pyridyl	55	48 49	3 1	2-F-Phenyl 4-Cl-Phenyl	
110	2	3-CH ₃ -4-pyridyl		50	2	4-Cl-Phenyl	
111	3	3-CH ₃ -4-pyridyl		51	3	4-Cl-Phenyl	
112	1	3,5-dimethylpyridin-4-yl		52	1	3-Cl-Phenyl	
113	2	3,5-dimethylpyridin-4-yl		53	2	3-Cl-Phenyl	
114	3	3,5-dimethylpyridin-4-yl	60	54	3	3-Cl-Phenyl	
115	1	2,6-dimethylpyridin-4-yl	· -	55 56	1	2-Cl-Phenyl	
116	2	2,6-dimethylpyridin-4-yl		56 57	2 3	2-Cl-Phenyl 2-Cl-Phenyl	
117	3	2,6-dimethylpyridin-4-yl		58	1	4-Br-Phenyl	
				59	2	4-Br-Phenyl	
				60	3		
1	1	- 111 1 - 1 1 - 1 - 1	41	00	3	4-Br-Phenyl	
		s include compounds having naceutically acceptable salt for		61	1 2	4-OCF ₃ -Phenyl	

TADIE	9-continued
IABLE	9-continued

	TABLE	E 9-continued		TABLE 10			
Entry	n	\mathbb{R}^3		Entry	n	R ³	
63	3	4-OCF ₃ -Phenyl	_	1	1	Phenyl	
64 65	1 2	3-OCF ₃ -Phenyl 3-OCF ₃ -Phenyl	5	2 3	2 3	Phenyl Phenyl	
66	3	3-OCF ₃ -Phenyl		4	1	4-OH-phenyl	
67	1	2-OCF ₃ -Phenyl		5	2	4-OH-phenyl	
68	2	2-OCF ₃ -Phenyl		6	3	4-OH-phenyl	
69	3	2-OCF ₃ -Phenyl		7	1	3-OH-phenyl	
70 71	1 2	4-isopropyl-phenyl 4-isopropyl-phenyl	10	8 9	2 3	3-OH-phenyl 3-OH-phenyl	
72	3	4-isopropyl-phenyl		10	1	2-OH-phenyl	
73	1	3-isopropyl-phenyl		11	2	2-OH-phenyl	
74	2	3-isopropyl-phenyl		12	3	2-OH-phenyl	
75 76	3	3-isopropyl-phenyl		13	1	4-CH ₃ -Phenyl	
76 77	1 2	2-isopropyl-phenyl 2-isopropyl-phenyl	15	14 15	2 3	4-CH ₃ -Phenyl 4-CH ₃ -Phenyl	
78	3	2-isopropyl-phenyl		16	1	3-CH ₃ -Phenyl	
79	1	4-cyclopropyl-phenyl		17	2	3-CH ₃ -Phenyl	
80	2	4-cyclopropyl-phenyl		18	3	3-CH ₃ -Phenyl	
81 82	3 1	4-cyclopropyl-phenyl 3-cyclopropyl-phenyl		19 20	1 2	2-CH ₃ -Phenyl 2-CH ₃ -Phenyl	
83	2	3-cyclopropyl-phenyl	20	21	3	2-CH ₃ -Thenyl	
84	3	3-cyclopropyl-phenyl		22	1	4-OCH ₃ -Phenyl	
85	1	2-cyclopropyl-phenyl		23	2	4-OCH ₃ -Phenyl	
86	2	2-cyclopropyl-phenyl		24	3	4-OCH ₃ -Phenyl	
87 88	3 1	2-cyclopropyl-phenyl 4-morpholino-phenyl		25 26	1 2	3-OCH ₃ -Phenyl 3-OCH ₃ -Phenyl	
89	2	4-morpholino-phenyl	25	27	3	3-OCH ₃ -Phenyl	
90	3	4-morpholino-phenyl		28	1	2-OCH ₃ -Phenyl	
91	1	3-morpholino-phenyl		29	2	2-OCH ₃ -Phenyl	
92	2	3-morpholino-phenyl		30	3	2-OCH ₃ -Phenyl	
93 94	3	3-morpholino-phenyl		31 32	1 2	4-CN-Phenyl 4-CN-Phenyl	
94 95	1 2	2-morpholino-phenyl 2-morpholino-phenyl	30	33	3	4-CN-Phenyl	
96	3	2-morpholino-phenyl		34	1	3-CN-Phenyl	
97	1	2-pyridyl		35	2	3-CN-Phenyl	
98	2	2-pyridyl		36 37	3 1	3-CN-Phenyl 2-CN-Phenyl	
99	3	2-pyridyl		38	2	2-CN-Phenyl	
100	1	3-pyridyl	35	39	3	2-CN-Phenyl	
101 102	2 3	3-pyridyl 3-pyridyl	55	40	1	4-F-Phenyl	
103	1	4-pyridyl		41 42	2 3	4-F-Phenyl 4-F-Phenyl	
104	2	4-pyridyl		43	1	3-F-Phenyl	
105	3	4-pyridyl		44	2	3-F-Phenyl	
106	1	2-CH ₃ -4-pyridyl	40	45	3	3-F-Phenyl	
107	2	2-CH ₃ -4-pyridyl	40	46	1	2-F-Phenyl	
108 109	3 1	2-CH ₃ -4-pyridyl 3-CH ₃ -4-pyridyl		47 48	2 3	2-F-Phenyl 2-F-Phenyl	
110	2	3-CH ₃ -4-pyridyl		49	1	4-Cl-Phenyl	
111	3	3-CH ₃ -4-pyridyl		50	2	4-Cl-Phenyl	
112	1	3,5-dimethylpyridin-4-yl	45	51	3	4-Cl-Phenyl	
113	2	3,5-dimethylpyridin-4-yl	43	52 53	1 2	3-Cl-Phenyl 3-Cl-Phenyl	
114	3	3,5-dimethylpyridin-4-yl		54	3	3-Cl-Phenyl	
115 116	1 2	2,6-dimethylpyridin-4-yl 2,6-dimethylpyridin-4-yl		55	1	2-Cl-Phenyl	
117	3	2,6-dimethylpyridin-4-yl		56 57	2	2-Cl-Phenyl	
			50	57 58	3 1	2-Cl-Phenyl 4-Br-Phenyl	
			30	59	2	4-Br-Phenyl	
Exemplary er	mbodiment	s include compounds having the		60	3	4-Br-Phenyl	
formula (XVII)	or a pharm	naceutically acceptable salt form		61	1	4-OCF ₃ -Phenyl	
thereof:	•	• •		62 63	2 3	4-OCF ₃ -Phenyl 4-OCF ₃ -Phenyl	
				64	1	3-OCF ₃ -Phenyl	
			55	65	2	3-OCF ₃ -Phenyl	
		(XVII))	66	3	3-OCF ₃ -Phenyl	
~	O			67 68	1 2	2-OCF ₃ -Phenyl 2-OCF ₃ -Phenyl	
	1			69	3	2-OCF ₃ -rhenyl 2-OCF ₃ -Phenyl	
	$\sim_{\scriptscriptstyle 0}$		60	70	1	4-isopropyl-phenyl	
	Ĭ	•	60	71 72	2	4-isopropyl-phenyl	
_	<u> </u>	$N - R^3$		72 73	3	4-isopropyl-phenyl	
	XI-1	$\langle \mathcal{N} / \rangle$		73 74	1 2	3-isopropyl-phenyl 3-isopropyl-phenyl	
	V_n	~ ~		75	3	3-isopropyl-phenyl	
				76	1	2-isopropyl-phenyl	
wherein non li-	miting over	mples of R ³ and n are defined	65	77	2	2-isopropyl-phenyl	
herein below in		imples of ix and if are defined		78	3	2-isopropyl-phenyl	
nerem below III	Table 10.						

TABLE 10-continued							TAR	UZ LE 11 -c or		
Entry	n	E TO-COILIN	R ³	_	Entry	n	R1 ^a	R1 ^b	R ²	
79	1	4-cvc	clopropyl-phenyl	_	13	1	CH ₃	CH ₃	4-CF ₃ -Phenyl	
80	2	4-cyc	clopropyl-phenyl	5	14	2	CH_3	CH_3	4-CF ₃ -Phenyl	
81	3		clopropyl-phenyl		15	3	CH ₃	CH ₃	4-CF ₃ -Phenyl	
82 83	1 2		clopropyl-phenyl clopropyl-phenyl		16 17	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl	
84	3		clopropyl-phenyl		18	3	CH ₂ CH ₃	CH ₂ CH ₃	4-CF ₃ -Phenyl	
85	1	2-cyc	clopropyl-phenyl		19	1	CH_3	CH_3	2-NH ₂ -Phenyl	
86	2		clopropyl-phenyl	10	20	2	CH_3	CH ₃	2-NH ₂ -Phenyl 2-NH ₂ -Phenyl	
87 88	3 1		clopropyl-phenyl orpholino-phenyl		21 22	1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2-NH ₂ -Phenyl	
89	2		rpholino-phenyl		23	2	CH ₂ CH ₃	CH ₂ CH ₃	2-NH ₂ -Phenyl	
90	3		rpholino-phenyl		24	3	CH_2CH_3	CH_2CH_3	2-NH ₂ -Phenyl	
91 92	1 2		orpholino-phenyl orpholino-phenyl		25 26	1 2	CH ₃ CH ₃	CH ₃ CH ₃	3-NH ₂ -Phenyl 3-NH ₂ -Phenyl	
93	3		orpholino-phenyl	15	27	3	CH ₃	CH ₃	3-NH ₂ -Phenyl	
94	1	2-mc	rpholino-phenyl		28	1	CH ₂ CH ₃	CH_2CH_3	3-NH ₂ -Phenyl	
95	2	2-mc	rpholino-phenyl		29	2	CH ₂ CH ₃	CH ₂ CH ₃	3-NH ₂ -Phenyl	
96 97	3 1	2-mc	orpholino-phenyl 2-pyridyl		30 31	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	3-NH ₂ -Phenyl 4-NH ₂ -Phenyl	
98	2		2-pyridyl		32	2	CH ₃	CH ₃	4-NH ₂ -Phenyl	
99	3		2-pyridyl	20	33	3	CH_3	CH_3	4-NH ₂ -Phenyl	
100	1 2		3-pyridyl		34	1	CH ₂ CH ₃	CH ₂ CH ₃	4-NH ₂ -Phenyl	
101 102	3		3-pyridyl 3-pyridyl		35 36	2 3	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-NH ₂ -Phenyl 4-NH ₂ -Phenyl	
103	1		4-pyridyl		37	1	CH ₃	CH ₃	2-tBu-Phenyl	
104	2		4-pyridyl	2.5	38	2	CH ₃	CH ₃	2-tBu-Phenyl	
105 106	3 1	2.0	4-pyridyl CH ₃ -4-pyridyl	25	39 40	3 1	CH₃ CH₂CH₃	CH ₃ CH ₂ CH ₃	2-tBu-Phenyl 2-tBu-Phenyl	
107	2		CH ₃ -4-pyridyl		41	2	CH ₂ CH ₃	CH ₂ CH ₃	2-tBu-Phenyl	
108	3		CH ₃ -4-pyridyl		42	3	CH ₂ CH ₃	CH ₂ CH ₃	2-tBu-Phenyl	
109	1		CH ₃ -4-pyridyl		43	1	CH ₃	CH ₃	3-tBu-Phenyl	
110 111	2 3		CH ₃ -4-pyridyl CH ₃ -4-pyridyl	30	44 45	2	CH ₃ CH ₃	CH ₃ CH ₃	3-tBu-Phenyl 3-tBu-Phenyl	
112	1		nethylpyridin-4-yl	30	46	1	CH ₂ CH ₃	CH ₂ CH ₃	3-tBu-Phenyl	
113	2		nethylpyridin-4-yl		47	2	CH ₂ CH ₃	CH ₂ CH ₃	3-tBu-Phenyl	
114	3 1		nethylpyridin-4-yl		48	3	CH ₂ CH ₃	CH ₂ CH ₃	3-tBu-Phenyl	
115 116	2		nethylpyridin-4-yl nethylpyridin-4-yl		49 50	1 2	CH ₃ CH ₃	CH ₃ CH ₃	4-tBu-Phenyl 4-tBu-Phenyl	
117	3		nethylpyridin-4-yl	35	51	3	CH ₃	CH ₃	4-tBu-Phenyl	
				33	52	1	CH_2CH_3	CH_2CH_3	4-tBu-Phenyl	
Exemplary e	mbodime	nts include (compounds having the		53 54	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-tBu-Phenyl 4-tBu-Phenyl	
			acceptable salt form		55	1	CH ₃	CH ₂ CH ₃	2-NO ₂ -Phenyl	
thereof:	i a pilari	naceaneany	acceptable balt form		56	2	CH_3	CH_3	2-NO ₂ -Phenyl	
				40	57	3	CH ₃	CH ₃	2-NO ₂ -Phenyl	
					58 59	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-NO ₂ -Phenyl 2-NO ₂ -Phenyl	
			(II)		60	3	CH ₂ CH ₃	CH ₂ CH ₃	2-NO ₂ -Phenyl	
O					61	1	CH_3	CH_3	3-NO ₂ -Phenyl	
\mathbb{R}^{1a}					62 63	2	CH ₃ CH ₃	CH ₃ CH ₃	3-NO ₂ -Phenyl 3-NO ₂ -Phenyl	
	\ 0			45	64	1	CH ₂ CH ₃	CH ₂ CH ₃	3-NO ₂ -Phenyl	
\mathbb{R}^{1b}	/	- ^			65	2	CH ₂ CH ₃	CH₂CH₃	3-NO ₂ -Phenyl	
	ጚ, /	$' \rightarrow \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ $	$V - R^2$		66	3	CH ₂ CH ₃	CH ₂ CH ₃	3-NO ₂ -Phenyl	
	()N	· L /			67 68	1 2	CH₃ CH₃	CH₃ CH₃	4-NO ₂ -Phenyl 4-NO ₂ -Phenyl	
	- •n	V ~			69	3	CH_3	CH_3	4-NO ₂ -Phenyl	
				50	70	1	CH ₂ CH ₃	CH ₂ CH ₃	4-NO ₂ -Phenyl	
wherein non-lin	miting exa	amples of R	R^{1a} , R^{1b} , R^2 and n are		71 72	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-NO₂-Phenyl 4-NO₂-Phenyl	
defined herein	below in	Table 11.			73	1	CH ₂ CH ₃	CH ₂ CH ₃	2-SCH ₃ -Phenyl	
					74	2	CH_3	CH ₃	2-SCH ₃ -Phenyl	
	7	TABLE 11			75 76	3	CH_3	CH ₃	2-SCH ₃ -Phenyl	
P-4	D 1 <i>a</i>	D 1 b	R ²	55	76 77	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl	
Entry n	R1ª	R1 ^b	κ-		78	3	CH ₂ CH ₃	CH ₂ CH ₃	2-SCH ₃ -Phenyl	
1 1	CH_3	CH_3	2-CF ₃ -Phenyl		79	1	CH_3	CH_3	3-SCH ₃ -Phenyl	
2 2	CH_3	CH ₃	2-CF ₃ -Phenyl		80 81	2	CH ₃ CH ₃	CH ₃ CH ₃	3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl	
3 3 4 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		82	1	CH ₂ CH ₃	CH ₂ CH ₃	3-SCH ₃ -Phenyl	
5 2	CH ₂ CH ₃	CH ₂ CH ₃	2-CF ₃ -Phenyl	60	83	2	CH ₂ CH ₃	CH ₂ CH ₃	3-SCH ₃ -Phenyl	
6 3	CH ₂ CH ₃	CH ₂ CH ₃	2-CF ₃ -Phenyl		84	3	CH ₂ CH ₃	CH ₂ CH ₃	3-SCH ₃ -Phenyl	
7 1 8 2	CH₃ CH₃	CH ₃ CH ₃	3-CF ₃ -Phenyl 3-CF ₃ -Phenyl		85 86	1 2	CH ₃ CH ₃	CH ₃ CH ₃	4-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl	
9 3	CH ₃	CH ₃ CH ₃	3-CF ₃ -Phenyl		87	3	CH ₃	CH ₃	4-SCH ₃ -Phenyl	
10 1	CH ₂ CH ₃	CH ₂ CH ₃	3-CF ₃ -Phenyl		88	1	$\mathrm{CH_{2}CH_{3}}$	CH ₂ CH ₃	4-SCH ₃ -Phenyl	
11 2	CH ₂ CH ₃	CH ₂ CH ₃	3-CF ₃ -Phenyl	65	89	2	CH ₂ CH ₃	CH ₂ CH ₃	4-SCH ₃ -Phenyl	
12 3	CH ₂ CH ₃	CH ₂ CH ₃	3-CF ₃ -Phenyl		90	3	CH ₂ CH ₃	CH ₂ CH ₃	4-SCH ₃ -Phenyl	

55	\mathbb{R}^2	R1 ^b	R1ª	n	Entry
_	2-CF ₃ -Phenyl	CH ₃	CH ₃	1	1
	2-CF ₃ -Phenyl	CH ₃	CH ₃	2	2
	2-CF ₃ -Phenyl	CH ₃	CH_3	3	3
	2-CF ₃ -Phenyl	CH ₂ CH ₃	CH ₂ CH ₃	1	4
60	2-CF ₃ -Phenyl	CH ₂ CH ₃	CH ₂ CH ₃	2	5
	2-CF ₃ -Phenyl	CH ₂ CH ₃	CH ₂ CH ₃	3	6
	3-CF ₃ -Phenyl	CH ₃	CH ₃	1	7
	3-CF ₃ -Phenyl	CH ₃	CH ₃	2	8
	3-CF ₃ -Phenyl	CH ₃	CH_3	3	9
	3-CF ₃ -Phenyl	CH ₂ CH ₃	CH ₂ CH ₃	1	10
65	3-CF ₃ -Phenyl	CH ₂ CH ₃	CH ₂ CH ₃	2	11
	3-CF ₃ -Phenyl	CH ₂ CH ₃	CH ₂ CH ₃	3	12

64 TABLE 11-continued

		TAB	LE 11 -c 01	ntinued		TABLE 11-continued				
Entry	n	$R1^a$	R1 ^b	R ²		Entry	n	$R1^a$	R1 ^b	\mathbb{R}^2
91	1	CH ₃	CH ₃	2-SO ₂ CH ₃ -Phenyl		169	1	CH ₃	CH ₃	2,5-di-CH ₃ -phenyl
92	2	CH_3	CH_3	2-SO ₂ CH ₃ -Phenyl	5	170	2	CH_3	CH_3	2,5-di-CH ₃ -phenyl
93	3	CH_3	CH ₃	2-SO ₂ CH ₃ -Phenyl		171 172	3	CH ₃	CH ₃ CH ₂ CH ₃	2,5-di-CH ₃ -phenyl
94 95	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-SO ₂ CH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl		172	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl
96	2	CH ₂ CH ₃	CH ₂ CH ₃	2-SO ₂ CH ₃ -Phenyl		174	2	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-CH ₃ -phenyl
97	1	$\mathrm{CH_3}$	CH_3	3-SO ₂ CH ₃ -Phenyl		175	1	CH_3	CH_3	2,6-di-CH ₃ -phenyl
98	2	CH ₃	CH ₃	3-SO ₂ CH ₃ -Phenyl	10	176	2	CH ₃	CH ₃	2,6-di-CH ₃ -phenyl
99 100	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	3-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl		177 178	1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl
101	2	CH ₂ CH ₃	CH ₂ CH ₃	3-SO ₂ CH ₃ -Phenyl		179	2	CH ₂ CH ₃	CH ₂ CH ₃	2,6-di-CH ₃ -phenyl
102	3	CH ₂ CH ₃	CH ₂ CH ₃	3-SO ₂ CH ₃ -Phenyl		180	3	CH ₂ CH ₃	CH ₂ CH ₃	2,6-di-CH ₃ -phenyl
103 104	1 2	CH₃ CH₃	CH ₃ CH ₃	4-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl		181 182	1 2	CH ₃	CH ₃ CH ₃	3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl
104	3	CH ₃	CH ₃	4-SO ₂ CH ₃ -Phenyl	15	183	3	CH ₃ CH ₃	CH ₃	3,4-di-CH ₃ -phenyl
106	1	CH ₂ CH ₃	CH ₂ CH ₃	4-SO ₂ CH ₃ -Phenyl		184	1	CH ₂ CH ₃	CH ₂ CH ₃	3,4-di-CH ₃ -phenyl
107	2	CH ₂ CH ₃	CH ₂ CH ₃	4-SO ₂ CH ₃ -Phenyl		185	2	CH ₂ CH ₃	CH ₂ CH ₃	3,4-di-CH ₃ -phenyl
108 109	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	4-SO ₂ CH ₃ -Phenyl 2-SO ₂ NH ₂ -Phenyl		186 187	1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
110	2	CH ₃	CH ₃	2-SO ₂ NH ₂ -Phenyl		188	2	CH ₃	CH_3	3,5-di-CH ₃ -phenyl
111	3	CH_3	CH ₃	2-SO ₂ NH ₂ -Phenyl	20	189	3	CH ₃	CH ₃	3,5-di-CH ₃ -phenyl
112	1	CH ₂ CH ₃	CH ₂ CH ₃	2-SO ₂ NH ₂ -Phenyl		190	1	CH ₂ CH ₃	CH ₂ CH ₃	3,5-di-CH ₃ -phenyl
113 114	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-SO ₂ NH ₂ -Phenyl 2-SO ₂ NH ₂ -Phenyl		191 192	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
115	1	CH_2CH_3	CH ₃	3-SO ₂ NH ₂ -Phenyl		193	1	CH ₃	CH ₃	2,3-di-Cl-phenyl
116	2	CH_3	CH ₃	3-SO ₂ NH ₂ -Phenyl		194	2	CH ₃	CH_3	2,3-di-Cl-phenyl
117	3	CH ₃	CH ₃	3-SO ₂ NH ₂ -Phenyl	25	195	3	CH ₃	CH ₃	2,3-di-Cl-phenyl
118 119	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-SO ₂ NH ₂ -Phenyl 3-SO ₂ NH ₂ -Phenyl		196 197	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2,3-di-Cl-phenyl 2,3-di-Cl-phenyl
120	3	CH ₂ CH ₃	CH ₂ CH ₃	3-SO ₂ NH ₂ -Phenyl		198	3	CH ₂ CH ₃	CH ₂ CH ₃	2,3-di-Cl-phenyl
121	1	CH ₃	CH ₃	4-SO ₂ NH ₂ -Phenyl		199	1	$\overline{\mathrm{CH}_{3}}$	$ m CH_3$	2,4-di-Cl-phenyl
122	2	CH_3	CH_3	4-SO ₂ NH ₂ -Phenyl		200	2	CH_3	CH_3	2,4-di-Cl-phenyl
123 124	3 1	CH₃ CH₂CH₃	CH ₃ CH ₂ CH ₃	4-SO ₂ NH ₂ -Phenyl 4-SO ₂ NH ₂ -Phenyl	30	201 202	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2,4-di-Cl-phenyl 2,4-di-Cl-phenyl
125	2	CH ₂ CH ₃	CH ₂ CH ₃	4-SO ₂ NH ₂ -Phenyl		203	2 3	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-Cl-phenyl
126	3	CH ₂ CH ₃	CH_2CH_3	4-SO ₂ NH ₂ -Phenyl		204	3	CH ₂ CH ₃	CH_2CH_3	2,4-di-Cl-phenyl
127	1 2	CH ₃	CH_3	2-CONH ₂ -Phenyl		205 206	1 2	CH ₃ CH ₃	CH_3	2,5-di-Cl-phenyl
128 129	3	CH₃ CH₃	CH ₃ CH ₃	2-CONH ₂ -Phenyl 2-CONH ₂ -Phenyl	2.5	200	3	CH ₃	CH ₃ CH ₃	2,5-di-Cl-phenyl 2,5-di-Cl-phenyl
130	1	CH ₂ CH ₃	CH ₂ CH ₃	2-CONH ₂ -Phenyl	35	280	1	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-Cl-phenyl
131	2	CH ₂ CH ₃	CH ₂ CH ₃	2-CONH ₂ -Phenyl		209	2	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-Cl-phenyl
132 133	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-CONH ₂ -Phenyl 3-CONH ₂ -Phenyl		210 211	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2,5-di-Cl-phenyl 2,6-di-Cl-phenyl
134	2	CH ₃	CH_3	3-CONH ₂ -Phenyl		211	2	CH ₃	CH ₃	2,6-di-Cl-phenyl
135	3	CH_3	CH_3	3-CONH ₂ -Phenyl	40	213	3	CH_3	CH_3	2,6-di-Cl-phenyl
136	1	CH ₂ CH ₃	CH ₂ CH ₃	3-CONH ₂ -Phenyl	40	214	1	CH ₂ CH ₃	CH ₂ CH ₃	2,6-di-Cl-phenyl
137 138	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-CONH ₂ -Phenyl 3-CONH ₂ -Phenyl		215 216	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2,6-di-Cl-phenyl 2,6-di-Cl-phenyl
139	1	CH ₃	CH ₃	4-CONH ₂ -Phenyl		217	1	CH ₃	CH ₃	3,4-di-Cl-phenyl
140	2	CH_3	CH_3	4-CONH ₂ -Phenyl		218	2	CH_3	CH_3	3,4-di-Cl-phenyl
141 142	3 1	CH ₃	CH ₃	4-CONH ₂ -Phenyl 4-CONH ₂ -Phenyl	45	219 220	3 1	CH ₃	CH ₃	3,4-di-Cl-phenyl 3,4-di-Cl-phenyl
143		CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	4-CONH ₂ -Phenyl	73	221	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3,4-di-Cl-phenyl
144	2	CH ₂ CH ₃	$CH_2^2CH_3$	4-CONH ₂ -Phenyl		222	3	CH ₂ CH ₃	CH ₂ CH ₃	3,4-di-Cl-phenyl
145	1	CH ₃	CH ₃	2-Br-Phenyl		223	1	CH ₃	CH ₃	3,5-di-Cl-phenyl
146 147	2	CH₃ CH₃	CH ₃ CH ₃	2-Br-Phenyl 2-Br-Phenyl		224 225	2	CH₃ CH₃	CH ₃ CH ₃	3,5-di-Cl-phenyl 3,5-di-Cl-phenyl
148	1	CH ₂ CH ₃	CH ₂ CH ₃	2-Br-Phenyl	50	226	1	CH ₂ CH ₃	CH ₂ CH ₃	3,5-di-Cl-phenyl
149	2	CH_2CH_3	CH ₂ CH ₃	2-Br-Phenyl		227	2	CH_2CH_3	CH ₂ CH ₃	3,5-di-Cl-phenyl
150	3	CH ₂ CH ₃	CH ₂ CH ₃	2-Br-Phenyl		228	3	CH ₂ CH ₃	CH ₂ CH ₃	3,5-di-Cl-phenyl
151 152	1 2	CH₃ CH₃	CH ₃ CH ₃	3-Br-Phenyl 3-Br-Phenyl		229 230	1 2	CH₃ CH₃	CH ₃ CH ₃	2-morpholino-4-CH ₃ -phenyl 2-morpholino-4-CH ₃ -phenyl
153	3	CH ₃	CH ₃	3-Br-Phenyl		231	3	CH ₃	CH ₃	2-morpholino-4-CH ₃ -phenyl
154	1	CH ₂ CH ₃	CH ₂ CH ₃	3-Br-Phenyl	55	232	1	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CH ₃ -phenyl
155 156	2	CH ₂ CH ₃	CH ₂ CH ₃	3-Br-Phenyl 3-Br-Phenyl		233 234	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CH ₃ -phenyl
156 157	1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2,3-di-CH ₃ -phenyl		234	1	CH ₂ CH ₃	CH ₂ CH ₃ CH ₃	2-morpholino-4-CH ₃ -phenyl 2-morpholino-4-CN-phenyl
158	2	CH_3	CH ₃	2,3-di-CH ₃ -phenyl		236	2	CH_3	CH_3	2-morpholino-4-CN-phenyl
159	3	CH ₃	CH ₃	2,3-di-CH ₃ -phenyl		237	3	CH ₃	CH ₃	2-morpholino-4-CN-phenyl
160	1	CH ₂ CH ₃	CH ₂ CH ₃	2,3-di-CH ₃ -phenyl	60	238	1	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CN-phenyl
161 162	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2,3-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl		239 240	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-morpholino-4-CN-phenyl 2-morpholino-4-CN-phenyl
163	1	$ m CH_3$	CH_3	2,4-di-CH ₃ -phenyl		241	1	$ m CH_3$	$ m CH_3$	2-morpholino-4-OH-phenyl
164	2	CH_3	CH_3	2,4-di-CH ₃ -phenyl		242	2	CH_3	CH_3	2-morpholino-4-OH-phenyl
165 166	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2,4-di-CH ₃ -phenyl 2,4-di-CH ₃ -phenyl		243 244	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2-morpholino-4-OH-phenyl 2-morpholino-4-OH-phenyl
167	2	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-CH ₃ -phenyl	65	245	2	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-OH-phenyl
168	3	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-CH ₃ -phenyl		246	3	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-OH-phenyl

66TABLE 12-continued

	IADI	LE 11-com.	illueu	_		IADI	LE 12-continued
Entry n	$R1^a$	R1 ^b	R ²		Entry	n	R ²
247 1	CH ₃	CH ₃	2,3 -dimethylpyridin-4-yl	_	39	3	2-SCH ₃ -Phenyl
248 2	CH ₃	CH ₃	2,3 -dimethylpyridin-4-yl	5	40	1	3-SCH ₃ -Phenyl
248 2 249 3	CH_3	CH ₃	2,3 -dimethylpyridin-4-yl		41	2	3-SCH ₃ -Phenyl
250 1	CH_2CH_3	CH_2CH_3	2,3 -dimethylpyridin-4-yl		42	3	3-SCH ₃ -Phenyl
	CH ₂ CH ₃	CH ₂ CH ₃	2,3 -dimethylpyridin-4-yl		43	1	4-SCH ₃ -Phenyl
252 3 253 1	CH ₂ CH ₃	CH ₂ CH ₃	2,3 -dimethylpyridin-4-yl 3 ,6-dimethy 1pyridin-4-yl		44 45	2 3	4-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
254 2	CH ₃ CH ₃	CH ₃ CH ₃	3 ,6-dimethy 1pyridin-4-yl	10	46	1	2-SO ₂ CH ₃ -Phenyl
254 2 255 3	CH ₃	CH ₃	3 ,6-dimethy 1pyridin-4-yl	10	47	2	2-SO ₂ CH ₃ -Phenyl
	CH ₂ CH ₃	CH ₂ CH ₃	3 ,6-dimethy 1pyridin-4-yl		48	3	2-SO ₂ CH ₃ -Phenyl
	CH ₂ CH ₃	CH ₂ CH ₃	3 ,6-dimethy 1pyridin-4-yl		49	1	3-SO ₂ CH ₃ -Phenyl
258 3	CH_2CH_3	CH_2CH_3	3,6-dimethylpyridin-4-yl		50	2	3-SO ₂ CH ₃ -Phenyl
			_		51	3	3-SO ₂ CH ₃ -Phenyl
				15	52 53	1	4-SO ₂ CH ₃ -Phenyl
			e compounds having the		54	2 3	4-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
	r a phar	maceuticall	ly acceptable salt form		55	1	2-SO ₂ NH ₂ -Phenyl
thereof:					56	2	2-SO ₂ NH ₂ -Phenyl
					57	3	2-SO ₂ NH ₂ -Phenyl
				20	58	1	3-SO ₂ NH ₂ -Phenyl
			(X)	20	59	2 3	3-SO ₂ NH ₂ -Phenyl
Ö			` ′		60		3-SO ₂ NH ₂ -Phenyl
					61 62	1 2	4-SO ₂ NH ₂ -Phenyl 4-SO ₂ NH ₂ -Phenyl
\wedge					63	3	$4-SO_2NH_2-Phenyl$
4	· · ·				64	1	2-CONH ₂ -Phenyl
	Ι,	∼		25	65	2	2-CONH ₂ -Phenyl
`		1	$N-R^2$		66	3	2-CONH ₂ -Phenyl
) N	1			67	1	3-CONH ₂ -Phenyl
	•••				68	2	3-CONH ₂ -Phenyl
					69 70	3 1	3-CONH ₂ -Phenyl
	•.•		S D 2 1 1 1 1 1	20	70	2	4-CONH ₂ -Phenyl 4-CONH ₂ -Phenyl
wherein non-lir	miting e	kamples of	f R ² and n are defined	30	72	3	4-CONH ₂ -Phenyl
herein below in	Table 1	2.			73	1	2-Br-Phenyl
					74	2 3	2-Br-Phenyl
		TABLE 12			75	3	2-Br-Phenyl
					76	1	3-Br-Phenyl
Entry	n		\mathbb{R}^2	35	77	2	3-Br-Phenyl
1			2 OF N 1		78 79	3 1	3-Br-Phenyl 2,3-di-CH ₃ -phenyl
$\frac{1}{2}$	1 2		2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		80	2	2,3-di-CH ₃ -phenyl
3	3		2-CF ₃ -Phenyl		81	3	2,3-di-CH ₃ -phenyl
4	1		3-CF ₃ -Phenyl		82	1	2,4-di-CH ₃ -phenyl
5	2		3-CF ₃ -Phenyl	40	83	2	2,4-di-CH ₃ -phenyl
6	3		3-CF ₃ -Phenyl	40	84	3	2,4-di-CH ₃ -phenyl
7	1		4-CF ₃ -Phenyl		85	1	2,5-di-CH ₃ -phenyl
8	2		4-CF ₃ -Phenyl		86	2 3	2,5-di-CH ₃ -phenyl
9	3		4-CF ₃ -Phenyl		87 88	1	2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl
10 11	1 2		2-NH ₂ -Phenyl 2-NH ₂ -Phenyl		89		2,6-di-CH ₃ -phenyl
12	3		2-NH ₂ -Phenyl	45	90	2 3	2,6-di-CH ₃ -phenyl
13	1		3-NH ₂ -Phenyl		91	1	3,4-di-CH ₃ -phenyl
14	2		3-NH ₂ -Phenyl		92	2 3	3,4-di-CH ₃ -phenyl
15	3		3-NH ₂ -Phenyl		93	3	3,4-di-CH ₃ -phenyl
16	1		4-NH ₂ -Phenyl		94	1	3,5-di-CH ₃ -phenyl
17	2		4-NH ₂ -Phenyl	50	95 06	2 3	3,5-di-CH ₃ -phenyl
18 19	3 1		4-NH ₂ -Phenyl	50	96 97	1	3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl
20	2		2-tBu-Phenyl 2-tBu-Phenyl		98	2	2,3-di-Cl-phenyl
21	3		2-tBu-Phenyl		99	2 3 1	2,3-di-Cl-phenyl
22	1		3-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
23	2		3-tBu-Phenyl		101	2 3 1	2,4-di-Cl-phenyl
24	3		3-tBu-Phenyl	55	102	3	2,4-di-Cl-phenyl
25	1		4-tBu-Phenyl		103	1	2,5-di-Cl-phenyl
26	2		4-tBu-Phenyl		104	2	2,5-di-Cl-phenyl
27 28	3 1		4-tBu-Phenyl 2-NO ₂ -Phenyl		105 106	2 3 1	2,5-di-Cl-phenyl 2,6-di-Cl-phenyl
28 29	2		2-NO ₂ -Phenyl 2-NO ₂ -Phenyl		107		2,6-di-Cl-phenyl
30	3		2-NO ₂ -Phenyl		108	2 3 1	2,6-di-Cl-phenyl
31	1		3-NO ₂ -Phenyl	60	109		3,4-di-Cl-phenyl
32	2		3-NO ₂ -Phenyl		110		3,4-di-Cl-phenyl
33	3		3-NO ₂ -Phenyl		111	2 3 1	3,4-di-Cl-phenyl
			4 N/O DL		112	1	3,5-di-Cl-phenyl
34	1		4-NO ₂ -Phenyl		112	~	
34 35	2		4-NO ₂ -Phenyl		113	2	3,5-di-Cl-phenyl
34 35 36	2 3		4-NO ₂ -Phenyl 4-NO ₂ -Phenyl	65	114	2 3	3,5-di-Cl-phenyl 3,5-di-Cl-phenyl
34 35	2		4-NO ₂ -Phenyl	65		2 3 1 2	3,5-di-Cl-phenyl

68 TABLE 13-continued

	TADLE	z 12-continued	_		IADLI	z 13-continued
Entry	n	R ²		Entry	n	\mathbb{R}^2
117	3	2-morpholino-4-CH ₃ -phenyl	_	38	2	2-SCH ₃ -Phenyl
118	1	2-morpholino-4-CN-phenyl	5	39	3	2-SCH ₃ -Phenyl
119	2	2-morpholino-4-CN-phenyl		40	1	3-SCH ₃ -Phenyl
120	3	2-morpholino-4-CN-phenyl		41	2	3-SCH ₃ -Phenyl
121 122	1 2	2-morpholino-4-OH-phenyl 2-morpholino-4-OH-phenyl		42 43	3 1	3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
123	3	2-morpholino-4-OH-phenyl		44	2	4-SCH ₃ -Phenyl
124	1	2,3-dimethylpyridin-4-yl	10	45	3	4-SCH ₃ -Phenyl
125	2	2,3-dimethylpyridin-4-yl		46	1	2-SO ₂ CH ₃ -Phenyl
126	3	2,3-dimethylpyridin-4-yl		47	2	2-SO ₂ CH ₃ -Phenyl
127	1	3,6-dimethylpyridin-4-yl		48	3	2-SO ₂ CH ₃ -Phenyl
128 129	2 3	3,6-dimethylpyridin-4-yl 3,6-dimethylpyridin-4-yl		49 50	1 2	3-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
129		5,0-dimentyipyi1diii-4-yi		51	3	3-SO ₂ CH ₃ -Phenyl
			15	52	1	4-SO ₂ CH ₃ -Phenyl
Exemplary en	nbodiment	ts include compounds having the		53	2	4-SO ₂ CH ₃ -Phenyl
		accutically acceptable salt form		54	3	4-SO ₂ CH ₃ -Phenyl
thereof:	a phann	accuracing acceptance suit form		55	1	2-SO ₂ NH ₂ -Phenyl
thereor.				56 57	2 3	2-SO ₂ NH ₂ -Phenyl 2-SO ₂ NH ₂ -Phenyl
			20	58	1	3-SO ₂ NH ₂ -Phenyl
				59	2	3-SO ₂ NH ₂ -Phenyl
0		(XI)		60	3	3-SO ₂ NH ₂ -Phenyl
Ĭ				61	1	4-SO ₂ NH ₂ -Phenyl
\wedge \downarrow				62	2	4-SO ₂ NH ₂ -Phenyl
\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	` o		25	63	3	4-SO ₂ NH ₂ -Phenyl
	/	^	23	64 65	1 2	2-CONH ₂ -Phenyl 2-CONH ₂ -Phenyl
	〈 /	$N-R^2$		66	3	2-CONH ₂ -Phenyl
	XI-N.	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \		67	1	3-CONH ₂ -Phenyl
	\setminus			68	2	3-CONH ₂ -Phenyl
				69	3	3-CONH ₂ -Phenyl
			30	70	1	4-CONH ₂ -Phenyl
wherein non-lim	iiting exam	ples of R and n are defined herein		71 72	2 3	4-CONH ₂ -Phenyl
below in Table	13.			73	1	4-CONH ₂ -Phenyl 2-Br-Phenyl
				74	2	2-Br-Phenyl
	T/	ABLE 13		75	3	2-Br-Phenyl
		IDED 13	35	76	1	3-Br-Phenyl
Entry	n	\mathbb{R}^2		77	2	3-Br-Phenyl
		- CF 71 1		78	3	3-Br-Phenyl
1 2	1	2-CF ₃ -Phenyl		79 80	1 2	2,3-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl
3	2 3	2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		81	3	2,3-di-CH ₃ -phenyl
4	1	3-CF ₃ -Phenyl		82	1	2,4-di-CH ₃ -phenyl
5	2	3-CF ₃ -Phenyl	40	83	2	2,4-di-CH ₃ -phenyl
6	3	3-CF ₃ -Phenyl		84	3	2,4-di-CH ₃ -phenyl
7	1	4-CF ₃ -Phenyl		85	1	2,5-di-CH ₃ -phenyl
8	2	4-CF ₃ -Phenyl		86 87	2 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl
10	3 1	4-CF ₃ -Phenyl 2-NH ₂ -Phenyl		88	1	2,6-di-CH ₃ -phenyl
11	2	2-NH ₂ -Phenyl	45	89	2	2,6-di-CH ₃ -phenyl
12	3	2-NH ₂ -Phenyl		90	3	2,6-di-CH ₃ -phenyl
13	1	3-NH ₂ -Phenyl		91	1	3,4-di-CH ₃ -phenyl
14	2	3-NH ₂ -Phenyl		92	2 3	3,4-di-CH ₃ -phenyl
15	3	3-NH ₂ -Phenyl		93 94	3 1	3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
16 17	1 2	4-NH ₂ -Phenyl 4-NH ₂ -Phenyl	50	95	2	3,5-di-CH ₃ -phenyl
18	3	4-NH ₂ -Phenyl	30	96	2 3	3,5-di-CH ₃ -phenyl
19	1	2-tBu-Phenyl		97	1	2,3-di-Cl-phenyl
20	2	2-tBu-Phenyl		98	2 3 1	2,3-di-Cl-phenyl
21	3	2-tBu-Phenyl		99	3	2,3-di-Cl-phenyl
22	1	3-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
23	2	3-tBu-Phenyl	55	101 102	2 3	2,4-di-Cl-phenyl 2,4-di-Cl-phenyl
24 25	3 1	3-tBu-Phenyl 4-tBu-Phenyl		102	1	2,4-di-Cl-phenyl
26	2	4-tBu-Phenyl		104	2	2,5-di-Cl-phenyl
27	3	4-tBu-Phenyl		105	2 3	2,5-di-Cl-phenyl
28	1	2-NO ₂ -Phenyl		106	1	2,6-di-Cl-phenyl
29	2	2-NO ₂ -Phenyl	60	107	2 3 1	2,6-di-Cl-phenyl
30	3	2-NO ₂ -Phenyl	•	108	3	2,6-di-Cl-phenyl
31	1	3-NO ₂ -Phenyl		109 110	2	3,4-di-Cl-phenyl 3,4-di-Cl-phenyl
32 33	2 3	3-NO ₂ -Phenyl 3-NO ₂ -Phenyl		110	2 3 1	3,4-di-Cl-phenyl
33 34	1	4-NO ₂ -Phenyl		112	1	3,5-di-Cl-phenyl
35	2	4-NO ₂ -Phenyl		113	2	3,5-di-Cl-phenyl
36	3	4-NO ₂ -Phenyl	65	114	3	3,5-di-Cl-phenyl
37	1	2-SCH ₃ -Phenyl		115	1	2-morpholino-4-CH ₃ -phenyl

70 TABLE 14-continued

	TABL	E 13-continued			TABL	E 14-continued
Entry	n	R ²		Entry	n	\mathbb{R}^2
116	2	2-morpholino-4-CH ₃ -phenyl		38	2	2-SCH ₃ -Phenyl
117	3	2-morpholino-4-CH ₃ -phenyl	5	39	3	2-SCH ₃ -Phenyl
118	1	2-morpholino-4-CN-phenyl		40	1	3-SCH ₃ -Phenyl
119 120	2 3	2-morpholino-4-CN-phenyl 2-morpholino-4-CN-phenyl		41 42	2 3	3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
121	1	2-morpholino-4-CN-phenyl		43	1	4-SCH ₃ -Phenyl
122	2	2-morpholino-4-OH-phenyl		44	2	4-SCH ₃ -Phenyl
123	3	2-morpholino-4-OH-phenyl	10	45	3	4-SCH ₃ -Phenyl
124	1	2,3-dimethylpyridin-4-yl		46	1	2-SO ₂ CH ₃ -Phenyl
125	2	2,3-dimethylpyridin-4-yl		47	2	2-SO ₂ CH ₃ -Phenyl
126	3	2,3-dimethylpyridin-4-yl		48	3	2-SO ₂ CH ₃ -Phenyl
127 128	1 2	3,6-dimethylpyridin-4-yl 3,6-dimethylpyridin-4-yl		49 50	1 2	3-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
129	3	3,6-dimethylpyridin-4-yl		51	3	3-SO ₂ CH ₃ -Phenyl
			15	52	1	4-SO ₂ CH ₃ -Phenyl
				53	2	4-SO ₂ CH ₃ -Phenyl
Exemplary er	nbodimen	its include compounds having the		54	3	4-SO ₂ CH ₃ -Phenyl
formula (XII) o	or a pharr	naceutically acceptable salt form		55	1	2-SO ₂ NH ₂ -Phenyl
thereof:	_	· -		56 57	2 3	2-SO ₂ NH ₂ -Phenyl 2-SO ₂ NH ₂ -Phenyl
			20	58	1	3-SO ₂ NH ₂ -Phenyl
				59	2	3-SO ₂ NH ₂ -Phenyl
		(XII)		60	3	3-SO ₂ NH ₂ -Phenyl
()	(All)		61	1	4-SO ₂ NH ₂ -Phenyl
$\overline{}$				62	2	4-SO ₂ NH ₂ -Phenyl
/ /	(25	63	3	4-SO ₂ NH ₂ -Phenyl
$\langle X \rangle$	` o	^	25	64 65	1 2	2-CONH ₂ -Phenyl
\sim /	/	$N - R^2$		66	3	2-CONH ₂ -Phenyl 2-CONH ₂ -Phenyl
_		T N		67	1	3-CONH ₂ -Phenyl
	(),"			68	2	3-CONH ₂ -Phenyl
		~		69	3	3-CONH ₂ -Phenyl
			30	70	1	4-CONH ₂ -Phenyl
wherein non-lir	niting exa	amples of R ² and n are defined		71	2	4-CONH ₂ -Phenyl
herein below in	Table 14			72 73	3 1	4-CONH ₂ -Phenyl 2-Br-Phenyl
				74	2	2-Br-Phenyl
	Т	ABLE 14		75	3	2-Br-Phenyl
	1.	ADEE 14	35	76	1	3-Br-Phenyl
Entry	n	\mathbb{R}^2	33	77	2	3-Br-Phenyl
				78	3	3-Br-Phenyl
1	1	2-CF ₃ -Phenyl		79	1	2,3-di-CH ₃ -phenyl
2	2	2-CF ₃ -Phenyl		80 81	2 3	2,3-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl
3 4	3 1	2-CF ₃ -Phenyl 3-CF ₃ -Phenyl		82	1	2,4-di-CH ₃ -phenyl
5	2	3-CF ₃ -Phenyl	40	83	2	2,4-di-CH ₃ -phenyl
6	3	3-CF ₃ -Phenyl		84	3	2,4-di-CH ₃ -phenyl
7	1	4-CF ₃ -Phenyl		85	1	2,5-di-CH ₃ -phenyl
8	2	4-CF ₃ -Phenyl		86	2	2,5-di-CH ₃ -phenyl
9	3	4-CF ₃ -Phenyl		87 88	3 1	2,5-di-CH ₃ -phenyl
10 11	1 2	2-NH ₂ -Phenyl 2-NH ₂ -Phenyl	45	89	2	2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl
12	3	2-NH ₂ -rhenyl 2-NH ₂ -Phenyl		90	3	2,6-di-CH ₃ -phenyl
13	1	3-NH ₂ -Phenyl		91	1	3,4-di-CH ₃ -phenyl
14	2	3-NH ₂ -Phenyl		92	2	3,4-di-CH ₃ -phenyl
15	3	3-NH ₂ -Phenyl		93	3	3,4-di-CH ₃ -phenyl
16	1	4-NH ₂ -Phenyl		94	1	3,5-di-CH ₃ -phenyl
17	2 3	4-NH ₂ -Phenyl	50	95 96	2 3	3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
18 19	1	4-NH ₂ -Phenyl 2-tBu-Phenyl		97	1	2,3-di-Cl-phenyl
20	2	2-tBu-Phenyl		98	2	2,3-di-Cl-phenyl
21	3	2-tBu-Phenyl		99	3	2,3-di-Cl-phenyl
22	1	3-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
23	2	3-tBu-Phenyl	55	101	2	2,4-di-Cl-phenyl
24	3	3-tBu-Phenyl		102	3	2,4-di-Cl-phenyl
25	1	4-tBu-Phenyl		103 104	1 2	2,5-di-Cl-phenyl 2,5-di-Cl-phenyl
26 27	2 3	4-tBu-Phenyl 4-tBu-Phenyl		105	3	2,5-di-Cl-phenyl
28	1	2-NO ₂ -Phenyl		106	1	2,6-di-Cl-phenyl
29	2	2-NO ₂ -Phenyl	60	107	2	2,6-di-Cl-phenyl
30	3	2-NO ₂ -Phenyl	60	108	3	2,6-di-Cl-phenyl
31	1	3-NO ₂ -Phenyl		109	1	3,4-di-Cl-phenyl
32	2	3-NO ₂ -Phenyl		110	2	3,4-di-Cl-phenyl
33	3	3-NO ₂ -Phenyl		111	3	3,4-di-Cl-phenyl
34	1	4-NO ₂ -Phenyl		112 113	1 2	3,5-di-Cl-phenyl 3,5-di-Cl-phenyl
35 36	2 3	4-NO ₂ -Phenyl 4-NO ₂ -Phenyl	65	113	3	3,5-di-Cl-phenyl
37	1	2-SCH ₃ -Phenyl		115	1	2-morpholino-4-CH ₃ -phenyl
· · ·	-	3,*		-**	-	

TABLE 15-continued

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Entry	n	R^2		Entry	n	\mathbb{R}^2
116	2	2-morpholino-4-CH ₃ -phenyl		38	2	2-SCH ₃ -Phenyl
117	3	2-morpholino-4-CH ₃ -phenyl	5	39	3	2-SCH ₃ -Phenyl
118	1	2-morpholino-4-CN-phenyl		40	1	3-SCH ₃ -Phenyl
119	2	2-morpholino-4-CN-phenyl		41	2	3-SCH ₃ -Phenyl
120	3	2-morpholino-4-CN-phenyl		42	3	3-SCH ₃ -Phenyl
121	1	2-morpholino-4-OH-phenyl		43	1	4-SCH ₃ -Phenyl
122	2	1 1 1		44	2	
	3	2-morpholino-4-OH-phenyl			3	4-SCH ₃ -Phenyl
123		2-morpholino-4-OH-phenyl	10	45		4-SCH ₃ -Phenyl
124	1	2,3-dimethylpyridin-4-yl		46	1	2-SO ₂ CH ₃ -Phenyl
125	2	2,3-dimethylpyridin-4-yl		47	2	2-SO ₂ CH ₃ -Phenyl
126	3	2,3-dimethylpyridin-4-yl		48	3	2-SO ₂ CH ₃ -Phenyl
127	1	3,6-dimethylpyridin-4-yl		49	1	3-SO ₂ CH ₃ -Phenyl
128	2	3,6-dimethylpyridin-4-yl		50	2	3-SO ₂ CH ₃ -Phenyl
129	3	3,6-dimethylpyridin-4-yl	15	51	3	3-SO ₂ CH ₃ -Phenyl
			13	52	1	4-SO ₂ CH ₃ -Phenyl
				53	2	4-SO ₂ CH ₃ -Phenyl
Exemplary en	nbodimei	nts include compounds having the		54	3	4-SO ₂ CH ₃ -Phenyl
				55	1	2-SO ₂ NH ₂ -Phenyl
	or a pnar	maceutically acceptable salt form		56	2	2-SO ₂ NH ₂ -Phenyl
ereof:				57	3	2-SO ₂ NH ₂ -Phenyl
			20	58	1	3-SO ₂ NH ₂ -Phenyl
				59	2	3-SO ₂ NH ₂ -Phenyl
		(XIII)		60	3	3-SO ₂ NH ₂ -Phenyl
	Ö	ζ/		61	1	4-SO ₂ NH ₂ -Phenyl
				62	2	4-SO ₂ NH ₂ -Phenyl
/ \	人			63	3	$4-SO_2NH_2$ -Phenyl
1 /			25	64	1	2-CONH ₂ -Phenyl
\mathcal{L}	γ	. ^ .		65	2	2-CONH ₂ -Phenyl
~ \		$N-R^2$		66	3	2-CONH ₂ -Phenyl
_	一、、	N IN		67	1	3-CONH ₂ -Phenyl
	M	-N		68	2	3-CONH ₂ -Phenyl
	\ <i>I</i> n			69	3	
						3-CONH ₂ -Phenyl
		_	30	70	1	4-CONH ₂ -Phenyl
erein non-lin	niting ex	amples of R ² and n are defined		71	2	4-CONH ₂ -Phenyl
rein below in				72	3	4-CONH ₂ -Phenyl
iem below m	Table 13	·•		73	1	2-Br-Phenyl
				74	2	2-Br-Phenyl
	Т	TABLE 15		75	3	2-Br-Phenyl
		THE IS	25	76	1	3-Br-Phenyl
Enter		\mathbb{R}^2	35	77	2	3-Br-Phenyl
Entry	n	K		78	3	3-Br-Phenyl
1		2-CF ₃ -Phenyl		79	1	2,3-di-CH ₃ -phenyl
1	1			80	2	2,3-di-CH ₃ -phenyl
2	2	2-CF ₃ -Phenyl		81	3	
3	3	2-CF ₃ -Phenyl				2,3-di-CH ₃ -phenyl
4	1	3-CF ₃ -Phenyl	40	82	1	2,4-di-CH ₃ -phenyl
		3-CF ₃ -Phenyl		83	2	2,4-di-CH ₃ -phenyl
5	2			84	3	2,4-di-CH ₃ -phenyl
6	2 3	3-CF ₃ -Phenyl				2,5-di-CH ₃ -phenyl
		3-CF ₃ -Phenyl 4-CF ₃ -Phenyl		85	1	
6 7	3 1				1 2	2,5-di-CH ₃ -phenyl
6 7 8	3 1 2	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl		85		2,5-di-CH ₃ -phenyl
6 7 8 9	3 1 2 3	$4-CF_3$ -Phenyl $4-CF_3$ -Phenyl $4-CF_3$ -Phenyl		85 86	2	
6 7 8 9 10	3 1 2 3 1	$4\text{-}\mathrm{CF}_3\text{-}\mathrm{Phenyl}$ $4\text{-}\mathrm{CF}_3\text{-}\mathrm{Phenyl}$ $4\text{-}\mathrm{CF}_3\text{-}\mathrm{Phenyl}$ $2\text{-}\mathrm{NH}_2\text{-}\mathrm{Phenyl}$	45	85 86 87 88	2 3 1	$2,5$ -di- CH_3 -phenyl $2,5$ -di- CH_3 -phenyl $2,6$ -di- CH_3 -phenyl
6 7 8 9 10 11	3 1 2 3 1 2	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl	45	85 86 87 88 89	2 3 1 2	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl
6 7 8 9 10 11 12	3 1 2 3 1 2 3	$4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl}$ $4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl}$ $4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl}$ $2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl}$ $2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl}$ $2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl}$	45	85 86 87 88 89 90	2 3 1 2 3	2.5 -di- $\mathrm{CH_3}$ -phenyl 2.5 -di- $\mathrm{CH_3}$ -phenyl 2.6 -di- $\mathrm{CH_3}$ -phenyl 2.6 -di- $\mathrm{CH_3}$ -phenyl 2.6 -di- $\mathrm{CH_3}$ -phenyl 2.6 -di- $\mathrm{CH_3}$ -phenyl
6 7 8 9 10 11 12	3 1 2 3 1 2 3 1	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \end{array}$	45	85 86 87 88 89 90	2 3 1 2 3 1	$2,5$ -di- $\mathrm{CH_3}$ -phenyl $2,5$ -di- $\mathrm{CH_3}$ -phenyl $2,6$ -di- $\mathrm{CH_3}$ -phenyl $2,6$ -di- $\mathrm{CH_3}$ -phenyl $2,6$ -di- $\mathrm{CH_3}$ -phenyl $3,4$ -di- $\mathrm{CH_3}$ -phenyl
6 7 8 9 10 11 12 13 14	3 1 2 3 1 2 3 1 2	$4-CF_3$ -Phenyl $4-CF_3$ -Phenyl $4-CF_3$ -Phenyl $2-NH_2$ -Phenyl $2-NH_2$ -Phenyl $2-NH_2$ -Phenyl $3-NH_2$ -Phenyl $3-NH_2$ -Phenyl $3-NH_2$ -Phenyl	45	85 86 87 88 89 90 91 92	2 3 1 2 3 1 2	2,5-di- $\mathrm{CH_{3}}$ -phenyl 2,5-di- $\mathrm{CH_{3}}$ -phenyl 2,6-di- $\mathrm{CH_{3}}$ -phenyl 2,6-di- $\mathrm{CH_{3}}$ -phenyl 2,6-di- $\mathrm{CH_{3}}$ -phenyl 3,4-di- $\mathrm{CH_{3}}$ -phenyl 3,4-di- $\mathrm{CH_{3}}$ -phenyl
6 7 8 9 10 11 12 13 14	3 1 2 3 1 2 3 1 2 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl	45	85 86 87 88 89 90 91 92 93	2 3 1 2 3 1 2 3	$2,5$ -di- CH_3 -phenyl $2,5$ -di- CH_3 -phenyl $2,6$ -di- CH_3 -phenyl $2,6$ -di- CH_3 -phenyl $2,6$ -di- CH_3 -phenyl $3,4$ -di- CH_3 -phenyl $3,4$ -di- CH_3 -phenyl $3,4$ -di- CH_3 -phenyl $3,4$ -di- CH_3 -phenyl
6 7 8 9 10 11 12 13 14 15	3 1 2 3 1 2 3 1 2 3 1 2 3 1	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ \end{array}$		85 86 87 88 89 90 91 92 93 94	2 3 1 2 3 1 2 3 1	2,5-di- $\mathrm{CH_3}$ -phenyl 2,5-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 3,4-di- $\mathrm{CH_3}$ -phenyl 3,4-di- $\mathrm{CH_3}$ -phenyl 3,5-di- $\mathrm{CH_3}$ -phenyl
6 7 8 9 10 11 12 13 14	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \end{array}$	45 50	85 86 87 88 89 90 91 92 93 94	2 3 1 2 3 1 2 3 1 2	2,5-di- $\mathrm{CH_3}$ -phenyl 2,5-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 3,4-di- $\mathrm{CH_3}$ -phenyl 3,4-di- $\mathrm{CH_3}$ -phenyl 3,5-di- $\mathrm{CH_3}$ -phenyl 3,5-di- $\mathrm{CH_3}$ -phenyl
6 7 8 9 10 11 12 13 14 15	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ \end{array}$		85 86 87 88 89 90 91 92 93 94 95 96	2 3 1 2 3 1 2 3 1 2 3 1 2 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
6 7 8 9 10 11 12 13 14 15 16 17	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \end{array}$		85 86 87 88 89 90 91 92 93 94	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	2,5-di- $\mathrm{CH_3}$ -phenyl 2,5-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 2,6-di- $\mathrm{CH_3}$ -phenyl 3,4-di- $\mathrm{CH_3}$ -phenyl 3,4-di- $\mathrm{CH_3}$ -phenyl 3,5-di- $\mathrm{CH_3}$ -phenyl 3,5-di- $\mathrm{CH_3}$ -phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \end{array}$		85 86 87 88 89 90 91 92 93 94 95 96	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl		85 86 87 88 89 90 91 92 93 94 95 96	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 2	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \end{array}$		85 86 87 88 89 90 91 92 93 94 95 96 97 98	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 3 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 1 2 3 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 1 2 3 1 1 2 3 1 1 1 2 3 1 1 1 1	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{Bu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{Bu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \end{array}$	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	3 1 2 3 2 3	$\begin{array}{l} 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{CF_3}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 4\text{-}\mathrm{NH_2}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 2\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{Phenyl} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}\mathrm{tBu}\text{-}\mathrm{tBu}\text{-}\mathrm{tBu} \\ 3\text{-}$		85 86 87 88 89 90 91 92 93 94 95 96 97 98 99	2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 3 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 2 3 1 2 2 3 1 2 3 1 2 2 3 1 2 3 1 2 3 1 2 3 1 2 2 2 3 3 1 2 2 2 2	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl
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6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 1 2 3 1 2 3 1 2 3 1 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 3 1	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 1 2 3 1 1 1 2 3 1 2 3 1 3 1	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl
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6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26	3 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 3 1 1 2 3 3 1 2 3 3 1 2 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 1 2 3 3 3 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-tBu-Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106	2 3 1 1 2 3 1 2 3 1 2 3 1 1 2 3 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 2 3 1 1 2 3 1 3 1	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,5-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27	3 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 1 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-tBu-Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105	2 3 1 2 2 3 1 2 3 1 2 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 2 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl
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6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 31	3 1 2 3 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-Bu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-tBu-Phenyl 2-NO ₂ -Phenyl 2-NO ₂ -Phenyl 3-NO ₂ -Phenyl 3-NO ₂ -Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108	2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-Cl ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 1 2 3 3 3 1 2 3 3 3 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-tBu-Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110	2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-D-Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110	2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 1 2 3 3 3 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 3,6-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,5-di-Cl-phenyl 3,5-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35	3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 2 3	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-TBu-Phenyl 4-NO ₂ -Phenyl 3-NO ₂ -Phenyl 3-NO ₂ -Phenyl 3-NO ₂ -Phenyl 4-NO ₂ -Phenyl 4-NO ₂ -Phenyl	50 55 60	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111	2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 2 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 3,6-di-Cl-phenyl 3,6-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,4-di-Cl-phenyl 3,5-di-Cl-phenyl
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 2-tBu-Phenyl 2-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 3-tBu-Phenyl 4-D-Phenyl	50	85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110	2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 3 3	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl 2,3-di-Cl-phenyl 2,3-di-Cl-phenyl 2,4-di-Cl-phenyl 2,4-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,5-di-Cl-phenyl 2,6-di-Cl-phenyl 2,6-di-Cl-phenyl 3,6-di-Cl-phenyl 3,4-di-Cl-phenyl 3,5-di-Cl-phenyl

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	TAB	LE 15-contin	nued	TABLE 16-continued				tinued	
Entry	n		R ²		Entry	n	R^{1a}	R^{1b}	R^2
116			olino-4-CH ₃ -phenyl	_	38	2 3	CH ₃	CH ₃	2-tBu-Phenyl
117 118			olino-4-CH ₃ -phenyl olino-4-CN-phenyl	5		3 1	CH ₃ CH ₂ CH ₃	CH₃ CH₂CH₃	2-tBu-Phenyl 2-tBu-Phenyl
119			olino-4-CN-phenyl			2	CH ₂ CH ₃	CH ₂ CH ₃	2-tBu-Phenyl
120			olino-4-CN-phenyl		42	3	CH ₂ CH ₃	CH ₂ CH ₃	2-tBu-Phenyl
121			olino-4-OH-phenyl		43	1	CH_3	CH ₃	3-tBu-Phenyl
122			olino-4-OH-phenyl		44	2	CH_3	CH ₃	3-tBu-Phenyl
123			olino-4-OH-phenyl	10		3	CH_3	CH_3	3-tBu-Phenyl
124			ethylpyridin-4-yl		46	1	CH_2CH_3	CH_2CH_3	3-tBu-Phenyl
125			ethylpyridin-4-yl			2	CH ₂ CH ₃	CH ₂ CH ₃	3-tBu-Phenyl
126			ethylpyridin-4-yl			3	CH ₂ CH ₃	CH ₂ CH ₃	3-tBu-Phenyl
127 128			ethylpyridin-4-yl ethylpyridin-4-yl			1 2	CH ₃ CH ₃	CH ₃ CH ₃	4-tBu-Phenyl 4-tBu-Phenyl
129			ethylpyridin-4-yl			3	CH ₃	CH ₃	4-tBu-Phenyl
		-,-		15		1	CH ₂ CH ₃	CH ₂ CH ₃	4-tBu-Phenyl
					53	2	CH ₂ CH ₃	CH ₂ CH ₃	4-tBu-Phenyl
Exemplary	embodim	ents include	compounds having the		54	3	CH_2CH_3	CH ₂ CH ₃	4-tBu-Phenyl
			acceptable salt form			1	CH_3	CH_3	2-NO ₂ -Phenyl
reof:	or a pine		acceptance can remi			2	CH_3	CH ₃	2-NO ₂ -Phenyl
1001.				20		3	CH ₃	CH ₃	2-NO ₂ -Phenyl
					58 59	1 2	CH ₂ CH ₃	CH ₂ CH ₃	2-NO ₂ -Phenyl
					60	3	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-NO ₂ -Phenyl 2-NO ₂ -Phenyl
	0		(VI)			1	CH ₂ CH ₃	CH ₂ CH ₃	3-NO ₂ -Phenyl
,	0 				62	2	CH ₃	CH ₃	3-NO ₂ -Phenyl
R^{1a}	L L				63	3	CH ₃	CH ₃	3-NO ₂ -Phenyl
	\ 0			25	64	1	CH₂CH₃	CH ₂ CH ₃	3-NO ₂ -Phenyl
\mathbb{R}^{1b}	Ĭ		$-R^3$		65	2	$\mathrm{CH_{2}CH_{3}}$	$\mathrm{CH_{2}CH_{3}}$	3-NO ₂ -Phenyl
_	_($/$ $/$ $^{\text{N}}$				3	CH_2CH_3	CH_2CH_3	3-NO ₂ -Phenyl
	X	N, /				1	CH ₃	CH ₃	4-NO ₂ -Phenyl
	(I_n)	~			68	2	CH ₃	CH ₃	4-NO ₂ -Phenyl
						1	CH₃ CH₂CH₃	CH₃ CH₂CH₃	4-NO ₂ -Phenyl 4-NO ₂ -Phenyl
				20					
	1	1 61	$a \mid a \mid b \mid b \mid b \mid a \mid a \mid b \mid b \mid a \mid a$	30		2	CH ₂ CH ₂	CH ₂ CH ₂	4-NU ₂ -Phenvi
			R^{1a} , R^{1b} , R^3 and n are	30		2	CH₂CH₃ CH₂CH₂	CH ₂ CH ₃ CH ₂ CH ₂	4-NO₂-Phenyl 4-NO₂-Phenyl
erein non- ined hereir			R^{1a} , R^{1b} , R^3 and n are	30	71 72	2 3 1	CH_2CH_3	CH_2CH_3	4-NO ₂ -Phenyl
			\mathbf{R}^{1a} , \mathbf{R}^{1b} , \mathbf{R}^{3} and \mathbf{n} are	30	71 72 73 74	1 2			
		Table 16.	\mathbf{R}^{1a} , \mathbf{R}^{1b} , \mathbf{R}^3 and \mathbf{n} are	30	71 72 73 74 75	1 2 3	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl
		TABLE 16.			71 72 73 74 75 76	1 2 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	$4-NO_2$ -Phenyl $2-SCH_3$ -Phenyl $2-SCH_3$ -Phenyl $2-SCH_3$ -Phenyl $2-SCH_3$ -Phenyl
		Table 16.	R^{1a} , R^{1b} , R^3 and n are	35	71 72 73 74 75 76 77	1 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl
ined hereir	n below ir	TABLE 16 R ^{1b}	\mathbb{R}^2		71 72 73 74 75 76 77 78	1 2 3 1 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl
Entry n	R ^{1a} CH ₃	TABLE 16 R ^{1b} CH ₃	R ² 2-CF ₃ -Phenyl		71 72 73 74 75 76 77 78 79	1 2 3 1 2 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2	R ^{1α} CH ₃ CH ₃	TABLE 16 R ^{1b} CH ₃ CH ₃	R ² 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		71 72 73 74 75 76 77 78 79 80	1 2 3 1 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3	R ^{1\alpha} CH ₃ CH ₃ CH ₃	TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃	R ² 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		71 72 73 74 75 76 77 78 79 80 81	1 2 3 1 2 3 1 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1	R ^{1a} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		71 72 73 74 75 76 77 78 79 80 81 82	1 2 3 1 2 3 1 2 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl	35	71 72 73 74 75 76 77 78 79 80 81 82	1 2 3 1 2 3 1 2 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	TABLE 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl 2-CF ₃ -Phenyl	35	71 72 73 74 75 76 77 78 79 80 81 82 83 84	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 3 4 1 1 5 2 6 3	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl	35	71 72 73 74 75 76 77 78 79 80 81 82 83 84 85	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 1 5 2 6 6 3 7 1 8 2 9 3	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 3-CF ₃ -Phenyl 3-CF ₃ -Phenyl	35	71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 1 5 2 6 3 7 1 8 2 9 3 10 1	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	TABLE 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₃ CH ₄ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 3-CF ₃ -Phenyl 3-CF ₃ -Phenyl 3-CF ₃ -Phenyl	35 40	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87	1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 3 1 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₄ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₄ CH ₄ CH ₅	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 1 5 2 6 3 7 1 8 2 9 3 10 1	R La CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	TABLE 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₄ CH ₃ CH ₅	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl	35	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88	1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 3 3 1 2 2 3 3 3 1 2 2 3 3 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₅ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 1 2 12 3	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl	35 40	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88	1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₆ CH ₆ CH ₇	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1	R ^{1a} CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl	35 40	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90	1 2 3 1 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 1 1 2 2 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl	35 40	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92	1 2 3 1 2 3 1 2 2 3 3 1 2 2 3 3 3 1 2 2 3 3 3 1 2 2 3 3 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3	R ¹ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl	35 40	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93	1 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 1 2 2 3 3 1 1 2 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₅ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1	R La CH3 CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH2CH3 CH3 CH3 CH4	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₅ CH ₆ CH ₆ CH ₇ CH ₇ CH ₇ CH ₈ CH ₇ CH ₈ CH ₈ CH ₈ CH ₉ CH ₈ CH ₉ CH ₈ CH ₉ CH ₉ CH ₉ CH ₉ CH ₉ CH ₉	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93	1 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 2 2 3 1 1 2 2 3 3 1 1 2 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2	R ¹ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl 4-CF ₃ -Phenyl	35 40	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 2 3 3 1 3 3 3 1 3 3 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₅ CH ₅ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₄ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 1 14 2 15 3 16 1 17 2 18 3 19 1	R ^{1a} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₅ CH ₆ CH ₆ CH ₇ CH ₇ CH ₇ CH ₈ CH ₇ CH ₈ CH ₈ CH ₈ CH ₉ CH ₈ CH ₉	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97	1 2 3 1 2 3 1 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3 1 2 2 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅	CH2CH3 CH3 CH4 CH3 CH4 CH5 CH5 CH5 CH5 CH5 CH6 CH6 CH6 CH6 CH6 CH6 CH6 CH7	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 3 4 1 1 5 2 6 3 7 1 8 2 9 3 3 10 1 11 1 2 12 3 13 1 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2	R ¹ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98	1 2 3 1 2 3 1 2 3 1 2 3 3 1 2 2 3 1 2	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₅ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₅ CH ₅ CH ₅ CH ₆ CH ₇	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1	R ld CH3 CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH3 CH2CH3 CH3 CH3 CH3	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 3 1 3 2 3 3 1 3 3 3 1 3 3 3 1 3 3 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1	R 1cd Selow in R 1cd	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₅ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₄ CH ₃ CH ₄ CH ₄ CH ₅	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 1 2 3 3 1 1 2 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1 23 2	R la CH3	Table 16. TABLE 16 R1b CH3 CH3 CH4 CH3 CH2CH3 CH4 CH3 CH4 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99	1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 2 3 1 1 2 3 3 1 1 2 3 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₄ CH ₃ CH ₄ CH ₅	CH2CH3 CH3CH3 CH4 CH4 CH5	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1 23 2 24 3	R ^{1d} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102	1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 2 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 1 3 3 3 1 3 3 3 1 3 3 3 1 3 3 3 1 3 3 3 3 1 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₄ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₅ CH	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1	R la CH3 CH3 CH4 CH3 CH3 CH2 CH3 CH3 CH2 CH3 CH3 CH2 CH3 CH3 CH2 CH3	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103	1 2 3 1 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₅ CH ₆ CH ₇	CH ₂ CH ₃ CH ₃ CH ₄ CH ₅ C	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1 23 2 24 3 25 1 26 2	R lea CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104	1 2 3 1 2 3	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ C	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1 23 2 24 3 25 1 26 2 27 3	R 1d CH3 CH3 CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH2CH3 CH3 CH2CH3 CH3 CH2CH3 CH3 CH3 CH3 CH3 CH3 CH2CH3 CH3 CH2CH3 CH3 CH3 CH2CH3 CH3 CH2CH3 CH3 CH3 CH3 CH3 CH3 CH3 CH3 CH3 CH3	Table 16. TABLE 16 R1b CH3 CH3 CH4 CH3 CH2CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4 CH4 CH4 CH4 CH4 CH4 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105	1 2 3 1 3 1	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₅ CH ₆ CH ₇	CH ₂ CH ₃ CH ₃ CH ₄ CH ₅ C	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl
Entry n 1	R lea CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH	Table 16. Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₄ CH ₃ CH ₄ CH ₃ CH ₄ CH ₃ CH ₄ CH ₄ CH ₄ CH ₅	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45 50	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 106 106 106 106 106 106 106 106 106	$\begin{smallmatrix} 1 & 2 & 3 & 1 & 2 & 3 & 1 & 2 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅	CH2CH3 CH3CH3 CH4CH3 CH4CH3 CH2CH3 CH2CH3 CH4CH3 CH4CH3 CH4CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH4CH3 CH2CH3 CH4CH3 CH4	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
Entry n 1	R la CH3 CH3 CH3 CH2 CH3 CH3 CH2 CH3 CH3 CH2 CH3 CH2 CH3 CH2 CH3 CH3 CH2 CH3 CH3 CH2 CH3	Table 16. TABLE 16 R1b CH3 CH3 CH4 CH3 CH2CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4 CH4 CH4 CH4 CH4 CH4 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 107 108	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₄ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₅ CH ₆ CH ₇ CH	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1 23 2 24 3 25 1 26 2 27 3 28 1 29 2 30 3 31 1	R ¹ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH	Table 16. TABLE 16 R ^{1b} CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45 50	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 106 107 108 108 108 108 108 108 108 108 108 108	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₄ CH	CH2CH3 CH3CH3 CH4CH3 CH4CH3 CH2CH3 CH2CH3 CH4CH3 CH4CH3 CH4CH3 CH4CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH4CH3 CH4CH4 CH	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
Entry n 1	R lea CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH	Table 16. TABLE 16 R1b CH3 CH3 CH4 CH4 CH4 CH3 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl	35 40 45 50	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 108 108 108 108 108 108 108 108 108	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH	CH2CH3 CH3CH3 CH4 CH3 CH4 CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH4 CH4 CH4 CH5 CH4 CH5 CH5 CH6 CH5 CH6 CH6 CH7 CH6 CH7	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
Entry n 1	R ld CH3 CH3 CH4 CH4	Table 16. TABLE 16 R1b CH3 CH3 CH2CH3 CH3 CH2CH3 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH4 CH3 CH4 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl 4-NH ₂ -Phenyl	35 40 45 50	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 108 108 108 108 108 108 108 108 108	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	CH2CH3 CH3CH3 CH4 CH4 CH4 CH5 CH5 CH5 CH5 CH5 CH5 CH5 CH6 CH6 CH6 CH6 CH6 CH6 CH6 CH7	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 3 4 1 1 5 2 6 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 2 24 3 22 1 23 2 2 24 3 22 1 23 2 2 27 3 28 1 26 2 27 3 28 1 29 2 23 3 3 3 1 1 3 2 2 3 3 3 3 3 3 3 3 3	R lea CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	Table 16. Table 16. Table 16. R1b CH3 CH3 CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH2CH3 CH3 CH2CH3 CH4 CH3 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl	35 40 45 50	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₄ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₅ CH	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl
Entry n 1 1 2 2 3 3 4 1 5 2 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 21 3 22 1 23 2 24 3 25 1 26 2 27 3 28 1 29 2 20 3 31 1 32 2 30 3 31 1 32 2 33 3 34 1 35 2	R 1d CH3 CH3 CH4 CH3 CH4 CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH2CH3 CH3 CH2CH3 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH3 CH4 CH4	Table 16. TABLE 16 R1b CH3 CH3 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl	3540455060	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH	CH ₂ CH ₃ CH ₃ CH ₄ CH ₃ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃
Entry n 1 1 2 2 3 3 3 4 1 1 5 2 6 6 3 7 1 8 2 9 3 10 1 11 2 12 3 13 1 1 14 2 15 3 16 1 17 2 18 3 19 1 20 2 2 24 3 22 1 23 2 2 24 3 22 1 23 2 2 27 3 28 1 26 2 27 3 28 1 29 2 23 3 3 3 1 1 3 2 2 3 3 3 3 3 3 3 3 3	R lea CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₂ CH ₃	Table 16. Table 16. Table 16. R1b CH3 CH3 CH3 CH2CH3 CH2CH3 CH2CH3 CH3 CH2CH3 CH3 CH2CH3 CH4 CH3 CH4	R ² 2-CF ₃ -Phenyl 3-CF ₃ -Phenyl 4-CF ₃ -Phenyl 2-NH ₂ -Phenyl 3-NH ₂ -Phenyl 4-NH ₂ -Phenyl	35 40 45 50	71 72 73 74 75 76 77 78 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114	$\begin{smallmatrix} 1 & 2 & 3 & 1 $	CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₃ CH ₃ CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₃ CH ₄ CH ₅ CH ₂ CH ₃ CH ₂ CH ₃ CH ₅ CH	4-NO ₂ -Phenyl 2-SCH ₃ -Phenyl 3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl

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TABLE 16-continued

76 TABLE 16-continued

	TABLE 10-continued					TABLE 10-continued				
Entry n	\mathbb{R}^{1a}	\mathbb{R}^{1b}	R ²		Entry	n	R^{1a}	R^{1b}	\mathbb{R}^2	
116 2	CH ₃	CH ₃	3-SO ₂ NH ₂ -Phenyl	5	194	2	CH ₃	CH ₃	2,3-di-Cl-phenyl	
117 3 118 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	3-SO ₂ NH ₂ -Phenyl 3-SO ₂ NH ₂ -Phenyl	3	195	3	CH_3	CH_3	2,3-di-Cl-phenyl	
119 2	CH ₂ CH ₃	CH ₂ CH ₃	3-SO ₂ NH ₂ -Phenyl		196	1	CH ₂ CH ₃	CH ₂ CH ₃	2,3-di-Cl-phenyl	
120 3	CH ₂ CH ₃	CH ₂ CH ₃	3-SO ₂ NH ₂ -Phenyl		197 198	2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2,3-di-Cl-phenyl 2,3-di-Cl-phenyl	
121 1 122 2	CH ₃ CH ₃	CH ₃ CH ₃	4-SO ₂ NH ₂ -Phenyl 4-SO ₂ NH ₂ -Phenyl		199	1	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-Cl-phenyl	
123 3	CH ₃	CH ₃	4-SO ₂ NH ₂ -Phenyl	10	200	2	CH ₃	CH ₃	2,4-di-Cl-phenyl	
124 1	CH ₂ CH ₃	CH ₂ CH ₃	4-SO ₂ NH ₂ -Phenyl	10	201	3	CH ₃	CH ₃	2,4-di-Cl-phenyl	
125 2	CH ₂ CH ₃	CH ₂ CH ₃	4-SO ₂ NH ₂ -Phenyl		202	1	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-Cl-phenyl	
126 3 127 1	CH ₂ CH ₃	CH ₂ CH ₃ CH ₃	4-SO ₂ NH ₂ -Phenyl 2-CONH ₂ -Phenyl		203	2	$\mathrm{CH_{2}CH_{3}}$	CH_2CH_3	2,4-di-Cl-phenyl	
127 1	CH ₃ CH ₃	CH ₃	2-CONH ₂ -Phenyl		204	3	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-Cl-phenyl	
129 3	CH ₃	CH ₃	2-CONH ₂ -Phenyl	15	205	1	CH ₃	CH ₃	2,5-di-Cl-phenyl	
130 1	CH_2CH_3	CH_2CH_3	2-CONH ₂ -Phenyl	13	206	2	CH ₃	CH ₃	2,5-di-Cl-phenyl	
131 2 132 3	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2-CONH ₂ -Phenyl 2-CONH ₂ -Phenyl		207 280	1	CH₃ CH₂CH₃	CH₃ CH₂CH₃	2,5-di-Cl-phenyl 2,5-di-Cl-phenyl	
132 3	CH_2CH_3	CH ₃	3-CONH ₂ -Phenyl		209	2	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-Cl-phenyl	
134 2	CH ₃	CH ₃	3-CONH ₂ -Phenyl		210	3	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-Cl-phenyl	
135 3	CH ₃	CH ₃	3-CONH ₂ -Phenyl	20	211	1	CH ₃	CH ₃	2,6-di-Cl-phenyl	
136 1 137 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3-CONH ₂ -Phenyl 3-CONH ₂ -Phenyl	20	212	2	CH_3	CH_3	2,6-di-Cl-phenyl	
138 3	CH ₂ CH ₃	CH ₂ CH ₃	3-CONH ₂ -Phenyl		213	3	CH_3	CH_3	2,6-di-Cl-phenyl	
139 1	CH_3	CH ₃	4-CONH ₂ -Phenyl		214	1	CH ₂ CH ₃	CH ₂ CH ₃	2,6-di-Cl-phenyl	
140 2	CH ₃	CH ₃	4-CONH ₂ -Phenyl		215	2	CH ₂ CH ₃	CH ₂ CH ₃	2,6-di-Cl-phenyl	
141 3 142 1	CH₃ CH₂CH₃	CH ₃ CH ₂ CH ₃	4-CONH ₂ -Phenyl 4-CONH ₂ -Phenyl	25	216 217	3 1	CH ₂ CH ₃	CH ₂ CH ₃ CH ₃	2,6-di-Cl-phenyl 3,4-di-Cl-phenyl	
143 2	CH ₂ CH ₃	CH ₂ CH ₃	4-CONH ₂ -Phenyl	23	217	2	CH ₃ CH ₃	CH ₃	3,4-di-Cl-phenyl	
144 3	CH ₂ CH ₃	CH ₂ CH ₃	4-CONH ₂ -Phenyl		219	3	CH ₃	CH ₃	3,4-di-Cl-phenyl	
145 1	CH ₃	CH ₃	2-Br-Phenyl		220	1	CH ₂ CH ₃	CH ₂ CH ₃	3,4-di-Cl-phenyl	
146 2 147 3	CH ₃ CH ₃	CH_3 CH_3	2-Br-Phenyl 2-Br-Phenyl		221	2	CH ₂ CH ₃	CH ₂ CH ₃	3,4-di-Cl-phenyl	
148 1	CH ₂ CH ₃	CH ₂ CH ₃	2-Br-Phenyl	30	222	3	$\mathrm{CH_{2}CH_{3}}$	$\mathrm{CH_{2}CH_{3}}$	3,4-di-Cl-phenyl	
149 2	CH ₂ CH ₃	CH ₂ CH ₃	2-Br-Phenyl	50	223	1	CH_3	CH_3	3,5-di-Cl-phenyl	
150 3	CH ₂ CH ₃	CH ₂ CH ₃	2-Br-Phenyl		224	2	CH ₃	CH ₃	3,5-di-Cl-phenyl	
151 1 152 2	CH ₃ CH ₃	CH ₃ CH ₃	3-Br-Phenyl 3-Br-Phenyl		225	3	CH ₃	CH ₃	3,5-di-Cl-phenyl	
153 3	CH ₃	CH ₃	3-Br-Phenyl		226 227	1 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3,5-di-Cl-phenyl 3,5-di-Cl-phenyl	
154 1	CH_2CH_3	CH_2CH_3	3-Br-Phenyl	35	228	3	CH ₂ CH ₃	CH ₂ CH ₃	3,5-di-Cl-phenyl	
155 2 156 3	CH ₂ CH ₃	CH ₂ CH ₃	3-Br-Phenyl		229	1	CH ₃	CH ₃	2-morpholino-4-CH ₃ -phenyl	
156 3 157 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	3-Br-Phenyl 2,3-di-CH ₃ -phenyl		230	2	CH_3	CH_3	2-morpholino-4-CH ₃ -phenyl	
158 2	CH ₃	CH ₃	2,3-di-CH ₃ -phenyl		231	3	CH_3	CH_3	2-morpholino-4-CH ₃ -phenyl	
159 3	CH ₃	CH ₃	2,3-di-CH ₃ -phenyl		232	1	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CH ₃ -phenyl	
160 1 161 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	2,3-di-CH ₃ -phenyl 2,3-di-CH ₃ -phenyl	40	233	2	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CH ₃ -phenyl	
162 3	CH ₂ CH ₃	CH ₂ CH ₃	2,3-di-CH ₃ -phenyl		234 235	3 1	CH ₂ CH ₃ CH ₃	CH ₂ CH ₃ CH ₃	2-morpholino-4-CH ₃ -phenyl 2-morpholino-4-CN-phenyl	
163 1	$\mathrm{CH_3}$	$\widetilde{\mathrm{CH}_{3}}$	2,4-di-CH ₃ -phenyl		236	2	CH ₃	CH ₃	2-morpholino-4-CN-phenyl	
164 2	CH ₃	CH ₃	2,4-di-CH ₃ -phenyl		237	3	CH ₃	CH ₃	2-morpholino-4-CN-phenyl	
165 3 166 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2,4-di-CH ₃ -phenyl 2,4-di-CH ₃ -phenyl		238	1	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CN-phenyl	
167 2	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-CH ₃ -phenyl	45	239	2	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-CN-phenyl	
168 3	CH ₂ CH ₃	CH ₂ CH ₃	2,4-di-CH ₃ -phenyl		240	3	$\mathrm{CH_{2}CH_{3}}$	CH_2CH_3	2-morpholino-4-CN-phenyl	
169 1 170 2	CH ₃	CH ₃	2,5-di-CH ₃ -phenyl		241	1	CH ₃	CH ₃	2-morpholino-4-OH-phenyl	
170 2 171 3	CH ₃ CH ₃	CH ₃ CH ₃	2,5-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl		242	2	CH ₃	CH ₃	2-morpholino-4-OH-phenyl	
172 1	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-CH ₃ -phenyl		243 244	3 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	2-morpholino-4-OH-phenyl 2-morpholino-4-OH-phenyl	
173 2	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-CH ₃ -phenyl	50	245	2	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-OH-phenyl	
174 3 175 1	CH ₂ CH ₃	CH ₂ CH ₃	2,5-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl		246	3	CH ₂ CH ₃	CH ₂ CH ₃	2-morpholino-4-OH-phenyl	
176 2	CH ₃ CH ₃	CH ₃ CH ₃	2,6-di-CH ₃ -phenyl		247	1	CH ₃	CH ₃	2,3-dimethylpyridin-4-yl	
177 3	CH ₃	CH_3	2,6-di-CH ₃ -phenyl		248	2	CH_3	CH_3	2,3-dimethylpyridin-4-yl	
178 1	CH ₂ CH ₃	CH ₂ CH ₃	2,6-di-CH ₃ -phenyl		249	3	CH_3	CH_3	2,3-dimethylpyridin-4-yl	
179 2 180 3	CH ₂ CH ₃ CH ₂ CH ₃	CH₂CH₃ CH₂CH₃	2,6-di-CH ₃ -phenyl 2,6-di-CH ₃ -phenyl	55	250	1	CH ₂ CH ₃	CH ₂ CH ₃	2,3-dimethylpyridin-4-yl	
181 1	CH ₂ CH ₃	CH ₃	3,4-di-CH ₃ -phenyl		251	2	CH ₂ CH ₃	CH ₂ CH ₃	2,3-dimethylpyridin-4-yl	
182 2	CH_3	CH_3	3,4-di-CH ₃ -phenyl		252	3	CH ₂ CH ₃	CH ₂ CH ₃	2,3-dimethylpyridin-4-yl 3,6-dimethy 1pyridin-4-yl	
183 3	CH ₃	CH ₃	3,4-di-CH ₃ -phenyl		253 254	1 2	CH ₃ CH ₃	CH ₃ CH ₃	3,6-dimethy 1pyridin-4-yl	
184 1 185 2	CH ₂ CH ₃ CH ₂ CH ₃	CH ₂ CH ₃ CH ₂ CH ₃	3,4-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl		255	3	CH ₃	CH ₃	3,6-dimethy 1pyridin-4-yl	
186 3	CH ₂ CH ₃	CH ₂ CH ₃	3,4-di-CH ₃ -phenyl	60	256	1	CH ₂ CH ₃	CH ₂ CH ₃	3,6-dimethy 1pyridin-4-yl	
187 1	CH_3	CH_3	3,5-di-CH ₃ -phenyl		257	2	CH ₂ CH ₃	CH ₂ CH ₃	3,63-dimethylpyridin-4-yl	
188 2	CH ₃	CH_3	3,5-di-CH ₃ -phenyl		258	3	CH ₂ CH ₃	CH ₂ CH ₃	3,6-dimethy 1pyridin-4-yl	
189 3 190 1	CH ₃ CH ₂ CH ₃	CH ₃ CH ₂ CH ₃	3,5-di-CH ₃ -phenyl 3,5-di-CH ₃ -phenyl							
191 2	CH ₂ CH ₃	CH ₂ CH ₃	3,5-di-CH ₃ -phenyl		Б		, ,,	,	1 11	
192 3	CH ₂ CH ₃	$\mathrm{CH_{2}CH_{3}}$	3,5-di-CH ₃ -phenyl	65					de compounds having the	
193 1	CH_3	CH_3	2,3-di-Cl-phenyl			(XI	V) or a ph	armaceutio	cally acceptable salt form	
					thereof:					

Exemplary embodiments include compounds having the formula (XIV) or a pharmaceutically acceptable salt form thereof:

TABLE 17-continued

		(VIII)			IABL	E 17-continued
O II		(XIV)	_	Entry	n	\mathbb{R}^2
人人				63	3	4-SO ₂ NH ₂ -Phenyl
LY '9)		5	64	1	2-CONH ₂ -Phenyl
\/	^	N - R^3		65	2	2-CONH ₂ -Phenyl
	LN.	\sim		66	3	2-CONH ₂ -Phenyl
,	\mathcal{T}_n	✓ · · ·		67 68	1	3-CONH_Phenyl
				68 69	2 3	3-CONH ₂ -Phenyl 3-CONH ₂ -Phenyl
	••	1 0 D3	10	70	1	4-CONH ₂ -Phenyl
		amples of R ³ and n are defined		71	2	4-CONH ₂ -Phenyl
in below in [Table 17			72	3	4-CONH ₂ -Phenyl
				73	1	2-Br-Phenyl
	Τ	ABLE 17		74 75	2	2-Br-Phenyl 2-Br-Phenyl
Entry	p	\mathbb{R}^2	15	76	1	3-Br-Phenyl
Entry	n	K		77	2	3-Br-Phenyl
1	1	2-CF ₃ -Phenyl		78	3	3-Br-Phenyl
2	2	2-CF ₃ -Phenyl		79	1	2,3-di-CH ₃ -phenyl
3 4	3 1	2-CF ₃ -Phenyl 3-CF ₃ -Phenyl		80	2	2,3-di-CH ₃ -phenyl
5	2	3-CF ₃ -Phenyl	20	81 82	3	2,3-di-CH ₃ -phenyl
6	3	3-CF ₃ -Phenyl		82 83	1 2	2,4-di-CH ₃ -phenyl 2,4-di-CH ₃ -phenyl
7	1	4-CF ₃ -Phenyl		84	3	2,4-di-CH ₃ -phenyl
8	2	4-CF ₃ -Phenyl		85	1	2,5-di-CH ₃ -phenyl
9 10	3 1	4-CF ₃ -Phenyl 2-NH ₂ -Phenyl		86	2	2,5-di-CH ₃ -phenyl
11	2	2-NH ₂ -Phenyl	25	87	3	2,5-di-CH ₃ -phenyl
12	3	2-NH ₂ -Phenyl		88	1	2,6-di-CH ₃ -phenyl
13	1	3-NH ₂ -Phenyl		89 90	2	2,6-di-CH ₃ -phenyl
14 15	2	3-NH ₂ -Phenyl		90 91	3 1	2,6-di-CH ₃ -phenyl 3,4-di-CH ₃ -phenyl
15 16	3 1	3-NH₂-Phenyl 4-NH₂-Phenyl		92	2	3,4-di-CH ₃ -phenyl
17	2	4-NH ₂ -Phenyl	30	93	3	3,4-di-CH ₃ -phenyl
18	3	4-NH ₂ -Phenyl		94	1	3,5-di-CH ₃ -phenyl
19	1	2-tBu-Phenyl		95	2	3,5-di-CH ₃ -phenyl
20 21	2 3	2-tBu-Phenyl 2-tBu-Phenyl		96	3	3,5-di-CH ₃ -phenyl
22	1	3-tBu-Phenyl		97 98	1 2	2,3-di-Cl-phenyl 2,3-di-Cl-phenyl
23	2	3-tBu-Phenyl	35	99	3	2,3-di-Cl-phenyl
24	3	3-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
25 26	1 2	4-tBu-Phenyl 4-tBu-Phenyl		101	2	2,4-di-Cl-phenyl
20 27	3	4-tBu-Phenyl		102	3	2,4-di-Cl-phenyl
28	1	2-NO ₂ -Phenyl		103	1	2,5-di-Cl-phenyl
29	2	2-NO ₂ -Phenyl	40	104	2	2,5-di-Cl-phenyl
30 31	3 1	2-NO ₂ -Phenyl 3-NO ₂ -Phenyl	-	105	3	2,5-di-Cl-phenyl
32	2	3-NO ₂ -Phenyl		106	1	2,6-di-Cl-phenyl
33	3	3-NO ₂ -Phenyl		107 108	2 3	2,6-di-Cl-phenyl 2,6-di-Cl-phenyl
34	1	4-NO ₂ -Phenyl		108	3 1	2,6-di-Cl-phenyl
35 36	2	4-NO ₂ -Phenyl	45	110	2	3,4-di-Cl-phenyl
36 37	3	4-NO ₂ -Phenyl	70	111	3	3,4-di-Cl-phenyl
37	1 2	2-SCH ₃ -Phenyl 2-SCH ₃ -Phenyl		112	1	3,5-di-Cl-phenyl
39	3	2-SCH ₃ -Phenyl		113	2	3,5-di-Cl-phenyl
40	1	3-SCH ₃ -Phenyl		114	3	3,5-di-Cl-phenyl
41 42	2	3-SCH ₃ -Phenyl	50	115	1	2-morpholino-4-CH ₃ -phenyl
42 43	3 1	3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl	50	116	2	2-morpholino-4-CH ₃ -phenyl
44	2	4-SCH ₃ -Phenyl		117	3	2-morpholino-4-CH ₃ -phenyl
45	3	4-SCH ₃ -Phenyl		118	1	2-morpholino-4-CN-phenyl
46	1	2-SO ₂ CH ₃ -Phenyl		119	2	2-morpholino-4-CN-phenyl
47 48	2	2-SO ₂ CH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl		120	3	2-morpholino-4-CN-phenyl
48 49	3 1	3-SO ₂ CH ₃ -Phenyl	55	121 122	1 2	2-morpholino-4-OH-phenyl 2-morpholino-4-OH-phenyl
50	2	3-SO ₂ CH ₃ -Phenyl		123	3	2-morpholino-4-OH-phenyl
51	3	3-SO ₂ CH ₃ -Phenyl		124	1	2,3-dimethylpyridin-4-yl
52 53	1	4-SO ₂ CH ₃ -Phenyl		125	2	2,3-dimethylpyridin-4-yl
53 54	2	4-SO ₂ CH ₃ -Phenyl 4-SO ₂ CH ₃ -Phenyl		126	3	2,3-dimethylpyridin-4-yl
55 55	3 1	2-SO ₂ CH ₃ -Phenyl	60	127	1	3,6-dimethylpyridin-4-yl
56	2	2-SO ₂ NH ₂ -Phenyl		128	2	3,6-dimethylpyridin-4-yl
57	3	2-SO ₂ NH ₂ -Phenyl		129	3	3,6-dimethylpyridin-4-yl
58 50	1	3-SO ₂ NH ₂ -Phenyl	_			
59 60	2	3-SO ₂ NH ₂ -Phenyl 3-SO ₂ NH ₂ -Phenyl		_		
61	1	4-SO ₂ NH ₂ -Thenyl				nts include compounds havir
	2	4-SO ₂ NH ₂ -Phenyl	fo	rmula (XV) o	r a mhar	maceutically acceptable salt

Exemplary embodiments include compounds having the formula (XV) or a pharmaceutically acceptable salt form thereof:

(XV)

TARLE	18-continued

0		(ΛV)		Entry	n	R^2
$ \bigcirc $				63	3	4-SO ₂ NH ₂ -Phenyl
LY \	O	A 2	5	64	1	2-CONH ₂ -Phenyl
_ \	/	N		65	2	2-CONH ₂ -Phenyl
\smile	\ !	/ × j		66	3	2-CONH ₂ -Phenyl
	M	\checkmark		67	1	3-CONH ₂ -Phenyl
	'n	•		68	2	3-CONH ₂ -Phenyl
			10	69	3	3-CONH ₂ -Phenyl
oin non lim	itina a	camples of R ³ and n are defined	10	70	1	4-CONH ₂ -Phenyl
				71	2	4-CONH ₂ -Phenyl
in below in	Table 18	3.		72	3	4-CONH ₂ -Phenyl
				73	1	2-Br-Phenyl
	-	FABLE 18		74	2	2-Br-Phenyl
			15	75	3	2-Br-Phenyl
Entry	n	\mathbb{R}^2		76	1	3-Br-Phenyl
1	1	2 CE Phoned		77	2	3-Br-Phenyl
1 2	1 2	2-CF ₃ -Phenyl 2-CF ₃ -Phenyl		78	3	3-Br-Phenyl
3	3	2-CF ₃ -Phenyl		79	1	2,3-di-CH ₃ -phenyl
4	1	3-CF ₃ -Phenyl		80	2 3	2,3-di-CH ₃ -phenyl
5	2	3-CF ₃ -Phenyl	20	81	1	2,3-di-CH ₃ -phenyl
6	3	3-CF ₃ -Phenyl		82		2,4-di-CH ₃ -phenyl
7	1	4-CF ₃ -Phenyl		83 84	2 3	2,4-di-CH ₃ -phenyl
8	2	4-CF ₃ -Phenyl		84 85	1	2,4-di-CH ₃ -phenyl 2,5-di-CH ₃ -phenyl
9	3	4-CF ₃ -Phenyl		86	2	2,5-di-CH ₃ -phenyl
10	1	2-NH ₂ -Phenyl	25	87	3	2,5-di-CH ₃ -phenyl
11	2	2-NH ₂ -Phenyl	23	88	1	2,6-di-CH ₃ -phenyl
12	3	2-NH ₂ -Phenyl		89	2	2,6-di-CH ₃ -phenyl
13 14	1 2	3-NH ₂ -Phenyl 3-NH ₂ -Phenyl		90	3	2,6-di-CH ₃ -phenyl
15	3	3-NH ₂ -Phenyl		91	1	3,4-di-CH ₃ -phenyl
16	1	4-NH ₂ -Phenyl		92	2	3,4-di-CH ₃ -phenyl
17	2	4-NH ₂ -Phenyl	30	93	3	3,4-di-CH ₃ -phenyl
18	3	4-NH ₂ -Phenyl		94	1	3,5-di-CH ₃ -phenyl
19	1	2-tBu-Phenyl		95	2	3,5-di-CH ₃ -phenyl
20	2	2-tBu-Phenyl		96	3	3,5-di-CH ₃ -phenyl
21	3	2-tBu-Phenyl		97	1	2,3-di-Cl-phenyl
22	1	3-tBu-Phenyl		98	2	2,3-di-Cl-phenyl
23	2	3-tBu-Phenyl	35	99	3	2,3-di-Cl-phenyl
24	3	3-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
25 26	1 2	4-tBu-Phenyl 4-tBu-Phenyl		101	2	2,4-di-Cl-phenyl
27	3	4-tBu-Phenyl		102	3	2,4-di-Cl-phenyl
28	1	2-NO ₂ -Phenyl		103	1	2,5-di-Cl-phenyl
29	2	2-NO ₂ -Phenyl	40	104	2	2,5-di-Cl-phenyl
30	3	2-NO ₂ -Phenyl	40	105	3	2,5-di-Cl-phenyl
31	1	3-NO ₂ -Phenyl		106	1	2,6-di-Cl-phenyl
32	2	3-NO ₂ -Phenyl		107	2	2,6-di-Cl-phenyl
33	3	3-NO ₂ -Phenyl		108	3	2,6-di-Cl-phenyl
34 35	1	4-NO ₂ -Phenyl 4-NO ₂ -Phenyl		109	1	3,4-di-Cl-phenyl
36	2	4-NO ₂ -Phenyl	45	110	2	3,4-di-Cl-phenyl
37	1	2-SCH ₃ -Phenyl		111	3	3,4-di-Cl-phenyl
38	2	2-SCH ₃ -Phenyl		112	1	3,5-di-Cl-phenyl
39	3	2-SCH ₃ -Phenyl		113	2	3,5-di-Cl-phenyl
40	1	3-SCH ₃ -Phenyl		114	3	3,5-di-Cl-phenyl
41	2	3-SCH ₃ -Phenyl		115	1	2-morpholino-4-CH ₃ -phenyl
42	3	3-SCH ₃ -Phenyl	50	116	2	2-morpholino-4-CH ₃ -phenyl
43	1	4-SCH ₃ -Phenyl		117	3	2-morpholino-4-CH ₃ -phenyl
44 45	2	4-SCH ₃ -Phenyl		118	1	2-morpholino-4-CN-phenyl
45 46	3 1	4-SCH ₃ -Phenyl 2-SO ₂ CH ₃ -Phenyl		119	2	2-morpholino-4-CN-phenyl
47	2	2-SO ₂ CH ₃ -Phenyl		120	3	2-morpholino-4-CN-phenyl
48	3	2-SO ₂ CH ₃ -Phenyl	55	121	1	2-morpholino-4-OH-phenyl
49	1	3-SO ₂ CH ₃ -Phenyl	رر	122	2	2-morpholino-4-OH-phenyl
50	2	3-SO ₂ CH ₃ -Phenyl		123	3	2-morpholino-4-OH-phenyl
51	3	3-SO ₂ CH ₃ -Phenyl		124	1	2,3-dimethylpyridin-4-yl
52	1	4-SO ₂ CH ₃ -Phenyl		125	2	2,3-dimethylpyridin-4-yl
53	2	4-SO ₂ CH ₃ -Phenyl		126	3	2,3-dimethylpyridin-4-yl
54	3	4-SO ₂ CH ₃ -Phenyl	60	126	1	3,6-dimethylpyridin-4-yl
55 56	1	2-SO ₂ NH ₂ -Phenyl		127	2	3,6-dimethylpyridin-4-yl
56 57	2	2-SO ₂ NH ₂ -Phenyl 2-SO ₂ NH ₂ -Phenyl		128	3	3,6-dimethylpyridin-4-yl
58	1	3-SO ₂ NH ₂ -Fhenyl	_	129	<i>J</i>	5,0-annemyipynam-4-yi
59	2	3-SO ₂ NH ₂ -Phenyl				
60	3	3-SO ₂ NH ₂ -Phenyl		E1-	.1 11	
61	1	4-SO ₂ NH ₂ -Phenyl				nts include compounds havin rmaceutically acceptable salt
	2					

formula (XVI) or a pharmaceutically acceptable salt form thereof:

TABLE 19-continued

		ATT.			IADL	E 19-continued
C) 	(XVI)	, -	Entry	n	R^2
				63	3	4-SO ₂ NH ₂ -Phenyl
$\langle X \rangle$	o	△ n³	5	64	1	2-CONH ₂ -Phenyl
\sim /	/	N^{-R^3}		65	2	2-CONH ₂ -Phenyl
_	\	<u>/</u>		66	3	2-CONH ₂ -Phenyl
	(\mathcal{A}_n)	\checkmark		67	1	3-CONH ₂ -Phenyl
				68	2	3-CONH ₂ -Phenyl
			10	69	3	3-CONH ₂ -Phenyl
rein non-lir	niting exa	amples of R ³ and n are defined	Į	70 71	1 2	4-CONH ₂ -Phenyl 4-CONH ₂ -Phenyl
in below in				72	3	4-CONH ₂ -Phenyl
				73	1	2-Br-Phenyl
	т	ABLE 19		74	2	2-Br-Phenyl
	1.	ABLE 19	15	75	3	2-Br-Phenyl
Entry	n	\mathbb{R}^2	13	76	1	3-Br-Phenyl
-			•	77	2	3-Br-Phenyl
1	1	2-CF ₃ -Phenyl		78	3	3-Br-Phenyl
2	2	2-CF ₃ -Phenyl		79	1	2,3-di-CH ₃ -phenyl
3 4	3 1	2-CF ₃ -Phenyl 3-CF ₃ -Phenyl		80	2	2,3-di-CH ₃ -phenyl
5	2	3-CF ₃ -Phenyl	20	81	3	2,3-di-CH ₃ -phenyl
6	3	3-CF ₃ -Phenyl		82 83	1 2	2,4-di-CH ₃ -phenyl
7	1	4-CF ₃ -Phenyl		83 84	3	2,4-di-CH ₃ -phenyl 2,4-di-CH ₃ -phenyl
8	2	4-CF ₃ -Phenyl		85	1	2,4-di-CH ₃ -phenyl
9	3	4-CF ₃ -Phenyl		86	2	2,5-di-CH ₃ -phenyl
10	1	2-NH ₂ -Phenyl	25	87	3	2,5-di-CH ₃ -phenyl
11 12	2 3	2-NH ₂ -Phenyl 2-NH ₂ -Phenyl	20	88	1	2,6-di-CH ₃ -phenyl
13	1	3-NH ₂ -Phenyl		89	2	2,6-di-CH ₃ -phenyl
14	2	3-NH ₂ -Phenyl		90	3	2,6-di-CH ₃ -phenyl
15	3	3-NH ₂ -Phenyl		91	1	3,4-di-CH ₃ -phenyl
16	1	4-NH ₂ -Phenyl		92	2	3,4-di-CH ₃ -phenyl
17	2	4-NH ₂ -Phenyl	30	93	3	3,4-di-CH ₃ -phenyl
18	3	4-NH ₂ -Phenyl		94	1	3,5-di-CH ₃ -phenyl
19 20	1 2	2-tBu-Phenyl 2-tBu-Phenyl		95	2	3,5-di-CH ₃ -phenyl
21	3	2-tBu-Phenyl		96	3	3,5-di-CH ₃ -phenyl
22	1	3-tBu-Phenyl		97 98	1 2	2,3-di-Cl-phenyl 2,3-di-Cl-phenyl
23	2	3-tBu-Phenyl	35	99	3	2,3-di-Cl-phenyl
24	3	3-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
25	1	4-tBu-Phenyl		101	2	2,4-di-Cl-phenyl
26 27	2 3	4-tBu-Phenyl 4-tBu-Phenyl		102	3	2,4-di-Cl-phenyl
28	1	2-NO ₂ -Phenyl		103	1	2,5-di-Cl-phenyl
29	2	2-NO ₂ -Phenyl	• •	104	2	2,5-di-Cl-phenyl
30	3	2-NO ₂ -Phenyl	40	105	3	2,5-di-Cl-phenyl
31	1	3-NO ₂ -Phenyl		106	1	2,6-di-Cl-phenyl
32	2	3-NO ₂ -Phenyl		107	2	2,6-di-Cl-phenyl
33	3	3-NO ₂ -Phenyl		108	3	2,6-di-Cl-phenyl
34 35	1 2	4-NO ₂ -Phenyl 4-NO ₂ -Phenyl		109	1	3,4-di-Cl-phenyl
36	3	4-NO ₂ -Phenyl	45	110	2	3,4-di-Cl-phenyl
37	1	2-SCH ₃ -Phenyl		111	3	3,4-di-Cl-phenyl
38	2	2-SCH ₃ -Phenyl		112	1	3,5-di-Cl-phenyl
39	3	2-SCH ₃ -Phenyl		113	2	3,5-di-Cl-phenyl
40	1	3-SCH ₃ -Phenyl		114	3	3,5-di-Cl-phenyl
41	2 3	3-SCH ₃ -Phenyl	50	115	1	2-morpholino-4-CH ₃ -phenyl
42 43	3 1	3-SCH ₃ -Phenyl 4-SCH ₃ -Phenyl	50	116	2	2-morpholino-4-CH ₃ -phenyl
44	2	4-SCH ₃ -Phenyl		117	3	2-morpholino-4-CH ₃ -phenyl
45	3	4-SCH ₃ -Phenyl		118	1	2-morpholino-4-CN-phenyl
46	1	2-SO ₂ CH ₃ -Phenyl		119	2	2-morpholino-4-CN-phenyl
47	2	2-SO ₂ CH ₃ -Phenyl		120	3	2-morpholino-4-CN-phenyl
48	3	2-SO ₂ CH ₃ -Phenyl	55	121	1	2-morpholino-4-OH-phenyl
49 50	1	3-SO ₂ CH ₃ -Phenyl		122	2	2-morpholino-4-OH-phenyl
50 51	2 3	3-SO ₂ CH ₃ -Phenyl 3-SO ₂ CH ₃ -Phenyl		123	3	2-morpholino-4-OH-phenyl
52	3 1	4-SO ₂ CH ₃ -Phenyl		124	1	2,3-dimethylpyridin-4-yl
53	2	4-SO ₂ CH ₃ -Thenyl		125	2	2,3-dimethylpyridin-4-yl
54	3	4-SO ₂ CH ₃ -Phenyl	60	126	3	2,3-dimethylpyridin-4-yl
55	1	2-SO ₂ NH ₂ -Phenyl	60	127	1	3,6-dimethylpyridin-4-yl
56	2	2-SO ₂ NH ₂ -Phenyl		128	2	3,6-dimethylpyridin-4-yl
57	3	2-SO ₂ NH ₂ -Phenyl		129	3	3,6-dimethylpyridin-4-yl
58 59	1 2	3-SO ₂ NH ₂ -Phenyl	_			
60	3	3-SO ₂ NH ₂ -Phenyl 3-SO ₂ NH ₂ -Phenyl		_		
61	1	4-SO ₂ NH ₂ -Flienyl	65	Exemplary en	nbodime	nts include compounds havin
				rmula (XVII)		

formula (XVII) or a pharmaceutically acceptable salt form thereof:

Entry

63

64

65 66

67

68

 \mathbb{R}^2

 $4-SO_2NH_2$ -Phenyl

2-CONH₂-Phenyl

2-CONH₂-Phenyl 2-CONH₂-Phenyl 3-CONH₂-Phenyl 3-CONH₂-Phenyl 3-CONH₂-Phenyl

3

3

1

2

0	(XVII)
∕ Ĭ	
N^{-R^3}	
MN X	
$\langle I_n \rangle$	

			10	69	3	3-CONH ₂ -Phenyl
11		1£ D34 4		70	1	4-CONH ₂ -Phenyl
		nples of R ³ and n are de	ппеа	71	2	4-CONH ₂ -Phenyl
below in	Table 20.			72	3	4-CONH ₂ -Phenyl
				73	1	2-Br-Phenyl
	ТА	BLE 20		74	2	2-Br-Phenyl
	1/1		15	75	3	2-Br-Phenyl
Entry	n	\mathbb{R}^2	13	76	1	3-Br-Phenyl
				77	2	3-Br-Phenyl
1	1	2-CF ₃ -Phenyl		78	3	3-Br-Phenyl
	2	2-CF ₃ -Phenyl		79	1	2,3-di-CH ₃ -phenyl
2 3	3	2-CF ₃ -Phenyl		80	2	2,3-di-CH ₃ -phenyl
4	1	3-CF ₃ -Phenyl	20	81	3	2,3-di-CH ₃ -phenyl
5	2	3-CF ₃ -Phenyl	20	82	1	2,4-di-CH ₃ -phenyl
6	3	3-CF ₃ -Phenyl		83	2	2,4-di-CH ₃ -phenyl
7	1	4-CF ₃ -Phenyl		84	3	2,4-di-CH ₃ -phenyl
8	2	4-CF ₃ -Phenyl		85	1	2,5-di-CH ₃ -phenyl
9	3	4-CF ₃ -Phenyl		86	2	2,5-di-CH ₃ -phenyl
10	1	2-NH ₂ -Phenyl	25	87	3	2,5-di-CH ₃ -phenyl
11	2	2-NH ₂ -Phenyl	23	88	1	2,6-di-CH ₃ -phenyl
12	3	2-NH ₂ -Phenyl		89	2	2,6-di-CH ₃ -phenyl
13	1	3-NH ₂ -Phenyl		90	3	2,6-di-CH ₃ -phenyl
14	2	3-NH ₂ -Phenyl		91	1	3,4-di-CH ₃ -phenyl
15 16	3 1	3-NH ₂ -Phenyl 4-NH ₂ -Phenyl		92	2	3,4-di-CH ₃ -phenyl
17	2	4-NH ₂ -Phenyl	30	93	3	3,4-di-CH ₃ -phenyl
18	3	4-NH ₂ -Phenyl	30	94	1	3,5-di-CH ₃ -phenyl
19	1	2-tBu-Phenyl		9 4 95	2	3,5-di-CH ₃ -phenyl
20	2	2-tBu-Phenyl		93 96	3	3,5-di-CH ₃ -phenyl
21	3	2-tBu-Phenyl		96 97	1	2,3-di-Cl-phenyl
22	1	3-tBu-Phenyl				
23	2	3-tBu-Phenyl	35	98 99	2 3	2,3-di-Cl-phenyl
24	3	3-tBu-Phenyl	33			2,3-di-Cl-phenyl
25	1	4-tBu-Phenyl		100	1	2,4-di-Cl-phenyl
26	2	4-tBu-Phenyl		101	2	2,4-di-Cl-phenyl
27	3	4-tBu-Phenyl		102	3	2,4-di-Cl-phenyl
28	1	2-NO ₂ -Phenyl		103	1	2,5-di-Cl-phenyl
29	2	2-NO ₂ -Phenyl	40	104	2	2,5-di-Cl-phenyl
30	3	2-NO ₂ -Phenyl		105	3	2,5-di-Cl-phenyl
31	1	3-NO ₂ -Phenyl		106	1	2,6-di-Cl-phenyl
32	2	3-NO ₂ -Phenyl		107	2	2,6-di-Cl-phenyl
33 34	3	3-NO ₂ -Phenyl		108	3	2,6-di-Cl-phenyl
3 4 35	1	4-NO ₂ -Phenyl 4-NO ₂ -Phenyl		109	1	3,4-di-Cl-phenyl
36	2 3	4-NO ₂ -Phenyl	45	110	2	3,4-di-Cl-phenyl
37	1	2-SCH ₃ -Phenyl		111	3	3,4-di-Cl-phenyl
38	2	2-SCH ₃ -Phenyl		112	1	3,5-di-Cl-phenyl
39	3	2-SCH ₃ -Phenyl		113	2	3,5-di-Cl-phenyl
40	1	3-SCH ₃ -Phenyl		114	3	3,5-di-Cl-phenyl
41	2	3-SCH ₃ -Phenyl		115	1	2-morpholino-4-CH ₃ -phenyl
42	3	3-SCH ₃ -Phenyl	50			
43	1	4-SCH ₃ -Phenyl		116	2	2-morpholino-4-CH ₃ -phenyl
44	2	4-SCH ₃ -Phenyl		117	3	2-morpholino-4-CH ₃ -phenyl
45	3	4-SCH ₃ -Phenyl		118	1	2-morpholino-4-CN-phenyl
46	1	2-SO ₂ CH ₃ -Phenyl		119	2	2-morpholino-4-CN-phenyl
47	2	2-SO ₂ CH ₃ -Phenyl		120	3	2-morpholino-4-CN-phenyl
48	3	2-SO ₂ CH ₃ -Phenyl	55	121	1	2-morpholino-4-OH-phenyl
49	1	3-SO ₂ CH ₃ -Phenyl		122	2	2-morpholino-4-OH-phenyl
50	2	3-SO ₂ CH ₃ -Phenyl		123	3	2-morpholino-4-OH-phenyl
51	3	3-SO ₂ CH ₃ -Phenyl		124	1	2,3-dimethylpyridin-4-yl
52	1	4-SO ₂ CH ₃ -Phenyl		125	2	2,3-dimethylpyridin-4-yl
53	2	4-SO ₂ CH ₃ -Phenyl		126	3	2,3-dimethylpyridin-4-yl
54 55	3	4-SO ₂ CH ₃ -Phenyl	60	127	1	3,6-dimethylpyridin-4-yl
55 56	1	2-SO ₂ NH ₂ -Phenyl		128	2	3,6-dimethylpyridin-4-yl
56 57	2 3	2-SO ₂ NH ₂ -Phenyl 2-SO ₂ NH ₂ -Phenyl			3	
58	1	3-SO ₂ NH ₂ -Phenyl		129	3	3,6-dimethylpyridin-4-yl
59	2	3-SO ₂ NH ₂ -Phenyl				
60	3	3-SO ₂ NH ₂ -Thenyl				_
61	1	4-SO ₂ NH ₂ -Phenyl	65 I	For the purp	oses of de	emonstrating the manner ir
62	2	4-SO ₂ NH ₂ -Filenyl				present invention are nam

4-SO₂NH₂-Phenyl

For the purposes of demonstrating the manner in which the compounds of the present invention are named and referred to herein, the compound having the formula:

has the chemical name 3-(2-(5-(pyridin-4-yl)hexahydropy- 10 rrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one.

For the purposes of demonstrating the manner in which the compounds of the present invention are named and referred to herein, the compound having the formula:

has the chemical name 3-(2-(6-(pyridin-4-yl)-2,6-diazaspiro [3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one.

For the purposes of the present invention, a compound depicted by the racemic formula, for example:

will stand equally well for either of the two enantiomers 40 having the formula:

or the formula:

60

or mixtures thereof, or in the case where a second chiral center is present, all diastereomers.

In all of the embodiments provided herein, examples of 65 suitable optional substituents are not intended to limit the scope of the claimed invention. The compounds of the

invention may contain any of the substituents, or combinations of substituents, provided herein.

Process

The present invention further relates to a process for preparing the sigma-2 receptor binders and sigma-2 receptor activity modulators of the present invention.

Compounds of the present teachings can be prepared in accordance with the procedures outlined herein, from commercially available starting materials, compounds known in the literature, or readily prepared intermediates, by employing standard synthetic methods and procedures known to those skilled in the art. Standard synthetic methods and procedures for the preparation of organic molecules and functional group transformations and manipulations can be readily obtained from the relevant scientific literature or from standard textbooks in the field. It will be appreciated that where typical or preferred process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions can vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures. Those skilled in the art of organic synthesis will recognize that the nature and order of the synthetic steps presented can be varied for the purpose of optimizing the formation of the compounds described herein.

The processes described herein can be monitored according to any suitable method known in the art. For example, product formation can be monitored by spectroscopic means, such as nuclear magnetic resonance spectroscopy (e.g., ¹H or ¹³C), infrared spectroscopy, spectrophotometry (e.g., UV-visible), mass spectrometry, or by chromatography such as high pressure liquid chromatography (HPLC), gas chromatography (GC), gel-permeation chromatography (GPC), or thin layer chromatography (TLC).

Preparation of the compounds can involve protection and deprotection of various chemical groups. The need for protection and deprotection and the selection of appropriate protecting groups can be readily determined by one skilled in the art. The chemistry of protecting groups can be found, for example, in Greene et al., *Protective Groups in Organic Synthesis*, 2d. Ed. (Wiley & Sons, 1991), the entire disclosure of which is incorporated by reference herein for all purposes.

The reactions or the processes described herein can be carried out in suitable solvents which can be readily selected by one skilled in the art of organic synthesis. Suitable solvents typically are substantially nonreactive with the reactants, intermediates, and/or products at the temperatures at which the reactions are carried out, i.e., temperatures that can range from the solvent's freezing temperature to the solvent's boiling temperature. A given reaction can be carried out in one solvent or a mixture of more than one solvent. Depending on the particular reaction step, suitable solvents for a particular reaction step can be selected.

The compounds of these teachings can be prepared by methods known in the art of organic chemistry. The reagents used in the preparation of the compounds of these teachings can be either commercially obtained or can be prepared by standard procedures described in the literature. For example, compounds of the present invention can be prepared according to the method illustrated in the General Synthetic Schemes:

General Synthetic Schemes for Preparation of Compounds

The reagents used in the preparation of the compounds of this invention can be either commercially obtained or can be prepared by standard procedures described in the literature. In accordance with this invention, compounds in the genus may be produced by one of the following reaction schemes.

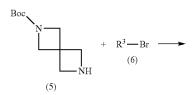
Compounds of the disclosure may be prepared according 10 to any of the process outlined in Schemes 1-8.

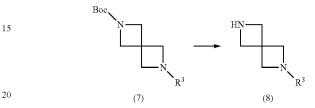
$$\begin{array}{c}
\underline{\text{Scheme 1}} \\
\text{HN} \\
& + R^2 - \text{Br} \\
& (2)
\end{array}$$

$$\begin{array}{c}
\text{(1)} \\
\end{array}$$

Box N
$$\mathbb{R}^2$$
 \mathbb{R}^2 \mathbb{R}^2 \mathbb{R}^2

Accordingly, a suitably substituted compound (1) a known compound or compound prepared by known methods, is reacted with a compound of the formula (2), a known compound or a compound prepared by known methods, in the presence of a palladium catalyst such as palladium acetate, palladium bis(triphenylphosphine) dichloride, palladium tetrakis(triphenylphospine), bis(acetonitrile) dichloropalladium [1,1'-Bis(diphenylphosphino) ferrocene]dichlo-Tris(dibenzylideneacetone)dipalladium(0), ropalladium, and the like, in the presence of a base such as potassium t-butoxide, sodium t-butoxide, lithium t-butoxide, potassium carbonate, sodium carbonate, lithium carbonate, cesium 45 carbonate, sodium hydroxide, lithium hydroxide, potassium hydroxide, and the like, optionally in the presence of an organic base such as triethylamine, diisopropylethyl amine, pyridine, and the like, optionally in the presence of a bis(diphenylphosphino) derived compound such as 2,2'-bis 50 (diphenylphosphino)-1,1'-binaphthalene, 2,2'-bis(di-p-tol ylphosphino)-1,1'-binaphthyl, 1,1'-binaphthalene-2,2'-diyl) bis[bis(3,5-dimethylphenyl)phosphine], 5,5'-bis[di(3,5-xylyl) phosphino]-4,4'-bi-1,3-benzodioxole, 5,5'-bis[di(3,5-ditert-butyl-4-methoxyphenyl) phosphino]-4,4'-bi-1,3-ben zodioxole, and the like, in a solvent such as toluene, benzene, xylene, 1,4-dioxane, tetrahydrofuran, methylene chloride, 1,2-dichloroethane, N,N-dimethylformamide, N,N-dimethylacetamide, and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (3). A compound of the formula (3) is reacted with an acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, and the like, optionally in the presence of an organic solvent such as methylene chloride, dichloro- 65 ethane, 1,4-dioxane, tetrahydrofuran, methanol, ethanol, and the like, to provide a compound of the formula (4).





A suitably substituted compound (5) a known compound or compound prepared by known methods, is reacted with a 25 compound of the formula (6), a known compound or a compound prepared by known methods, in the presence of a palladium catalyst such as palladium acetate, palladium bis(triphenylphosphine) dichloride, palladium tetrakis(triphenylphospine), bis(acetonitrile) dichloropalladium [1,1'-Bis (diphenylphosphino) ferrocene]dichloropalladium, Tris (dibenzylideneacetone)dipalladium(0), and the like, in the presence of a base such as potassium t-butoxide, sodium t-butoxide, lithium t-butoxide, potassium carbonate, sodium carbonate, lithium carbonate, cesium carbonate, sodium hydroxide, lithium hydroxide, potassium hydroxide, and the like, optionally in the presence of an organic base such as triethylamine, diisopropylethyl amine, pyridine, and the like, optionally in the presence of a bis(diphenylphosphino) derived compound such as 2,2'-bis(diphenylphosphino)-1, 1'-binaphthalene, 2,2'-bis(di-p-tolylphosphino)-1,1'-binaphthyl, 1,1'-binaphthalene-2,2'-diyl)bis[bis(3,5-dimethylphenyl)phosphine], 5,5'-bis[di(3,5-xylyl) phosphino]-4,4'-bi-1, 5,5'-bis[di(3,5-di-tert-butyl-4-methoxy 3-benzodioxole. phenyl)phosphino]-4,4'-bi-1,3-benzodioxole, and the like, in a solvent such as toluene, benzene, xvlene, 1.4-dioxane, tetrahydrofuran, methylene chloride, 1.2-dichloroethane, N,N-dimethylformamide, N,N-dimethylacetamide, and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (7). A compound of the formula (7) is reacted with an acid such as trifluoroacetic acid, hydrochloric acid, sulfuric acid, and the like, optionally in the presence of an organic solvent such as methylene chloride, dichloroethane, 1,4-dioxane, tetrahydrofuran, methanol, ethanol, and the like, to provide a compound of the formula (8).

$$\begin{array}{c}
 & \underline{\text{Scheme 3}} \\
 & \underline{\text{HN}} \\
 & \underline{\text{N}} \\
 & \underline{\text{Bn}}
\end{array}$$

$$\begin{array}{c}
 & \underline{\text{Scheme 3}} \\
 & \underline{\text{N}} \\
 & \underline{\text{In}} \\
 &$$

Bn -continued HN
$$R^2$$
 R^2 R^2

A suitably substituted compound (9) a known compound 10 or compound prepared by known methods, is reacted with a compound of the formula (10), a known compound or a compound prepared by known methods, in the presence of a palladium catalyst such as palladium acetate, palladium bis(triphenylphosphine) dichloride, palladium tetrakis(triphenylphospine), bis(acetonitrile) dichloropalladium [1,1'-Bis (diphenylphosphino) ferrocene]dichloropalladium, (dibenzylideneacetone)dipalladium(0), and the like, in the presence of a base such as potassium t-butoxide, sodium t-butoxide, lithium t-butoxide, potassium carbonate, sodium 20 carbonate, lithium carbonate, cesium carbonate, sodium hydroxide, lithium hydroxide, potassium hydroxide, and the like, optionally in the presence of an organic base such as triethylamine, diisopropylethyl amine, pyridine, and the like, optionally in the presence of a bis(diphenylphosphino) derived compound such as 2,2'-bis(diphenylphosphino)-1, 1'-binaphthalene, 2,2'-bis(di-p-tolylphosphino)-1,1'-binaphthyl, 1,1'-binaphthalene-2,2'-diyl)bis[bis(3,5-dimethylphenyl)phosphine], 5,5'-bis[di(3,5-xylyl) phosphino]-4,4'-bi-1, 30 5,5'-bis[di(3,5-di-tert-butyl-4-methoxyp 3-benzodioxole, henyl)phosphino]-4,4'-bi-1,3-benzodioxole, and the like, in a solvent such as toluene, benzene, xylene, 1,4-dioxane, tetrahydrofuran, methylene chloride, 1,2-dichloroethane, N,N-dimethylformamide, N,N-dimethylacetamide, and the 35 like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (11). A compound of the formula (11) is reacted with hydrogen in the presence of a palladium catalyst such as palladium on carbon, palladium on celite, palladium on barium sulfate, 40 palladium acetate, palladium bis(triphenylphosphine) dichloride, palladium tetrakis(triphenylphospine), and the like, in a solvent such as methanol, ethanol, isopropanol, ethyl acetate, tetrahydrofuran, 1,4-dioxane, and the like to provide a compound of the formula (12).

A suitably substituted compound (13) a known compound 65 or compound prepared by known methods, is reacted with a compound of the formula (14), a known compound or a

compound prepared by known methods, in the presence of a palladium catalyst such as palladium acetate, palladium bis(triphenylphosphine) dichloride, palladium tetrakis(triphenvlphospine), bis(acetonitrile) dichloropalladium [1.1'-Bis (diphenylphosphino) ferroceneldichloropalladium, Tris (dibenzylideneacetone)dipalladium(0), and the like, in the presence of a base such as potassium t-butoxide, sodium t-butoxide, lithium t-butoxide, potassium carbonate, sodium carbonate, lithium carbonate, cesium carbonate, sodium hydroxide, lithium hydroxide, potassium hydroxide, and the like, optionally in the presence of an organic base such as triethylamine, diisopropylethyl amine, pyridine, and the like, optionally in the presence of a bis(diphenylphosphino) derived compound such as 2,2'-bis(diphenylphosphino)-1, 1'-binaphthalene, 2,2'-bis(di-p-tolylphosphino)-1,1'-binaphthyl, 1,1'-binaphthalene-2,2'-diyl)bis[bis(3,5-dimethylphenyl)phosphine], 5,5'-bis[di(3,5-xylyl) phosphino]-4,4'-bi-1, 5,5'-bis[di(3,5-di-tert-butyl-4-methoxy 3-benzodioxole, phenyl)phosphino]-4,4'-bi-1,3-benzodioxole, and the like, in a solvent such as toluene, benzene, xylene, 1,4-dioxane, tetrahydrofuran, methylene chloride, 1,2-dichloroethane, N,N-dimethylformamide, N,N-dimethylacetamide, and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (15). A compound of the formula (15) is reacted with hydrogen in the presence of a palladium catalyst such as palladium on carbon, palladium on celite, palladium on barium sulfate, palladium acetate, palladium bis(triphenylphosphine) dichloride, palladium tetrakis(triphenylphospine), and the like, in a solvent such as methanol, ethanol, isopropanol, ethyl acetate, tetrahydrofuran, 1,4-dioxane, and the like to provide a compound of the formula (16).

Scheme 5

$$R^{la}$$
 R^{la}
 R^{la}

Scheme 6

A suitably substituted compound of formula (17), a known compound or compound prepared by known methods, is reacted with a compound of the formula (18), wherein X is a leaving group such as chlorine, bromine, iodine, mesylate, tosylate, and the like, in the presence of a base such as lithium diisopropylamide, sodium diisopropylamide, potassium diisopropylamide, lithium bis(trimethylsilyl)amide, sodium bis(trimethylsilyl)amide, potassium bis(trimethvlsilvl)amide, sodium hydride, and the like in an organic solvent such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, to provide a compound of the formula (19). A compound of the formula (19) is then treated with paraformaldehyde in the presence of an acid such as sulfuric acid, hydrochloric acid, and the like, in an the presence of acetic acid, and optionally in an organic solvent such as methanol, ethanol, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, 30 optionally with heating, optionally with microwave irradiation to provide a compound of the formula (20). A compound of the formula (20) is then treated with a base such as sodium hydroxide, potassium hydroxide, lithium hydroxide, and the like, in an solvent such as water, methanol, ethanol, 35 isopropanol, and the like, optionally with heating, and then treated with an acid such as sulfuric acid, hydrochloric acid, and the like, in a solvent such as water, methanol, ethanol, isopropanol, and the like, to provide a compound of the formula (21). A compound of the formula (21) is then 40 converted to a compound of the formula (22), wherein LG is a leaving group such as mesylate, tosylate, nosylate, bromide, and the like, using methods that are known to one skilled in the art. Thus, a compound of the formula (21) is treated with a sulfonyl chloride such as methanesulfonyl 45 chloride, toluenesulfonyl chloride p-nitrophenyl sulfonyl chloride, and the like, in the presence of a base such as triethylamine, diisopropyl amine, pyridine, 2,6-lutidine, and the like, in an organic solvent such as methylene chloride, dichloroethane, tetrahydrofuran, 1,4-dioxane, N,N-dimeth- 50 ylformamide, tetrahydrofuran, 1,4-dioxane and the like to provide a compound of the formula (22). Alternatively, a compound of the formula (21) is reacted with carbon tetrabromide in the presence of triphenylphosphine in a solvent such as methylene chloride, dichloroethane, tetrahydro- 55 furan, 1,4-dioxane, N,N-dimethylformamide, tetrahydrofuran, 1,4-dioxane and the like, optionally with heating, optionally with microwave irradiation, to provide a compound of the formula (22). A compound of the formula (22) is reacted with a compound of the formula (23), a known 60 compound or compound prepared by known methods, in an organic solvent such as tetrahydrofuran, 1,4-dioxane, 1,2dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, optionally in the presence of a base such as triethylamine, diisopropylethylamine, pyridine, 2,6 lutidine, 65 and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (24).

5
$$R^{la}$$
OH
 (26)
 R^{la}
OH
 (27)
OH
 (27)
OH
 (28)
 (28)
 (29)
OH
 (28)
 (29)
OH
 (28)
 (29)
 (30)
 (30)
 (30)
 (32)

A suitably substituted compound of formula (25), a known compound or compound prepared by known methods, is reacted with a compound of the formula (26), wherein X is a leaving group such as chlorine, bromine, iodine, mesylate, tosylate, and the like, in the presence of a base such as lithium diisopropylamide, sodium diisopropylamide, potassium diisopropylamide, lithium bis(trimethylsilyl)amide, sodium bis(trimethylsilyl)amide, potassium bis(trimethylsilyl)amide, sodium hydride, n-butyl lithium, sec-butyl lithium, tert-butyl lithium, and the like in an organic solvent such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, to provide a compound of the formula (27). A compound of the formula (27) is then treated with paraformaldehyde in the presence of an acid such as sulfuric acid, hydrochloric acid, and the like, in the presence of acetic acid, and optionally in an organic solvent such as methanol, ethanol, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (28). A compound of the formula (28) is then treated with a base such as sodium hydroxide, potassium hydroxide, lithium hydroxide, and the like, in an solvent such as water, methanol, ethanol, isopropanol, and the like, optionally with heating, and then treated with an acid such as sulfuric acid, hydrochloric acid, and the like, in a solvent such as water, methanol, ethanol, isopropanol, and the like, optionally with heating, to provide a compound of the formula (29). A compound of the formula (29) is then converted to a compound of the formula (30), wherein LG is a leaving group such as mesylate, tosylate, nosylate, bromide, and the like, using methods that are known to one skilled in the art. Thus, a compound of the formula (29) is treated with a sulfonyl chloride such as methanesulfonyl chloride, toluenesulfonyl chloride p-nitrophenyl sulfonyl

chloride, and the like, in the presence of a base such as triethylamine, diisopropyl amine, pyridine, 2,6-lutidine, and the like, in an organic solvent such as methylene chloride, dichloroethane, tetrahydrofuran, 1,4-dioxane, N,N-dimethvlformamide, tetrahydrofuran, 1.4-dioxane and the like to 5 provide a compound of the formula (30). Alternatively, a compound of the formula (29) is reacted with carbon tetrabromide in the presence of triphenylphosphine in a solvent such as methylene chloride, dichloroethane, tetrahydrofuran, 1,4-dioxane, N,N-dimethylformamide, tetrahydrofuran, 1,4-dioxane and the like, optionally with heating, optionally with microwave irradiation, to provide a compound of the formula (30). A compound of the formula (30) is reacted with a compound of the formula (31), a known compound or compound prepared by known methods, in an organic solvent such as tetrahydrofuran, 1,4-dioxane, 1,2dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, optionally in the presence of a base such as triethylamine, diisopropylethylamine, pyridine, 2,6 lutidine, and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (32).

Compounds of formula (37) may be prepared according to the process outlined in Scheme 7.

Scheme 7

$$R^{1a}$$
 R^{1a}
 R^{1a}

A compound of the formula (33) is reacted with a base 45 such as sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate, lithium carbonate and the like, in the presence of a solvent such as methanol, ethanol, isopropanol, water, and the like, optionally with heating, optionally with microwave irradiation to 50 provide a compound of the formula (34). A compound of the formula (34) is then reacted with iodine in the presence of a base such as sodium bicarbonate, potassium bicarbonate, lithium bicarbonate, sodium carbonate, potassium carbonate, lithium bicarbonate, sodium hydroxide, potassium 55 hydroxide, lithium hydroxide, and the like, in the presence of a solvent such as tetrahydrofuran, ethyl ether, 1,4-dioxane, and the like to provide a compound of the formula (35). A compound of the formula (35) is reacted with a compound of the formula (36), a known compound or 60 compound prepared by known methods, in an organic solvent such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, optionally in the presence of a base such as triethylamine, diisopropylethylamine, pyridine, 2,6 lutidine, and the 65 like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (37).

Compounds of formula (46) may be prepared according to the process outlined in Scheme 8.

Scheme 8

$$R^{la} \longrightarrow OH$$

$$R^{l$$

A compound of the formula (38) is reacted with ruthenium chloride in the presence of sodium periodate in a solvent such as acetonitrile, methanol, ethanol, isopropanol, and the like, to provide a compound of the formula (39). A compound of the formula (39) is reacted with a compound of the formula (40), a known compound or compound prepared by known methods, wherein x is a halogen, in the presence of a solvent such as ethyl ether, tetrahydrofuran, 1,4-dioxane and the like to provide a compound of the formula (41). A compound of the formula (41) is reacted with ruthenium chloride in the presence of sodium periodate

(46)

in a solvent such as acetonitrile, methanol, ethanol, isopropanol, and the like, to provide a compound of the formula (42). A compound of the formula (42) is reacted with a reducing agent such as lithium borohydride, sodium borohydride, sodium cyanoborohydride and the like, in a solvent 5 such as methanol, ethanol, isopropanol, acetonitrile, and the like to provide a compound of the formula (42). A compound of the formula (43) is then converted to a compound of the formula (44), wherein LG is a leaving group such as mesylate, tosylate, nosylate, bromide, and the like, using methods that are known to one skilled in the art. Thus, a compound of the formula (43) is treated with a sulfonyl chloride such as methanesulfonyl chloride, toluenesulfonyl chloride p-nitrophenyl sulfonyl chloride, and the like, in the presence of a base such as triethylamine, diisopropyl amine, pyridine, 2,6-lutidine, and the like, in an organic solvent such as methylene chloride, dichloroethane, tetrahydrofuran, 1,4-dioxane, N,N-dimethylformamide, tetrahydrofuran, 1,4-dioxane and the like to provide a compound of the formula (44). Alternatively, a compound of the formula (43) is reacted with carbon tetrabromide in the presence of 20 triphenylphosphine in a solvent such as methylene chloride, dichloroethane, tetrahydrofuran, 1,4-dioxane, N,N-dimethylformamide, tetrahydrofuran, 1,4-dioxane and the like, optionally with heating, optionally with microwave irradiation, to provide a compound of the formula (44). A compound of the formula (44) is reacted with a compound of the formula (45), a known compound or compound prepared by known methods, in an organic solvent such as tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, dimethylformamide, dimethylacetamide, and the like, optionally in the presence of a base such as triethylamine, diisopropylethylamine, pyridine, 2,6 lutidine, and the like, optionally with heating, optionally with microwave irradiation to provide a compound of the formula (46).

The Examples provided below provide representative methods for preparing exemplary compounds of the present invention. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds of the present invention.

EXAMPLES

The practice of the invention is illustrated by the following non-limiting examples. The Examples provided below provide representative methods for preparing exemplary compounds of the present invention. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds of the present invention.

In the examples that follow, ¹H-NMR spectra were obtained on a Varian Mercury 300-MHz NMR. Purity (%) and mass spectral data were determined with a Waters Alliance 2695 HPLC/MS (Waters Symmetry C18, 4.6×75 mm, 3.5 m) with a 2996 diode array detector from 210-400 ⁵⁵ mm

Example 1: Preparation of methyl 2,2-dimethylpent-4enoate: This reaction was performed in oven-dried glassware under a nitrogen atmosphere. To a well-stirred solution of freshly prepared lithium diisopropylamide (1M, 1.10 equiv) in dry 35 ml tetrahydrofuran, isobutyric acid methyl ester (3.32 g, 32.6 mmol, 1.0 equiv) was added dropwise during 0.5 hours at -78° C. The mixture was allowed to stir at this temperature for 30 min followed by the addition of allyl bromide (5.35 g, 44.0 mmol) and Hexamethylphosphoramide (HMPA) (2.91 g, 16.3 mmol) dropwise over 0.5 h. The reaction mixture was stirred overnight at room temperature, quenched with 10% HCl (while cooling in ice bath) until acidic (pH=2). The organic layer was separated and the aqueous layer was extracted with hexanes (3×100 mL). The extract was washed with 10% NaHCO₃ (200 mL) and brine (200 mL). The solution was then dried over MgSO₄, concentrated in vacuo and distilled to give pure product. ¹H NMR (400 MHz, CDCl₃) δ 5.73 (dd, J=9.4, 17.7, 1H), 5.04 (dd, J=1.9, 13.5, 2H), 4.12 (q, J=7.1, 2H), 2.28 (d, J=7.4, 2H), 1.25 (t, J=7.1, 3H), 1.17 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 177.42, 134.42, 117.88, 77.68, 77.36, 77.04, 60.35, 44.91, 42.25, 24.92, 14.35

The following compounds can be prepared by the procedure of methyl 2,2-dimethylpent-4-enoate. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 2: Preparation of Ethyl 2,2-diethylpent-4-enoate: The title compound was prepared according to the procedure for methyl 2,2-dimethylpent-4-enoate, except 2-ethyl-butyric acid ethyl ester was substituted for isobutyric acid methyl ester ¹H NMR (300 MHz, CDCl₃) δ 5.68 (dd, J=9.9, 17.2, 1H), 5.16-4.97 (m, 2H), 4.14 (q, J=7.1, 2H), 2.33 (d, J=7.4, 2H), 1.59 (dt, J=6.5, 7.5, 5H), 1.26 (t, J=7.1, 3H), 0.80 (t, J=7.5, 6H)

Example 3: Preparation of 1-allylcyclobutanecarboxylic acid: This reaction was performed in oven-dried glassware under a nitrogen atmosphere. To a well-stirred solution of freshly prepared lithium diisopropylamide (1M, 10.76 mmol, 2.30 equiv) in dry 107 ml tetrahydrofuran, cyclobutanecarboxylic acid (4.68 g, 46.8 mmol, 1.0 equiv) was added dropwise during 0.5 hours at 0° C. The mixture was heated to 50° C. for 6 hours, then cooled to 0° C. followed by the addition of NaI (0.697 g, 4.68 mmol, 0.1 equiv) in one portion and a mixture of allyl bromide (7.58 g, 63.2 mmol,

1.35 equiv) and HMPA (4.18 g, 23.4 mmol, 0.5 equiv) dropwise over 0.5 hr. The reaction mixture was stirred overnight at room temperature, quenched with 10% HCl (while cooling in ice bath) until acidic (pH=2). The organic layer was separated and the aqueous layer was extracted with ether (3×250 mL). The organic phases were combined and washed with brine. The solution was then dried over MgSO₄ and concentrated in vacuo to afford a crude oil which was purified through flash chromatography (silica; ethyl acetate/hexanes, 1%~10%). ¹H NMR (400 MHz, CDCl₃) δ 5.77 (ddt, J=7.1, 10.2, 17.2, 1H), 5.17-4.99 (m, 2H), 2.59-2.38 (m, 4H), 2.07-1.84 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 184.04, 133.90, 118.19, 47.20, 41.74, 29.57, 15.65; Rf, 0.43 (Hexane:Ethyl Acetate 10:1); HRMS (CI): [M+H], calcd for C₃H₁₃O₂, 141.0916; found 141.0911.

The following compounds can be prepared by the procedure of 1-allylcyclobutanecarboxylic acid. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 4: Preparation of 1-allylcyclopentanecarboxylic 35 acid: The title compound was prepared according to the procedure for 1-allylcyclobutanecarboxylic acid, except cyclopentane carboxylic acid was substituted for cyclobutanecarboxylic acid: 1 H NMR (400 MHz, CDCl₃) δ 5.77 40 (ddt, J=7.2, 10.2, 17.4, 1H), 5.17-4.94 (m, 2H), 2.38 (d, J=7.2, 2H), 2.20-2.02 (m, 2H), 1.79-1.47 (m, 6H). 13 C NMR (101 MHz, CDCl₃) δ 184.94, 134.96, 118.02, 53.75, 42.96, 35.89, 25.47. Rf, 0.50 (Hexane:Ethyl Acetate 10:1); HRMS 45 (CI): [M+H], calcd for $C_9H_{15}O_2$, 155.1072; found 155.1068.

Example 5: Preparation of 1-allylcyclohexanecarboxylic acid: The title compound was prepared according to the procedure for 1-allylcyclobutanecarboxylic acid, except cyclohexane carboxylic acid was substituted for cyclobutanecarboxylic acid: ¹H NMR (400 MHz, CDCl₃) δ 12.13 (broad, 1H), 5.83-5.63 (m, 1H), 5.12-5.00 (m, 2H), 2.27 (m, 2H), 2.04 (m, 2H), 1.66-1.50 (m, 3H), 1.49-1.33 (m, 2H), 1.33-1.17 (m, 3H).

Example 6: Preparation of 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one: A mixture of glacial acetic acid (28.6 g, 477 mmol, 53.6 equiv), paraformaldehyde (0.80 g, 26.7 mmol, 3.0 equiv) and $\rm H_2SO_4$ (0.5 g, 4.45 mmol, 0.57 equiv) was stirred for 30 min at 70° C. before methyl 2,2-dimethylpent-4-enoate (1.26 g, 8.9 mmol, 1.0 equiv) was added dropwise during 10 min. The reaction mixture was then maintained at 70–80° C. and allowed to stir overnight. Acetic acid was removed under reduced pressure and the reaction was quenched with 10% NaHCO $_3$ solution. The mixture was then extracted with ethyl acetate (3×50 mL) and the combined organic phase was concentrated in vacuo to give a crude oil. The crude oil was used for next step without further purification.

A mixture of the crude oil (200 mg, 1.0 mmol, 1 equiv) 25 and 30% NaOH (800 mg NaOH, 20 mmol, 20 equiv) aqueous solution was refluxed for 2 hours. The mixture was cooled in an ice bath and excess 30% H₂SO₄ was added until acidic (pH<2). The resulting mixture was extracted with ethyl acetate (3×25 mL), the combined organic phase was washed with 10% NaHCO₃, (50 mL), brine (50 mL), dried over MgSO₄ and concentrated in vacuo to give a crude product which was further purified by column chromatography (Ethyl acetate/Hexanes, 10%~60%) ¹H NMR (400 MHz, CDCl₃) δ 4.70-4.60 (m, 1H), 3.90-3.78 (m, 2H), 2.22 (dd, J=5.9, 12.7, 1H), 1.98-1.87 (m, 2H), 1.80 (dd, J=5.9, 12.7, 1H), 1.28 (d, J=4.8, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 182.26, 75.01, 59.58, 43.93, 40.62, 38.69, 25.31, 24.61; Rf, 0.34 (Hexane:Ethyl Acetate 1:1); Anal. Calcd for C₈H₁₄O₃: C, 60.74; H, 8.92. Found: C, 60.47; H, 8.86.

The following compounds can be prepared by the procedure of 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

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Example 7: Preparation of 3,3-diethyl-5-(2-hydroxyethyl) dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one, except ethyl 2,2-diethylpent-4-enoate was substituted for methyl 2,2-dimethylpent-4-enoate: $^1\mathrm{H}$ NMR (400 MHz, CDCl_3) δ 4.62 (dtd, J=5.3, 7.3, 9.5, 1H), 3.78 (t, J=6.1, 2H), 3.20 (s, 1H), 2.19 (dd, J=6.8, 13.1, 1H), 1.97-1.81 (m, 3H), 1.70-1.56 (m, 4H), 0.93 (dt, J=7.5, 20.7, 6H); $^{13}\mathrm{C}$ NMR (101 MHz, CDCl_3) δ 181.46, 75.10, 58.91, 48.77, 39.13, 37.76, 29.21, 28.30, 8.83, 8.73; Rf, 0.36 (Hexane:Ethyl Acetate 5:2); Anal. Calcd for $\mathrm{C}_{10}\mathrm{H}_{13}\mathrm{O}_3$: C, 64.49; H, 9.74. Found: C, 64.20; H, 9.57.

Example 8: Preparation of 7-(2-hydroxyethyl)-6-oxaspiro [3.4] octan-5-one: The title compound was prepared according to the procedure for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one, except 1-allylcyclobutanecarboxylic acid was substituted for methyl 2,2-dimethylpent-4-enoate: $^1\mathrm{H}$ NMR (400 MHz, CDCl_3) δ 4.60-4.50 (m, 1H), 3.82 (t, 15 J=5.9, 2H), 2.61-2.40 (m, 3H), 2.19-1.96 (m, 5H). 1.92-185 (m, 2H); $^{13}\mathrm{C}$ NMR (101 MHz, CDCl_3) δ 181.25, 75.46, 59.66, 44.62, 42.42, 38.47, 31.95, 29.64, 16.79; Rf, 0.40 (Hexane:Ethyl Acetate 1:2); calcd for $\mathrm{C_9H_{15}O_3}$, 171.1021; $_{20}$ found 171.1016.

Example 9: Preparation of 3-(2-hydroxyethyl)-2-oxaspiro [4.4]nonan-1-one: The title compound was prepared according to the procedure for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one, except 1-allylcyclopentanecarboxylic 35 acid was substituted for methyl 2,2-dimethylpent-4-enoate: $^1\mathrm{H}$ NMR (400 MHz, CDCl_3) δ 4.65-4.56 (m, 1H), 3.84-3.76 (m, 2H), 2.74 (s, 1H), 2.28 (dd, J=5.8, 12.6, 1H), 2.20-2.10 (m, 1H), 2.00-1.56 (m, 10H); $^{13}\mathrm{C}$ NMR (101 MHz, CDCl_3) $_{40}$ δ 183.02, 75.77, 59.20, 50.35, 43.41, 38.41, 37.49, 36.93, 25.67, 25.58; Rf, 0.46 (Hexane:Ethyl Acetate 1:2); HRMS (CI): [M+H], calcd for C $_{10}\mathrm{H}_{703}$, 185.1178; found 185.1171.

Example 10: Preparation of 3-(2-hydroxyethyl)-2-oxaspiro[4.5]decan-1-one: The title compound was prepared 55 according to the procedure for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one, except 1-allylcyclohexanecarboxylic acid was substituted for methyl 2,2-dimethylpent-4-enoate: $^1\mathrm{H}$ NMR (400 MHz, CDCl_3) δ 4.62 (m, 1H), 60 3.82 (t, J=5.9, 2H), 2.43 (dd, J=6.2, 12.9, 1H), 2.22 (s, 1H), 2.00-1.17 (m, 13H). $^{13}\mathrm{C}$ NMR (101 MHz, CDCl_3) δ 181.96, 75.37, 59.55, 45.13, 39.88, 38.91, 34.54, 31.71, 25.57, 22.42, 22.36; Rf, 0.46 (Hexane:Ethyl Acetate 1:2); Anal. Calcd for $\mathrm{C}_{11}\mathrm{H}_{18}\mathrm{O}_3$: C, 66.64; H, 9.15. Found: C, 66.48; H, 9.17.

Example 11: Preparation of 2-(4,4-dimethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenzenesulfonate: To a stirred solution of 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one (0.316 g, 2 mmol, 1.0 equiv) and triethylamine (0.152 g, 1.5 mmol, 1.5 equiv) in dry dichloromethane, a solution of p-TosCl (0.475 g, 2.5 mmol, 1.25 equiv) in dichloromethane was added drop wise at 0° C. The resulting mixture was stirred at 0° C. for 1 hour and allowed to stir overnight at room temperature. Then, the reaction mixture was diluted with dichloromethane (50 mL), washed with 10% HCl, brine, dried over MgSO₄ and concentrated in vacuo to afford yellowish oil. This crude product was then purified by flash chromatography (silica gel; Ethyl acetate/ Hexanes, 0%~40%) to afford desired tosylate. ¹H NMR (300 MHz, CDCl₃) & 7.72 (m, 2H), 7.29 (m, 2H), 4.39 (m, 1H), 4.10 (m, 2H), 2.38 (s, 3H), 2.09 (m, 1H), 1.93 (m, 2H), 1.65 (m, 1H), 1.16 (d, J=4.8, 6H); ¹³C NMR (101 MHz, CDCl₃) ¹³C NMR (101 MHz, CDCl₃) δ 181.26, 145.16, 132.53, 130.03, 127.84, 77.68, 77.36, 77.04, 72.93, 66.83, 42.99, 40.23, 34.97, 24.82, 24.12, 21.57; HRMS (CI): [M+H] 313.1; Anal. Calcd for C₁₅H₂₀O₅S: C, 57.67; H, 6.45. Found: C, 57.85; H, 6.63.

The following compounds can be prepared by the procedure of 2-(4,4-dimethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenzenesulfonate. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 12: Preparation of 2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenzenesulfonate: The title compound was prepared according to the procedure for 2-(4,4-dimethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenzenesulfonate, except 3,3-diethyl-5-(2-hydroxyethyl)dihydrofuran-2(3H)-one was substituted for 5-(2-Hydroxyethyl)-3,3-dimethyl-dihydro-furan-2-one: ¹H NMR (300 MHz, CDCl₃) δ 7.79 (d, J=8.3 Hz, 2H), 7.36 (d, J=8.0 Hz, 2H), 4.55-4.33 (m, 1H), 4.14 (dd, J=6.5, 13.3 Hz, 3H), 2.46 (s, 3H), 2.21-1.84 (m, 3H), 1.83-1.68 (m, 1H), 1.58 (t, J=7.4 Hz, 4H), 0.89 (dt, J=7.5, 18.0 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 180.33, 145.30, 132.72, 130.15, 128.03, 77.68, 77.36, 77.04, 73.18, 66.95, 48.67, 37.53, 35.82, 29.14, 28.23, 21.76, 8.81, 8.74. Anal. Calcd for C₁₇H₂₄O₅S: C, 59.98; H, 7.11. Found: C, 60.27; H, 7.25.

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180.41, 145.24, 132.68, 130.10, 128.02, 73.38, 66.76, 44.33,

Example 13: Preparation of 2-(5-oxo-6-oxaspiro[3.4]octan-7-yl)ethyl 4-methylbenzenesulfonate: The title compound was prepared according to the procedure for 2-(4,4-dimethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenze nesulfonate, except 7-(2-hydroxyethyl)-6-oxaspiro[3.4]octan-5-one was substituted for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one: ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, J=8.3 Hz, 2H), 7.35 (d, J=8.0 Hz, 2H), 4.37 (tdd, J=8.8, 6.0, 4.3 Hz, 1H), 4.21-4.05 (m, 2H), 2.57-2.32 (m, 6H), 2.19-1.82 (m, 7H); ¹³C NMR (101 MHz, CDCl₃) δ ¹⁰

41.79, 35.10, 31.72, 29.28, 21.76, 16.51.

Example 14: Preparation of 2-(1-oxo-2-oxaspiro[4.4] nonan-3-yl)ethyl 4-methylbenzenesulfonate: The title compound was prepared according to the procedure for 2-(4,4-dimethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenze nesulfonate, except 3-(2-hydroxyethyl)-2-oxaspiro[4.4] nonan-1-one was substituted for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one: ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, J=8.3 Hz, 2H), 7.36 (d, J=8.0 Hz, 2H), 4.51-4.35 (m, 1H), 4.25-4.06 (m, 2H), 2.45 (s, 3H), 2.28-2.08 (m, 2H), 2.08-1.91 (m, 2H), 1.87-1.52 (m, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 181.90, 145.26, 132.76, 130.12, 128.07, 73.71, 66.85, 50.19, 43.07, 37.44, 36.81, 35.19, 25.61, 25.50, 21.79

Example 15: Preparation of 2-(1-oxo-2-oxaspiro[4.5]decan-3-yl)ethyl 4-methylbenzenesulfonate: The title compound was prepared according to the procedure for 2-(4,4-dimethyl-5-oxotetrahydrofuran-2-yl)ethyl 4-methylbenzene sulfonate, except 3-(2-hydroxyethyl)-2-oxaspiro[4.5]decan-1-one was substituted for 5-(2-Hydroxy-ethyl)-3,3-dimethyl-dihydro-furan-2-one: ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, J=8.3 Hz, 2H), 7.36 (d, J=8.0 Hz, 2H), 4.51-4.38 (m, 1H), 4.26-4.12 (m, 2H), 2.45 (s, 3H), 2.36 (dd, J=12.9, 6.2 Hz, 1H), 2.12-1.87 (m, 2H), 1.85-1.68 (m, 3H), 1.65-1.50 (m, 5H), 1.43-1.14 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 180.97, 145.27, 132.76, 130.12, 128.07, 73.28, 66.85, 44.96, 39.48, 35.58, 34.35, 31.52, 25.37, 22.23, 22.16, 21.80.

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Example 16: Preparation of 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2(3H)-one: To a solution of 3,3-diethyl-5-(2-hydroxyethyl)dihydrofuran-2(3H)-one (8.03 g, 43.0 mmol, 1 eq.) in tetrahydrofuran (143 mL) was added triphenylphosphine (16.94 g, 64.6 mmol, 1.5 eq.). The resulting solution was cooled to 0° C. and carbon tetrabromide (21.44 g, 64.6 mmol, 1.5 eq.) was added in one portion. The reaction was allowed to stir at 22° C. overnight. The reaction mixture was diluted with ether and filtered and concentrated onto Celite in vacuo and further purified by column chromatography (ethyl acetate/hexanes, 0%~30%, solid load). ¹H NMR (400 MHz, CDCl₃) 84.60 (m, 1H), 3.53 (dd, J=5.5, 7.6 Hz, 2H), 2.27-2.07 (m, 3H), 1.82 (dd, J=9.3, 13.0 Hz, 1H), 1.69-1.57 (m, 4H), 0.93 (dt, J=7.5, 25.7 Hz, 6H).

Example 17: Preparation of 3-(2-bromoethyl)-2-oxaspiro [4.5]decan-1-one: The title compound was prepared according to the procedure for 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2(3H)-one, except 3-(2-hydroxyethyl)-2-oxaspiro [4.5]decan-1-one was substituted for 3,3-diethyl-5-(2-hydroxyethyl)dihydrofuran-2(3H)-one: ¹H NMR (400 MHz, CDCl₃) &4.61 (m, 1H), 3.53 (dd, J=5.5, 7.6 Hz, 2H), 2.44 (dd, J=6.4, 12.9 Hz, 1H), 2.29-2.07 (m, 2H), 1.88-1.70 (m, 3H), 1.69-1.54 (m, 4H), 1.53-1.44 (m, 1H), 1.44-1.18 (m, 3H).

$$\frac{\text{NaOH}}{\text{MeOH, H}_2\text{O}}$$

ethyl 2,2-diethylpent-4-enoate

Example 18: Preparation of 2,2-diethylpent-4-enoic acid: Ethyl 2,2-diethylpent-4-enoate (0.2 g, 0.28 mmol) is mixed with NaOH (0.4 g, 10 mmol), MeOH (2.5 mL) and $\rm H_2O$ (2.5 mL) in a microwave vial. The mixture is then heated in a microwave reactor at 160° C. for 2 hours. The mixture was then acidified with 10% HCl, washed with ether (3×30 ml). The combined organic phase was dried over MgSO₄ and concentrated in vacuo to give a crude product which was used in the next step without further purification.

65 Example 19: Preparation of 3,3-diethyl-5-(iodomethyl) dihydrofuran-2(3H)-one: 2,2-diethylpent-4-enoic acid (1.77 g, 11.67 mmol) is stirred with tetrahydrofuran (34 mL), ether

(12 mL) and saturated NaHCO₃ solution (57 mL). The mixture is protected from sunlight. I2 was dissolved in 12 mL of tetrahydrofuran and added to the mixture in one portion at 0° C. The mixture was allowed to stir overnight at room temperature. Saturated sodium thiosulfate is added to the mixture to quench the reaction. The mixture was extracted with ethyl acetate (3×50 mL). The combined organic phase was dried over MgSO₄ and concentrated in vacuo to give a crude oil which was purified by flash chromatography (silica gel; Ethyl acetate/Hexanes, 0%~25%). ¹H NMR (400 MHz, CDCl₃) & 4.42 (dtd, J=9.0, 7.3, 4.6 Hz, 1H), 3.41 (dd, J=10.2, 4.6 Hz, 1H), 3.23 (dd, J=10.2, 7.5 Hz, 1H), 2.25 (dd, J=13.3, 6.9 Hz, 1H), 1.86 (dd, J=13.3, 9.1 Hz, 1H), 1.63 (m, 4H), 0.94 (dt, J=10.4, 7.5 Hz, 6H). MS (LC/MS, M+H⁺): 283.0

The following compounds can be prepared by the procedure of 3,3-diethyl-5-(iodomethyl)dihydrofuran-2(3H)-one. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 20: Preparation of 3-(iodomethyl)-2-oxaspiro [4.4]nonan-1-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(iodomethyl)dihydrofuran-2(3H)-one, except 1-allylcyclopentanecarboxylic acid was substituted for 2,2-diethylpent-4-enoic acid: $^{1}\mathrm{H}$ NMR (400 MHz, CDCl $_{3}$) δ 4.48-4.34 (m, 1H), 3.39 (dd, J=10.2, 4.9 Hz, 1H), 3.23 (dd, J=10.2, 7.5 Hz, 1H), 2.35 (dd, J=12.9, 6.1 Hz, 1H), 2.20-2.04 (m, 1H), 1.93-1.54 (m, 8H); $^{13}\mathrm{C}$ NMR (101 MHz, CDCl $_{3}$) δ 181.57, 75.96, 50.71, 43.44, 37.84, 36.89, 25.45, 25.36, 7.02; MS (LC/MS, M+H+): 281.0

Example 21: Preparation of 3-(iodomethyl)-2-oxaspiro [4.5]decan-1-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(iodomethyl)dihydrofuran-2(3H)-one, except 1-allylcyclohexanecarboxylic acid was substituted for 2,2-diethylpent-4-enoic acid: $^1\mathrm{H}$ NMR (400 MHz, CDCl₃) δ 4.42 (dtd, J=9.2, 6.9, 4.6 Hz, 1H), 3.41 (dd, J=10.3, 4.6 Hz, 1H), 3.26 (dd, J=10.2, 7.3 Hz, 1H), 2.50 (dd, J=13.1, 6.5 Hz, 1H), 1.85-1.49 (m, 8H), 1.44-1.20 (m, 3H); MS (LC/MS, M+H⁺): 295.0

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Example 22: Preparation of 3-hydroxy-2-oxaspiro[4.4] nonan-1-one: To a stirred mixture of 1-allylcyclopentanecarboxylic acid (10.93 g, 71 mmol, 1 equiv), RuCl₃ stock solution (0.514 g, 0.035M in water, 0.035 equiv) and CH₃CN (500 mL), NaIO₄ (30.8 g, 142 mmol, 2.04 equiv) was added in portions over a period of 30 min at room temperature. The suspension was allowed to stir at room temperature for another 30 min. The reaction was quenched with saturated aqueous solution of Na₂S₂O₃ and the two layers were separated. The aqueous layer was extracted with ethyl acetate (3×200 mL). The combined organic layer was washed with brine, dried over anhydrous MgSO₄, filtered, and concentrated. The residue was purified by flash column chromatography (silica gel; Ethyl acetate/Hexanes, 10%~50%) to give desired product. ¹H NMR (400 MHz, CDCl₃) δ 5.87 (s, 1H), 5.28 (s, 1H), 2.06 (dd, J=35.1, 28.9 Hz, 4H), 1.90-1.44 (m, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 183.20, 49.58, 43.94, 38.28, 25.42.

The following compounds can be prepared by the procedure of 3-hydroxy-2-oxaspiro[4.4]nonan-1-one. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 23: Preparation of 3-hydroxy-2-oxaspiro[4.5] decan-1-one: The title compound was prepared according to the procedure for 3-hydroxy-2-oxaspiro[4.4]nonan-1-one, except 1-allylcyclohexanecarboxylic acid was substituted for 1-allylcyclopentanecarboxylic acid: ¹H NMR (400 MHz, CDCl₃) δ 5.86 (t, J=4.5 Hz, 1H), 4.47 (broad, 1H), 2.18 (m, 2H), 1.83-1.43 (m, 7H), 1.32 (d, J=5.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 181.91, 96.88, 44.52, 40.54, 34.06, 25.28, 22.23.

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Example 24: Preparation of 3-(but-3-en-1-yl)-2-oxaspiro [4.4]nonan-1-one: This reaction was performed in ovendried glassware under a nitrogen atmosphere. To a wellstirred solution of freshly prepared but-1-ene magnesium bromide Grignard reagent (96 mmol, 1M, 3 equiv) in dry ether, 3-hydroxy-2-oxaspiro[4.4]nonan-1-one (5.0 g, 32.0 mmol, 1.0 equiv) was added dropwise during 0.5 hours at 0° C. The reaction mixture was stirred overnight at room 60 temperature, quenched with 10% HCl (while cooling in ice bath) until acidic (pH=2). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×200 mL). The extract was washed with 10% NaHCO₃ (100 mL) and brine (200 mL). The solution was then dried 65 over MgSO₄, concentrated in vacuo and purified by flash column chromatography (silica gel; Ethyl acetate/Hexanes, 0%~25%) to give desired product. ¹H NMR (400 MHz,

CDCl₃) δ 5.79 (ddt, J=16.9, 10.2, 6.7 Hz, 1H), 5.15-4.88 (m, 2H), 4.36 (ddt, J=9.7, 7.9, 5.5 Hz, 1H), 2.18 (m, 4H), 1.93-1.46 (m, 10H); 13 C NMR (101 MHz, CDCl₃) δ 182.55, 137.26, 115.62, 77.19, 50.28, 43.24, 37.51, 36.91, 34.83, 29.70, 25.56, 25.47.

The following compounds can be prepared by the procedure of 3-(but-3-en-1-yl)-2-oxaspiro[4.4]nonan-1-one. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 25: Preparation of 3-(but-3-en-1-yl)-2-oxaspiro [4.5]decan-1-one: The title compound was prepared according to the procedure for 3-(but-3-en-1-yl)-2-oxaspiro[4.4] nonan-1-one, except 3-hydroxy-2-oxaspiro[4.5]decan-1-one 25 was substituted for 3-hydroxy-2-oxaspiro[4.4]nonan-1-one: ¹H NMR (400 MHz, CDCl₃) δ 5.80 (ddt, J=16.9, 10.2, 6.6 Hz, 1H), 5.17-4.89 (m, 2H), 4.48-4.31 (m, 1H), 2.36 (dd, J=12.9, 6.3 Hz, 1H), 2.30-2.08 (m, 2H), 1.87-1.17 (m, 13H); ¹³C NMR (101 MHz, CDCl₃) δ 181.68, 137.31, 115.67, 30 76.77, 45.04, 39.55, 35.31, 34.43, 31.70, 29.75, 25.42, 22.29, 22.22

Example 26: Preparation of 3-(1-oxo-2-oxaspiro[4.4] nonan-3-yl)propyl 4-methylbenzenesulfonate: To a stirred mixture of 3-(but-3-en-1-yl)-2-oxaspiro[4.4]nonan-1-one (0.194 g, 1 mmol, 1 equiv), RuCl₃ stock solution (7.2 mg, 0.035M in water, 0.035 equiv) and CH₃CN (6 mL), NaIO₄ (434 mg, 2.04 mmol, 2.04 equiv) was added in portions over a period of 5 min at room temperature. The suspension was allowed to stir at room temperature for another 30 min. The reaction was quenched with saturated aqueous solution of Na₂S₂O₃ and the two layers were separated. The aqueous layer was extracted with ethyl acetate (3×20 mL). The combined organic layer was washed with brine, dried over anhydrous MgSO₄, filtered, and concentrated. The crude aldehyde was used for the next step without further purification.

This reaction was performed in oven-dried glassware under a nitrogen atmosphere. To a well-stirred solution of the crude aldehyde (0.196 g, 1 mmol, 1 equiv) in dry methanol, NaBH₄ (74 mg, 2.0 mmol, 2 equiv) was added to 60 the mixture in one portion at 0° C. The reaction mixture was stirred at room temperature for another 1 h, quenched with brine (while cooling in ice bath). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3×20 mL). The combined organic phase was then 65 dried over MgSO₄, concentrated in vacuo. The crude alcohol was used for the next step without further purification.

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To a stirred solution of the crude alcohol (0.396 g, 2 mmol, 1.0 equiv) and Et₃N (0.303 g, 3 mmol, 1.5 equiv) in dry dichloromethane, a solution of p-TosCl (0.475 g, 2.5 mmol, 1.25 equiv) in dichloromethane was added drop wise at 0° C. The resulting mixture was stirred at 0° C. for 1 hour and allowed to stir overnight at room temperature. Then, the reaction mixture was diluted with dichloromethane (50 mL). washed with 10% HCl, brine, dried over MgSO₄ and concentrated in vacuo to afford yellowish oil. This crude product was then purified by flash chromatography (silica gel; Ethyl acetate/Hexanes, 0%~40%) to afford desired tosylate. ¹H NMR (400 MHz, CDCl₃) δ 7.82-7.71 (m, 2H), 7.35 (m, 2H), 4.37-4.23 (m, 1H), 4.06 (qdd, J=10.0, 6.7, 5.2 Hz, 2H), 2.45 (s, 3H), 2.15 (m, 2H), 1.92-1.50 (m, 12H); 13C NMR ¹⁵ (101 MHz, CDCl₃) δ 182.29, 145.03, 133.05, 130.04, 128.00, 76.90, 69.91, 50.24, 43.20, 37.53, 36.92, 31.74, 25.59, 25.49, 25.37, 21.76.

The following compounds can be prepared by the procedure of 3-(1-oxo-2-oxaspiro[4.4]nonan-3-yl)propyl 4-methylbenzenesulfonate. The skilled practitioner will know how to substitute the appropriate reagents, starting materials and purification methods known to those skilled in the art, in order to prepare the compounds provided herein.

Example 27: Preparation of 3-(1-oxo-2-oxaspiro[4.5]de-can-3-yl)propyl 4-methylbenzenesulfonate: The title compound was prepared according to the procedure for 3-(1-oxo-2-oxaspiro[4.4]nonan-3-yl)propyl

4-methylbenzenesulfonate, except 3-(but-3-en-1-yl)-2-oxaspiro[4.5]decan-1-one was substituted for 3-(but-3-en-1-yl)-2-oxaspiro[4.4]nonan-1-one: ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, J=8.3 Hz, 2H), 7.35 (d, J=8.0 Hz, 2H), 4.39-4.26 (m, 1H), 4.16-3.97 (m, 2H), 2.44 (s, 3H), 2.32 (dt, J=15.8, 7.9 Hz, 1H), 1.98-1.13 (m, 16H); ¹³C NMR (101 MHz, CDCl₃) δ 181.36, 145.03, 133.05, 130.03, 127.99, 76.46, 69.91, 44.97, 39.54, 34.40, 32.15, 31.68, 25.37, 25.36, 22.25, 22.18, 21.76

Example 28: Preparation of 5-(2-(5-benzylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one: A solution of 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2(3H)-one (0.400 g, 1.53 mmol, 1 eq.), acetonitrile (8 mL), 2-benzyloctahydropyrrolo[3,4-c]pyrrole (0.340 g, 1.68 mmol, 1.1 eq.) and $\rm K_2CO_3$ (1.05 g, 7.65 mmol, 5 eq.) was heated and stirred at 80° C. for 24 hours. The resulting mixture was then filtered and concentrated in vacuo to give a crude residue that was further purified by column chromatography (methanol/dichloromethane, 0%~10%). $^1\rm H$ NMR (400 MHz, CDCl₃) δ 7.25-7.14 (m, 4H), 7.14-7.06 (m, 1H), 4.38 (m, 1H), 3.46 (s, 2H), 2.64-2.48 (m, 6H), 2.48-

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2.38 (m, 2H), 2.28-2.13 (m, 4H), 2.02 (dd, J=6.8, 13.0 Hz, 1H), 1.87-1.59 (m, 3H), 1.58-1.44 (m, 4H), 0.83 (dt, J=7.3, 21.4 Hz, 6H); MS (LC/MS, M+H+): m/z 371.2

Example 29: Preparation of 3-(2-(5-benzylhexahydropy-rrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one: The title compound was prepared according to the procedure for 5-(2-(5-benzylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one, except 3-(2-bromoethyl)-2-oxaspiro[4.5]decan-1-one was substituted for 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2 (3H)-one: $^1\!H$ NMR (400 MHz, CDCl₃) δ 7.26-7.17 (m, 4H), 7.17-7.10 (m, 1H), 4.40 (m, 1H), 3.50 (s, 2H), 2.69-2.52 (m, 6H), 2.49 (t, J=7.4 Hz, 2H), 2.30 (dd, J=6.3, 12.8 Hz, 1H), 2.27-2.16 (m, 4H), 1.88-1.61 (m, 5H), 1.61-1.45 (m, 4H), 1.44-1.37 (m, 1H), 1.36-1.07 (m, 3H); MS (LC/MS, M+H^+): 25 m/z 383.2

Example 30: Preparation of 3,3-diethyl-5-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: A mixture of 5-(2-(5-benzylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one (540 mg, 1.46 mmol, 1 eq.), Pd/C (108 mg, 20% wt) and MeOH (5.0 mL) was stirred at 22° C. under 1 atm of H₂ (filled balloon) for 3 days. The mixture was filtered through a plug of Celite, washed with MeOH (50 mL) and concentrated in vacuo to give a crude product that was used in following steps without further purification. 1 H NMR (400 MHz, CDCl₃) 84.42 (m, 1H), 2.83 (b, 1H), 2.69 (m, 2H), 2.55-2.39 (m, 4H), 2.33 (m, 2H), 2.26 (t, J=7.0 Hz, 2H), 2.14 (dd, J=1.7, 9.0 Hz, 2H), 1.91 (dd, J=6.7, 13.0 Hz, 1H), 1.71-1.47 (m, 3H), 1.45-1.32 (m, 4H), 0.69 (dt, J=7.4, 19.2 50 Hz, 6H); MS (LC/MS, M+H $^{+}$): m/z 281.2

Example 31: Preparation of 3-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one, except 3-(2-(5-benzylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]

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decan-1-one was substituted for 5-(2-(5-benzylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one: ¹H NMR (400 MHz, CDCl₃) 84.55 (m, 1H), 2.94 (m, 2H), 2.82-2.63 (m, 5H), 2.63-2.46 (m, 3H), 2.42 (m, 2H), 1.97-1.60 (m, 8H), 1.59-1.43 (m, 3H), 1.43-1.22 (m, 4H); MS (LC/MS, M+H⁺): m/z 293.2

Example 32: Preparation of 3,3-diethyl-5-(2-(5-(pyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: A solution of 3,3-diethyl-5-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2 (3H)-one (0.180 g, 0.642 mmol, 1 eq.), 1-butanol (6.4 mL), 4-bromopyridine hydrochloride (0.249 g, 1.28 mmol, 2.0 eq.) and triethylamine (0.325 g, 3.21 mmol, 5 eq.) was heated and stirred at 120° C. for 24 hours. The resulting solution was concentrated in vacuo to give a crude residue that was further purified by column chromatography (methanol/dichloromethane, 0%~10%, w/0.1% NH₄OH). ¹H NMR (400 MHz, CDCl₃) 88.13 (dd, J=1.4, 3.5 Hz, 2H), 6.32 (dd, J=1.5, 3.5 Hz, 2H), 4.37 (m, 1H), 3.45 (dd, J=8.3, 9.2 Hz, 30 2H), 3.12 (dt, J=3.4, 9.9 Hz, 2H), 2.90 (m, 2H), 2.62 (m, 2H), 2.50 (t, J=7.4 Hz, 2H), 2.46 (m, 2H), 2.02 (dd, J=6.8, 13.0 Hz, 1H), 1.85-1.61 (m, 3H), 1.52 (q, J=7.5 Hz, 4H), 0.82 (dt, J=5.7, 13.2 Hz, 6H); MS (LC/MS, M+H+): m/z 358.2

Example 33: Preparation of 3-(2-(5-(pyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(pyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2 (3H)-one, except 3-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one was substituted for 3,3-diethyl-5-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: ¹H NMR (400 MHz, CDCl₃) 88.13 (d, J=5.6 Hz, 2H), 6.33 (d, J=6.2 Hz, 2H), 4.38 (m, 1H), 3.46 (m, 2H), 3.13 (dt, J=3.7, 10.0 Hz, 2H), 2.91 (m, 2H), 2.68-2.57 (m, 2H), 2.55-2.41 (m, 4H), 2.28 (dd, J=6.2, 12.8 Hz, 1H), 1.95-1.43 (m, 9H), 1.43-1.33 (m, 1H), 1.32-1.04 (m, 3H); MS (LC/MS, M+H⁺): m/z 370.2.

Example 34: Preparation of 1-(benzyloxy)-2-bromobenzene: To a solution of 2-bromophenol (1.0 g, 5.78 mmol, 1.01 eq.) in acetonitrile (14 mL) was added benzyl bromide (0.975 g, 5.7 mmol, 1.0 eq.) and K₂CO₃ (1.09 g, 7.87 mmol, 1.38 eq.). This mixture was allowed to stir at 22° C. 5 overnight. The reaction was filtered and concentrated in vacuo to give a crude residue that was further purified by column chromatography (hexanes/ethyl acetate, 0%~10%). ¹H NMR (400 MHz, CDCl₃) 87.60 (dd, J=1.6, 7.8 Hz, 1H), 7.51 (m, 2H), 7.42 (t, J=7.6 Hz, 2H), 7.35 (m, 1H), 7.29-7.22 (m, 1H), 6.97 (dd, J=1.2 8.3 Hz, 1H), 6.88 (td, J=1.3, 7.6 Hz, 1H), 5.19 (s, 2H).

Example 35: Preparation of 1-(benzyloxy)-3-bromobenzene: The title compound was prepared according to the procedure for 1-(benzyloxy)-2-bromobenzene, except 3-bromophenol was substituted for 2-bromophenol: ¹H NMR (400 MHz, CDCl₃) δ7.50-7.34 (m, 5H), 7.23-7.10 (m, 25 3H), 6.95 (m, 1H), 5.08 (s, 2H).

Example 36: Preparation of 1-(benzyloxy)-4-bromobenzene: The title compound was prepared according to the procedure for 1-(benzyloxy)-2-bromobenzene, except 4-bromophenol was substituted for 2-bromophenol: ^{1}H NMR (400 MHz, CDCl₃) δ 7.51-7.33 (m, 7H), 6.91 (d, J=9.1 Hz, 2H), 5.08 (s, 2H).

Example 37: Preparation of 4-(2-bromophenyl)morpholine: This reaction was performed in oven-dried glassware under a nitrogen atmosphere. To a solution of 1,2-dibromobenzene (1.0 g, 4.24 mmol, 1.0 eq.) and morpholine (0.370 g, 4.24 mmol, 1.0 eq.) in anhydrous toluene (10.6 mL) was added the following in this order: Pd₂(dba)₃ (0.097 g, 5 mol %), BINAP (0.197 g, 7.5 mol %), and NaOtBu (0.448 g, 5.08 mmol, 1.2 eq.). The resulting mixture was allowed to stir at 80° C. overnight, under a sweep of N₂. The reaction mixture was cooled to 22° C. and then filtered through a plug of Celite. The collected filtrate was concentrated in vacuo to give a crude residue that was further purified by column chromatography (hexanes/ethyl acetate, 65 0%~20%). ¹H NMR (400 MHz, CDCl₃) 87.55 (dd, J=1.5, 7.9 Hz, 1H), 7.25 (td, J=1.4, 7.8 Hz, 1H), 7.00 (dd, J=1.4, 8.0

Hz, 1H), 6.89 (td, J=1.4, 7.7 Hz, 1H), 3.83 (m, 4H), 2.99 (m, 4H); MS (LC/MS, M+H+): m/z 241.9, 243.8

Example 38: Preparation of tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: This reaction was performed in oven-dried glassware under a nitrogen atmosphere. To a solution of 2,6-diazaspiro[3.3]heptane-2carboxylic acid tert-butyl ester hemioxylate (0.300 g, 1.23 mmol, 1.1 eq.) and bromobenzene (0.176 g, 1.12 mmol, 1.0 15 eq.) in anhydrous toluene (14 mL) was added the following in this order: Pd₂(dba)₃ (0.030 g, 2.5 mol %), BINAP (0.0450 g, 1.5/Pd), triethylamine (0.125 g, 1.23 mmol, 1.1 eq.) and NaOtBu (0.355 g, 3.69 mmol, 3.3 eq.). The resulting mixture was allowed to stir at 110° C. overnight, under 20 a sweep of N₂. The reaction mixture was cooled to 22° C. and then filtered through a plug of Celite. The collected filtrate was concentrated in vacuo to give a crude residue that was further purified by column chromatography (hexanes/ ethyl acetate, 0%~30%). ¹H NMR (400 MHz, CDCl₃) δ7.21 (m, 2H), 6.93 (m, 1H), 6.74 (d, J=8.3 Hz, 2H), 4.23 (s, 4H), 4.19 (s, 4H), 1.38 (s, 9H); MS (LC/MS, M+H+): m/z 275.2

Example 39: Preparation of tert-butyl 6-(pyridin-4-yl)-2, 6-diazaspiro[3.3]heptane-2-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except 4-bromopyridine hydrochloride was substituted for bromobenzene and 2 equivalents of triethylamine was utilized: ¹H NMR (400 MHz, CDCl₃) 88.09 (d, J=6.5 Hz, 2H), 6.28 (d, J=6.7 Hz, 2H), 4.12 (s, 4H), 4.06 (s, 4H), 1.37 (s, 9H); MS (LC/MS, M+H⁺): m/z 276.2

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Example 40: Preparation of tert-butyl 6-(3-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except 4-bromo-3-methylpyridine hydrochloride was substituted for bromobenzene and 2 equivalents of triethylamine was utilized: ¹H NMR (400 MHz, CDCl₃) 88.05 (d, J=5.5 Hz, 1H), 7.94 (s, 1H), 6.12 (d, J=5.4 Hz, 1H), 4.08 (s, 4H), 4.02 (s, 4H), 2.10 (s, 3H) 1.37 (s, 9H); MS (LC/MS, M+H⁺): m/z 290.2

Example 41: Preparation of tert-butyl 6-(2-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except 4-bromo-2-methylpyridine was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 88.05 (d, J=5.5 Hz, 1H), 6.07-6.00 (m, 2H), 4.02 (s, 4H), 3.95 (s, 4H), 2.35 (s, 3H), 1.37 (s, 9H); MS (LC/MS, M+H⁺): m/z 290.2

Example 42: Preparation of tert-butyl 6-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate:
The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except 4-bromo-2,6-dimethylpyridine was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) δ 5.90 (s, 2H), 4.01 (s, 4H), 3.92 (s, 4H), 2.32 (s, 6H), 1.37 (s, 9H); 25 MS (LC/MS, M+H*i m/z 304.2

Example 43: Preparation of tert-butyl 5-(3-methylpyridin-35 4-yl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate, 4-bromo-3-methylpyridine hydrochloride was substituted for bromobenzene and 2 equivalents of triethylamine was utilized: ¹H NMR (400 MHz, CDCl₃) 88.03 (d, J=5.8 Hz, 1H), 7.97 (s, 1H), 6.37 (d, J=5.8 Hz, 1H), 3.64-3.44 (m, 4H), 3.33-3.10 (m, 4H), 2.86 (b, 2H), 2.24 (s, 3H), 1.38 (s, 9H); MS (LC/MS, M+H⁺): m/z 304.2

Example 44: Preparation of tert-butyl 5-(2-methylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 4-bromo-2-methylpyridine was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.99 (d, J=5.9 Hz, 1H), 65 6.13 (d, J=2.2 Hz, 1H), 6.09 (dd, J=2.4, 5.8 Hz, 1H), 3.54 (dd, J=7.2, 11.2 Hz, 2H), 3.42 (b, 2H), 3.21 (m, 1H),

Example 45: Preparation of tert-butyl 5-(2,6-dimethylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3]heptane-2-carboxylic acid tert-butyl ester hemioxylate and 4-bromo-2,6-dimethylpyridine was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 85.98 (s, 2H), 3.52 (m, 2H), 3.41 (m, 2H), 3.21 (m, 1H), 3.16-2.99 (m, 3H), 2.86 (b, 2H), 2.29 (s, 6H), 1.34 (s, 9H); MS (LC/MS, M+H⁺): m/z 318.2.

Example 46: Preparation of tert-butyl 5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3]heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-2-methylbenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) δ7.18-7.10 (m, 2H), 6.96-6.89 (m, 2H), 3.69 (b, 2H), 3.36 (b, 2H), 3.18 (b, 2H), 3.05 (b, 2H), 2.91 (b, 2H), 2.33 (s, 3H), 1.52 (s, 9H); MS (LC/MS, M+H⁺): m/z 303.2

Example 47: Preparation of tert-butyl 5-(m-tolyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3]heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-3-methylbenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.17 (t, J=7.8 Hz, 1H), 6.59 (d, J=7.5 Hz, 1H), 6.46-6.37 (m, 2H), 3.68 (b, 2H), 3.52 (b, 2H), 3.42 (m, 1H), 3.29 (m, 1H), 3.23 (m, 2H), 2.97 (b, 2H), 2.38 (s, 3H), 1.54 (s, 9H); MS (LC/MS, M+H⁺): m/z 303.2

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Example 48: Preparation of tert-butyl 5-(p-tolyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3]heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-4-methylbenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.09 (d, J=8.1 Hz, 2H), 6.52 (d, J=8.5 Hz, 2H), 3.68 (m, 2H), 3.57 (b, 2H), 3.42 (m, 1H), 3.28 (m, 1H), 3.21 (m, 2H), 3.00 (b, 2H), 2.30 (s, 3H), 1.51 (s, 9H); MS (LC/MS, M+H⁺): m/z 303.2.

Example 49: Preparation of tert-butyl 5-(2-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate:
The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-2-methoxybenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 86.91-6.78 (m, 3H), 6.76-6.67 (m, 1H), 3.80 (s, 3H), 3.61 (b, 2H), 3.45 (b, 2H), 3.40-3.22 (m, 2H), 3.14 (b, 2H), 2.90 (b, 2H), 1.46 (s, 9H); MS (LC/MS, M+H⁺): m/z 319.2.

Example 50: Preparation of tert-butyl 5-(3-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate:
The title compound was prepared according to the procedure 50 for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-3-methoxybenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.13 (t, J=8.1 Hz, 1H), 6.29 (dd, J=2.2, 8.1 Hz, 1H), 6.18 (dd, J=1.8, 8.1 Hz, 1H), 6.10 (t, J=2.2 Hz, 1H), 3.79 (s, 3H), 3.63 (m, 2H), 3.50 (m, 2H), 3.37 (m, 1H), 3.30-3.11 (m, 3H), 2.95 (b, 2H), 1.48 (s, 9H); MS (LC/MS, M+H⁺): m/z 319.2

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Example 51: Preparation of tert-butyl 5-(4-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-4-methoxybenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) &6.83 (d, J=9.0 Hz, 2H), 6.50 (d, J=9.0 Hz, 2H), 3.73 (s, 3H), 3.62 (m, 2H), 3.48-3.29 (m, 3H), 3.23 (m, 1H), 3.12 (dd, J=3.5, 9.3 Hz, 2H), 2.93 (b, 2H), 1.46 (s, 9H); MS (LC/MS, M+H⁺): m/z 319.2.

Example 52: Preparation of tert-butyl 5-(2-cyanophenyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2 (1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 2-bromobenzonitrile was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.39 (dd, J=1.6, 7.8 Hz, 1H), 7.30 (m, 1H), 6.66 (t, J=7.5 Hz, 1H), 6.59 (d, J=8.5 Hz, 1H), 3.80 (m, 2H), 3.61 (m, 2H), 3.52 (m, 1H), 3.44 (m, 1H), 3.28 (m, 2H), 2.95 (b, 2H), 1.42 (s, 9H); MS (LC/MS, M+H+): m/z 314.2.

Example 53: Preparation of tert-butyl 5-(3-cyanophenyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2 (1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 3-bromobenzonitrile was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.22 (m, 1H), 6.88 (d, J=7.5 Hz, 1H), 6.71-6.64 (m, 2H), 3.62 (m, 2H), 3.49 (m, 2H), 3.31 (m, 1H), 3.23 (m, 1H), 3.16 (dd, J=3.9, 9.7 Hz, 2H), 2.99 (b, 2H), 1.42 (s, 9H); MS (LC/MS, M+H⁺): m/z 314.2

Example 54; Preparation of tert-butyl 5-(4-cyanophenyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2 (1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and

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4-bromobenzonitrile was substituted for bromobenzene: 1 H NMR (400 MHz, CDCl₃) 87.35 (d, J=8.9 Hz, 2H), 6.41 (d, J=8.9 Hz, 2H), 3.57 (m, 2H), 3.50 (m, 2H), 3.26 (m, 1H), 3.21-3.06 (m, 3H), 2.95 (b, 2H), 1.37 (s, 9H); MS (LC/MS, M+H⁺): m/z 314.2.

Example 55: Preparation of tert-butyl 5-(2-(benzyloxy) phenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate:
The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3,3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3,3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-(benzyloxy)-2-bromobenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.36-7.23 (m, 4H), 7.20 (m, 1H), 6.79 (m, 2H), 6.72 (m, 1H), 6.65 (m, 1H), 4.94 (s, 2H), 3.50 (b, 2H), 3.33 (m, 2H), 3.27-3.02 (m, 3H), 2.76 (b, 2H), 1.35 (s, 9H); MS (LC/MS, M+H+): m/z 395.2.

Example 56: Preparation of tert-butyl 5-(3-(benzyloxy) phenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3,3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3,3] heptane-2-carboxylate was substituted for 2,6-diazaspiro[3,3] heptane-2-carboxylate was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.47 (m, 2H), 7.41 (t, J=7.6 Hz, 2H), 7.34 (m, 1H), 7.17 (t, J=8.2 Hz, 1H), 6.39 (dd, J=1.7, 8.0 Hz, 1H), 6.23 (m, 2H), 5.08 (s, 2H), 3.66 (m, 2H), 3.53 (m, 2H), 3.40 (m, 1H), 3.33-3.14 (m, 3H), 2.99 (b, 2H), 1.49 (s, 9H); MS (LC/MS, M+H⁺): m/z 395.2.

Example 57: Preparation of tert-butyl 5-(4-(benzyloxy) phenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: 55 The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylate was substituted for 2,6-diazaspiro[3.3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 60 1-(benzyloxy)-4-bromobenzene was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.46 (m, 2H), 7.40 (t, J=7.8 Hz, 2H), 7.34 (m, 1H), 6.95 (d, J=9.0 Hz, 2H), 6.54 (d, J=8.8 Hz, 2H), 5.03 (s, 2H), 3.67 (b, 2H), 3.47 (b, 2H), 3.40 (m, 1H), 3.28 (m, 1H), 3.18 (dd, J=3.4, 9.3 Hz, 65 2H), 2.99 (b, 2H), 1.50 (s, 9H); MS (LC/MS, M+H⁺): m/z 395.2.

Example 58: Preparation of tert-butyl 5-(2-morpholinophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3,3]heptane-2-carboxylate, except tert-butyl hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for 2,6-diazaspiro[3,3] heptane-2-carboxylic acid tert-butyl ester hemioxylate and 4-(2-bromophenyl)morpholine was substituted for bromobenzene: ¹H NMR (400 MHz, CDCl₃) 87.04-6.89 (m, 3H), 6.85 (d, J=7.8 Hz, 1H), 3.85 (t, J=4.5 Hz, 4H), 3.62 (b, 2H), 3.48-3.21 (m, 6H), 3.04 (t, J=4.5 Hz, 4H), 2.92 (b, 2H), 1.48 (s, 9H); MS (LC/MS, M+H*): m/z 374.2.

Example 59: Preparation of 2-benzyl-5-(2-isopropylphenyl)octahydropyrrolo[3,4-c]pyrrole: The title compound was prepared according to the procedure for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate, except 2-benzyloctahydropyrrolo[3,4-c]pyrrole was substituted for 2,6-diazaspiro[3.3]heptane-2-carboxylic acid tert-butyl ester hemioxylate and 1-bromo-2-isopropylbenzene was substituted for bromobenzene. The product was purified by column chromatography (dichloromethane/MeOH, 0%~5%).

¹H NMR (400 MHz, CDCl₃) 87.54-7.33 (m, 6H), 7.32-7.11 (m, 3H), 3.77 (s, 2H), 3.65 (sept, J=6.9 Hz, 1H), 3.15 (m, 2H), 3.09-2.99 (m, 4H), 2.96 (m, 2H), 2.47 (dd, J=4.9, 8.8 Hz, 2H), 1.39 (d, J=6.9 Hz, 9H) MS (LC/MS, M+H⁺): m/z 321.2.

Example 60: Preparation of 2-phenyl-2,6-diazaspiro[3.3] heptane trifluoroacetate: To a solution of tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate (0.054 g, 0.196 mmol, 1 eq.) in dichloromethane (1 mL) at 0° C. was added trifluoroacetic acid (1 mL). The reaction was allowed to stir at 22° C. for 30 minutes before being diluted with MeOH and concentrated in vacuo to afford the product as a TFA salt. MS (LC/MS, M+H+): m/z 175.2.

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Example 61: Preparation of 2-(pyridin-4-yl)-2,6-diazaspiro[3.3]heptane ditrifluoroacetate: The title compound was prepared according to the procedure for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tert-butyl 6-(pyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate was substituted for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, M+H+): m/z 176.2.

Example 62: Preparation of 2-(3-methylpyridin-4-yl)-2, 6-diazaspiro[3.3]heptane ditrifluoroacetate: The title compound was prepared according to the procedure for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tertbutyl 6-(3-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate was substituted for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, M+H+): m/z 190.2.

Example 63: Preparation of 2-(2-methylpyridin-4-yl)-2, 6-diazaspiro[3.3]heptane ditrifluoroacetate: The title compound was prepared according to the procedure for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tertbutyl 6-(2-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate was substituted for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, M+H+): m/z 190.2.

Example 64: Preparation of 2-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane: The title compound was prepared according to the procedure for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tert-butyl 6-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro[3.3]heptane-2-carboxylate was substituted for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, 55 M+H $^+$): m/z 204.2.

Example 65: Preparation of 2-(3-methylpyridin-4-yl)oc- 65 tahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate: The title compound was prepared according to the procedure for

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2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tert-butyl 5-(3-methylpyridin-4-yl)hexahydropyrrolo[3,4-c] pyrrole-2(1H)-carboxylate was substituted for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, M+H+): m/z 204.2.

Example 66: Preparation of 2-(2-methylpyridin-4-yl)octahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate: The title compound was prepared according to the procedure for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tert-butyl 5-(2-methylpyridin-4-yl)hexahydropyrrolo[3,4-c] pyrrole-2(1H)-carboxylate was substituted for tert-butyl 6-phenyl-2,6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, M+H⁺): m/z 204.2.

Example 67: Preparation of 2-(2,6-dimethylpyridin-4-yl) octahydropyrrolo[3,4-c]pyrrole: The title compound was prepared according to the procedure for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate, except tert-butyl 5-(2,6-dimethylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrole-2 (1H)-carboxylate was substituted for tert-butyl 6-phenyl-2, 6-diazaspiro[3.3]heptane-2-carboxylate: MS (LC/MS, M+H+): m/z 218.2.

Example 68: Preparation of 2-(o-tolyl)octahydropyrrolo [3,4-c]pyrrole: To a solution of tert-butyl 5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate (0.490 g, 1.62 mmol, 1 eq.) in dichloromethane (4 mL) at 0° C. was added trifluoroacetic acid (2 mL). The reaction was allowed to stir at 22° C. for 30 minutes before being diluted with MeOH and concentrated in vacuo to afford the product as a TFA salt. The salt was then suspended in sat. NaHCO₃ solution and the free based product was extracted with methylene chloride (3×15 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentration in vacuo to afford the product as a free base: MS (LC/MS, M+H⁺): m/z 203.2.

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Example 69: Preparation of 2-(m-tolyl)octahydropyrrolo [3,4-c]pyrrole: The title compound was prepared according to the procedure for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole, except tert-butyl 5-(m-tolyl)hexahydropyrrolo[3,4-c] pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5 5-(m-tolyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z 203.2.

Example 70: Preparation of 2-(p-tolyl)octahydropyrrolo 15 [3,4-c]pyrrole: The title compound was prepared according to the procedure for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole, except 5-(p-tolyl)hexahydropyrrolo[3,4-c]pyrrole-2 (1H)-carboxylate was substituted for tert-butyl 5-(o-tolyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: MS 20 $(LC/MS, M+H^{+}): m/z 203.2$

Example 71: Preparation of 2-(2-methoxyphenyl)octahydropyrrolo[3,4-c]pyrrole: The title compound was prepared according to the procedure for 2-(o-tolyl)octahydropyrrolo [3,4-c]pyrrole, except tert-butyl 5-(2-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(o-tolyl)hexahydropyrrolo[3,4-c] pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z 219.2.

Example 72: Preparation of 2-(4-methoxyphenyl)octahy- 45 dropyrrolo[3,4-c]pyrrole: The title compound was prepared according to the procedure for 2-(o-tolyl)octahydropyrrolo [3,4-c]pyrrole, except tert-butyl 5-(4-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(o-tolyl)hexahydropyrrolo[3,4-c] 50 carboxylate: MS (LC/MS, M+H+): m/z 219.2. pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H⁺): m/z 219.2.

Example 73: Preparation of 3-(hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)benzonitrile: The title compound was prepared according to the procedure for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole, except tert-butyl 5-(3-cyanophenyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate substituted for tert-butyl 5-(o-tolyl)hexahydropyrrolo[3,4-c] pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z 214.2

Example 74: Preparation of 4-(hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)benzonitrile: The title compound was prepared according to the procedure for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole, except tert-butyl 5-(4-cyanophenyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate substituted for tert-butyl 5-(o-tolyl)hexahydropyrrolo[3,4-c] pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z

Example 75: Preparation of 2-(hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)benzonitrile hydrochloride: To a solution of tert-butyl 5-(2-cyanophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate (0.408 g, 1.30 mmol, 1 eq.) in MeOH (1 mL) at 0° C. was added 1M methanolic HCl (3 mL). The reaction was allowed to stir at 22° C. overnight before being diluted with MeOH and concentrated in vacuo to afford the product as a HCl salt. MS (LC/MS, M+H+): m/z 214.2.

Example 76: Preparation of 2-(3-methoxyphenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride: The title compound was prepared according to the procedure for 2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile hydrochloride. except tert-butyl 5-(3-methoxyphenyl)hexahydropyrrolo[3, 4-c|pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(2-cyanophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-

Example 77: Preparation of 2-(2-(benzyloxy)phenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride: The title compound was prepared according to the procedure for 2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile hydrochl oride, except tert-butyl 5-(2-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(2-cyanophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z 295.2.

Example 78: Preparation of 2-(3-(benzyloxy)phenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride: The title compound was prepared according to the procedure for 2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile hydrochloride, except tert-butyl 5-(3-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(2-cyanophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z 295.2.

Example 79: Preparation of 2-(4-(benzyloxy)phenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride: The title compound was prepared according to the procedure for 2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile hydrochloride, except tert-butyl 5-(4-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(2-cyanophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H+): m/z 295.2.

Example 80: Preparation of 4-(2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)phenyl)morpholine hydrochloride: The title compound was prepared according to the procedure for 2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile hydrochloride, except tert-butyl 5-(2-morpholinophenyl) hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate was substituted for tert-butyl 5-(2-cyanophenyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carboxylate: MS (LC/MS, M+H⁺): m/z 274.2.

Example 81: Preparation of 2-(2-isopropylphenyl)octahydropyrrolo[3,4-c]pyrrole: To a dry round bottom flask, 0.04 g of 10% Pd/C (20% wt) was added and wet with a small 65 amount of ethyl acetate. Following, a solution of 2-benzyl-5-(2-isopropylphenyl)octahydropyrrolo[3,4-c]pyrrole (0.20

g, 0.624 mmol, 1 eq.) in MeOH (2.1 mL) was added slowly to the Pd/C containing round bottom flask. This system was then flushed $3\times$ with H_2 , using a balloon filled with H_2 . The reaction was allowed to stir under 1 atm H_2 for 5 days at room temperature. The Pd/C was removed via filtration through a plug of Celite. The filtrate was concentrated in vacuo to afford a crude oil of 2-(2-isopropylphenyl)octahydropyrrolo[3,4-c]pyrrole which was used in the next step without further purification. MS (LC/MS, M+H⁺): m/z 231.2.

Example 82: Preparation of 3-(2-(6-(pyridin-4-yl)-2,6diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1one trifluoroacetate: A mixture of 3-(2-bromoethyl)-2-oxaspiro[4.5]decan-1-one (0.057 g, 0.221 mmol, 1 eq.), acetonitrile (2 mL), 2-(pyridin-4-yl)-2,6-diazaspiro[3.3]heptane ditrifluoroacetate (0.098 g, 0.266 mmol, 1.2 eq.) and K₂CO₃ (0.153 g, 1.11 mmol, 5 eq.) was refluxed and stirred for 3 days. The resulting mixture was then filtered and concentrated in vacuo to give a crude residue that was first purified by column chromatography (methanol/dichloromethane, 0%~10% w/0.1% NH₄OH). The resulting fractions were further purified by column chromatography on a C18 column. (acetonitrile/H₂O, 0%~100%, w/0.1% TFA) ¹H NMR (400 MHz, MeOD) δ8.11 (d, J=7.4 Hz, 2H), 6.67 (d, J=7.1 Hz, 2H), 4.70-4.17 (b, 9H), 3.44 (m, 2H), 2.54 (dd, J=6.2, 12.9 Hz, 1H), 2.10-1.99 (m, 1H), 1.98-1.86 (m, 1H), 1.83-1.61 (m, 6H), 1.60-1.44 (m, 3H), 1.43-1.21 (m, 2H); 40 MS (LC/MS, M+H⁺): =356.2.

Example 83: Preparation of 3,3-diethyl-5-(2-(6-phenyl-2, 6-diazaspiro[3.3]heptan-2-yl)ethyl)dihydrofuran-2(3H)one: A mixture of 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2(3H)-one (0.080 g, 0.324 mmol, 1 eq.), acetonitrile (2 mL), 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate (0.288 g, 0.389 mmol, 1.2 eq.) and K₂CO₃ (0.224 g, 1.62 mmol, 5 eq.) was refluxed and stirred for 3 days. The resulting mixture was then filtered and concentrated in vacuo to give a crude residue that was first purified by chromatography (methanol/dichloromethane, 0%~10%). ¹H NMR (400 MHz, CDCl₃) δ7.13 (m, 2H), 6.67 (t, J=7.4 Hz, 1H), 6.37 (d, J=8.2 Hz, 2H), 4.36 (m, 1H), 3.85 (s, 4H), 3.29 (s, 4H), 2.48 (t, J=7.1 Hz, 2H), 2.04 (dd, J=6.7, 13.0 Hz, 1H), 1.71 (dd, J=9.4, 13.1 Hz, 1H), 1.67-1.43 (m, 6H), 1.83-1.61 (m, 6H), 0.85 (dt, J=7.5, 21.9 Hz, 6H); MS (LC/MS, M+H+): 343.2.

Example 84: Preparation of 3-(2-(6-phenyl-2,6-diazaspiro 10 [3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]decan-1-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl) ethyl)dihydrofuran-2(3H)-one, except 3-(2-bromoethyl)-2-oxaspiro[4.5]decan-1-one was substituted for 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2(3H)-one: 1 H NMR (400 MHz, CDCl₃) δ 7.13 (m, 2H), 6.67 (t, J=7.4 Hz, 1H), 6.37 (d, J=8.5 Hz, 2H), 4.38 (m, 1H), 3.86 (s, 4H), 3.29 (s, 4H), 2.50 (t, J=7.9 Hz, 2H), 2.30 (dd, J=6.2, 12.9 Hz, 1H), 1.81-1.45 (m, 9H), 1.45-1.37 (m, 1H), 1.37-1.08 (m, 3H); MS (LC/ 20 MS, M+H⁺): m/z 355.2.

Example 85: Preparation of 3,3-diethyl-5-(2-(5-(2-isopropylphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl) dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)dihydrofuran-2(3H)-one, except 2-(2-isopropylphenyl)octahydropyrrolo[3,4-c]pyrrole was substituted for 2-phenyl-2,6-diazaspiro[3.3]heptane trifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 87.18 (dd, J=1.5, 7.4 Hz, 1H), 7.10-6.90 (m, 3H), 4.43 (m, 1H), 3.38 (sept, J=6.9 Hz, 1H), 3.01-2.84 (m, 4H), 2.83-2.66 (m, 4H), 2.52 (t, J=6.8 Hz, 2H), 2.19 (m, 2H), 2.06 (dd, J=6.8, 13.1 Hz, 1H), 1.91-1.67 (m, 3H), 1.63-1.44 (m, 4H), 1.15 (d, J=6.9 Hz, 6H), 0.86 (dt, J=7.3, 19.3 Hz, 6H); MS (LC/MS, M+H⁺): m/z 399.2.

Example 86: Preparation of 3-(2-(5-(2-isopropylphenyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro [4.5]decan-1-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)dihydrofuran-2(3H)-one, except 3-(2-bromoethyl)-2-oxaspiro[4.5]decan-1-one was substituted for 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2

(3H)-one and 2-(2-isopropylphenyl)octahydropyrrolo[3,4-c] pyrrole was substituted for 2-phenyl-2,6-diazaspiro[3.3] heptane trifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 87.18 (dd, J=1.5, 7.0 Hz, 1H), 7.09-6.94 (m, 3H), 4.44 (m, 1H), 3.37 (sept, J=6.8 Hz, 1H), 2.99-2.83 (m, 4H), 2.82-2.66 (m, 4H), 2.52 (t, J=7.2 Hz, 2H), 2.32 (dd, J=6.3, 12.7 Hz, 1H), 2.24-2.12 (m, 2H), 1.93-1.81 (m, 1H), 1.80-1.46 (m, 8H), 1.46-1.37 (m, 1H), 1.37-1.04 (m, 9H) MS (LC/MS, M+H⁺): m/z 411.2.

Example 87: Preparation of 3-(2-(5-(3-methylpyridin-4yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one: A mixture of 3-(2-bromoethyl)-2-oxaspiro[4.5]decan-1-one (0.100 g, 0.383 mmol, 1 eq.), acetonitrile (4 mL), 2-(3-methylpyridin-4-yl)octahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate (0.299 g, 0.766 mmol, 2 eq.) and K₂CO₃ (0.264 g, 1.91 mmol, 5 eq.) was refluxed and stirred for 3 days. The resulting mixture was then filtered and concentrated in vacuo to give a crude residue that was first purified by column chromatography on a C18 column. (acetonitrile/H₂O, 0%~100%, w/0.1% NH₄OH). The resulting fractions were further purified by column chromatography (methanol/dichloromethane, 0%~10% w/0.1% NH₄OH). ¹H NMR (400 MHz, CDCl₃) δ8.06 (d, J=18.7 Hz, 2H), 6.49 (d, J=4.7 Hz, 1H), 4.38 (m, 1H), 3.20 (m, 2H), 3.04 (m, 2H), 2.83-2.66 (m, 4H), 2.47 (m, 2H), 2.35-2.21 (m, 3H), 2.17 (s, 3H), 1.85-1.74 (m, 1H), 1.74-1.40 (m, 8H), 40 1.40-1.32 (m, 1H), 1.31-1.02 (m, 3H); MS (LC/MS, M+H+): m/z 384.2.

Example 88: Preparation of 3-(2-(5-(2-methylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxas-piro[4.5]decan-1-one: The title compound was prepared according to the procedure for 3-(2-(5-(3-methylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxas-piro[4.5]decan-1-one, except 2-(2-methylpyridin-4-yl)octahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate was substituted for 2-(3-methylpyridin-4-yl)octahydropyrrolo[3, 4-c]pyrrole ditrifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 87.99 (d, J=5.4 Hz, 1H), 6.23-6.07 (m, 2H), 4.35 (m, 1H), 3.40 (t, J=8.5 Hz, 2H), 3.08 (dt, J=3.3, 9.9 Hz, 2H), 2.85 (b, 2H), 2.65-2.53 (m, 2H), 2.52-2.36 (m, 4H), 2.32 (s, 3H), 2.25 (dd, J=6.3, 12.8 Hz, 1H), 1.84-1.39 (m, 9H), 1.39-1.29 (m, 1H), 1.28-1.01 (m, 3H); MS (LC/MS, M+H⁺): m/z 384.2

Example 89: Preparation of 3-(2-(5-(2,6-dimethylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one: The title compound was prepared according to the procedure for 3-(2-(5-(3-methylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one, except 2-(2,6-dimethylpyridin-4-yl) octahydropyrrolo[3,4-c]pyrroleditrifluoroacetate was substituted for 2-(3-methylpyridin-4-yl)octahydropyrrolo[3, 4-c]pyrrole ditrifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 86.02 (s, 2H), 4.35 (m, 1H), 3.38 (m, 2H), 3.08 (dt, J=3.1, 9.9 Hz, 2H), 2.84 (b, 2H), 2.68-2.53 (m, 2H), 2.53-2.36 (m, 4H), 2.36-2.17 (m, 7H), 1.84-1.39 (m, 9H), 1.38-1.30 (m, 1H), 1.28-0.97 (m, 3H); MS (LC/MS, M+H⁺): m/z 398.2.

Example 90: Preparation of 3-(2-(6-(3-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5] decan-1-one: The title compound was prepared according to the procedure for 3-(2-(5-(3-methylpyridin-4-yl)hexahydro-pyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one, except 2-(3-methylpyridin-4-yl)-2,6-diazaspiro[3.3] heptane ditrifluoroacetate was substituted for 2-(3- 45 methylpyridin-4-yl)octahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 88.02 (d, J=5.2 Hz, 1H), 7.90 (s, 1H), 6.11 (d, J=5.6 Hz, 1H), 4.38 (m, 1H), 4.06 (s, 4H), 3.29 (s, 4H), 2.49 (t, J=7.8 Hz, 2H), 2.30 (dd, J=6.2, 12.9 Hz, 1H), 2.11 (s, 3H), 1.83-1.45 (m, 9H), 1.45-1.37 (m, 1H), 1.37-1.08 (m, 3H); MS (LC/MS, M+H⁺): m/z 370.2.

Example 91: Preparation of 3-(2-(6-(2-methylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5]

decan-1-one: The title compound was prepared according to the procedure for 3-(2-(5-(3-methylpyridin-4-yl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one, except 2-(2-methylpyridin-4-yl)-2,6-diazaspiro[3.3] heptane ditrifluoroacetate was substituted for 2-(3-methylpyridin-4-yl)octahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 88.03 (d, J=5.4 Hz, 1H), 6.07-5.97 (m, 2H), 4.38 (m, 1H), 3.91 (s, 4H), 3.28 (s, 4H), 2.55-2.41 (m, 2H), 2.34 (s, 3H), 2.30 (dd, J=6.2, 12.8 Hz, 1H), 1.82-1.45 (m, 9H), 1.45-1.37 (m, 1H), 1.37-1.07 (m, 3H); MS (LC/MS, M+H+): m/z 370.2.

Example 92: Preparation of 3-(2-(6-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)-2-oxaspiro[4.5] decan-1-one: The title compound was prepared according to the procedure for 3-(2-(5-(3-methylpyridin-4-yl)hexahydro-pyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-2-oxaspiro[4.5]decan-1-one, except 2-(2,6-dimethylpyridin-4-yl)-2,6-diazaspiro [3.3]heptane ditrifluoroacetate was substituted for 2-(3-methylpyridin-4-yl)octahydropyrrolo[3,4-c]pyrrole ditrifluoroacetate. A third purification was need via column chromatography on a C18 column. (acetonitrile/H₂O, 0%~100%, w/0.1% HCOOH): ¹H NMR (400 MHz, CDCl₃) 85.97 (s, 2H), 4.45 (m, 1H), 4.21 (s, 4H), 3.55 (s, 4H), 2.70 (m, 2H), 2.57 (s, 6H), 2.40 (dd, J=6.2, 12.7 Hz, 1H), 1.91-1.54 (m, 9H), 1.54-1.45 (m, 1H), 1.45-1.13 (m, 3H); MS (LC/MS, M+H⁺): m/z 384.2.

Example 93: Preparation of 3,3-diethyl-5-(2-(5-(o-tolyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: A mixture of 5-(2-bromoethyl)-3,3-diethyldihydrofuran-2(3H)-one (0.075 g, 0.301 mmol, 1 eq.), acetonitrile (3 mL), 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole (0.073 g, 0.361 mmol, 1.2 eq.) and N,N-diisopropylethyl amine (0.116 g, 0.903 mmol, 3 eq.) was microwaved at 120° C. for 4 hrs. The resulting solution was concentrated in vacuo to give a crude residue that was first purified by chromatography (methanol/dichloromethane, 0%~10%). ¹H NMR (400 MHz, CDCl₃) δ7.15 (m, 2H), 6.96 (m, 2H), 4.50 (m, 1H), 3.08-2.92 (m, 6H), 2.86 (b, 2H), 2.60 (t, J=6.9 Hz, 2H), 2.37-2.24 (m, 5H), 2.14 (dd, J=6.7, 13.0 Hz, 1H), 1.99-1.75 (m, 3H), 1.64 (m, 4H), 0.94 (dt, J=7.4, 18.1 Hz, 6H); MS (LC/MS, M+H⁺): m/z 371.2.

Example 94: Preparation of 3,3-diethyl-5-(2-(5-(m-tolyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexa hydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2 (3H)-one, except 2-(m-tolyl)octahydropyrrolo[3,4-c]pyrrole was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: $^1\mathrm{H}$ NMR (400 MHz, CDCl $_3$) $\delta 7.13$ (t, J=8.0 Hz, 1H), 6.58 (d, J=7.4 Hz, 1H), 6.53-6.45 (m, 2H), 4.47 (m, 1H), 3.37 (m, 2H), 3.18 (dt, J=2.8, 9.4 Hz, 2H), 2.95 (b, 2H), 2.86 (m, 2H), 2.59 (t, J=7.0 Hz, 2H), 2.41 (dd, J=4.0, 8.9 Hz, 2H), 2.33 (s, 3H), 2.12 (dd, J=6.6, 13.0 Hz, 1H), 1.97-1.73 (m, 3H), 1.62 (q, J=7.5 Hz, 4H), 0.92 (dt, J=7.5, 14.8 Hz, 6H); MS (LC/MS, M+H+): m/z 371.2.

Example 95: Preparation of 3,3-diethyl-5-(2-(5-(p-tolyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexa hydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2 (3H)-one, except 2-(p-tolyl)octahydropyrrolo[3,4-c]pyrrole was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: $^1\mathrm{H}$ NMR (400 MHz, CDCl $_3$) $\delta6.89$ (d, J=8.4 Hz, 2H), 6.45 (d, J=8.4 Hz, 2H), 4.32 (m, 1H), 3.17 (m, 2H), 2.99 (dt, J=3.0, 9.2 Hz, 2H), 2.78 (b, 2H), 2.70 (m, 2H), 2.42 (t, J=6.9 Hz, 2H), 2.42 (dd, J=4.0, 8.8 Hz, 2H), 2.11 (s, 3H), 2.97 (dd, J=6.8, 13.0 Hz, 1H), 1.81-1.57 (m, 3H), 1.45 (q, J=7.2 Hz, 4H), 0.76 (dt, J=7.5, 14.7 Hz, 6H); MS (LC/MS, M+H^+): m/z 371.2.

Example 96: Preparation of 2-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl)hexahydropyrrolo[3,4-c]pyrrol-2 (1H)-yl)benzonitrile: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one, except 2-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile hydrochloride was substituted for

2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: 1 H NMR (400 MHz, CDCl $_{3}$) 87.45 (dd, J=1.5, 7.6 Hz, 1H), 7.36 (m, 1H), 6.81-6.68 (m, 2H), 4.45 (m, 1H), 3.62 (m, 2H), 3.45 (td, J=2.0, 8.6 Hz, 2H), 2.92 (b, 2H), 2.74 (m, 2H), 2.63-2.53 (m, 2H), 2.52-2.46 (m, 2H), 2.11 (dd, J=6.8, 13.0 Hz, 1H), 1.94-1.70 (m, 3H), 1.58 (qd, J=2.6, 7.4 Hz, 4H), 0.88 (dt, J=7.3, 14.8 Hz, 6H); MS (LC/MS, M+H⁺): m/z 382.2.

Example 97: Preparation of 3-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl)hexahydropyrrolo[3,4-c]pyrrol-2 (1H)-yl)benzonitrile: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(0-tolyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one, except 3-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile was substituted for 2-(0-tolyl) octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) 87.26 (m, 1H), 6.95 (d, J=7.5 Hz, 1H), 6.82-6.75 (m, 2H), 4.44 (m, 1H), 3.44 (t, J=8.7 Hz, 2H), 3.15 (dt, J=3.8, 9.4 Hz, 2H), 2.98 (b, 2H), 2.73 (m, 2H), 2.57 (t, J=7.0 Hz, 2H), 3.0 (dd, J=3.1, 9.1 Hz, 2H), 2.10 (dd, J=6.8, 12.9 Hz, 1H), 1.94-1.70 (m, 3H), 1.59 (q, J=7.3 Hz, 4H), 0.89 (dt, J=5.4, 14.9 Hz, 6H); MS (LC/MS, M+H⁺): m/z 382.2.

Example 98: Preparation of 4-(5-(2-(4,4-diethyl-5-oxotetrahydrofuran-2-yl)ethyl)hexahydropyrrolo[3,4-c]pyrrol-2 (1H)-yl)benzonitrile: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one, except 4-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)benzonitrile was substituted for 2-(o-tolyl) octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) 87.44 (d, J=8.9 Hz, 2H), 6.54 (d, J=8.7 Hz, 2H), 4.44 (m, 1H), 3.55 (t, J=9.0 Hz, 2H), 3.23 (dt, J=3.6, 9.9 Hz, 2H), 3.00 (b, 2H), 2.72 (m, 2H), 2.64-2.50 (m, 4H), 2.10 (dd, J=6.7, 13.1 Hz, 1H), 1.94-1.71 (m, 3H), 1.59 (q, J=7.5 Hz, 4H), 0.89 (dt, J=5.1, 14.9 Hz, 6H); MS (LC/MS, M+H⁺): m/z 382.2.

Example 99: Preparation of 3,3-diethyl-5-(2-(5-(2-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihyd rofuran-2(3H)-one, except 2-(2-methoxyphenyl)octahy dropyrrolo[3,4-c]pyrrole was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) 86.83-6.61 (m, 4H), 4.34 (m, 1H), 3.71 (s, 3H), 3.23 (q, J=7.5 Hz, 2H), 2.86 (m, 2H), 2.72 (b, 2H), 2.58 (b, 2H), 2.44 (m, 2H), 2.31 (dt, J=3.2, 8.8 Hz, 2H), 1.98 (dd, J=6.8, 13.1 Hz, 1H), 1.84-1.73 (m, 1H), 1.73-1.58 (m, 2H), 1.47 (qd, J=1.5, 7.5 Hz, 4H), 0.77 (dt, J=7.3, 15.8 Hz, 6H); MS (LC/MS, M+H⁺): m/z 387.2.

Example 100: Preparation of 3,3-diethyl-5-(2-(5-(3-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one, except 2-(3-methoxyphenyl)octahydropyrrolo[3,4-c]pyrrole was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) 35 87.14 (t, J=8.2 Hz, 1H), 6.30 (m, 2H), 6.20 (t, J=2.2 Hz, 1H), 4.46 (m, 1H), 3.79 (s, 3H), 3.38 (t, J=8.2 Hz, 2H), 3.17 (dt, J=3.0, 9.5 Hz, 2H), 2.94 (b, 2H), 2.86-2.77 (m, 2H), 2.57 (t, J=7.1 Hz, 2H), 2.42 (dd, J=3.9, 9.0 Hz, 2H), 2.11 (dd, J=6.8, 13.0 Hz, 1H), 1.95-1.72 (m, 3H), 1.61 (qd, J=1.5, 7.5 Hz, 4H), 0.91 (dt, J=7.4, 14.8 Hz, 6H); MS (LC/MS, M+H+): m/z 387.2.

Example 101: Preparation of 3,3-diethyl-5-(2-(5-(4-methoxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl) dihydrofuran-2(3H)-one, except 2-(4-methoxyphenyl)oct ahydropyrrolo[3,4-c]pyrrole was substituted for 2-(o-tolyl) octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) 86.83 (d, J=9.0 Hz, 2H), 6.65 (d, J=9.0 Hz, 2H), 4.46 (m, 1H), 3.76 (s, 3H), 3.28 (m, 2H), 3.10 (dt, J=3.2, 9.1 Hz, 2H), 2.92 (b, 2H), 2.84 (b, 2H), 2.63-2.51 (m, 2H), 2.39 (dd, J=4.0, 8.7 Hz, 2H), 2.11 (dd, J=6.8, 13.0 Hz, 1H), 65 1.97-1.71 (m, 3H), 1.61 (qd, J=1.3, 7.4 Hz, 4H), 0.91 (dt, J=7.3, 14.8 Hz, 6H); MS (LC/MS, M+H⁺): m/z 387.2.

Example 102: Preparation of 3,3-diethyl-5-(2-(5-(2-morpholinophenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihy drofuran-2(3H)-one, except 4-(2-(hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)phenyl)morpholine hydrochloride was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) 87.05-6.94 (m, 3H), 6.91-6.83 (m, 1H), 4.49 (m, 1H) 3.85 (t, J=4.7 Hz, 4H), 3.68-3.42 (m, 4H), 3.22-2.84 (m, 10H), 2.61 (b, 2H), 2.30 (b, 1H), 2.19 (dd, J=6.7, 13.2 Hz, 1H), 2.05-1.90 (m, 1H), 1.84 (dd, J=9.3, 13.2 Hz, 1H), 1.67-1.56 (m, 4H), 0.91 (dt, J=7.3, 16.5 Hz, 6H); MS (LC/MS, M+H⁺): m/z 442.2.

Example 103: Preparation of 5-(2-(5-(2-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(o-tolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one, except 2-(2-(benzyloxy)phenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: $^1\mathrm{H}$ NMR (400 MHz, CDCl $_3$) 87.46-7.29 (m, 5H), 7.01-6.86 (m, 3H), 6.81 (dd, J=1.4, 7.7 Hz, 1H), 5.03 (s, 2H), 4.43 (m, 1H), 3.61 (b, 2H), 3.36 (t, J=10.6 Hz, 2H), 3.17-2.97 (m, 3H), 2.91 (td, J=5.3, 12.2 Hz, 1H), 2.86-2.73 (m, 2H), 2.58-2.37 (m, 2H), 2.30 (m, 1H), 2.17 (dd, J=6.7, 13.1 Hz, 1H), 1.92-1.73 (m, 2H), 1.61 (q, J=7.4 Hz, 4H), 0.91 (dt, J=7.0, 13.9 Hz, 6H); MS (LC/MS, M+H+): m/z 463.2.

Example 104: Preparation of 5-(2-(5-(3-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-di-

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ethyldihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(otolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihy drofuran-2(3H)-one, except 2-(3-(benzyloxy)phenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₃) δ7.39-7.33 (m, 2H), 7.33-7.26 (m, 2H), 7.26-7.20 (m, 1H), 7.05 (m, 1H), 6.29 (dd, J=1.7, 8.1 Hz, 1H), 6.24-6.18 (m, 2H), 4.96 (s, 2H), 4.37 (m, 1H), 3.28 (m, 2H), 3.08 (dt, J=2.9, 9.3 Hz, 2H), 2.93-2.81 (m, 2H), 2.81-2.69 (m, 2H), 2.50 (t, J=7.2 Hz, 2H), 2.33 (dd, J 3.9, 8.9 Hz, 2H), 2.02 (dd, J=6.7, 13.0 Hz, 1H), 1.87-1.63 (m, 3H), 1.52 (qd, J=1.2, 7.4 Hz, 4H), 0.82 (dt, J=7.4, 14.9 Hz, 6H); MS (LC/MS, M+H+): m/z 463.2.

Example 105: Preparation of 5-(2-(5-(4-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(otolyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihy drofuran-2(3H)-one, except 2-(4-(benzyloxy)phenyl)octahydropyrrolo[3,4-c]pyrrole hydrochloride was substituted for 2-(o-tolyl)octahydropyrrolo[3,4-c]pyrrole: ¹H NMR (400 MHz, CDCl₂) 87.37-7.31 (m, 2H), 7.31-7.25 (m, 2H), 7.24-7.18 (m, 1H), 6.81 (d, J=9.0 Hz, 2H), 6.55 (d, J=9.0 Hz, 2H), 4.92 (s, 2H), 4.37 (m, 1H), 3.19 (m, 2H), 3.01 (dt, 35) J=3.1, 9.3 Hz, 2H), 2.89-2.80 (m, 2H), 2.80-2.70 (m, 2H), 2.48 (t, J=6.9 Hz, 2H), 2.29 (dd, J 3.9, 8.6 Hz, 2H), 2.02 (dd, J=6.7, 13.1 Hz, 1H), 1.87-1.62 (m, 3H), 1.52 (q, J=7.3 Hz, 4H), 0.82 (dt, J=7.5, 14.5 Hz, 6H); MS (LC/MS, M+H⁺): m/z 463.2.

Example 106: Preparation of 3,3-diethyl-5-(2-(5-(2-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one: To a dry round bottom flask, 0.013 g of 10% Pd/C (20% wt) was added and wet with a 55 small amount of ethyl acetate. Following, a solution of 5-(2-(5-(2-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one (0.065 g, 0.140 mmol, 1 eq.) in MeOH (1.5 mL) was added slowly to the Pd/C containing round bottom flask. This 60 system was then flushed 3× with H₂, using a balloon filled with H_2 . The reaction was allowed to stir under 1 atm H_2 for overnight at room temperature. The Pd/C was removed via filtration through a plug of Celite. The filtrate was concentrated in vacuo to give a crude residue that was first purified 65 by column chromatography (methanol/dichloromethane, 0%~10%). ¹H NMR (400 MHz, CDCl₃) 87.13 (dd, J=1.3,

7.8 Hz, 1H), 7.05 (td, J=1.3, 7.7 Hz, 1H), 6.93 (dd, J=1.3, 8.1 Hz, 1H), 6.85 (td, J=1.4, 7.7 Hz, 1H), 4.52 (m, 1H), 3.12-3.00 (m, 2H), 2.98-2.74 (m, 6H), 2.65 (t, J=7.3 Hz, 2H), 2.58-2.46 (m, 2H), 2.16 (dd, J=6.7, 13.1 Hz, 1H), 2.00-1.76 (m, 3H), 1.64 (q, J=7.5 Hz, 4H), 0.95 (dt, J=7.4, 22.8 Hz, 6H); MS (LC/MS, M+H+): m/z 373.2.

Example 107: Preparation of 3,3-diethyl-5-(2-(5-(3-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(2hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one, except 5-(2-(5-(3-(benz vloxy)phenyl) hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)-3,3-diethyldihydrofuran-2(3H)-one was substituted for 5-(2-(5-(2-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c] pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one: ¹H NMR (400 MHz, CDCl₃) δ6.85 (t, J=8.1 Hz, 1H), 6.00 (td, J=1.8, 7.6 Hz, 2H), 5.91 (t, J=2.3 Hz, 1H), 4.24 (m, 1H), 3.18-3.05 (m, 2H), 2.97 (d, J=9.2 Hz, 2H), 2.83-2.64 (m, 4H), 2.44 (t, J=7.3 Hz, 2H), 2.25 (m, 2H), 1.91 (dd, J=6.7, 13.1 Hz, 1H), 1.77-1.53 (m, 3H), 1.40 (q, J=7.4 Hz, 4H), 0.70 (dt, J=7.4, 15.6 Hz, 6H); MS (LC/MS, M+H+): m/z 373.2.

Example 108: Preparation of 3,3-diethyl-5-(2-(5-(4-hydroxyphenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl) ethyl)dihydrofuran-2(3H)-one trifluoroacetate: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(5-(2-hydroxyphenyl)hexahydropyrrolo[3, 4-c|pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one, except 5-(2-(5-(4-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one was substituted for 5-(2-(5-(2-(benzyloxy)phenyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)-3,3-diethyldihydrofuran-2(3H)-one and the reaction time was extended to 3 days. A second purification was need via column chromatography on a C18 column. (acetonitrile/H₂O, 0%-100%, w/0.1% TFA): ¹H NMR (400 MHz, MeOD) δ6.78-6.67 (m, 4H), 4.54 (m, 1H), 3.69 (b, 2H), 3.45 (dd, J=7.2, 9.6 Hz, 2H), 3.40-3.09 (m, 6H), 2.98 (m, 2H), 2.28 (dd, J=6.7, 13.2 Hz, 1H), 2.20-1.97 (m, 2H), 1.91 (dd, J=9.4, 13.2 Hz, 1H), 1.74-1.52 (m, 4H), 0.94 (dt, J=5.0, 14.9 Hz, 6H); MS (LC/MS, M+H+):m/z 373.2.

Example 109: Preparation of 3,3-diethyl-5-(2-(5-phenyl-hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)ethyl)dihydrofuran-2(3H)-one: The title compound was prepared according to the procedure for 3,3-diethyl-5-(2-(6-phenyl-2,6-diazaspiro[3.3]heptan-2-yl)ethyl)dihydrofuran-2(3H)-one, except 2-phenyloctahydropyrrolo[3,4-c]pyrrole dihydrochloride was substituted for 2-phenyl-2,6-diazaspiro[3.3] heptane trifluoroacetate: ¹H NMR (400 MHz, CDCl₃) 87.14 (m, 2H), 6.64 (t, J=7.2 Hz, 1H), 6.57 (d, J=8.5 Hz, 2H), 4.37 (m, 1H), 3.29 (t, J=8.1 Hz, 2H), 3.08 (dt, J=2.7, 9.3 Hz, 2H), 2.92-2.79 (b, 2H), 2.78-2.65 (m, 2H), 2.47 (t, J=6.9 Hz, 2H), 2.32 (dd, J=4.0, 8.9 Hz, 2H), 2.02 (dd, J=6.7, 13.1 Hz, 1H), 1.87-1.61 (m, 3H), 1.51 (q, J=7.3 Hz, 4H), 0.81 (dt, J=7.5, 13.9 Hz, 6H); MS (LC/MS, M+H⁺): m/z 357.2

Formulations

The present invention also relates to compositions or formulations which comprise the sigma-2 receptor binders and sigma-2 receptor activity modulators according to the present invention. In general, the compositions of the present invention comprise an effective amount of one or more compounds of the disclosure and salts thereof according to the present invention which are effective for providing modulation of sigma-2 receptor activity; and one or more excipients.

For the purposes of the present invention the term "excipient" and "carrier" are used interchangeably throughout the description of the present invention and said terms are defined herein as, "ingredients which are used in the practice of formulating a safe and effective pharmaceutical composition."

The formulator will understand that excipients are used primarily to serve in delivering a safe, stable, and functional pharmaceutical, serving not only as part of the overall vehicle for delivery but also as a means for achieving 45 effective absorption by the recipient of the active ingredient. An excipient may fill a role as simple and direct as being an inert filler, or an excipient as used herein may be part of a pH stabilizing system or coating to insure delivery of the ingredients safely to the stomach. The formulator can also 50 take advantage of the fact the compounds of the present invention have improved cellular potency, pharmacokinetic properties, as well as improved oral bioavailability.

The present teachings also provide pharmaceutical compositions that include at least one compound described 55 herein and one or more pharmaceutically acceptable carriers, excipients, or diluents. Examples of such carriers are well known to those skilled in the art and can be prepared in accordance with acceptable pharmaceutical procedures, such as, for example, those described in Remington's Pharmaceutical Sciences, 17th edition, ed. Alfonoso R. Gennaro, Mack Publishing Company, Easton, PA (1985), the entire disclosure of which is incorporated by reference herein for all purposes. As used herein, "pharmaceutically acceptable" refers to a substance that is acceptable for use in pharmaceutical applications from a toxicological perspective and does not adversely interact with the active ingredient.

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Accordingly, pharmaceutically acceptable carriers are those that are compatible with the other ingredients in the formulation and are biologically acceptable. Supplementary active ingredients can also be incorporated into the pharmaceutical compositions.

Compounds of the present teachings can be administered orally or parenterally, neat or in combination with conventional pharmaceutical carriers. Applicable solid carriers can include one or more substances which can also act as flavoring agents, lubricants, solubilizers, suspending agents, fillers, glidants, compression aids, binders or tablet-disintegrating agents, or encapsulating materials. The compounds can be formulated in conventional manner, for example, in a manner similar to that used for known sigma-2 receptor activity modulators. Oral formulations containing a compound disclosed herein can comprise any conventionally used oral form, including tablets, capsules, buccal forms, troches, lozenges and oral liquids, suspensions or solutions. In powders, the carrier can be a finely divided solid, which is an admixture with a finely divided compound. In tablets, a compound disclosed herein can be mixed with a carrier having the necessary compression properties in suitable proportions and compacted in the shape and size desired. The powders and tablets can contain up to 99% of the 25 compound.

Capsules can contain mixtures of one or more compound(s) disclosed herein with inert filler(s) and/or diluent(s) such as pharmaceutically acceptable starches (e.g., corn, potato or tapioca starch), sugars, artificial sweetening agents, powdered celluloses (e.g., crystalline and microcrystalline celluloses), flours, gelatins, gums, and the like.

Useful tablet formulations can be made by conventional compression, wet granulation or dry granulation methods and utilize pharmaceutically acceptable diluents, binding 35 agents, lubricants, disintegrants, surface modifying agents (including surfactants), suspending or stabilizing agents, including, but not limited to, magnesium stearate, stearic acid, sodium lauryl sulfate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, microcrystalline cellulose, sodium carboxymethyl cellulose, carboxymethylcellulose calcium, polyvinylpyrrolidine, alginic acid, acacia gum, xanthan gum, sodium citrate, complex silicates, calcium carbonate, glycine, sucrose, sorbitol, dicalcium phosphate, calcium sulfate, lactose, kaolin, mannitol, sodium chloride, low melting waxes, and ion exchange resins. Surface modifying agents include nonionic and anionic surface modifying agents. Representative examples of surface modifying agents include, but are not limited to, poloxamer 188, benzalkonium chloride, calcium stearate, cetostearl alcohol, cetomacrogol emulsifying wax, sorbitan esters, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, magnesium aluminum silicate, and triethanolamine. Oral formulations herein can utilize standard delay or time-release formulations to alter the absorption of the compound(s). The oral formulation can also consist of administering a compound disclosed herein in water or fruit juice, containing appropriate solubilizers or emulsifiers as needed.

Liquid carriers can be used in preparing solutions, suspensions, emulsions, syrups, elixirs, and for inhaled delivery. A compound of the present teachings can be dissolved or suspended in a pharmaceutically acceptable liquid carrier such as water, an organic solvent, or a mixture of both, or a pharmaceutically acceptable oils or fats. The liquid carrier can contain other suitable pharmaceutical additives such as solubilizers, emulsifiers, buffers, preservatives, sweeteners, flavoring agents, suspending agents, thickening agents, col-

ors, viscosity regulators, stabilizers, and osmo-regulators. Examples of liquid carriers for oral and parenteral administration include, but are not limited to, water (particularly containing additives as described herein, e.g., cellulose derivatives such as a sodium carboxymethyl cellulose solution), alcohols (including monohydric alcohols and polyhydric alcohols, e.g., glycols) and their derivatives, and oils (e.g., fractionated coconut oil and *arachis* oil). For parenteral administration, the carrier can be an oily ester such as ethyl oleate and isopropyl myristate. Sterile liquid carriers are used in sterile liquid form compositions for parenteral administration. The liquid carrier for pressurized compositions can be halogenated hydrocarbon or other pharmaceutically acceptable propellants.

Liquid pharmaceutical compositions, which are sterile 15 solutions or suspensions, can be utilized by, for example, intramuscular, intraperitoneal or subcutaneous injection. Sterile solutions can also be administered intravenously. Compositions for oral administration can be in either liquid or solid form.

Preferably the pharmaceutical composition is in unit dosage form, for example, as tablets, capsules, powders, solutions, suspensions, emulsions, granules, or suppositories. In such form, the pharmaceutical composition can be sub-divided in unit dose(s) containing appropriate quantities 25 of the compound. The unit dosage forms can be packaged compositions, for example, packeted powders, vials, ampoules, prefilled syringes or sachets containing liquids. Alternatively, the unit dosage form can be a capsule or tablet itself, or it can be the appropriate number of any such 30 compositions in package form. Such unit dosage form can contain from about 1 mg/kg of compound to about 500 mg/kg of compound, and can be given in a single dose or in two or more doses. Such doses can be administered in any manner useful in directing the compound(s) to the recipi- 35 ent's bloodstream, including orally, via implants, parenterally (including intravenous, intraperitoneal and subcutaneous injections), rectally, vaginally, and transdermally.

When administered for the treatment or inhibition of a particular disease state or disorder, it is understood that an 40 effective dosage can vary depending upon the particular compound utilized, the mode of administration, and severity of the condition being treated, as well as the various physical factors related to the individual being treated. In therapeutic applications, a compound of the present teachings can be 45 provided to a patient already suffering from a disease in an amount sufficient to cure or at least partially ameliorate the symptoms of the disease and its complications. The dosage to be used in the treatment of a specific individual typically must be subjectively determined by the attending physician. 50 The variables involved include the specific condition and its state as well as the size, age and response pattern of the patient.

In some cases it may be desirable to administer a compound directly to the airways of the patient, using devices such as, but not limited to, metered dose inhalers, breath-operated inhalers, multidose dry-powder inhalers, pumps, squeeze-actuated nebulized spray dispensers, aerosol dispensers, and aerosol nebulizers. For administration by intranasal or intrabronchial inhalation, the compounds of the present teachings can be formulated into a liquid composition, a solid composition, or an aerosol composition. The liquid composition can include, by way of illustration, one or more compounds of the present teachings dissolved, partially dissolved, or suspended in one or more pharmaceutically acceptable solvents and can be administered by, for example, a pump or a squeeze-actuated nebulized spray

dispenser. The solvents can be, for example, isotonic saline or bacteriostatic water. The solid composition can be, by way of illustration, a powder preparation including one or more compounds of the present teachings intermixed with lactose or other inert powders that are acceptable for intrabronchial use, and can be administered by, for example, an aerosol dispenser or a device that breaks or punctures a capsule encasing the solid composition and delivers the solid composition for inhalation. The aerosol composition can include, by way of illustration, one or more compounds of the present teachings, propellants, surfactants, and co-solvents, and can be administered by, for example, a metered device. The propellants can be a chlorofluorocarbon (CFC), a hydrofluoroalkane (HFA), or other propellants that are physiologically and environmentally acceptable.]

Compounds described herein can be administered parenterally or intraperitoneally. Solutions or suspensions of these compounds or a pharmaceutically acceptable salts, hydrates, or esters thereof can be prepared in water suitably mixed with a surfactant such as hydroxyl-propylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof in oils. Under ordinary conditions of storage and use, these preparations typically contain a preservative to inhibit the growth of microorganisms.

The pharmaceutical forms suitable for injection can include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In some embodiments, the form can sterile and its viscosity permits it to flow through a syringe. The form preferably is stable under the conditions of manufacture and storage and can be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol and liquid polyethylene glycol), suitable mixtures thereof, and vegetable oils.

Compounds described herein can be administered transdermally, i.e., administered across the surface of the body and the inner linings of bodily passages including epithelial and mucosal tissues. Such administration can be carried out using the compounds of the present teachings including pharmaceutically acceptable salts, hydrates, or esters thereof, in lotions, creams, foams, patches, suspensions, solutions, and suppositories (rectal and vaginal).

Transdermal administration can be accomplished through the use of a transdermal patch containing a compound, such as a compound disclosed herein, and a carrier that can be inert to the compound, can be non-toxic to the skin, and can allow delivery of the compound for systemic absorption into the blood stream via the skin. The carrier can take any number of forms such as creams and ointments, pastes, gels, and occlusive devices. The creams and ointments can be viscous liquid or semisolid emulsions of either the oil-inwater or water-in-oil type. Pastes comprised of absorptive powders dispersed in petroleum or hydrophilic petroleum containing the compound can also be suitable. A variety of occlusive devices can be used to release the compound into the blood stream, such as a semi-permeable membrane covering a reservoir containing the compound with or without a carrier, or a matrix containing the compound. Other occlusive devices are known in the literature.

Compounds described herein can be administered rectally or vaginally in the form of a conventional suppository. Suppository formulations can be made from traditional materials, including cocoa butter, with or without the addition of waxes to alter the suppository's melting point, and

glycerin. Water-soluble suppository bases, such as polyethylene glycols of various molecular weights, can also be used.

Lipid formulations or nanocapsules can be used to introduce compounds of the present teachings into host cells either in vitro or in vivo. Lipid formulations and nanocapsules can be prepared by methods known in the art.

To increase the effectiveness of compounds of the present teachings, it can be desirable to combine a compound with 10 other agents effective in the treatment of the target disease. For example, other active compounds (i.e., other active ingredients or agents) effective in treating the target disease can be administered with compounds of the present teachings. The other agents can be administered at the same time or at different times than the compounds disclosed herein.

Compounds of the present teachings can be useful for the treatment or inhibition of a pathological condition or disorder in a mammal, for example, a human subject. The present teachings accordingly provide methods of treating or inhibiting a pathological condition or disorder by providing to a mammal a compound of the present teachings including its pharmaceutically acceptable salt) or a pharmaceutical composition that includes one or more compounds of the present teachings in combination or association with pharmaceutically acceptable carriers. Compounds of the present teachings can be administered alone or in combination with other therapeutically effective compounds or therapies for the treatment or inhibition of the pathological condition or disorder.

Non-limiting examples of compositions according to the present invention include from about 0.001 mg to about 1000 mg of one or more compounds of the disclosure according to the present invention and one or more excipients; from about 0.01 mg to about 100 mg of one or more 40 compounds of the disclosure according to the present invention and one or more excipients; and from about 0.1 mg to about 10 mg of one or more compounds of the disclosure according to the present invention; and one or more excipi- 45 ents.

Procedures

The following procedure may be utilized in evaluating 50 and selecting compounds as sigma-2 receptor binders and sigma-2 receptor activity modulators.

Radiolabel Binding Studies for the sigma-2 receptor:

A solution of the compound of the disclosure to be tested $\,$ is prepared as a 1-mg/ml stock in Assay Buffer or DMSO according to its solubility. A similar stock of the reference compound Haloperidol is also prepared as a positive control. Eleven dilutions (5× assay concentration) of the compound of the disclosure and Haloperidol are prepared in the Assay Buffer by serial dilution to yield final corresponding assay concentrations ranging from 10 pM to 10 μM .

A stock concentration of 5 nM ³H-1,3-di-(2-tolyl)guanidine (³H-DTG) is prepared in 50 mM Tris-HCl, 10 mM MgCl₂, 1 mM EDTA, pH 7.4 (Assay Buffer). Aliquots (50

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 μ l) of radioligand are dispensed into the wells of a 96-well plate containing 100 μ l of Assay Buffer. Duplicate 50- μ l aliquots of the compound of the disclosure test and Haloperidol positive control reference compound serial dilutions are added.

Membrane fractions of cells expressing recombinant sigma-2 receptors (50 μ L) are dispensed into each well. The membranes are prepared from stably transfected cell lines expressing sigma-2 receptors cultured on 10-cm plates by harvesting PBS-rinsed monolayers, resuspending and lysing in chilled, hypotonic 50 mM Tris-HCl, pH 7.4, centrifuging at 20,000×g, decanting the supernatant and storing at -80° C.; the membrane preparations are resuspended in 3 ml of chilled Assay Buffer and homogenized by several passages through a 26 gauge needle before using in the assay.

The 250-µl reactions are incubated at room temperature for 1.5 hours, then harvested by rapid filtration onto 0.3% polyethyleneimine-treated, 96-well filter mats using a 96-well Filtermate harvester. Four rapid 500-µl washes are performed with chilled Assay Buffer to reduce non-specific binding. The filter mats are dried, then scintillant is added to the filters and the radioactivity retained on the filters is counted in a Microbeta scintillation counter.

Raw data (dpm) representing total radioligand binding (i.e., specific+non-specific binding) are plotted as a function of the logarithm of the molar concentration of the competitor (i.e., test or reference compound). Non-linear regression of the normalized (i.e., percent radioligand binding compared to that observed in the absence of test or reference compound) raw data is performed in Prism 4.0 (GraphPad Software) using the built-in three parameter logistic model describing ligand competition binding to radioligand-labeled sites:

 $y=bottom+[(top-bottom)/(1+10\times-log IC_{50})]$

where bottom equals the residual radioligand binding measured in the presence of 10 μ M reference compound (i.e., non-specific binding) and top equals the total radioligand binding observed in the absence of competitor. The log IC $_{50}$ (i.e., the log of the ligand concentration that reduces radioligand binding by 50%) is thus estimated from the data and used to obtain the Ki by applying the Cheng-Prusoff approximation:

 $\mathit{Ki=}IC_{50}/(1+[\mathrm{ligand}]/\mathit{KD})$

where [ligand] equals the assay radioligand concentration and KD equals the affinity constant of the radioligand for the target receptor.

Compounds of the disclosure are also screened at a single concentration of $10 \,\mu\text{M}$ using the same method described for the Radiolabel Binding Studies for sigma-2 receptors to determine the percent inhibition of $^3\text{H-DTG}$ binding.

Results for representative compounds according to the present invention are listed in Table 21.

TABLE 21

Radiolabel Binding Studies for the sigma-2 receptors results for exemplary compounds of the disclosure

the disclosure	
Entry Structure	Sigma-2 IC ₅₀ (nm
	3.5
	29
3 O N N N N N N N N N N N N N N N N N N	39
	2.0
5 O_N_N_N_N_	2.4
	3.9
7 0 N N N	11

TABLE 21-continued

Radiolabel Binding Studies for the sigma-2 receptors results for exemplary compounds of the disclosure

Entry Structure	Sigma-2 IC ₅₀ (nr
8 O N N	N 24
9 O O N N N	34 N
10 O N N	59 N
$\begin{array}{c} 11 \\ 0 \\ 0 \\ \end{array}$	30
$\begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \end{array}$	3.9 N
O O N N	1.2 N
$\begin{array}{c} \\ \\ \\ \\ \\ \end{array}$	1.5

TABLE 21-continued

Radiolabel Binding Studies for the sigma-2 receptors results for exemplary compounds of
the disclosure

the disclosure	
Entry Structure	Sigma-2 IC ₅₀ (nm)
15 O N N	53
O NC	6.8
O O N N N CN	7.0
18 O O N N O CY	9.6 N
19 0 N	6.5
	25
21 0 0 N N	, 22

What is claimed is:

1. A compound having formula (VIII):

$$\mathbb{R}^{la}$$

$$\mathbb{R}^{lb}$$

$$\mathbb{N}$$

$$\mathbb{R}^{3}$$

$$(VIII) 5$$

or a pharmaceutically acceptable salt thereof, wherein:

R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C₁₋₆ linear alkyl, and C_{1-6} branched alkyl, R^{1a} and R^{1b} may be taken together with the atom to which they are bound to form a cyclohexyl; and

R³ is optionally substituted phenyl or optionally substituted pyridyl.

2. The compound of claim 1, wherein R^{1a} and R^{1b} are each independently C_{1-6} linear alkyl or C_{1-6} branched alkyl. 25 **3**. The compound of claim **2**, wherein R^{1a} and R^{1b} are

each independently methyl or ethyl.

4. The compound of claim 1, wherein R³ is selected from a group consisting of phenyl, 4-OH-phenyl, 3-OH-phenyl, 2-OH-phenyl, 4-CH₃-phenyl, 3-CH₃-phenyl, 2-CH₃-phenyl, 30 4-OCH₃-phenyl, 3-OCH₃-phenyl, 2-OCH₃-phenyl, 4-CNphenyl, 3-CN-phenyl, 2-CN-phenyl, 4-F-phenyl, 3-F-phenyl, 2-F-phenyl, 4-Cl-phenyl, 3-Cl-phenyl, 2-Cl-phenyl, 4-OCF₃-phenyl, 3-OCF₃-phenyl, 2-OCF₃-phenyl, 4-isopropyl-phenyl, 3-isopropyl-phenyl, 2-isopropyl-phenyl, 4-cy- 35 clopropyl-phenyl, 3-cyclopropyl-phenyl, 2-cyclopropyl-4-morpholino-phenyl, 3-morpholino-phenyl, phenyl, 2-morpholino-phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-CH₃-4-pyridyl, 3-CH₃-4-pyridyl, 3,5-dimethylpyridin-4yl, 2,6-dimethylpyridin-4-yl, 2-CF₃-phenyl, 3-CF₃-phenyl, 40 4-CF₃-phenyl, 2-NH₂-phenyl, 3-NH₂-phenyl, 4-NH₂-phenyl, 2-tBu-phenyl, 3-tBu-phenyl, 4-tBu-phenyl, 2-NO₂-phenyl, 3-NO₂-phenyl, 4-NO₂-phenyl, 2-SCH₃-phenyl, 3-SCH₃-phenyl, 4-SCH₃-phenyl, 2-SO₂CH₃-phenyl, 3-SO₂CH₃-phenyl, 4-SO₂CH₃-phenyl, 2-SO₂NH₂-phenyl, $3-SO_2NH_2-phenyl,\ 4-SO_2NH_2-phenyl,\ 2-CO_2NH_2-phenyl,$ 3-CO₂NH₂-phenyl, 4-CO₂NH₂-phenyl, 2-Br-phenyl, 3-Brphenyl, 4-Br-phenyl, 2,3-di-CH₃-phenyl, 2,4-di-CH₃-phenyl, 2,5-di-CH₃-phenyl, 2,6-di-CH₃-phenyl, 3,4-di-CH₃phenyl, 3,5-di-CH₃-phenyl, 2,3-di-Cl-phenyl, 2,4-di-Cl- ⁵⁰ phenyl, 2,5-di-Cl-phenyl, 2,6-di-Cl-phenyl, 3,4-di-Clphenyl, 3,5-di-Cl-phenyl, 2-morpholino-4-CH₃-phenyl, 2-morpholino-4-CN-phenyl, 2-morpholino-4-OH-phenyl, 2,3-dimethylpyridin-4-yl, and 3,6-dimethylpyridin-4-yl.

5. The compound of claim 4, wherein R³ is unsubstituted 55 phenyl, 4-pyridyl, 3-CH₃-4-pyridyl, 2-CH₃-4-pyridyl, or 2,6-dimethylpyridin-4-yl.

6. The compound of claim 1, wherein the compound is selected from a group consisting of

or a pharmaceutically acceptable salt thereof.