

POLYCYCLIC AMINES FOR OPIOID RECEPTOR MODULATION

BACKGROUND

There is a continuing need for new opioid receptors modulators for the management of pain with reduced or fewer side effects. There is also a continuing need for new opioid receptors modulators for the treatment migraine, depression, cognitive disorders, Parkinson's disease, locomotor disfunction, pruritus, diarrhea, irritable bowel syndrome and gastro-intestinal disorders, bladder dysfunctions, overactive bladder, urinary incontinence, neurogenic bladder, interstitial cystitis, drug addiction, alcohol addiction, drug overdose, premature ejaculation, cough, lung edema, cardiac disorders, cardioprotection, and respiratory depression, and as immunomodulatory and anti-tumor agents. A number of such opioid receptor modulators are disclosed in US Pat. No. 10,676,456 (incorporated by reference). Some additional new compounds are shown below.

SUMMARY

The present invention provides polycyclic amines, prodrugs and pharmaceutically acceptable salts thereof ("compounds of the invention"), which are useful in the treatment of diseases through the modulation of opioid receptors; similar to the compounds and their uses disclosed in US Pat. No. 10,676,456. The process of making the compounds listed below are disclosed in or similar to processes of making compounds disclosed in US Pat. No. 10,676,456.

The compounds of the invention are useful for preventing or treating a disease or condition selected from the group consisting of cardioprotection, cardiac disorders, analgesia, functional pain, inflammatory pain, peripherally mediated and neuropathic pain, non-somatic pain, arthritis, mental illness, cognitive disorders, depression, Parkinson's disease, locomotor disfunction, urogenital tract disorders, bladder dysfunction, overactive bladder, urinary incontinence, neurogenic bladder, psoriasis, pruritus, emesis, acne, skin lesions, non-ulcerogenic dyspepsia, gastro-intestinal

disorders, functional bowel disease, diarrhea, inflammatory bowel disease, irritable bowel syndrome, interstitial cystitis, sexual dysfunctions, drug addiction, alcohol addiction, drug overdose, premature ejaculation, asthma, cough, lung edema, disorders of respiratory function, respiratory depression, functional distension, and disorders of motility or secretion. These compounds are also useful for immunomodulation, inhibiting or preventing organ or skin graft rejection, or treating tumors or cancer. All such treatment involves administering, to a patient, an effective amount of one or more of the compounds of the invention.

The present invention also includes a pharmaceutical composition comprising a pharmaceutically acceptable carrier and one or more of the compounds of the invention.

These and other aspects and embodiments of the invention will be apparent from the detailed description that follows.

DETAILED DESCRIPTION

Certain compounds of the invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are encompassed within the scope of the present invention. Certain compounds of the invention may exist in multiple crystalline or amorphous forms. In general, all physical forms are equivalent for the uses contemplated by the present invention and are intended to be within the scope of the present invention.

The compounds of the invention, or their pharmaceutically acceptable salts, may have asymmetric carbon atoms or double bonds in their structure. The compounds of the invention and their pharmaceutical acceptable salts may therefore exist as single stereoisomers, racemates, and as mixtures of enantiomers, diastereomers and geometric isomers. All such single stereoisomers, racemates and mixtures thereof are intended to be within the scope of the invention. Absolute configuration of certain

carbon atoms within the compounds, if known, are indicated by the appropriate absolute descriptors R or S.

The compounds of the invention may be synthesized in the form of racemic mixtures of enantiomers which can be separated from one another following art-known resolution procedure. The racemic compounds of the invention may be converted into the corresponding diastereomeric salt forms by reaction with a suitable chiral acid. Said diastereomeric salt forms are subsequently separated, for example, by selective or fractional crystallization and the enantiomers are liberated therefrom by alkali. An alternative manner of separating the enantiomeric forms of the compounds of the invention involves liquid chromatography using a chiral stationary phase. Said pure stereochemically isomeric forms may also be derived from the corresponding pure stereochemically isomeric forms of the appropriate starting materials, provided that the reaction occurs stereospecifically. Preferably if a specific stereoisomer is desired, said compound will be synthesized by stereospecific methods of preparation. These methods will advantageously employ enantiomerically pure starting materials.

The compounds of the invention may also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the compounds may be radiolabeled with radioactive isotopes, such as for example tritium (³H), iodine-125 (¹²⁵I) or carbon-14 (¹⁴C). All isotopic variations of the compounds of the invention, whether radioactive or not, are encompassed within the scope of the present invention.

"Therapeutic" as used herein, includes prevention, treatment and/or prophylaxis for humans as well as other animals.

"Pharmaceutically or therapeutically effective dose or amount" refers to a dosage level sufficient to induce a desired biological result. That result may be the alleviation

of the signs, symptoms or causes of a disease or any other alteration of a biological system that is desired. The precise dosage will vary according to a variety of factors, including but not limited to the age and size of the subject, the disease and the treatment being effected.

A "host" or "patient" or "subject" is a living mammal, human or animal, for whom therapy is desired. The "host," "patient" or "subject" generally refers to the recipient of the therapy to be practiced according to the method of the invention. It should be noted that the invention described herein may be used for veterinary as well as human applications and that the term "host" should not be construed in a limiting manner. In the case of veterinary applications, the dosage ranges can be determined as described below, taking into account the body weight of the animal.

As used herein, the term "pharmaceutically acceptable" means approved by a regulatory agency of a federal or a state government or listed in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals and, more particularly, in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered and includes, but is not limited to such sterile liquids as water and oils.

The term "pharmaceutically acceptable salts" is meant to include salts of the active compounds which are prepared with relatively nontoxic acids or bases, depending on the particular substituents found on the compounds described herein. When compounds of the invention contain relatively acidic functionalities, base addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amino, or magnesium salt, or a similar salt. When compounds of the invention contain relatively basic functionalities, acid

addition salts can be obtained by contacting the neutral form of such compounds with a sufficient amount of the desired acid, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable acid addition salts include those derived from inorganic acids like hydrochloric, hydrobromic, nitric, carbonic, monohydrogencarbonic, phosphoric, monohydrogenphosphoric, dihydrogenphosphoric, sulfuric, monohydrogensulfuric, hydroiodic, or phosphorous acids and the like, as well as the salts derived from relatively nontoxic organic acids like acetic, propionic, isobutyric, maleic, malonic, benzoic, succinic, suberic, fumaric, lactic, mandelic, phthalic, benzenesulfonic, p-tolylsulfonic, citric, tartaric, methanesulfonic, and the like. Also included are salts of amino acids such as arginate and the like, and salts of organic acids like glucuronic or galactunoric acids and the like (see, for example, Berge et al., "Pharmaceutical Salts", Journal of Pharmaceutical Science 66: 1-19 (1977)). Certain specific compounds of the invention contain both basic and acidic functionalities that allow the compounds to be converted into either base or acid addition salts.

Other examples of pharmaceutically acceptable salts of the invention include salts derived from an appropriate base, such as an alkali metal (for example, sodium, potassium), an alkaline earth metal (for example, calcium, magnesium), ammonium and NR'_4 (wherein R' is C_1 - C_4 alkyl). Pharmaceutically acceptable salts of the invention having an amino group include salts of: organic carboxylic acids such as acetic, lactic, tartaric, malic, lactobionic, fumaric, and succinic acids; organic sulfonic acids such as methanesulfonic, ethanesulfonic, isethionic, benzenesulfonic and p-toluenesulfonic acids; and inorganic acids such as hydrochloric, hydrobromic, sulfuric, phosphoric and sulfamic acids. Pharmaceutically acceptable salts of the invention having a hydroxyl group consist of the anion of such compounds in combination with a suitable cation such as Na^+ , NH_4^+ , or NR'_4^+ , (wherein R' is for example a C_1 - C_4 group).

The neutral forms of the compounds of the invention are preferably regenerated by contacting the salt with a base or acid and isolating the parent compound in the

conventional manner. The parent form of the compound may differ from the various salt forms in certain physical properties, such as solubility in polar solvents.

In addition to salt forms, the invention provides compounds which are in a prodrug form. Prodrugs of the compounds described herein are those compounds that readily undergo chemical changes under physiological conditions to provide the compounds of the invention.

Additionally, prodrugs can be converted to the compounds of the invention by chemical or biochemical methods in an ex vivo environment. For example, prodrugs can be slowly converted to the compounds of the invention when placed in a transdermal patch reservoir with a suitable enzyme or chemical reagent. Prodrugs are often useful because, in some situations, they may be easier to administer than the parent drug. They may, for instance, be bioavailable by oral administration whereas the parent drug is not. The prodrug may also have improved solubility in pharmaceutical compositions over the parent drug. A wide variety of prodrug derivatives are known in the art, such as those that rely on hydrolytic cleavage or oxidative activation of the prodrug. An example, without limitation, of a prodrug would be a compound of the present invention which is administered as an ester (the "prodrug"), but then is metabolically hydrolyzed to the carboxylic acid, the active entity. Additional examples include peptidyl derivatives of a compound of the invention. Certain compounds of the invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are intended to be encompassed within the scope of the invention. Certain compounds of the invention may exist in multiple crystalline or amorphous forms. In general, all physical forms are equivalent for the uses contemplated by the invention and are intended to be within the scope of the invention.

A "pharmaceutical composition" is a formulation comprising the disclosed compounds in a form suitable for administration to a subject. A pharmaceutical composition of the invention is preferably formulated to be compatible with its intended route of administration. Examples of routes of administration include, but are not limited to, oral and parenteral, e.g., intravenous, intradermal, subcutaneous, inhalation, topical, transdermal, transmucosal, and rectal administration.

The compounds of the invention can combine with an exogenous receptor or be used as complexing compounds, and may be used for binding with an opioid receptor. Further, the compounds may be used as a conjugate in an agonist/antagonist pair that is employed for transductional assay of neurotransmitter function in appertaining cellular or differentiated tissue systems, as well as for receptor assay, differential binding, and specificity applications for cellular, histological, and corporeal monitoring and assessment purposes.

The compounds of the invention can be administered for therapeutic intervention in a pharmaceutical composition containing the compound and a pharmaceutically acceptable carrier. The invention contemplates the use of any means and/or of modality of administration of the compositions of the invention.

The compounds of the invention include their physiologically functional derivatives. "Physiologically functional derivative" includes a pharmaceutically acceptable salt, ether, ester or salt of an ether or ester of the compounds of the invention or any other compound which, upon administration to the recipient, is capable of providing (directly or indirectly) a compound of the invention or an active metabolite or residue thereof. Phenolic C₁-C₆ alkyl ethers are a sub-class of physiologically functional derivatives of the compounds of the invention.

The compounds of the invention when used in pharmaceutical or diagnostic applications preferably are prepared in a racemic mixture or an essentially pure

enantiomer form, with an enantiopurity of at least 90% enantiomeric excess (EE), preferably at least 95% EE, more preferably at least 98% EE, and most preferably at least 99% EE. Enantiomeric excess values provide a quantitative measure of the excess of the percentage amount of a major isomer over the percentage amount of a minor isomer which is present therewith, and may be readily determined by suitable methods well-known and established in the art, as for example chiral high pressure liquid chromatography (HPLC), chiral gas chromatography (GC), nuclear magnetic resonance (NMR) using chiral shift reagents, etc.

Subjects to be treated by administration of the compounds of the invention are preferably human subjects, but also include non-human mammals and other animals (e.g., bird, dog, cat, cow, horse).

Depending on the specific condition to be treated, subjects may be administered compounds of the invention at any suitable therapeutically effective and safe dosage, as may readily be determined within the skill of the art, and without undue experimentation, with extrapolation from the animal dosages set forth herein in the examples. In *in vitro* tests for agonist/antagonist activity, such as receptor binding affinity tests, and inhibition of electrically stimulated muscle twitch tests, compounds of the invention exhibit potency.

In general, while the effective dosage of compounds of the invention for therapeutic use may be widely varied in the broad practice of the invention, depending on the specific application, condition, or disease state involved, as readily determinable within the skill of the art, suitable therapeutic doses of the compounds of the invention, for each of the appertaining compositions described herein, and for achievement of therapeutic benefit in treatment of each of the conditions described herein, will be in the range of 10 micrograms (μg) to 100 milligrams (mg) per kilogram body weight of the recipient per day, preferably in the range of 50 μg to 75

mg per kilogram body weight per day, and most preferably in the range of 100 μ g to 50 mg per kilogram body weight per day. The desired dose is preferably presented as one, two, three, four, five, six, or more sub-doses administered at appropriate intervals throughout the day. These sub-doses may be administered in unit dosage forms, for example, containing from 10 μ g to 1000 mg, preferably from 50 μ g to 500 mg, more preferably from 50 μ g to 250 mg, and most preferably from 50 μ g to 10 mg of active ingredient per unit dosage form. Alternatively, if the condition of the recipient so requires, the doses may be administered as a continuous infusion.

The mode of administration and dosage forms will affect the therapeutic amounts of the compounds which are desirable and efficacious for the given treatment application.

For example, orally administered dosages typically are at least twice, e.g., 2-10 times, the dosage levels used in parenteral administration methods, for the same active ingredient. In oral administration, dosage levels for delta receptor binding compounds of the invention may be on the order of 5-200 mg/70 kg body weight/day. In tablet dosage forms, typical active agent dose levels are on the order of 10-100 mg per tablet.

The compounds of the invention may be administered per se as well as in the form of pharmaceutically acceptable esters, salts, and ethers, as well as other physiologically functional derivatives of such compounds.

The present invention also contemplates pharmaceutical compositions, both for veterinary and for human medical use, which comprise as the active agent one or more compound(s) of the invention.

In such pharmaceutical compositions, the active agent preferably is utilized together with one or more pharmaceutically acceptable carrier(s) therefor and optionally any other therapeutic ingredients. The carrier(s) preferably are compatible with the other ingredients of the formulation and not unduly deleterious to the recipient thereof. The active agent is preferably in a pharmaceutically acceptable amount effective to achieve the desired pharmacological effect.

The formulations include those suitable for parenteral as well as non-parenteral administration, and specific administration modalities include oral, rectal, topical, sub-lingual, mucosal, transdermal, nasal, ophthalmic, subcutaneous, intramuscular, intravenous, transdermal, spinal, intrathecal, intra-articular, intra-arterial, sub-arachnoid, bronchial, lymphatic, and intra-uterine administration. Formulations suitable for oral administration are preferred.

When the active agent is utilized in a formulation comprising a liquid solution, the formulation advantageously may be administered parenterally. When the active agent is employed in a liquid suspension formulation or as a powder in a biocompatible carrier formulation, the formulation may be advantageously administered orally, rectally, or bronchially.

When the active agent is utilized directly in the form of a powdered solid, the active agent may be advantageously administered orally. Alternatively, it may be administered bronchially, via nebulization of the powder in a carrier gas, to form a gaseous dispersion of the powder which is inspired by the patient from a breathing circuit comprising a suitable nebulizer device.

In some applications, it may be advantageous to utilize the active agent in a "vectorized" form, such as by encapsulation of the active agent in a liposome or other encapsulant medium, or by fixation of the active agent, e.g., by covalent bonding,

chelation, or associative coordination, on a suitable biomolecule, such as those selected from proteins, lipoproteins, glycoproteins, and polysaccharides.

The formulations comprising the compounds of the invention may conveniently be presented in unit dosage forms and may be prepared by any of the methods well known in the art of pharmacy. Such methods generally include the step of bringing the compound(s) into association with a carrier that constitutes one or more accessory ingredients. Typically, the formulations are prepared by uniformly and intimately bringing the active compound(s) into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product into dosage forms of the desired formulation.

Formulations of the present invention suitable for oral administration may be presented as discrete units such as capsules, cachets, tablets, or lozenges, each containing a predetermined amount of the active ingredient as a powder or granules; or a suspension in an aqueous liquor or a non-aqueous liquid, such as a syrup, an elixir, an emulsion, or a draught.

A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing in a suitable machine, with the active compound being in a free-flowing form such as a powder or granules which optionally is mixed with a binder, disintegrant, lubricant, inert compound, surface active agent, or discharging agent. Molded tablets comprised of a mixture of the powdered active compound with a suitable carrier may be made by molding in a suitable machine.

A syrup may be made by adding the active compound to a concentrated aqueous solution of a sugar, for example sucrose, to which may also be added any accessory ingredient(s). Such accessory ingredient(s) may include flavorings, suitable

preservative, agents to retard crystallization of the sugar, and agents to increase the solubility of any other ingredient, such as a polyhydroxy alcohol, for example glycerol or sorbitol.

Formulations suitable for parenteral administration conveniently comprise a sterile aqueous preparation of the active compound, which preferably is isotonic with the blood of the recipient (e.g., physiological saline solution). Such formulations may include suspending agents and thickening agents and liposomes or other microparticulate systems which are designed to target the compound to blood components or one or more organs. The formulations may be presented in unit-dose or multi-dose form.

Nasal spray formulations comprise purified aqueous solutions of the active compounds with preservative agents and isotonic agents. Such formulations are preferably adjusted to a pH and isotonic state compatible with the nasal mucous membranes.

Formulations for rectal administration may be presented as a suppository with a suitable carrier such as cocoa butter, hydrogenated fats, or hydrogenated fatty carboxylic acids.

Ophthalmic formulations are prepared by a similar method to the nasal spray, except that the pH and isotonic factors are preferably adjusted to match that of the eye.

Topical formulations comprise the active compound dissolved or suspended in one or more media, such as mineral oil, petroleum, polyhydroxy alcohols, or other bases used for topical pharmaceutical formulations.

Transdermal formulations may be prepared by incorporating the active agent in a thixotropic or gelatinous carrier such as a cellulosic medium, e.g., methyl cellulose or hydroxyethyl cellulose, with the resulting formulation then being packed in a transdermal device adapted to be secured in dermal contact with the skin of a wearer.

In addition to the aforementioned ingredients, formulations of this invention may further include one or more accessory ingredient(s) selected from diluents, buffers, flavoring agents, binders, disintegrants, surface active agents, thickeners, lubricants, preservatives (including antioxidants), and the like.

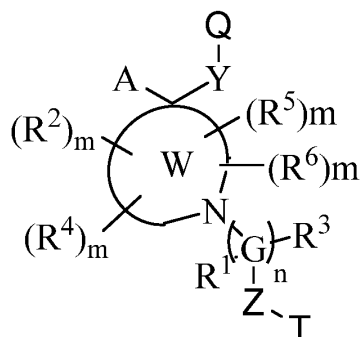
The disease state or physiological condition involved in such therapeutic intervention may be of any type or kind noted above, e.g., centrally mediated disorders; pain, depression, drug addiction, and drug dependence, alcohol addiction; and peripherally mediated neuropathic pain, cough, lung edema, gastro-intestinal disorders, arthritis, psoriasis, asthma, inflammatory bowel disease, disorders of respiratory function, functional bowel disease, irritable bowel syndrome, diarrhea, functional distension, pain (e.g., functional pain, trauma pain, etc.), non-ulcerogenic dyspepsia, urogenital tract disorders, premature ejaculation, overactive bladder, urinary incontinence, organ transplant rejection, skin graft rejection, cardiac disorders, cardioprotection, emesis, acne and skin lesions.

The compounds of the present invention may be readily synthesized within the skill of the art and in view of the illustrative synthesis examples hereinafter set forth.

The invention is further illustrated by the following non-limiting preparation schemes and other examples.

PREPARATION OF OPIOID RECEPTOR MODULATORS

The following exemplary schemes illustrate methods of preparing the compounds of the invention, wherein the compounds of the invention have a structure according to Formula I, and include pharmaceutically acceptable salts and other derivatives of this structure:

**(Formula I)**

wherein:

A includes substituted or unsubstituted: alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, and arylalkyl;

Y includes substituted or unsubstituted: alkyl, heteroalkyl, cycloalkyl, and heterocycloalkyl;

Q includes: substituted or unsubstituted: aryl, heteroaryl, and null;

W includes substituted or unsubstituted, saturated or unsaturated: (i) 4- to 8- membered heterocyclic rings including an N-substituent as an atom of the ring; and (ii) bicyclic or heterobicyclic fused rings wherein each ring has 4- to 10- members, and wherein at least one of the rings includes an N-substituent as an atom of the ring;

G includes substituted or unsubstituted alkyl or an N atom;

Z includes substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and null;

If Z is null then T is null, but if Z is not null, T is selected from: (i) the moieties H, OH, NH₂, NO₂, -SO₂NH₂, halogen, (ii) substituted or unsubstituted: alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl;

n is an integer from 1-4 when G is alkyl and is 1 when G is an N atom;

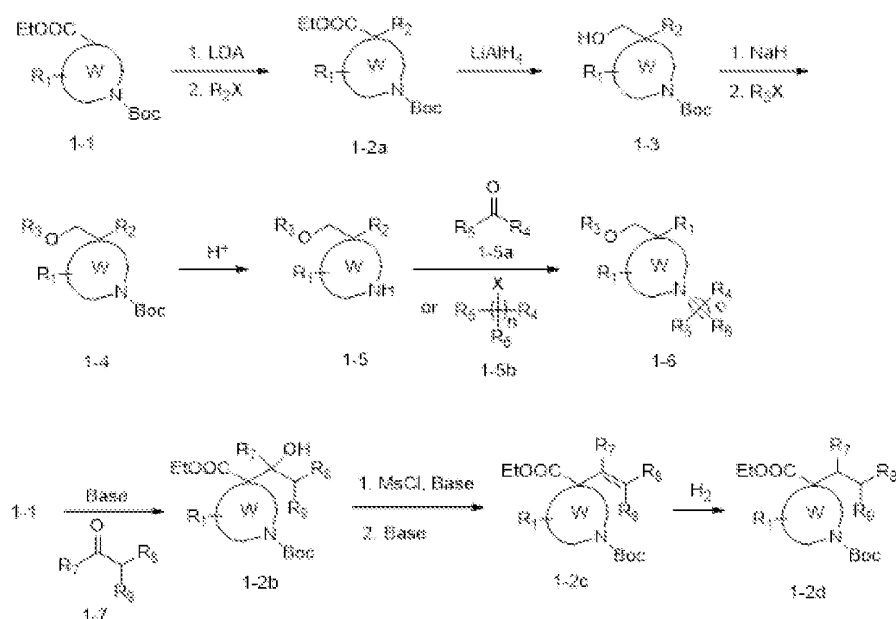
R^1 and R^3 are members independently selected from H and substituted or unsubstituted: alkyl, heteroalkyl, 3- to 7- membered cycloalkyl, 3- to 7- membered heterocycloalkyl, aryl, and heteroaryl;

m is an integer from 0-8 and can be same or different for each of R^2 , R^4 , R^5 and R^6 , and wherein R^2 , R^4 , R^5 and R^6 are each independently selected from H and substituted or unsubstituted: alkyl, heteroalkyl, 3- to 7- membered cycloalkyl, 3- to 7- membered heterocycloalkyl, and where m is greater than 1 for any of R^2 , R^4 , R^5 and R^6 , each member in such a multi-member R^2 , R^4 , R^5 and R^6 chain can be the same or different; and further provided that the total number of R^2 , R^4 , R^5 and R^6 having an m value greater than 0 is always less than or equal to the number of W ring positions available for covalent bonding; and

R^1 and R^3 , or R^1 or R^3 and Z, or R^2 and A, or R^2 and Y together with groups to which they may be joined, optionally form a substituted or unsubstituted 3- to 7- membered ring.

Scheme 1

Compounds where “A” of Formula I is an alkyl or heteroalkyl moiety are synthesized as illustrated in Scheme 1. The synthesis of compounds **1-6** is exemplified.

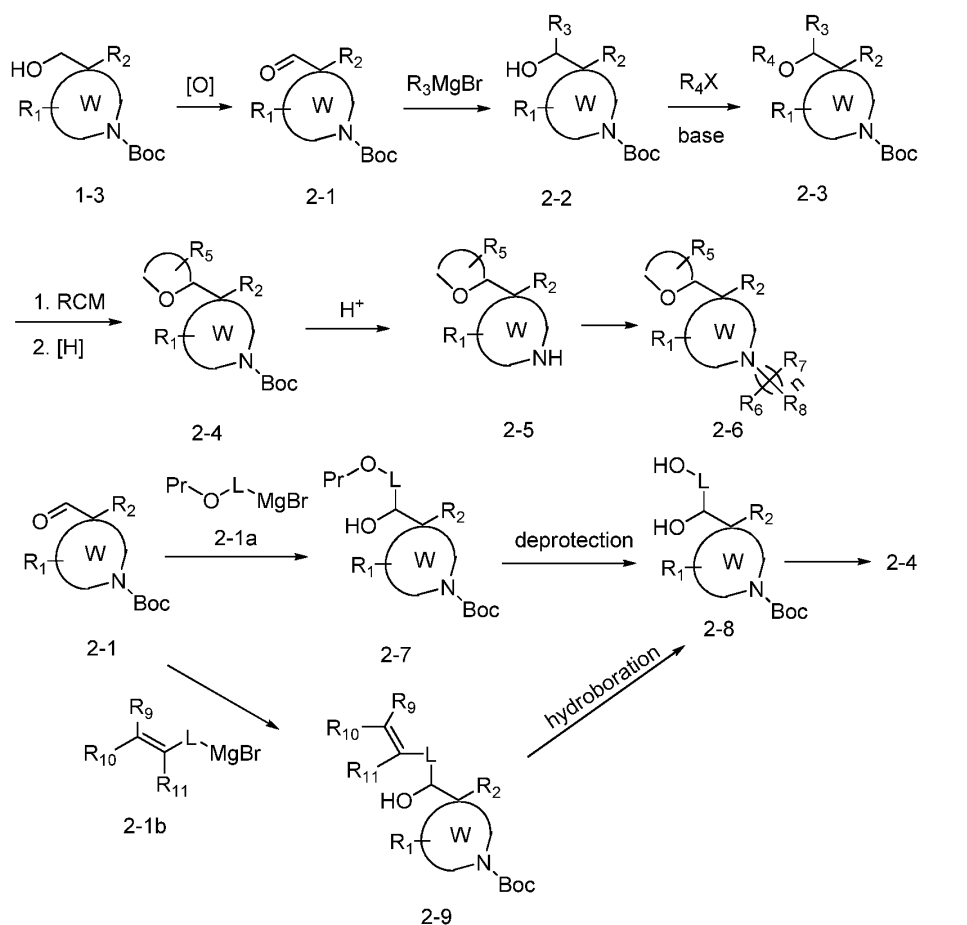


wherein for Scheme I above, X is selected from: Cl, Br, I, p-toluenesulfonyl (Tos), methanesulfonyl (Ms) and trifluoromethanesulfonyl (Tf).

In Scheme I, a substituted cyclic ester **1-1** is deprotonated in the presence of a strong base, such as LDA, LHMDs, or the like, followed by alkylation to produce **1-2a**. Reduction of **1-2a** followed by alkylation gives the ether **1-4**. Deprotection of the Boc group of **1-4** is carried out in the presence of an acid, such as TFA, HCl or the like. Reductive amination of **1-5** with a suitable aldehyde or ketone **1-5a** or alkylation of **1-5** with **1-5b** under basic conditions gives **1-6**. The compounds with different moieties from R¹ are exemplified by the synthesis of intermediates such as **1-2b**, **1-2c**, or **1-2d**. Reaction of **1-1** with a suitable ketone or aldehyde **1-7** gives the intermediate **1-2b**. Activation of the hydroxyl group of **1-2b** using MsCl followed by the elimination in the presence of bases, such as DBU or the like, produces the unsaturated intermediates **1-2c**. Hydrogenation of **1-2c** gives the intermediate **1-2d**.

Scheme 2

Compounds where “A” of Formula I is a cyclic alkyl or cyclic heteroalkyl moiety are synthesized as illustrated in Scheme 2. The synthesis of compounds **2-6** is used as an example.



L: alkyl or heteroalkyl linkers; Pr: protection groups

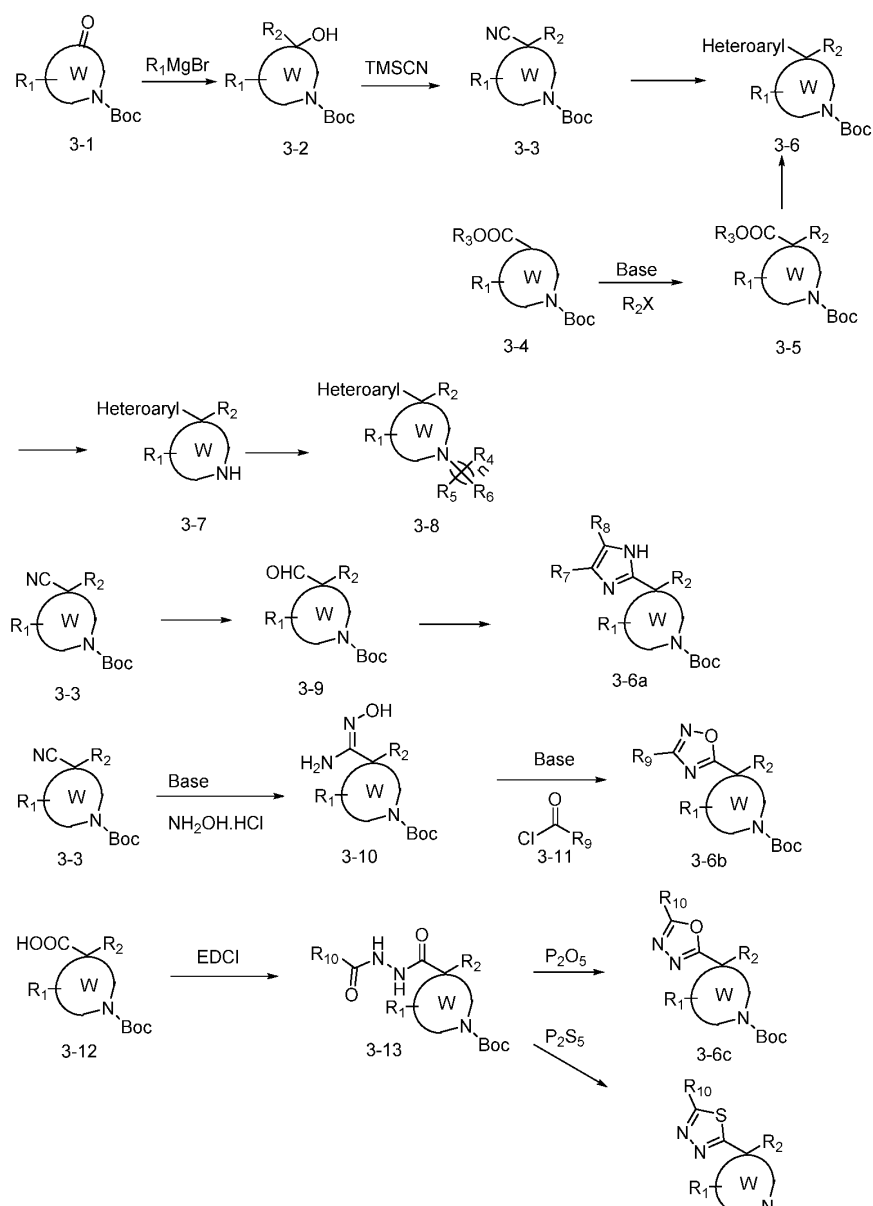
Oxidation of **1-3** to **2-1** is carried out by Swern oxidation or other oxidants, such as Dess-Martin Periodinane or the like. Grignard reaction of aldehyde **2-1** with an unsaturated or a saturated Grignard reagent, followed by alkylation with an unsaturated or a saturated alkylating reagent under basic condition gives **2-3**. Ring-closing metathesis (RCM) of **2-3** with a catalyst, such as Grubbs ruthenium-carbene complexes or the like, yields an unsaturated oxygen-containing heterocyclic **2-4** or a saturated oxygen-containing heterocyclic **2-4** after hydrogenation. Alternatively, the synthesis of **2-4** is achieved by a Grignard reaction of **2-1** with **2-1a** or **2-1b**, followed by either deprotection of the intermediate **2-7** or hydroboration of double bond of the intermediate **2-9** to give the corresponding diol **2-8**. The diol **2-8** is converted to **2-4** by intramolecular cyclization under Mitsunobu

reaction condition or displacement of the corresponding mesylates, tosylates, or the like.

Finally, the synthesis of **2-6** from **2-4** is achieved using the same methodology as the conversion of **1-4** to **1-6** in Scheme 1.

Scheme 3

Compounds where “A” of Formula I is a heteroaryl moiety are synthesized as illustrated in Scheme 3 and exemplified by the synthesis of **3-8**.

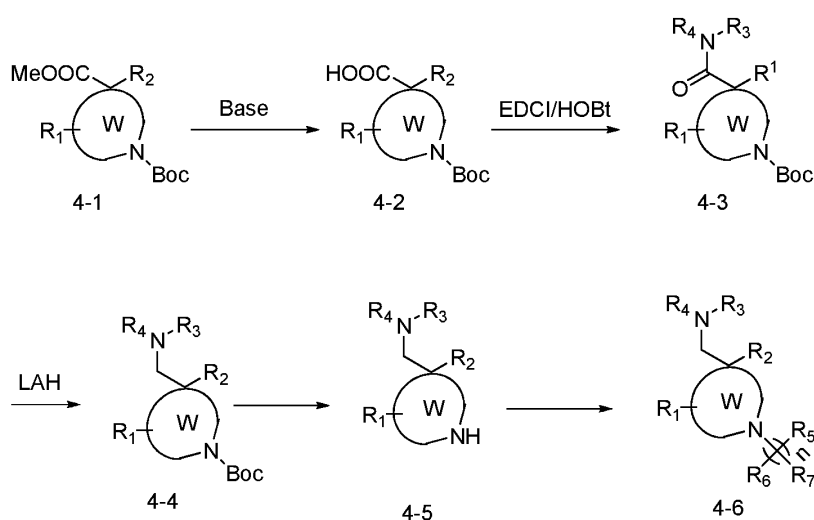


The cyano intermediate **3-3** and the ester intermediate **3-5** are prepared from substituted **3-2** by cynidation and **3-4** by alkylation as described in Scheme 1. The cyano group of **3-3** and the ester group of **3-5** are converted to heterocyclic rings such as imidazole, thiazole, thiadiazole, oxadiazole **3-6** (**3-6a**, **3-6b**, **3-6c** and **3-6d**), etc. through the corresponding intermediates such as amide, thioamide, hydrazide,

thiohydrazide or N-hydroxy-imidamide using the common methods exemplified in the scheme 3. The conversion of **3-6** to **3-8** is achieved using the methodology illustrated in Scheme 1.

Scheme 4

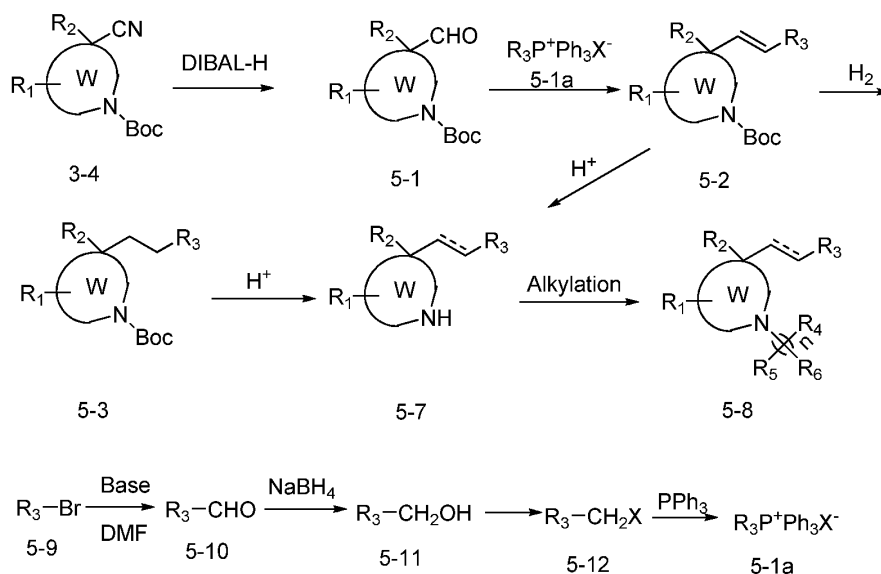
Compounds where “A” of Formula I is a heteroalkyl moiety are synthesized as illustrated in Scheme 4 and exemplified by the synthesis of **4-6**.



A suitable substituted cyclic amide **4-3** is prepared from the corresponding ester **4-1** by hydrolysis using bases, such as NaOH, LiOH, KOH, or the like, followed by coupling with an amine in the presence of coupling reagents, such as EDCI/HOBt, DCC, HATU, or the like. Reduction of **4-3** using BH_3 or $LiAlH_4$, followed by deprotection of Boc group of **4-4** and alkylation of **4-5** as described in Scheme 1 yields compound **4-6**.

Scheme 5

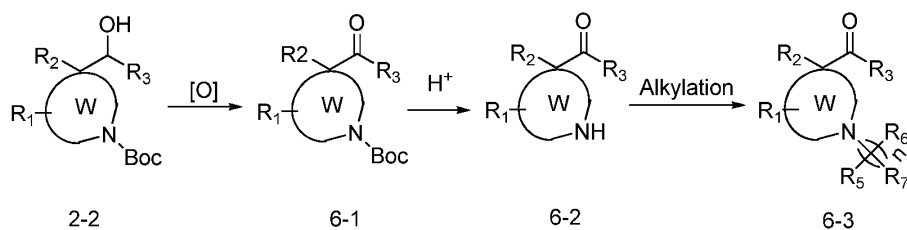
As illustrated in Scheme 5, compounds where Y and Q of Formula I are certain moieties are synthesized.



Reduction of CN group to aldehyde **5-1**, followed by Wittig reaction with a quaternary phosphonium salt such as **5-1a** produces compound **5-2**. Hydrogenation of the double bond of **5-2** followed by deprotection or deprotection of **5-2** followed by the alkylation gives either an unsaturated or a saturated compound **5-8**. The quaternary phosphonium salt **5-1a** is prepared from a suitable bromide **5-9**. Conversion of a suitable bromide **5-9** to the corresponding aldehyde **5-10**, followed by reduction of the aldehyde with a suitable reducing agent, such as NaBH₄ or the like, gives alcohol **5-11**. Halogenation of alcohol **5-11**, followed by the treatment with PPh₃ gives a quaternary phosphonium salt **5-1a**.

Scheme 6

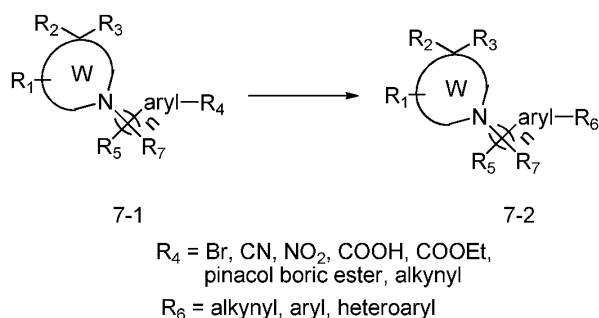
As illustrated in Scheme 6, compounds where Y and Q of Formula I are other moieties than in Scheme 5 are synthesized.



Alcohol **2-2** is oxidized with oxidants such as Dess-Martin Periodic acid, PCC, or the like to form ketone **6-1**. Deprotection of the Boc group of **6-1**, followed by alkylation generates **6-3**.

Scheme 7

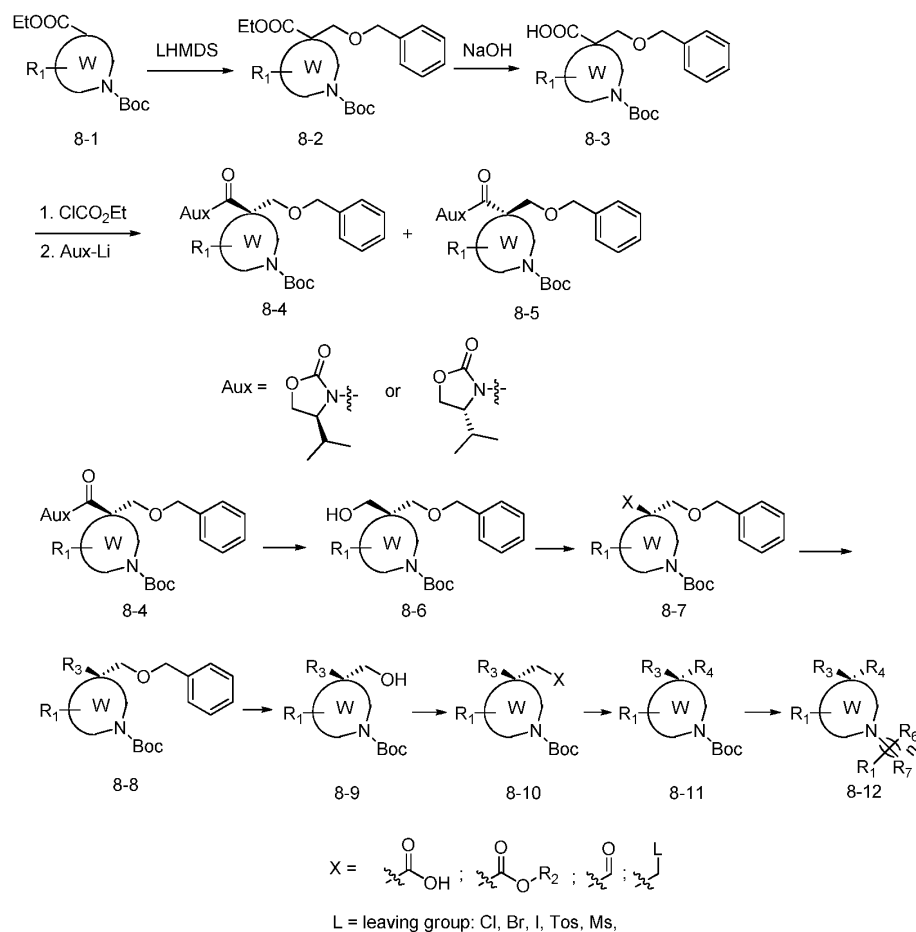
As illustrated in Scheme 7, compounds where Z and T of Formula I are particular moieties are synthesized.



The starting **7-1** is a group of intermediates which are prepared according to the schemes 1 to 6. The aryl group of **7-1** is a substituted or an unsubstituted aryl group, such as benzene, thiazolyl, thiophenyl, furanyl, imidazolyl, thiadiazolyl, oxadiazolyl, tetrazolyl. The R_4 is a functional group such as Br, I, CN, COOH, COOEt, boric acid. The conversion of R_4 to R_6 is achieved via Suzuki coupling of boric acid with Br or I, or the cyclization of hydrazide of ester with acid or the cyclization of N-hydroxy-imidamide with an acyl chloride.

Scheme 8

Scheme 8 illustrates one of the approaches for the synthesis of stereo isomers. In addition, the synthesis of the two enantiomerically pure isomers is also achieved by the chiral separation via chiral HPLC, chiral resolution, or column chromatography methods.

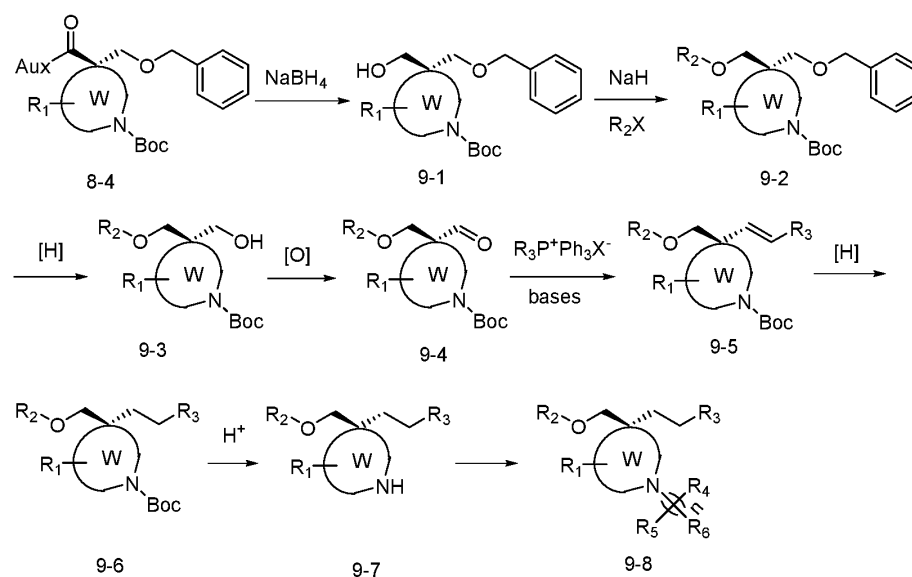


In scheme 8, ester **8-2**, prepared according to scheme 1, is hydrolyzed to acid **8-3** using inorganic bases, such as LiOH, NaOH, KOH, or the like. Acid **8-3** is activated to its corresponding acid chloride or mixed anhydride, followed by reaction with lithiated chiral auxiliary salt provides a mixture of diastereomers **8-4** and **8-5**. The separation of diastereomeric mixture provides the single enantiomers **8-4** and **8-5**.

The enantiomerically pure intermediates such as **8-4** and **8-5** are further transformed into a variety of the key intermediates, such as **8-8** and **8-10**, in enantiomerically pure form, using the methodologies illustrated in the schemes **1-7**. Some examples are illustrated in Scheme 9 and Scheme 10 below.

Scheme 9

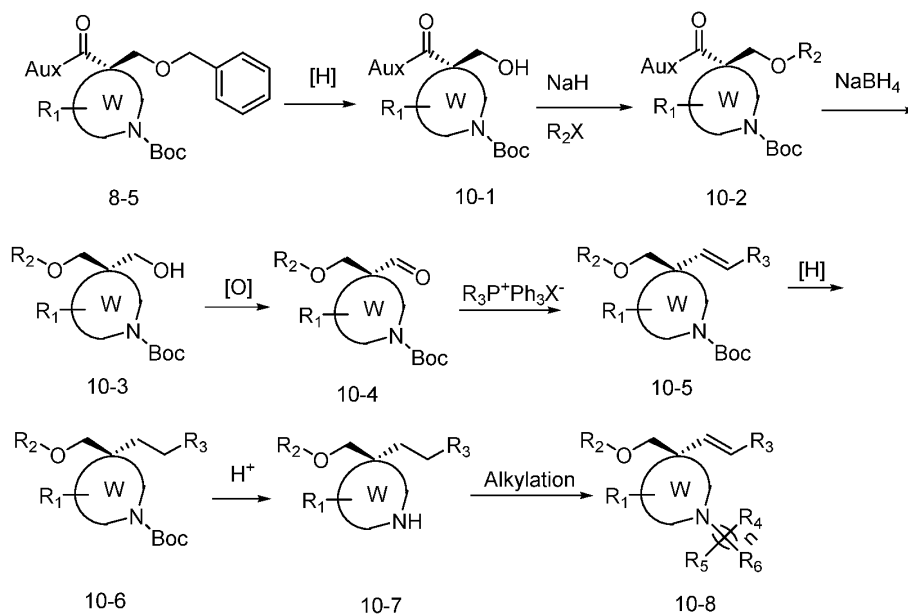
Scheme 9 shows an example for the synthesis of enantiomerically pure compounds **9-8** starting from **8-4**.



The enantiomerically pure intermediate **8-4** described in Scheme 8 is reduced using NaBH_4 to a chiral alcohol **9-1**. The transformation of alcohol **9-1** to **9-8** is carried out according to the methodologies described in schemes 1 to 5. Using the same methodology as demonstrated in Scheme 9, the enantiomer of **9-8** is synthesized starting from the enantiomerically pure intermediate **8-5**.

Scheme 10

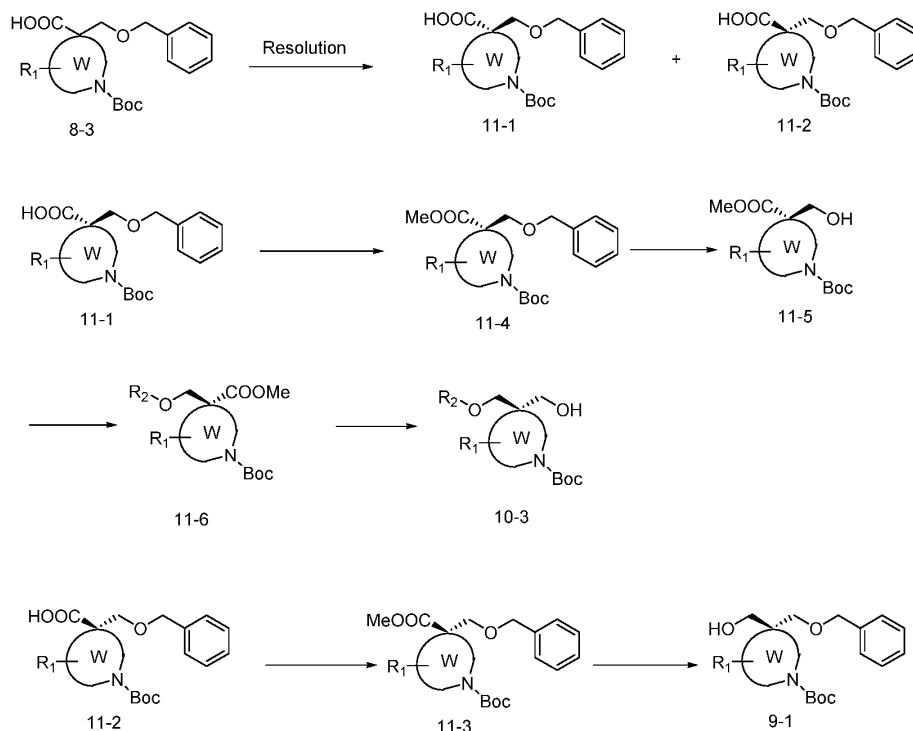
Scheme 10 shows an example for the synthesis of enantiomerically pure compounds **10-8** starting from **8-5**.



The enantiomerically pure compound **10-8** is synthesized starting from **8-5** according to the methodologies described in scheme 9. Using the same methodology as demonstrated in Scheme 10, the enantiomer of **10-8** is synthesized starting from the enantiomerically pure intermediate **8-4**.

Scheme 11

Scheme 11 shows an example for the synthesis of enantiomerically intermediate **10-3** and **9-1** starting from **8-3** by chiral resolution.



The enantiomerically intermediate **10-3** and **9-1** was synthesized starting from **8-3** according to the methodologies described in scheme 9 and 10. Using the same methodology as demonstrated in Scheme 11, the enantiomer of **10-3** and **9-1** is synthesized starting from the enantiomerically pure intermediate **11-2**.

Formulation of the Compounds (Compositions)

For preparing pharmaceutical compositions from the compounds of the present invention, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances, which may also act as diluents, flavoring agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

In powders, the carrier is a finely divided solid, which is in a mixture with the finely divided active component. In tablets, the active component is mixed with the carrier

having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

The powders and tablets preferably contain from 5% or 10% to 70% of the active compound. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component with or without other carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid dosage forms suitable for oral administration.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides or cocoa butter, is first melted and the active component is dispersed homogeneously therein, as by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool, and thereby to solidify.

Liquid form preparations include solutions, suspensions, and emulsions, for example, water or water/propylene glycol solutions. For parenteral injection, liquid preparations can be formulated in solution in aqueous polyethylene glycol solution.

Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavors, stabilizers, and thickening agents as desired. Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well-known suspending agents.

Also included are solid form preparations, which are intended to be converted, shortly before use, to liquid form preparations for oral administration. Such liquid forms include solutions, suspensions, and emulsions. These preparations may contain, in

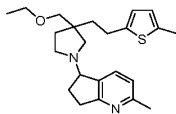
addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

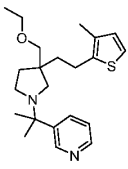
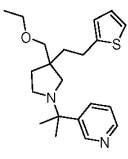
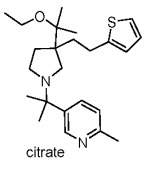
The pharmaceutical preparation is preferably in unit dosage form. In such form the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form.

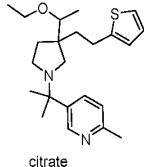
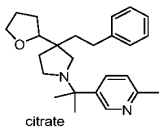
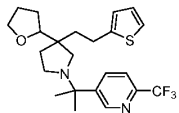
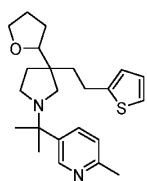
The quantity of active component in a unit dose preparation may be varied or adjusted to provide a pharmaceutically acceptable dosage of the active component.

The compounds of the invention and for some of them, their properties, are listed below in Tables I to VI.

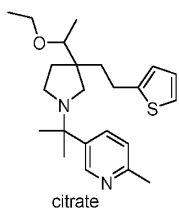
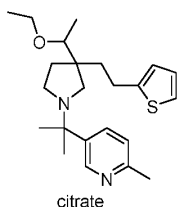
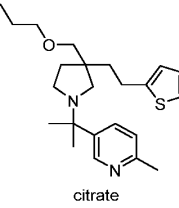
Table I: Compounds with a pyrrolidine ring and a pyridine or pyridine-like molecule bonded to the pyrrolidine N-constituent

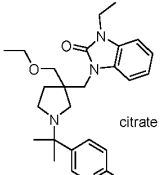
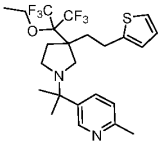
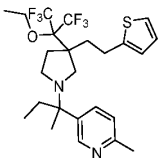
Compound No.	Structure	Name	MS (ESI+): [M+H] ⁺	H-NMR
1		5-((R or S)-3-(ethoxymethyl)-3-(2-(5-methylthiophen-2-yl)ethyl)pyrrolidin-1-yl)-2-methyl-6,7-dihydro-5H-cyclopenta[b]pyridine	385	¹ H NMR (300 MHz, CDCl ₃): δ 7.52 (d, J = 7.5 Hz, 1H), 6.95 (d, J = 7.8 Hz, 1H), 6.53-6.51 (m, 2H), 4.25-4.15 (m, 1H), 3.45 (q, J = 5.1 Hz, 2H), 3.31-3.23 (m, 2H), 3.15-3.03 (m, 1H), 2.95-2.81 (m, 1H), 2.79-2.60 (m, 3H), 2.60-2.55 (m, 1H), 2.52 (s, 3H), 2.42 (s, 3H), 2.39-2.35 (m, 1H), 2.18-2.10 (m, 2H), 2.10-1.98 (m, 1H), 1.90-1.75 (m, 2H), 1.65-1.59 (m, 2H), 1.17 (t, J = 7.2 Hz, 3H).

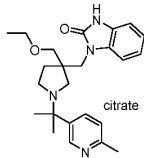
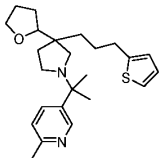
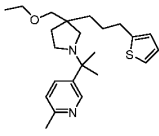
2		(S or R)-3-(2-(3-(ethoxymethyl)-3-(2-(3-methylthiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)pyridine	373	¹ H NMR (300 MHz, MeOD): δ 8.70 (s, 1H), 8.38-8.36 (m, 1H), 8.00-7.97 (m, 1H), 7.41-7.37 (m, 1H), 7.01 (d, <i>J</i> = 5.1 Hz, 1H), 6.73 (d, <i>J</i> = 5.1 Hz, 1H), 3.48 (q, <i>J</i> = 6.9 Hz, 2H), 3.33-3.30 (m, 2H), 3.29-3.27 (m, 2H), 2.68-2.55 (m, 4H), 2.53 (d, <i>J</i> = 9.3 Hz, 1H), 2.32 (d, <i>J</i> = 9.3 Hz, 1H), 2.11 (s, 3H), 1.78-1.64 (m, 2H), 1.62-1.55 (m, 2H), 1.44 (s, 6H), 1.17 (t, <i>J</i> = 6.9 Hz, 3H)
3		(S or R)-3-(2-(3-(ethoxymethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)pyridine	359	¹ H NMR (300 MHz, MeOD): δ 8.70 (s, 1H), 8.37 (d, <i>J</i> = 3.9 Hz, 1H), 7.98 (d, <i>J</i> = 8.1 Hz, 1H), 7.38 (m, 1H), 7.13 (dd, <i>J</i> = 5.1, 1.2 Hz, 1H), 6.87 (dd, <i>J</i> = 5.1, 3.3 Hz, 1H), 6.76 (d, <i>J</i> = 2.4 Hz, 1H), 3.47 (q, <i>J</i> = 6.9 Hz, 2H), 3.34-3.30 (m, 2H), 2.78 (t, <i>J</i> = 8.4 Hz, 2H), 2.64-2.60 (m, 2H), 2.52 (d, <i>J</i> = 9.3 Hz, 1H), 2.31 (d, <i>J</i> = 9.3 Hz, 1H), 1.82-1.77 (m, 2H), 1.59 (t, <i>J</i> = 6.9 Hz, 2H), 1.43 (s, 6H), 1.16 (t, <i>J</i> = 6.9 Hz, 3H)
4		(S or R)-5-(2-(3-(2-ethoxypropan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	402	¹ H NMR (300 MHz, MeOD): δ 8.77 (s, 1H), 8.13 (dd, <i>J</i> = 8.4, 2.4 Hz, 1H), 7.46 (d, <i>J</i> = 8.4 Hz, 1H), 7.17-7.16 (m, 1H), 6.90-6.87 (m, 1H), 6.80-6.79 (m, 1H), 3.50-3.29 (m, 7H), 3.12-3.08 (m, 1H), 2.80 (q, <i>J</i> = 15.6 Hz, 4H), 2.56 (s, 3H), 2.37-2.25 (m, 1H), 1.92 (s, 6H), 1.87-1.78 (m, 3H), 1.13 (d, <i>J</i> = 8.7 Hz, 6H), 1.02 (t, <i>J</i> = 6.9 Hz, 3H)

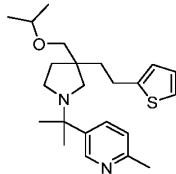
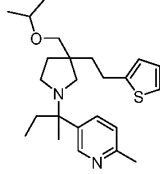
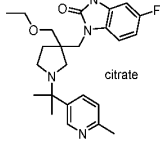
5		5-(2-((S&R)-3-((S or R)-1-ethoxyethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	388	¹ H NMR (300 MHz, MeOD): δ 8.75-8.67 (m, 1H), 8.15-8.03 (m, 1H), 7.45 (t, <i>J</i> = 6.6 Hz, 1H), 7.18-7.17 (m, 1H), 6.90-6.88 (m, 1H), 6.81 (s, 1H), 3.56-3.50 (m, 2H), 3.40-3.31 (m, 2H), 3.25-3.15 (m, 3H), 2.87-2.75 (m, 6H), 2.58 (s, 3H), 2.33-2.08 (m, 2H), 1.90 (d, <i>J</i> = 7.8 Hz, 6H), 1.87-1.62 (m, 2H), 1.36-1.00 (m, 6H)
6		2-methyl-5-(2-((3R or S)-3-phenethyl-3-(tetrahydrofuran-2-yl)pyrrolidin-1-yl)propan-2-yl)pyridine citrate	379	¹ H NMR (300 MHz, MeOD): δ 8.73-8.71 (m, 1H), 8.07 (t, <i>J</i> = 8.4 Hz, 1H), 7.45 (dd, <i>J</i> = 8.4, 2.4 Hz, 1H), 7.27-7.12 (m, 5H), 3.92-3.80 (m, 2H), 3.65-3.26 (m, 2H), 3.47-3.38 (m, 2H), 3.31 (q, <i>J</i> = 1.5 Hz, 1H), 2.80 (q, <i>J</i> = 15.3 Hz, 4H), 2.61-2.50 (m, 5H), 2.20 (m, 1H), 2.15-1.95 (m, 3H), 1.87 (s, 3H), 1.85 (s, 3H), 1.77-1.72 (m, 3H), 1.28-1.15 (m, 1H)
7		5-(2-((3R or S)-3-(tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-(trifluoromethyl)pyridine	439	¹ H NMR (300 MHz, MeOD): δ 8.89 (s, 1H), 8.00 (d, <i>J</i> = 4.8 Hz, 1H), 7.62 (d, <i>J</i> = 8.1 Hz, 1H), 7.12-7.11 (m, 1H), 6.92-6.91 (m, 1H), 6.80 (s, 1H), 3.86-3.82 (m, 2H), 3.74-3.71 (m, 1H), 2.90-2.85 (m, 2H), 2.70-2.51 (m, 3H), 2.47-2.36 (m, 2H), 1.96-1.42 (m, 13H)
8		2-methyl-5-(2-((R or S)-3-((S or R)-tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)pyridine	387	¹ H NMR (300 MHz, CDCl ₃): δ 8.60 (d, <i>J</i> = 1.5 Hz, 1H), 7.72 (dd, <i>J</i> = 6.0, 1.5 Hz, 1H), 7.11-7.08 (m, 2H), 6.91 (dd, <i>J</i> = 2.4, 3.9 Hz, 1H), 6.79 (d, <i>J</i> = 1.8 Hz, 1H), 3.87-3.83 (m, 2H), 3.73-3.71 (m, 1H), 3.00-2.88 (m, 1H), 2.87-2.78 (m, 1H), 2.59-2.53

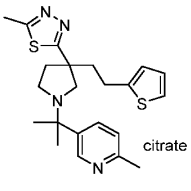
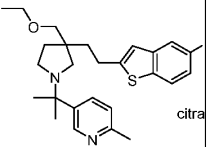
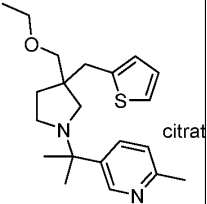
				(m, 3H), 2.51 (s, 3H), 2.43 (d, $J = 6.9$ Hz, 1H), 2.00-1.91 (m, 1H), 1.90-1.85 (m, 3H), 1.78-1.71 (m, 3H), 1.61-1.52 (m, 1H), 1.39 (d, $J = 0.9$ Hz, 6H)
9		2-methyl-5-(2-((3S or R)-3-(tetrahydrofuran-2-yl)-3-(thiophen-2-ylmethyl)pyrrolidin-1-yl)propan-2-yl)pyridine	371	^1H NMR (300 MHz, CDCl_3): δ 8.57 (s, 1H), 7.63 (d, $J = 7.5$ Hz, 1H), 7.12 (s, 1H), 7.07 (d, $J = 8.1$ Hz, 1H), 6.93 (s, 1H), 6.81 (s, 1H), 3.88-3.78 (m, 1H), 3.76-3.69 (m, 3H), 3.15-3.10 (m, 1H), 2.95-2.83 (m, 1H), 2.52 (s, 3H), 2.48-2.36 (m, 3H), 1.76-1.60 (m, 6H), 1.36 (s, 3H), 1.35 (s, 3H)
10		5-(2-((R or S)-3-((S or R)-ethoxy(phenyl)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	449	^1H NMR (300 MHz, MeOD): δ 8.68 (d, $J = 2.1$ Hz, 1H), 8.02 (dd, $J = 8.3, 2.1$ Hz, 1H), 7.43-7.34 (m, 5H), 7.32-7.26 (m, 1H), 7.14 (d, $J = 5.1$ Hz, 1H), 6.88-6.85 (m, 1H), 6.74 (d, $J = 2.4$ Hz, 1H), 4.39 (s, 1H), 3.41-3.35 (m, 2H), 3.28-3.25 (m, 2H), 3.16-3.06 (m, 2H), 2.92-2.83 (m, 2H), 2.84-2.71 (m, 4H), 2.56 (s, 3H), 2.25-2.13 (m, 1H), 2.90-2.81 (m, 1H), 1.77-1.73 (m, 6H), 1.61-1.50 (m, 2H), 1.05 (t, $J = 6.9$ Hz, 3H)
11		5-(2-((R or S)-3-((R or S)-ethoxy(phenyl)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	449	^1H NMR (300 MHz, CDCl_3): δ 8.53 (d, $J = 2.4$ Hz, 1H), 7.60 (dd, $J = 8.1, 2.4$ Hz, 1H), 7.32-7.28 (m, 5H), 7.10-7.04 (m, 2H), 6.90 (dd, $J = 5.1, 3.6$ Hz, 1H), 6.76 (d, $J = 2.4$ Hz, 1H), 4.20 (s, 1H), 3.41-3.30 (m, 1H), 3.27-3.12 (m, 1H), 3.05-2.92 (m, 1H), 2.91-2.82 (m, 1H), 2.74 (d, $J = 9.2$ Hz, 1H), 2.52 (s, 3H),

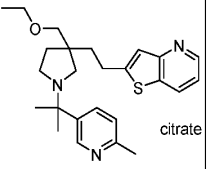
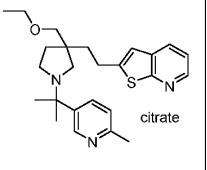
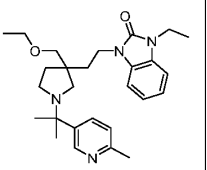
				2.51-2.45 (m, 1H), 2.41-2.30 (m, 1H), 2.24 (d, $J = 9.0$ Hz, 1H), 2.02-1.88 (m, 2H), 1.71-1.65 (m, 2H), 1.37 (s, 3H), 1.34 (s, 3H), 1.15 (t, $J = 6.9$ Hz, 3H)
12		5-(2-((R or S)-3-((R or S)-1-ethoxyethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	387	^1H NMR (300 MHz, MeOD): δ 8.70 (d, $J = 2.1$ Hz, 1H), 8.05 (dd, $J = 8.1, 2.4$ Hz, 1H), 7.41 (d, $J = 8.1$ Hz, 1H), 7.16 (dd, $J = 5.1, 1.2$ Hz, 1H), 6.88 (dd, $J = 5.1, 3.3$ Hz, 1H), 6.79 (d, $J = 3.3$ Hz, 1H), 3.61-3.58 (m, 1H), 3.50-3.34 (m, 1H), 3.32-3.30 (m, 2H), 3.25-3.22 (m, 2H), 3.21-3.19 (m, 1H), 2.92-2.82 (m, 2H), 2.80-2.70 (m, 4H), 2.56 (s, 3H), 2.09-1.95 (m, 1H), 1.94-1.85 (m, 3H), 1.82 (s, 6H), 1.10-1.03 (m, 6H)
13		5-(2-((R or S)-3-((S or R)-1-ethoxyethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	387	^1H NMR (300 MHz, MeOD): δ 8.69 (d, $J = 2.1$ Hz, 1H), 8.03 (d, $J = 8.7$ Hz, 1H), 7.42 (d, $J = 7.2$ Hz, 1H), 7.17 (dd, $J = 4.8, 1.2$ Hz, 1H), 6.88 (dd, $J = 3.3, 5.1$ Hz, 1H), 6.79 (d, $J = 3.0$ Hz, 1H), 3.68-3.60 (m, 1H), 3.49-3.43 (m, 1H), 3.30-3.18 (m, 4H), 3.17-2.98 (m, 2H), 2.86-2.71 (m, 4H), 2.56 (s, 3H), 2.25-2.12 (m, 1H), 2.10-1.90 (m, 1H), 1.82 (s, 6H), 1.81-1.76 (m, 2H), 1.71-1.60 (m, 1H), 1.13-1.03 (m, 6H)
14		(R or S)-2-methyl-5-(2-((3-(propoxymethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)pyridine) citrate	387	^1H NMR (300 MHz, MeOD): δ 8.68 (d, $J = 2.1$ Hz, 1H), 8.03 (d, $J = 6.3$ Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.15 (d, $J = 5.1$ Hz, 1H), 6.88 (dd, $J = 5.1, 3.6$ Hz, 1H), 6.78 (d, $J = 3.3$ Hz, 1H), 3.50-3.38 (m, 2H), 3.25-3.20 (m, 2H),

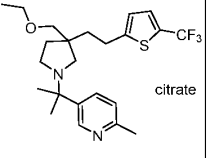
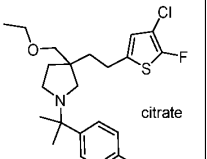
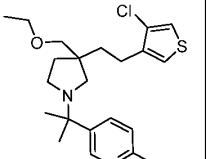
				3.12-3.08 (m, 1H), 2.92-2.87 (m, 2H), 2.78-2.72 (m, 4H), 2.56 (s, 3H), 2.15-1.92 (m, 2H), 1.90-1.81 (m, 4H), 1.79 (s, 6H), 1.70-1.48 (m, 3H), 0.89 (t, $J=7.5$ Hz, 3H)
15		(R or S)-1-((3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-ethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	437	^1H NMR (300 MHz, MeOD): δ 8.56 (d, $J = 2.4$ Hz, 1H), 7.91 (d, $J = 8.3$ Hz, 1H), 7.27 (d, $J = 8.2$ Hz, 1H), 7.13 (d, $J = 6.8$ Hz, 1H), 7.10-6.96 (m, 3H), 3.92-3.81 (m, 3H), 3.40-3.30 (m, 4H), 3.31 (m, 2H), 3.18 (s, 2H), 2.91 (d, $J = 11.5$ Hz, 1H), 2.78-2.61 (m, 4H), 2.45 (s, 3H), 1.96 (m, 1H), 1.83-1.72 (m, 1H), 1.65 (s, 3H), 1.64 (s, 3H), 1.20 (t, $J = 7.2$ Hz, 3H), 1.06 (t, $J = 6.9$ Hz, 3H)
16		(R or S)-5-(2-(3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	509	^1H NMR (300 MHz, CDCl_3): δ 8.51 (d, $J = 2.1$ Hz, 1H), 7.64 (dd, $J = 8.1, 2.4$ Hz, 1H), 7.07-7.02 (m, 2H), 6.86 (dd, $J = 5.1, 3.3$ Hz, 1H), 6.74-6.73 (m, 1H), 3.96-3.80 (m, 2H), 3.01 (t, $J = 8.7$ Hz, 2H), 2.89 (d, $J = 9.6$ Hz, 1H), 2.60-2.56 (m, 2H), 2.55 (s, 3H), 2.36-2.28 (m, 2H), 2.15-2.08 (m, 1H), 2.00-1.80 (m, 2H), 1.61 (s, 6H), 1.13 (t, $J = 6.9$ Hz, 3H)
17		5-(2-((R or S)-3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine citrate	523	^1H NMR (300 MHz, MeOD): δ 8.50 (d, $J = 2.1$ Hz, 1H), 7.92-7.87 (m, 1H), 7.35 (dd, $J = 8.4, 2.7$ Hz, 1H), 7.19-7.16 (m, 1H), 6.93-6.90 (m, 1H), 6.85-6.75 (m, 1H), 4.08-3.90 (m, 2H), 3.19-3.10 (m, 1H), 3.05-2.98 (m, 2H), 2.91-2.75 (m, 4H), 2.54 (s, 3H), 2.50-2.35 (m, 2H), 2.22-2.10 (m, 1H), 2.09-1.90

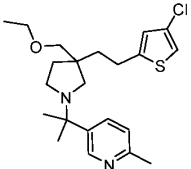
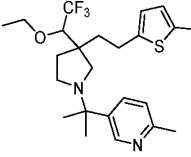
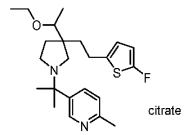
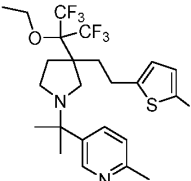
				(m, 2H), 1.89-1.75 (m, 2H), 1.46 (s, 3H), 1.35-1.30 (m, 2H), 1.22-1.16 (m, 3H), 0.71-0.64 (m, 3H)
18		(R or S)-1-((3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	409	¹ H NMR (300 MHz, MeOD) δ 8.61 (s, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.10-7.03 (m, 1H), 6.99-6.90 (m, 3H), 3.85 (s, 2H), 3.48-3.06 (m, 10H), 2.84-2.63 (q, J = 15.6 Hz, 4H), 2.46 (s, 3H), 1.94 (m, 2H), 1.76 (s, 6H), 1.04 (t, J = 6.9 Hz, 3H)
19		2-methyl-5-(2-((3R or 3S)-3-(tetrahydrofuran-2-yl)-3-(3-(thiophen-2-yl)propyl)pyrrolidin-1-yl)propan-2-yl)pyridine	399	¹ H NMR (300 MHz, CDCl ₃): δ 8.58 (d, J = 2.1 Hz, 1H), 7.69 (dd, J = 8.1, 2.4 Hz, 1H), 7.12-7.05 (m, 2H), 6.93-6.90 (m, 1H), 6.78 (d, J = 3.3 Hz, 1H), 3.90-3.75 (m, 2H), 3.74-3.62 (m, 1H), 2.89-2.75 (m, 2H), 2.64-2.45 (m, 6H), 2.35-2.25 (m, 1H), 1.90-1.80 (m, 4H), 1.72-1.58 (m, 4H), 1.52-1.44 (m, 2H), 1.43-1.36 (m, 6H)
20		(R or S)-5-(2-(3-(ethoxymethyl)-3-(3-(thiophen-2-yl)propyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	387	¹ H NMR (300 MHz, CDCl ₃): δ 8.58 (d, J = 2.4 Hz, 1H), 7.68 (dd, J = 8.4, 2.4 Hz, 1H), 7.11-7.05 (m, 2H), 6.90 (dd, J = 8.4, 3.3 Hz, 1H), 6.78-6.77 (m, 1H), 3.49 (s, 2H), 3.44 (dd, J = 14.1, 7.5 Hz, 2H), 3.24 (dd, J = 15.2, 8.7 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 2.60-2.55 (m, 1H), 2.54-2.50 (m, 4H), 2.43 (d, J = 9.0 Hz, 1H), 2.23 (d, J = 9.0 Hz, 1H), 1.55-1.48 (m, 4H), 1.36 (s, 6H), 1.15 (t, J = 6.9 Hz, 3H)

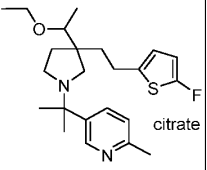
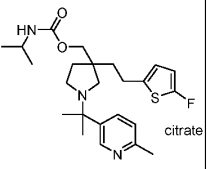
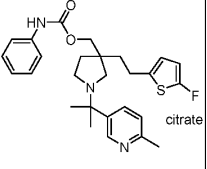
21		(R or S)-5-(2-(3-(isopropoxymethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	387	¹ H NMR (300 MHz, CDCl ₃): δ 8.59 (d, <i>J</i> = 2.1 Hz, 1H), 7.71 (dd, <i>J</i> = 8.1, 2.4 Hz, 1H), 7.10-7.06 (m, 2H), 6.91 (dd, <i>J</i> = 5.1, 3.3 Hz, 1H), 6.77 (d, <i>J</i> = 2.4 Hz, 1H), 3.52-3.48 (m, 1H), 3.26 (q, <i>J</i> = 8.7 Hz, 2H), 2.79 (t, <i>J</i> = 8.4 Hz, 2H), 2.58-2.52 (m, 5H), 2.28 (d, <i>J</i> = 9.0 Hz, 1H), 2.95-2.75 (m, 2H), 2.55-2.50 (m, 2H), 1.37 (s, 6H), 1.30-1.26 (m, 1H), 1.14-1.12 (m, 6H)
22		5-(2-((R or S)-3-(isopropoxymethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine	401	¹ H NMR (300 MHz, CDCl ₃): δ 8.52 (s, 1H), 7.64 (dd, <i>J</i> = 8.1, 2.4 Hz, 1H), 7.10-7.07 (m, 2H), 6.91 (d, <i>J</i> = 2.1 Hz, 1H), 6.77 (d, <i>J</i> = 0.9 Hz, 1H), 3.55-3.45 (m, 1H), 3.35-3.20 (m, 2H), 2.85-2.72 (m, 2H), 2.70-2.60 (m, 1H), 2.53 (s, 3H), 2.50-2.40 (m, 2H), 2.35-2.18 (m, 1H), 1.90-1.73 (m, 3H), 1.68-1.62 (m, 1H), 1.57-1.52 (m, 2H), 1.34 (s, 3H), 1.15-1.11 (m, 6H), 0.62 (t, <i>J</i> = 7.2 Hz, 3H)
23		(R or S)-1-((3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-ethyl-5-fluoro-1,3-dihydro-2H-benzo[d]imidazol-2-onecitrate	455	¹ H NMR (300 MHz, MeOD): δ 8.68 (s, 1H), 8.04 (d, <i>J</i> = 8.1 Hz, 1H), 7.40 (d, <i>J</i> = 7.9 Hz, 1H), 7.20-7.16 (m, 1H), 7.06-7.02 (m, 1H), 6.85 (t, 9.6 Hz, 1H), 3.94-3.90 (m, 4H), 3.50-3.27 (m, 7H), 3.05 (d, <i>J</i> = 11.4 Hz, 1H), 2.81 (q, <i>J</i> = 15.6 Hz, 4H), 2.56 (s, 3H), 2.10-1.99 (m, 2H), 1.84-1.73 (m, 6H), 1.32-1.24 (m, 3H), 1.15 (t, <i>J</i> = 6.9 Hz, 3H)

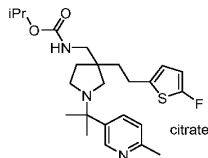
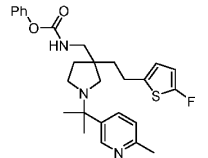
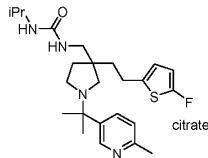
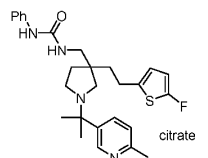
24		(R or S)-2-methyl-5-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)-1,3,4-thiadiazole citrate	413	¹ H NMR (300 MHz, MeOD): δ 8.55 (s, 1H), 7.95 (dd, <i>J</i> = 8.1, 2.4 Hz, 1H), 7.30 (d, <i>J</i> = 8.4 Hz, 1H), 7.07 (d, <i>J</i> = 4.8 Hz, 1H), 6.78 (t, <i>J</i> = 4.2 Hz, 1H), 6.67 (d, <i>J</i> = 2.7 Hz, 1H), 3.42 (d, <i>J</i> = 11.2 Hz, 1H), 3.05-2.96 (m, 1H), 2.94-2.83 (m, 1H), 2.70 (m, 6H), 2.52 (m, 2H), 2.47 (s, 3H), 2.30 (m, 1H), 2.11 (s, 3H), 2.03-1.93 (m, 1H), 1.85 (m, 1H), 1.61 (s, 6H)
25		(R or S)-5-(2-(3-(ethoxymethyl)-3-(2-(5-fluorobenzo[b]thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	450	¹ H NMR (300 MHz, MeOD): δ 8.68 (s, 1H), 8.02 (d, <i>J</i> = 8.1 Hz, 1H), 7.73 (dd, <i>J</i> = 9.0, 4.8 Hz, 1H), 7.39 (s, 1H), 7.36 (s, 1H), 7.07-7.00 (m, 2H), 3.50-3.45 (m, 2H), 3.38-3.43 (m, 2H), 3.27-3.20 (m, 2H), 3.15-3.08 (m, 1H), 2.92-2.85 (m, 3H), 2.79 (q, <i>J</i> = 15.6 Hz, 4H), 2.54 (s, 3H), 1.98-1.82 (m, 4H), 1.77 (s, 6H), 1.14 (t, <i>J</i> = 6.9 Hz, 3H).
26		(S or R)-5-(2-(3-(ethoxymethyl)-3-(thiophen-2-ylmethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	359	¹ H NMR (300 MHz, MeOD): δ 8.70 (s, 1H), 8.04 (d, <i>J</i> = 6.0 Hz, 1H), 7.44 (d, <i>J</i> = 8.2 Hz, 1H), 7.24 (d, <i>J</i> = 5.3 Hz, 1H), 6.95-6.90 (m, 1H), 6.82 (s, 1H), 3.47-3.40 (m, 2H), 3.20-3.19 (m, 3H), 3.10-3.07 (m, 3H), 3.05-2.98 (m, 2H), 2.82 (q, <i>J</i> = 15.6 Hz, 4H), 2.59 (s, 3H), 2.06-1.96 (m, 1H), 1.93-1.86 (m, 1H), 1.83 (s, 6H), 1.15 (t, <i>J</i> = 7.0 Hz, 3H).

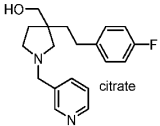
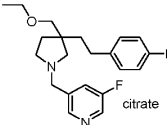
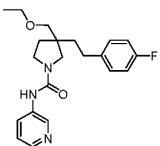
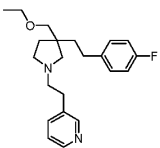
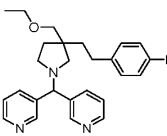
27		(R or S)-2-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thieno[3,2-b]pyridine citrate	424	¹ H NMR (300 MHz, MeOD): δ 8.66 (d, <i>J</i> = 2.1 Hz, 1H), 8.53 (dd, <i>J</i> = 4.8, 1.2 Hz, 1H), 8.27 (d, <i>J</i> = 8.1 Hz, 1H), 8.01 (dd, <i>J</i> = 4.8, 1.2 Hz, 1H), 7.36 (d, <i>J</i> = 8.4 Hz, 1H), 7.30 (dd, <i>J</i> = 7.8, 3.6 Hz, 1H), 7.23 (s, 1H), 3.52-3.44 (m, 2H), 3.38-3.35 (m, 2H), 3.18-3.10 (m, 2H), 3.08-3.02 (m, 1H), 2.96 (t, <i>J</i> = 8.4 Hz, 2H), 2.92-2.87 (m, 1H), 2.80 (q, <i>J</i> = 15.6 Hz, 4H), 2.53 (s, 3H), 2.00-1.83 (m, 4H), 1.74 (s, 6H), 1.14 (t, <i>J</i> = 6.9 Hz, 3H)
28		(R or S)-2-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thieno[2,3-b]pyridine citrate	424	¹ H NMR (300 MHz, MeOD): δ 8.68 (d, <i>J</i> = 1.8 Hz, 1H), 8.40 (d, <i>J</i> = 3.3 Hz, 1H), 8.10-8.02 (m, 2H), 7.39-7.34 (m, 2H), 7.08 (s, 1H), 3.50-3.42 (m, 2H), 3.38-3.36 (m, 1H), 3.25-3.18 (m, 2H), 3.15-3.10 (m, 1H), 3.09-3.00 (m, 1H), 2.99-2.88 (m, 3H), 2.81 (q, <i>J</i> = 15.6 Hz, 4H), 2.54 (s, 3H), 2.02-1.88 (m, 4H), 1.77 (s, 6H), 1.14 (t, <i>J</i> = 7.2 Hz, 3H)
29		(S & R)-1-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-ethyl-1,3-dihydro-2H-benzo[d]imidazol-2-one	451	¹ H NMR (300 MHz, MeOD): δ 8.67 (d, <i>J</i> = 1.9 Hz, 1H), 8.03 (dd, <i>J</i> = 8.2, 2.4 Hz, 1H), 7.39 (d, <i>J</i> = 8.3 Hz, 1H), 7.18-7.14 (m, 4H), 4.01-3.87 (m, 4H), 3.49-3.41 (m, 2H), 3.38-3.34 (m, 2H), 3.23-3.18 (m, 2H), 3.10 (d, <i>J</i> = 11.5 Hz, 1H), 2.94 (d, <i>J</i> = 11.7 Hz, 1H), 2.80 (q, <i>J</i> = 15.5 Hz, 4H), 2.55 (s, 3H), 2.01-1.82 (m, 4H), 1.77 (s, 6H), 1.29 (t, <i>J</i> = 7.2 Hz, 3H), 1.13 (t, <i>J</i> = 7.0 Hz, 3H).

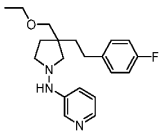
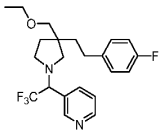
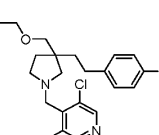
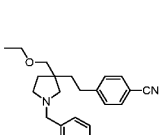
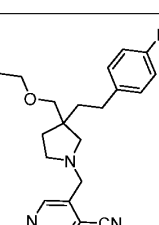
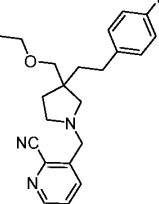
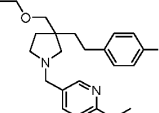
30		(R or S)-5-(2-(3-(ethoxymethyl)-3-(2-(5-(trifluoromethyl)thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	425	¹ H NMR (300 MHz, MeOD): δ 8.70 (d, J = 2.5 Hz, 1H), 8.06 (dd, J = 8.3, 2.6 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 3.8 Hz, 1H), 6.87 (d, J = 3.5 Hz, 1H), 3.52-3.43 (m, 2H), 3.37-3.33 (m, 1H), 3.28-3.22 (m, 2H), 3.17 (d, J = 11.7 Hz, 1H), 2.98 (d, J = 11.7 Hz, 1H), 2.80 (m, 7H), 2.56 (s, 3H), 2.05-1.84 (m, 4H), 1.81 (s, 6H), 1.13 (t, J = 7.0 Hz, 3H).
31		(R or S)-5-(2-(3-(2-(4-chloro-5-fluorothiophen-2-yl)ethyl)-3-(ethoxymethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	425	¹ H NMR (300 MHz, MeOD): δ 8.68 (d, J = 2.4 Hz, 1H), 8.04 (dd, J = 8.3, 2.5 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 6.48 (d, J = 3.4 Hz, 1H), 3.49-3.41 (m, 2H), 3.40-3.37 (m, 2H), 3.35-3.32 (m, 2H), 3.30-3.22 (m, 2H), 3.09 (d, J = 11.5 Hz, 1H), 2.80 (q, J = 15.5 Hz, 4H), 2.69-2.59 (m, 2H), 2.56 (s, 3H), 2.09-1.82 (m, 3H), 1.78 (s, 6H), 1.13 (t, J = 7.0 Hz, 3H).
32		(R or S)-5-(2-(3-(2-(4-chlorothiophen-3-yl)ethyl)-3-(ethoxymethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	407	¹ H NMR (500 MHz, MeOD): δ 8.54 (d, J = 2.1 Hz, 1H), 7.87 (dd, J = 8.2, 2.3 Hz, 1H), 7.28-7.22 (m, 2H), 7.12 (d, J = 3.4 Hz, 1H), 3.47 (q, J = 7.0 Hz, 2H), 3.34-3.32 (m, 1H), 3.30-3.29 (m, 1H), 2.69-2.62 (m, 2H), 2.56-2.52 (m, 3H), 2.50 (s, 3H), 2.37 (d, J = 9.2 Hz, 1H), 1.74-1.66 (m, 2H), 1.63 (t, J = 6.9 Hz, 2H), 1.45 (s, 6H), 1.16 (t, J = 7.0 Hz, 3H).

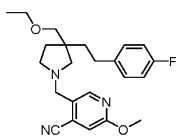
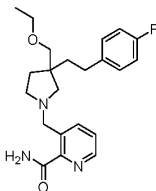
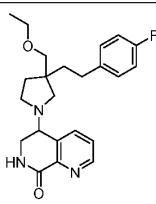
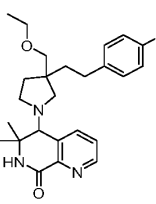
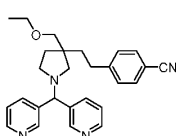
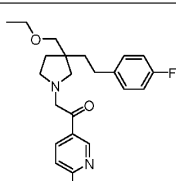
33		(R or S)-5-(2-(3-(2-(4-chlorothiophen-2-yl)ethoxy)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	407	¹ H NMR (300 MHz, CDCl ₃): δ 8.66 (s, 1H), 7.74 (t, <i>J</i> = 6.3 Hz, 1H), 7.21 (d, <i>J</i> = 8.0 Hz, 1H), 6.89 (d, <i>J</i> = 6.2 Hz, 1H), 6.66 (m, 1H), 3.73 (t, <i>J</i> = 7.3 Hz, 1H), 3.68-3.21 (m, 7H), 2.87-2.69 (m, 2H), 2.60 (s, 3H), 2.05-1.89 (m, 2H), 1.86-1.71 (m, 2H), 1.63 (s, 6H), 1.17-1.12 (m, 3H).
34		5-(2-((R & S)-3-((S or R)-1-ethoxy-2,2,2-trifluoroethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	459	¹ H NMR (300 MHz, MeOD): δ 8.59 (dd, <i>J</i> = 9.0, 2.1 Hz, 1H), 7.69 (d, <i>J</i> = 8.1 Hz, 1H), 7.09 (d, <i>J</i> = 8.1 Hz, 1H), 6.33 (t, <i>J</i> = 3.0 Hz, 1H), 6.23 (dd, <i>J</i> = 2.1, 1.2 Hz, 1H), 3.95-3.82 (m, 1H), 3.55-3.45 (m, 2H), 2.91-2.80 (m, 1H), 2.69-2.60 (m, 2H), 2.53 (s, 3H), 2.48-2.39 (m, 1H), 2.10-1.85 (m, 2H), 1.84-1.55 (m, 4H), 1.39 (s, 6H), 1.15 (t, <i>J</i> = 6.9 Hz, 3H)
35		5-(2-((R or S)-3-((S or R)-1-ethoxyethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	405	¹ H NMR (300 MHz, MeOD): δ 8.69 (s, 1H), 8.04 (d, <i>J</i> = 8.1 Hz, 1H), 7.41 (d, <i>J</i> = 8.1 Hz, 1H), 6.41 (m, 1H), 6.30 (d, <i>J</i> = 2.1 Hz, 1H), 3.65-3.57 (m, 1H), 3.48-3.39 (m, 1H), 3.28-3.14 (m, 4H), 3.12-2.95 (m, 2H), 2.75 (q, <i>J</i> = 15.5 Hz, 4H), 2.68-2.63 (m, 2H), 2.56 (s, 3H), 2.24-2.08 (m, 1H), 2.06-1.94 (m, 1H), 1.69 (s, 6H), 1.68-1.59 (m, 1H), 1.12-1.02 (m, 6H)
36		(R or S)-5-(2-(3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1	527	¹ H NMR (300 MHz, MeOD): δ 8.58 (d, <i>J</i> = 1.8 Hz, 1H), 7.68 (dd, <i>J</i> = 8.1, 1.8 Hz, 1H), 7.10 (d, <i>J</i> = 8.1 Hz, 1H), 6.36 (d, <i>J</i> = 3.3 Hz, 1H), 6.25 (dd, <i>J</i> = 3.6, 1.8 Hz, 1H),

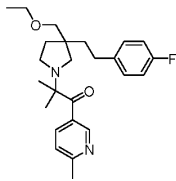
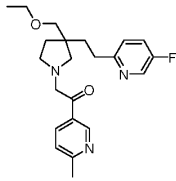
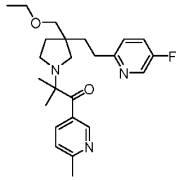
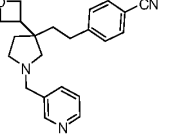
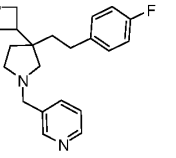
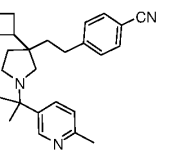
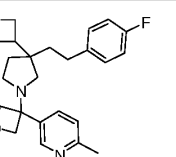
		-yl)propan-2-yl)-2-methylpyridine		3.97-3.88 (m, 2H), 2.95-2.89 (m, 3H), 2.71-2.56 (m, 2H), 2.53 (s, 3H), 2.45-2.30 (m, 2H), 2.18-2.02 (m, 1H), 1.92-1.80 (m, 1H), 1.72-1.65 (m, 1H), 1.40 (s, 6H), 1.20 (t, $J = 6.9$ Hz, 3H).
37		5-(2-((R or S)-3-((R or S)-1-ethoxyethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	405	^1H NMR (300 MHz, MeOD): δ 8.70 (d, $J = 1.8$ Hz, 1H), 8.06 (dd, $J = 8.4, 2.4$ Hz, 1H), 7.42 (d, $J = 8.4$ Hz, 1H), 6.41 (d, $J = 3.6$ Hz, 1H), 6.30 (m, 1H), 3.63-3.55 (m, 1H), 3.50-3.44 (m, 1H), 3.38-3.32 (m, 2H), 3.26-3.18 (m, 2H), 2.96-2.88 (m, 1H), 2.76 (q, $J = 15.5$ Hz, 4H), 2.69-2.61 (m, 2H), 2.56 (s, 3H), 2.05-1.97 (m, 1H), 1.95-1.89 (m, 1H), 1.83 (s, 6H), 1.80-1.74 (m, 2H), 1.11-1.00 (m, 6H)
38		(R or S)-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl isopropylcarbamate citrate	448	^1H NMR (300 MHz, MeOD): δ 8.66 (s, 1H), 8.04 (d, $J = 8.2$ Hz, 1H), 7.40 (d, $J = 8.2$ Hz, 1H), 6.42 (m, 1H), 6.35-6.25 (m, 1H), 4.08-3.91 (m, 2H), 3.83-3.73 (m, 2H), 3.18 (m, 2H), 2.97 (d, $J = 10.9$ Hz, 1H), 2.90-2.73 (m, 6H), 2.71-2.64 (m, 2H), 2.56 (s, 3H), 1.85-1.78 (m, 2H), 1.73 (s, 6H), 1.10 (d, $J = 6.5$ Hz, 6H).
39		(R or S)-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl phenylcarbamate citrate	482	^1H NMR (300 MHz, MeOD): δ 8.66 (s, 1H), 8.05 (d, $J = 8.2$ Hz, 1H), 7.42 (d, $J = 7.8$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 1H), 7.28 (t, $J = 7.9$ Hz, 2H), 7.03 (t, $J = 7.3$ Hz, 1H), 6.43 (m, 1H), 6.28 (m, 1H), 4.09 (q, $J = 11.1$ Hz, 2H), 3.18 (m, 2H), 2.99 (m, 1H),

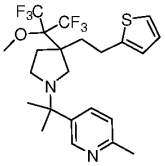
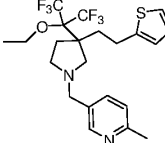
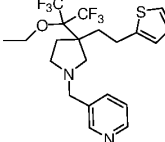
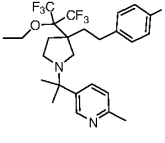
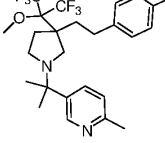
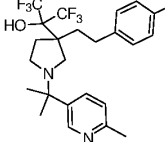
				2.90-2.68 (m, 5H), 2.49 (s, 3H), 1.96-1.79 (m, 4H), 1.73 (s, 6H).
40		isopropyl (S or R)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl) carbamate citrate	448	¹ H NMR (300 MHz, MeOD): δ 8.66 (s, 1H), 8.03 (d, J = 7.2 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 6.42 (t, J = 3.3 Hz, 1H), 6.28 (dd, J = 2.4, 1.2 Hz, 1H), 4.88-4.68 (m, 2H), 3.25-3.13 (m, 4H), 3.05-2.93 (m, 1H), 2.73 (q, J = 15.6 Hz, 4H), 2.71-2.62 (m, 2H), 2.55 (s, 3H), 1.92-1.80 (m, 2H), 1.75 (s, 6H), 1.68-1.63 (m, 2H), 1.26 (m, 6H)
41		phenyl (S or R)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl) carbamate	482	¹ H NMR (300 MHz, MeOD): δ 8.53 (d, J = 1.2 Hz, 1H), 7.89 (dd, J = 6.0, 2.4 Hz, 1H), 7.36 (t, J = 7.8 Hz, 2H), 7.23 (d, J = 8.1 Hz, 1H), 7.20 (m, 1H), 7.08 (d, J = 7.8 Hz, 2H), 6.42 (t, J = 3.3 Hz, 1H), 6.28 (dd, J = 3.3, 2.1 Hz, 1H), 2.85-2.70 (m, 7H), 2.55 (m, 1H), 2.49 (s, 3H), 1.80-1.60 (m, 4H), 1.45 (s, 6H)
42		(S or R)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-isopropylurea citrate	447	¹ H NMR (300 MHz, MeOD): δ 8.72 (s, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 6.50-6.40 (m, 1H), 6.35-6.25 (m, 1H), 3.91-3.73 (m, 1H), 3.22-3.09 (m, 3H), 2.90 (d, J = 4.8 Hz, 1H), 2.88-2.65 (m, 8H), 2.57 (s, 3H), 1.88-1.68 (m, 10H), 1.12 (m, 6H).
43		(S or R)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-phenylurea citrate	481	¹ H NMR (300 MHz, MeOD): δ 8.71 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.41-7.33 (m, 3H), 7.27 (t, J = 7.8 Hz, 2H), 7.00 (t, J = 7.2 Hz, 1H),

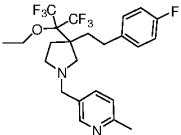
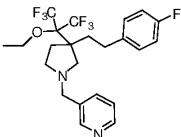
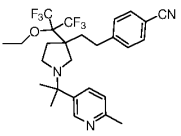
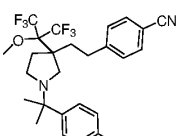
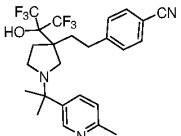
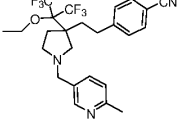
		hyl)-3-phenylurea citrate		6.48-6.44 (m, 1H), 6.34-6.26 (m, 1H), 3.44-3.34 (m, 3H), 3.18 (m, 1H), 2.95 (m, 1H), 2.91-2.68 (m, 7H), 2.50 (s, 3H), 2.00-1.87 (m, 2H), 1.84 (m, 6H), 1.81-1.71 (m, 2H).
44		(R or S)-3-(3-(4-fluorophenethyl)-1-(pyridin-3-yl)methyl)pyrrolidin-3-yl)methanol citrate	315	¹ H NMR (300 MHz, MeOD): δ 8.69 (s, 1H), 8.63 (d, J = 4.8 Hz, 1H), 8.03 (s, 1H), 7.54 (s, 1H), 7.21 (dd, J = 8.4, 5.4 Hz, 2H), 6.98 (t, J = 8.6 Hz, 2H), 4.45-4.26 (m, 2H), 3.57 (s, 4H), 3.06 (d, J = 10.5 Hz, 1H), 2.87-2.71 (m, 5H), 2.59 (t, J = 8.6 Hz, 2H), 2.04 (s, 2H), 1.81 (d, J = 9.2 Hz, 2H).
45		(R or S)-3-(3-(3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)-5-fluoropyridine citrate	361	¹ H NMR (300 MHz, MeOD): δ 8.58 (s, 2H), 7.91 (d, J = 9.1 Hz, 1H), 7.26-7.15 (m, 2H), 6.98 (t, J = 8.6 Hz, 2H), 4.54-4.35 (m, 2H), 3.61-3.51 (m, 2H), 3.49-3.34 (m, 5H), 3.15 (d, J = 11.5 Hz, 1H), 2.81 (q, J = 15.6 Hz, 4H), 2.59 (s, 2H), 2.04 (s, 2H), 1.84 (d, J = 11.9 Hz, 2H), 1.22 (t, J = 7.0 Hz, 3H).
46		(R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)-N-(pyridin-3-yl)pyrrolidine-1-carboxamide		
47		(R or S)-3-(2-(3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)ethyl)pyridine		
48		(R or S)-3,3'-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methylene)dipyridine		

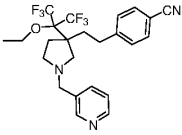
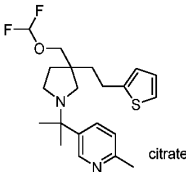
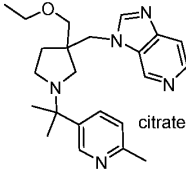
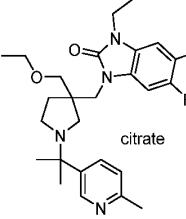
		dine		
49		(R or S)-N-(3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)pyridin-3-amine		
50		3-(1-((R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)-2,2,2-trifluoroethyl)pyridine		
51		(R or S)-3,5-dichloro-4-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)pyridine		
52		(R or S)-4-(2-(3-(ethoxymethyl)-1-(pyridin-3-ylmethyl)pyrrolidin-3-yl)ethyl)benzonitrile		
53		(R or S)-3-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)isonicotinonitrile		
54		(R or S)-3-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)picolinonitrile		
55		(R or S)-5-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)-2-methoxy pyridine		

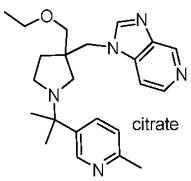
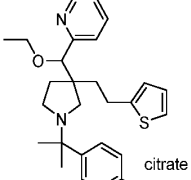
56		(R or S)-5-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)-2-methoxyisonicotinonitrile		
57		(R or S)-3-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)picolinamide		
58		5-((R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)-6,7-dihydro-1,7-naphthyridin-8(5H)-one		
59		5-((R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)-6,6-dimethyl-6,7-dihydro-1,7-naphthyridin-8(5H)-one		
60		(R or S)-4-(2-(1-(di(pyridin-3-yl)methyl)-3-(ethoxymethyl)pyrrolidin-3-yl)ethyl)benzonitrile		
61		(R or S)-2-(3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)-1-(6-methylpyridin-3-yl)ethan-1-one		

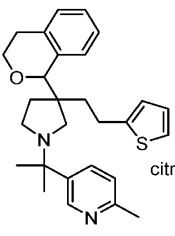
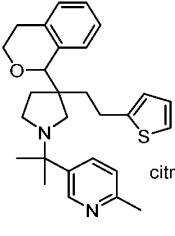
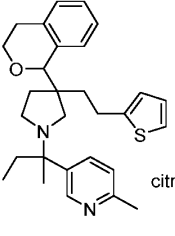
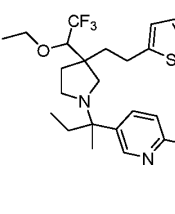
62		(R or S)-2-(3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)-2-methyl-1-(6-methylpyridin-3-yl)propan-1-one		
63		(R or S)-2-(3-(ethoxymethyl)-3-(2-(5-fluoropyridin-2-yl)ethyl)pyrrolidin-1-yl)-1-(6-methylpyridin-3-yl)ethan-1-one		
64		(R or S)-2-(3-(ethoxymethyl)-3-(2-(5-fluoropyridin-2-yl)ethyl)pyrrolidin-1-yl)-2-methyl-1-(6-methylpyridin-3-yl)propan-1-one		
65		(R or S)-4-(2-(3-(oxetan-3-yl)-1-(pyridin-3-yl)methyl)pyrrolidin-3-yl)ethylbenzonitrile		
66		(R or S)-3-((3-(4-fluorophenethyl)-3-(oxetan-3-yl)pyrrolidin-1-yl)methyl)pyridine		
67		(R or S)-4-(2-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(oxetan-3-yl)pyrrolidin-3-yl)ethyl)benzonitrile		
68		(R or S)-5-(3-(3-(4-fluorophenethyl)-3-(oxetan-3-yl)pyrrolidin-1-yl)oxetan-3-yl)-2-methylpyridine		

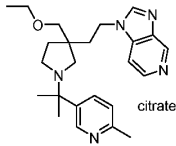
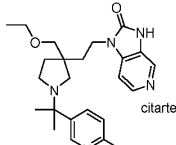
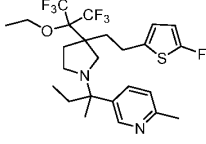
69		(R or S)-5-(2-(3-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
70		(R or S)-5-((3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)methyl)-2-methylpyridine		
71		(R or S)-3-((3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)methyl)pyridine		
72		(R or S)-5-(2-(3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
73		(R or S)-5-(2-(3-(4-fluorophenethyl)-3-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
74		(R or S)-1,1,1,3,3,3-hexafluoro-2-(3-(4-fluorophenethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin		

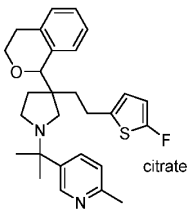
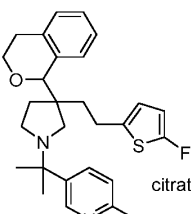
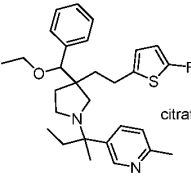
		-3-yl)propan-2-ol		
75		(R or S)-5-((3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)-2-methylpyridine		
76		(R or S)-3-((3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)pyridine		
77		(R or S)-4-(2-(3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)benzonitrile		
78		(R or S)-4-(2-(3-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)benzonitrile		
79		(R or S)-4-(2-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)benzonitrile		
80		(R or S)-4-(2-(3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-1-(6-methylpyridin-3-yl)		

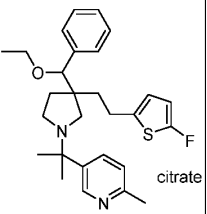
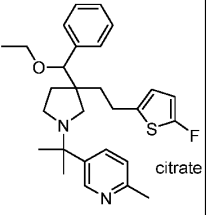
		methyl)pyrrolidin-3-yl)ethyl)benzonitrile		
81		(R or S)-4-(2-(3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-1-(pyridin-3-ylmethyl)pyrrolidin-3-yl)ethyl)benzonitrile		
82		(R or S)-5-(2-(3-((difluoromethoxy)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	395	¹ H NMR (300 MHz, MeOD) : δ 8.63 (s, 1H), 7.98 (dd, J = 5.7, 2.7 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.17 (dd, J = 3.9, 1.2 Hz, 1H), 6.88 (dd, J = 3.6, 1.2 Hz, 1H), 6.79 (d, J = 3.3 Hz, 1H), 6.38 (t, J = 75.3 Hz, 1H), 3.88-3.75 (m, 2H), 3.05-2.98 (m, 2H), 2.93-2.78 (m, 6H), 2.75-2.65 (m, 2H), 2.54 (s, 3H), 1.89-1.80 (m, 4H), 1.65 (s, 6H)
83		(R or S)-3-((3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3H-imidazo[4,5-c]pyridine citrate	422	¹ H NMR (300 MHz, MeOD): δ 8.98 (s, 1H), 8.59 (d, J = 2.4 Hz, 1H), 8.45-8.31 (m, 2H), 7.96 (m, 1H), 7.79 (m, 1H), 7.34 (d, J = 8.2 Hz, 1H), 4.53-4.37 (m, 2H), 3.41 (t, J = 7.1 Hz, 2H), 3.21-3.09 (m, 2H), 3.02-2.96 (m, 1H), 2.93-2.75 (m, 4H), 2.75-2.66 (m, 3H), 2.55 (s, 3H), 1.96-1.85 (m, 1H), 1.70 (m, 1H), 1.57 (m, 6H), 1.16 (t, J = 7.0 Hz, 3H).
84		(R or S)-1-((3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-ethyl-5,6-difluoro-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	473	¹ H NMR (300 MHz, MeOD): δ 8.59 (s, 1H), 7.97 (dd, J = 8.3, 2.6 Hz, 1H), 7.31 (d, J = 8.3 Hz, 1H), 7.14-7.08 (m, 2H), 3.91-3.75 (m, 4H), 3.46-3.26 (m, 4H), 3.13 (m, 1H), 2.91 (m, 1H), 2.75-2.64 (m, 6H), 2.47 (s, 3H), 1.96

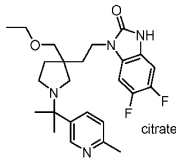
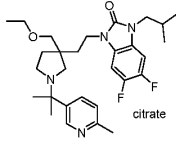
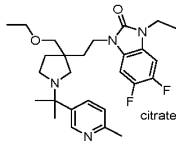
				(m, 1H), 1.80 (m, 1H), 1.70 (d, $J = 3.2$ Hz, 6H), 1.18 (t, $J = 7.2$ Hz, 3H), 1.08 (t, $J = 7.0$ Hz, 3H).
85		(R or S)-1-((3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-1H-imidazo[4,5-c]pyridine citrate	394	^1H NMR (300 MHz, MeOD): δ 9.04 (s, 1H), 8.60 (d, $J = 2.3$ Hz, 1H), 8.42 (s, 1H), 8.38 (d, $J = 5.8$ Hz, 1H), 8.01 (dd, $J = 8.2, 2.4$ Hz, 1H), 7.76 (d, $J = 5.7$ Hz, 1H), 7.37 (d, $J = 8.2$ Hz, 1H), 4.64-4.45 (m, 2H), 3.38 (m, 2H), 3.13 (m, 2H), 2.91 (m, 2H), 2.99-2.80 (m, 4H), 2.76 (m, 2H), 2.56 (s, 3H), 1.97 (m, 1H), 1.60-1.58 (m, 7H), 1.17 (t, $J = 7.0$ Hz, 3H).
86		5-(2-((S or R)-3-((R&S)-ethoxy(pyridin-2-yl)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	450	^1H NMR (300 MHz, MeOD): δ 8.64 (t, $J = 3.0$ Hz, 1H), 8.54 (t, $J = 3.9$ Hz, 1H), 8.02-7.96 (m, 1H), 7.88-7.79 (m, 1H), 7.50-7.45 (m, 1H), 7.43-7.34 (m, 2H), 7.15-7.11 (m, 1H), 6.88-6.83 (m, 1H), 6.75-6.71 (m, 1H), 4.49 (s, 0.5H), 4.47 (s, 0.5H), 3.73 (d, $J = 11.4$ Hz, 0.5 H), 3.46 (d, $J = 11.4$ Hz, 0.5 H), 3.39-3.35 (m, 2H), 3.30-3.25 (m, 1H), 3.23-3.03 (m, 2H), 3.01-2.96 (m, 1H), 2.83-2.73 (m, 5H), 2.56 (m, 3H), 2.41-2.20 (m, 1H), 1.93-1.84 (m, 1H), 1.76 (m, 6H), 1.74-1.42 (m, 2H), 1.17-1.06 (m, 3H)

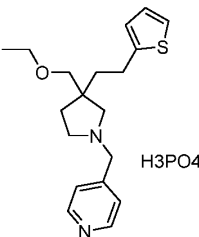
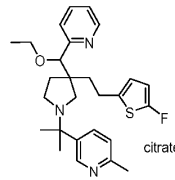
87		5-(2-((R or S)-3-((S or R)-isochroman-1-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	447	¹ H NMR (300 MHz, MeOD): δ 8.72 (s, 1H), 8.06 (s, 1H), 7.42 (s, 1H), 7.20-7.18 (m, 4H), 7.09 (d, <i>J</i> = 4.8 Hz, 1H), 6.82 (t, <i>J</i> = 3.3 Hz, 1H), 6.56 (s, 1H), 4.11-4.05 (m, 1H), 3.61-3.50 (m, 2H), 3.10-3.05 (m, 1H), 2.98-2.86 (m, 2H), 2.75 (q, <i>J</i> = 15.6 Hz, 4H), 2.65-2.55 (m, 4H), 2.54-2.45 (m, 4H), 2.20-2.00 (m, 2H), 1.83 (s, 6H), 1.70-2.55 (m, 2H)
88		5-(2-((R or S)-3-((R or S)-isochroman-1-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	447	¹ H NMR (300 MHz, MeOD): δ 8.65 (s, 1H), 7.98 (d, <i>J</i> = 6.9 Hz, 1H), 7.39 (d, <i>J</i> = 7.8 Hz, 1H), 7.21-7.16 (m, 5H), 6.88 (t, <i>J</i> = 3.9 Hz, 1H), 6.75 (s, 1H), 4.08-4.06 (m, 1H), 3.56-3.46 (m, 2H), 3.16-3.08 (m, 1H), 2.85 (q, <i>J</i> = 15.5 Hz, 4H), 2.58 (s, 6H), 2.19 (t, <i>J</i> = 7.5 Hz, 1H), 2.09-1.97 (m, 3H), 1.87-1.81 (m, 8H), 1.66-1.54 (m, 2H)
89		5-(2-((R or S)-3-((S or R)-isochroman-1-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine citrate	461	¹ H NMR (300 MHz, MeOD): δ 8.68 (s, 1H), 8.06 (s, 1H), 7.46 (s, 1H), 7.20 (m, 4H), 7.10 (t, <i>J</i> = 5.7 Hz, 1H), 6.81 (m, 1H), 6.55 (m, 1H), 4.15-4.02 (m, 1H), 3.62-3.45 (m, 4H), 3.21-2.95 (m, 2H), 2.80 (q, <i>J</i> = 15.5 Hz, 4H), 2.58-2.49 (m, 6H), 2.47-2.25 (m, 2H), 2.19-2.05 (m, 2H), 1.95-1.78 (m, 4H), 1.76-1.50 (m, 2H), 0.90-0.81 (m, 3H)
90		5-(2-((R or S)-3-((S&R)-1-ethoxy-2,2,2-trifluoroethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine	473	¹ H NMR (300 MHz, MeOD): δ 8.54 (m, 1H), 7.65-7.59 (m, 1H), 7.10 (d, <i>J</i> = 7.8 Hz, 1H), 6.33 (s, 1H), 6.23 (d, <i>J</i> = 1.8 Hz, 1H), 4.01-3.80 (m, 1H), 3.64-3.42 (m, 2H), 3.04-2.64 (m, 3H), 2.54 (s, 6H),

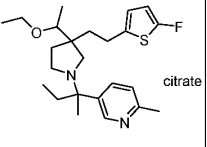
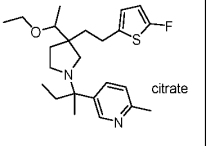
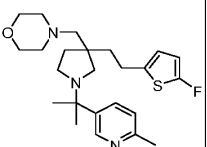
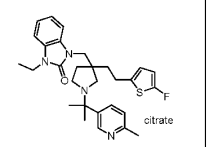
				2.00-1.91 (m, 1H), 1.90-1.74 (m, 3H), 1.72-1.61 (m, 2H), 1.35 (s, 3H), 1.24-1.17 (m, 2H), 1.16-1.06 (m, 1H), 0.63 (t, $J = 7.2$ Hz, 3H)
91		1-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1H-imidazo[4,5-c]pyridine citrate	408	^1H NMR (300 MHz, MeOD): δ 8.98 (s, 1H), 8.66 (s, 1H), 8.47 (s, 1H), 8.40 (d, $J = 5.8$ Hz, 1H), 8.08-7.97 (m, 1H), 7.75 (d, $J = 5.7$ Hz, 1H), 7.39 (d, $J = 8.5$ Hz, 1H), 4.45 (t, $J = 8.2$ Hz, 2H), 3.48 (q, $J = 7.0$ Hz, 3H), 3.39 (m, 2H), 3.24-3.12 (m, 2H), 3.10-3.02 (m, 1H), 2.81 (q, $J = 15.6$ Hz, 4H), 2.55 (s, 3H), 2.21-2.05 (m, 2H), 1.95-1.85 (m, 2H), 1.75 (s, 6H), 1.16 (t, $J = 7.0$ Hz, 3H).
92		1-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one citrate	424	^1H NMR (500 MHz, MeOD): δ 8.66 (d, $J = 2.1$ Hz, 1H), 8.33 (s, 1H), 8.22 (d, $J = 5.4$ Hz, 1H), 8.02 (dd, $J = 8.3$, 2.4 Hz, 1H), 7.39 (d, $J = 8.3$ Hz, 1H), 7.17 (d, $J = 5.4$ Hz, 1H), 3.94 (t, $J = 7.7$ Hz, 2H), 3.46 (t, $J = 7.1$ Hz, 2H), 3.38 (q, $J = 9.2$ Hz, 2H), 3.22-3.10 (m, 2H), 3.05 (d, $J = 11.3$ Hz, 1H), 2.90 (d, $J = 11.4$ Hz, 1H), 2.80 (q, $J = 15.5$ Hz, 4H), 2.55 (s, 3H), 2.01-1.82 (m, 4H), 1.74 (s, 6H), 1.14 (t, $J = 7.0$ Hz, 3H).
93		5-(2-((R or S)-3-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl))pyrrolidin-3-yl)ethyl)-1H-imidazo[4,5-c]pyridine	541	^1H NMR (300 MHz, MeOD): δ 8.51 (dd, $J = 11.4$, 1.8 Hz, 1H), 7.68-7.55 (m, 1H), 7.11 (d, $J = 8.1$ Hz, 1H), 6.38-6.26 (m, 1H), 6.25 (d, $J = 1.8$ Hz,

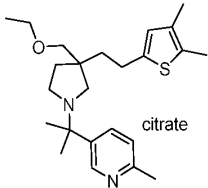
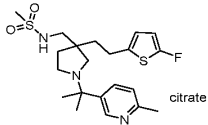
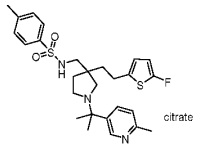
		yl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine		1H), 4.01-3.82 (m, 2H), 3.11-2.75 (m, 4H), 2.55 (s, 3H), 2.51-2.45 (m, 1H), 2.40-2.27 (m, 2H), 2.23-1.98 (m, 1H), 1.97-1.70 (m, 4H), 1.41-1.32 (m, 3H), 1.21-1.15 (m, 3H), 0.63 (t, $J = 7.2$ Hz, 3H)
94		5-(2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-3-((R or S)-isochroman-1-yl)pyrrolidin-1-yl)propyl)-2-methylpyridine citrate	465	¹ HNMR (300 MHz, MeOD): δ 8.61 (d, $J = 2.1$ Hz, 1H), 7.94 (m, 1H), 7.35 (d, $J = 8.4$ Hz, 1H), 7.19-7.08 (m, 4H), 6.31 (d, $J = 3.0$ Hz, 1H), 6.27 (t, $J = 3.6$ Hz, 1H), 4.15-4.02 (m, 1H), 3.55-3.49 (m, 1H), 3.20-3.11 (m, 2H), 3.07-3.01 (m, 1H), 2.98-2.88 (m, 2H), 2.87-2.84 (m, 1H), 2.79 (q, $J = 15.6$ Hz, 4H), 2.74-2.66 (m, 2H), 2.64-2.60 (m, 1H), 2.55 (s, 3H), 2.25-2.18 (m, 1H), 1.95-1.82 (m, 2H), 1.81-1.75 (m, 1H), 1.71 (m, 6H).
95		5-(2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-3-((S or R)-isochroman-1-yl)pyrrolidin-1-yl)propyl)-2-methylpyridine citrate	465	¹ HNMR (300 MHz, MeOD): δ 8.74 (s, 1H), 8.10 (d, $J = 6.0$ Hz, 1H), 7.45 (d, $J = 8.1$ Hz, 1H), 7.26-7.20 (m, 4H), 6.23-6.22 (m, 1H), 6.18 (d, $J = 2.7$ Hz, 1H), 4.15-4.02 (m, 1H), 3.52-3.49 (m, 2H), 3.15-3.05 (m, 1H), 2.79 (q, $J = 15.6$ Hz, 4H), 2.74 (s, 3H), 2.54-2.43 (m, 2H), 2.38-2.28 (m, 2H), 2.20-2.08 (m, 2H), 1.87 (s, 6H), 1.80-1.75 (m, 1H), 1.65-1.60 (m, 1H), 1.18 (t, $J = 6.9$ Hz, 3H).
96		5-(2-((R or S)-3-((R or S)-ethoxy(phenyl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)butyl)-2-methylpyridine citrate	481	¹ HNMR (300 MHz, MeOD): δ 8.69 (d, $J = 2.1$ Hz, 1H), 8.04 (d, $J = 8.1$ Hz, 1H), 7.52-7.47 (m, 1H), 7.40-7.34 (m, 3H), 7.26 (d, $J = 6.9$ Hz, 1H), 7.22 (t, $J = 3.9$ Hz, 1H), 6.37 (d, $J = 3.9$ Hz, 1H), 6.28

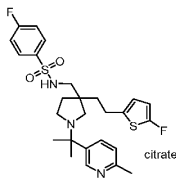
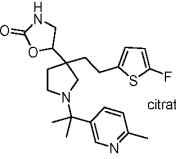
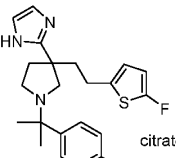
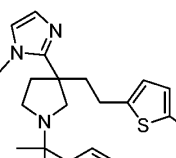
		dine citrate		(m, 1H), 4.39 (m, 1H), 3.58-3.40 (m, 2H), 3.30-3.12 (m, 4H), 3.11-2.93 (m, 1H), 2.79 (q, $J = 15.6$ Hz, 4H), 2.78-2.70 (m, 3H), 2.60 (d, $J = 6.3$ Hz, 3H), 2.28-2.20 (m, 1H), 2.10-2.00 (m, 1H), 1.83 (m, 3H), 1.75-1.62 (m, 1H), 1.58 (m, 1H), 1.03 (t, $J = 7.2$ Hz, 3H), 0.82 (t, $J = 6.9$ Hz, 3H)
97		5-(2-((R or S)-3-((R or S)-ethoxy(phenyl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	467	¹ HNMR (300 MHz, MeOD): δ 8.75 (s, 1H), 8.09 (d, $J = 8.4$ Hz, 1H), 7.48 (d, $J = 8.4$ Hz, 1H), 7.40-7.34 (m, 3H), 7.24 (d, $J = 6.3$ Hz, 2H), 6.37 (s, 1H), 6.29 (t, $J = 2.9$ Hz, 1H), 4.40 (s, 1H), 3.56-3.50 (m, 1H), 3.49-3.38 (m, 3H), 3.28-3.22 (m, 2H), 2.98-2.90 (m, 2H), 2.79 (q, $J = 15.6$ Hz, 4H), 2.60 (s, 3H), 2.32-2.21 (m, 1H), 2.08-1.97 (m, 1H), 1.88 (m, 6H), 1.70-1.52 (m, 2H), 1.03 (t, $J = 6.9$ Hz, 3H).
98		5-(2-((R or S)-3-((S or R)-ethoxy(phenyl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	467	¹ HNMR (300 MHz, MeOD): δ 8.70 (d, $J = 1.8$ Hz, 1H), 8.03 (m, 1H), 7.43 (d, $J = 8.1$ Hz, 1H), 7.35-7.28 (m, 5H), 6.37 (t, $J = 3.3$ Hz, 1H), 6.30-6.28 (m, 1H), 4.40 (s, 1H), 3.47-3.40 (m, 2H), 3.25-3.15 (m, 2H), 3.08-2.90 (m, 2H), 2.79 (q, $J = 15.6$ Hz, 4H), 2.75-2.65 (m, 2H), 2.59 (s, 3H), 2.38-2.30 (m, 1H), 2.15-1.92 (m, 1H), 1.84 (m, 6H), 1.70-1.62 (m, 1H), 1.58-1.49 (m, 1H), 1.11 (t, $J = 7.2$ Hz, 3H).

99		1-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-5,6-difluoro-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	459	¹ H NMR (300 MHz, MeOD): δ 8.67 (d, <i>J</i> = 1.8 Hz, 1H), 8.03 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 7.40 (d, <i>J</i> = 8.3 Hz, 1H), 7.11 (t, <i>J</i> = 8.5 Hz, 1H), 7.01 (t, <i>J</i> = 8.5 Hz, 1H), 3.85 (t, <i>J</i> = 7.8 Hz, 2H), 3.46 (m, 3H), 3.38 (m, 2H), 3.24-3.15 (m, 2H), 3.08 (d, <i>J</i> = 11.4 Hz, 1H), 2.91 (d, <i>J</i> = 11.7 Hz, 1H), 2.80 (q, <i>J</i> = 15.5 Hz, 4H), 2.56 (s, 3H), 1.95-1.83 (m, 3H), 1.77 (s, 6H), 1.14 (t, <i>J</i> = 7.0 Hz, 3H).
100		1-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyrrolidin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-5,6-difluoro-3-isobutyl-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	515	¹ H NMR (300 MHz, MeOD): δ 8.68 (s, 1H), 8.04 (d, <i>J</i> = 8.9 Hz, 1H), 7.41 (d, <i>J</i> = 8.3 Hz, 1H), 7.20 (ddd, <i>J</i> = 16.9, 10.0, 6.9 Hz, 2H), 3.89 (t, <i>J</i> = 7.5 Hz, 2H), 3.67 (d, <i>J</i> = 7.5 Hz, 2H), 3.46 (q, <i>J</i> = 7.0 Hz, 2H), 3.36 (m, 2H), 3.22 (m, 2H), 3.11 (d, <i>J</i> = 11.5 Hz, 1H), 2.96 (d, <i>J</i> = 11.7 Hz, 1H), 2.80 (q, <i>J</i> = 15.5 Hz, 4H), 2.56 (s, 3H), 2.19-2.08 (m, 1H), 2.01-1.82 (m, 4H), 1.79 (s, 6H), 1.14 (t, <i>J</i> = 7.0 Hz, 3H), 0.93 (d, <i>J</i> = 4.8 Hz, 6H).
101		1-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyrrolidin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-ethyl-5,6-difluoro-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	487	¹ H NMR (300 MHz, MeOD): δ 8.65 (s, 1H), 8.00 (d, <i>J</i> = 6.2 Hz, 1H), 7.38 (d, <i>J</i> = 8.1 Hz, 1H), 7.24 (dd, <i>J</i> = 10.1, 6.9 Hz, 1H), 7.15 (dd, <i>J</i> = 10.1, 7.0 Hz, 1H), 3.96-3.84 (m, 4H), 3.46 (q, <i>J</i> = 6.9 Hz, 3H), 3.37 (s, 2H), 3.14 (m,

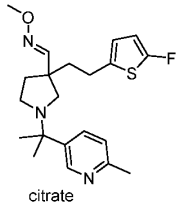
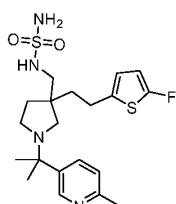
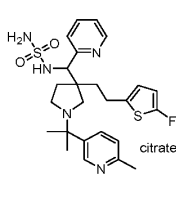
				2H), 3.02 (m, 1H), 2.80 (q, J = 15.5 Hz, 4H), 2.55 (s, 3H), 1.97-1.78 (m, 4H), 1.73 (s, 6H), 1.27 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H).
102		(S)-4-((3-(ethoxymethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)methyl)pyridine H ₃ PO ₄ salt	331	¹ H NMR (300 MHz, MeOD): δ 8.46 (d, J = 5.2 Hz, 2H), 7.45 (s, 2H), 7.13 (dd, J = 5.2, 1.2 Hz, 1H), 6.87 (dd, J = 5.2, 3.4 Hz, 1H), 6.78 (d, J = 3.4 Hz, 1H), 3.66 (s, 2H), 3.49 (q, J = 7.0 Hz, 2H), 3.34 (d, J = 3.5 Hz, 2H), 2.81 (t, J = 7.8 Hz, 2H), 2.63 (q, J = 7.0 Hz, 2H), 2.56 (d, J = 9.6 Hz, 1H), 2.34 (d, J = 9.6 Hz, 1H), 1.86 (m, 2H), 1.68 (t, J = 6.9 Hz, 2H), 1.18 (t, J = 7.0 Hz, 3H).
103		5-(2-((R or S)-3-((S&R)-ethoxy(pyridin-2-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	468	¹ H NMR (300 MHz, MeOD): δ 8.68 (s, 1H), 8.56 (s, 1H), 8.05 (m, 1H), 7.84 (m, 1H), 7.53-7.31 (m, 3H), 6.43-6.32 (m, 1H), 6.31-6.22 (m, 1H), 4.47 (m, 1H), 3.79 (d, J = 11.7 Hz, 1H), 3.51 (d, J = 11.5 Hz, 1H), 3.25-3.15 (m, 1H), 3.08 (d, J = 11.4 Hz, 1H), 3.02-2.87 (m, 2H), 2.79 (q, J = 15.5 Hz, 4H), 2.70-2.63 (m, 1H), 2.58 (s, 3H), 2.42-2.23 (m, 1H), 2.12-1.89 (m, 1H), 1.82 (s, 6H), 1.79-1.59 (m, 2H), 1.52-1.36 (m, 1H), 1.18-1.01 (m, 3H).

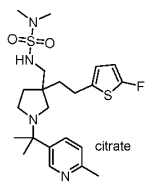
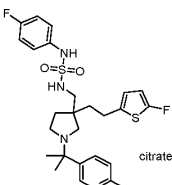
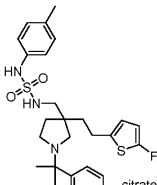
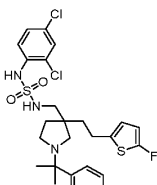
104		5-(2-((R or S)-3-((S or R)-1-ethoxyethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine citrate	419	¹ H NMR (300 MHz, MeOD): δ 8.64 (s, 1H), 8.00 (d, <i>J</i> = 7.8 Hz, 1H), 7.45 (d, <i>J</i> = 8.1 Hz, 1H), 6.41 (m, 1H), 6.30 (m, 1H), 3.64-3.57 (m, 1H), 3.50-3.38 (m, 2H), 3.26-3.07 (m, 4H), 2.75 (q, <i>J</i> = 15.6 Hz, 4H), 2.71-2.61 (m, 2H), 2.57 (s, 3H), 2.53-2.44 (m, 1H), 2.21-2.11 (m, 1H), 2.07-2.00 (m, 1H), 1.80 (s, 3H), 1.76-1.57 (m, 3H), 1.13-1.02 (m, 6H), 0.78 (t, <i>J</i> = 7.2 Hz, 3H)
105		5-(2-((R or S)-3-((R or S)-1-ethoxyethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine citrate	419	¹ H NMR (300 MHz, MeOD): δ 8.65 (s, 1H), 8.00 (d, <i>J</i> = 8.1 Hz, 1H), 7.45 (d, <i>J</i> = 8.1 Hz, 1H), 6.41 (d, <i>J</i> = 3.9 Hz, 1H), 6.30 (m, 1H), 3.64-3.56 (m, 1H), 3.50-3.42 (m, 2H), 3.22-3.08 (m, 2H), 2.77 (q, <i>J</i> = 15.6 Hz, 4H), 2.68-2.62 (m, 2H), 2.56 (s, 3H), 2.55-2.47 (m, 2H), 2.07-2.00 (m, 2H), 1.82 (s, 6H), 1.75-1.69 (m, 1H), 1.08-0.99 (m, 6H), 0.80 (t, <i>J</i> = 7.2 Hz, 3H)
106		(S or R)-4-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)morpholine	432	¹ H NMR (300 MHz, MeOD): δ 8.53 (d, <i>J</i> = 1.8 Hz, 1H), 7.85 (dd, <i>J</i> = 8.1, 2.1 Hz, 1H), 7.25 (d, <i>J</i> = 8.1 Hz, 1H), 6.38 (t, <i>J</i> = 3.3 Hz, 1H), 6.28 (m, 1H), 3.63 (t, <i>J</i> = 4.5 Hz, 4H), 2.68-2.58 (m, 4H), 2.52 (s, 3H), 2.50-2.38 (m, 6H), 2.36-2.28 (m, 2H), 1.82-1.70 (m, 2H), 1.66-1.54 (m, 2H), 1.42 (s, 6H)
107		(S or R)-1-ethyl-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-	507	¹ H NMR (300 MHz, MeOD): δ 8.59 (s, 1H), 7.90 (s, 1H), 7.30 (t, <i>J</i> = 5.1 Hz, 1H), 7.17 (d, <i>J</i> = 18.9 Hz, 4H), 6.43 (s, 1H), 6.29 (s, 1H), 3.99 (d, <i>J</i> = 4.0 Hz, 4H), 3.14-3.05 (m,

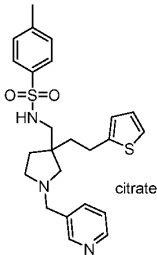
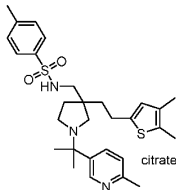
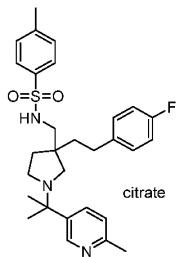
		3-yl)methyl)-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate		¹ H, 2.98 (s, 2H), 2.90-2.68 (m, 5H), 2.52 (d, <i>J</i> = 3.3 Hz, 3H), 2.07-1.95 (m, 1H), 1.87-1.77 (m, 3H), 1.65-1.55 (m, 6H), 1.35-1.29 (m, 5H).
108		(R or S)-5-(2-(3-(2-(4,5-dimethylthiophen-2-yl)ethyl)-3-(ethoxymethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	401	¹ H NMR (300 MHz, MeOD): δ 8.70 (s, 1H), 8.06 (d, <i>J</i> = 7.8 Hz, 1H), 7.43 (d, <i>J</i> = 8.3 Hz, 1H), 6.43 (s, 1H), 3.43 (q, <i>J</i> = 6.6 Hz, 2H), 3.18 (d, <i>J</i> = 11.8 Hz, 1H), 2.96 (d, <i>J</i> = 11.8 Hz, 1H), 2.80 (q, <i>J</i> = 15.5 Hz, 4H), 2.70-2.59 (m, 4H), 2.57 (s, 3H), 2.24 (s, 3H), 2.09-1.91 (m, 5H), 1.90-1.67 (m, 10H), 1.12 (t, <i>J</i> = 6.9 Hz, 3H).
109		(R or S)-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)methanesulfonamide citrate	440	¹ H NMR (300 MHz, MeOD): δ 8.63 (d, <i>J</i> = 1.8 Hz, 1H), 8.00 (dd, <i>J</i> = 8.1, 2.4 Hz, 1H), 7.36 (d, <i>J</i> = 8.1 Hz, 1H), 6.43 (t, <i>J</i> = 3.6 Hz, 1H), 6.29 (dd, <i>J</i> = 3.9, 2.1 Hz, 1H), 3.12-3.02 (m, 4H), 3.01-2.95 (m, 1H), 2.94 (s, 3H), 2.77 (q, <i>J</i> = 15.6 Hz, 4H), 2.72-2.64 (m, 3H), 2.54 (s, 3H), 1.92-1.75 (m, 4H), 1.74 (s, 6H)
110		(R or S)-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-4-methylbenzenesulfonamide citrate	516	¹ H NMR (300 MHz, MeOD): δ 8.67 (s, 1H), 8.07 (d, <i>J</i> = 8.1 Hz, 1H), 7.72 (d, <i>J</i> = 8.1 Hz, 2H), 7.39 (t, <i>J</i> = 8.4 Hz, 3H), 6.40 (t, <i>J</i> = 3.6 Hz, 1H), 6.27 (dd, <i>J</i> = 3.6, 2.1 Hz, 1H), 3.32-3.30 (m, 3H), 3.29-3.18 (m, 2H), 3.15-3.05 (m, 1H), 2.90-2.80 (m, 3H), 2.75 (q, <i>J</i> = 15.6 Hz, 4H), 2.65-2.60 (m, 1H), 2.55 (s, 3H), 2.42 (s, 3H), 1.95-1.82 (m, 2H), 1.72 (s, 6H)

111		(S or R)-4-fluoro-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)benzenesulfonamide citrate	520	¹ H NMR (300 MHz, MeOD): δ 8.65 (s, 1H), 8.03 (d, <i>J</i> = 7.9 Hz, 1H), 7.90 (dd, <i>J</i> = 8.7, 4.9 Hz, 2H), 7.49-7.24 (m, 3H), 6.50-6.37 (m, 1H), 6.35-6.22 (m, 1H), 3.20-2.99 (m, 3H), 2.95-2.69 (m, 8H), 2.67-2.50 (m, 5H), 1.87-1.68 (m, 9H).
112		(S & R)-5-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)oxazolidin-2-one citrate	418	¹ H NMR (300 MHz, MeOD): δ 8.61 (s, 1H), 8.00 (d, <i>J</i> = 8.1 Hz, 1H), 7.36 (d, <i>J</i> = 8.0 Hz, 1H), 6.44 (t, <i>J</i> = 3.4 Hz, 1H), 6.30 (dd, <i>J</i> = 3.7, 2.1 Hz, 1H), 4.88-4.70 (m, 1H), 3.69-3.42 (m, 2H), 2.98-2.61 (m, 10H), 2.54 (s, 3H), 1.97-1.68 (m, 4H), 1.61 (s, 6H).
113		(R or S)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(1H-imidazol-2-yl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	399	¹ H NMR (300 MHz, MeOD): δ 8.43 (s, 1H), 7.79 (d, <i>J</i> = 8.3 Hz, 1H), 7.34-7.23 (m, 3H), 6.36-6.29 (m, 1H), 6.28-6.23 (m, 1H), 3.15 (m, 1H), 3.05-2.95 (m, 2H), 2.93-2.73 (m, 5H), 2.57-2.45 (m, 5H), 2.41-2.29 (m, 1H), 2.24-2.01 (m, 3H), 1.51 (d, <i>J</i> = 7.7 Hz, 6H).
114		(R or S)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(1-methyl-1H-imidazol-2-yl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	413	¹ H NMR (300 MHz, MeOD): δ 8.55 (d, <i>J</i> = 1.9 Hz, 1H), 7.92 (dd, <i>J</i> = 8.3, 2.3 Hz, 1H), 7.32 (d, <i>J</i> = 8.3 Hz, 1H), 7.16 (d, <i>J</i> = 1.3 Hz, 1H), 7.04 (d, <i>J</i> = 1.2 Hz, 1H), 6.33-6.18 (m, 2H), 3.74 (s, 3H), 3.05 (m, 2H), 2.90-2.72 (m, 5H), 2.53 (s, 3H), 2.50-2.43 (m, 1H), 2.40-2.08 (m, 6H), 1.56

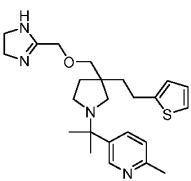
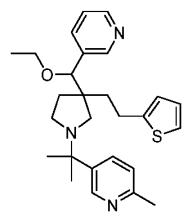
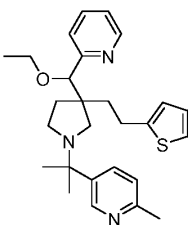
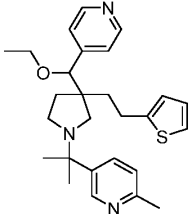
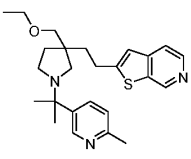
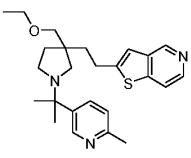
				(s, 6H).
115		(R or S)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(4H-1,2,4-triazol-1-yl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine	400	¹ H NMR (300 MHz, MeOD): δ 8.56 (s, 1H), 8.01 (s, 1H), 7.66 (t, <i>J</i> = 4.1 Hz, 1H), 7.12 (d, <i>J</i> = 8.1 Hz, 1H), 6.28-6.19 (m, 1H), 6.18 (d, <i>J</i> = 2.1 Hz, 1H), 3.10-3.00 (m, 1H), 2.99-2.85 (m, 1H), 2.80-2.68 (m, 1H), 2.66-2.55 (m, 2H), 2.53 (s, 3H), 2.50-2.42 (m, 1H), 2.40-2.25 (m, 2H), 2.15-2.05 (m, 1H), 1.98-1.88 (m, 1H), 1.45 (s, 3H), 1.45 (s, 3H).
116		(R or S)-5-(2-(3-((cyclopropylmethoxy)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	417	¹ H NMR (300 MHz, MeOD): δ 8.73 (s, 1H), 8.09 (dd, <i>J</i> = 8.4, 1.7 Hz, 1H), 7.45 (d, <i>J</i> = 8.0 Hz, 1H), 6.46-6.39 (m, 1H), 6.32-6.26 (m, 1H), 3.40-3.34 (m, 4H), 3.27-3.32 (m, 3H), 3.00 (d, <i>J</i> = 12.2 Hz, 1H), 2.82 (q, <i>J</i> = 15.6 Hz, 4H), 2.66 (t, <i>J</i> = 8.0 Hz, 2H), 2.57 (s, 3H), 2.06-1.99 (m, 1H), 1.93-1.83 (m, 8H), 1.79 (d, <i>J</i> = 8.3 Hz, 1H), 1.02-0.89 (m, 1H), 0.56-0.46 (m, 2H), 0.22-0.13 (m, 2H).
117		(R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidine-3-carboxamide citrate	376	¹ H NMR (300 MHz, MeOD): δ 8.61 (s, 1H), 7.98 (d, <i>J</i> = 7.3 Hz, 1H), 7.36 (d, <i>J</i> = 8.5 Hz, 1H), 6.43-6.36 (m, 1H), 6.31-6.25 (m, 1H), 3.05-2.94 (m, 2H), 2.81 (q, <i>J</i> = 15.5 Hz, 4H), 2.68 (m, 1H), 2.62-2.57 (m, 1H), 2.55 (s, 3H), 2.42-2.28 (m, 1H), 2.16-2.00 (m, 2H), 1.97-1.72

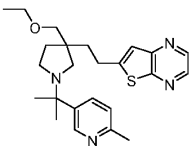
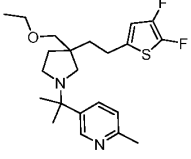
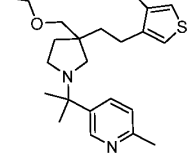
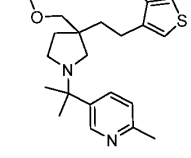
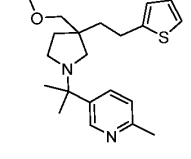
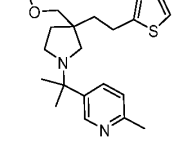
				(m, 3H), 1.64 (s, 6H).
118		(R or S,E)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidine-3-carbaldehyde O-methyl oxime citrate	390	¹ H NMR (500 MHz, MeOD): δ 8.65 (d, J = 2.1 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.39 (d, J = 8.3 Hz, 1H), 7.30 (s, 1H), 6.40 (t, J = 3.6 Hz, 1H), 6.28 (dd, J = 3.9, 2.1 Hz, 1H), 3.78 (s, 3H), 3.36-3.32 (m, 1H), 3.24-3.15 (m, 1H), 3.05 (m, 1H), 2.93-2.88 (m, 1H), 2.81 (q, J = 15.5 Hz, 4H), 2.69-2.57 (m, 2H), 2.56 (s, 3H), 2.24-2.17 (m, 1H), 1.97-1.89 (m, 2H), 1.89-1.82 (m, 1H), 1.72 (s, 6H).
119		(S or R)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)sulfamoyl amine	441	¹ H NMR (300 MHz, MeOD): δ 8.51 (s, 1H), 7.87 (dd, J = 5.7, 2.4 Hz, 1H), 7.26 (d, J = 8.1 Hz, 1H), 6.42 (s, 1H), 6.28 (t, J = 3.0 Hz, 1H), 3.04 (s, 2H), 2.78-2.51 (m, 5H), 2.50 (s, 3H), 2.34 (m, 1H), 1.80-1.71 (m, 3H), 1.68-1.51 (m, 1H), 1.30 (s, 6H)
120		(S or R)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)(pyridin-2-yl)methyl)sulfamoyl amine	518	¹ H NMR (300 MHz, MeOD): δ 8.63 (s, 1H), 8.59-8.51 (m, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.48 (dd, J = 22.1, 7.7 Hz, 1H), 7.41-7.26 (m, 2H), 6.40-6.34 (m, 1H), 6.28 (t, J = 3.1 Hz, 1H), 4.57 (d, J = 15.3 Hz, 1H), 3.52 (d, J = 10.4 Hz, 1H), 2.96-2.75 (m, 7H), 2.56 (s, 3H), 2.33-2.28 (m, 1H), 1.85-1.75 (m, 1H), 1.71 (d, J = 4.1 Hz, 6H), 1.58-1.43 (m, 2H).

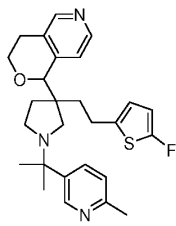
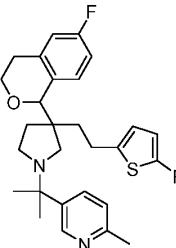
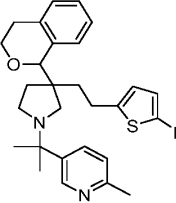
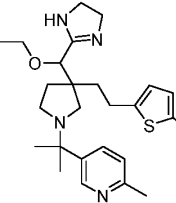
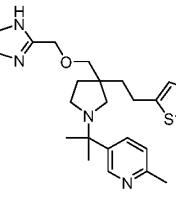
121		(S or R)- ((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)sulfamoyl dimethylamine	469	¹ H NMR (300 MHz, MeOD): δ 8.64 (s, 1H), 8.01 (d, J = 7.5 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 6.43 (s, 1H), 6.29 (s, 1H), 3.11-3.00 (m, 5H), 2.91-2.61 (m, 14H), 2.55 (s, 3H), 1.95-1.74 (m, 3H), 1.61 (s, 6H).
122		(R or S)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)sulfamoyl 4-fluorophenylamine citrate	535	¹ H NMR (300 MHz, MeOD): δ 8.65 (d, J = 2.3 Hz, 1H), 8.04 (dd, J = 8.7, 2.3 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1H), 7.22 (dd, J = 8.9, 4.7 Hz, 2H), 7.04 (t, J = 8.5 Hz, 2H), 6.36 (d, J = 3.6 Hz, 1H), 6.27 (dd, J = 3.9, 2.1 Hz, 1H), 3.18 (t, J = 7.0 Hz, 2H), 3.09 (d, J = 11.6 Hz, 1H), 2.98 (s, 2H), 2.92-2.69 (m, 5H), 2.63-2.49 (m, 5H), 1.89-1.79 (m, 2H), 1.75 (s, 6H), 1.71-1.64 (m, 2H).
123		(R or S)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)sulfamoyl 4-methylphenylamine		¹ H NMR (300 MHz, MeOD): δ 8.58 (s, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.35 (d, J = 7.9 Hz, 1H), 7.10 (s, 4H), 6.33 (s, 1H), 6.26 (s, 1H), 2.95 (s, 3H), 2.89-2.69 (m, 5H), 2.62-2.49 (m, 6H), 2.26 (s, 3H), 1.79-1.69 (m, 5H), 1.60 (s, 6H).
124	 Exact Mass: 584.12 tPSA: 73.8 CLogP: 6.67	(R or S)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)sulfamoyl 2,4-dichlorophenyl	531	¹ H NMR (300 MHz, MeOD): δ 8.60 (s, 1H), 7.96 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 2.4 Hz, 1H), 7.33 (dd, J = 19.1, 8.4 Hz, 2H), 6.36 (s, 1H), 6.31-6.24 (m, 1H), 3.05-2.98

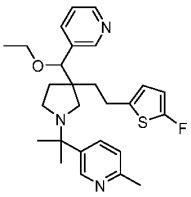
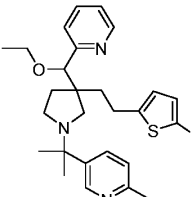
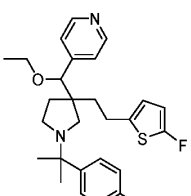
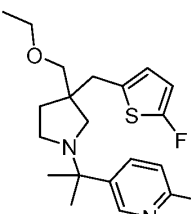
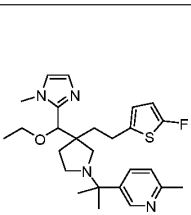
		amine		(m, 3H), 2.89-2.73 (m, 6H), 2.66-2.57 (m, 3H), 2.55 (s, 3H), 1.83-1.70 (m, 4H), 1.64 (s, 6H).
125		(S or R)-4-methyl-N-((1-(pyridin-3-ylmethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)methyl)benzenesulfonamide citrate	456	¹ H NMR (300 MHz, MeOD): δ 8.63 (s, 1H), 8.57 (d, <i>J</i> = 4.9 Hz, 1H), 7.99 (d, <i>J</i> = 7.9 Hz, 1H), 7.74 (d, <i>J</i> = 8.0 Hz, 2H), 7.52 – 7.48 (m, 1H), 7.38 (d, <i>J</i> = 7.9 Hz, 2H), 7.19-7.11 (m, 1H), 6.88 (dd, <i>J</i> = 5.1, 3.5 Hz, 1H), 6.81 (d, <i>J</i> = 3.4 Hz, 1H), 4.19 (s, 2H), 3.23-3.11 (m, 3H), 2.91 (d, <i>J</i> = 7.0 Hz, 2H), 2.88-2.69 (m, 7H), 2.42 (s, 3H), 1.99-1.81 (m, 4H).
126		(S or R)-N-((3-(2-(4,5-dimethylthiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-4-methylbenzenesulfonamide citrate	526	¹ H NMR (300 MHz, MeOD): δ 8.65 (s, 1H), 8.02 (d, <i>J</i> = 8.3 Hz, 1H), 7.71 (d, <i>J</i> = 8.0 Hz, 2H), 7.39 (t, <i>J</i> = 6.9 Hz, 3H), 6.41 (s, 1H), 3.22-3.15 (m, 2H), 3.10-3.06 (m, 1H), 2.89-2.71 (m, 8H), 2.62-2.53 (m, 5H), 2.43 (s, 3H), 2.23 (s, 3H), 2.02 (s, 3H), 1.87-1.83 (m, 1H), 1.77-1.69 (m, 8H).
127		(S or R)-N-((3-(4-fluorophenethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-4-methylbenzenesulfonamide citrate	510	¹ H NMR (300 MHz, MeOD): δ 8.65 (s, 1H), 8.02 (d, <i>J</i> = 8.1 Hz, 1H), 7.73 (d, <i>J</i> = 8.0 Hz, 2H), 7.39 (d, <i>J</i> = 8.0 Hz, 3H), 7.20-7.11 (m, 2H), 6.95 (t, <i>J</i> = 8.7 Hz, 2H), 3.15 (t, <i>J</i> = 5.8 Hz, 2H), 3.05 (d, <i>J</i> = 11.0 Hz, 1H), 2.87-2.71 (m, 7H), 2.55 (s, 3H), 2.51-2.44 (m, 2H), 2.43 (s, 3H),

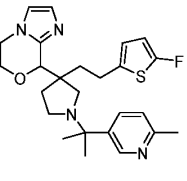
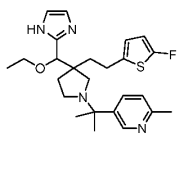
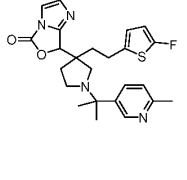
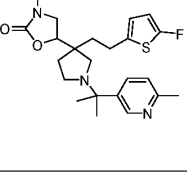
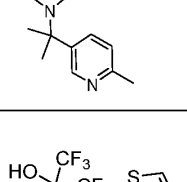
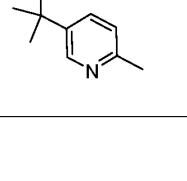
				1.90-1.79 (m, 2H), 1.74 (s, 6H), 1.70-1.59 (m, 2H).
128		(R or S)-5-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thieno[3,4-b]pyrazine		
129		(R or S)-5-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-7-fluorothieno[3,4-b]pyrazine		
130		1-((R or S)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)-3,4-dihydro-1H-pyrano[4,3-c]pyridine		
131		5-(2-((3R or S)-3-(6-fluoroisochroman-1-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
132		5-(2-((3R or S)-3-((4,5-dihydro-1H-imidazol-2-yl)(ethoxymethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

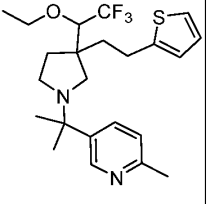
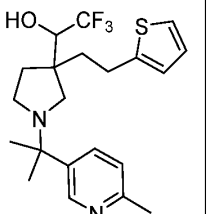
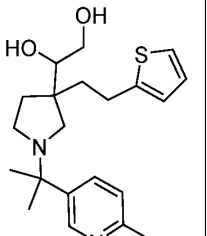
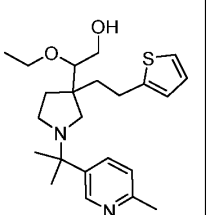
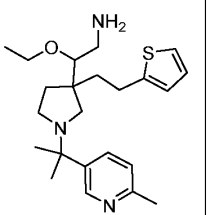
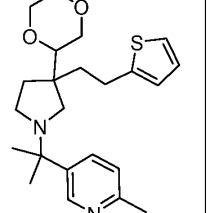
133		(R or S)-5-(2-(3-(((4,5-dihydro-1H-imidazol-2-yl)methoxy)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
134		5-(2-((S or R)-3-((S or R)-ethoxy(pyridin-3-yl)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
135		5-(2-((S or R)-3-((S or R)-ethoxy(pyridin-2-yl)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
136		5-(2-((3R or S)-3-(ethoxy(pyridin-4-yl)methyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
137		(R or S)-2-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thieno[2,3-c]pyridine		
138		(R or S)-2-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thieno[3,2-c]pyridine		

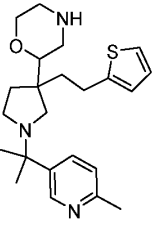
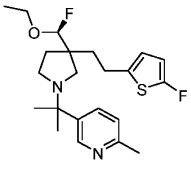
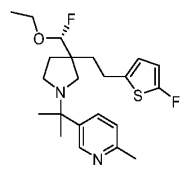
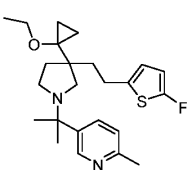
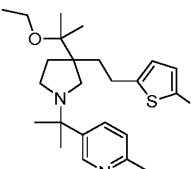
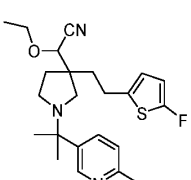
		yridine		
139		(R or S)-6-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thieno[2,3-b]pyrazine		
140		(R or S)-5-(2-(3-(2-(4,5-difluorothiophen-2-yl)ethyl)-3-(ethoxymethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
141		(R or S)-4-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thiophene-3-carbonitrile		
142		(R or S)-5-(2-(3-(ethoxymethyl)-3-(2-(4-fluorothiophen-3-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
143		(R or S)-5-(2-(3-(ethoxymethyl)-3-(2-(4-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
144		(R or S)-5-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thiophene-3-carbonitrile		

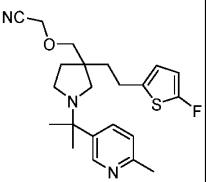
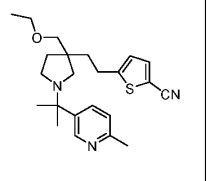
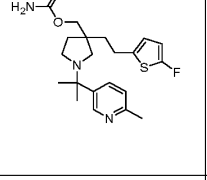
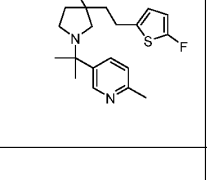
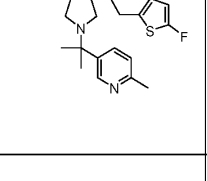
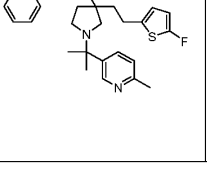
145		1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-3,4-dihydro-1H-pyrano[4,3-c]pyridine		
146		5-(2-((3R or S)-3-(6-fluoroisochroman-1-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
147		5-(2-((3R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(isochroman-1-yl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
148		5-(2-((3R or S)-3-((4,5-dihydro-1H-imidazol-2-yl)(ethoxymethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
149		(R or S)-5-(2-(3-(((4,5-dihydro-1H-imidazol-2-yl)methoxy)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

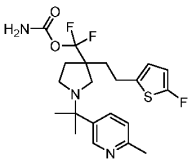
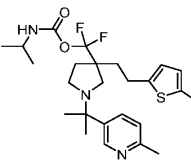
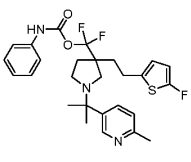
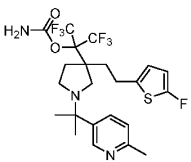
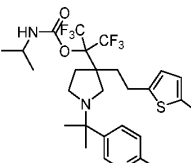
150		5-(2-((S or R)-3-((R or S)-ethoxy(pyridin-3-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
151		5-(2-((S or R)-3-((R or S)-ethoxy(pyridin-2-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
152		5-(2-((S or R)-3-((R or S)-ethoxy(pyridin-4-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
153		(S or R)-5-(2-(3-(ethoxymethyl)-3-((5-fluorothiophen-2-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
154		5-(2-((3R or S)-3-(ethoxy(1-methyl-1H-imidazol-2-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

155		8-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-5,6-dihydro-8H-imidazo[2,1-c][1,4]oxazine		
156		5-(2-((3R or S)-3-(ethoxy(1H-imidazol-2-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
157		7-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-5H,7H-imidazo[1,2-c]oxazol-5-one		
158		3-ethyl-5-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)oxazolidin-2-one		
159		(R or S)-2-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)propan-2-ol		
160		(R or S)-1,1,1,3,3,3-hexafluoro-2-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)propan-2-ol		

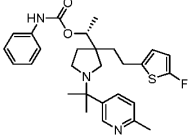
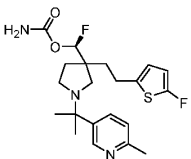
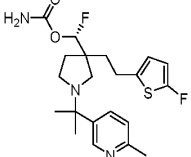
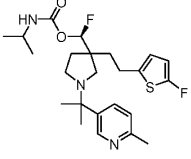
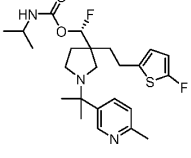
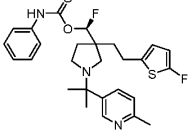
161		(R or S)-5-(2-(3-(1-ethoxy-2,2,2-trifluoroethyl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
162		(R or S)-2,2,2-trifluoro-1-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)ethan-1-ol		
163		(R or S)-1-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)ethane-1,2-diol		
164		(R or S)-2-ethoxy-2-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)ethan-1-ol		
165		(R or S)-2-ethoxy-2-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)ethan-1-amine		
166		(R or S)-5-(2-(3-(1,4-dioxan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

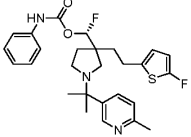
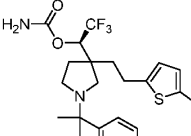
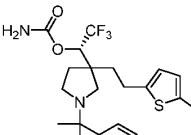
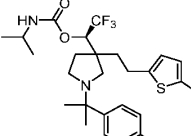
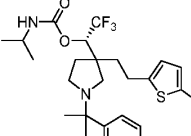
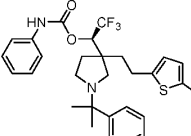
167		(R or S)-2-(1-(2-(6-methylpyridin-3-yl)propan-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-3-yl)morpholine		
168		5-(2-((R or S)-3-((S)-ethoxyfluoromethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
169		5-(2-((R or S)-3-((R)-ethoxyfluoromethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
170		(R or S)-5-(2-(3-(1-ethoxycyclopropyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
171		(R or S)-5-(2-(3-(2-ethoxypropan-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
172		2-ethoxy-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)acetonitrile		

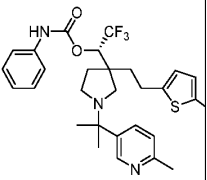
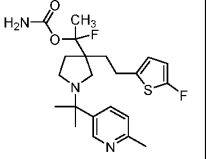
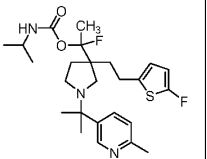
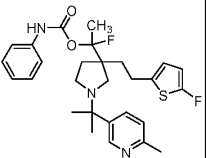
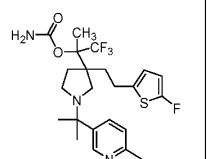
173		(R or S)-2-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methoxy)acetonitrile		
174		(R or S)-5-(2-(3-(ethoxymethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)thiophene-2-carbonitrile		
175		(R or S)-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl carbamate		
176		(R or S)-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl carbamate		
177		(R or S)-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl isopropylcarbamate		
178		(R or S)-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl phenylcarbamate		

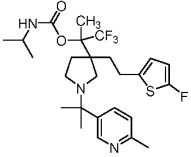
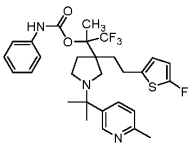
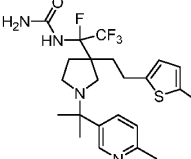
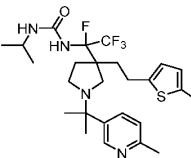
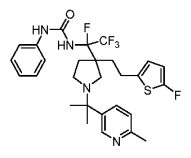
179		(R or S)-difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl carbamate		
180		(R or S)-difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl isopropylcarbamate		
181		(R or S)-difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl phenylcarbamate		
182		(R or S)-1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl carbamate		
183		(R or S)-1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl isopropylcarbamate		

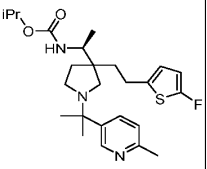
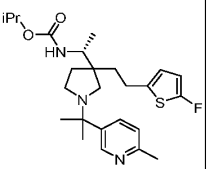
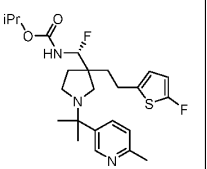
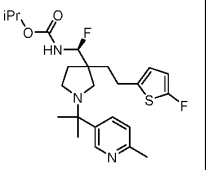
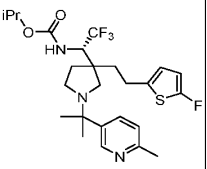
184		(R or S)-1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl phenylcarbamate		
185		(S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl carbamate		
186		(R)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl carbamate		
187		(S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl isopropylcarbamate		
188		(R)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl isopropylcarbamate		
189		(S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl phenylcarbamate		

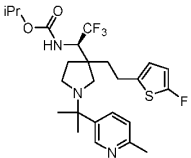
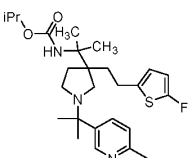
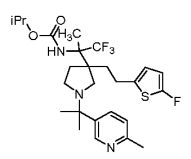
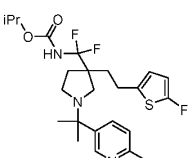
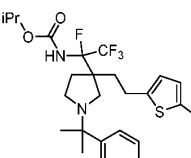
190		(R)-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl phenylcarbamate		
191		(S)-fluoro((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl carbamate		
192		(R)-fluoro((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl carbamate		
193		(S)-fluoro((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl isopropylcarbamate		
194		(R)-fluoro((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl isopropylcarbamate		
195		(S)-fluoro((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl phenylcarbamate		

196		(R)-fluoro((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl phenylcarbamate		
197		(R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl carbamate		
198		(S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl carbamate		
199		(R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl isopropylcarbamate		
200		(S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl isopropylcarbamate		
201		(R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl isopropylcarbamate		

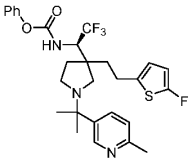
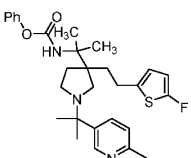
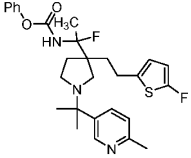
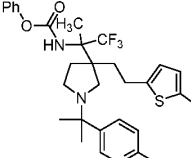
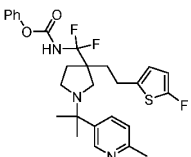
		3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl phenylcarbamate		
202		(S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl phenylcarbamate		
203		1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl carbamate		
204		1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl isopropylcarbamate		
205		1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl phenylcarbamate		
206		1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl carbamate		

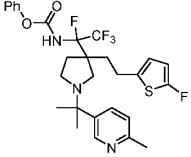
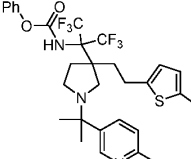
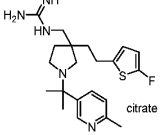
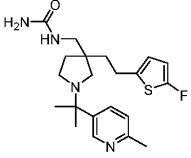
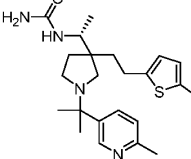
207		1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)propan- 2-yl isopropylcarbamate		
208		1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)propan- 2-yl phenylcarbamate		
209		1-(1,2,2,2-tetrafluor o-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)ethyl)ur ea		
210		1-isopropyl-3-(1,2,2, 2-tetrafluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)ethyl)ur ea		
211		1-phenyl-3-(1,2,2,2-t etrafluoro-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)ethyl)ur ea		

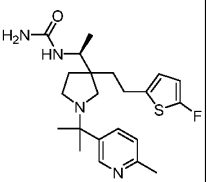
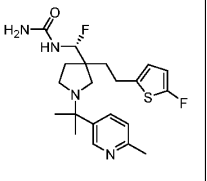
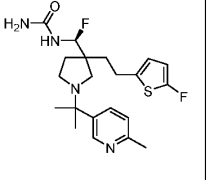
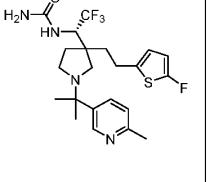
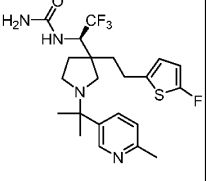
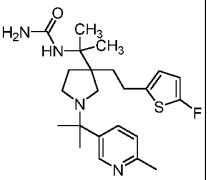
212		isopropyl ((S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate isopropyl ((1S)-1-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
213		isopropyl ((R)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
214		isopropyl ((R)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		
215		isopropyl ((S)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		
216		isopropyl ((S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		

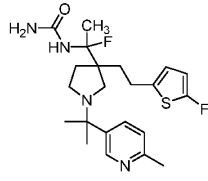
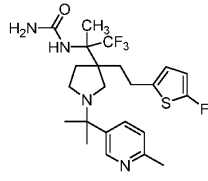
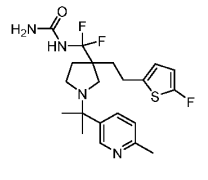
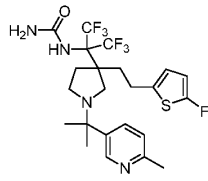
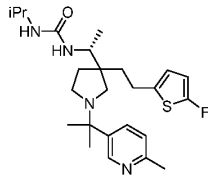
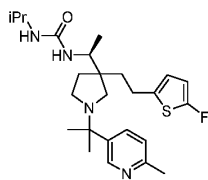
		2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
217		isopropyl ((R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
218		isopropyl (R or S)-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)carbamate		
219		isopropyl (1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)carbamate		
220		isopropyl (R or S)-(difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		
221		isopropyl (1,2,2,2-tetrafluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)ca		

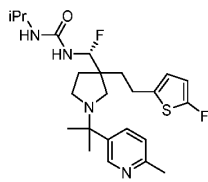
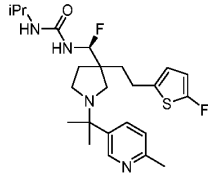
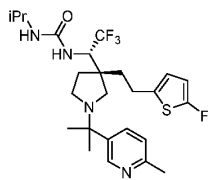
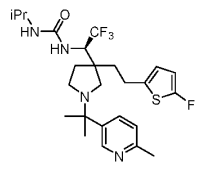
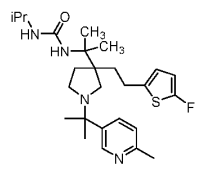
		rbamate		
222		isopropyl (R or S)-(1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)carbamate		
223		phenyl ((R)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
224		phenyl ((S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
225		phenyl ((R)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		
226		phenyl ((S)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		
227		phenyl ((S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(		

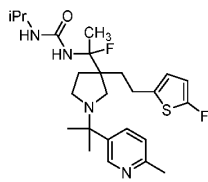
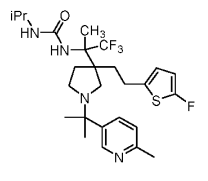
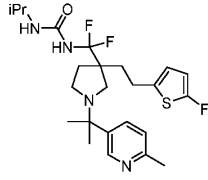
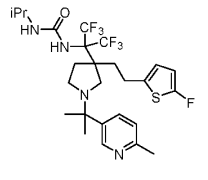
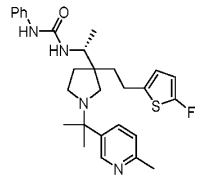
		2-(6-methylpyridin-3-yl)propan-2-ylpyrrolidin-3-ylethyl)carbamate		
228		phenyl ((R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
229		phenyl (R or S)-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)carbamate		
230		phenyl (1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)carbamate		
231		phenyl (1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)carbamate		
232		phenyl (R or S)-(difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)carbamate		

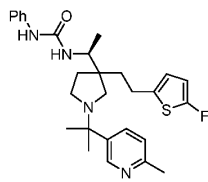
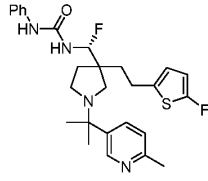
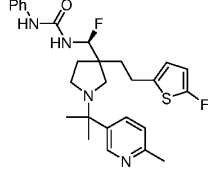
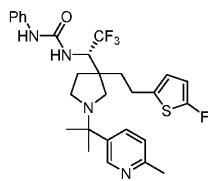
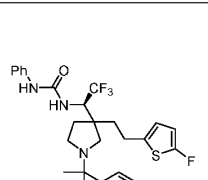
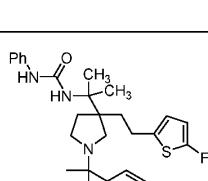
233		phenyl (1,2,2,2-tetrafluoro- 1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)ethyl)ca rbamate		
234		phenyl (R or S)-(1,1,1,3,3,3-hexaf luoro-2-(3-(2-(5-fluo rothiophen-2-yl)ethy l)-1-(2-(6-methylpyr idin-3-yl)propan-2-y l)pyrrolidin-3-yl)pro pan-2-yl)carbamate		
235		(R or S)-1-((3-(2-(5-fluoro thiophen-2-yl)ethyl) -1-(2-(6-methylpyrid in-3-yl)propan-2-yl) pyrrolidin-3-yl)meth yl)guanidine citrate	404	¹ H NMR (300 MHz, MeOD): δ 8.78 (s, 1H), 8.27 (d, <i>J</i> = 6.6 Hz, 1H), 7.52 (d, <i>J</i> = 7.8 Hz, 1H), 6.46 (s, 1H), 6.32 (s, 1H), 3.11-2.99 (m, 2H), 2.94-2.76 (m, 7H), 2.71-2.55 (m, 5H), 2.05-1.90 (m, 2H), 1.88-1.72 (m, 9H).
236		(S or R)-1-((3-(2-(5-fluor othiophen-2-yl)ethyl)-1-(2-(6-methylpyri din-3-yl)propan-2-yl)pyrrolidin-3-yl)met hyl)urea		
237		1-((R)-1-((R or S)-3-(2-(5-fluorothio phen-2-yl)ethyl)-1-(2-(6-methylpyridin- 3-yl)propan-2-yl)pyr rolidin-3-yl)ethyl)ur ea		

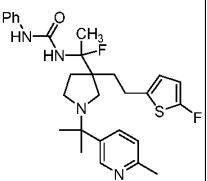
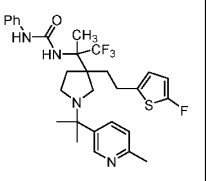
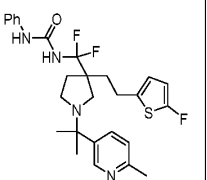
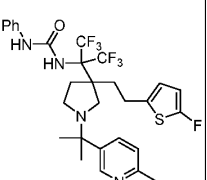
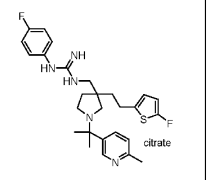
238		1-((S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
239		1-((R)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
240		1-((S)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
241		1-((S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
242		1-((R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
243		(R or S)-1-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)urea		

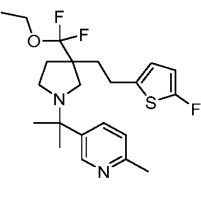
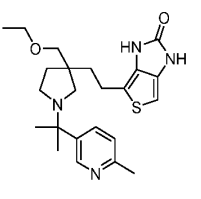
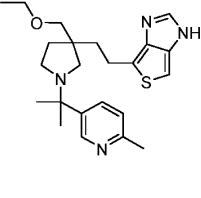
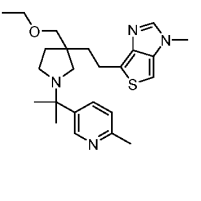
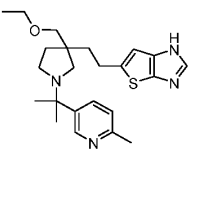
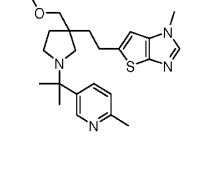
244		1-(1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
245		1-(1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)urea		
246		(R or S)-1-(difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
247		(R or S)-1-(1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)urea		
248		1-((R)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-isopropylurea		
249		1-((S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-isopropylurea		

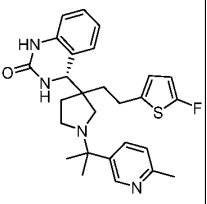
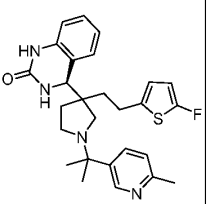
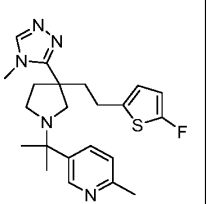
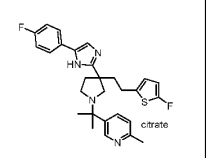
250		1-((R)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-isopropylurea		
251		1-((S)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-isopropylurea		
252		1-isopropyl-3-((S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
253		1-isopropyl-3-((R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
254		(R or S)-1-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyrrolidin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)-3-isopropylurea		

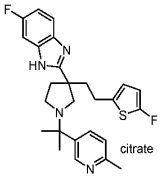
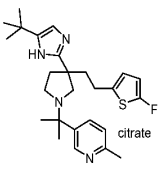
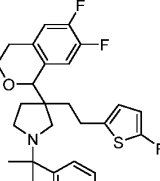
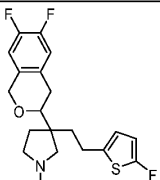
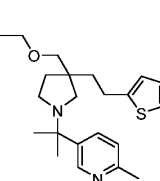
255		1-(1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-isopropylurea		
256		1-isopropyl-3-(1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)urea		
257		(R or S)-1-(difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-isopropylurea		
258		(R or S)-1-(1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)-3-isopropylurea		
259		1-((R)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-phenylurea		

260		1-((S)-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-phenylurea		
261		1-((R)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-phenylurea		
262		1-((S)-fluoro((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-phenylurea		
263		1-phenyl-3-((S)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
264		1-phenyl-3-((R)-2,2,2-trifluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)urea		
265		(R or S)-1-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)-3-phenylurea		

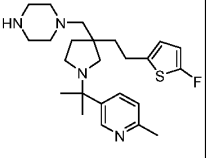
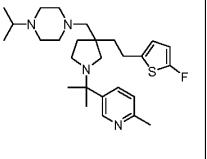
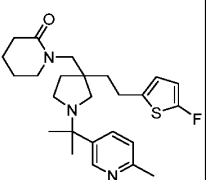
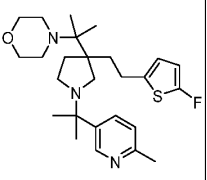
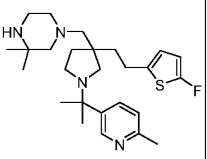
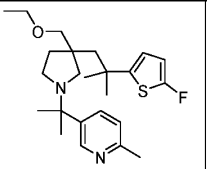
		rea		
266		1-(1-fluoro-1-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-3-phenylurea		
267		1-phenyl-3-(1,1,1-trifluoro-2-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)urea		
268		(R or S)-1-(difluoro(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-phenylurea		
269		(R or S)-1-(1,1,1,3,3,3-hexafluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)-3-phenylurea		
270		(R or S)-1-(4-fluorophenyl)-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3-phenylurea	498	¹ H NMR (300 MHz, MeOD): δ 8.76 (s, 1H), 8.21 (s, 1H), 7.47 (d, <i>J</i> = 8.3 Hz, 1H), 7.32 (dd, <i>J</i> = 8.8, 4.5 Hz, 2H), 7.21 (t, <i>J</i> = 8.5 Hz, 2H), 6.47 (s, 1H), 6.35-6.27 (m, 1H), 3.48-3.41 (m, 2H), 2.94-2.74 (m, 7H), 2.72-2.64 (m, 2H), 2.58 (s, 3H), 2.10-1.91 (m, 2H), 1.83-1.74 (m, 9H).

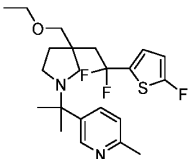
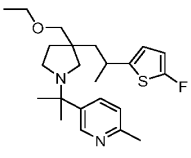
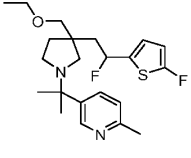
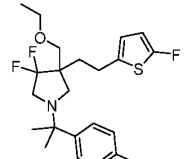
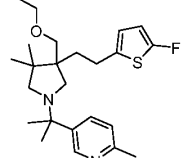
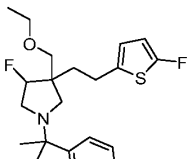
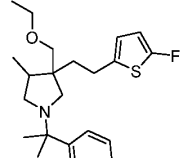
271		(R or S)-5-(2-(3-(ethoxydi fluoromethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
272		(R or S)-4-(2-(3-(ethoxym ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1H-thieno[3,4-d]imidazol-2(3H)-one		
273		(R or S)-4-(2-(3-(ethoxym ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1H-thieno[3,4-d]imidazole		
274		(R or S)-4-(2-(3-(ethoxym ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1-methyl-1H-thieno[3,4-d]imidazole		
275		(R or S)-5-(2-(3-(ethoxym ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1H-thieno[2,3-d]imidazole		
276		(R or S)-5-(2-(3-(ethoxym ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)ethyl)-1-methyl-1H-thieno[2,3-d]imidazole		

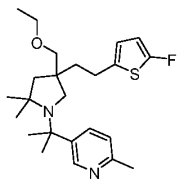
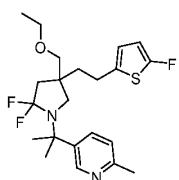
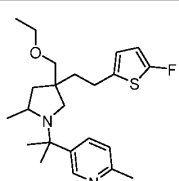
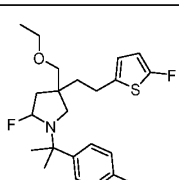
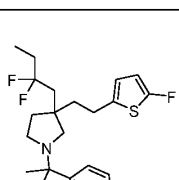
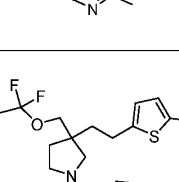
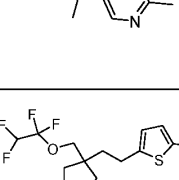
		ole		
277		(S)-4-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-3,4-dihydroquinazolin-2(1H)-one		
278		(R)-4-((R or S)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-3,4-dihydroquinazolin-2(1H)-one		
279		(R or S)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(4-methyl-4H-1,2,4-triazol-3-yl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
280		(S or R)-5-(2-(3-(5-(4-fluorophenyl)-1H-imidazol-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	493	¹ H NMR (300 MHz, MeOD): δ 8.62 (s, 1H), 7.99 (dd, <i>J</i> = 8.4, 2.3 Hz, 1H), 7.70 (dd, <i>J</i> = 8.5, 5.3 Hz, 2H), 7.46-7.31 (m, 2H), 7.14 (t, <i>J</i> = 8.8 Hz, 2H), 6.31 (t, <i>J</i> = 3.6 Hz, 1H), 6.22 (dd, <i>J</i> = 3.9, 2.1 Hz, 1H), 3.72 (d, <i>J</i> = 11.1 Hz, 1H), 3.41-3.28 (m, 1H), 3.21 (d, <i>J</i> = 10.9 Hz, 2H), 2.92-2.73 (m, 4H), 2.68-2.59 (m, 1H), 2.48 (s, 4H), 2.41-2.27 (m, 1H), 2.22 (m, 3H), 1.74 (d, <i>J</i> = 5.0 Hz, 6H).

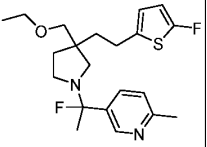
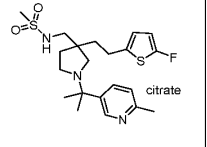
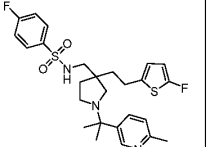
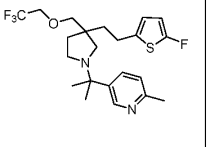
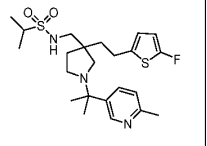
281		(S or R)-6-fluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-1H-benzo[d]imidazole citrate	467	¹ H NMR (300 MHz, MeOD): δ 8.62 (s, 1H), 8.00 (d, <i>J</i> = 8.0 Hz, 1H), 7.51 (dd, <i>J</i> = 8.7, 4.6 Hz, 1H), 7.27 (dd, <i>J</i> = 22.7, 8.5 Hz, 2H), 7.04 (s, 1H), 6.27 (s, 1H), 6.19 (s, 1H), 3.73 (d, <i>J</i> = 10.0 Hz, 1H), 3.39-3.33 (m, 1H), 3.25-3.10 (m, 2H), 2.93-2.74 (m, 6H), 2.48 (s, 3H), 2.35-2.11 (m, 4H), 1.72 (d, <i>J</i> = 6.7 Hz, 6H).
282		(S or R)-5-(2-(3-(5-(tert-butyl)-1H-imidazol-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine citrate	455	¹ H NMR (300 MHz, MeOD): δ 8.45 (s, 1H), 7.85 (d, <i>J</i> = 8.2 Hz, 1H), 7.34 (d, <i>J</i> = 8.1 Hz, 1H), 7.06 (s, 1H), 6.30 (s, 1H), 6.24 (s, 1H), 3.11 (d, <i>J</i> = 9.3 Hz, 1H), 3.05-2.96 (m, 2H), 2.93-2.74 (m, 4H), 2.65-2.43 (m, 6H), 2.36-2.25 (m, 1H), 2.22-2.11 (m, 2H), 1.99 (s, 1H), 1.50 (d, <i>J</i> = 6.2 Hz, 6H), 1.34 (s, 9H).
283		5-(2-((R or S)-3-((R)-6,7-difluoroisochroman-1-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
284		5-(2-((R or S)-3-((R)-6,7-difluoroisochroman-3-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
285		(R or S)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(isobutoxymethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

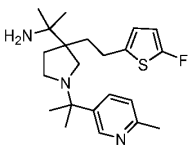
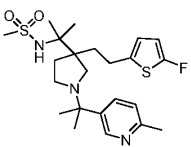
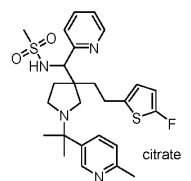
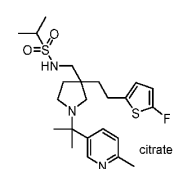
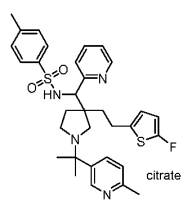
286		(S or R)-1-(4-fluorophenyl)-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
287		(S or R)-1-(4-chlorophenyl)-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
288		(S or R)-1-(3,4-difluorophenyl)-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
289		(S or R)-1-(5-fluoropyridin-2-yl)-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)urea		
290		5-(2-((R or S)-3-(ethoxy(pyridin-3-yl)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)butan-2-yl)-2-methylpyridine		
291		(S or R)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-(piperidin-1-yl)methyl)pyrrolidin-1-yl)-2-methylpyridine		

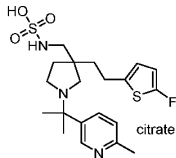
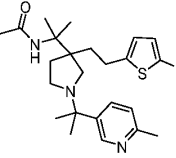
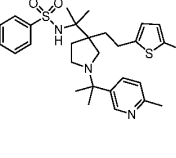
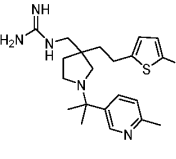
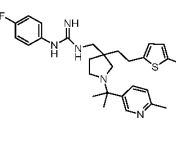
		yl)propan-2-yl)-2-methylpyridine		
292		(S or R)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)piperazine		
293		(S or R)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-4-isopropylpiperazine		
294		(R or S)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)piperidin-2-one		
295		(R or S)-4-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)morpholine		
296		(S or R)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)-3,3-dimethylpiperazine		
297		5-(2-(3-(ethoxymethyl)-3-(2-(5-fluorothiophen-2-yl)-2-methylpropyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

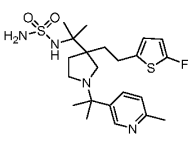
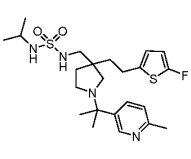
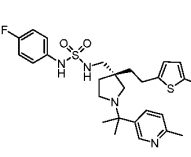
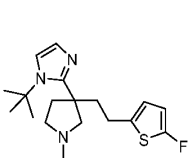
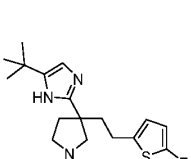
		ethylpyridine		
298		5-(2-(3-(2,2-difluoro-2-(5-fluorothiophen-2-yl)ethyl)-3-(ethoxymethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
299		5-(2-(3-(ethoxymethyl)-3-(2-(5-fluorothiophen-2-yl)propyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
300		5-(2-(3-(ethoxymethyl)-3-(2-fluoro-2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
301		5-(2-(3-(ethoxymethyl)-4,4-difluoro-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
302		5-(2-(3-(ethoxymethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)-4,4-dimethylpyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
303		5-(2-(3-(ethoxymethyl)-4-fluoro-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
304		5-(2-(3-(ethoxymethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)-4-methylpyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

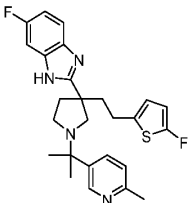
305		5-(2-(4-(ethoxymethyl)-4-(2-(5-fluorothiophen-2-yl)ethyl)-2,2-dimethylpyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
306		5-(2-(4-(ethoxymethyl)-2,2-difluoro-4-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
307		5-(2-(4-(ethoxymethyl)-4-(2-(5-fluorothiophen-2-yl)ethyl)-2-methylpyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
308		5-(2-(4-(ethoxymethyl)-2-fluoro-4-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
309		(S or R)-5-(2-(3-(2,2-difluorobutyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
310		(R or S)-5-(2-(3-((1,1-difluoroethoxy)methyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
311		(R or S)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-((1,1,2,2-tetrafluoroethoxy)methyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

		n-2-yl)-2-methylpyridine		
312		5-(1-((R or S)-3-(ethoxymethyl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)-1-fluoroethyl)-2-methylpyridine		
313		(S or R)-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)methanesulfonamide citrate	440	¹ H NMR (300 MHz, MeOD): δ 8.67 (s, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.41 (d, J = 8.2 Hz, 1H), 6.44 (t, J = 3.6 Hz, 1H), 6.29 (dd, J = 3.9, 2.1 Hz, 1H), 3.26-3.17 (m, 2H), 3.15-3.06 (m, 3H), 2.94 (s, 3H), 2.90-2.72 (m, 6H), 2.71-2.64 (m, 2H), 2.56 (s, 3H), 1.92-1.83 (m, 2H), 1.78 (s, 6H), 1.75-1.72 (m, 1H).
314		(S or R)-4-fluoro-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)benzenesulfonamide		
315		(S or R)-5-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-3-((2,2,2-trifluoroethoxy)methyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
316		(S or R)-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)propane-2-sulfonamide		

317		(S or R)-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-amine		
318		(S or R)-N-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)methanesulfonamide		
319		N-((R & S)-((S or R)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)(pyridin-2-yl)methyl)methanesulfonamide citrate	517	¹ H NMR (300 MHz, MeOD): δ 8.58 (d, <i>J</i> = 7.5 Hz, 2H), 7.96 (d, <i>J</i> = 8.4 Hz, 1H), 7.82 (t, <i>J</i> = 7.9 Hz, 1H), 7.53 (d, <i>J</i> = 7.7 Hz, 1H), 7.37 (d, <i>J</i> = 7.8 Hz, 2H), 6.39 (s, 1H), 6.28 (s, 1H), 4.64 (s, 1H), 3.50 (m, 1H), 2.88-2.72 (m, 8H), 2.70-2.62 (m, 1H), 2.56-2.52 (m, 6H), 2.32-2.18 (m, 1H), 1.93-1.90 (m, 1H), 1.87-1.50 (m, 8H).
320		(S or R)-N-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)propane-2-sulfonamide citrate	468	¹ H NMR (300 MHz, MeOD): δ 8.64 (s, 1H), 8.00 (d, <i>J</i> = 8.2 Hz, 1H), 7.38 (d, <i>J</i> = 8.1 Hz, 1H), 6.44 (s, 1H), 6.30 (d, <i>J</i> = 3.0 Hz, 1H), 3.34 (s, 3H), 3.15-3.03 (m, 4H), 2.80 (q, <i>J</i> = 15.5 Hz, 4H), 2.70-2.63 (m, 3H), 2.55 (s, 3H), 1.85-1.75 (m, 3H), 1.72 (s, 6H), 1.33 (d, <i>J</i> = 6.7 Hz, 6H).
321		N-((R & S)-((S or R)-3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)(pyridin-2-yl)methyl)-4-methylbenzenesulfonamide citrate	593	¹ H NMR (300 MHz, MeOD): δ 8.61 (s, 1H), 8.40-8.28 (m, 1H), 8.09-7.81 (m, 1H), 7.41 (q, <i>J</i> = 7.9, 7.1 Hz, 4H), 7.14-7.08 (m, 1H), 6.98 (dd, <i>J</i> = 34.6, 8.0 Hz, 3H), 6.37 (s, 1H), 6.27 (t, <i>J</i> = 3.1 Hz, 1H),

		hyllbenzenesulfonamide citrate		4.41 (s, 1H), 3.55 (m, 1H), 3.08-2.67 (m, 1H), 2.88-2.72 (m, 8H), 2.55 (d, $J = 7.2$ Hz, 3H), 2.27 (m, 3H), 2.22-2.17 (m, 1H), 1.93-1.60 (m, 9H).
322		(S or R)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)sulfamic acid citrate	442	^1H NMR (300 MHz, MeOD): δ 8.70 (s, 1H), 8.11 (d, $J = 4.8$ Hz, 1H), 8.46 (d, $J = 8.1$ Hz, 1H), 6.45 (s, 1H), 6.30 (s, 1H), 3.60-3.54 (m, 2H), 3.11-3.03 (m, 2H), 2.88-2.81 (m, 6H), 2.79-2.62 (m, 2H), 2.58 (s, 3H), 2.15-1.93 (m, 2H), 1.87 (s, 6H), 1.76 (d, $J = 8.4$ Hz, 2H).
323		(S or R)-N-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)acetamide		
324		(S or R)-N-(2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl)benzenesulfonamide		
325		(R or S)-1-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)guanidine		
326		(R or S)-1-(4-fluorophenyl)-3-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl)guanidine		

		l)guanidine		
327		(R or S)-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)propan-2-yl sulfamoylamine		
328		(R or S)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl) sulfamoyl propan-2-yl-amine		
329		(R or S)-((3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)methyl) sulfamoyl 4-fluorophenylamine		
330		(S or R)-5-(2-(3-(1-(tert-butyl)-1H-imidazol-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		
331		(S or R)-5-(2-(3-(5-(tert-butyl)-1H-imidazol-2-yl)-3-(2-(5-fluorothiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-2-methylpyridine		

332		(S or R)-6-fluoro-2-(3-(2-(5-fluorothiophen-2-yl)ethyl)-1-(2-(6-methylpyridin-3-yl)propan-2-yl)pyrrolidin-3-yl)-1H-benzo[d]imidazole		
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Legend for Tables I, III, V; 4th & 5th Columns: Electrospray ionization (ESI) was used in mass spectrometry for the compounds with a measured mass result shown in the fourth column. The right-most (fifth) column shows the ¹H NMR of such compounds in MeOD at 300 MHz.

Table II: Chirality and *in vivo* testing of certain compounds of Table I

Compound No.	Configuration	ED ₅₀ (mg/kg) at 30 min on C57BL/6 mice in Warm-water Tail-flick Test
1	S	++
2	S	++
3	S	++
4	S	++
5	(S&R, S)	++
6	S	++
7	S	++
8	S	++
9	S	++
10	(S, S or R)	++
11	(S, S or R)	++
12	(S, S or R)	++
13	(S, S or R)	++
14	S	++
15	S	++
16	S	++
17	S	+
18	S	++
19	S	++
20	S	++

21	S	++
22	S	++
23	S	++
24	S	++
25	S	++
26	S	++
27	S	++
28	S	++
29	(S&R)	++
30	S	++
31	S	++
32	S	++
33	S	++
34	(R&S, S)	++
35	(S or R, S)	++
36	S	++
37	(S or R, S)	++
38	S	++
39	S	++
40	S	++
41	S	++
42	S	++
43	S	++
44	R	++
45	R	+
82	S	++
83	S	++
84	S	++
85	S	++
86	(S, R&S)	++
87	(S, S or R)	++
88	(S, S or R)	++
89	(S, S or R)	++
90	(S, R&S)	++
91	(R&S)	++
92	(R&S)	++
93	S	++

94	(S, S or R)	++
95	(S, S or R)	++
96	(S, S or R)	++
97	(S, S or R)	++
98	(S, S or R)	++
99	(R&S)	++
100	(R&S)	++
101	(R&S)	++
102	S	+
103	(S, R&S)	++
104	(S, S or R)	++
105	(S, S or R)	++
106	S	++
107	S	++
108	S	++
109	S	++
110	S	+
111	S	++
112	(R&S, S)	++
113	S	++
114	S	++
115	S	++
116	S	++
117	S	++
118	S	++
119	S	++
120	S	++
121	S	++
122	R	++
123	R	++
124	R	+
125	S	+
126	S	++
127	S	++
235	R	+
270	R	+
280	S	++

281	S	++
282	S	++
313	S	++
319	(R&S, S)	++
320	S	++
321	(R&S, S)	++
322	S	++

Legend for Table II, middle column:

“S” means the S enantiomer was tested with the result shown in the right-most column.

“R” means the R enantiomer was tested with the result shown in the right-most column.

“R&S” means the racemate was tested.

“S, S or R” means the compound has two chiral centers and can possibly have four diastereomers. The compound with S at the 1st chiral center and S or R at the 2nd chiral center was tested.

“R, R&S” means the compound has two chiral centers and can possibly have four diastereomers. The compound with R at the 1st chiral center and the racemate at the 2nd chiral center was tested.

“S, R&S” means the compound has two chiral centers and can possibly have four diastereomers. The compound with S at the 1st chiral center and the racemate at the 2nd chiral center was tested.

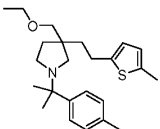
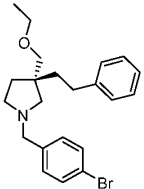
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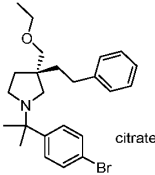
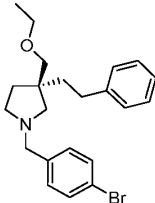
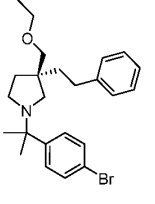
Right-most Column in Table II:

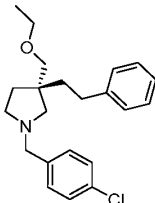
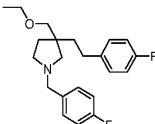
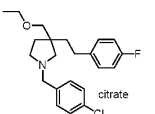
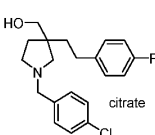
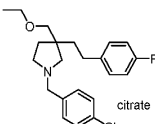
Shows results from an antinociception and warm-water tail-flick test, using male C57BL/6 mice (20-30 g; 6-12 wks), maintained on a 12-h light/dark cycle with rodent chow and water available ad libitum, and housed separately until testing. Antinociception was assessed using the 55°C warm-water tail-flick test. The latency to the first sign of a rapid tail flick was taken as the behavioral endpoint. Each mouse was first tested for baseline latency by immersing its tail in the water and recording

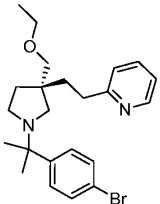
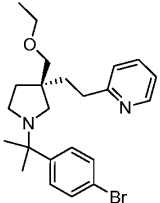
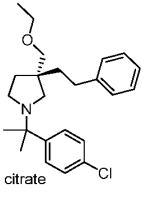
the time to response. Mice not responding within 2 secs were excluded from further testing. Responsive mice were then s.c. administered the test compound and tested for antinociception at 30 min, 60 min, 90 min, and 120 min time points afterward. Antinociception was calculated using the following formula: percentage of antinociception = $100 \times (\text{test latency} - \text{control latency}) / (20 - \text{control latency})$. To avoid tissue damage, a maximum score was assigned (100%) to animals that failed to respond within 20 secs.

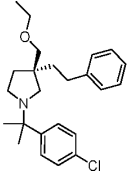
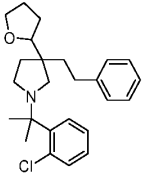
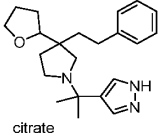
Table III: New Compounds with a pyrrolidine ring and a non- pyridine-like molecule bonded to the pyrrolidine N-constituent

Compound No.	Structure	Name	MS (ESI+): [M+H] ⁺	H-NMR
1		(R or S)-3-(ethoxymethyl)-3-(2-(5-methylthiophen-2-yl)ethyl)-1-(2-(p-tolyl)propan-2-yl)pyrrolidine	386	¹ H NMR (300 MHz, CDCl ₃): δ 7.39-7.28 (m, 2H), 7.03 (d, J = 8.0 Hz, 2H), 6.46 (s, 2H), 3.43-3.36 (m, 2H), 3.19 (q, J = 8.8 Hz, 2H), 2.62 (t, J = 8.4 Hz, 2H), 2.49 (dd, J = 11.1, 6.9 Hz, 2H), 2.39 (d, J = 9.0 Hz, 1H), 2.35 (s, 3H), 2.25 (d, J = 9.1 Hz, 1H), 1.78-1.67 (m, 2H), 1.47 (t, J = 6.8 Hz, 2H), 1.33 (t, J = 7.2 Hz, 3H), 1.28 (s, 6H), 1.09 (t, J = 7.2 Hz, 3H).
2		(S)-1-(4-bromobenzyl)-3-(ethoxymethyl)-3-phenethylpyrrolidine	402	¹ H NMR (300 MHz, MeOD): δ 7.53 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.30-7.21 (m, 2H), 7.19-7.10 (m, 3H), 3.86-3.77 (m, 2H), 3.51

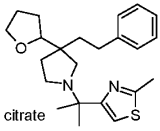
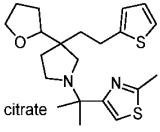
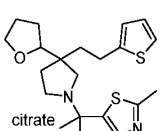
				(q, $J = 7.2$ Hz, 2H), 3.37 (s, 2H), 2.91-2.77 (m, 3H), 2.60-2.51 (m, 3H), 1.86-1.71 (m, 4H), 1.21 (t, $J = 6.9$ Hz, 3H).
3		(S)-1-(2-(4-bromophenyl)propan-2-yl)-3-(ethoxymethyl)-3-phenethylpyrrolidine citrate	430	^1H NMR (300 MHz, MeOD): δ 7.68-7.59 (m, 4H), 7.27-7.22 (m, 2H), 7.17-7.12 (m, 3H), 3.52 (q, $J = 8.4$ Hz, 2H), 3.42-3.39 (m, 3H), 3.25-3.14 (m, 2H), 2.97-2.88 (m, 1H), 2.85-2.69 (m, 4H), 2.55-2.49 (m, 2H), 2.04-1.81 (m, 2H), 1.78 (s, 6H), 1.18 (t, $J = 6.9$ Hz, 3H).
4		(R)-1-(4-bromobenzyl)-3-(ethoxymethyl)-3-phenethylpyrrolidine	402	^1H NMR (300 MHz, MeOD): δ 7.43 (d, $J = 8.1$ Hz, 2H), 7.33-7.25 (m, 2H), 7.22-7.14 (m, 5H), 3.52-3.43 (m, 4H), 3.35-3.25 (m, 2H), 2.62-2.57 (m, 5H), 2.28 (d, $J = 9.6$ Hz, 1H), 1.81-1.68 (m, 2H), 1.69-1.61 (m, 2H), 1.18 (t, $J = 6.9$ Hz, 3H).
5		(R)-1-(2-(4-bromophenyl)propan-2-yl)-3-(ethoxymethyl)-3-phenethylpyrrolidine	430	^1H NMR (300 MHz, MeOD): δ 7.41-7.36 (m, 4H), 7.28-7.22 (m, 2H), 7.18-7.11 (m, 3H), 3.48 (q, $J = 6.9$ Hz, 2H), 3.33-3.25 (m, 2H), 2.62-2.52 (m, 4H), 2.48 (d, $J = 9.0$ Hz, 1H), 2.31 (d, $J = 9.0$ Hz, 1H), 1.82-1.65 (m, 2H), 1.68-1.51 (m, 2H), 1.33 (s, 6H), 1.18 (t, $J = 6.9$ Hz, 3H).

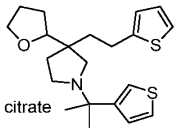
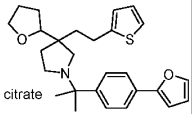
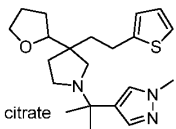
6		(S)-1-(4-chlorobenzyl)-3-(ethoxymethyl)-3-phenethylpyrrolidine	358	¹ H NMR (300 MHz, MeOD): δ 7.34-7.31 (m, 4H), 7.25-7.21 (m, 2H), 7.16-7.12 (m, 3H), 3.52 (s, 2H), 3.48 (q, J = 6.9 Hz, 2H), 3.33-3.30 (m, 2H), 2.65-2.59 (m, 3H), 2.58-2.51 (m, 2H), 2.33-2.30 (m, 1H), 1.78-1.64 (m, 4H), 1.18 (t, J = 6.9 Hz, 3H).
7		(R or S)-3-(ethoxymethyl)-1-(4-fluorobenzyl)-3-(4-fluorophenethyl)pyrrolidine		
8		(R or S)-1-(4-chlorobenzyl)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidine citrate	376	¹ H NMR (300 MHz, MeOD): δ 7.50 (s, 4H), 7.20 (t, J = 6.8 Hz, 2H), 6.98 (t, J = 8.6 Hz, 2H), 4.50-4.20 (m, 2H), 3.64-3.51 (m, 3H), 3.49-3.39 (m, 4H), 3.21-3.08 (m, 1H), 2.81 (q, J = 15.6 Hz, 4H), 2.65-2.51 (m, 2H), 2.17-1.96 (m, 2H), 1.92-1.74 (m, 2H), 1.21 (t, J = 6.9 Hz, 3H).
9		(R or S)-1-(4-chlorobenzyl)-3-(4-fluorophenethyl)pyrrolidine-3-ylmethanol citrate	348	¹ H NMR (300 MHz, MeOD): δ 7.50 (s, 4H), 7.21 (dd, J = 8.4, 5.4 Hz, 2H), 6.98 (t, J = 8.6 Hz, 2H), 4.86-4.68 (m, 2H), 4.44-4.23 (m, 2H), 3.60-3.53 (m, 2H), 2.92-2.72 (m, 6H), 2.59 (t, J = 8.4 Hz, 2H), 2.13-1.99 (m, 2H), 1.87-1.72 (m, 2H).
10		(S or R)-1-(4-chlorobenzyl)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidine citrate	376	¹ H NMR (300 MHz, MeOD): δ 7.50 (s, 4H), 7.20 (dd, J = 8.3, 5.4 Hz, 2H), 6.98 (t, J = 8.6 Hz, 2H), 4.36 (q, J = 12.9 Hz, 2H), 3.56 (dd, J = 7.2, 2.2 Hz, 2H),

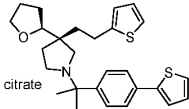
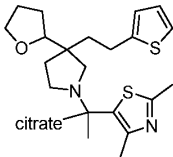
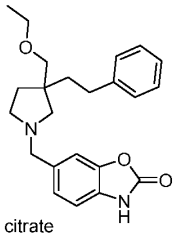
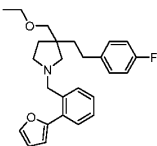
				3.45 (s, 2H), 3.35 (s, 3H), 3.14 (d, $J = 11.9$ Hz, 1H), 2.94-2.71 (m, 4H), 2.59 (s, 2H), 2.05 (s, 2H), 1.83 (q, $J = 8.5$ Hz, 2H), 1.22 (t, $J = 7.0$ Hz, 3H).
11		(S)-2-(2-(1-(2-(4-bromophenyl)propan-2-yl)-3-(ethoxymethyl)pyrrolidin-3-yl)ethyl)pyridine	431	^1H NMR (300 MHz, MeOD): δ 8.43 (d, $J = 4.2$ Hz, 1H), 7.79-7.73 (m, 1H), 7.68-7.59 (m, 4H), 7.31-7.24 (m, 2H), 3.45 (q, $J = 6.9$ Hz, 2H), 3.40-3.32 (m, 3H), 3.19-3.13 (m, 1H), 2.98-2.95 (m, 1H), 2.70 (t, $J = 8.1$ Hz, 2H), 2.03-1.95 (m, 1H), 1.83-1.74 (m, 10H), 1.14 (t, $J = 6.9$ Hz, 3H).
12		(R)-2-(2-(1-(2-(4-bromophenyl)propan-2-yl)-3-(ethoxymethyl)pyrrolidin-3-yl)ethyl)pyridine	431	^1H NMR (300 MHz, MeOD): δ 8.43 (d, $J = 4.2$ Hz, 1H), 7.79-7.73 (m, 1H), 7.68-7.60 (m, 4H), 7.31-7.24 (m, 2H), 3.45 (q, $J = 6.9$ Hz, 2H), 3.36-3.32 (m, 3H), 3.19-3.13 (m, 1H), 2.98-2.91 (m, 1H), 2.70 (t, $J = 8.1$ Hz, 2H), 2.03-1.95 (m, 1H), 1.83-1.74 (m, 10H), 1.14 (t, $J = 6.9$ Hz, 3H).
13		(S)-1-(2-(4-chlorophenyl)propan-2-yl)-3-(ethoxymethyl)-3-phenethylpyrrolidine citrate	386	^1H NMR (300 MHz, MeOD): δ 7.50 (d, $J = 2.1$ Hz, 2H), 7.28-7.20 (m, 4H), 7.13-7.10 (m, 3H), 3.49 (q, $J = 6.9$ Hz, 2H), 3.32-3.31 (m, 2H), 2.62-2.59 (m, 2H), 2.53-2.47 (m, 3H), 2.29 (d, $J = 9$ Hz, 1H), 1.69-1.60 (m, 4H), 1.38

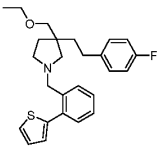
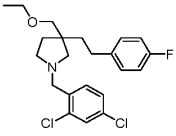
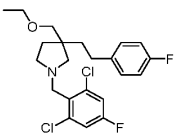
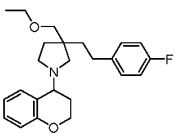
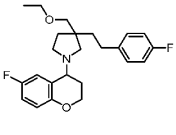
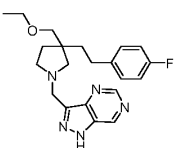
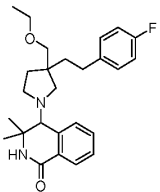
				(s, 6H), 1.14 (t, $J = 6.9$ Hz, 3H).
14		(R)-1-(2-(4-chlorophenyl)propan-2-yl)-3-(ethoxymethyl)-3-phenethylpyrrolidine	386	^1H NMR (300 MHz, MeOD): δ 7.65 (d, $J = 8.7$ Hz, 2H), 7.44 (d, $J = 8.7$ Hz, 2H), 7.23-7.21 (m, 2H), 7.15-7.13 (m, 3H), 3.49 (q, $J = 6.9$ Hz, 2H), 3.34-3.30 (m, 4H), 3.14-3.09 (m, 2H), 2.98 (d, $J = 10.5$ Hz, 1H), 2.75 (d, $J = 11.1$ Hz, 1H), 2.54 (t, $J = 8.4$ Hz, 2H), 1.90-1.74 (m, 2H), 1.68 (s, 6H), 1.17 (t, $J = 6.9$ Hz, 3H).
15		(S or R)-1-(2-(2-chlorophenyl)propan-2-yl)-3-phenethyl-3-((S&R)-tetrahydrofuran-2-yl)pyrrolidine	398	^1H NMR (300 MHz, MeOD): δ 7.72-7.68 (m, 1H), 7.68-7.58 (m, 1H), 7.49-7.47 (m, 2H), 7.27-7.16 (m, 5H), 4.01-3.96 (m, 2H), 3.80 (m, 1H), 3.45-3.34 (m, 3H), 3.08-3.04 (m, 1H), 2.80 (q, $J = 15.3$ Hz, 4H), 2.69-2.63 (m, 2H), 2.28 (t, $J = 8.4$ Hz, 2H), 2.02 (m, 3H), 2.00 (d, $J = 8.7$ Hz, 6H), 1.96-1.83 (m, 2H), 1.76-1.51 (m, 1H).
16		4-(2-((S or R)-3-phenethyl-3-((S&R)-tetrahydrofuran-2-yl)pyrrolidin-1-yl)propan-2-yl)-1H-pyrazole citrate	354	^1H NMR (300 MHz, MeOD): δ 7.98 (s, 1H), 7.93 (s, 1H), 7.25-7.03 (m, 5H), 3.93-3.85 (m, 2H), 3.59-3.49 (m, 3H), 3.16-3.10 (m, 2H), 2.80 (q, $J = 15.3$ Hz, 4H), 2.75 (m, 1H), 2.63-2.60 (m, 1H), 2.16-0.98 (m, 5H), 1.70 (s, 6H), 1.60 (m, 1H), 1.54-1.29 (m, 2H).

17		(S or R)-1-(2-(4-(furan-2-yl)phenyl)propan-2-yl)-3-phenethyl-3-((S&R)-tetrahydrofuran-2-yl)pyrrolidine	431	¹ H NMR (300 MHz, MeOD): δ 7.84-7.61 (m, 5H), 7.30-7.00 (m, 5H), 6.89 (d, <i>J</i> = 3.3 Hz, 1H), 6.56 (d, <i>J</i> = 4.5 Hz, 1H), 4.93 (br s, 1H), 3.45-3.31 (m, 2H), 2.80 (q, <i>J</i> = 15.3 Hz, 4H), 2.68-2.45 (m, 2H), 2.30-1.95 (m, 4H), 1.88 (s, 6H), 1.86-1.60 (m, 4H), 1.39-1.29 (m, 4H).
18		5-(2-((S or R)-3-phenethyl-3-((S&R)-tetrahydrofuran-2-yl)pyrrolidin-1-yl)propan-2-yl)-1-phenyl-1H-pyrazole citrate	431	¹ H NMR (300 MHz, MeOD): δ 7.62 (s, 1H), 7.61-7.47 (m, 5H), 7.28-7.14 (m, 5H), 6.60 (d, <i>J</i> = 5.1 Hz, 1H), 3.88-3.70 (m, 3H), 2.90-2.70 (m, 8H), 2.58-2.53 (t, <i>J</i> = 9.0 Hz, 2H), 1.93-1.84 (m, 4H), 1.71-1.57 (m, 3H), 1.49-1.46 (m, 7H).
19		2-methyl-5-(2-((S or R)-3-phenethyl-3-((S&R)-tetrahydrofuran-2-yl)pyrrolidin-1-yl)propan-2-yl)thiazole citrate	385	¹ H NMR (300 MHz, MeOD): δ 7.87 (d, <i>J</i> = 6.3 Hz, 1H), 7.27-7.12 (m, 5H), 3.89-3.81 (m, 1H), 3.49-3.41 (m, 2H), 3.40 (m, 3H), 3.30 (s, 1H), 3.32-3.10 (m, 1H), 2.80 (q, <i>J</i> = 15.3 Hz, 4H), 3.71 (s, 3H), 3.61-3.50 (m, 2H), 2.20-2.01 (m, 2H), 2.00-1.90 (m, 2H), 1.85-1.80 (m, 6H), 1.78-1.73 (m, 3H).
20		1-methyl-5-(2-((S or R)-3-phenethyl-3-((S&R)-tetrahydrofuran-2-yl)pyrrolidin-1-yl)propan-2-yl)-1H-pyrazole citrate	368	¹ H NMR (300 MHz, MeOD): δ 7.38 (s, 1H), 7.28-7.23 (m, 2H), 7.17-7.15 (m, 3H), 6.31 (m, 1H), 4.11 (s, 3H), 3.93-3.79 (m, 1H), 3.76-3.70 (m, 2H),

		citrate		2.91-2.75 (m, 4H), 2.71-2.58 (m, 6H), 2.00-1.75 (m, 8H), 1.63-1.62 (m, 6H).
21		2-methyl-4-(2-((S or R)-3-phenethyl-3- ((S&R)-tetrahydr ofuran-2-yl)pyrrol idin-1-yl)propan- 2-yl)thiazole citrate	385	¹ H NMR (300 MHz, MeOD): δ 7.61 (s, 1H), 7.29-7.24 (m, 2H), 7.19-7.14 (m, 3H), 4.04-3.81 (m, m, 2H), 3.66-3.39 (m, 3H), 3.26 (s, 3H), 3.03 (m, 1H), 2.43 (q, J = 15.6 Hz, 4H), 2.72-2.66 (m, 5H), 2.24-2.16 (m, 2H), 2.14-2.00 (m, 2H), 1.80 (s, 6H), 1.62-1.53 (m, 2H).
22		2-methyl-4-(2-((S or R)-3-((S&R)-tetra hydrofuran-2-yl)- 3-(2-(thiophen-2- yl)ethyl)pyrrolidi n-1-yl)propan-2-y l)thiazole citrate	391	¹ H NMR (300 MHz, MeOD): δ 7.61 (d, J = 5.1 Hz, 1H), 7.19 (dd, J = 2.4, 1.2 Hz, 1H), 6.90 (dd, J = 3.6, 1.5 Hz, 1H), 6.82 (s, 1H), 3.93-3.90 (m, 2H), 3.88-3.65 (m, 1H), 3.56-3.44 (m, 3H), 2.92-2.80 (m, 7H), 2.77-2.68 (m, 3H), 2.11-1.95 (m, 6H), 1.80-1.73 (m, 8H).
23		2-methyl-5-(2-((S or R)-3-((S&R)-tetra hydrofuran-2-yl)- 3-(2-(thiophen-2- yl)ethyl)pyrrolidi n-1-yl)propan-2-y l)thiazole citrate	391	¹ H NMR (300 MHz, MeOD): δ 7.81-7.76 (m, 1H), 7.17 (d, J = 4.8 Hz, 1H), 6.89(s, 1H), 6.80 (s, 1H), 3.89-3.81 (m, 1H), 3.70-3.57 (m, 2H), 3.22-3.19 (m, 2H), 3.09-3.05 (m, 1H), 2.87-2.77 (m, 6H), 2.71-2.68 (m, 3H), 2.03-1.87 (m, 6H), 1.82-1.73 (m, 8H), 1.72-1.56 (m, 1H).

24		(S or R)-3-((S&R)-tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)-1-(2-(thiophen-3-yl)propan-2-yl)pyrrolidine citrate	376	¹ H NMR (300 MHz, MeOD): δ 7.79-7.78 (m, 1H), 7.61-7.59 (m, 1H), 7.40-7.39 (m, 1H), 7.17 (d, <i>J</i> = 5.1 Hz, 1H), 6.90-6.87 (m, 1H), 6.80-6.78 (m, 1H), 3.89-3.84 (m, 2H), 3.78-3.55 (m, 2H), 3.78-3.55 (m, 1H), 3.42-3.31 (m, 3H), 3.24-3.06 (m, 1H), 2.78 (q, <i>J</i> = 15.3 Hz, 4H), 2.23-1.93 (m, 1H), 1.95-1.90 (m, 4H), 1.84 (s, 6H), 1.80-1.61 (m, 2H), 1.55-1.31 (m, 1H).
25		(S or R)-1-(2-(4-(furan-2-yl)phenyl)propan-2-yl)-3-((S&R)-tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidine citrate	436	¹ H NMR (300 MHz, MeOD): δ 7.84-7.81 (m, 2H), 7.76-7.70 (m, 2H), 7.61 (s, 1H), 7.11-7.01 (m, 1H), 6.89 (d, <i>J</i> = 3.3 Hz, 1H), 6.81-6.80 (m, 2H), 6.56-6.55 (m, 1H), 3.90-3.72 (m, 2H), 3.69-3.65 (m, 1H), 3.55-3.36 (m, 2H), 3.26-3.00 (m, 2H), 2.91-2.75 (m, 6H), 2.25-2.02 (m, 2H), 1.99-1.89 (m, 2H), 1.87 (s, 6H), 1.82-1.75 (m, 4H).
26		1-methyl-4-(2-((S or R)-3-((S&R)-tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)-1H-pyrazole citrate	374	¹ H NMR (300 MHz, MeOD): δ 7.97 (s, 1H), 7.74 (s, 1H), 7.19 (s, 1H), 6.91 (s, 1H), 6.91-6.75 (m, 1H), 3.99-3.88 (m, 5H), 3.75-3.35 (m, 5H), 3.12-3.03 (m, 1H), 2.84 (q, <i>J</i> = 15.3 Hz, 4H), 2.73-2.66 (m, 1H),

				2.22-2.16 (m, 6H), 1.96 (s, 6H), 1.77-1.30 (m, 2H).
27		(S or R)-3-((S&R)-tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)-1-(2-(4-(thiophen-2-yl)phenyl)propan-2-yl)pyrrolidine citrate	452	¹ H NMR (300 MHz, MeOD): δ 7.80-7.69 (m, 4H), 7.49-7.44 (m, 2H), 7.13-7.08 (m, 2H), 6.85-6.74 (m, 2H), 4.88-3.37 (m, 5H), 3.25-2.91 (m, 2H), 2.86-2.74 (m, 6H), 2.17-1.73 (m, 14H).
28		2,4-dimethyl-5-(2-((S or R)-3-((S&R)-tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidin-1-yl)propan-2-yl)thiazole citrate	405	¹ H NMR (300 MHz, MeOD): δ 7.17 (d, J = 4.8 Hz, 1H), 6.90 (br s, 1H), 6.81 (br s, 1H), 3.90-3.86 (m, 2H), 3.75-3.70 (m, 2H), 3.20-2.95 (m, 3H), 2.94-2.86 (m, 4H), 2.85-2.70 (m, 4H), 2.60-2.58 (m, 3H), 2.53-2.51 (m, 3H), 1.93-1.79 (m, 6H), 1.72-1.68 (m, 6H).
29		(R or S)-6-((3-(ethoxymethyl)-3-phenethylpyrrolidin-1-yl)methyl)benzo[d]oxazol-2(3H)-one citrate	381	¹ H NMR (300 MHz, MeOD): δ 7.40 (s, 1H), 7.32 (d, J = 8.1 Hz, 1H), 7.28-7.23 (m, 2H), 7.20-7.13 (m, 4H), 4.44-4.31 (q, J = 12.9 Hz, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.45-3.31 (m, 5H), 3.12 (m, 1H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.57 (m, 2H), 2.10-1.99 (m, 2H), 1.89-1.80 (m, 2H), 1.21 (t, J = 7.2 Hz, 3H).
30		(R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)-1-(2-(furan-2-yl)benzyl)pyrrolidine citrate		

		rolidine		
31		(R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)-1-(2-(thiophen-2-yl)benzyl)pyrrolidine		
32		(R or S)-1-(2,4-dichlorobenzyl)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidine		
33		(R or S)-1-(2,6-dichloro-4-fluorobenzyl)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidine		
34		(3R or S)-1-(chroman-4-yl)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidine		
35		(3R or S)-3-(ethoxymethyl)-1-(6-fluorochroman-4-yl)-3-(4-fluorophenethyl)pyrrolidine		
36		(R or S)-3-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)-1H-pyrazolo[4,3-d]pyrimidine		
37		4-((R or S)-3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-one		

38		(R or S)-3-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)pyridazine-4-carbonitrile		
39		(R or S)-3-((3-(ethoxymethyl)-3-(4-fluorophenethyl)pyrrolidin-1-yl)methyl)-4-(trifluoromethyl)pyridazine		
40		(R or S)-4-(2-(1-(bis(2-methylthiazol-4-yl)methyl)-3-(ethoxymethyl)pyrrolidin-3-yl)ethyl)benzonitrile		
41		(3R or S)-1-(1,1,1,3,3,3-hexafluoro-2-(p-tolyl)propan-2-yl)-3-(tetrahydrofuran-2-yl)-3-(2-(thiophen-2-yl)ethyl)pyrrolidine		

*Legend for 4th & 5th columns in Table III is same as for Table I.

Table IV: Chirality and *in vivo* testing of compound Nos. 1 to 25 of Table III

Compound	Configuration tested	ED ₅₀ (mg/kg) at 30 min on C57BL/6 mice in Warm-water Tail-flick Test (same as Table II)
1	S	++
2	S	+

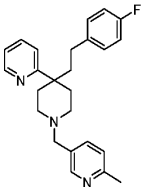
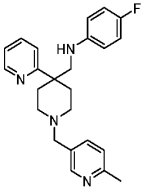
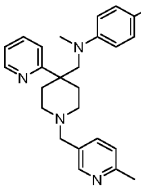
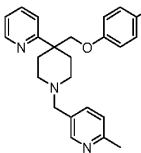
3	S	++
4	R	+
5	R	++
6	S	+
7	S	++
8	R	+
9	R	+
10	S	+
11	S	++
12	S	++
13	S	++
14	S	++
15	(S, S&R)	+
16	(S, S&R)	++
17	(S, S&R)	++
18	(S, S&R)	+
19	(S, S&R)	++
21	(S, S&R)	++
22	(S, S&R)	++
23	(S, S&R)	++
24	(S, S&R)	++
24	(S, S&R)	++
25	(S, S&R)	++
26	(S, S&R)	++
27	(S, S&R)	+
28	(S, S&R)	+
29	S	+

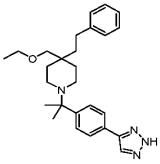
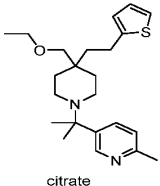
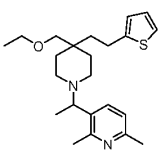
Legend for Table IV, middle column

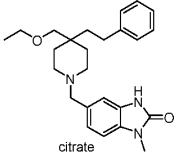
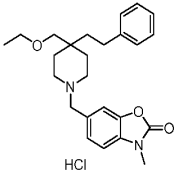
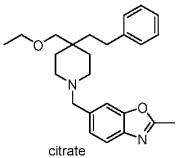
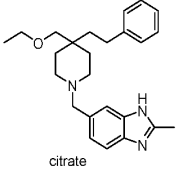
“S, S&R” means the compound has two chiral centers and can possibly have four diastereomers. The compound with S at the 1st chiral center and the racemate at the 2nd chiral center was tested.

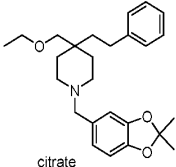
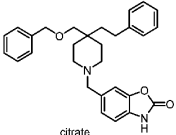
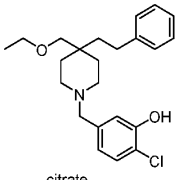
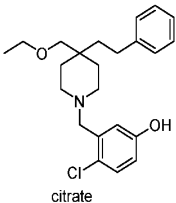
Table V: New Compounds with a pyridine ring and other groups bonded to the pyridine N-constituent

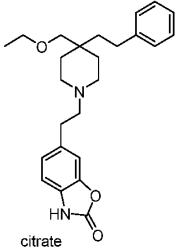
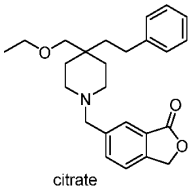
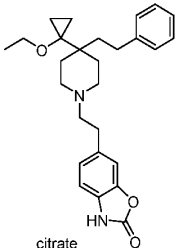
Compound	Structure	Name	MS (ESI+): [M+H] ⁺	H-NMR
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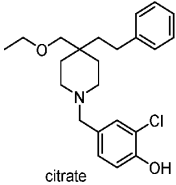
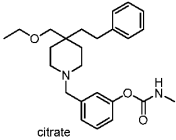
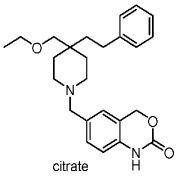
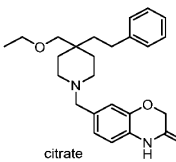
1		5-((4-(4-fluorophenyl)-4-(pyridin-2-yl)piperidin-1-yl)methyl)-2-methylpyridine	390	¹ H NMR (300 MHz, MeOD): δ 8.56 (d, J = 4.2 Hz, 1H), 8.31 (d, J = 1.5 Hz, 1H), 7.80 (td, J = 7.5, 1.5 Hz, 1H), 7.69 (dd, J = 8.1, 2.0 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.39-7.21 (m, 2H), 7.02-6.82 (m, 4H), 3.45 (s, 2H), 2.75-2.68 (m, 2H), 2.50 (s, 3H), 2.47-2.43 (m, 2H), 2.19-2.14 (m, 4H), 1.93-1.85 (m, 4H).
2		4-fluoro-N-((1-((6-methylpyridin-3-yl)methyl)-4-(pyridin-2-yl)piperidin-4-yl)methyl)aniline	391	¹ H NMR (300 MHz, MeOD): δ 8.55 (d, J = 3.6 Hz, 1H), 8.30 (d, J = 1.8 Hz, 1H), 7.72-7.65 (m, 2H), 7.48 (d, J = 7.8 Hz, 1H), 7.24-7.18 (m, 2H), 6.70 (t, J = 8.7 Hz, 2H), 6.40-6.30 (m, 2H), 3.43 (s, 2H), 3.29 (s, 2H), 2.72-2.66 (m, 2H), 2.49-2.47 (m, 5H), 1.88 (t, J = 8.4 Hz, 2H), 1.98-1.94 (m, 2H).
3		4-fluoro-N-methyl-N-((1-((6-methylpyridin-3-yl)methyl)-4-(pyridin-2-yl)piperidin-4-yl)methyl)aniline	405	¹ H NMR (300 MHz, MeOD): δ 8.55 (dd, J = 4.5, 0.9 Hz, 1H), 8.27 (d, J = 1.8 Hz, 1H), 7.65-7.60 (m, 2H), 7.40 (d, J = 8.1 Hz, 1H), 7.24-7.18 (m, 2H), 6.73-6.67 (m, 2H), 6.4-6.35 (m, 2H), 3.42 (s, 2H), 3.34 (s, 2H), 2.73 (d, J = 8.7 Hz, 2H), 2.62 (s, 3H), 2.60-2.56 (m, 2H), 2.48 (s, 3H), 2.02-1.87 (m, 4H).
4		5-((4-(4-fluorophenyl)-4-(pyridin-2-yl)piperidin-1-yl)methyl)-2-methylpyridine	392	¹ H NMR (300 MHz, MeOD): δ 8.52 (s, 1H), 8.32 (s, 1H), 7.80-7.75 (m, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.28-7.21 (m, 2H), 6.93-6.86 (m, 2H), 6.75-6.72

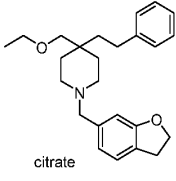
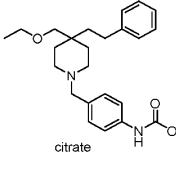
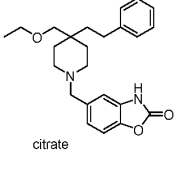
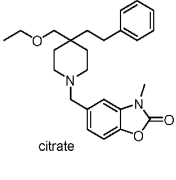
				(m, 2H), 4.00 (s, 2H), 3.45 (s, 2H), 2.72-2.68 (m, 2H), 2.57-2.46 (m, 5H), 2.28-2.20 (m, 2H), 2.18-2.03 (m, 2H).
5		1-(2-(4-(2H-1,2,3-triazol-4-yl)phenyl)propan-2-yl)-4-(ethoxymethyl)-4-phenethylpiperidine	433	¹ H NMR (300 MHz, MeOD): δ 8.26 (s, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.4 Hz, 2H), 7.24-7.20 (m, 2H), 7.15-7.12 (m, 3H), 3.48-3.42 (m, 4H), 3.28-3.22 (m, 2H), 2.54-2.48 (m, 2H), 1.90 (s, 6H), 1.84-1.70 (m, 4H), 1.67-1.55 (m, 2H), 1.35-1.28 (m, 2H), 1.19-1.17 (m, 3H).
6		5-(2-(4-(ethoxymethyl)-4-(2-(thiophen-2-yl)ethyl)piperidin-1-yl)propan-2-yl)-2-methylpyridine citrate	387	¹ H NMR (300 MHz, MeOD): δ 8.70 (s, 1H), 8.05-8.03 (m, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.16 (d, J = 5.1 Hz, 1H), 6.90-6.87 (m, 1H), 6.80-6.79 (m, 1H), 3.52-3.41 (m, 4H), 3.24-3.13 (m, 4H), 2.90-2.72 (m, 6H), 2.58 (s, 3H), 1.97-1.86 (m, 2H), 1.85 (s, 6H), 1.77-1.70 (m, 4H), 1.23 (t, J = 7.2 Hz, 3H).
7		3-(1-(4-(ethoxymethyl)-4-(2-(thiophen-2-yl)ethyl)piperidin-1-yl)ethyl)-2,6-dimethylpyridine	387	¹ H NMR (300 MHz, MeOD): δ 8.21 (s, 1H), 7.25 (s, 1H), 7.14 (dd, J = 5.1, 1.2 Hz, 1H), 6.88 (dd, J = 5.1, 2.4 Hz, 1H), 6.81-6.80 (m, 1H), 3.79 (br s, 2H), 3.53 (q, J = 6.9 Hz, 2H), 3.38 (s, 2H), 3.29-3.26 (m, 5H), 2.85-2.79 (m, 2H), 2.51 (s, 3H), 2.31 (s, 3H), 1.85-1.80 (m, 2H), 1.70-1.43 (m, 5H), 1.17 (t, J = 6.9 Hz, 3H).

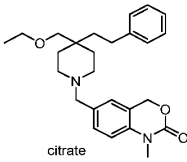
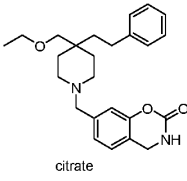
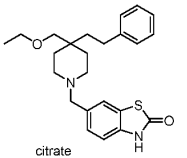
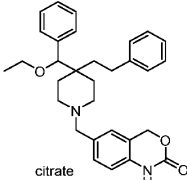
8		5-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-1-methyl-1,3-dihydro-2H-benzo[d]imidazol-2-one citrate	407	¹ H NMR (300 MHz, MeOD): δ 7.27-7.12 (m, 8H), 4.30 (s, 2H), 3.54 (q, $J = 7.2$ Hz, 2H), 3.32-3.30 (m, 5H), 3.21 (m, 4H), 2.79 (q, $J = 15.6$ Hz, 4H), 2.61-2.53 (m, 2H), 1.90-1.71 (m, 6H), 1.18 (t, $J = 7.2$ Hz, 3H).
9		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-3-methylbenzo[d]oxazol-2(3H)-one HCl	406	¹ H NMR (300 MHz, D ₂ O): δ 7.32-7.24 (m, 4H), 7.22-7.18 (m, 4H), 4.26-4.25 (m, 2H), 3.50-3.44 (m, 3H), 3.35 (s, 3H), 3.32-3.28 (m, 3H), 3.06-2.98 (m, 2H), 2.51-2.47 (m, 2H), 1.89-1.51 (m, 6H), 1.08 (t, $J = 7.2$ Hz, 3H).
10		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-2-methylbenzo[d]oxazole citrate	392	¹ H NMR (300 MHz, MeOD): δ 7.78 (s, 1H), 7.71 (d, $J = 8.1$ Hz, 1H), 7.49 (d, $J = 8.4$ Hz, 1H), 7.27-7.12 (m, 5H), 4.42 (s, 2H), 3.54 (q, $J = 7.2$ Hz, 2H), 3.47-3.45 (m, 2H), 3.22 (m, 4H), 2.79 (q, $J = 15.3$ Hz, 4H), 2.66 (s, 3H), 2.59-2.54 (m, 2H), 1.91-1.86 (m, 2H), 1.77-1.72 (m, 4H), 1.18 (t, $J = 7.2$ Hz, 3H).
11		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-2-methyl-1H-benzo[d]imidazole citrate	391	¹ H NMR (300 MHz, MeOD): δ 7.68 (s, 1H), 7.57 (d, $J = 8.1$ Hz, 1H), 7.32 (d, $J = 8.4$ Hz, 1H), 7.27-7.12 (m, 5H), 4.40 (s, 2H), 3.54 (q, $J = 7.2$ Hz, 2H), 3.40 (s, 2H), 3.26 (m, 4H), 2.78 (q, $J = 15.6$ Hz, 4H), 2.60 (s, 3H), 2.58-2.54 (m, 2H), 1.86-1.75 (m, 6H), 1.17 (t, $J =$

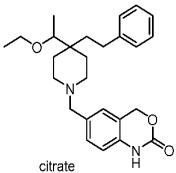
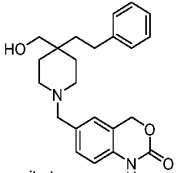
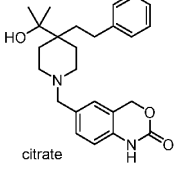
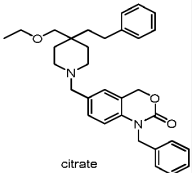
				7.2 Hz, 3H).
12		1-((2,2-dimethylbenzo[d][1,3]dioxol-5-yl)methyl)-4-(ethoxymethyl)-4-phenethylpiperidine citrate	409	¹ H NMR (300 MHz, MeOD): δ 7.28-7.15 (m, 5H), 6.93-6.90 (m, 2H), 6.81 (d, J = 7.8 Hz, 1H), 4.18 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.40 (m, 2H), 3.22 (m, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.54 (m, 2H), 1.87-1.71 (m, 6H), 1.66 (s, 6H), 1.18 (t, J = 7.2 Hz, 3H).
13		6-((4-((benzyloxy)methyl)-4-phenethylpiperidin-1-yl)methyl)benzo[d]oxazol-2(3H)-one citrate	459	¹ H NMR (300 MHz, MeOD): δ 7.37-7.30 (m, 5H), 7.28-7.22 (m, 4H), 7.17-7.12 (m, 4H), 4.52 (s, 2H), 4.27 (s, 2H), 3.54 (s, 2H), 3.17 (m, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.55-2.49 (m, 2H), 1.91-1.86 (m, 2H), 1.82-1.71 (m, 4H).
14		2-chloro-5-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)phenol citrate	388	¹ H NMR (300 MHz, MeOD): δ 7.33 (d, J = 8.7 Hz, 1H), 7.28-7.09 (m, 5H), 7.05 (s, 1H), 6.87 (d, J = 8.7 Hz, 1H), 4.33 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.42 (s, 2H), 3.34-3.29 (m, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.54 (m, 2H), 1.91-1.87 (m, 2H), 1.78-1.68 (m, 4H), 1.29 (t, J = 7.2 Hz, 3H).
15		4-chloro-3-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)phenol citrate	388	¹ H NMR (300 MHz, MeOD): δ 7.32-7.23 (m, 3H), 7.20-7.14 (m, 2H), 7.12-7.10 (m, 2H), 7.04 (d, J = 8.1 Hz, 1H), 4.44 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.42 (s, 2H), 3.34 (m, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.54 (m, 2H), 1.93-1.88

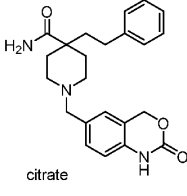
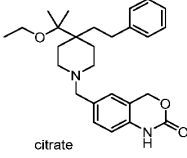
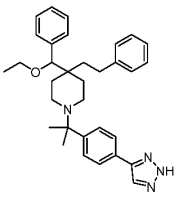
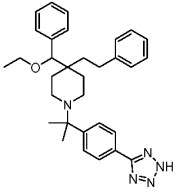
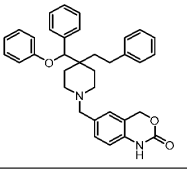
				(m, 2H), 1.79-1.69 (m, 4H), 1.21 (t, $J = 7.2$ Hz, 3H).
16		6-(2-(4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)ethyl)benzo[d]oxazol-2(3H)-one citrate	409	^1H NMR (300 MHz, MeOD): δ 7.40-7.19 (m, 4H), 7.15-7.10 (m, 2H), 7.05 (d, $J = 7.8$ Hz, 2H), 3.67-3.34 (q, $J = 7.2$ Hz, 2H), 3.31-3.30 (m, 4H), 3.18-3.00 (m, 4H), 3.11-3.00 (m, 2H), 2.78 (q, $J = 15.6$ Hz, 4H), 2.61-2.56 (m, 2H), 1.92-1.55 (m, 6H), 1.22 (t, $J = 6.9$ Hz, 3H).
17		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)isobenzofuran-1(3H)-one citrate	394	^1H NMR (300 MHz, MeOD): δ 8.02 (s, 1H), 7.90 (d, $J = 7.2$ Hz, 1H), 7.73 (d, $J = 7.2$ Hz, 1H), 7.29-7.12 (m, 5H), 5.43 (s, 2H), 4.37 (s, 2H), 3.54 (q, $J = 7.2$ Hz, 2H), 3.40 (s, 2H), 3.18 (m, 4H), 2.78 (q, $J = 15.6$ Hz, 4H), 2.59-2.54 (m, 2H), 1.89-1.84 (m, 2H), 1.75-1.69 (m, 4H), 1.29 (t, $J = 6.9$ Hz, 3H).
18		6-(2-(4-(1-ethoxycyclopropyl)-4-phenethylpiperidin-1-yl)ethyl)benzo[d]oxazol-2(3H)-one citrate	435	^1H NMR (300 MHz, MeOD): δ 7.26-7.20 (m, 4H), 7.16-7.10 (m, 3H), 7.04 (d, $J = 7.8$ Hz, 1H), 3.54 (q, $J = 7.2$ Hz, 2H), 3.44 (m, 2H), 3.31-3.21 (m, 2H), 3.23-3.08 (m, 4H), 2.86-2.71 (m, 6H), 2.05-2.00 (m, 2H), 1.87 (d, $J = 14.4$ Hz, 2H), 1.67-1.59 (m, 2H), 1.14 (t, $J = 6.9$ Hz, 3H), 0.89 (m, 2H), 0.74 (m, 2H).

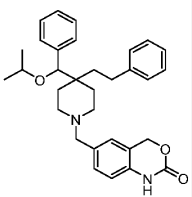
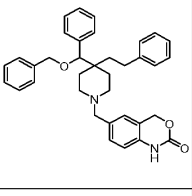
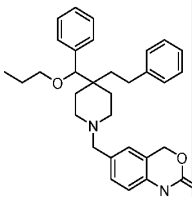
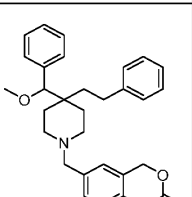
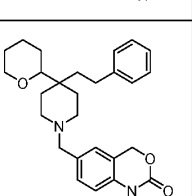
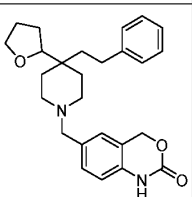
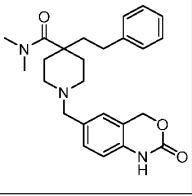
19		2-chloro-4-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)phenol citrate	388	¹ H NMR (300 MHz, MeOD): δ 7.49 (s, 1H), 7.28-7.23 (m, 3H), 7.20-7.12 (m, 3H), 6.98 (d, J = 8.4 Hz, 1H), 4.18 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.39 (m, 2H), 3.20 (m, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.64-2.53 (m, 2H), 1.85-1.71 (m, 6H), 1.19 (t, J = 7.2 Hz, 3H).
20		3-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)phenyl methylcarbamate citrate	410	¹ H NMR (300 MHz, MeOD): δ 7.49 (t, J = 7.6 Hz, 1H), 7.34-7.12 (m, 8H), 4.28 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.40 (s, 2H), 3.23 (br s, 4H), 2.80-2.71 (m, 7H), 2.60-2.54 (m, 2H), 1.86-1.75 (m, 6H), 1.20 (t, J = 6.9 Hz, 3H).
21		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	408	¹ H NMR (300 MHz, MeOD): δ 7.40 (d, J = 8.1 Hz, 1H), 7.34 (s, 1H), 7.28-7.12 (m, 5H), 6.96 (d, J = 7.8 Hz, 1H), 5.35 (s, 2H), 4.22 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.39 (br s, 2H), 3.20 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.54 (m, 2H), 1.90-1.59 (m, 6H), 1.20 (t, J = 6.9 Hz, 3H).
22		7-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-2H-benzo[b][1,4]oxazin-3(4H)-one citrate	408	¹ H NMR (300 MHz, MeOD): δ 7.28-7.07 (m, 7H), 6.97 (d, J = 8.1 Hz, 1H), 4.61 (s, 2H), 4.19 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.40 (br s, 2H), 3.20 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.54 (m, 2H), 1.85-1.62 (m, 6H), 1.19 (t, J = 7.2 Hz, 3H).

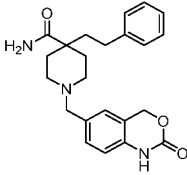
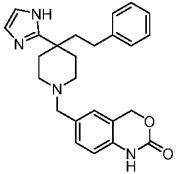
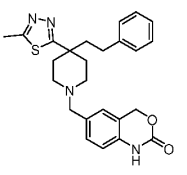
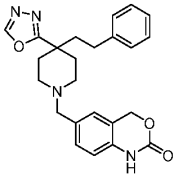
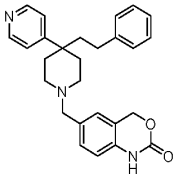
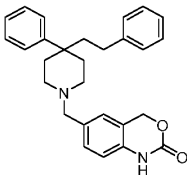
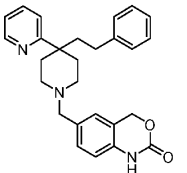
23		1-((2,3-dihydrobenzofuran-6-yl)methyl)-4-(ethoxymethyl)-4-phenethylpiperidine citrate	379	¹ H NMR (300 MHz, MeOD): δ 7.31-7.23 (m, 3H), 7.20-7.12 (m, 3H), 6.94 (d, J = 6.6 Hz, 1H), 6.87 (s, 1H), 4.58 (t, J = 8.7 Hz, 2H), 4.20 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.34 (br s, 2H), 3.29-3.20 (m, 6H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.54 (m, 2H), 1.86-1.74 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H).
24		methyl (4-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)phenyl)carbamate citrate	410	¹ H NMR (300 MHz, MeOD): δ 7.56 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.28-7.12 (m, 5H), 4.23 (s, 2H), 3.74 (s, 3H), 3.57 (q, J = 7.2 Hz, 2H), 3.39 (br s, 2H), 3.22 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.54 (m, 2H), 1.86-1.74 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H).
25		5-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)benzo[d]oxazol-2(3H)-one citrate	394	¹ H NMR (300 MHz, MeOD): δ 7.39-7.23 (m, 5H), 7.22-7.12 (m, 3H), 4.19 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.47 (br s, 2H), 3.21 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.54 (m, 2H), 1.85-1.75 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H).
26		5-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-3-methylbenzo[d]oxazol-2(3H)-one citrate	408	¹ H NMR (300 MHz, MeOD): δ 7.35-7.29 (m, 2H), 7.25-7.12 (m, 6H), 4.32 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.43-3.20 (m, 5H), 3.22 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.54 (m, 2H), 1.91-1.65 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H).

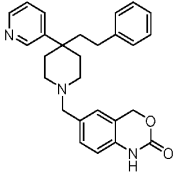
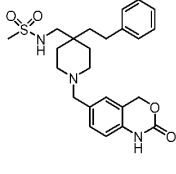
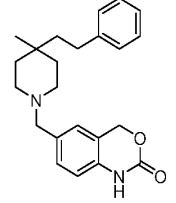
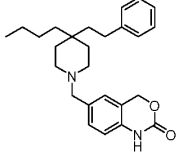
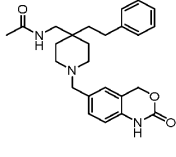
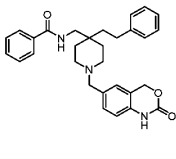
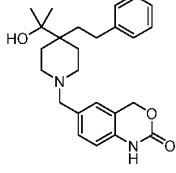
27		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-1-methyl-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	422	¹ H NMR (300 MHz, MeOD): δ 7.52 (d, J = 8.4 Hz, 1H), 7.39 (s, 1H), 7.28-7.12 (m, 6H), 5.28 (s, 2H), 4.31 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.40-3.34 (m, 5H), 3.20 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.54 (m, 2H), 1.90-1.71 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H)
28		7-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-3,4-dihydro-2H-benzo[e][1,3]oxazin-2-one citrate	408	¹ H NMR (300 MHz, MeOD): δ 7.33-7.12 (m, 8H), 4.51 (s, 2H), 4.22 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.39 (s, 2H), 3.16 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.54 (m, 2H), 1.89-1.70 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H).
29		6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)benzo[d]thiazol-2(3H)-one citrate	410	¹ H NMR (300 MHz, MeOD): δ 7.64 (s, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.28-7.12 (m, 6H), 4.28 (s, 2H), 3.53 (q, J = 7.2 Hz, 2H), 3.40 (br s, 2H), 3.22 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.59-2.21 (m, 2H), 1.90-1.71 (m, 6H), 1.19 (t, J = 6.9 Hz, 3H).
30		6-((4-(ethoxy(phenyl)methyl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	484	¹ H NMR (300 MHz, MeOD): δ 7.38-7.30 (m, 7H), 7.25-7.20 (m, 2H), 7.17-7.13 (m, 3H), 6.94 (d, J = 8.1 Hz, 1H), 5.33 (s, 2H), 4.37 (s, 1H), 4.21 (s, 2H), 3.41-3.36 (m, 2H), 3.30-3.26 (m, 2H), 3.10-3.08 (m, 2H), 2.78 (q, J = 15.6 Hz, 4H), 2.67-2.61 (m, 2H), 2.04-1.61 (m, 6H), 1.67 (t, J =

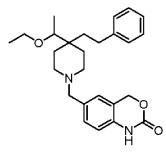
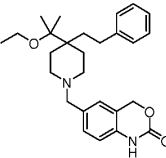
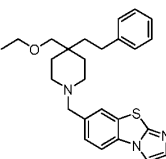
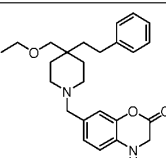
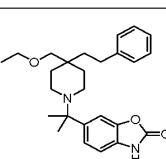
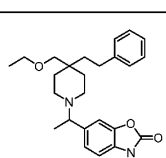
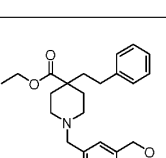
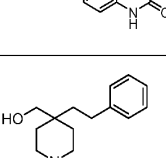
				6.9 Hz, 3H).
31		6-((4-(1-ethoxyethyl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	422	¹ H NMR (300 MHz, MeOD): δ 7.41 (d, J = 8.4 Hz, 1H), 7.36 (s, 1H), 7.29-7.13 (m, 5H), 6.96 (d, J = 8.1 Hz, 1H), 5.35 (s, 2H), 4.23 (s, 2H), 3.71-3.66 (m, 1H), 3.42-3.34 (m, 4H), 3.12 (br s, 2H), 2.78 (q, J = 15.6 Hz, 4H), 2.71-2.50 (m, 2H), 2.03-1.82 (m, 3H), 1.72-1.62 (m, 3H), 1.17-1.13 (m, 6H).
32		6-((4-(hydroxymethyl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	380	¹ H NMR (300 MHz, MeOD): δ 7.41 (d, J = 8.7 Hz, 1H), 7.36 (s, 1H), 7.28-7.11 (m, 5H), 6.96 (d, J = 7.8 Hz, 1H), 5.35 (s, 2H), 4.24 (s, 2H), 3.53 (s, 2H), 3.11 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H), 2.60-2.54 (m, 2H), 1.84-1.73 (m, 6H).
33		6-((4-(2-hydroxypropan-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	408	¹ H NMR (300 MHz, MeOD): δ 7.42 (d, J = 8.1 Hz, 1H), 7.37 (s, 1H), 7.29-7.13 (m, 5H), 6.96 (d, J = 8.1 Hz, 1H), 5.35 (s, 2H), 4.25 (s, 2H), 3.39 (s, 2H), 3.05 (q, J = 12.9 Hz, 2H), 2.85-2.68 (m, 6H), 2.08 (t, J = 11.7 Hz, 2H), 1.79-1.75 (m, 4H), 1.27 (s, 6H).
34		1-benzyl-6-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	498	¹ H NMR (300 MHz, MeOD): δ 7.39-7.32 (m, 2H), 7.30-7.22 (m, 4H), 7.18-7.11 (m, 6H), 7.00 (d, J = 8.4 Hz, 1H), 5.38 (s, 2H), 5.19 (s, 2H), 4.19 (s, 2H), 3.54 (q, J = 7.2 Hz, 2H), 3.45 (s, 2H), 3.16 (br s, 4H), 2.78 (q, J = 15.6 Hz, 4H).

				2.57-2.52 (m, 2H), 1.87-1.68 (m, 6H), 1.17 (t, $J = 6.9$ Hz, 3H).
35		1-((2-oxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)methyl)-4-phenethylpiperidine-4-carboxamide citrate	393	^1H NMR (300 MHz, MeOD): δ 7.42 (d, $J = 8.1$ Hz, 1H), 7.33 (s, 1H), 7.28-7.15 (m, 5H), 6.98 (d, $J = 7.8$ Hz, 1H), 5.35 (s, 2H), 4.28 (s, 2H), 3.41-3.10 (m, 2H), 3.07-3.06 (m, 2H), 2.80 (q, $J = 15.6$ Hz, 4H), 2.58-2.45 (m, 4H), 1.82-1.68 (m, 4H).
36		6-((4-(2-ethoxypropan-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one citrate	436	^1H NMR (300 MHz, MeOD): δ 7.42 (d, $J = 7.8$ Hz, 1H), 7.35 (s, 1H), 7.29-7.13 (m, 5H), 6.98 (d, $J = 7.5$ Hz, 1H), 5.35 (s, 2H), 4.27 (s, 2H), 3.54-3.42 (m, 4H), 3.11 (br s, 2H), 2.89-2.73 (m, 6H), 2.09 (m, 2H), 1.84-1.79 (m, 4H), 1.22 (s, 6H), 1.15 (t, $J = 7.2$ Hz, 3H).
37		1-(2-(4-(2H-1,2,3-triazol-4-yl)phenyl)propan-2-yl)-4-(ethoxy(phenyl)methyl)-4-phenethylpiperidine		
38		1-(2-(4-(2H-tetrazol-5-yl)phenyl)propan-2-yl)-4-(ethoxy(phenyl)methyl)-4-phenethylpiperidine		
39		6-((4-phenethyl-4-(phenoxymethyl)piperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		

40		6-((4-(isopropoxy(p henyl)methyl)-4-phe nethylpiperidin-1-yl) methyl)-1H-benzo[d][1,3]oxazin-2(4H)- one		
41		6-((4-((benzyloxy)(p henyl)methyl)-4-phe nethylpiperidin-1-yl) methyl)-1H-benzo[d][1,3]oxazin-2(4H)- one		
42		6-((4-phenethyl-4-(p henyl(propoxy)meth yl)piperidin-1-yl)me thyl)-1H-benzo[d][1, 3]oxazin-2(4H)-one		
43		6-((4-(methoxy(phen yl)methyl)-4-phenet hylpiperidin-1-yl)me thyl)-1H-benzo[d][1, 3]oxazin-2(4H)-one		
44		6-((4-phenethyl-4-(t etrahydro-2H-pyran- 2-yl)piperidin-1-yl) methyl)-1H-benzo[d][1,3]oxazin-2(4H)- one		
45		6-((4-phenethyl-4-(t etrahydrofuran-2-yl) piperidin-1-yl)methy l)-1H-benzo[d][1,3] oxazin-2(4H)-one		
46		N,N-dimethyl-1-((2- oxo-2,4-dihydro-1H- benzo[d][1,3]oxazin -6-yl)methyl)-4-phe nethylpiperidine-4-c arboxamide		

47		1-((2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)methyl)-4-phenethylpiperidine-4-carboxamide		
48		6-((4-(1H-imidazol-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
49		6-((4-(5-methyl-1,3,4-thiadiazol-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
50		6-((4-(1,3,4-oxadiazol-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
51		6-((4-phenethyl-4-(pyridin-4-yl)piperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
52		6-((4-phenethyl-4-phenylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
53		6-((4-phenethyl-4-(pyridin-2-yl)piperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		

54		6-((4-phenethyl-4-(pyridin-3-yl)piperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
55		N-((1-((2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)methyl)-4-phenethylpiperidin-4-yl)methyl)methanesulfonamide		
56		6-((4-methyl-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
57		6-((4-butyl-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
58		N-((1-((2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)methyl)-4-phenethylpiperidin-4-yl)methyl)acetamide		
59		N-((1-((2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)methyl)-4-phenethylpiperidin-4-yl)methyl)benzamide		
60		6-((4-(2-hydroxypropan-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		

61		6-((4-(1-ethoxyethyl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
62		6-((4-(2-ethoxypropan-2-yl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		
63		7-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)benzo[d]imidazo[2,1-b]thiazole		
64		7-((4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)methyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one		
65		6-(2-(4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)propan-2-yl)benzo[d]oxazol-2(3H)-one		
66		6-(1-(4-(ethoxymethyl)-4-phenethylpiperidin-1-yl)ethyl)benzo[d]oxazol-2(3H)-one		
67		ethyl 1-((2-oxo-2,4-dihydro-1H-benzo[d][1,3]oxazin-6-yl)methyl)-4-phenethylpiperidine-4-carboxylate		
68		6-((4-(hydroxymethyl)-4-phenethylpiperidin-1-yl)methyl)-1H-benzo[d][1,3]oxazin-2(4H)-one		

*Legend for 4th & 5th columns in Table V is same as for Table I.

Table VI: *in vivo* testing of compound Nos. 1 to 36 of Table V

Compound No.	ED50 (mg/kg) at 30 min on C57BL/6 mice in Warm-water Tail-flick Test (same conditions as Table II)
1	+
2	+
3	++
4	++
5	++
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	+
36	+

The specific methods, processes, compounds and compositions described herein are representative of preferred and other embodiments, and are exemplary and not intended as limitations on the scope of the invention. Other objects, aspects, and embodiments will occur to those skilled in the art upon consideration of this specification, and are encompassed within the spirit of the invention as defined by the scope of the claims. It will be readily apparent to one skilled in the art that various substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. The invention illustratively described herein suitably may be practiced in the absence of any element or elements, or limitation or limitations, which is not specifically disclosed herein as essential. Thus, for example, in each instance herein, in embodiments or examples of the present invention, any of the terms "comprising", "including", "containing", "having" etc. are to be read expansively and without limitation. The methods and processes illustratively described herein suitably may be practiced in differing orders of steps, and that they are not necessarily restricted to the orders of steps indicated herein or in the claims. It is also noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference, and the plural include singular forms, unless the context clearly dictates otherwise. Under no circumstances may the patent be interpreted to be limited to the specific examples or embodiments or methods specifically disclosed herein. Under no circumstances may the patent be interpreted to be limited by any statement made by any Examiner or any other official or employee of the Patent and Trademark Office unless such statement is specifically and without qualification or reservation expressly adopted in a responsive writing by Applicants.

The invention has been described broadly and generically herein. Each of the narrower species and subgeneric groupings falling within the generic disclosure also

form part of the invention. The terms and expressions that have been employed are used as terms of description and not of limitation, and there is no intent in the use of such terms and expressions to exclude any equivalent of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention as claimed. Thus, it will be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.