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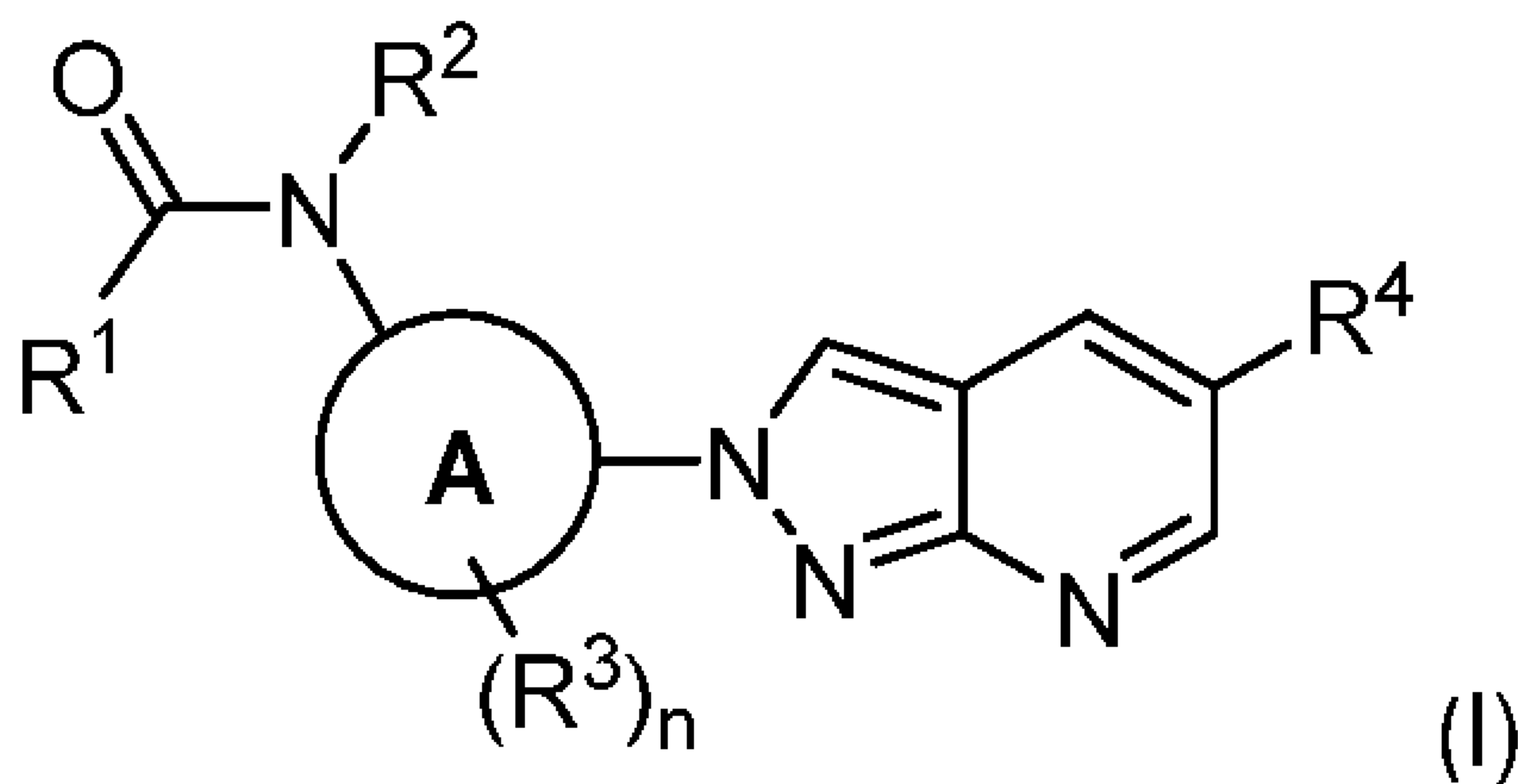
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(54) Title: 5,6-FUSED-BICYCLIC COMPOUNDS AND COMPOSITIONS FOR THE TREATMENT OF PARASITIC DISEASES



(57) **Abrégé/Abstract:**

The present invention provides a compound of Formula (I) or a pharmaceutically acceptable salt thereof; (I) a method for manufacturing the compounds of the invention, and its therapeutic uses. The present invention further provides a combination of pharmacologically active agents and a pharmaceutical composition.

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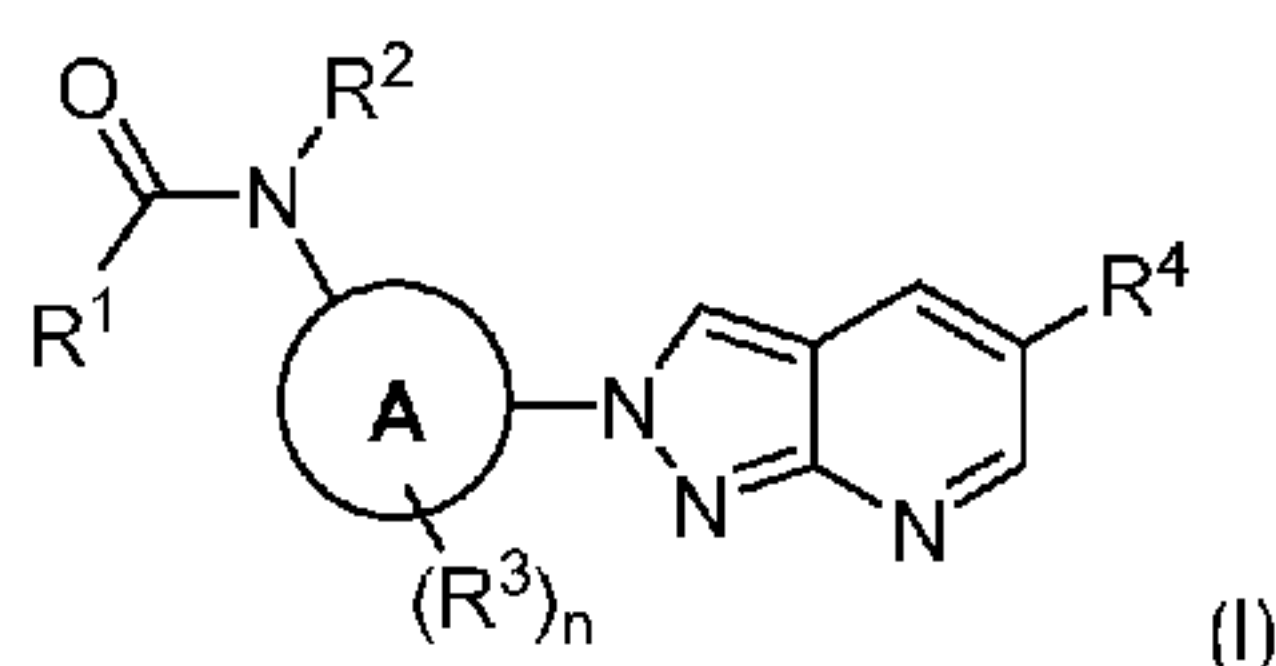
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(54) Title: 5,6-FUSED-BICYCLIC COMPOUNDS AND COMPOSITIONS FOR THE TREATMENT OF PARASITIC DISEASES



(57) Abstract: The present invention provides a compound of Formula (I) or a pharmaceutically acceptable salt thereof; (I) a method for manufacturing the compounds of the invention, and its therapeutic uses. The present invention further provides a combination of pharmacologically active agents and a pharmaceutical composition.

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5,6-FUSED-BICYCLIC COMPOUNDS AND COMPOSITIONS FOR THE TREATMENT OF PARASITIC DISEASES

CROSS-REFERENCE TO RELATED APPLICATIONS

The application claims the benefit of U.S. provisional application serial no. 62/513,211 filed
5 31 May 2017, and U.S. provisional serial no. 62/581,919 filed 6 November 2017; each of which
is incorporated by reference herein in its entirety.

FIELD OF THE INVENTION

The present invention relates to compounds having antiparasitic activity against
kinatoplastid protozoa.

10 BACKGROUND OF THE INVENTION

Leishmaniasis is a disease caused by protozoan parasites that belong to the genus
Leishmania and is transmitted by the bite of certain species of sand fly. There are four main
forms of Leishmaniasis. Cutaneous leishmaniasis is the most common form of leishmaniasis.
Visceral leishmaniasis, the most serious form in which the parasites migrate to the vital organs,
15 is caused by the parasite *Leishmania donovani*, and is potentially fatal if untreated. It affects as
many as 12 million people worldwide, with 1.5–2 million new cases each year. The visceral
form of leishmaniasis has an estimated incidence of 500,000 new cases and 60,000 deaths
each year.

The two main therapies for visceral leishmaniasis are the antimony derivatives sodium
20 stibogluconate (Pentostam®) and meglumine antimoniate (Glucantim®). Sodium
stibogluconate has been used for about 70 years and resistance to this drug is a growing
problem. In addition, the treatment is relatively long and painful, and can cause undesirable
side effects. Amphotericin (AmBisome®) is now the treatment of choice. Miltefosine
(Impavido®) and paromomycin are the other treatment alternatives.

25 Amphotericin (AmBisome) is expensive and has to be given intravenously. Paromomycin
requires intramuscular injections for 3 weeks; compliance is a major issue. Miltefosine is an oral
drug and has shown to be more effective and better tolerated than other drugs. However, there
are problems associated with the use of miltefosine that arise from its teratogenicity and
pharmacokinetics. Miltefosine was shown to be much slower eliminated from the body and was
30 still detectable five months after the end of treatment. The presence of subtherapeutic
miltefosine concentrations in the blood beyond five months after treatment might contribute to
the selection of resistant parasites; moreover, the measures for preventing the teratogenic risks
of miltefosine must be reconsidered. Currently, no vaccines are in routine use.

Chagas disease, also called American trypanosomiasis, is a tropical parasitic disease
35 caused by the flagellate protozoan *Trypanosoma cruzi*. *T. cruzi* is commonly transmitted to
humans and other mammals by the blood-sucking "kissing bugs" of the subfamily Triatominae
(family Reduviidae). Each year, an estimated 10 to 15 million people across the world are

infected with Chagas disease, most of whom do not know they are infected. Every year, 14,000 people die as a consequence of the disease. In Central and South America, Chagas kills more people than any other parasite-borne disease, including malaria. The CDC estimates that more than 300,000 persons with *Trypanosoma cruzi* infection live in the United States.

5 The symptoms of Chagas disease vary over the course of an infection. In the early, acute stage, symptoms are mild and usually produce no more than local swelling at the site of infection. The initial acute phase is responsive to antiparasitic treatments, with 60-90% cure rates. After 4-8 weeks, individuals with active infections enter the chronic phase of Chagas disease that is asymptomatic for 60-80% of chronically infected individuals through their lifetime.
10 However, the remaining 20-40% of infected people will develop debilitating and sometimes life-threatening medical problems over the course of their lives.

Treatment for Chagas disease focuses on killing the parasite and managing signs and symptoms. During the acute phase of Chagas disease, the drugs currently available for treatment are benznidazole and nifurtimox. Once Chagas disease reaches the chronic phase,
15 medications are not effective for curing the disease. Instead, treatment depends on the specific signs and symptoms. However, problems with these current therapies include their diverse side effects, the length of treatment, and the requirement for medical supervision during treatment. Resistance to the two frontline drugs has already occurred. The antifungal agent Amphotericin b has been proposed as a second-line drug, but is costly and relatively toxic. There is no vaccine
20 against Chagas disease.

Human African trypanosomiasis (HAT), also known as African sleeping sickness, is a vector-borne parasitic disease caused by the protozoa *Trypanosoma brucei*. There are two subspecies that infect humans, *T.b. gambiense* and *T.b. rhodesiense*, with the former accounting for over 95% of reported cases and the latter accounting for the remaining reported
25 cases. The parasites are transmitted to humans by tsetse fly (*Glossina* genus) bites, which have acquired their infection from human beings or from animals harboring the human pathogenic parasites. About 48,000 people died of sleeping sickness in 2008. Public health efforts in prevention and the eradication of the tsetse fly population have been successful in controlling the spread of the disease; under 10,000 new cases were reported in 2009 according to WHO
30 figures, which represents a huge decrease from the estimated 300,000 new cases in 1998.

African trypanosomiasis symptoms occur in two stages. In the first stage, known as the haemolymphatic phase, the trypanosomes multiply in subcutaneous tissues, blood and lymph. The haemolymphatic phase is characterized by bouts of fever, headaches, joint pains and itching. In the second stage, the neurological phase, the parasites cross the blood-brain barrier
35 to infect the central nervous system. It is in this stage when more obvious signs and symptoms of the disease appear (e.g., changes of behavior, confusion, sensory disturbances and poor coordination). Disturbance of the sleep cycle, which gives the disease its name, is an important

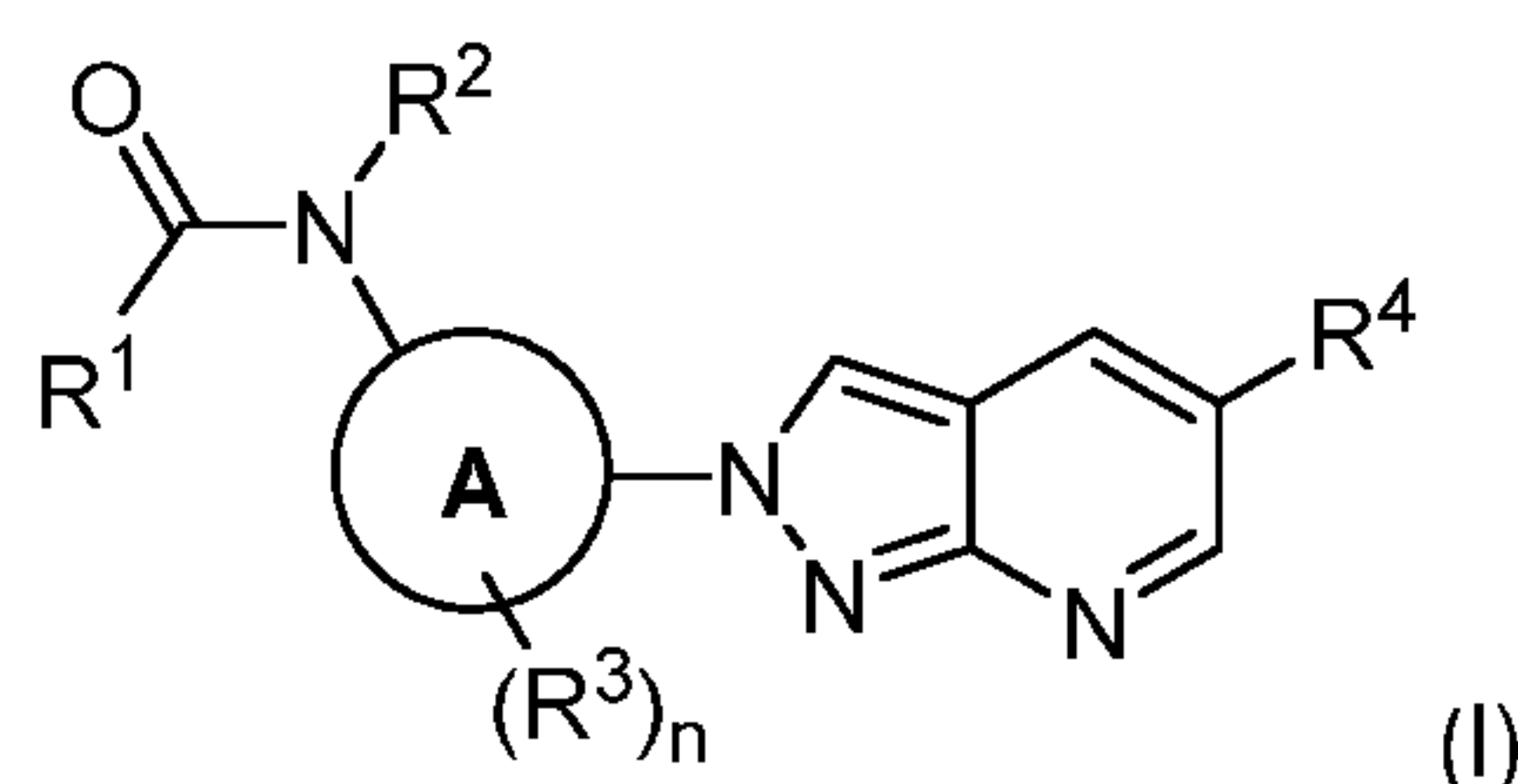
feature of the second stage of the disease. Without treatment, the disease is invariably fatal, with progressive mental deterioration leading to coma, systemic organ failure, and death.

Four drugs are registered for the treatment of sleeping sickness. The protocol depends on the stage of the disease. The current standard treatment for first-stage disease is intravenous or intramuscular pentamidine (for *T.b. gambiense*), or intravenous suramin (for *T.b. rhodesiense*). The current standard treatment for second-stage disease is intravenous melarsoprol, or intravenous melarsoprol in combination with oral nifurtimox, intravenous eflornithine only or eflornithine in combination with nifurtimox. All of the drugs have undesirable or potentially serious side effects. For example, 3-10% of patients those injected with melarsoprol (Arsobal®), developed reactive encephalopathy (convulsions, progressive coma, or psychotic reactions), and 10-70% of such cases result in death.

Thus, there remains a need for new and better treatments and therapies for leishmaniasis, Chagas disease and HAT.

SUMMARY OF THE INVENTION

Within certain aspects, provided herein is a compound of Formula (I) or subformulae thereof:



or a pharmaceutically acceptable salt, or stereoisomer thereof; wherein

Ring A is phenyl or pyridinyl;

R¹ is selected from:

(a) C₁₋₆alkyl that is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen and C₃₋₆cycloalkyl; and said C₃₋₆cycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl;

(b) C₁₋₄alkoxy that is unsubstituted or substituted by C₁₋₄haloalkyl;

(c) -NR^{5a}R^{5b} wherein R^{5a} and R^{5b} are independently hydrogen, C₁₋₄alkyl or C₁₋₄haloalkyl; or R^{5a} and R^{5b} together with the nitrogen atom to which both are attached form a 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O and S as ring atoms;

wherein the 4 to 7-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, C₁₋₄alkyl, and C₁₋₄alkoxy; or two substituents on the same or different ring atoms of the 4- to 7-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused Ring B attached to the 4- to 7-membered heterocycloalkyl;

wherein Ring B is C₃₋₆cycloalkyl or a 3- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms;

(d) monocyclic C₃₋₆cycloalkyl, C₃₋₆ cycloalkenyl or spiropentyl; each of which is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen, cyano, C₁₋₄alkyl, and C₁₋₄haloalkyl, and C₁₋₄alkoxy;

(e) phenyl or a 5-6 membered heteroaryl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms; each of which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, di-C₁₋₄alkylamino-C₁₋₄alkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄ hydroxyalkyl, C₁₋₄alkoxy, and C₃₋₆cycloalkyl;

R² and R⁷ are independently hydrogen or C₁₋₄alkyl;

R³ is hydrogen or halogen, and n is 0 or 1; and

R⁴ is selected from

(a) hydrogen;

(b) halogen;

(c) C₁₋₆haloalkyl or C₁₋₆alkyl that is unsubstituted or substituted by C₃₋₆cycloalkyl; and said C₃₋₆cycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl;

(d) -NR^{6a}R^{6b} wherein R^{6a} is hydrogen or C₁₋₄alkyl; R^{6b} is hydrogen, C₁₋₄alkoxycarbonyl, C₁₋₄ haloalkyl, C₃₋₆ cycloalkyl, or C₁₋₄alkyl that is unsubstituted or substituted by C₁₋₄alkoxy; or

R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- to 7-membered heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms;

wherein the 4- to 7-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkoxy, oxo, 1,1-dioxo, -C(O)-OR⁷ or a 4-6 membered heterocycloalkyl comprising 1-2 heteroatoms independently selected from N, O and S; or two substituents on the same or different ring atoms of the 4- to 7-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused Ring C attached to the 4- to 7-membered heterocycloalkyl;

wherein Ring C is selected from C₃₋₆cycloalkyl, and 3- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and is independently unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, and oxo;

(e) C₃₋₆cycloalkyl;

(f) 4- to 6-membered heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms; and is unsubstituted or substituted by -C(O)OR⁸, -C(O)R⁸ wherein R⁸ is C₁₋₄ alkyl, and arylC₁₋₄ alkyl that is unsubstituted or substituted by 1 to 2 halo substituents; and

(g) 5- to 6-membered heteroaryl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms; which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, C₁₋₄alkyl, C₁₋₄ hydroxyalkyl, and C₃₋₆cycloalkyl.

In another aspect, the invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula (I) or subformulae thereof, or a pharmaceutically acceptable salt or stereoisomer thereof; and one or more pharmaceutically acceptable carriers.

In yet another aspect, the invention provides a combination, in particular a pharmaceutical combination, comprising a therapeutically effective amount of a compound of Formula (I) or subformulae thereof, or a pharmaceutically acceptable salt or stereoisomer thereof; and one or more therapeutically active agent(s).

Compounds of Formula (I) or subformulae thereof, in free form or in pharmaceutically acceptable salt form, may be useful as a therapy for a disease or condition that can benefit from inhibition of growth and proliferation of kinetoplastid parasites. In one aspect, the present invention provides a compound of Formula (I) or subformulae thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, for use in treating, preventing, inhibiting, ameliorating, or eradicating the pathology and/or symptomology of a disease caused by a kinetoplastid parasite. In another aspect, the present invention provides the use of a compound selected from Formula (I), or subformulae thereof, or a pharmaceutically acceptable salt or stereoisomer thereof, in the manufacture of a medicament for treating a disease in a subject caused by a kinetoplastid parasite. The kinetoplastid parasites include, but is not limited to, a parasite of the *Leishmania* genus, for example, *Leishmania donovani*, *Leishmania infantum*, *Leishmania braziliensis*, *Leishmania panamensis*, *Leishmania guayanensis*, *Leishmania amazonensis*, *Leishmania mexicana*, *Leishmania tropica*, *Leishmania major*; or a parasite of the *Trypanosoma* genus, for example, *Trypanosoma cruzi* and *Trypanosoma brucei*. Accordingly, compounds of the invention may be useful in the treatment of an indication selected from: leishmaniasis, Chagas disease (also call American Trypanosomiasis), more particularly, Chagas disease caused by the protozoa *Trypanosoma cruzi*; and human African trypanosomiasis, more particularly, Human African Trypanosomiasis caused by the protozoa *Trypanosoma brucei*.

Unless specified otherwise, the term "compounds of the present invention" refers to compounds of Formula I and subformulae thereof, salts of the compound, hydrates or solvates of the compounds, salts, as well as all stereoisomers (including diastereoisomers and enantiomers), tautomers and isotopically labeled compounds (including deuterium substitutions). Compounds of the present invention further comprise polymorphs of compounds of Formula (I) (or subformulae thereof) and salts thereof.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

As used herein, the term "a," "an," "the" and similar terms used in the context of the present invention (especially in the context of the claims) are to be construed to cover both the singular and plural unless otherwise indicated herein or clearly contradicted by the context.

As used herein, the term "C₁₋₆alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, having from one to six carbon atoms, and which is attached to the rest of the molecule by a single bond. The term "C₁₋₄alkyl" is to be construed accordingly. As used herein, the term "*n*-alkyl" refers to straight chain (un-branched) alkyl radical as defined herein. Examples of C₁₋₆alkyl include, but are not limited to, methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, isobutyl (-CH₂CH(CH₃)₂), *sec*-butyl (-CH(CH₃)CH₂CH₃), *t*-butyl (-C(CH₃)₃), *n*-pentyl, isopentyl (-CH₂)₂CH(CH₃)₂), neopentyl (-CH₂C(CH₃)₃), *tert*-pentyl (-C(CH₃)₂CH₂CH₃), 2-pentan-yl (-CH(CH₃)(CH₂)₂CH₃), *n*-hexyl, and the like.

As used herein, the term "C₁₋₄alkylamino" refers to a radical of the formula -NH-R^a, where R^a is a C₁₋₄alkyl radical as defined above.

As used herein, the term "di-(C₁₋₄alkyl)amino" refers to a radical of the formula -N(R^a)-R^a, where each R^a is a C₁₋₄alkyl radical, which may be the same or different, as defined above.

As used herein, the term "C₁₋₆alkoxy" refers to a radical of the formula -OR_a, where R_a is a C₁₋₆alkyl radical as generally defined above. Examples of C₁₋₆alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, pentoxy, and hexoxy

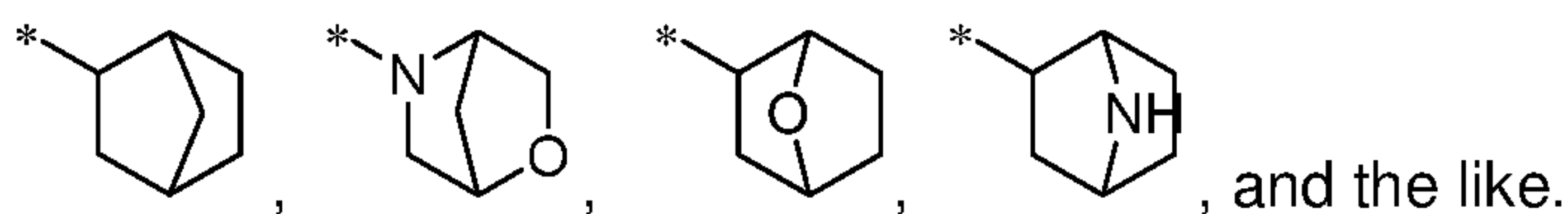
As used herein, the term "C₁₋₄alkoxyC₁₋₄alkyl" refers to a radical of the formula -R^a-O-R^a where each R^a is independently a C₁₋₆alkyl radical as defined above. The oxygen atom may be bonded to any carbon atom in either alkyl radical. Examples of C₁₋₄alkoxyC₁₋₄alkyl include, but are not limited to, methoxy-methyl, methoxy-ethyl, ethoxy-ethyl, 1-ethoxy-propyl and 2-methoxy-butyl.

As used herein, the term "C₁₋₆alkoxycarbonyl" refers to a radical of the formula -C(=O)-O-R^a where R^a is a C₁₋₆alkyl radical as defined above.

"Aryl" as used herein refers to a 6-14 membered monocyclic or polycyclic aromatic ring assembly where all the ring atoms are carbon atoms. Typically, the aryl is a 6 membered monocyclic, a 10-12 membered bicyclic or a 14-membered fused tricyclic aromatic ring system. C_Xaryl and C_{X-Y}aryl as used herein describe an aryl group where X and Y indicate the number of carbon atoms in the ring system. C₆₋₁₄aryls include, but are not limited to, phenyl, biphenyl, naphthyl, azulenyl, and anthracenyl.

"Bridging ring" or "bridged rings" as used herein refers to a polycyclic ring system where two ring atoms that are common to two rings are not directly bound to each other. One or more rings of the ring system may include C₃₋₆cycloalkyl or 4- to 6-membered heterocyclic rings

comprising heteroatoms selecting from N, O and S as ring atoms. Non-exclusive examples of bridging rings include adamantanyl, azabicyclo[3.2.1]oct-3-en-3-yl,



As used herein, the term “cyano” means the radical $^*-\text{C}\equiv\text{N}$.

5 The term “cycloalkyl” refers to nonaromatic carbocyclic ring that is a fully hydrogenated ring, including mono-, bi- or poly-cyclic, fused, bridged or spiro, ring systems. Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, bicyclo[1,1,1]pentanyl, cyclohexyl, norbornyl, and cubanyl.

“Fused ring”, as used herein, refers to a multi-ring assembly wherein the rings
10 comprising the ring assembly are so linked that the ring atoms that are common to two rings are directly bound to each other. The fused ring assemblies may be saturated, partially saturated, aromatics, carbocyclics, heterocyclics, and the like. Non-exclusive examples of common fused rings include decalin, naphthalene, anthracene, phenanthrene, indole, benzofuran, purine, quinoline, and the like.

15 “Halogen” or “halo” refers to bromo, chloro, fluoro or iodo; preferably fluoro, chloro or bromo.

As used herein, “C₁₋₆haloalkyl” refers to a C₁₋₆alkyl radical as defined above, substituted by one or more halo radicals as defined above. Examples of C₁₋₆haloalkyl include, but are not limited to, trifluoromethyl, difluoromethyl, fluoromethyl, trichloromethyl, 2,2,2-trifluoroethyl, 1,3-
20 dibromopropan-2-yl, 3-bromo-2-fluoropropyl and 1,4,4-trifluorobutan-2-yl.

The term “heteroaryl” refers to aromatic moieties containing at least one heteroatom (e.g., oxygen, sulfur, nitrogen or combinations thereof) within a 5- to 10-membered aromatic ring system. Examples of heteroaryl include, but are not limited to pyrrolyl, pyrazolyl, indolyl, indazolyl, thienyl, furanyl, benzofuranyl, oxazolyl, isoxazolyl, imidazolyl, triazolyl, tetrazolyl, triazinyl, pyridyl, pyrimidinyl, pyrazinyl, thiazolyl, purinyl, benzimidazolyl, quinolinyl, isoquinolinyl, quinoxalinyl, benzopyranyl, benzothiophenyl, benzoimidazolyl, benzoxazolyl and
25 1H-benzo[d][1,2,3]triazolyl. The heteroaromatic moiety may consist of a single or fused ring system. A typical single heteroaryl ring is a 5- to 6-membered ring containing one to four heteroatoms independently selected from N, O and S and a typical fused heteroaryl ring system is a 9- to 10-membered ring system containing one to four heteroatoms independently
30 selected from N, O and S. The fused heteroaryl ring system may consist of two heteroaryl rings fused together or a heteroaryl fused to an aryl (e.g., phenyl).

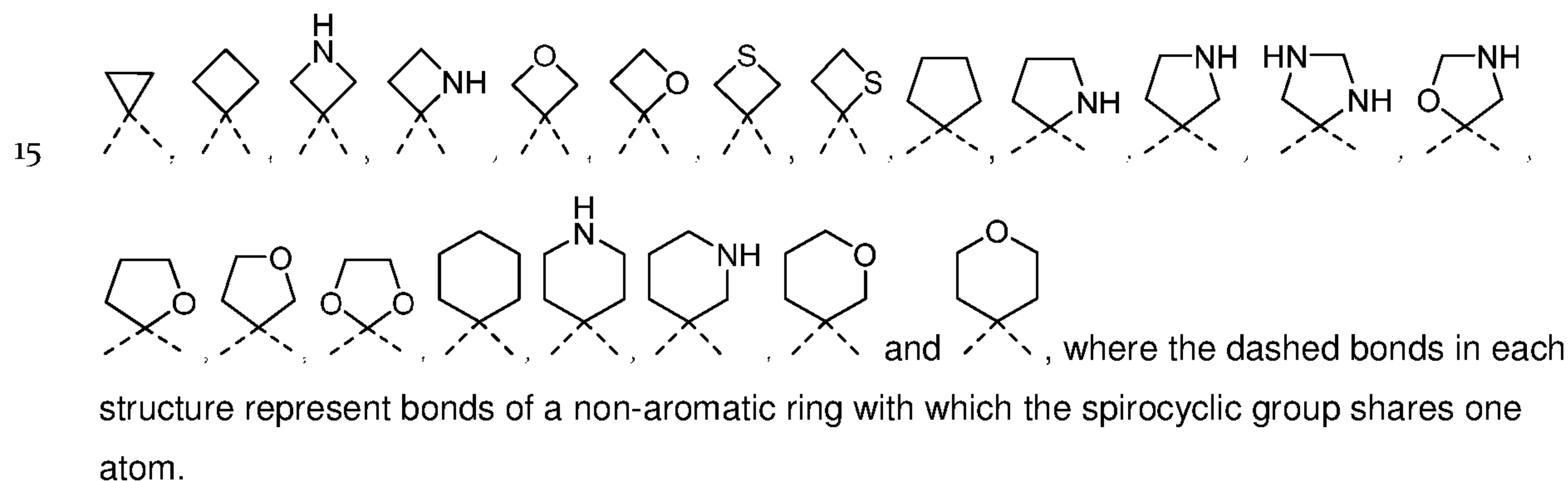
As used herein, the term “heteroatoms” refers to nitrogen (N), oxygen (O) or sulfur (S) atoms. Unless otherwise indicated, any heteroatom with unsatisfied valences is assumed to
35 have hydrogen atoms sufficient to satisfy the valences, and when the heteroatom is sulfur, it can be unoxidized (S) or oxidized to S(O) or S(O)₂.

The term “hydroxyl” or “hydroxy”, as used herein, refers to the radical $-\text{OH}$.

"Heterocycloalkyl" means cycloalkyl, as defined in this application, provided that one or more of the ring carbons indicated, are replaced by a moiety selected from -O-, -N=, -NH-, -S-, -S(O)- and -S(O)₂-. Examples of 3 to 8 membered heterocycloalkyl include, but are not limited to oxiranyl, aziridinyl, azetidiny, imidazolidinyl, pyrazolidinyl, tetrahydrofuranyl, tetrahydrothienyl, tetrahydrothienyl 1,1-dioxide, oxazolidinyl, thiazolidinyl, pyrrolidinyl, pyrrolidinyl-2-one, morpholinyl, piperazinyl, piperidinyl, pyrazolidinyl, hexahydropyrimidinyl, 1,4-dioxo-8-aza-spiro[4.5]dec-8-yl, thiomorpholinyl, sulfanomorpholinyl, sulfonomorpholinyl and octahydropyrrolo[3,2-b]pyrrolyl.

The term "oxo", as used herein, refers to the divalent radical =O.

The term "spiro" as used herein includes C₃₋₆cycloalkyl or 4- to 6-membered heterocyclic rings having one or two heteroatoms selected from N, O and S as ring members, wherein the spiro ring is fused onto a single carbon atom of a non-aromatic ring, making the carbon atom shared by both rings a spirocyclic center. The spiro ring can optionally be substituted as defined, e.g., halo, hydroxyl or C₁₋₄alkyl. Illustrative examples of spiro groups are:



As referred to herein, the term "substituted" means that at least one hydrogen atom is replaced with a non-hydrogen group, provided that normal valencies are maintained and that the substitution results in a stable compound. When a substituent is oxo (*i.e.*, =O), then 2 hydrogens on the atom are replaced. In cases wherein there are nitrogen atoms (*e.g.*, amines) present in compounds of the present invention, these may be converted to N-oxides by treatment with an oxidizing agent (*e.g.*, mCPBA and/or hydrogen peroxides) to give other compounds of the invention.

As a person of ordinary skill in the art would be able to understand, for example, a ketone (-CH-C(=O)-) group in a molecule may tautomerize to its enol form(-C=C(OH)-). Thus, this invention is intended to cover all possible tautomers even when a structure depicts only one of them.

When any variable occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-3 R groups, then said group may be unsubstituted or substituted with up to three R groups, and at each occurrence R is selected independently from the definition of R.

As used herein, "X—*" denotes the point of attachment of X, to other part of the molecule.

The term "IC₅₀", as used herein, refers to the molar concentration of an inhibitor that produces 50% of the inhibition effect.

5 The term "EC₅₀", as used herein, refers to the molar concentration of an inhibitor or modulator that produces 50% efficacy.

As used herein, the term "pharmaceutical composition" refers to a compound of the invention, or a pharmaceutically acceptable salt thereof, together with at least one pharmaceutically acceptable carrier, in a form suitable for topical or parenteral administration.

10 As used herein, the term "pharmaceutically acceptable carrier" refers to a substance useful in the preparation or use of a pharmaceutical composition and includes, for example, suitable diluents, solvents, dispersion media, surfactants, antioxidants, preservatives, isotonic agents, buffering agents, emulsifiers, absorption delaying agents, salts, drug stabilizers, binders, excipients, disintegration agents, lubricants, wetting agents, sweetening agents,
15 flavoring agents, dyes, and combinations thereof, as would be known to those skilled in the art (see, for example, Remington The Science and Practice of Pharmacy, 22nd Ed. Pharmaceutical Press, 2013, pp. 1049-1070).

As used herein, the term "inhibit", "inhibition" or "inhibiting" refers to the reduction or suppression of a given condition, symptom, or disorder, or disease, or a significant decrease in
20 the baseline activity of a biological activity or process.

As used herein, the term "prevent", "preventing" or "prevention" of any disease or disorder refers to the prophylactic treatment of the disease or disorder; or delaying the onset or progression of the disease or disorder.

As used herein, the term "subject" refers to primates (*e.g.*, humans, male or female,
25 dogs, rabbits, guinea pigs, pigs, rats and mice). In certain embodiments, the subject is a primate. In yet other embodiments, the subject is a human.

The term "a therapeutically effective amount" of a compound of the present invention refers to an amount of the compound of the present invention that will elicit the biological or medical response of a subject, for example, reduction or inhibition of an enzyme or a protein
30 activity, or ameliorate symptoms, alleviate conditions, slow or delay disease progression, or prevent a disease, etc. In one non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a subject, is effective to (1) at least partially alleviate, inhibit, prevent and/or ameliorate a condition, or a disorder or a disease caused by the proliferation of a kinetoplastid
35 parasite; or (2) reduce or inhibit the proliferation of a kinetoplastid parasite.

As used herein, the term "treat", "treating" or "treatment" of any disease or disorder refers to alleviating or ameliorating the disease or disorder (*i.e.*, slowing or arresting the development of the disease or at least one of the clinical symptoms thereof); or alleviating or ameliorating at

least one physical parameter or biomarker associated with the disease or disorder, including those which may not be discernible to the patient.

Embodiments of the Invention

The present invention relates to compounds having antiparasitic activity against kinatoplastid protozoa. It relates particularly to compounds that inhibit growth of kinatoplastid parasite cells through inhibition of the parasitic proteasome, and thereof useful as a therapy for leishmaniasis, Chagas disease and African sleeping sickness.

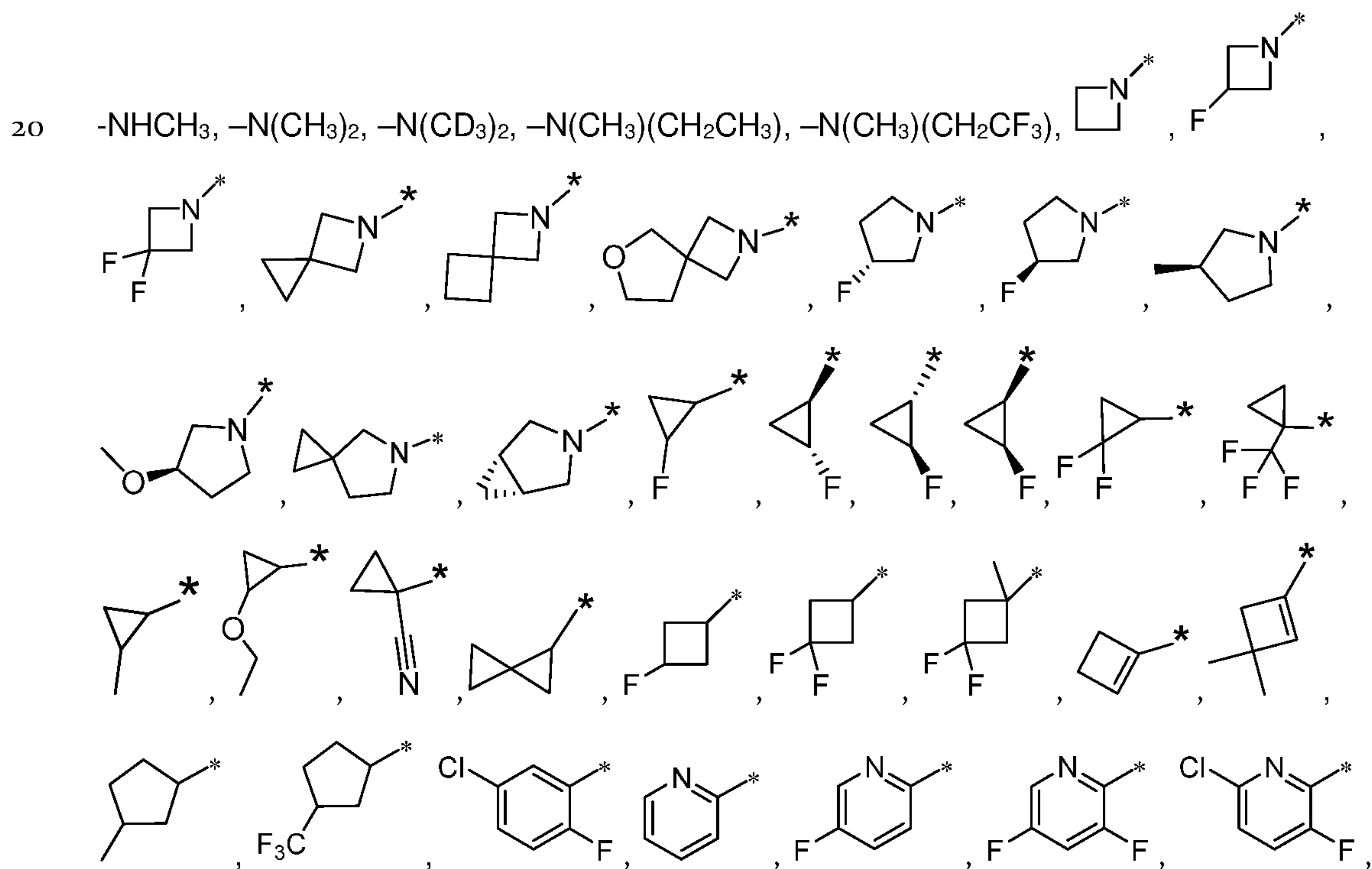
Various (enumerated) embodiments of the invention are described herein. Features specified in each embodiment may be combined with other specified features to provide further embodiments of the present invention.

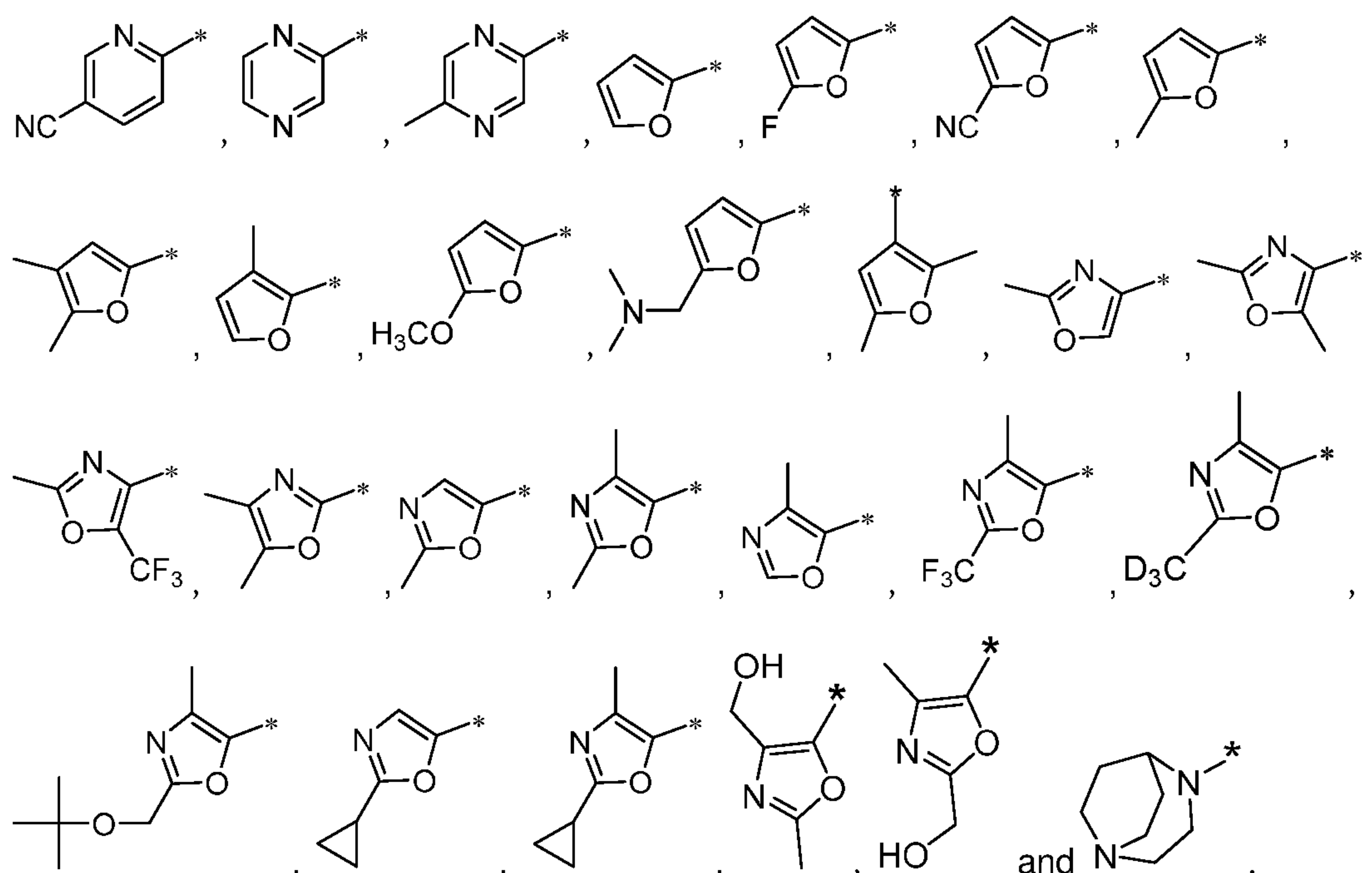
Embodiment 1. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, as described in the Summary of the Invention.

Embodiment 2. The compound according to Embodiment 1 or a pharmaceutically acceptable salt thereof, wherein Ring A is phenyl.

Embodiment 3. The compound according to Embodiment 1 or a pharmaceutically acceptable salt thereof, wherein Ring A is pyridinyl.

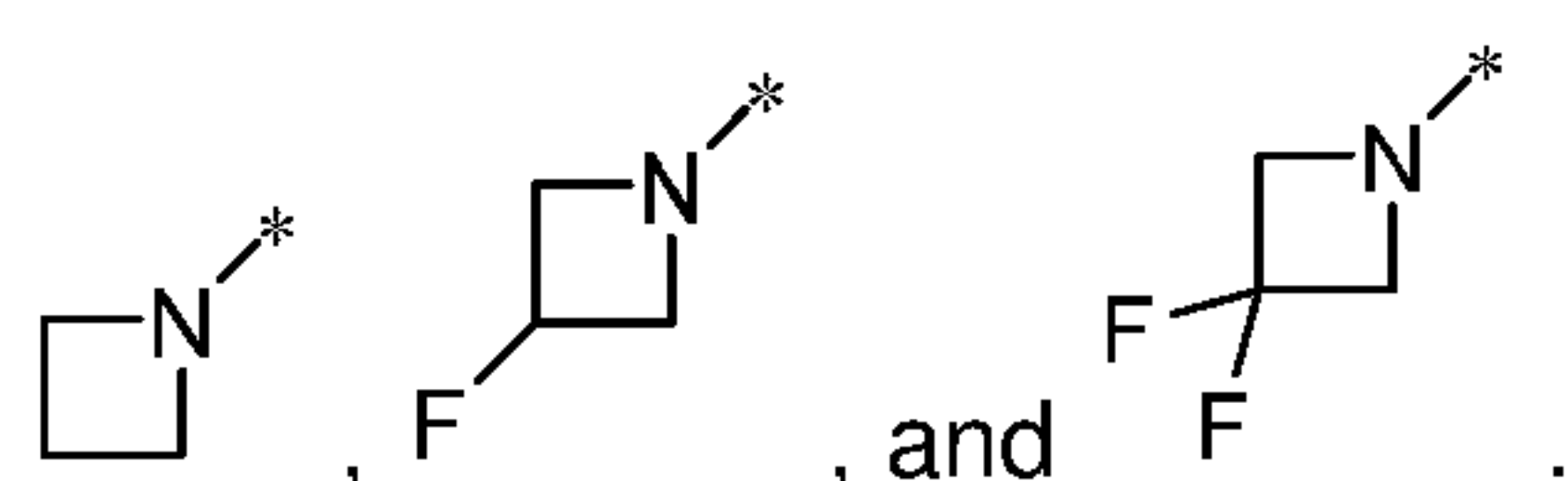
Embodiment 4. The compound according to any one of Embodiments 1-3 or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from $-(CH_2)_{1-3}CF_3$, $-(CH_2)-CH(CH_3)-CF_3$, $-(CH_2)-C(CH_3)_3$, $-O(CH_2)_2CF_3$, $-(CH_2)_{0-2}$ -cyclopropyl, $-(CH_2)_{0-2}$ -cyclobutyl,





5 **Embodiment 5.** The compound according to any one of Embodiments 1-3 or a pharmaceutically acceptable salt thereof, wherein R¹ is azetidynyl, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl; or two substituents on the same ring atom of the azetidynyl, together with the ring atom to which both are attached, form a spiro cyclopropyl or spiro tetrahydrofuranyl attached to the azetidynyl ring.

10 **Embodiment 6.** The compound according to any one of Embodiments 1-3 or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from

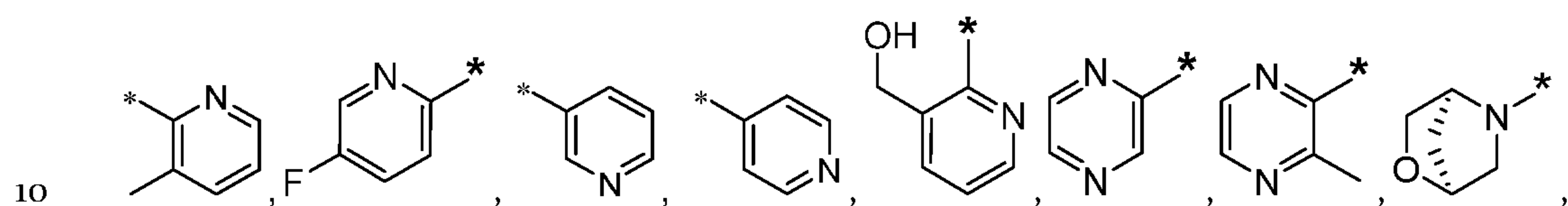
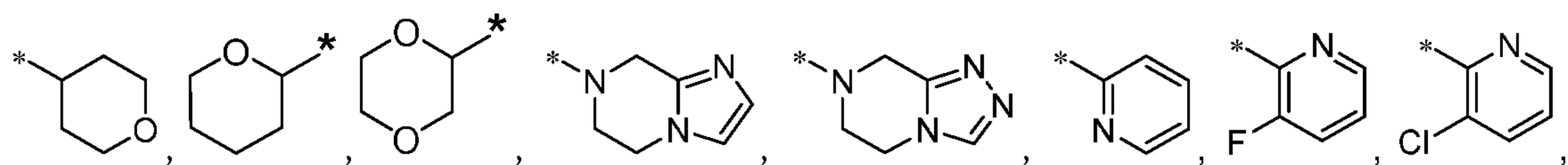
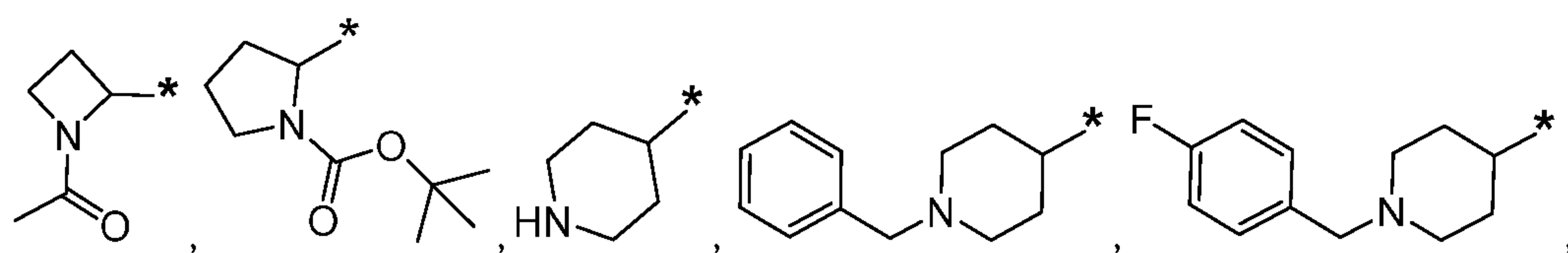
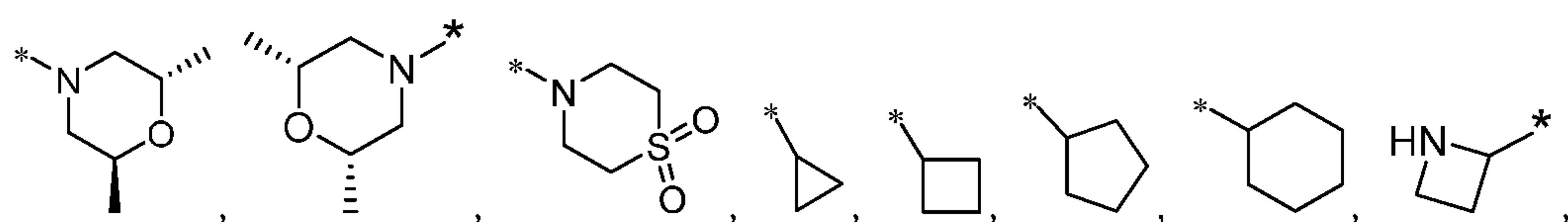
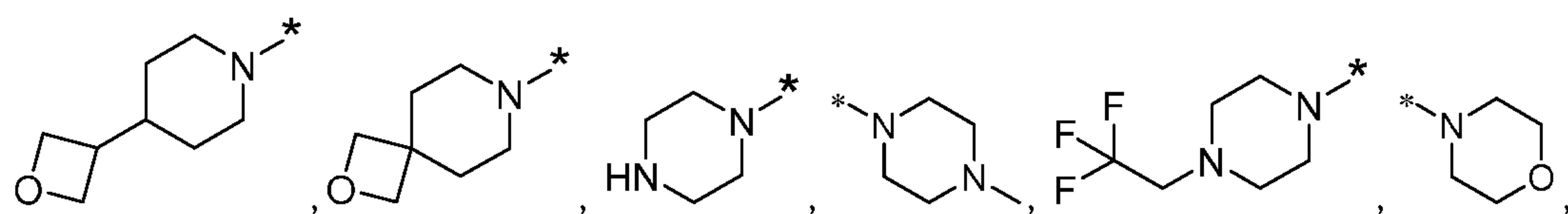
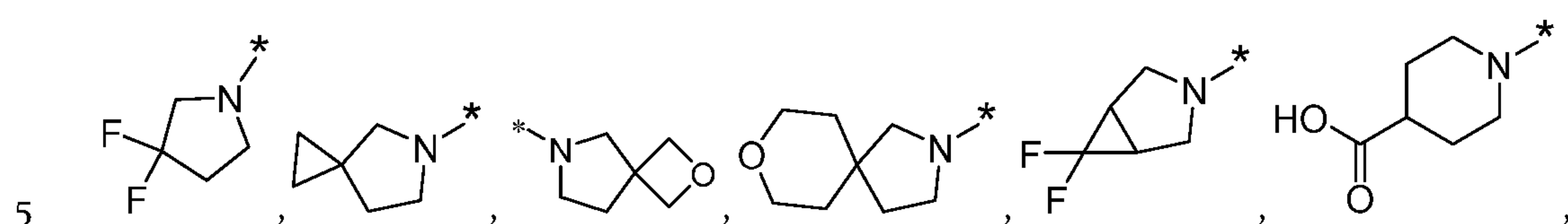
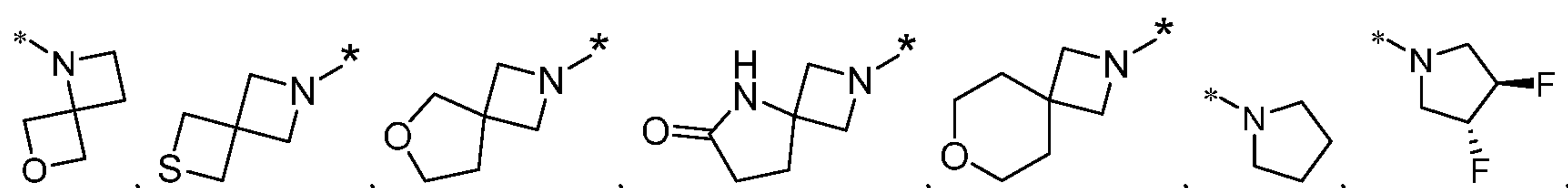
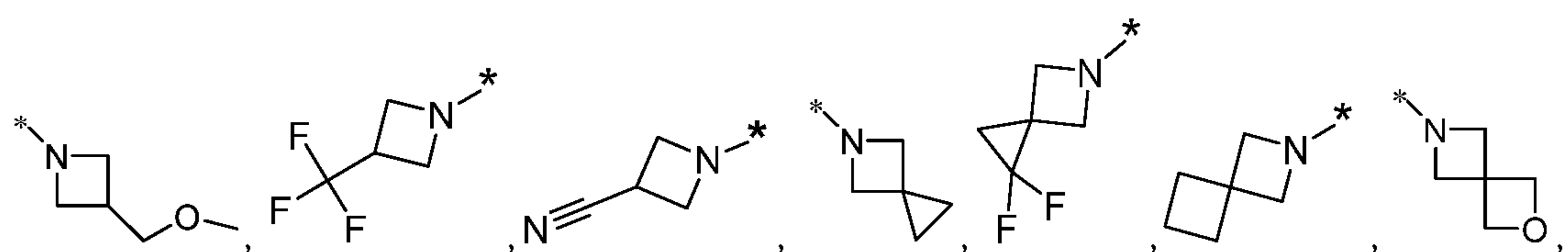
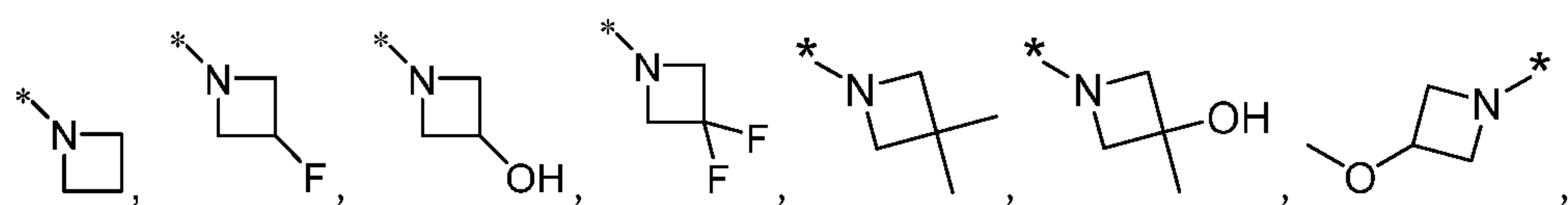
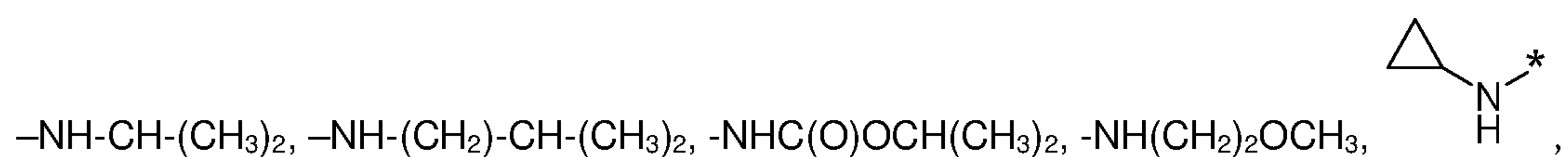


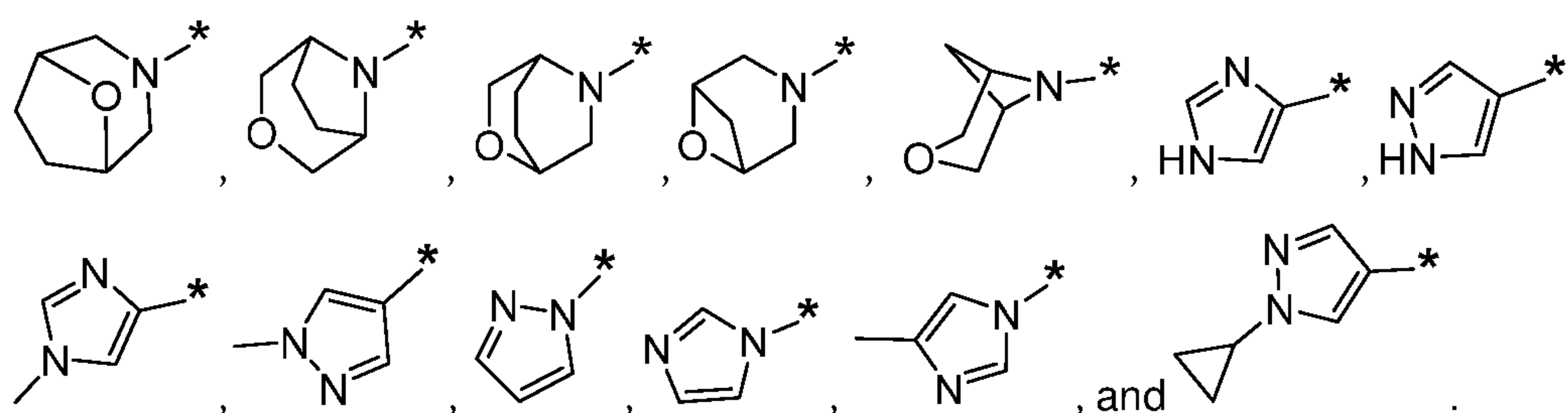
Embodiment 7. The compound according to any one of Embodiments 1-6 or a pharmaceutically acceptable salt thereof, wherein R³ is halo and n is 1.

15 **Embodiment 8.** The compound according to Embodiment 7 or a pharmaceutically acceptable salt thereof, wherein R³ is fluoro.

Embodiment 9. The compound according to any one of Embodiments 1-8 or a pharmaceutically acceptable salt thereof, wherein R⁴ is selected from hydrogen, chloro, bromo, methyl, *iso*-propyl, $-(CH_2)_{1-2}CH(CH_3)_2$, $-(CH_2)_{0-1}C(CH_3)_3$, $-C(CH_3)_2CH_2CH_3$, $-CH(CH_3)(CH_2)_{1-2}CH_3$, $-CH_2$ -cyclobutyl, $-(CH_2)_{0-1}CF_3$, $-NH-(CH_2)_{0-1}CH_3$, $-N-(CD_3)_2$, $-N(CH_3)_2$,

20





Embodiment 10. The compound according to any one of Embodiments 1-8 or a pharmaceutically acceptable salt thereof, wherein R^4 is $-NR^{6a}R^{6b}$;

5 R^{6a} is hydrogen or C_{1-4} alkyl;

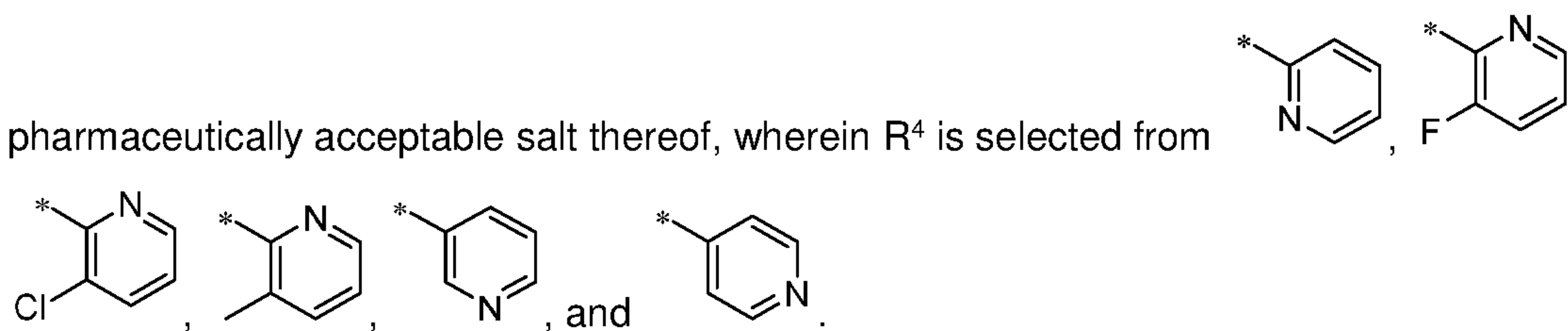
R^{6b} is hydrogen, C_{1-4} alkoxycarbonyl or C_{1-4} alkyl that is unsubstituted or substituted by C_{1-4} alkoxy; or R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- to 6-membered heterocycloalkyl optionally comprising 1 to 2 additional heteroatoms independently selected from N, O and S as ring atoms;

10 wherein the 4- to 6-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy, and oxo; or two substituents on the same or different ring atoms of the 4- to 6-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused, Ring C attached to the 4- to 6-membered heterocycloalkyl;

15 wherein Ring C is selected from C_{3-6} cycloalkyl; and 3- to 5-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and Ring C is independently unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, and oxo.

Embodiment 11. The compound according to any one of Embodiments 1-8 or a

20 pharmaceutically acceptable salt thereof, wherein R^4 is selected from



Embodiment 12. The compound according to any one of Embodiments 1-3 or a pharmaceutically acceptable salt thereof;

25 wherein R^1 is azetidiny, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C_{1-4} alkyl; or two substituents on the same ring atom of the azetidiny, together with the ring atom to which both are attached, form a spiro cyclopropyl or spiro tetrahydrofuranyl attached to the azetidiny ring;

R^2 is hydrogen or C_{1-4} alkyl;

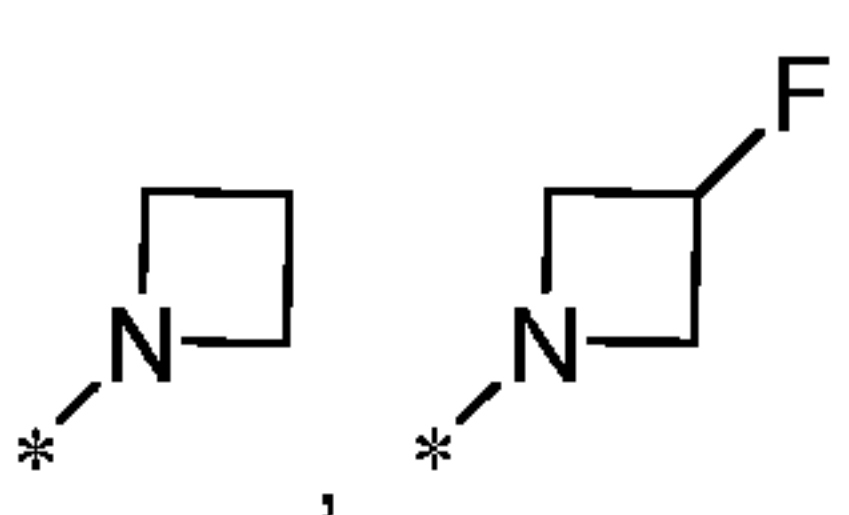
R^3 is selected from halo, and n is 1; and

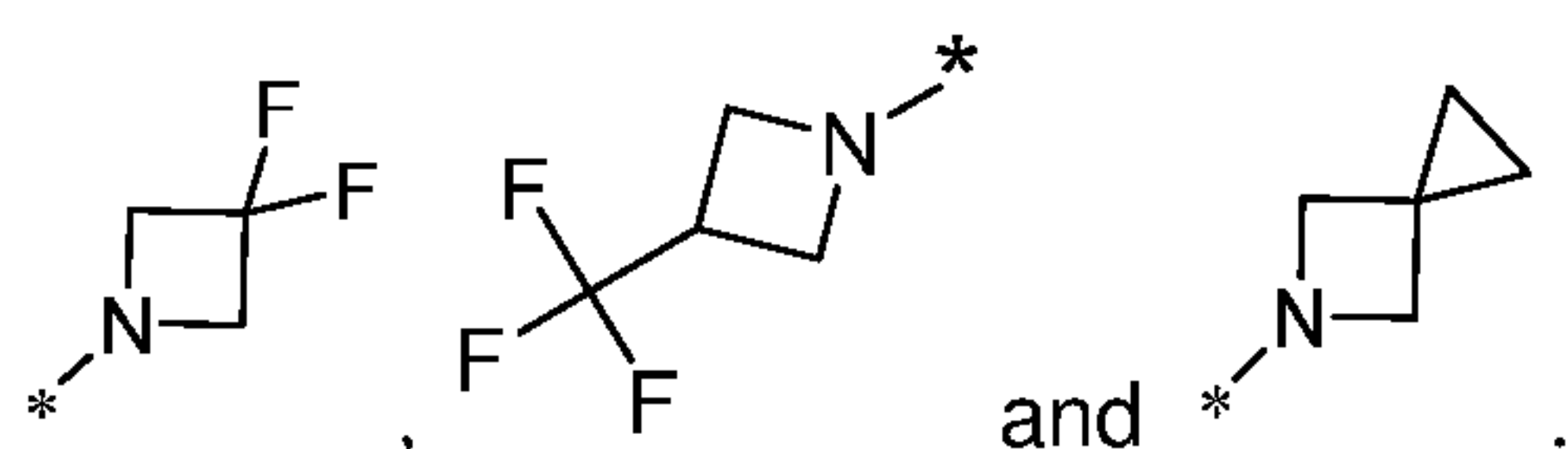
R^4 is $-NR^{6a}R^{6b}$ wherein R^{6a} is hydrogen or C_{1-4} alkyl; R^{6b} is hydrogen, C_{1-4} alkoxycarbonyl, or C_{1-4} alkyl that is unsubstituted or substituted by C_{1-4} alkoxy; or R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- to 6-membered heterocycloalkyl optionally comprising 1 to 2 additional heteroatoms independently selected from N, O and S as ring atoms;

wherein the 4- to 6-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} alkoxy, and oxo; or two substituents on the same or different ring atoms of the 4- to 6-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused, Ring C attached to the 4- to 6-membered heterocycloalkyl;

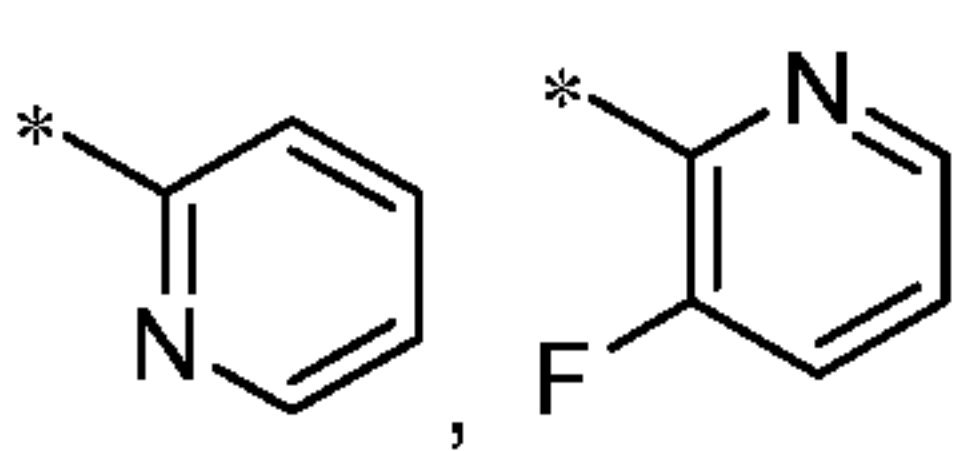
wherein Ring C is selected from C_{3-6} cycloalkyl; 3- to 5-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and Ring C is independently unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and oxo.

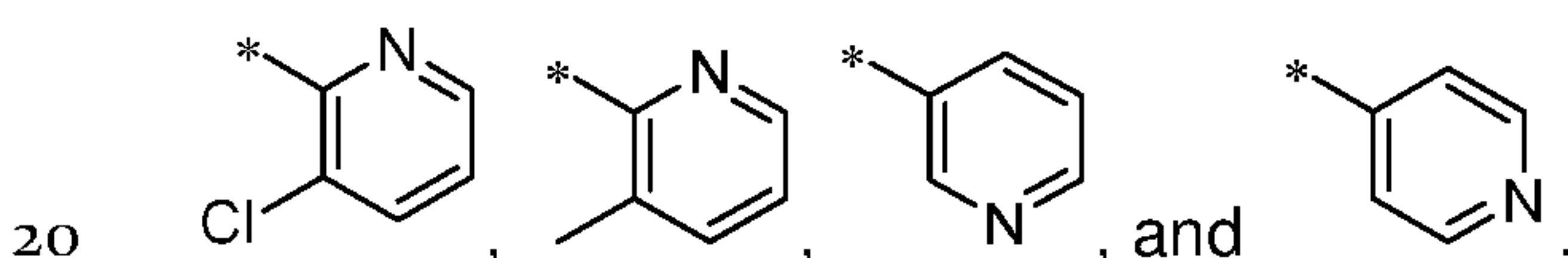
Embodiment 13. The compound according to any one of Embodiments 1-12 or a

pharmaceutically acceptable salt thereof, wherein R^4 is selected from ,

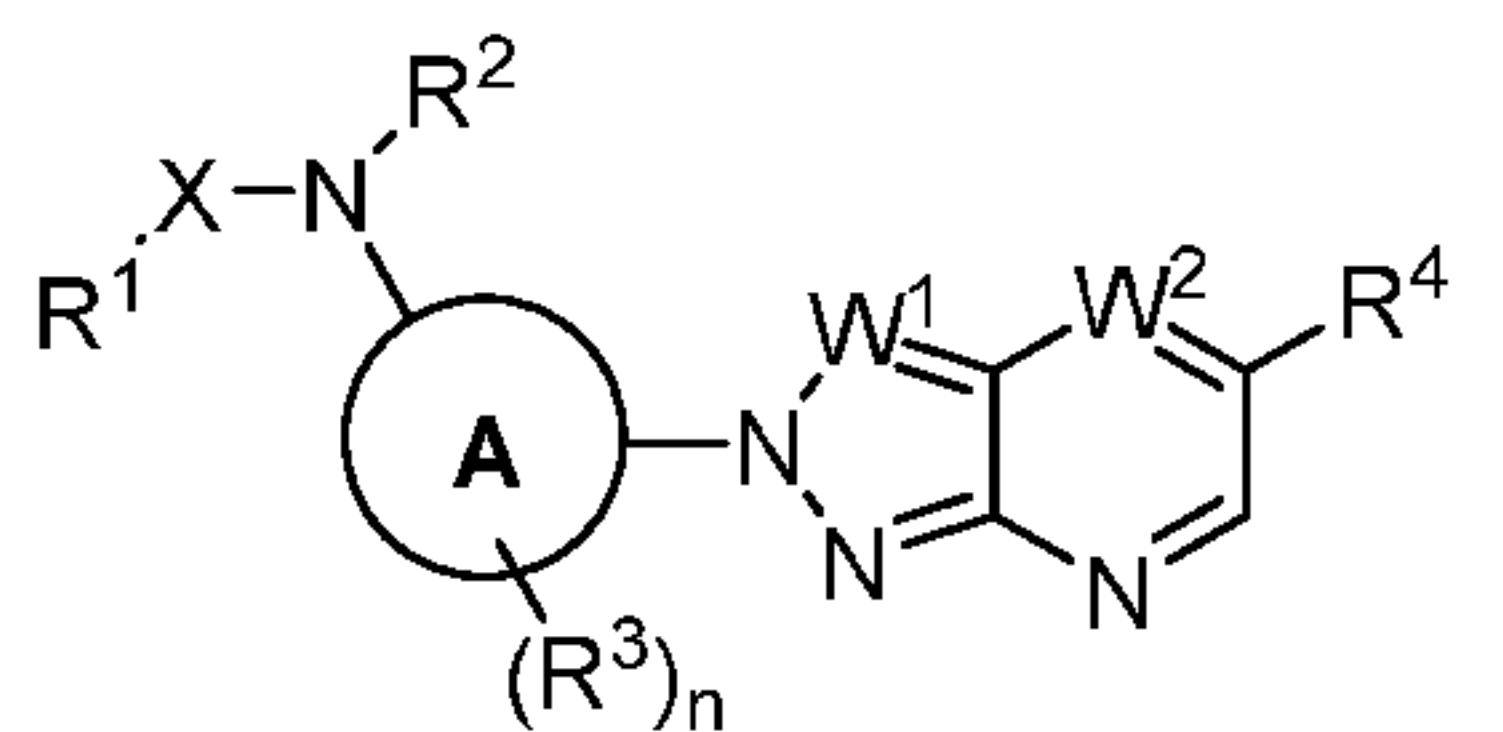


Embodiment 14. The compound according to any one of Embodiments 1-12 or a

pharmaceutically acceptable salt thereof, wherein R^4 is selected from ,



Embodiment 15. A compound of Formula (I) or a pharmaceutically acceptable salt thereof:



or a pharmaceutically acceptable salt, or stereoisomer thereof; wherein

W^1 and W^2 are each independently CH or N;

Ring A is phenyl or pyridyl;

X is $-C(O)-$ or $-S(O)_2-$;

R¹ is selected from

- (a) C₁₋₄alkyl that is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen and C₃₋₆cycloalkyl, wherein the C₃₋₆cycloalkyl substituent is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl;
- 5 (b) C₁₋₄alkoxy that is unsubstituted or substituted by C₁₋₄haloalkyl;
- (c) -NR^{5a}R^{5b}, wherein
 - (1) R^{5a} and R^{5b} are each independently hydrogen or C₁₋₄alkyl; or
 - (2) R^{5a} and R^{5b} together with the nitrogen atom to which both are attached form a 4- to 6-membered heterocycloalkyl optionally comprising 1 to 3 additional heteroatoms independently selected from N, O and S as ring atoms, wherein
 - 10 the 4 to 6-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxy, and oxo; or
 - two substituents on the same or different ring atoms of the 4- to 6-membered heterocycloalkyl, together with the atoms to which they are attached, form a
 - 15 spiro, bridged or fused Ring B attached to the 4- to 6-membered heterocycloalkyl; wherein Ring B is selected from
 - (i) C₃₋₆cycloalkyl,
 - (ii) 3- to 5-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and
 - 20 (iii) 5- to 6-membered heteroaryl comprising 1 to 3 heteroatoms independently selected from N or O as ring atoms;
 - wherein Ring B of (i) to (iii) are each unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, and oxo;
- 25 (d) monocyclic C₃₋₆cycloalkyl and polycyclic C₅₋₉cycloalkyl, each of which is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, and C₁₋₄alkoxycarbonyl;
- (e) 4- to 6-membered heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxy, oxo, and C₁₋₄alkylcarbonyl;
- 30 (f) phenyl that is unsubstituted or substituted by 1 to 2 substituents independently select from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkylamino-C₁₋₄alkyl, di-C₁₋₄alkylamino-C₁₋₄alkyl, C₁₋₄alkoxy, and C₃₋₆cycloalkyl;
- 35 (g) monocyclic 5- to 6-membered heteroaryl and polycyclic 7- to 10-membered heteroaryl, each of which comprises 1 to 2 heteroatoms independently selected from N, O and S as ring atoms, and each of which is unsubstituted or substituted by 1 to 2 substituents

independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkylamino-C₁₋₄alkyl, di-C₁₋₄alkylamino-C₁₋₄alkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkoxy, and C₃₋₆cycloalkyl;

R² is hydrogen or C₁₋₄alkyl;

R³ is halogen or C₁₋₄alkyl, and n is 0, 1 or 2;

5 R⁴ is selected from

(a) halogen;

(b) C₁₋₆alkyl that is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen and C₃₋₆cycloalkyl, wherein the C₃₋₆cycloalkyl substituent is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl;

10 (c) -NR^{6a}R^{6b}, wherein

(1) R^{6a} is hydrogen or C₁₋₄alkyl;

(2) R^{6b} is hydrogen or C₁₋₄alkyl that is unsubstituted or substituted by C₁₋₄alkoxy or C₁₋₄alkoxycarbonyl;

(3) or R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- to 6-membered heterocycloalkyl optionally comprising 1 to 2 additional heteroatoms independently selected from N, O and S as ring atoms, wherein

the 4- to 6-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2

substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl,

C₁₋₄haloalkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkoxy, and oxo; or

20 two substituents on the same or different ring atoms of the 4- to 6-membered

heterocycloalkyl, together with the atoms to which they are attached, form a

spiro, bridged or fused Ring C attached to the 4- to 6-membered

heterocycloalkyl; wherein Ring C is selected from

(i) C₃₋₆cycloalkyl,

25 (ii) 3- to 5-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and

(iii) 5- to 6-membered heteroaryl comprising 1 to 3 heteroatoms independently selected from N or O as ring atoms;

wherein Ring C of (i) to (iii) are each unsubstituted or substituted by 1 to 2

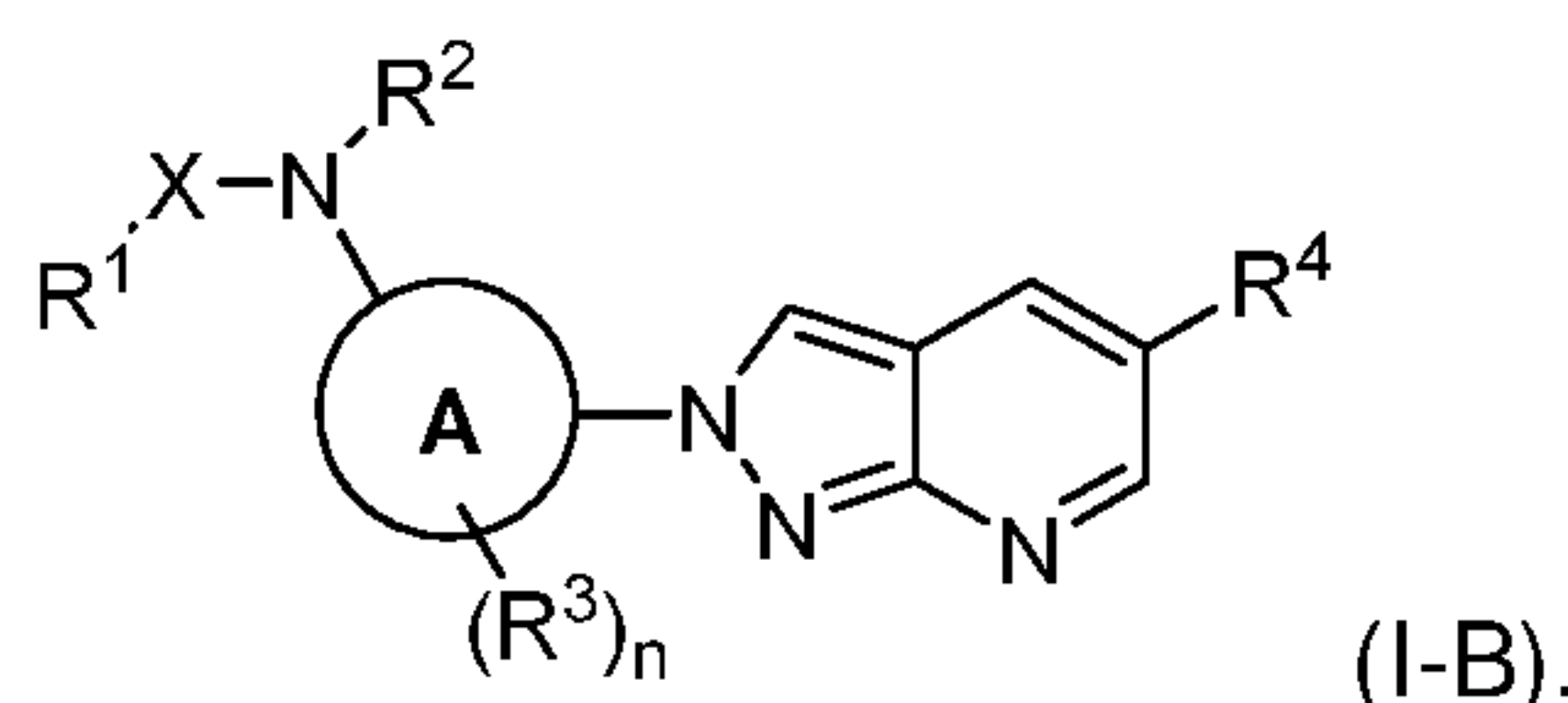
30 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, and oxo;

(d) C₃₋₆cycloalkyl that is unsubstituted or substituted by 1 to 2 substituents selected from halogen, cyano, C₁₋₄alkyl, and C₁₋₄haloalkyl;

35 (e) 4- to 6-membered heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl, C₁₋₄haloalkyl, and oxo;

- (f) phenyl that is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkylamino-C₁₋₄alkyl, di-C₁₋₄alkylamino-C₁₋₄alkyl, C₁₋₄alkoxy, and C₃₋₆cycloalkyl;
- (g) 5- to 6-membered heteroaryl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkylaminoC₁₋₄alkyl, di-C₁₋₄alkylaminoC₁₋₄alkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkoxy, and C₃₋₆cycloalkyl.

Embodiment 16. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 15, wherein the compound is of Formula (I-B):



Embodiment 17. A compound or a pharmaceutically acceptable salt thereof, according to Embodiment 15 or 16, wherein Ring A is phenyl.

Embodiment 18. A compound or a pharmaceutically acceptable salt thereof, according to Embodiment 15 or 16, wherein Ring A is pyridinyl.

Embodiment 19. A compound or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 15-18, wherein X is -C(O)-.

Embodiment 20. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 15-19, wherein R¹ is azetidiny, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl; or two substituents on the same ring atom of the azetidiny, together with the ring atom to which both are attached, form a spiro cyclopropyl or spiro tetrahydrofuranyl attached to the azetidiny ring.

Embodiment 21. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 20, wherein R¹ is

Embodiment 22. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 20, wherein R¹ is

Embodiment 23. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 20, wherein R¹ is

Embodiment 24. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 15-23, wherein R^3 is selected from halo or C_{1-4} alkyl, and n is 1.

Embodiment 25. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 24, wherein R^3 is halo.

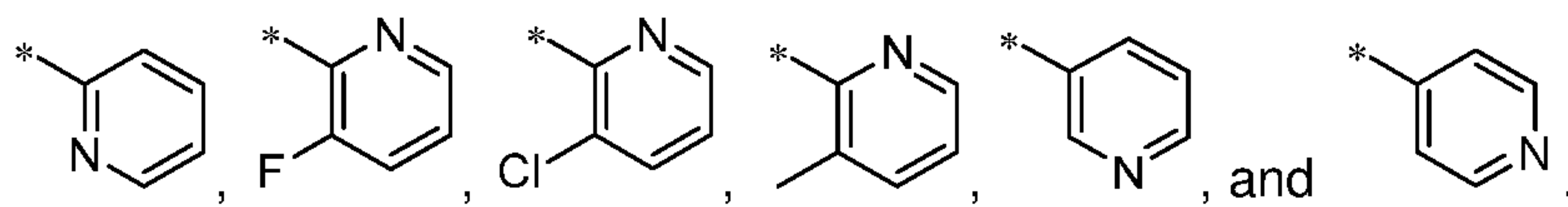
Embodiment 26. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 25, wherein R^3 is fluoro.

Embodiment 27. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 15-26, wherein R^4 is $-NR^{6a}R^{6b}$; wherein R^{6a} is hydrogen or C_{1-4} alkyl; and R^{6b} is hydrogen or C_{1-4} alkyl that is unsubstituted or substituted by C_{1-4} alkoxy or C_{1-4} alkoxycarbonyl; or wherein R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- to 6-membered heterocycloalkyl optionally comprising 1 to 2 additional heteroatoms independently selected from N, O and S as ring atoms;

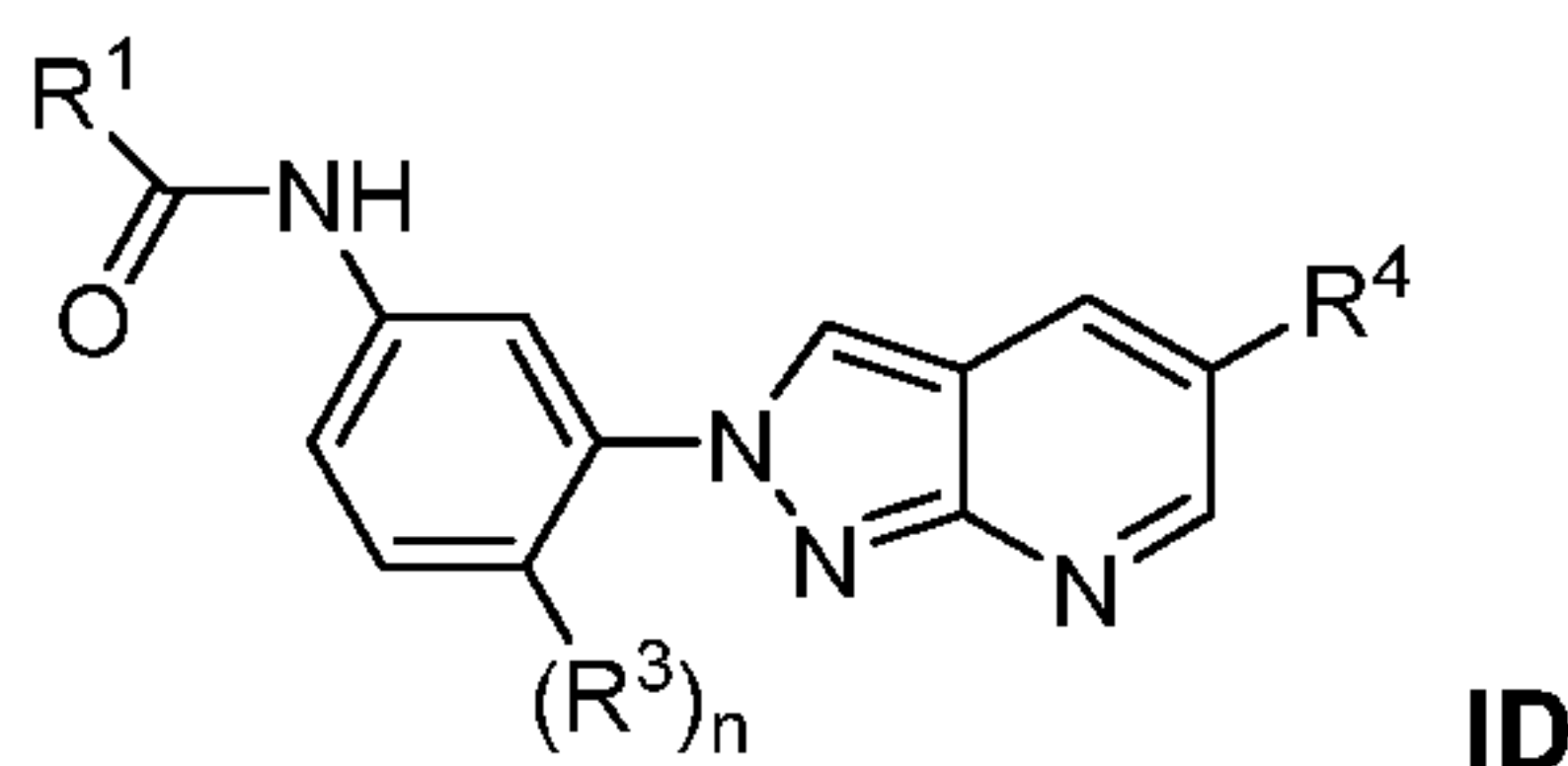
wherein the 4- to 6-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} alkoxy, and oxo; or two substituents on the same or different ring atoms of the 4- to 6-membered heterocycloalkyl together with the atoms to which they are attached form a spiro, bridged or fused Ring C attached to the 4- to 6-membered heterocycloalkyl;

wherein Ring C is selected from C_{3-6} cycloalkyl; 3- to 5-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and 5-membered heteroaryl comprising 1 to 3 heteroatoms independently selected from N or O as ring atoms; and Ring C is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, C_{1-4} alkyl, C_{1-4} haloalkyl, and oxo.

Embodiment 28. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 15-27, wherein R^4 is selected from



Embodiment 29. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to Embodiment 15, wherein the compound is of Formula (I)D:



wherein R_1 is selected from

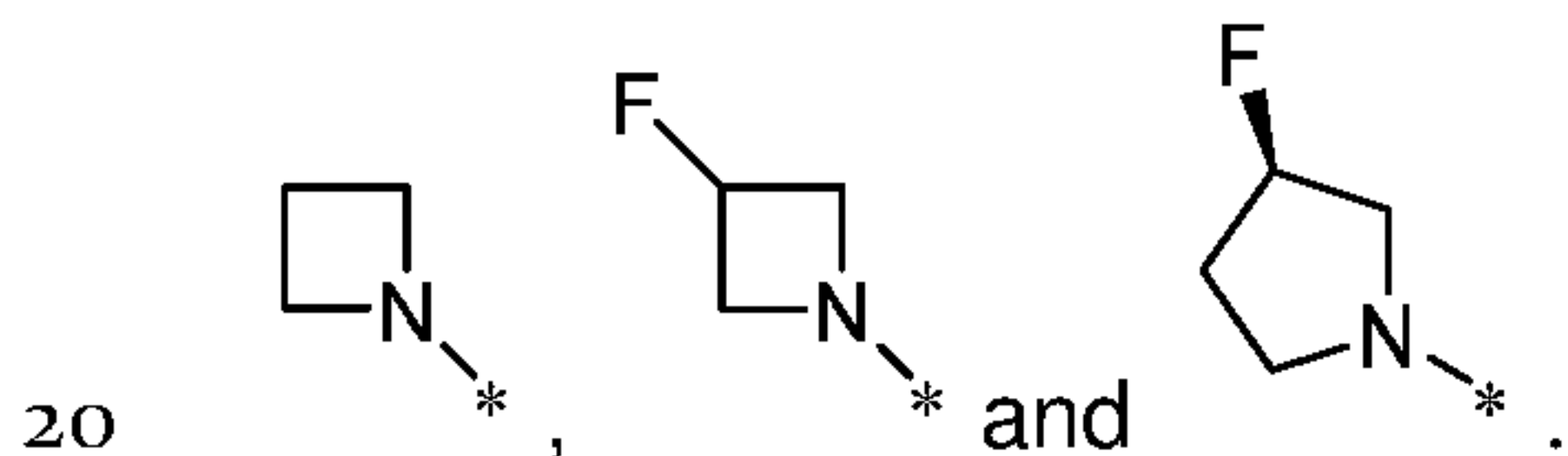
- (a) $-NR^{5a}R^{5b}$, wherein R^{5a} and R^{5b} together with the nitrogen atom to which both are attached form a 4- to 5-membered heterocycloalkyl, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C_{1-4} alkyl; and
- (b) monocyclic 5-membered heteroaryl comprising 1 to 2 heteroatoms independently selected from N and O as ring atoms, and each of which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C_{1-4} alkyl;

R^3 is halogen or C_{1-4} alkyl, and n is 0 or 1;

R^4 is selected from

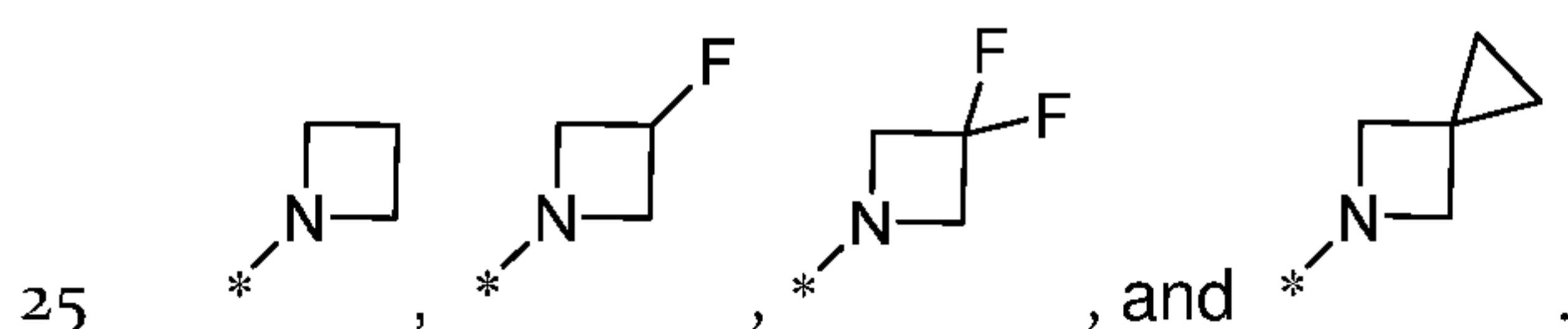
- (a) $-NR^{6a}R^{6b}$, wherein R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- or 5-membered heterocycloalkyl, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, hydroxyl and C_{1-4} alkyl; or 2 substituents on the same or different ring atoms of the 4- or 5-membered heterocycloalkyl together with the atoms to which they are attached form a spiro Ring C attached to the 4- to 5-membered heterocycloalkyl, wherein Ring C is C_{3-6} cycloalkyl; and
- (b) 6-membered heteroaryl comprising 1 to 2 nitrogen atoms as ring atoms, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C_{1-4} alkyl.

Embodiment 30. The compound according to Embodiment 29, wherein R^1 is selected from

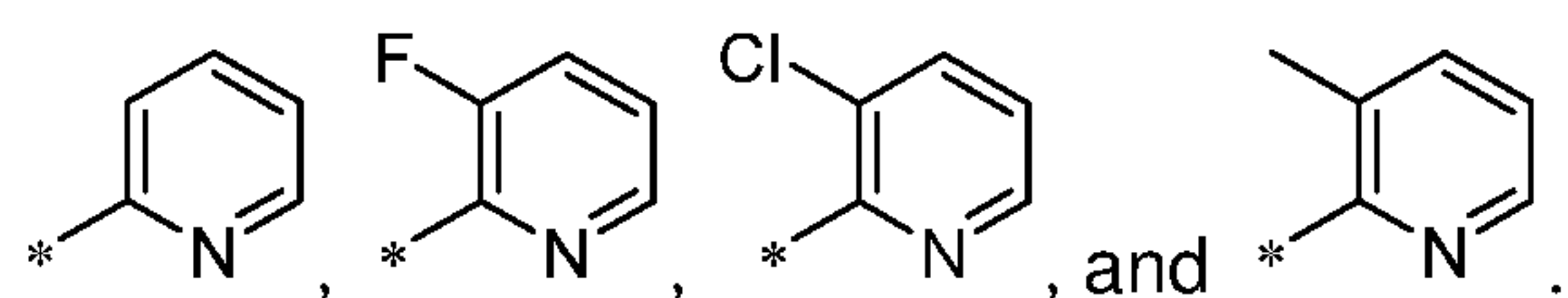


Embodiment 31. A compound of Formula (I)D or a pharmaceutically acceptable salt thereof, according to Embodiments 29 or 30, wherein R^3 is fluoro or chloro, and n is 1.

Embodiment 32. A compound of Formula (I)D or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 29-31, wherein R^4 is selected from



Embodiment 33. A compound of Formula (I)D or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 29-31 wherein R^4 is selected from



Embodiment 34. A compound of Formula (I) or a pharmaceutically acceptable salt thereof, selected from Table 1.

Table 1

1	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
2	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
3	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
4	(3R)-3-fluoro-N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
5	3,3-difluoro-N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
6	3-fluoro-N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
7	N-{4-fluoro-3-[5-(2-methylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
8	3,3-difluoro-N-{4-fluoro-3-[5-(2-methylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
9	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
10	N-{3-[5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
11	5-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
12	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropanecarboxamide
13	2-cyclopropyl-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}acetamide
14	3-fluoro-N-{4-fluoro-3-[5-(2-methylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
15	N-(3-{5-cyclopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
16	N-{4-fluoro-3-[5-(2-methylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
17	N-(3-{5-cyclopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-2,4-dimethyl-1,3-oxazole-5-carboxamide
18	N-(3-{5-cyclopentyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
19	N-(3-{5-cyclohexyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
20	N-(3-{5-cyclobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
21	N-{3-[5-(2,2-dimethylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
22	N-(3-{5-tert-butyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
23	3-fluoro-N-{4-fluoro-3-[5-(pentan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
24	3-fluoro-N-{4-fluoro-3-[5-(2-methylbutan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
25	N-{3-[5-(butan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide

26	N-{3-[5-(cyclobutylmethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
27	3-fluoro-N-{4-fluoro-3-[5-(3-methylbutyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
28	3-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
29	N-(3-{5-cyclopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide
30	N-(3-{5-cyclopentyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide
31	N-(3-{5-cyclobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide
32	N-{3-[5-(2,2-dimethylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
33	N-(3-{5-tert-butyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide
34	3,3-difluoro-N-{4-fluoro-3-[5-(pentan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
35	3,3-difluoro-N-{4-fluoro-3-[5-(2-methylbutan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
36	N-{3-[5-(butan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
37	N-{3-[5-(cyclobutylmethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
38	3,3-difluoro-N-{4-fluoro-3-[5-(3-methylbutyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
39	3,3-difluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
40	N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
41	(3R)-3-fluoro-N-{4-fluoro-3-[5-(2-methylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
42	(3R)-N-(3-{5-cyclopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
43	(3R)-N-(3-{5-cyclopentyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
44	(3R)-N-(3-{5-cyclohexyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
45	(3R)-N-(3-{5-cyclobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
46	(3R)-N-{3-[5-(2,2-dimethylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide
47	(3R)-N-(3-{5-tert-butyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
48	(3R)-3-fluoro-N-{4-fluoro-3-[5-(pentan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
49	(3R)-3-fluoro-N-{4-fluoro-3-[5-(2-methylbutan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
50	(3R)-N-{3-[5-(butan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide

51	(3R)-N-{3-[5-(cyclobutylmethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide
52	(3R)-3-fluoro-N-{4-fluoro-3-[5-(3-methylbutyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
53	(3R)-3-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
54	N-{4-fluoro-3-[5-(2-methylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
55	N-(3-{5-cyclopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)furan-2-carboxamide
56	N-(3-{5-cyclopentyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)furan-2-carboxamide
57	N-(3-{5-cyclohexyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)furan-2-carboxamide
58	3-fluoro-N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
59	N-{3-[5-(2,2-dimethylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}furan-2-carboxamide
60	N-{4-fluoro-3-[5-(2-methylbutan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
61	N-{3-[5-(butan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}furan-2-carboxamide
62	N-{3-[5-(cyclobutylmethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}furan-2-carboxamide
63	N-{4-fluoro-3-[5-(3-methylbutyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
64	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
65	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-5-methylpyrazine-2-carboxamide
66	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methylcyclopentane-1-carboxamide
67	5-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyridine-2-carboxamide
68	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-methyl-5-(trifluoromethyl)-1,3-oxazole-4-carboxamide
69	2-cyclopropyl-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}acetamide
70	3,5-difluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyridine-2-carboxamide
71	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-(trifluoromethyl)cyclopentane-1-carboxamide
72	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,5-dimethylfuran-3-carboxamide
73	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4-methyl-1,3-oxazole-5-carboxamide
74	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,5-dimethyl-1,3-oxazole-4-carboxamide
75	2-cyclopropyl-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-1,3-oxazole-5-carboxamide
76	2-cyclopropyl-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4-methyl-1,3-oxazole-5-carboxamide
77	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-methyloxolane-2-carboxamide

78	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4-methyl-2-(trifluoromethyl)-1,3-oxazole-5-carboxamide
79	2-[(tert-butoxy)methyl]-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4-methyl-1,3-oxazole-5-carboxamide
80	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}oxane-2-carboxamide
81	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4,5-dimethyl-1,3-oxazole-2-carboxamide
82	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyridine-2-carboxamide
83	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-methyl-1,3-oxazole-5-carboxamide
84	5-cyano-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyridine-2-carboxamide
85	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-methyl-1,3-oxazole-4-carboxamide
86	6-chloro-3-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyridine-2-carboxamide
87	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrazine-2-carboxamide
88	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}oxolane-2-carboxamide
89	5-chloro-2-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}benzamide
90	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropanecarboxamide
91	N-(3-{5-cyclopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)azetidine-1-carboxamide
92	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
93	N-(3-{5-cyclobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)azetidine-1-carboxamide
94	N-{3-[5-(2,2-dimethylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
95	N-{4-fluoro-3-[5-(pentan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
96	N-{3-[5-(butan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
97	N-{3-[5-(cyclobutylmethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
98	N-{4-fluoro-3-[5-(3-methylbutyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
99	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
100	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
101	N-(3-{5-cyclobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-2,4-dimethyl-1,3-oxazole-5-carboxamide
102	N-{3-[5-(2,2-dimethylpropyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
103	N-(3-{5-tert-butyl-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-2,4-dimethyl-1,3-oxazole-5-carboxamide
104	N-{4-fluoro-3-[5-(2-methylbutan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide

105	N-{3-[5-(butan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
106	N-{3-[5-(cyclobutylmethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
107	N-{4-fluoro-3-[5-(3-methylbutyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
108	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
109	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-5-methylfuran-2-carboxamide
110	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-5-methoxyfuran-2-carboxamide
111	5-[(dimethylamino)methyl]-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
112	5-cyano-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
113	5-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
114	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4,5-dimethylfuran-2-carboxamide
115	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methylfuran-2-carboxamide
116	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-1-benzofuran-2-carboxamide
117	3,3-difluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-1-methylcyclobutane-1-carboxamide
118	3,3-difluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclobutane-1-carboxamide
119	methyl 8-({4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}carbamoyl)cubane-1-carboxylate
120	methyl 3-({4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}carbamoyl)bicyclo[1.1.1]pentane-1-carboxylate
121	3-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclobutane-1-carboxamide
122	N-{4-fluoro-3-[5-(morpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
123	propan-2-yl N-{2-[2-fluoro-5-(furan-2-amido)phenyl]-2H-pyrazolo[3,4-b]pyridin-5-yl}carbamate
124	3,3-difluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
125	N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide
126	N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
127	(3R)-N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
128	N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-2,4-dimethyl-1,3-oxazole-5-carboxamide
129	N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)azetidine-1-carboxamide
130	N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)furan-2-carboxamide

131	3-fluoro-N-{4-fluoro-3-[5-(pyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
132	3-fluoro-N-{4-fluoro-3-[5-(morpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
133	(3R)-N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide
134	(3R)-3-fluoro-N-{4-fluoro-3-[5-(pyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
135	(3R)-3-fluoro-N-{4-fluoro-3-[5-(morpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
136	propan-2-yl N-[2-(2-fluoro-5-[(3R)-3-fluoropyrrolidine-1-carbonyl]amino)phenyl]-2H-pyrazolo[3,4-b]pyridin-5-yl]carbamate
137	N-{4-fluoro-3-[5-(morpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
138	propan-2-yl N-(2-{5-[(azetidine-1-carbonyl)amino]-2-fluorophenyl}-2H-pyrazolo[3,4-b]pyridin-5-yl)carbamate
139	N-{4-fluoro-3-[5-(methylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
140	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}furan-2-carboxamide
141	N-{4-fluoro-3-[5-(pyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
142	1-{4-fluoro-3-[5-(methylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methylurea
143	1-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-dimethylurea
144	N-{3-[5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
145	3,3-difluoro-N-{4-fluoro-3-[5-(morpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
146	propan-2-yl N-(2-{5-[(3,3-difluoroazetidine-1-carbonyl)amino]-2-fluorophenyl}-2H-pyrazolo[3,4-b]pyridin-5-yl)carbamate
147	N-{3-[5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
148	3-fluoro-N-{4-fluoro-3-[5-(oxan-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
149	(3R)-N-{3-[5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide
150	(3R)-3-fluoro-N-{4-fluoro-3-[5-(oxan-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
151	N-{3-[5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}furan-2-carboxamide
152	3-fluoro-N-{4-fluoro-3-[5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
153	N-{4-fluoro-3-[5-(methylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
154	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
155	N-{3-[5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
156	3-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
157	N-{4-fluoro-3-[5-(pyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide

158	N-{4-fluoro-3-[5-(morpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
159	propan-2-yl N-{2-[5-(dimethyl-1,3-oxazole-5-amido)-2-fluorophenyl]-2H-pyrazolo[3,4-b]pyridin-5-yl}carbamate
160	N-{4-fluoro-3-[5-(oxan-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
161	3,3-difluoro-N-{4-fluoro-3-[5-(pyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
162	(3R)-3-fluoro-N-{4-fluoro-3-[5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
163	N-{4-fluoro-3-[5-(pyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
164	N-{4-fluoro-3-[5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
165	3,3-difluoro-N-{4-fluoro-3-[5-(oxan-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
166	3,3-difluoro-N-{4-fluoro-3-[5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
167	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
168	propan-2-yl N-(2-{2-fluoro-5-[(3-fluoroazetidine-1-carbonyl)amino]phenyl}-2H-pyrazolo[3,4-b]pyridin-5-yl)carbamate
169	N-{4-fluoro-3-[5-(oxan-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
170	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
171	3-fluoro-N-[4-fluoro-3-(5-{2-oxa-6-azaspiro[3.3]heptan-6-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
172	3-fluoro-N-(4-fluoro-3-{5-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
173	4,4,4-trifluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}butanamide
174	3,3,3-trifluoropropyl N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}carbamate
175	N-{4-fluoro-3-[5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2,4-dimethyl-1,3-oxazole-5-carboxamide
176	N-{4-fluoro-3-[5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
177	N-(3-{5-[(2S,6S)-2,6-dimethylmorpholin-4-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
178	N-{3-[5-(1,1-dioxo-1 λ ⁶ ,4-thiomorpholin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
179	3-fluoro-N-{4-fluoro-3-[5-(4-methylpiperazin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
180	3-fluoro-N-[4-fluoro-3-(5-{5H,6H,7H,8H-imidazo[1,2-a]pyrazin-7-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
181	3-fluoro-N-{4-fluoro-3-[5-(3-hydroxyazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
182	3-fluoro-N-{4-fluoro-3-[5-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide

183	3-fluoro-N-[4-fluoro-3-(5-{2-oxa-6-azaspiro[3.4]octan-6-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
184	3-fluoro-N-[4-fluoro-3-(5-{8-oxa-3-azabicyclo[3.2.1]octan-3-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
185	3-fluoro-N-(4-fluoro-3-{5-[(2-methoxyethyl)amino]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
186	3-fluoro-N-[4-fluoro-3-(5-{5H,6H,7H,8H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
187	3-fluoro-N-{4-fluoro-3-[5-(3-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
188	N-{3-[5-(3-chloropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
189	3-fluoro-N-{4-fluoro-3-[5-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
190	N-(3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
191	3-fluoro-N-[4-fluoro-3-(5-{6-oxa-1-azaspiro[3.3]heptan-1-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
192	3-fluoro-N-(4-fluoro-3-{5-[3-(methoxymethyl)azetidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
193	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoroazetidine-1-carboxamide
194	N-(3-{5-[(3R,4R)-3,4-difluoropyrrolidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
195	(3R)-3-fluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
196	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
197	3-fluoro-N-[4-fluoro-3-(5-{2-oxa-5-azabicyclo[2.2.2]octan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
198	3-fluoro-N-(4-fluoro-3-{5-[(2-methylpropyl)amino]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
199	N-{3-[5-(ethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
200	3-fluoro-N-(4-fluoro-3-{5-[(propan-2-yl)amino]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
201	3-fluoro-N-[4-fluoro-3-(5-{1-oxa-6-azaspiro[3.3]heptan-6-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
202	3-fluoro-N-[4-fluoro-3-(5-{6-oxa-2-azaspiro[3.4]octan-2-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
203	3-fluoro-N-[4-fluoro-3-(5-{7-oxa-2-azaspiro[3.5]nonan-2-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
204	N-[3-(5-{6,6-difluoro-3-azabicyclo[3.1.0]hexan-3-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoroazetidine-1-carboxamide
205	3-fluoro-N-{4-fluoro-3-[5-(3-methoxyazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
206	5-cyano-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}furan-2-carboxamide
207	2-ethoxy-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide

208	2,2-difluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide
209	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-1-(trifluoromethyl)cyclopropane-1-carboxamide
210	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclobutanecarboxamide
211	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-methylcyclopropane-1-carboxamide
212	3,3,3-trifluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}propanamide
213	4,4,4-trifluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methylbutanamide
214	5,5,5-trifluoro-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pentanamide
215	3-cyclopropyl-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}propanamide
216	2-cyclobutyl-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}acetamide
217	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3,3-dimethylbutanamide
218	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclobut-1-ene-1-carboxamide
219	1-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3,3-bis(² H ₅)methylurea
220	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-5-azaspiro[2.4]heptane-5-carboxamide
221	(3R)-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methylpyrrolidine-1-carboxamide
222	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-5-azaspiro[2.3]hexane-5-carboxamide
223	(1R,5S)-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-azabicyclo[3.1.0]hexane-3-carboxamide
224	3-ethyl-1-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methylurea
225	(3R)-N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methoxypyrrolidine-1-carboxamide
226	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-azaspiro[3.3]heptane-2-carboxamide
227	1-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-methyl-3-(2,2,2-trifluoroethyl)urea
228	1-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3,3-dimethylurea
229	N-{4-fluoro-3-[5-(propan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-1,4-diazabicyclo[3.2.2]nonane-4-carboxamide
230	N-(3-{5-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
231	3-fluoro-N-[4-fluoro-3-(5-{6-oxa-1-azaspiro[3.3]heptan-1-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
232	3-fluoro-N-(4-fluoro-3-{5-[3-(methoxymethyl)azetidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
233	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoroazetidine-1-carboxamide
234	N-(3-{5-[(3R,4R)-3,4-difluoropyrrolidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide

235	3-fluoro-N-[4-fluoro-3-(5-{3-oxa-8-azabicyclo[3.2.1]octan-8-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
236	1-(2-{2-fluoro-5-[(3-fluoroazetidine-1-carbonyl)amino]phenyl}-2H-pyrazolo[3,4-b]pyridin-5-yl)piperidine-4-carboxylic acid
237	3-fluoro-N-(4-fluoro-3-{5-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
238	3-fluoro-N-(4-fluoro-3-{5-[4-(oxetan-3-yl)piperidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
239	3-fluoro-N-[4-fluoro-3-(5-{2-thia-6-azaspiro[3.3]heptan-6-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
240	3-fluoro-N-[4-fluoro-3-(5-{6-oxa-3-azabicyclo[3.1.1]heptan-3-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
241	N-[3-(5-{5-azaspiro[2.4]heptan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoroazetidine-1-carboxamide
242	N-[3-(5-{5-azaspiro[2.4]heptan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-5-azaspiro[2.4]heptane-5-carboxamide
243	N-[3-(5-{2-azaspiro[3.3]heptan-2-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoroazetidine-1-carboxamide
244	3-fluoro-N-[4-fluoro-3-(5-{8-oxa-2-azaspiro[4.5]decan-2-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
245	3-fluoro-N-[4-fluoro-3-(5-{6-oxo-2,5-diazaspiro[3.4]octan-2-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
246	N-[4-fluoro-3-(5-{6-oxa-2-azaspiro[3.4]octan-2-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]-6-oxa-2-azaspiro[3.4]octane-2-carboxamide
247	tert-butyl 2-(2-{5-[(azetidine-1-carbonyl)amino]-2-fluorophenyl}-2H-pyrazolo[3,4-b]pyridin-5-yl)pyrrolidine-1-carboxylate
248	3-fluoro-N-[4-fluoro-3-(5-{2-oxa-7-azaspiro[3.5]nonan-7-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
249	N-{3-[5-(cyclopropylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
250	N-(4-fluoro-3-{5-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
251	3-fluoro-N-{4-fluoro-3-[5-(3-hydroxy-3-methylazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
252	3,3-difluoro-N-(4-fluoro-3-{5-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
253	(3R)-3-fluoro-N-(4-fluoro-3-{5-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)pyrrolidine-1-carboxamide
254	N-(3-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-5-azaspiro[2.3]hexane-5-carboxamide
255	N-{3-[5-(3,3-dimethylazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
256	(1S,2R)-2-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide
257	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]azetidine-1-carboxamide
258	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3,3-difluoroazetidine-1-carboxamide
259	(3R)-N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoropyrrolidine-1-carboxamide

260	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-5-azaspiro[2.3]hexane-5-carboxamide
261	N-[3-(5-{1,1-difluoro-5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-3-fluoroazetidine-1-carboxamide
262	N-{3-[5-(3,3-difluoropyrrolidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
263	3-fluoro-N-[4-fluoro-3-(5-{3-oxa-6-azabicyclo[3.1.1]heptan-6-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
264	N-{3-[5-(azetidin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
265	3-fluoro-N-(4-fluoro-3-{5-[3-(trifluoromethyl)azetidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
266	N-{3-[5-(3-cyanoazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
267	N-{3-[5-(1-acetylazetidin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
268	(1S,2R)-N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2-fluorocyclopropane-1-carboxamide
269	(1R,2S)-2-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide
270	3-fluoro-N-{4-fluoro-3-[5-(piperazin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
271	(1R,2S)-N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2-fluorocyclopropane-1-carboxamide
272	(1R,2S)-N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]-2-fluorocyclopropane-1-carboxamide
273	(1S,2R)-2-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide
274	N-(4-fluoro-3-{5-[3-(trifluoromethyl)azetidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
275	(3R)-3-fluoro-N-(4-fluoro-3-{5-[3-(trifluoromethyl)azetidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)pyrrolidine-1-carboxamide
276	N-(3-{5-chloro-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
277	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-4-(hydroxymethyl)-2-methyl-1,3-oxazole-5-carboxamide
278	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-(² H ₃)methyl-4-methyl-1,3-oxazole-5-carboxamide
279	N-(4-fluoro-3-{5-[3-(trifluoromethyl)azetidin-1-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)-2,4-dimethyl-1,3-oxazole-5-carboxamide
280	N-{2-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]pyridin-4-yl}azetidine-1-carboxamide
281	3,3-difluoro-N-{2-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]pyridin-4-yl}azetidine-1-carboxamide
282	N-[2-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-yl]azetidine-1-carboxamide
283	N-{4-chloro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3-fluoroazetidine-1-carboxamide
284	N-{4-chloro-3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide

285	N-{4-chloro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
286	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-chlorophenyl]azetidine-1-carboxamide
287	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
288	N-{4-fluoro-3-[5-(oxan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
289	N-{3-[5-(1,4-dioxan-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
290	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
291	3-fluoro-N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
292	N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
293	3-fluoro-N-{4-fluoro-3-[5-(piperidin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
294	3-fluoro-N-{4-fluoro-3-[5-(pyrazin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
295	3-fluoro-N-{4-fluoro-3-[5-(1H-imidazol-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
296	N-{3-[5-(1-benzylpiperidin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
297	3-fluoro-N-{4-fluoro-3-[5-(1H-pyrazol-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
298	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
299	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
300	(3R)-N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide
301	3-fluoro-N-{4-fluoro-3-[5-(1-methyl-1H-imidazol-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
302	(3R)-3-fluoro-N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
303	3,3-difluoro-N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
304	3-fluoro-N-{4-fluoro-3-[5-(1-methyl-1H-pyrazol-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
305	3-fluoro-N-[4-fluoro-3-(5-{1-[(4-fluorophenyl)methyl]piperidin-4-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl]azetidine-1-carboxamide
306	N-(3-{5-[bis(² H ₃)methylamino]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)azetidine-1-carboxamide
307	N-(3-{5-[bis(² H ₃)methylamino]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide
308	(3R)-N-(3-{5-[bis(² H ₃)methylamino]-2H-pyrazolo[3,4-b]pyridin-2-yl}-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide
309	3,3-difluoro-N-{4-fluoro-3-[5-(3-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide

310	N-{3-[5-(3-chloropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3,3-difluoroazetidine-1-carboxamide
311	3-fluoro-N-(4-fluoro-3-{2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
312	3-fluoro-N-{4-fluoro-3-[5-(3-methylpyrazin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
313	N-{4-fluoro-3-[5-(3-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
314	N-(3-{5-[bis(² H ₃)methylamino]-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide
315	N-{3-[5-(3-chloropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}azetidine-1-carboxamide
316	(3R)-N-{3-[5-(3-chloropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoropyrrolidine-1-carboxamide
317	(3R)-3-fluoro-N-{4-fluoro-3-[5-(3-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
318	3-fluoro-N-(4-fluoro-3-{5-methyl-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)azetidine-1-carboxamide
319	3-fluoro-N-{4-fluoro-3-[5-(1H-pyrazol-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
320	N-{4-fluoro-3-[5-(trifluoromethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
321	3-fluoro-N-{4-fluoro-3-[5-(trifluoromethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
322	(3R)-3-fluoro-N-{4-fluoro-3-[5-(trifluoromethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
323	3-fluoro-N-{4-fluoro-3-[5-(1H-imidazol-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
324	3,3-difluoro-N-{4-fluoro-3-[5-(trifluoromethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
325	N-{3-[5-(1-cyclopropyl-1H-pyrazol-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-3-fluoroazetidine-1-carboxamide
326	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}cyclopropanecarboxamide
327	N-{4-fluoro-3-[5-(3-fluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropanecarboxamide
328	3-fluoro-N-{4-fluoro-3-[5-(4-methyl-1H-imidazol-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
329	3-fluoro-N-{4-fluoro-3-[5-(5-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
330	N-{4-fluoro-3-[5-(5-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
331	N-{3-[5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}cyclopropanecarboxamide
332	N-{4-fluoro-3-[5-(3-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropanecarboxamide
333	N-{3-[5-(3-chloropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}cyclopropanecarboxamide
334	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-2-(hydroxymethyl)-4-methyl-1,3-oxazole-5-carboxamide

335	N-(4-fluoro-3-{5-[3-(hydroxymethyl)pyridin-2-yl]-2H-pyrazolo[3,4-b]pyridin-2-yl}phenyl)-2,4-dimethyl-1,3-oxazole-5-carboxamide
336	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrrolidine-1-carboxamide
337	N-[3-(5-{5-azaspiro[2.3]hexan-5-yl}-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl]pyrrolidine-1-carboxamide
338	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}pyrrolidine-1-carboxamide
339	(1R,2S)-N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]-4-fluorophenyl}-2-fluorocyclopropane-1-carboxamide
340	(3R)-N-(2-{5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl}pyridin-4-yl)-3-fluoropyrrolidine-1-carboxamide
341	N-{2-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]pyridin-4-yl}azetidine-1-carboxamide
342	3-fluoro-N-{2-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]pyridin-4-yl}azetidine-1-carboxamide
343	N-{3-[5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
344	N-{3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}azetidine-1-carboxamide
345	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}pyrazine-2-carboxamide
346	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}spiro[2.2]pentane-1-carboxamide
347	N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3,3-dimethylcyclobut-1-ene-1-carboxamide
348	1-cyano-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide
349	(1S,2S)-2-fluoro-N-{4-fluoro-3-[5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}cyclopropane-1-carboxamide
350	N-{4-fluoro-3-[5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl]phenyl}-3,3-dimethylcyclobut-1-ene-1-carboxamide
351	N-(4-fluoro-3-(5-isopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-2,4-dimethyloxazole-5-carboxamide
352	N-(4-fluoro-3-(5-phenyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-2,4-dimethyloxazole-5-carboxamide
353	3,3-difluoro-N-(4-fluoro-3-(5-phenyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide

Embodiment 35. A compound of Formula (I) or a pharmaceutically acceptable salt thereof according to Embodiment 34, wherein said compound is selected from compounds 1-76, 78-79, 81-87, 89-115, 117-118 and 121-353 of Table 1.

Embodiment 36. A pharmaceutical composition comprising a compound of Formula (I) or a pharmaceutically acceptable salt thereof according to any one of Embodiments 1-35, and at least one excipient.

Embodiment 37. A combination comprising a compound of Formula (I) or a pharmaceutically acceptable salt thereof according to any one of Embodiments 1-35, or a pharmaceutical composition thereof according to Embodiment 36, and one or more therapeutically active agents.

Embodiment 38. A compound according to any one of Embodiments 1-35, or a pharmaceutical composition according to Embodiment 36, for use in therapy.

Embodiment 39. A compound according to any one of Embodiments 1-35, or a pharmaceutical composition according to Embodiment 36, for use in the treatment of a disease selected from leishmaniasis, Chagas diseases and human African trypanosomiasis.

Embodiment 40. Use of a compound according to any one of Embodiments 1-35, or a pharmaceutical composition according to Embodiment 36, in the manufacture of a medicament for the treatment of a disease selected from leishmaniasis, Chagas diseases and human African trypanosomiasis.

Embodiment 41. A method of inhibiting growth and proliferation of a kinetoplastid parasite in a subject, comprising administering to a subject in need thereof, a therapeutically effective amount of a compound of Formula (I) or a pharmaceutically acceptable salt thereof, according to any one of Embodiments 1-35.

Embodiment 42. A method of treating a disorder or disease caused by a kinetoplastid parasite, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I) or a pharmaceutically acceptable salt thereof according to any one of Embodiments 1-35, and optionally in combination with a second agent; wherein the disease is selected from leishmaniasis, Chagas diseases and human African trypanosomiasis.

Embodiment 43. The method according to Embodiment 42, wherein said disease is leishmaniasis selected from visceral leishmaniasis and cutaneous leishmaniasis.

Embodiment 44. The method according to Embodiment 43, wherein said second agent selected from stibogluconate, meglumine antimoniate, amphotericin, miltefosine, and paromomycin.

Embodiment 45. The method according to Embodiment 42, wherein said disease is Chagas disease; and said second agent is selected from benznidazole, nifurtimox and amphotericin.

Embodiment 46. The method according to Embodiment 42, wherein said disease is human African trypanosomiasis; and said second agent is pentamidine, suramin, melarsoprol, eflornithine, and nifurtimox.

Depending on the choice of the starting materials and procedures, the compounds can be present in the form of one of the possible stereoisomers or as mixtures thereof, for example as pure optical isomers, or as stereoisomer mixtures, such as racemates and diastereoisomer mixtures, depending on the number of asymmetric carbon atoms. The present invention is meant to include all such possible stereoisomers, including racemic mixtures, diasteriomic mixtures and optically pure forms. Optically active (*R*)- and (*S*)- stereoisomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. If the compound contains a double bond, the substituent may be E or Z configuration. If the

compound contains a disubstituted cycloalkyl, the cycloalkyl substituent may have a cis- or trans-configuration. All tautomeric forms are also intended to be included.

As used herein, the terms "salt" or "salts" refers to an acid addition or base addition salt of a compound of the invention. "Salts" include in particular "pharmaceutical acceptable salts". The term "pharmaceutically acceptable salts" refers to salts that retain the biological effectiveness and properties of the compounds of this invention and, which typically are not biologically or otherwise undesirable. In many cases, the compounds of the present invention are capable of forming acid and/or base salts by virtue of the presence of amino and/or carboxyl groups or groups similar thereto.

Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids. Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, sulfosalicylic acid, and the like.

Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases. Inorganic bases from which salts can be derived include, for example, ammonium salts and metals from columns I to XII of the periodic table. In certain embodiments, the salts are derived from sodium, potassium, ammonium, calcium, magnesium, iron, silver, zinc, and copper; particularly suitable salts include ammonium, potassium, sodium, calcium and magnesium salts. Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like. Certain organic amines include isopropylamine, benzathine, choline, diethanolamine, diethylamine, lysine, meglumine, piperazine and tromethamine.

In another aspect, the present invention provides compounds of Formula (I) or subformulae thereof, in acetate, ascorbate, adipate, aspartate, benzoate, besylate, bromide/hydrobromide, bicarbonate/carbonate, bisulfate/sulfate, camphorsulfonate, caprate, chloride/hydrochloride, chlortheophyllonate, citrate, ethandisulfonate, fumarate, gluceptate, gluconate, glucuronate, glutamate, glutarate, glycolate, hippurate, hydroiodide/iodide, isethionate, lactate, lactobionate, laurylsulfate, malate, maleate, malonate, mandelate, mesylate, methylsulphate, mucate, naphthoate, napsylate, nicotinate, nitrate, octadecanoate, oleate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, polygalacturonate, propionate, sebacate, stearate, succinate, sulfosalicylate, sulfate, tartrate, tosylate trifenate, trifluoroacetate or xinafoate salt form.

In another aspect, the present invention provides compounds of Formula (I) or subformulae thereof, in sodium, potassium, ammonium, calcium, magnesium, iron, silver, zinc, copper,

isopropylamine, benzathine, choline, diethanolamine, diethylamine, lysine, meglumine, piperazine or tromethamine salt form.

Any formula given herein represent unlabeled forms as well as isotopically labeled forms of the compounds. Isotopically labeled compounds have structures depicted by the formulas given herein except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Isotopes that can be incorporated into compounds of the invention include, for example, isotopes of hydrogen.

Further, incorporation of certain isotopes, particularly deuterium (i.e., ^2H or D) may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements or an improvement in therapeutic index or tolerability. It is understood that deuterium in this context is regarded as a substituent of a compound of Formula (I). The concentration of deuterium, may be defined by the isotopic enrichment factor. The term "isotopic enrichment factor" as used herein means the ratio between the isotopic abundance and the natural abundance of a specified isotope. If a substituent in a compound of this invention is denoted as being deuterium, such compound has an isotopic enrichment factor for each designated deuterium atom of at least 3500 (52.5% deuterium incorporation at each designated deuterium atom), at least 4000 (60% deuterium incorporation), at least 4500 (67.5% deuterium incorporation), at least 5000 (75% deuterium incorporation), at least 5500 (82.5% deuterium incorporation), at least 6000 (90% deuterium incorporation), at least 6333.3 (95% deuterium incorporation), at least 6466.7 (97% deuterium incorporation), at least 6600 (99% deuterium incorporation), or at least 6633.3 (99.5% deuterium incorporation). It should be understood that the term "isotopic enrichment factor" can be applied to any isotope in the same manner as described for deuterium.

Other examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, and chlorine, such as ^3H , ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{18}F , ^{31}P , ^{32}P , ^{35}S , ^{36}Cl , ^{123}I , ^{124}I , ^{125}I respectively. Accordingly it should be understood that the invention includes compounds that incorporate one or more of any of the aforementioned isotopes, including for example, radioactive isotopes, such as ^3H and ^{14}C , or those into which non-radioactive isotopes, such as ^2H and ^{13}C are present. Such isotopically labelled compounds are useful in metabolic studies (with ^{14}C), reaction kinetic studies (with, for example ^2H or ^3H), detection or imaging techniques, such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT) including drug or substrate tissue distribution assays, or in radioactive treatment of patients. In particular, an ^{18}F or labeled compound may be particularly desirable for PET or SPECT studies. Isotopically-labeled compounds of formula (I) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations using an appropriate isotopically-labeled reagents in place of the non-labeled reagent previously employed.

Any asymmetric atom (e.g., carbon or the like) of the compound(s) of the present invention can be present in racemic or enantiomerically enriched, for example the (*R*)-, (*S*)- or (*R,S*)- configuration. In certain embodiments, each asymmetric atom has at least 50 % enantiomeric excess, at least 60 % enantiomeric excess, at least 70 % enantiomeric excess, at least 80 %
 5 enantiomeric excess, at least 90 % enantiomeric excess, at least 95 % enantiomeric excess, or at least 99 % enantiomeric excess in the (*R*)- or (*S*)- configuration. Substituents at atoms with unsaturated double bonds may, if possible, be present in *cis*- (*Z*)- or *trans*- (*E*)- form.

Accordingly, as used herein a compound of the present invention can be in the form of one of the possible stereoisomers, rotamers, atropisomers, tautomers or mixtures thereof, for
 10 example, as substantially pure geometric (*cis* or *trans*) stereoisomers, diastereomers, optical isomers (antipodes), racemates or mixtures thereof.

Any resulting mixtures of stereoisomers can be separated on the basis of the physicochemical differences of the constituents, into the pure or substantially pure geometric or optical isomers, diastereomers, racemates, for example, by chromatography and/or fractional
 15 crystallization.

Any resulting racemates of final products or intermediates can be resolved into the optical antipodes by known methods, e.g., by separation of the diastereomeric salts thereof, obtained with an optically active acid or base, and liberating the optically active acidic or basic compound. In particular, a basic moiety may thus be employed to resolve the compounds of the present
 20 invention into their optical antipodes, e.g., by fractional crystallization of a salt formed with an optically active acid, e.g., tartaric acid, dibenzoyl tartaric acid, diacetyl tartaric acid, di-*O,O'*-*p*-toluoyl tartaric acid, mandelic acid, malic acid or camphor-10-sulfonic acid. Racemic products can also be resolved by chiral chromatography, e.g., high pressure liquid chromatography (HPLC) using a chiral adsorbent.

25 **Pharmacology and Utility**

In one aspect, the invention relates to small molecules compounds of Formula (I) that target the proteasome of kinetoplastid parasites and are useful as a therapy; particularly, for preventing and treating diseases and conditions that are caused by the infection of kinetoplastid parasites. The activity of a compound according to the present invention can be assessed by
 30 the *in vitro* and *in vivo* methods described in the Biological Assay section *infra*. It is understood that the assays illustrate the invention without in any way limiting the scope of the invention.

Thus, as a further aspect, the present invention provides for the use of a compound of Formula (I) or subformulae thereof, or a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, as a therapy for a disease or condition that can benefit from inhibition of
 35 growth and proliferation of kinetoplastid parasites; and for the manufacture of a medicament, such as for the treatment of a disease caused by the growth and proliferation of a kinetoplastid parasite. In one embodiment, the disease being treated is selected from leishmaniasis, Chagas disease and Human African trypanosomiasis. In another embodiment, the disease

being treated is Leishmaniasis caused by the parasite including, but is not limited to, *Leishmania donovani*, *Leishmania infantum*, *Leishmania braziliensis*, *Leishmania panamensis*, *Leishmania guayanensis*, *Leishmania amazonensis*, *Leishmania mexicana*, *Leishmania tropica*, *Leishmania major*. In one embodiment, the disease being treated is visceral leishmaniasis. In another embodiment, the disease being treated is cutaneous leishmaniasis. In another embodiment, the disease being treated is Chagas disease caused by *Trypanosoma cruzi*. In yet another embodiment, the disease being treated is human African trypanosomiasis caused by *Trypanosoma brucei*, *Trypanosoma brucei gambiense* or *Trypanosoma brucei rhodesiense*.

In accordance with the foregoing, the present invention further provides a method for preventing or treating leishmaniasis, Chagas disease or Human African trypanosomiasis in a subject in need of such treatment, comprising administering to said subject a therapeutically effective amount of a compound selected from Formula (I) or subformulae thereof, a pharmaceutically acceptable salt or stereoisomer thereof. The required dosage will vary depending on the mode of administration, the particular condition to be treated and the effect desired.

Pharmaceutical Compositions, Dosage and Administration

In another aspect, the present invention provides a pharmaceutical composition comprising a compound of the present invention, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. In a further embodiment, the composition comprises at least two pharmaceutically acceptable carriers, such as those described herein. The pharmaceutical composition can be formulated for particular routes of administration such as oral administration, parenteral administration (e.g. by injection, infusion, transdermal or topical administration), and rectal administration. Topical administration may also pertain to inhalation or intranasal application. The pharmaceutical compositions of the present invention can be made up in a solid form (including, without limitation, capsules, tablets, pills, granules, powders or suppositories), or in a liquid form (including, without limitation, solutions, suspensions or emulsions). Tablets may be either film coated or enteric coated according to methods known in the art. Typically, the pharmaceutical compositions are tablets or gelatin capsules comprising the active ingredient together with one or more of:

- a) diluents, e.g., lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and/or glycine;
- b) lubricants, e.g., silica, talcum, stearic acid, its magnesium or calcium salt and/or polyethyleneglycol; for tablets also
- c) binders, e.g., magnesium aluminum silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and/or polyvinylpyrrolidone; if desired
- d) disintegrants, e.g., starches, agar, alginic acid or its sodium salt, or effervescent mixtures; and
- e) absorbents, colorants, flavors and sweeteners.

The pharmaceutical composition or combination of the present invention can be in unit dosage of about 1-1000 mg of active ingredient(s) for a subject of about 50-70 kg, or about 1-500 mg or about 1-250 mg or about 1-150 mg or about 0.5-100 mg, or about 1-50 mg of active ingredients. The therapeutically effective dosage of a compound, the pharmaceutical
5 composition, or the combinations thereof, is dependent on the species of the subject, the body weight, age and individual condition, the disorder or disease or the severity thereof being treated. A physician, clinician or veterinarian of ordinary skill can readily determine the effective amount of each of the active ingredients necessary to prevent, treat or inhibit the progress of the disorder or disease.

10 The above-cited dosage properties are demonstrable *in vitro* and *in vivo* tests using advantageously mammals, *e.g.*, mice, rats, dogs, monkeys or isolated organs, tissues and preparations thereof. The compounds of the present invention can be applied *in vitro* in the form of solutions, *e.g.*, aqueous solutions, and *in vivo* either enterally, parenterally, advantageously intravenously, *e.g.*, as a suspension or in aqueous solution. The dosage *in*
15 *vitro* may range between about 10^{-3} molar and 10^{-9} molar concentrations. A therapeutically effective amount *in vivo* may range depending on the route of administration, between about 0.1-500 mg/kg, or between about 1-100 mg/kg.

Compounds of the invention can be administered in therapeutically effective amounts in combination with one or more therapeutic agents (pharmaceutical combinations). The
20 compound of the present invention may be administered either simultaneously with, or before or after, one or more other therapeutic agent. The compound of the present invention may be administered separately, by the same or different route of administration, or together in the same pharmaceutical composition as the other agents. A therapeutic agent is, for example, a chemical compound, peptide, antibody, antibody fragment or nucleic acid, which is
25 therapeutically active or enhances the therapeutic activity when administered to a patient in combination with a compound of the invention.

Products provided as a combined preparation include a composition comprising the compound of Formula (I) or subformulae thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, and the other therapeutic agent(s) together in the same pharmaceutical
30 composition, or the compound of Formula (I) and the other therapeutic agent(s) in separate form, *e.g.* in the form of a kit. In one embodiment, the invention provides a pharmaceutical composition comprising a compound of Formula (I) or subformulae thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof, and another therapeutic agent(s). Optionally, the pharmaceutical composition may comprise a pharmaceutically acceptable carrier, as
35 described above. In another embodiment, the invention provides a product comprising a compound of Formula (I) and at least one other therapeutic agent as a combined preparation for simultaneous, separate or sequential use in therapy.

In one embodiment, the invention provides a kit comprising two or more separate pharmaceutical compositions, at least one of which contains a compound of Formula (I) or subformulae thereof, a pharmaceutically acceptable salt thereof, or a stereoisomer thereof. In one embodiment, the kit comprises means for separately retaining said compositions, such as a container, divided bottle, or divided foil packet. An example of such a kit is a blister pack, as typically used for the packaging of tablets, capsules and the like. The kit of the invention may be used for administering different dosage forms, for example, oral and parenteral, for administering the separate compositions at different dosage intervals, or for titrating the separate compositions against one another. To assist compliance, the kit of the invention typically comprises directions for administration.

In the combination therapies of the invention, the compound of the invention and the other therapeutic agent may be manufactured and/or formulated by the same or different manufacturers. Moreover, the compound of the invention and the other therapeutic may be brought together into a combination therapy: (i) prior to release of the combination product to physicians (*e.g.* in the case of a kit comprising the compound of the invention and the other therapeutic agent); (ii) by the physician themselves (or under the guidance of the physician) shortly before administration; (iii) in the patient themselves, *e.g.* during sequential administration of the compound of the invention and the other therapeutic agent.

Accordingly, the invention provides the use of a compound of Formula (I) for treating a disease or condition caused by the growth and proliferation of a kinetoplastid parasite, wherein the medicament is prepared for administration with another therapeutic agent. The invention also provides the use of another therapeutic agent for treating a disease or condition caused by the growth and proliferation of a kinetoplastid parasite, wherein the medicament is administered with a compound of Formula (I).

The invention also provides the use of a compound of Formula (I) for treating a disease or condition caused by the growth and proliferation of a kinetoplastid parasite, wherein the patient has previously (*e.g.* within 24 hours) been treated with another therapeutic agent. The invention also provides the use of another therapeutic agent for treating a disease or condition caused by the growth and proliferation of a kinetoplastid parasite, wherein the patient has previously (*e.g.* within 24 hours) been treated with a compound of Formula (I).

In one embodiment, for the treatment of Leishmaniasis, the other therapeutic agent is selected from tsetibogluconate, meglumine antimoniate, Amphotericin, Miltefosine and paromomycin. In one embodiment, for the treatment of Chagas disease, the other therapeutic agent is selected from benznidazole, nifurtimox and/or Amphotericin. In another embodiment, for treatment of human African trypanosomiasis, the other therapeutic agent is selected from pentamidine, suramin, melarsoprol, eflornithine, and/or nifurtimox. Where the compounds of the invention are administered in conjunction with other therapies, dosages of the co-administered

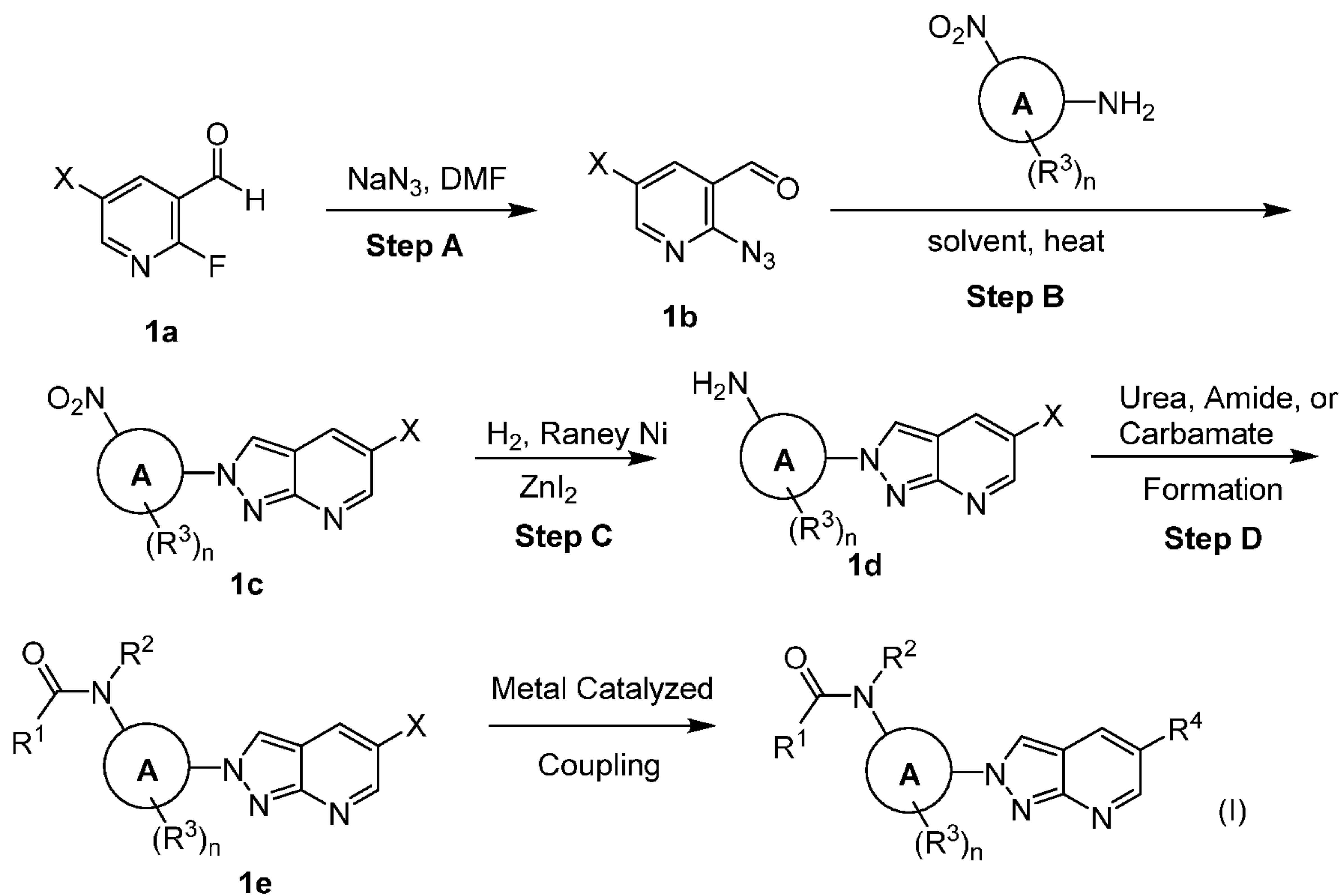
compounds will of course vary depending on the type of co-drug employed, on the specific drug employed, on the condition being treated and so forth.

PREPARATION OF COMPOUNDS

The compounds of the present invention can be prepared in a number of ways known to one skilled in the art of organic synthesis in view of the methods, reaction schemes and examples provided herein. For illustrative purposes, the reaction schemes depicted below provide potential routes for synthesizing the compounds of the present invention as well as key intermediates. For a more detailed description of the individual reaction steps, see the Examples section below. Those skilled in the art will appreciate that other synthetic routes may be used to synthesize the inventive compounds. Although specific starting materials and reagents are depicted in the schemes and discussed below, other starting materials and reagents can be substituted to provide a variety of derivatives and/or reaction conditions. In addition, many of the compounds prepared by the methods described below can be further modified in light of this disclosure using conventional chemistry well known to those skilled in the art. All methods described herein can be performed in any suitable order, unless otherwise indicated or otherwise clearly contradicted by context.

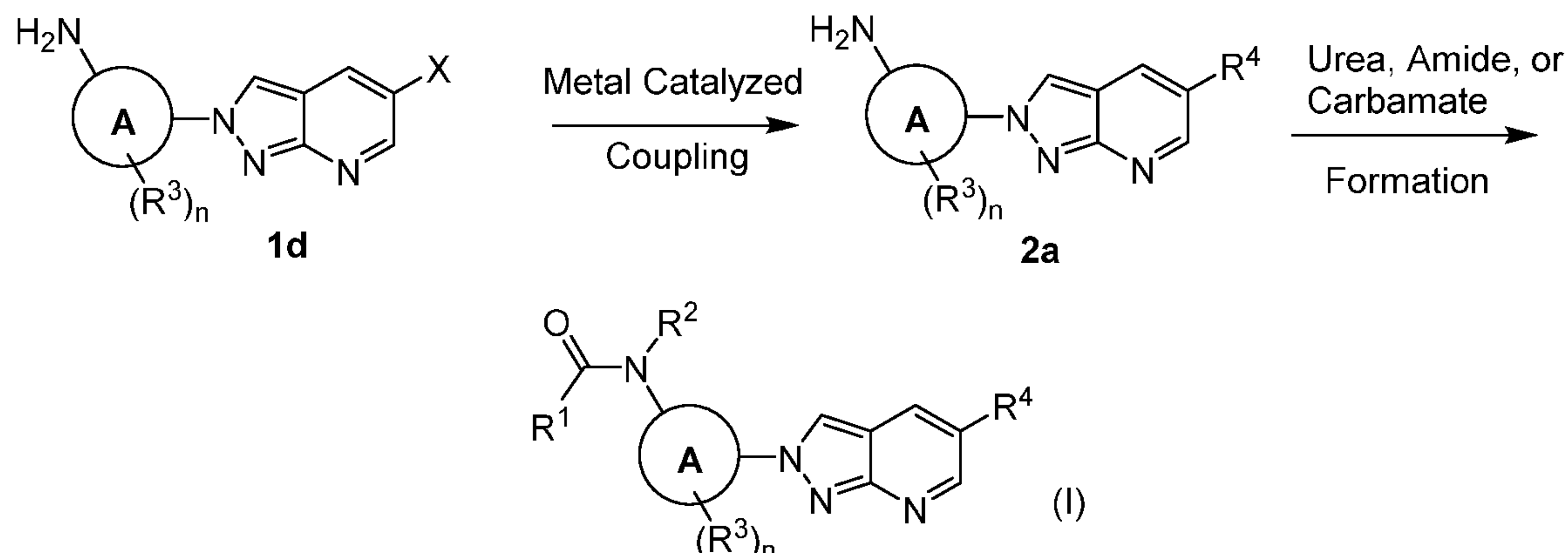
Compounds of Formula (I) can be prepared as generally illustrated in Schemes 1-3 below, wherein R^1 , R^2 , R^3 , R^4 and n are as defined in the Summary of the Invention.

Compounds of Formula (I) can be prepared as generally illustrated in Schemes 1-3 below, wherein X is chloro, bromo or trifluoromethyl; and R^1 , R^2 , R^3 , R^4 and n are as defined in the Summary of the Invention.



Scheme 1

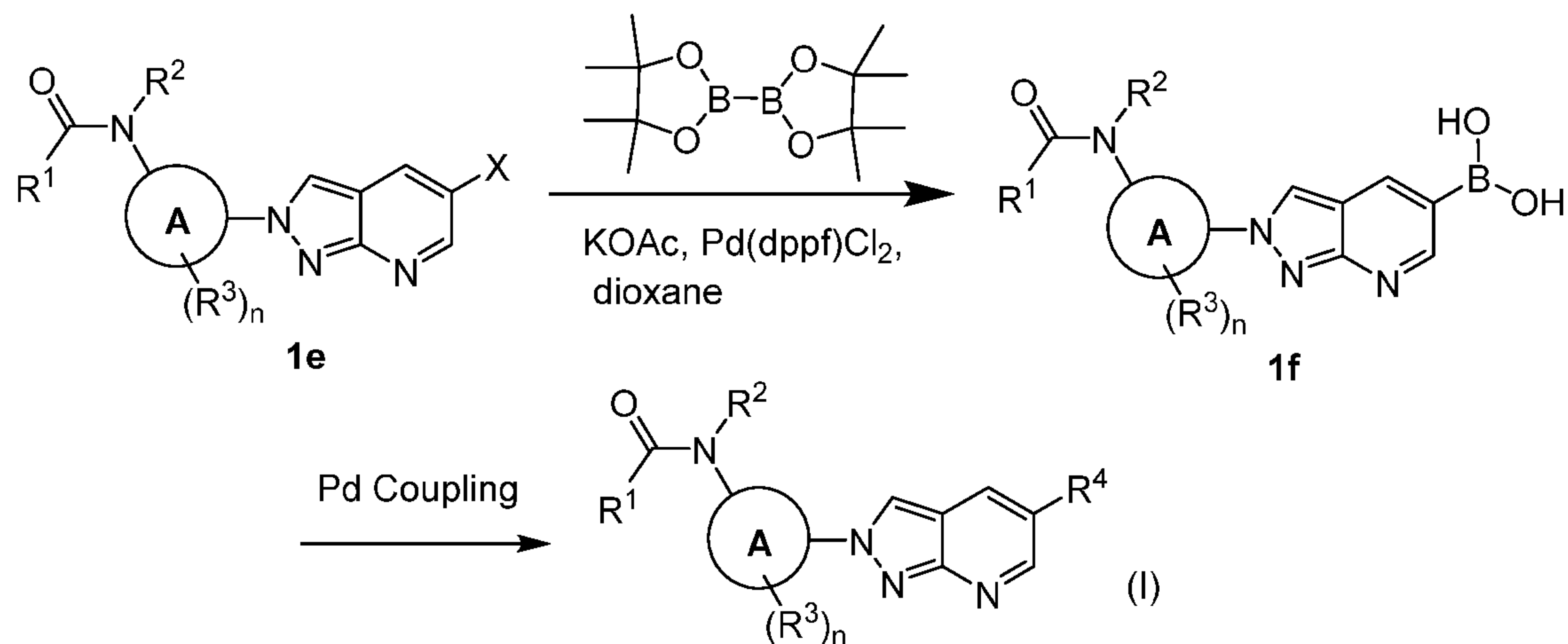
Alternatively, Formula (I) can be prepared from intermediate (**1d**) following the procedures in Scheme 2.



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Scheme 2

Alternatively, Formula (I) can be prepared from intermediate (**1e**) following the procedures in Scheme 3.

**Scheme 3**

The invention further includes any variant of the present processes, in which an intermediate product obtainable at any stage thereof is used as starting material and the remaining steps are carried out, or in which the starting materials are formed *in situ* under the reaction conditions, or in which the reaction components are used in the form of their salts or optically pure material. Compounds of the invention and intermediates can also be converted into each other according to methods generally known to those skilled in the art.

Examples

The Examples herein merely illuminate the invention and does not limit the scope of the invention otherwise claimed.

Temperatures are given in degrees Celsius. If not mentioned otherwise, all evaporations are performed under reduced pressure, typically between about 15 mm Hg and 100 mm Hg (= 20-133 mbar). The structure of final products, intermediates and starting materials is confirmed by standard analytical methods, e.g., microanalysis and spectroscopic characteristics, e.g., MS, IR, NMR.

All starting materials, building blocks, reagents, acids, bases, dehydrating agents, solvents, and catalysts utilized to synthesis the compounds of the present invention are either commercially available or can be produced by organic synthesis methods known to one of ordinary skill in the art (Houben-Weyl 4th Ed. 1952, Methods of Organic Synthesis, Thieme, Volume 21). Further, the compounds of the present invention can be produced by organic synthesis methods known to one of ordinary skill in the art as shown in the following examples. Where desired, conventional protecting groups are used to protect reactive functional groups in accordance with standard practice, for example, see T.W. Greene and P.G.M. Wuts in "Protecting Groups in Organic Synthesis", John Wiley and Sons, 1991.

Unless specified otherwise, the starting materials are generally available from non-excluding commercial sources such as Aldrich Chemicals (Milwaukee, Wis.), TCI Fine Chemicals (Japan), Shanghai Chemhere Co., Ltd.(Shanghai, China), Aurora Fine Chemicals LLC (San Diego, CA), FCH Group (Ukraine), Lancaster Synthesis, Inc. (Windham, N.H.), Acros Organics (Fairlawn, N.J.), Maybridge Chemical Company, Ltd. (Cornwall, England), Tyger Scientific (Princeton, N.J.), AstraZeneca Pharmaceuticals (London, England), Chembridge Corporation (USA), Matrix Scientific (USA), Conier Chem & Pharm Co., Ltd (China), Enamine Ltd (Ukraine), Combi-Blocks, Inc. (San Diego, USA), Oakwood Products, Inc. (USA), Apollo Scientific Ltd. (UK), Allichem LLC. (USA), Rieke Metals (USA), Silicycle Inc (Canada) and Ukrorgsyntez Ltd (Latvia); or are readily prepared using methods well known to those skilled in the art (e.g., prepared by methods generally described in Louis F. Fieser and Mary Fieser, Reagents for Organic Synthesis, v. 1-19, Wiley, New York (1967-1999 ed.), Larock, R.C., *Comprehensive Organic Transformations*, 2nd-ed., Wiley-VCH Weinheim, Germany (1999), or Beilsteins Handbuch der organischen Chemie, 4, Aufl. ed. Springer-Verlag, Berlin, including supplements (also available via the Beilstein online database).

Abbreviations

Abbreviations as used herein, are defined as follows: "1x" for once, "2x" for twice, "3x" for thrice, "°C" for degrees Celsius, "aq" for aqueous, "Col" for column, "eq" for equivalent or equivalents, "g" for gram or grams, "mg" for milligram or milligrams, "L" for liter or liters, "mL" or "ml" for milliliter or milliliters, "μL" or "μl" for microliter or microliters, "N" for normal, "M" for molar, "μM" for micromolar, "nM" for nanomolar, "mol" for mole or moles, "mmol" for millimole or millimoles, "min" for minute or minutes, "h" or "hrs" for hour or hours, "RT" for room temperature, "ON" for overnight, "atm" for atmosphere, "psi" for pounds per square inch, "conc." for concentrate, "aq" for aqueous, "sat" or "sat'd" for saturated, "MW" for molecular

weight, "mw" or "μwave" for microwave, "mp" for melting point, "Wt" for weight, "MS" or "Mass Spec" for mass spectrometry, "ESI" for electrospray ionization mass spectroscopy, "HR" for high resolution, "HRMS" for high resolution mass spectrometry, "LCMS" for liquid chromatography mass spectrometry, "HPLC" for high pressure liquid chromatography, "RP HPLC" for reverse phase HPLC, "TLC" or "tlc" for thin layer chromatography, "NMR" for nuclear magnetic resonance spectroscopy, "nOe" for nuclear Overhauser effect spectroscopy, "1H" for proton, "δ" for delta, "s" for singlet, "d" for doublet, "t" for triplet, "q" for quartet, "m" for multiplet, "br" for broad, "Hz" for hertz, "ee" for "enantiomeric excess" and "α", "β", "R", "r", "S", "s", "E", and "Z" are stereochemical designations familiar to one skilled in the art.

The following abbreviations used herein below have the corresponding meanings:

10	AIBN	azobisisobutyronitrile
	Bn	benzyl
	Boc	<i>tert</i> -butoxy carbonyl
	Boc ₂ O	di- <i>tert</i> -butyl dicarbonate
15	Bu	butyl
	Cs ₂ CO ₃	cesium carbonate anhydrous
	CHCl ₃	chloroform
	DAST	diethylaminosulfurtrifluoride
	DBA	dibenzylideneacetone
20	DBU	2,3,4,6,7,8,9,10-octahydropyrimido[1,2-a]azepine
	DCM	dichloromethane
	DIEA	N,N-Diisopropylethylamine
	DMAP	4-dimethylaminopyridine
	DMF	dimethylformamide
25	DMSO	dimethylsulfoxide
	DPP	diphenylphosphine
	DPPA	diphenylphosphoryl azide
	Dppf	1,1'-Bis(diphenylphosphino)ferrocene
	EA	ethyl acetate
30	Equiv.	equivalence
	Et	ethyl
	Et ₂ O	diethyl ether
	EtOH	ethanol
	EtOAc	ethyl acetate
35	FA	formic acid
	HATU	2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
	HCl	hydrochloric acid

	<i>i</i> -Bu	isobutyl
	<i>i</i> -Pr	isopropyl
	KOAc	potassium acetate
	LiAlH ₄	lithium aluminium hydride
5	Me	methyl
	mCPBA	3-chloroperoxybenzoic acid
	MeCN	acetonitrile
	MnO ₂	manganese dioxide
	N ₂	nitrogen
10	NaBH ₄	sodium borohydride
	NaHCO ₃	sodium bicarbonate
	Na ₂ SO ₄	sodium sulfate
	NBS	<i>N</i> -Bromosuccinimide
	Ph	phenyl
15	PPh ₃	triphenylphosphine
	Ph ₃ P=O	triphenylphosphine oxide
	R _f	retention factor
	RT	room temperature (°C)
	SFC	supercritical fluid chromatography
20	<i>t</i> -Bu or Bu ^t	<i>tert</i> -butyl
	T3P®	Propane phosphonic acid anhydride
	TEA	triethylamine
	TFA	trifluoroacetic acid
	THF	tetrahydrofuran
25	Troc	2,2,2-Trichloroethyl

LCMS**Method 1:**

Waters Acquity UPLC system:

- Acquity Binary Gradient Manager with Degasser
- 30 -Acquity Column Compartment set at 50°C
- Acquity Diode Array Detector

Leap Technologies HTS Pal Autosampler

Antek Chemiluminescent Nitrogen Detector (CLND)

Waters 3100 Mass Spectrometer

- 35 HPLC Column: Thermo Synchronis C18 30x2.1mm

Mobile Phase: (A)95% H₂O/5% MeOH/IPA (75/25, v/v) + 0.05% formic acid, (B) MeOH/IPA (75/25, v/v) + 0.035% formic acid

Gradient: 0.4 mL/minute, initial 2% B for 1.0 minutes, ramp to 95% B over 2.5 minutes, until 4.0 minutes, return to 2% B to at 4.25 minutes until end of run at 5.0.

MS Scan: 150 to 1000amu in 1 second

Diode Array Detector: 190nm – 400nm

5 Method 2:

Waters Acquity UPLC system:

-Acquity Binary Gradient Manager with Degasser

-Acquity Column Compartment set at 50 °C

-Acquity Diode Array Detector

10 -Acquity ELSD

Leap Technologies HTS Pal Autosampler

Waters Qda Mass Detector

HPLC Column: Waters Acquity C18 1.7 μ m 2.1 x 30 mm

Mobile Phase: (A)H₂O + 0.05%TFA and (B)Acetonitrile + 0.05%TFA

15 Gradient: 1 mL/minute, initial 5% B for 0.1 minutes, ramp to 95% B over 1.5 minutes,hold until 1.6 minutes then to 100%B at 1.7 and return to 5% B to at 1.9 minutes until end of run at 2.25.

MS Scan: 160 to 1000 amu in 0.4 seconds

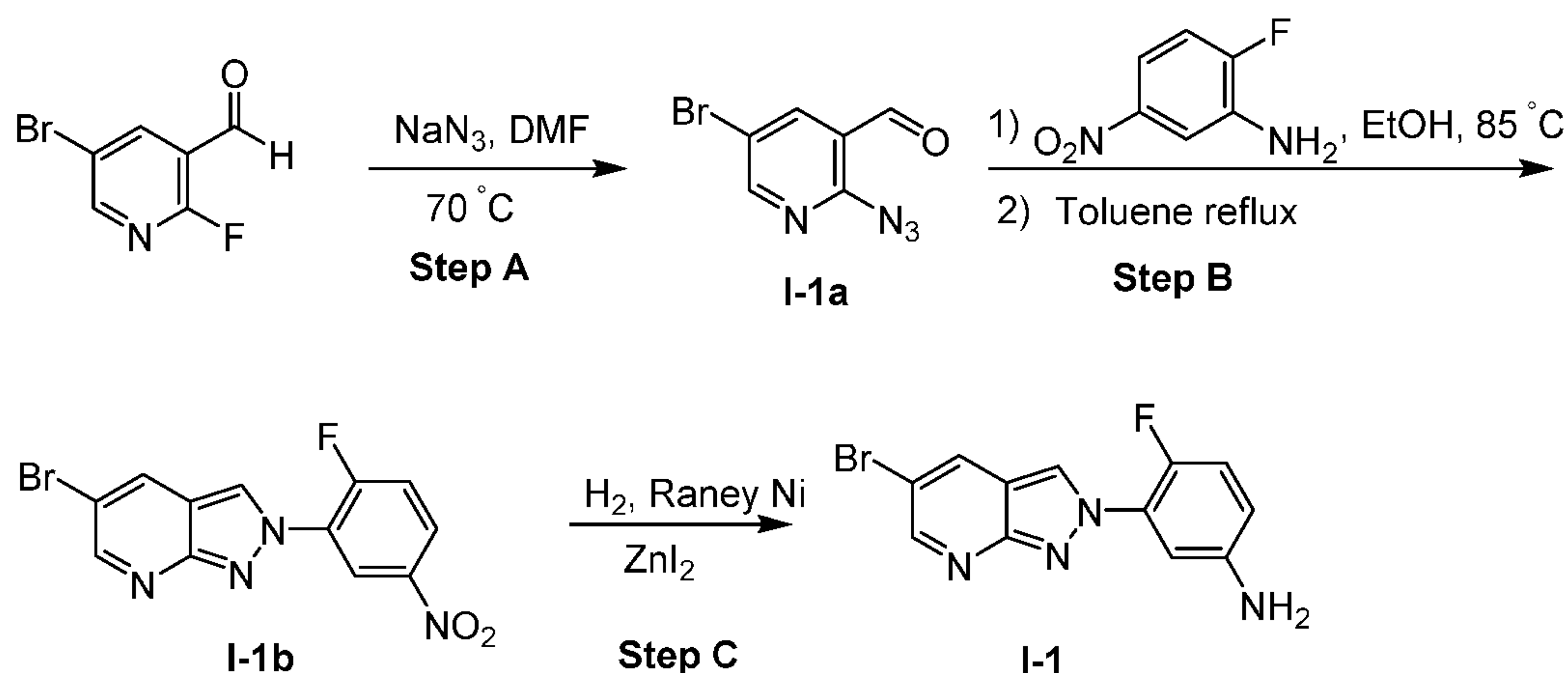
Diode Array Detector: 214 nm – 400nm

NMR. Proton spectra are recorded on a Bruker AVANCE II 400 MHz with 5 mm QNP

20 Cryoprobe or a Bruker AVANCE III 500 MHz with 5 mm QNP probe unless otherwise noted.

Chemical shifts are reported in ppm relative to dimethyl sulfoxide (δ 2.50), chloroform (δ 7.26), methanol (δ 3.34), or dichloromethane (δ 5.32). A small amount of the dry sample (2-5 mg) is dissolved in an appropriate deuterated solvent (1 mL).

Intermediate 1: 3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluoroaniline (**I-1**)



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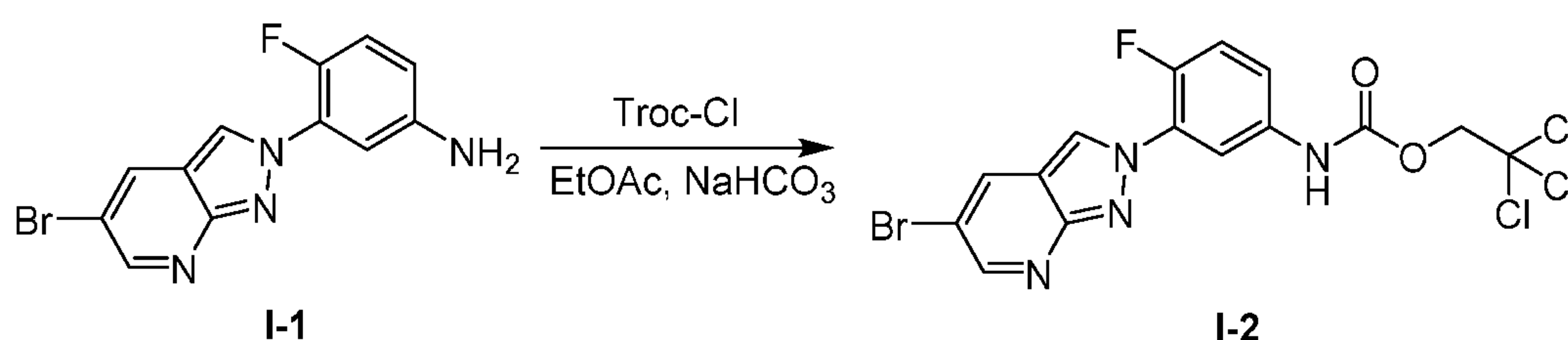
Step A: The reaction mixture of NaN_3 (8 g, 122.5 mmol, 1 eq), 5-bromo-2-fluoro-pyridine-3-carbaldehyde (25 g, 122.5 mmol, 1 eq) in DMF (250 mL) was stirred at 70 °C for 1 hour. The reaction mixture was diluted with ethyl acetate (500 mL) and poured into ice-water (500 mL).

The water layer was separated and extracted with ethyl acetate (500 mL*6). The combined organic layers were washed with brine (300 mL*3), dried over sodium sulfate and concentrated. The residue was triturated with Et₂O (100 mL) to give compound **I-1a** as a yellow solid. ¹H NMR: (400 MHz, DMSO-*d*₆) δ ppm 10.26 - 10.46 (m, 1 H), 10.12 (d, *J*=1.51 Hz, 1 H), 8.64 (d, *J*=1.51 Hz, 1 H). For safe handling of low molecular weight azides, several batches of this reaction were carried out and combined for use in Step B.

Step B: The reaction mixture of **I-1a** (30 g, 132.1 mmol, 1 eq) and 2-fluoro-5-nitro-aniline (20.6 g, 132.1 mmol, 1 eq) in EtOH (500 mL) was stirred at 85 °C for 4 hours under a N₂ atmosphere. The reaction mixture was concentrated in vacuo. Toluene (700 mL) was added to the crude material and the reaction mixture was refluxed for 16 hr. The reaction mixture was concentrated and the material was purified by silica gel chromatography eluting with 0-50% EtOAc in DCM. The resulting material was triturated with EtOAc (100 mL) to give **I-1b** as a yellow solid. ¹H NMR: (400 MHz, DMSO-*d*₆) δ ppm 9.04 (d, *J*=2.26 Hz, 1 H), 8.85 (dd, *J*=6.53, 3.01 Hz, 1 H), 8.79 (d, *J*=2.26 Hz, 1 H), 8.60 - 8.71 (m, 1 H), 8.47 (dt, *J*=9.03, 3.39 Hz, 1 H), 7.92 (dd, *J*=10.54, 9.29 Hz, 1 H).

Step C: The reaction mixture of compound **I-1b** (25 g, 74.2 mmol, 1 eq), diiodozinc (9.5 g, 29.7 mmol, 0.4 eq) and Raney-Ni (50 g, 583.6 mmol, 7.9 eq) in THF (500 mL) was stirred at 20 °C for 12 hour under 15 psi of H₂. The reaction mixture was diluted with MeOH (450 mL), filtered and the filter cake was washed with MeOH (200 mL*3). The filtrate was concentrated and triturated with water (500 mL) and dried in vacuo to give **I-1** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 8.81 (br d, *J*=1.51 Hz, 1 H), 8.71 (br d, *J*=1.76 Hz, 1 H), 8.58 (br d, *J*=1.76 Hz, 1 H), 7.10 - 7.41 (m, 2 H), 6.56 - 6.85 (m, 1 H), 5.45 (br s, 2 H).

Intermediate 2: 2,2,2-trichloroethyl (3-(5-bromo-2H-pyrazolo[3,4-*b*]pyridin-2-yl)-4-fluorophenyl)carbamate (**I-2**)

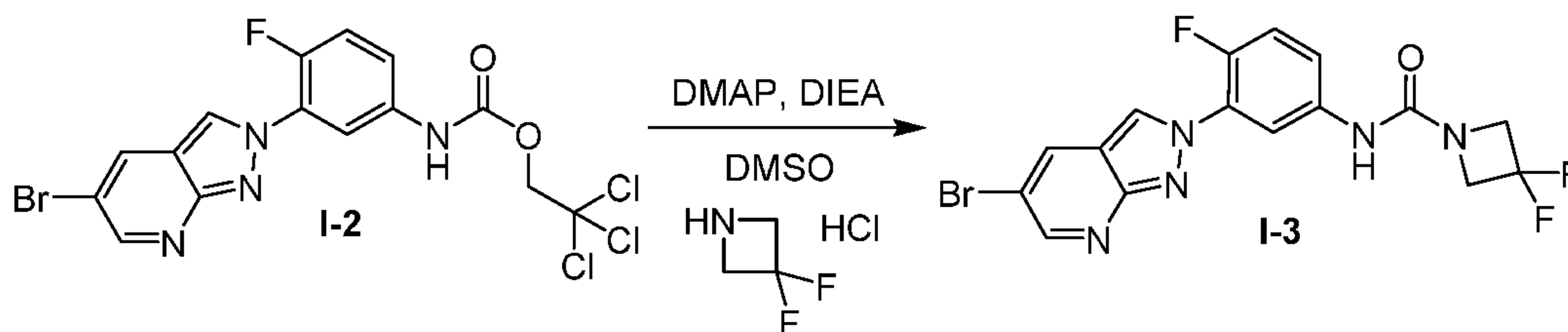


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To a solution **I-1** (5 g, 16.3 mmol, 1 eq) in EtOAc (150 mL) was added saturated aqueous NaHCO₃ (150 mL). The reaction mixture was cooled to 0 °C followed by dropwise addition of 2,2,2-trichloroethyl carbonochloridate (6.9 g, 32.6 mmol, 2 eq). The mixture was stirred at 0 °C for 2 hr and then stirred at 25 °C for 20hr. The solid was collected by filtration and washed with water (150 mL) and ethyl acetate (20 mL) to give compound **I-2** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm, 10.57 (br s, 1 H), 8.92 (d, *J*=2.51 Hz, 1 H), 8.76 (d, *J*=2.26 Hz, 1 H), 8.63 (d, *J*=2.51 Hz, 1 H), 8.27 (br d, *J*=4.52 Hz, 1 H), 7.62 - 7.67 (m, 1 H), 7.55 - 7.61 (m, 1 H), 4.99 (s, 2 H).

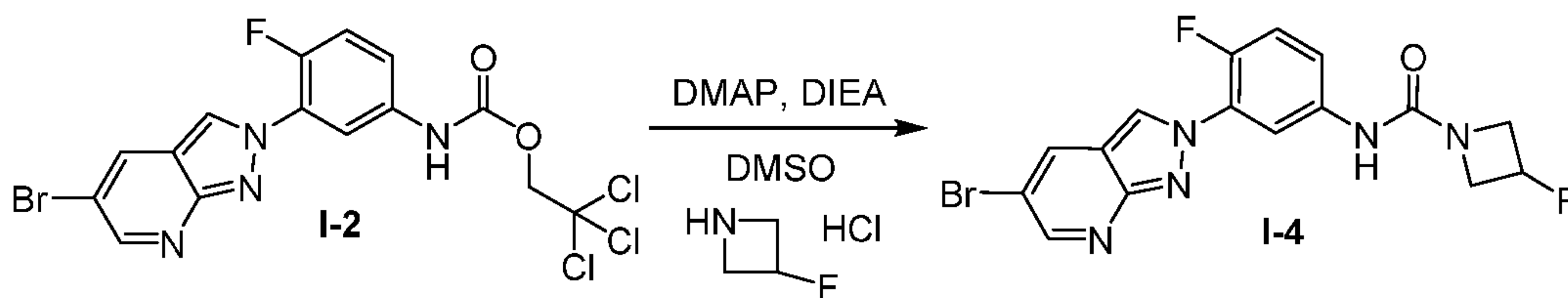
30

Intermediate 3: N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide (**I-3**) (also Compound **125**)



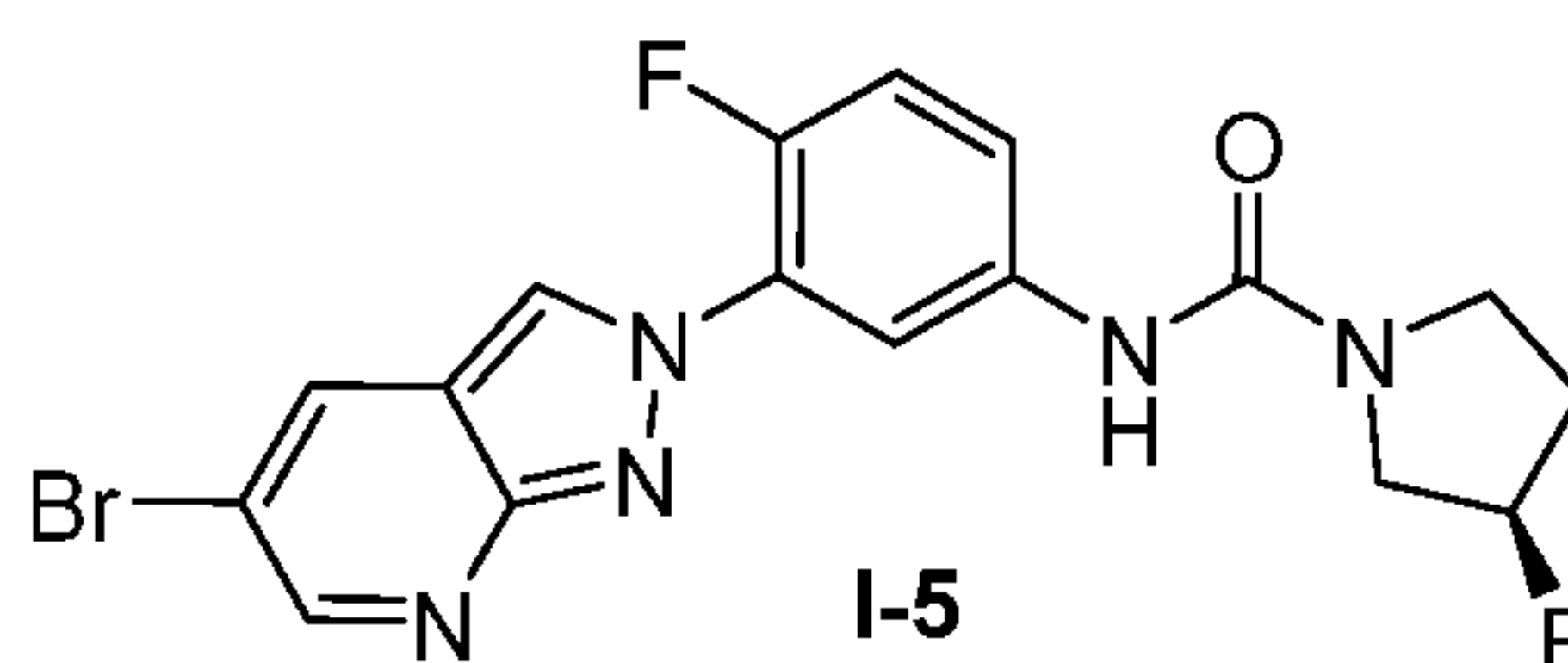
To a solution of **I-2** (2 g, 4.14 mmol, 1 eq) and 3,3-difluoroazetidine HCl (1.1 g, 8.3 mmol, 2 eq) in DMSO (15 mL) was added DMAP (25.3 mg, 207 μ mol, 0.05 eq) and DIEA (1.1 g, 8.3 mmol, 1.45 mL, 2 eq). The mixture was stirred at 60 °C for 15 hrs. The product was precipitated out by addition of 60 mL water and 10 mL ethyl acetate and collected by filtration. The filter cake was washed with 40 mL of water and 10 mL of ethyl acetate and the resulting solid was dried under reduced pressure to give a **I-3** as a white solid. ^1H NMR (400 MHz, DMSO- d_6), δ ppm, 9.25 (s, 1 H), 8.91 (br s, 1 H), 8.76 (br s, 1 H), 8.63 (br s, 1 H), 8.25 (br s, 1 H), 7.69 (br s, 1 H), 7.51 (br t, $J=10.16$ Hz, 1 H), 4.41 (br t, $J=12.67$ Hz, 4 H).

Intermediate 4: N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide (**I-4**) (also Compound **126**)



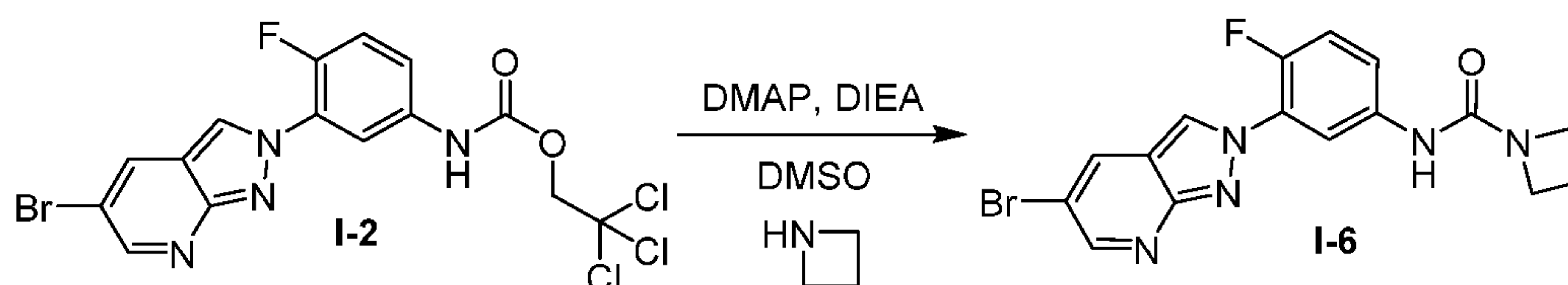
To a solution of **I-2** (2 g, 4.14 mmol, 1 eq) and 3-fluoroazetidine HCl (924 mg, 8.28 mmol, 2 eq) in DMSO (15 mL) was added DMAP (25.3 mg, 207 μ mol, 0.05 eq) and DIEA (1.07 g, 8.28 mmol, 1.45 mL, 2 eq). The mixture was stirred at 60 °C for 15 hrs. The product was precipitated out by addition of 60 mL water and 10 mL ethyl acetate and collected by filtration. The filter cake was washed with 40 mL of water and 10 mL of ethyl acetate and the resulting solid was dried under reduced pressure to give a **I-4** as a solid. ^1H NMR (400 MHz, DMSO- d_6), δ ppm, 8.98 (s, 1 H), 8.90 (d, $J=2.51$ Hz, 1 H), 8.76 (d, $J=2.51$ Hz, 1 H), 8.63 (d, $J=2.51$ Hz, 1 H), 8.24 (dd, $J=7.03, 2.76$ Hz, 1 H), 7.67 - 7.74 (m, 1 H), 7.49 (dd, $J=11.17, 9.16$ Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.25 - 4.39 (m, 2 H), 3.96 - 4.10 (m, 2 H).

Intermediate 5: (*R*)-N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide (**I-5**) (also Compound **127**)



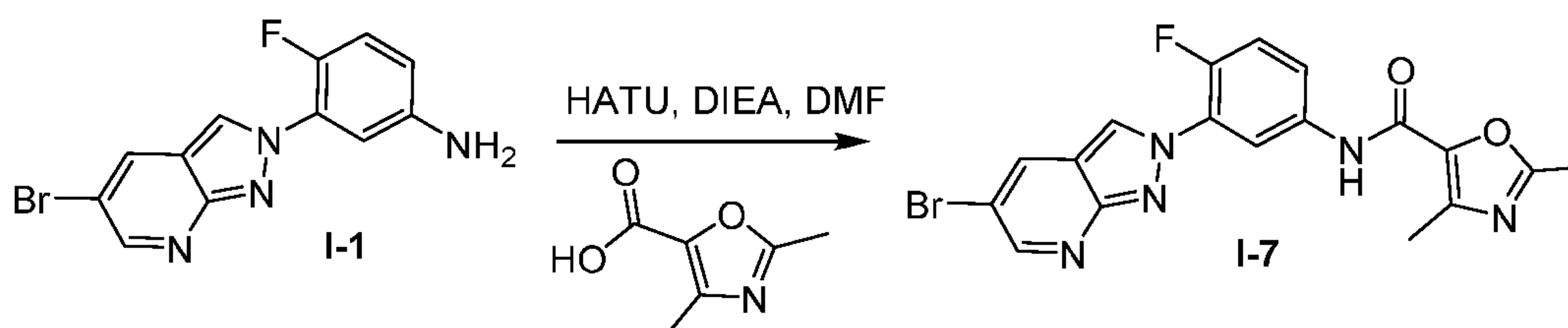
The intermediate **I-5** was prepared in a similar manner as intermediate **I-3** using (*R*)-3-fluoropyrrolidine HCl as a starting material. ¹H NMR (400 MHz, DMSO-*d*₆), δ ppm, 8.90 (d, *J*=2.26 Hz, 1 H), 8.76 (d, *J*=2.51 Hz, 1 H), 8.66 (s, 1 H), 8.63 (d, *J*=2.26 Hz, 1 H), 8.27 (dd, *J*=7.03, 2.76 Hz, 1 H), 7.71 - 7.77 (m, 1 H), 7.48 (dd, *J*=11.17, 9.16 Hz, 1 H), 5.28 - 5.48 (m, 1 H), 3.40 - 3.78 (m, 4 H), 2.01 - 2.27 (m, 2 H).

Intermediate 6: *N*-(3-(5-bromo-2H-pyrazolo[3,4-*b*]pyridin-2-yl)-4-fluorophenyl)azetidine-1-carboxamide **I-6** (also compound **129**)



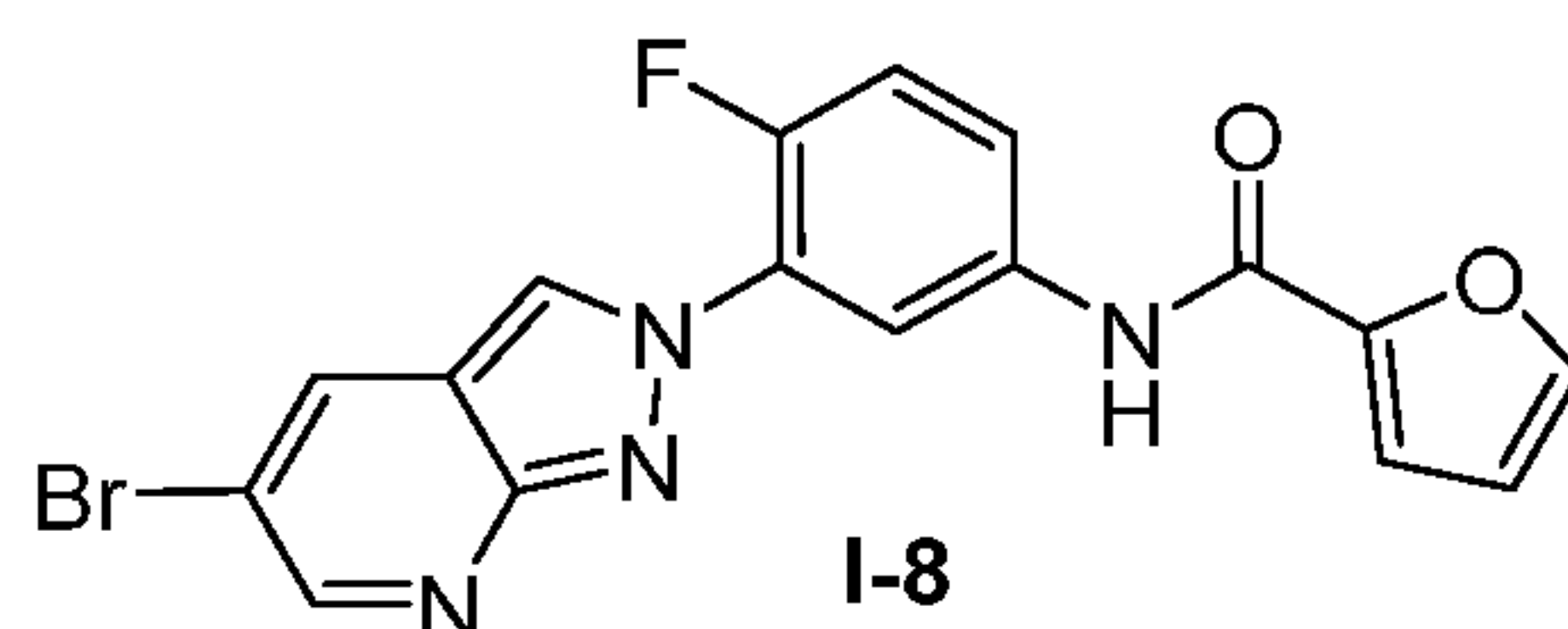
To a solution of **I-2** (1.6 g, 3.32 mmol, 1 eq) and azetidine (379 mg, 6.63 mmol, 2 eq) in DMSO (15 mL) was added DMAP (20.3 mg, 166 μmol, 0.05 eq) and DIEA (857 mg, 6.63 mmol, 2 eq). The mixture was stirred at 60 °C for 15 hrs. The product was precipitated out by addition of 60 mL water and 10 mL ethyl acetate and collected by filtration. The filter cake was washed with 40 mL of water and 10 mL of ethyl acetate and the resulting solid was dried under reduced pressure. The resulting solid was triturated with 10 mL of ethyl acetate to give a **I-6** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆), δ ppm, 8.89 (d, *J*=2.01 Hz, 1 H), 8.70 - 8.80 (m, 2 H), 8.62 (d, *J*=2.26 Hz, 1 H), 8.25 (dd, *J*=6.90, 2.38 Hz, 1 H), 7.72 (br d, *J*=9.03 Hz, 1 H), 7.46 (br t, *J*=10.16 Hz, 1 H), 3.98 (br t, *J*=7.53 Hz, 4 H), 2.20 (quin, *J*=7.59 Hz, 2 H).

Intermediate 7: *N*-(3-(5-bromo-2H-pyrazolo[3,4-*b*]pyridin-2-yl)-4-fluorophenyl)-2,4-dimethyloxazole-5-carboxamide (**I-7**) (also Compound **128**)



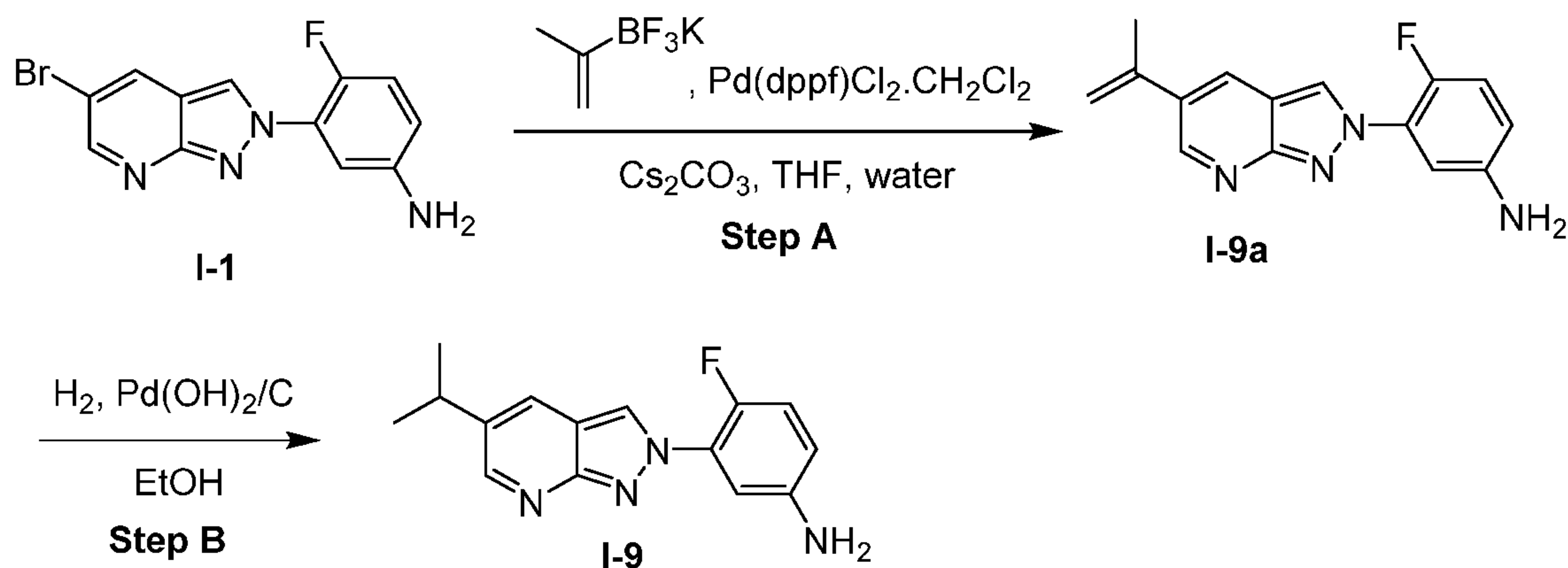
To a solution of **I-1** (1 g, 3.3 mmol, 1 eq) and 2,4-dimethyloxazole-5-carboxylic acid (552.1 mg, 3.9 mmol, 1.2 eq) in DMF (15 mL) was added HATU (1.5 g, 3.9 mmol, 1.2 eq) and DIEA (632 mg, 4.9 mmol, 854 μL, 1.50 eq). The mixture was stirred at 25 °C for 13 hours. Saturated aqueous NaHCO₃ (40 mL) was added to the reaction mixture and the solid was collected by filtration. The filter cake was washed with water (30 mL) and ethyl acetate (10 mL). The resulting solid was triturated in water (20 mL) to give **I-7** as a brown solid. ¹H NMR (400 MHz, DMSO-*d*₆), δ ppm, 10.53 (s, 1 H), 8.94 (d, *J*=2.51 Hz, 1 H), 8.77 (d, *J*=2.26 Hz, 1 H), 8.64 (d, *J*=2.26 Hz, 1 H), 8.58 (dd, *J*=7.15, 2.64 Hz, 1 H), 7.89 - 7.97 (m, 1 H), 7.59 (dd, *J*=11.17, 9.16 Hz, 1 H), 2.52 - 2.53 (s, 3 H), 2.40 (s, 3 H).

Intermediate 8: N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)furan-2-carboxamide (**I-8**) (also Compound **130**)



The intermediate **I-8** was prepared in a similar manner as intermediate **I-7** using furan-2-carboxylic acid as a starting material. ¹H NMR (400 MHz, DMSO-*d*₆), δ ppm, 10.58 (br s, 1 H), 8.94 (d, *J*=2.26 Hz, 1 H), 8.77 (d, *J*=2.26 Hz, 1 H), 8.64 (d, *J*=2.26 Hz, 1 H), 8.53 (dd, *J*=7.03, 2.51 Hz, 1 H), 7.92 - 8.02 (m, 2 H), 7.60 (dd, *J*=11.04, 9.29 Hz, 1 H), 7.40 (d, *J*=3.26 Hz, 1 H), 6.74 (dd, *J*=3.26, 1.51 Hz, 1 H).

Intermediate 9: 4-fluoro-3-(5-isopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline (**I-9**)

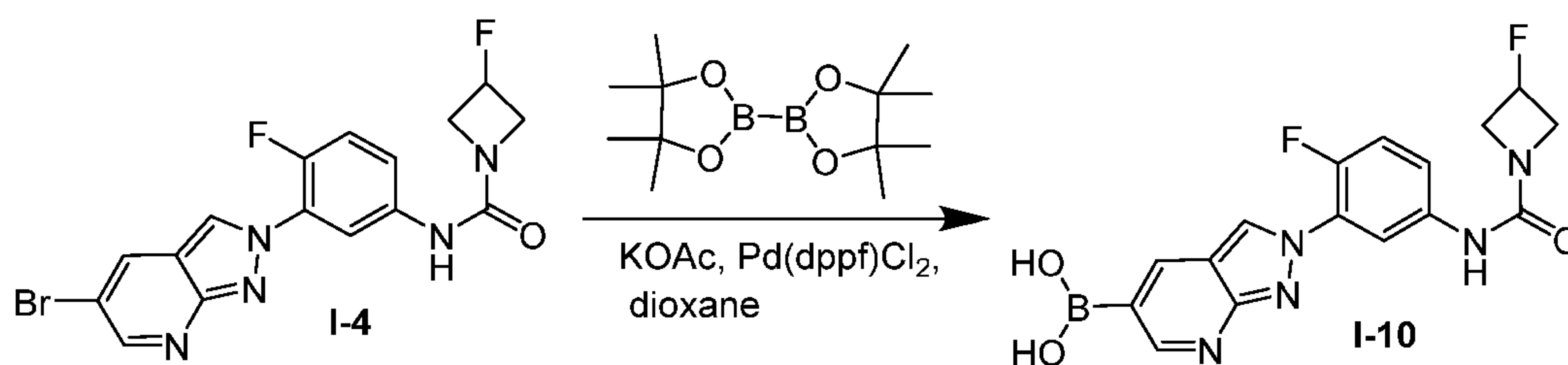


Step A: To a solution of intermediate **I-1** (4 g, 13.0 mmol, 1 eq) in THF (60 mL) and H₂O (9 mL) was added Cs₂CO₃ (12.7 g, 39.1 mmol, 3 eq), Pd(dppf)Cl₂·CH₂Cl₂ (531.8 mg, 651.2 μmol, 0.05 eq) and potassium trifluoro(prop-1-en-2-yl)borate (2.2 g, 14.7 mmol, 1.1 eq). The mixture was stirred at 80 °C for 16 hr. The reaction mixture was extracted with EtOAc (100 mL * 2). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by silica chromatography eluting with petroleum ether: EtOAc = 1:2) to give compound **I-9a** as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 9.00 (d, *J*=2.26 Hz, 1 H), 8.78 (d, *J*=2.38 Hz, 1 H), 8.23 (d, *J*=2.26 Hz, 1 H), 7.09 - 7.29 (m, 2 H), 6.68 (dt, *J*=8.88, 3.34 Hz, 1 H), 5.64 (s, 1 H), 5.44 (s, 2 H), 5.22 (s, 1 H), 2.18 (s, 3 H), M+H = 269.1.

Step B: To a solution of intermediate **I-9a** (3.4 g, 12.7 mmol, 1 eq) in EtOH (216 mL) was added 20% Pd(OH)₂/C (5.3 g, 7.60 mmol, 0.6 eq) and the mixture was stirred at 25 °C for 4 hr under a 15 psi H₂ atmosphere. The reaction mixture was filtered through celite and the filter cake was washed with ethanol (30 mL). The filtrate was concentrated, the resulting residue was dissolved in EtOAc (10 mL) and 4M HCl in EtOAc (2 mL) was added. The solid was collected by filtration and dried under vacuo to give the HCl salt of **I-9** as a yellow solid. ¹H NMR (400 MHz,

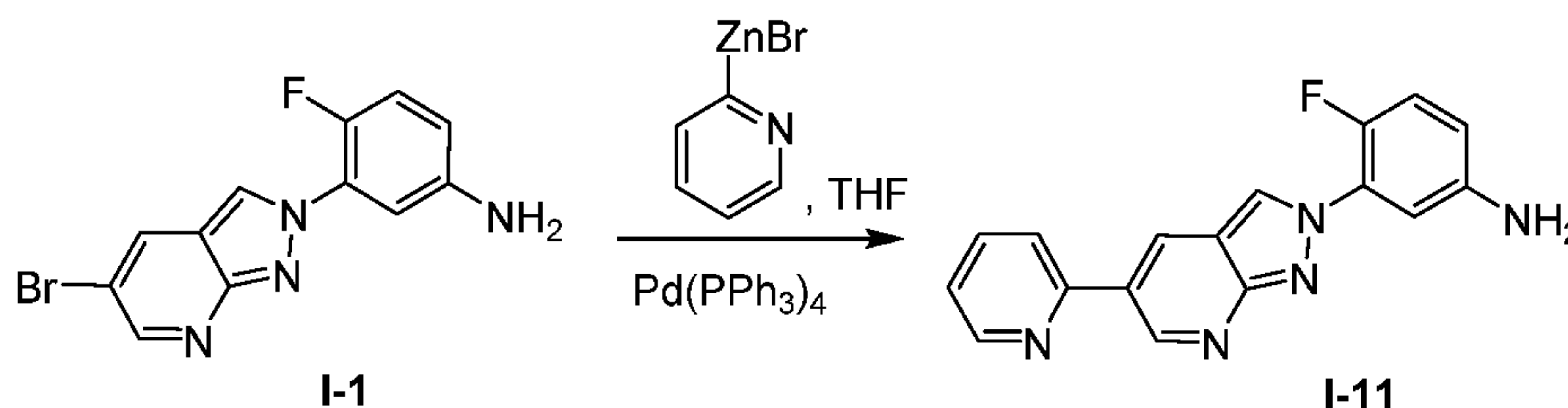
DMSO- d_6) δ ppm 9.10 (d, $J=2.26$ Hz, 1 H), 8.90 (d, $J=2.01$ Hz, 1 H), 8.47 (br d, $J=1.63$ Hz, 1 H), 8.07 (br dd, $J=6.46, 2.45$ Hz, 1 H), 7.72 (br dd, $J=10.85, 9.10$ Hz, 1 H), 7.58 (dt, $J=8.50, 3.28$ Hz, 1 H), 3.07 - 3.25 (m, 1 H), 1.32 (d, $J=6.78$ Hz, 6 H), $M+H = 271.1$.

Intermediate 10: (2-(2-fluoro-5-(3-fluoroazetidine-1-carboxamido)phenyl)-2H-pyrazolo[3,4-b]pyridin-5-yl)boronic acid (**I-10**)



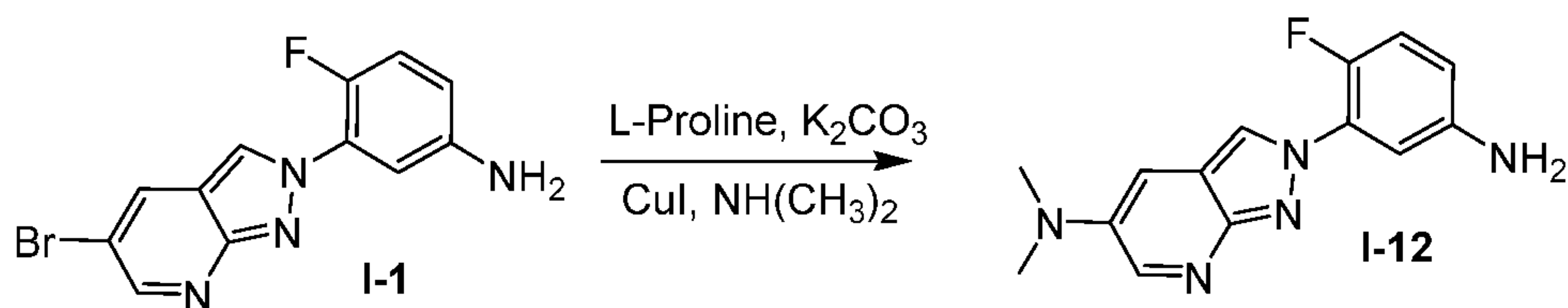
To a solution of intermediate **I-4** (300 mg, 734.9 μ mol, 1 eq) in dioxane (18 mL) was added 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (223.9 mg, 881.9 μ mol, 1.2 eq), Pd(dppf)Cl₂ (53.8 mg, 73.5 μ mol, 0.1 eq) and KOAc (144.3 mg, 1.5 mmol, 2 eq). The mixture was stirred at 100 °C for 16 hr. The reaction mixture was concentrated and the residue was washed with EtOAc (5 mL), water (5 mL), and dried under reduced pressure to give compound **I-10** as a black solid. ¹H NMR (400 MHz, DMSO- d_6) δ ppm 9.00 (br s, 2 H), 8.70 (br s, 1 H), 8.45 (br s, 1 H), 8.24 (br s, 1 H), 7.69 (br s, 1 H), 7.56 (br s, 1 H), 7.50 (br s, 1 H), 6.59 (br s, 1 H), 5.25 - 5.56 (m, 1 H), 4.33 (br s, 2 H), 3.90 - 4.13 (m, 2 H), $M+H = 374.2$.

Intermediate 11: 4-fluoro-3-(5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline **I-11**



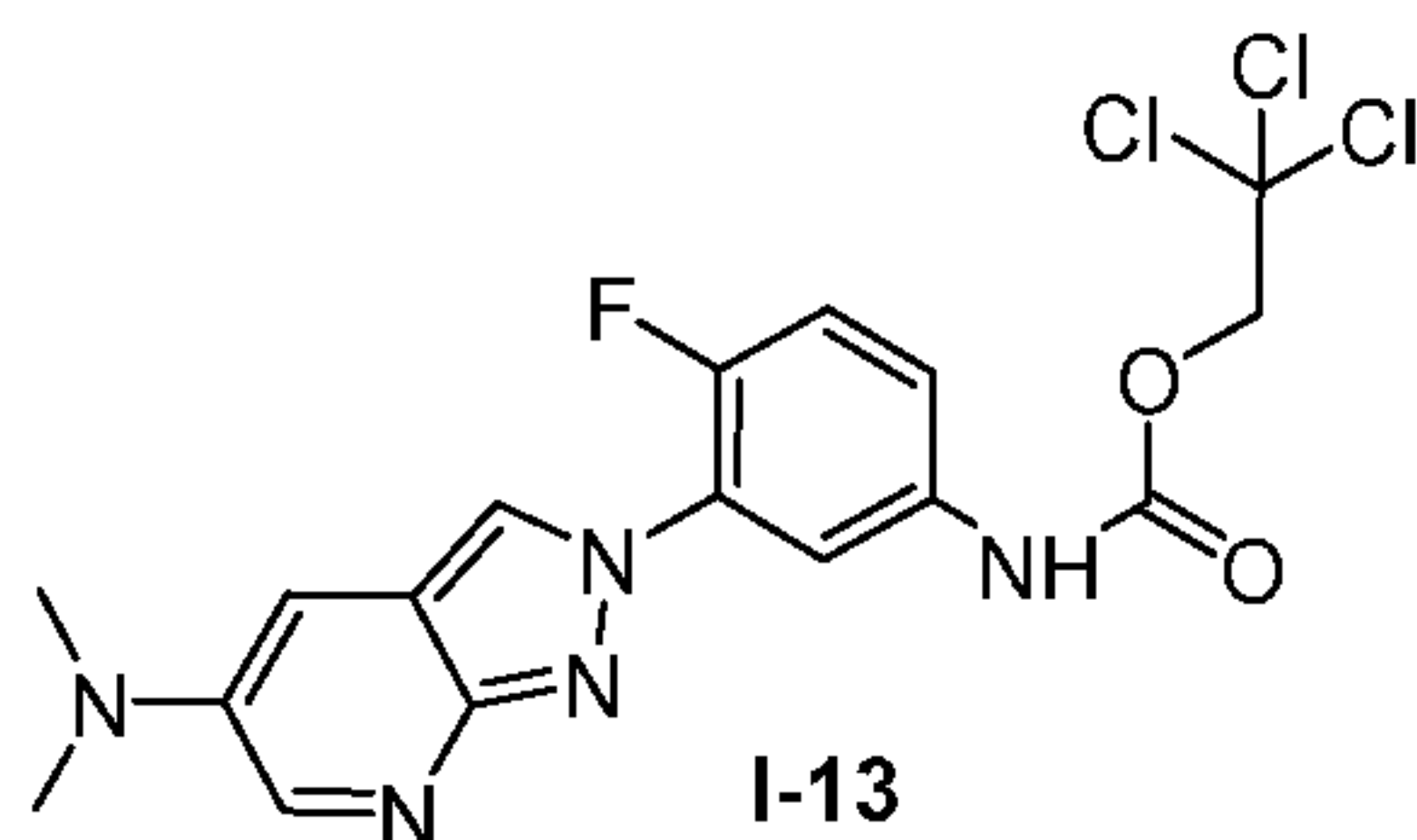
I-1 (947 mg, 3.1 mmol) and Pd(PPh₃)₄ (178 mg, 0.15 mmol) were combined in a flask and placed under a nitrogen atmosphere. Pyridin-2-ylzinc(II) bromide 0.5 M in THF (24.7 mL, 12.3 mmol) was added and the reaction was heated to 65 °C for 4 hrs. The reaction was quenched with water and concentrated. The crude material was purified by C18 flash chromatography eluting with 10-80% acetonitrile in water to give **I-11** as a pale yellow solid. ¹H NMR (400 MHz, DMSO- d_6) δ 9.45 (d, $J = 2.3$ Hz, 1H), 8.93 (dd, $J = 3.4, 2.4$ Hz, 2H), 8.73 (ddd, $J = 4.8, 1.8, 0.9$ Hz, 1H), 8.12 (dt, $J = 8.0, 1.0$ Hz, 1H), 7.95 (td, $J = 7.7, 1.8$ Hz, 1H), 7.46 - 7.40 (m, 1H), 7.26 - 7.16 (m, 2H), 6.69 (ddd, $J = 8.9, 3.9, 2.9$ Hz, 1H), 5.46 (s, 2H).

Intermediate 12: 2-(5-amino-2-fluorophenyl)-N,N-dimethyl-2H-pyrazolo[3,4-b]pyridin-5-amine (**I-12**)



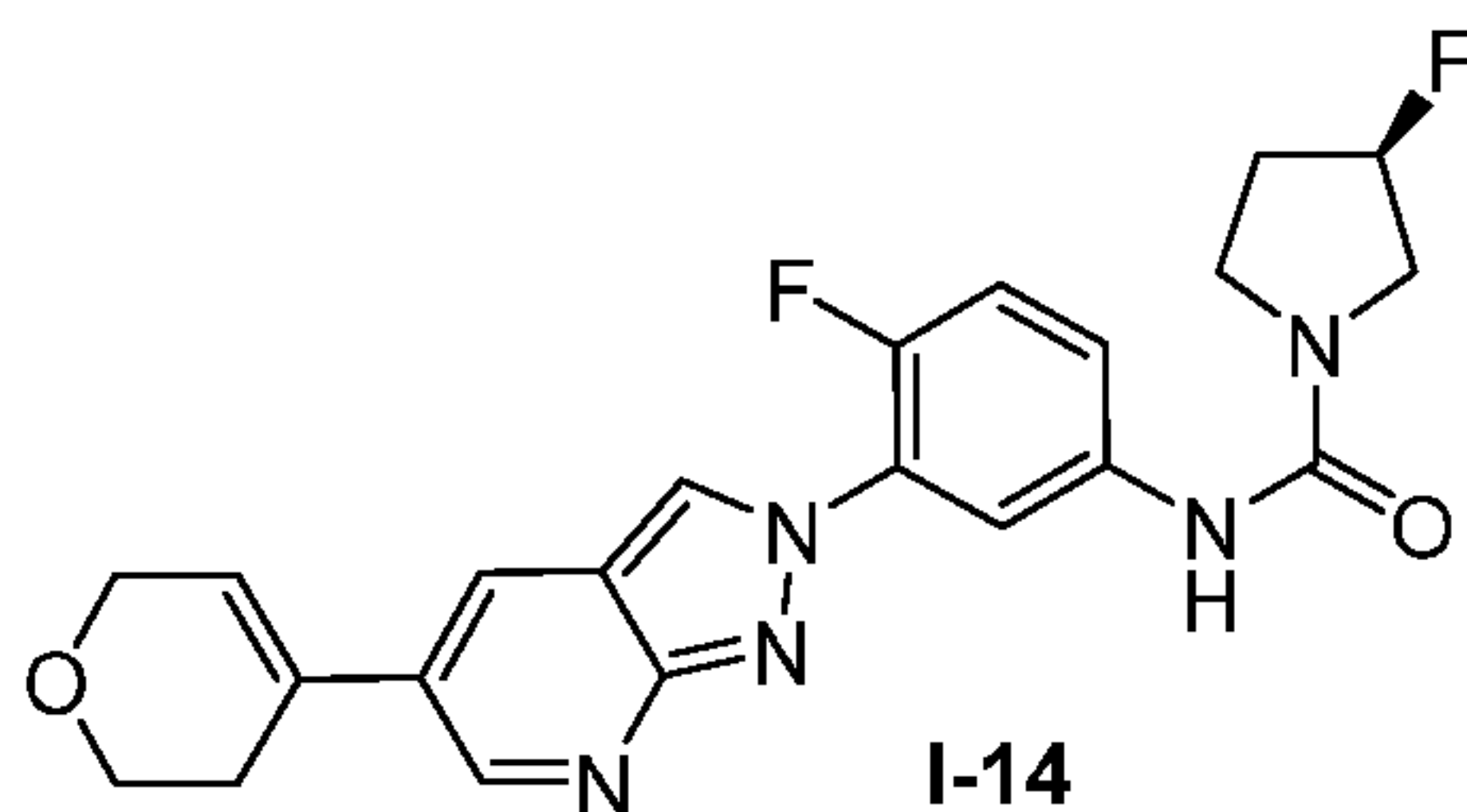
The reaction mixture of *N*-methylmethanamine (4.4 g, 98.7 mmol, 5 mL, 50.5 eq), **I-1** (0.6 g, 1.9 mmol, 1 eq), *L*-proline (22.5 mg, 195.4 μ mol, 0.1 eq), CuI (37.2 mg, 195.4 μ mol, 0.1 eq) and K₂CO₃ (540 mg, 3.9 mmol, 2 eq) in DMSO (5 mL) was stirred at 90 °C for 12 hrs. The reaction was quenched with 10% aqueous NH₄OH (20 mL) and extracted with ethyl acetate (25 mL*4). The combined ethyl acetate layers were washed with brine (15 mL*3), dried over sodium sulfate and concentrated. The residue was purified by silica chromatography eluting with 20% ethyl acetate and 20% DCM in petroleum ether to give **I-12** as a yellow solid. ¹H NMR: (400 MHz, DMSO-*d*₆) δ ppm 8.68 (br s, 1 H), 8.48 (br s, 1 H), 7.16 (br s, 3 H), 6.63 (br s, 1 H), 5.38 (br s, 2 H), 2.95 (br s, 6 H). M+H = 391.1.

Intermediate 13: 2,2,2-trichloroethyl (3-(5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)carbamate (**I-13**)



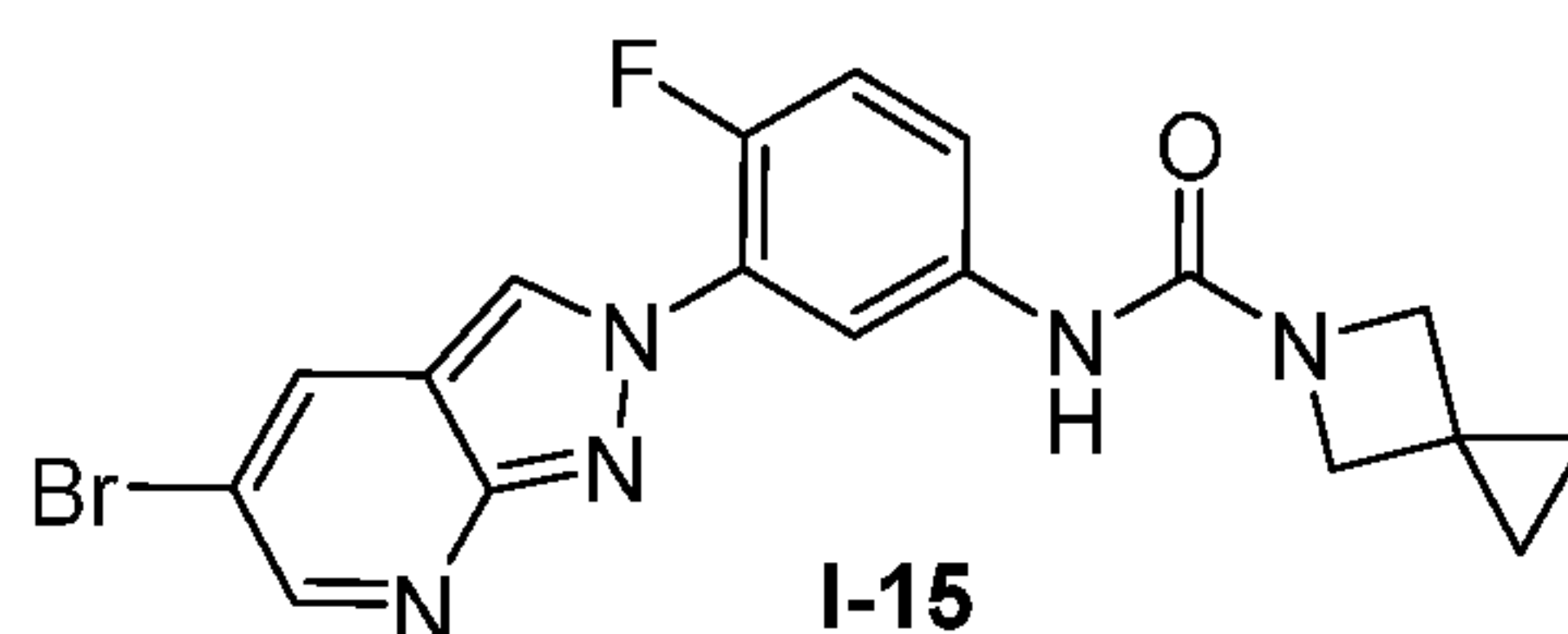
The synthesis of **I-13** is described in Example 9.

Intermediate 14: (R)-N-(3-(5-(3,6-dihydro-2H-pyran-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-3-fluoropyrrolidine-1-carboxamide (**I-14**)



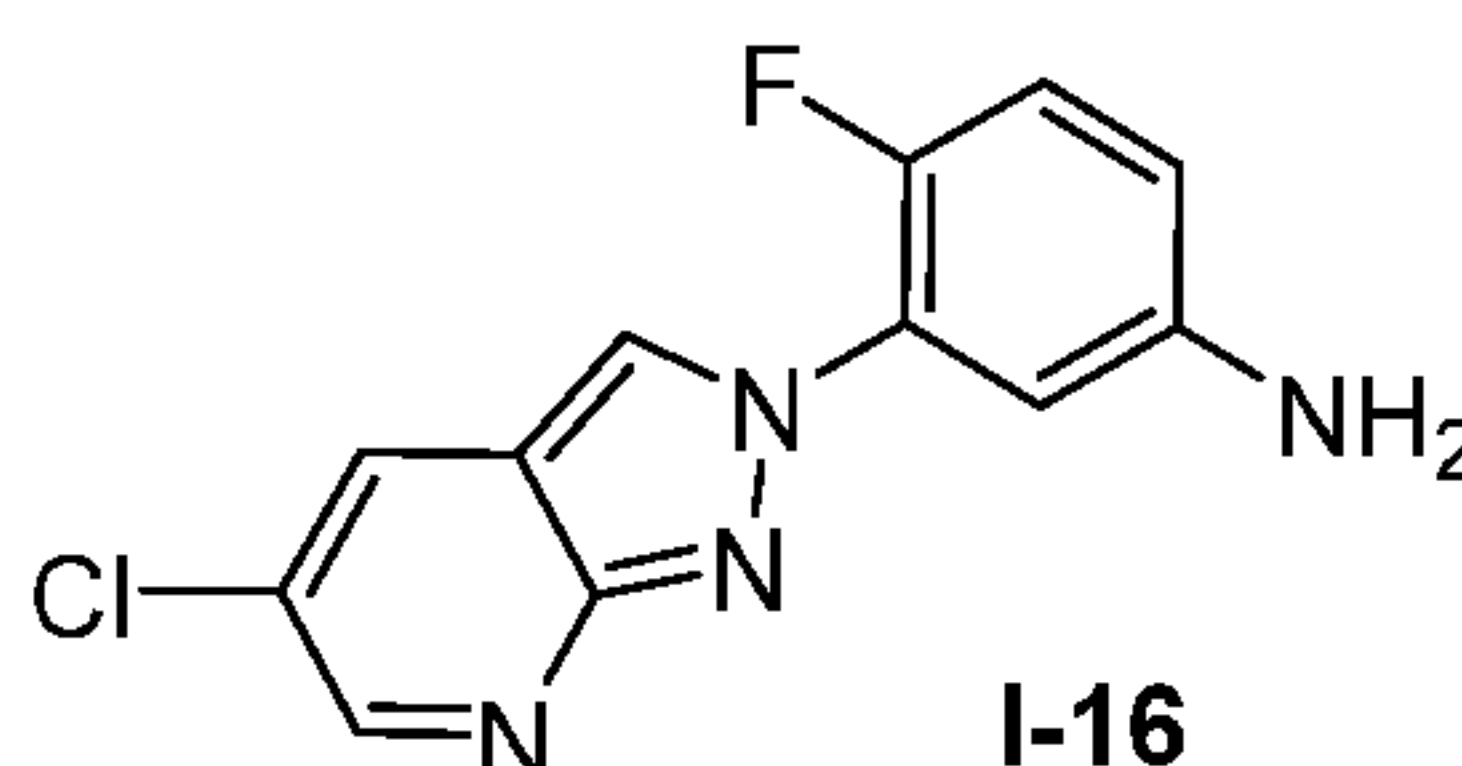
The synthesis of **I-14** is described in Example 18.

Intermediate 15: N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-5-azaspiro[2.3]hexane-5-carboxamide **I-15** (also Compound **254**)



Intermediate **I-15** (compound **254**) was prepared in a similar manner as intermediate **I-3** using 5-azaspiro[2.3]hexane hemioxalate as a starting material. ¹H NMR (400 MHz, DMSO-*d*₆), δ ppm, 8.90 (d, *J*=2.45 Hz, 1 H), 8.85 (s, 1 H), 8.74 - 8.78 (m, 1 H), 8.61 - 8.65 (m, 1 H), 8.26 (dd, *J*=7.09, 2.69 Hz, 1 H), 7.69 - 7.76 (m, 1 H), 7.47 (dd, *J*=11.25, 9.29 Hz, 1 H), 4.05 (s, 4 H), 0.66 (s, 4 H). Method 1: RT = 2.95 min.; M+H = 416.0, 418.0.

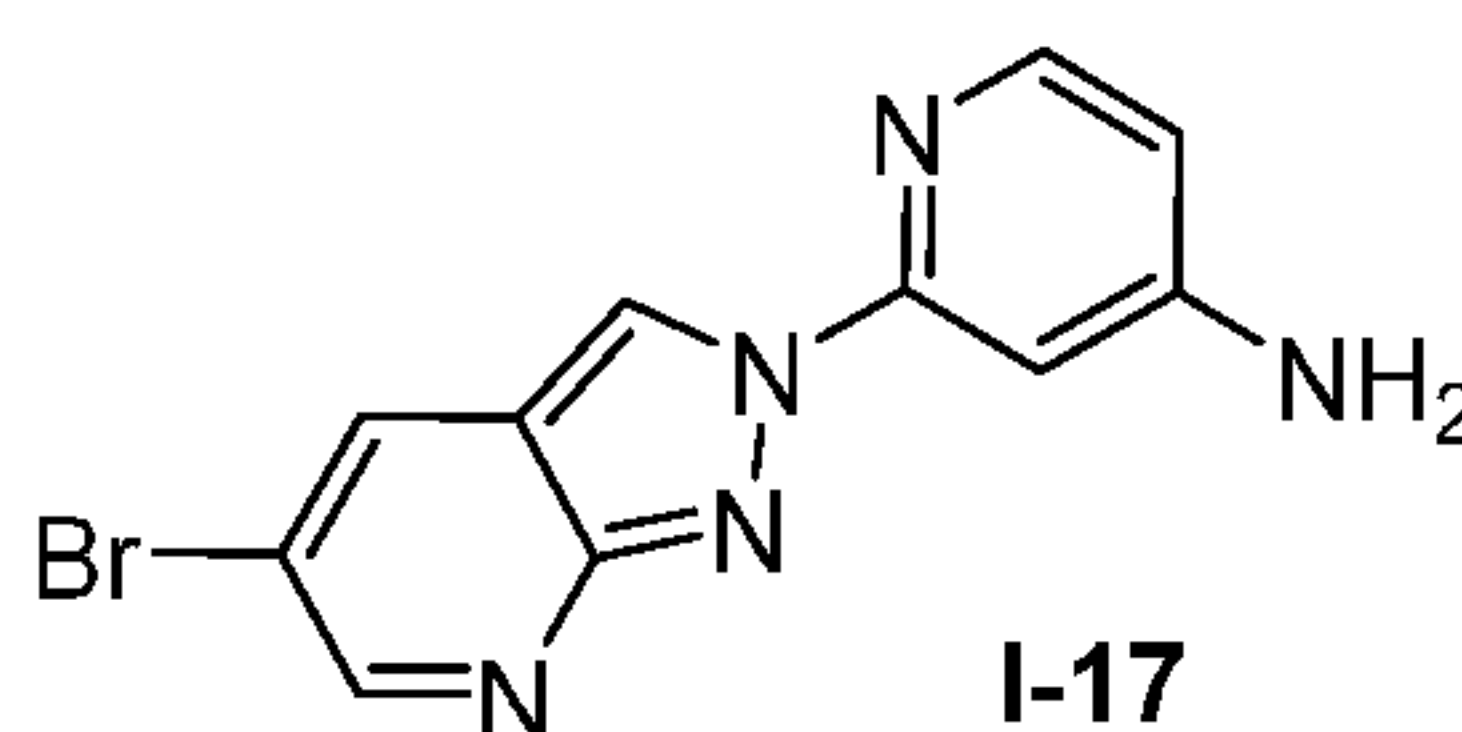
Intermediate 16: 3-(5-chloro-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluoroaniline (**I-16**)



10

Intermediate **I-16** was prepared in a similar manner as intermediate **I-1** using 5-chloro-2-fluoronicotinaldehyde as the starting material. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 8.82 (d, *J*=2.26 Hz, 1 H), 8.67 (d, *J*=2.51 Hz, 1 H), 8.44 (d, *J*=2.51 Hz, 1 H), 7.12 - 7.28 (m, 2 H), 6.61 - 6.75 (m, 1 H), 5.44 (br s, 2 H).

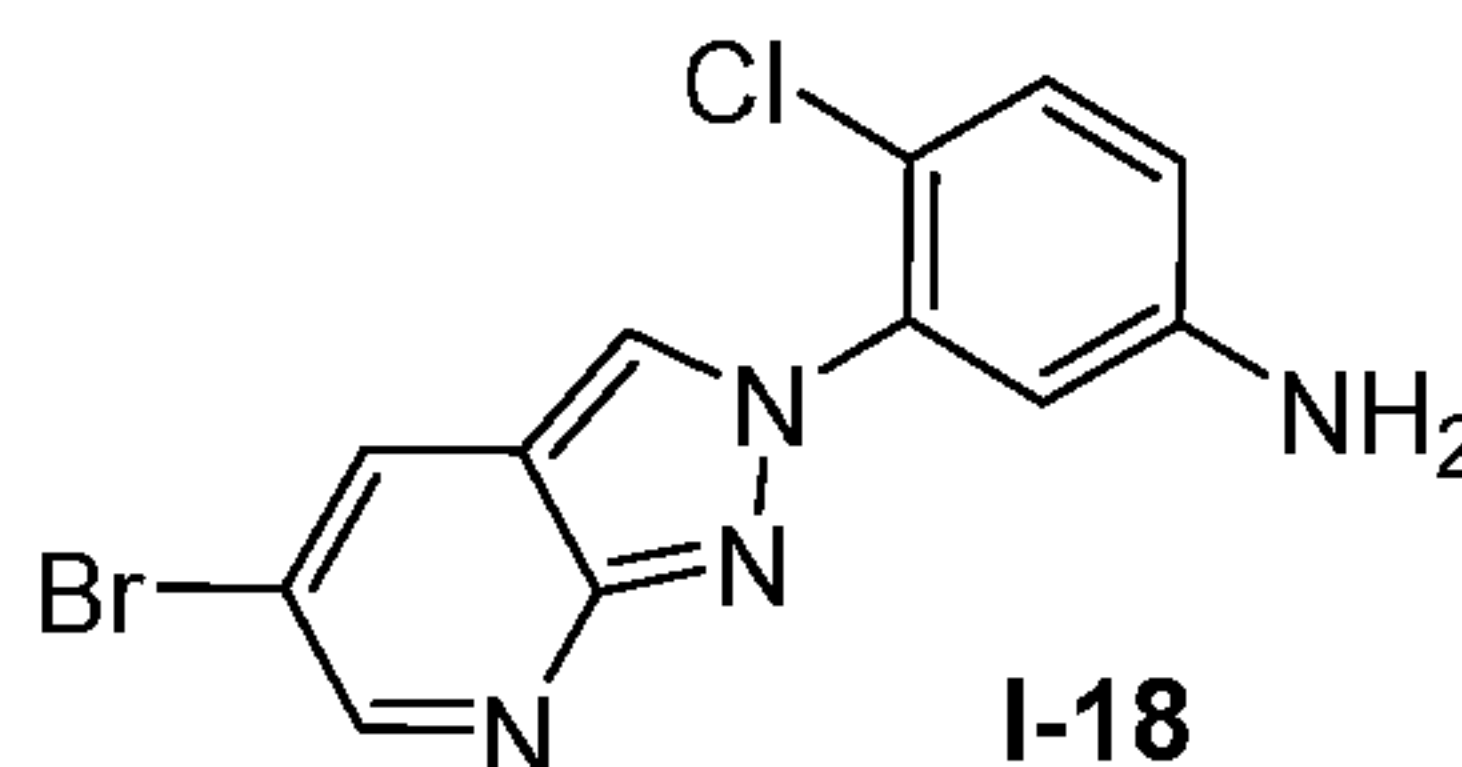
Intermediate 17: 2-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-amine (**I-17**)



20

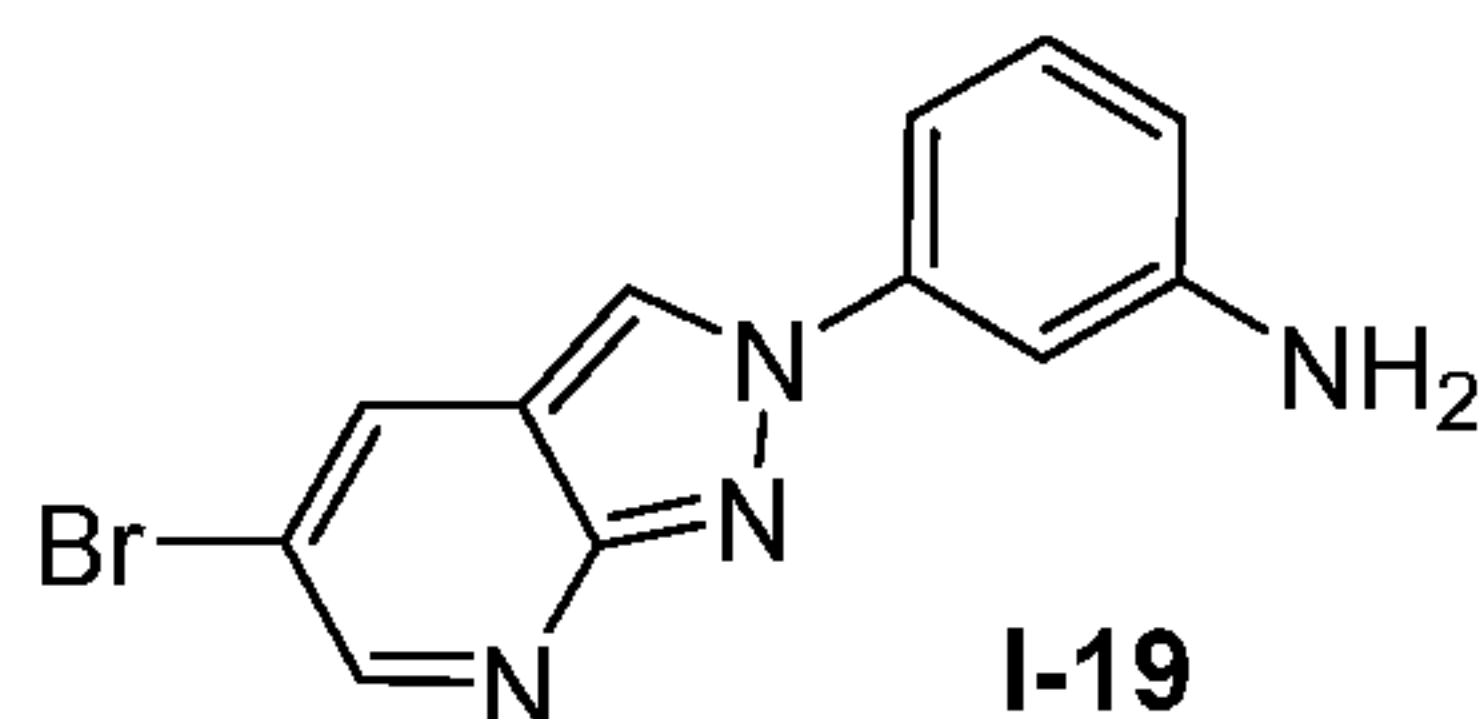
Intermediate **I-17** was prepared in a similar manner as intermediate **I-1** using 4-nitropyridin-2-amine as a starting material in Step B. ¹H NMR (400 MHz, DMSO) δ ppm 9.19 (br s, 1 H), 8.73 (br s, 1 H), 8.59 (br s, 1 H), 8.01 (br d, *J* = 5.27 Hz, 1 H), 7.42 (br s, 1 H), 6.54 - 6.74 (m, 3 H).

Intermediate 18: 3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-chloroaniline (**I-18**)



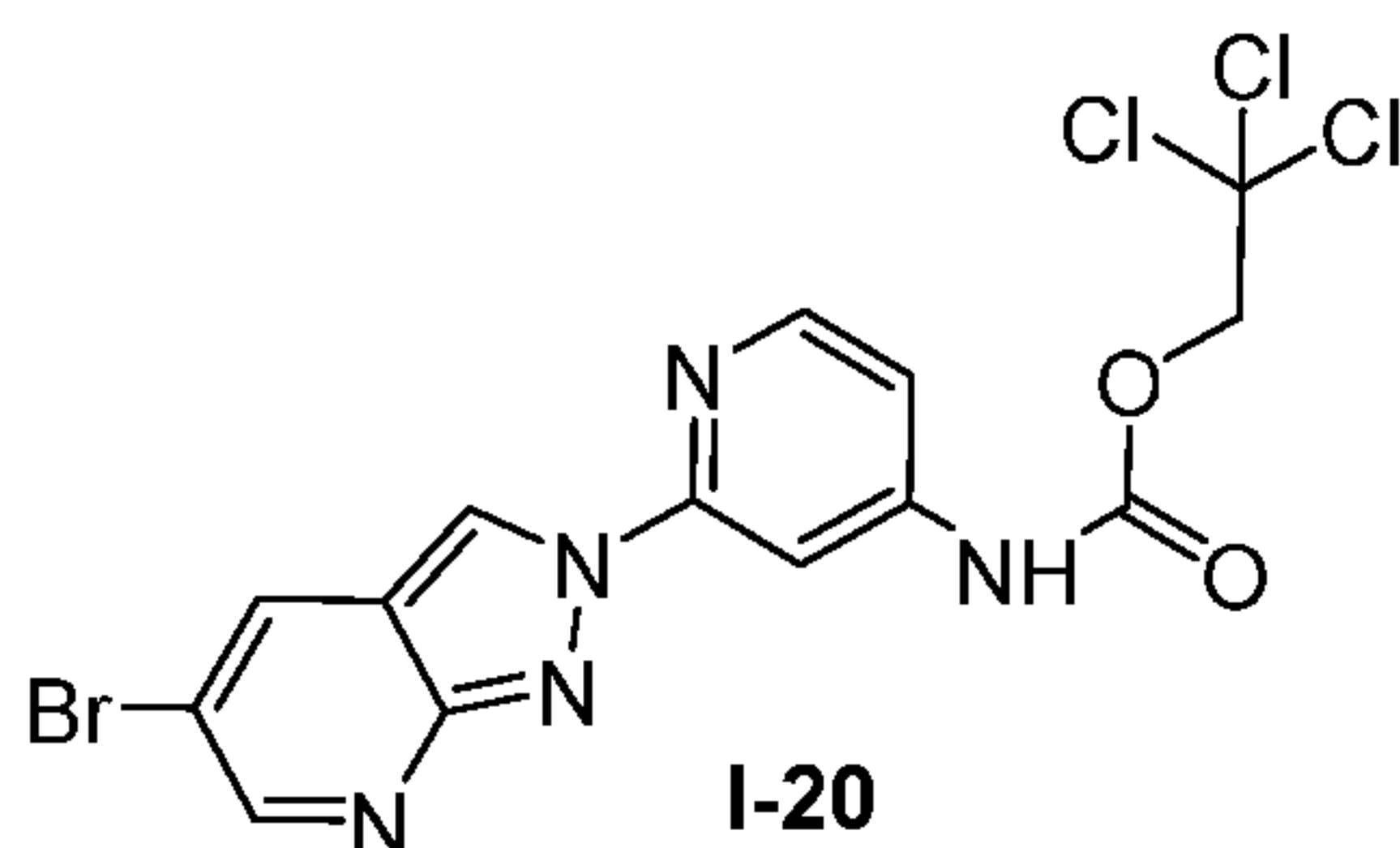
Intermediate **I-18** was prepared in a similar manner as intermediate **I-1** using 2-chloro-5-nitro-aniline as a starting material in Step B. M+H=325.0.

Intermediate 19: 3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline (**I-19**)



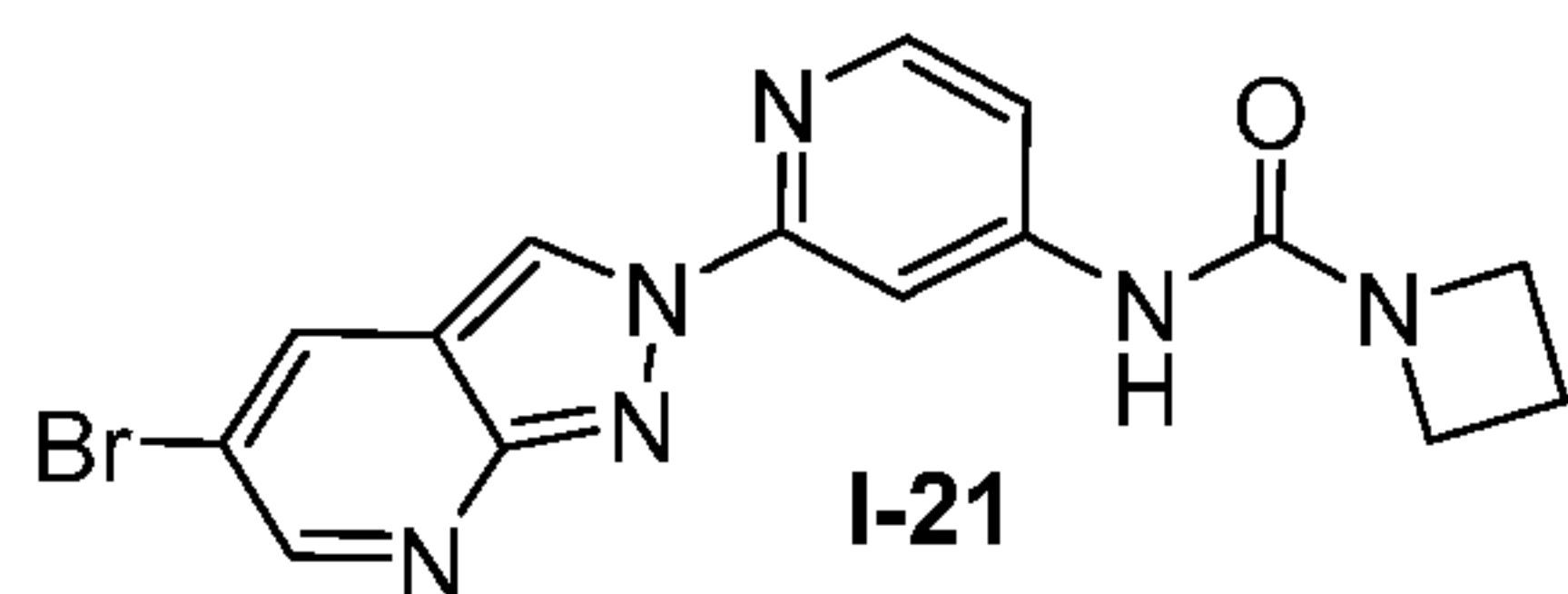
Intermediate **I-19** was prepared in a similar manner as intermediate **I-1** using 3-nitroaniline as a starting material in Step B. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 8.99 (s, 1 H), 8.69 (d, *J*=2.44 Hz, 1 H), 8.56 (d, *J*=2.45 Hz, 1 H), 7.31 (t, *J*=2.08 Hz, 1 H), 7.12 - 7.26 (m, 2 H), 6.61 - 6.72 (m, 1 H), 5.56 (br s, 2 H).

Intermediate 20: 2,2,2-trichloroethyl (2-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-yl)carbamate (**I-20**)



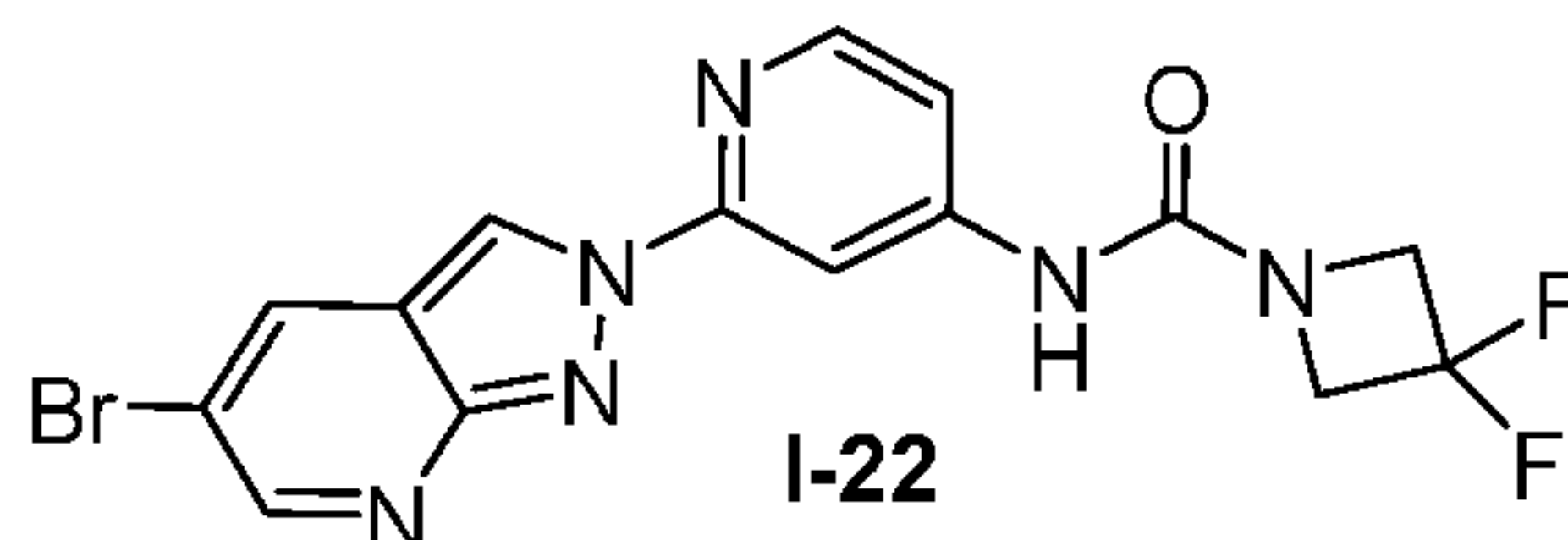
The synthesis of **I-20** is described in Example 21.

Intermediate 21: 3-(2-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-yl)-1,1-dimethylurea (**I-21**)



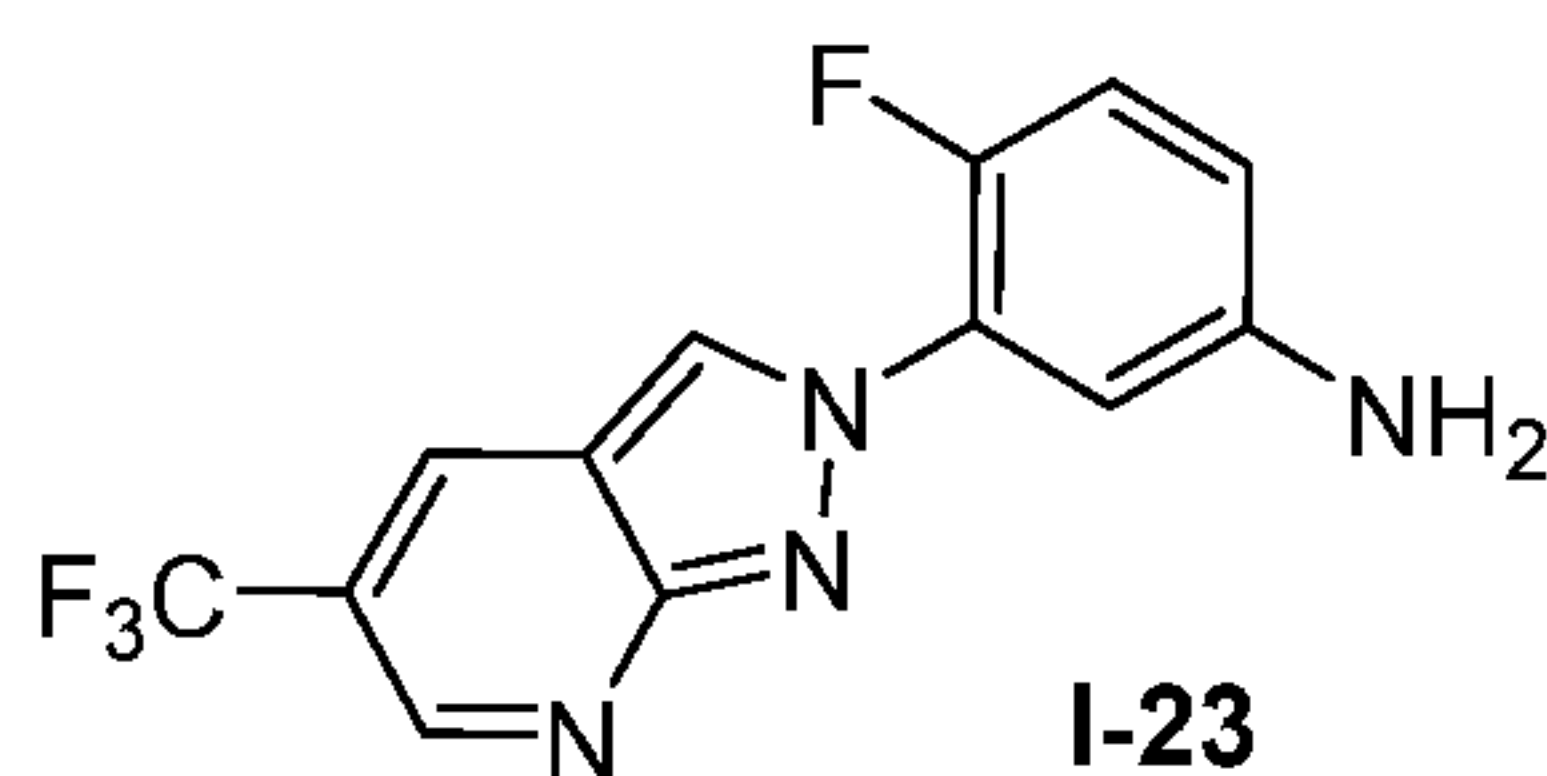
The synthesis of **I-21** is described in Example 21.

Intermediate 22: N-(2-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-yl)-3,3-difluoroazetidine-1-carboxamide (**I-22**)



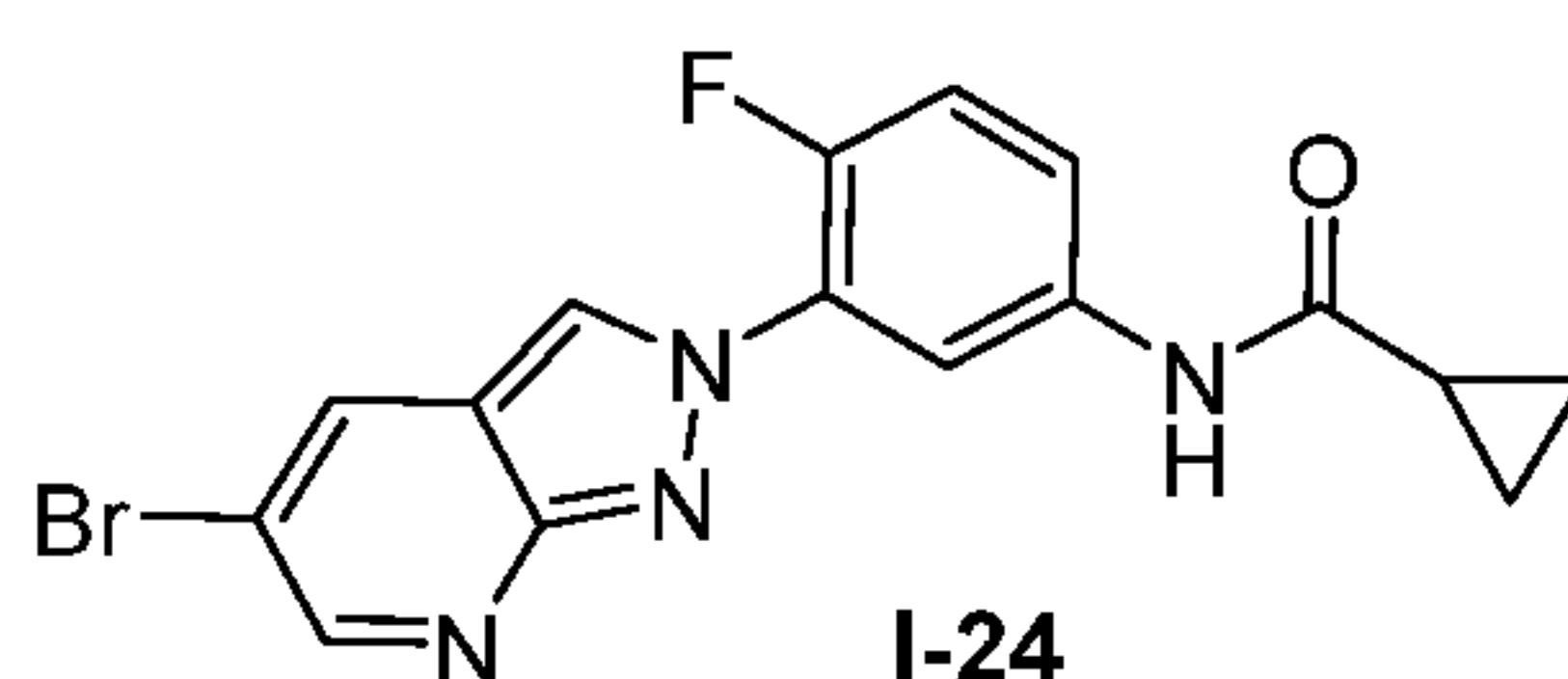
The synthesis of **I-22** is described in Example 22.

Intermediate 23: 4-fluoro-3-(5-(trifluoromethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline (**I-23**)



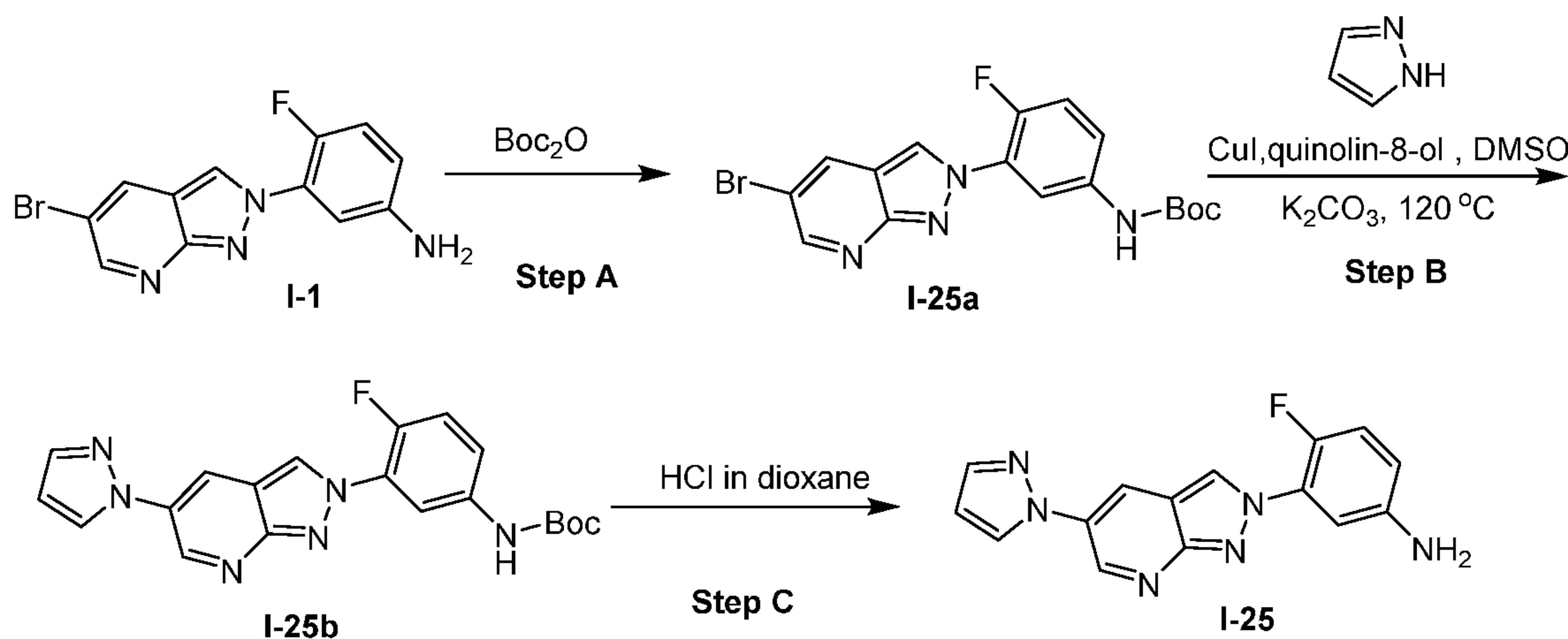
Intermediate **I-23** was prepared in a similar manner as intermediate **I-1** using 2-fluoro-5-(trifluoromethyl)nicotinaldehyde as a starting material. ¹H NMR (400 MHz, DMSO), δ ppm, 9.06 (d, $J = 2.01$ Hz, 1 H), 8.98 (d, $J = 2.26$ Hz, 1 H), 8.85 (s, 1 H), 7.16 - 7.30 (m, 2 H), 6.72 (dt, $J = 8.91, 3.33$ Hz, 1 H), 5.48 (s, 2 H).

- 5 **Intermediate 24:** N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)cyclopropanecarboxamide (**I-24**)



Intermediate **I-24** was prepared in a similar manner as intermediate **I-7** using cyclopropanecarboxylic acid as a starting material. ¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.90 (d, $J = 2.38$ Hz, 1 H), 8.75 (d, $J = 2.38$ Hz, 1 H), 8.62 (d, $J = 2.38$ Hz, 1 H), 8.38 (dd, $J = 7.03, 2.51$ Hz, 1 H), 8.25 - 8.30 (m, 1H), 7.66 - 7.75 (m, 1 H), 7.53 (dd, $J = 11.17, 9.16$ Hz, 1 H), 1.72 - 1.83 (m, 1 H), 0.83 (d, $J = 6.15$ Hz, 4 H).

Intermediate 25: 3-(5-(1H-pyrazol-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluoroaniline (**I-25**)

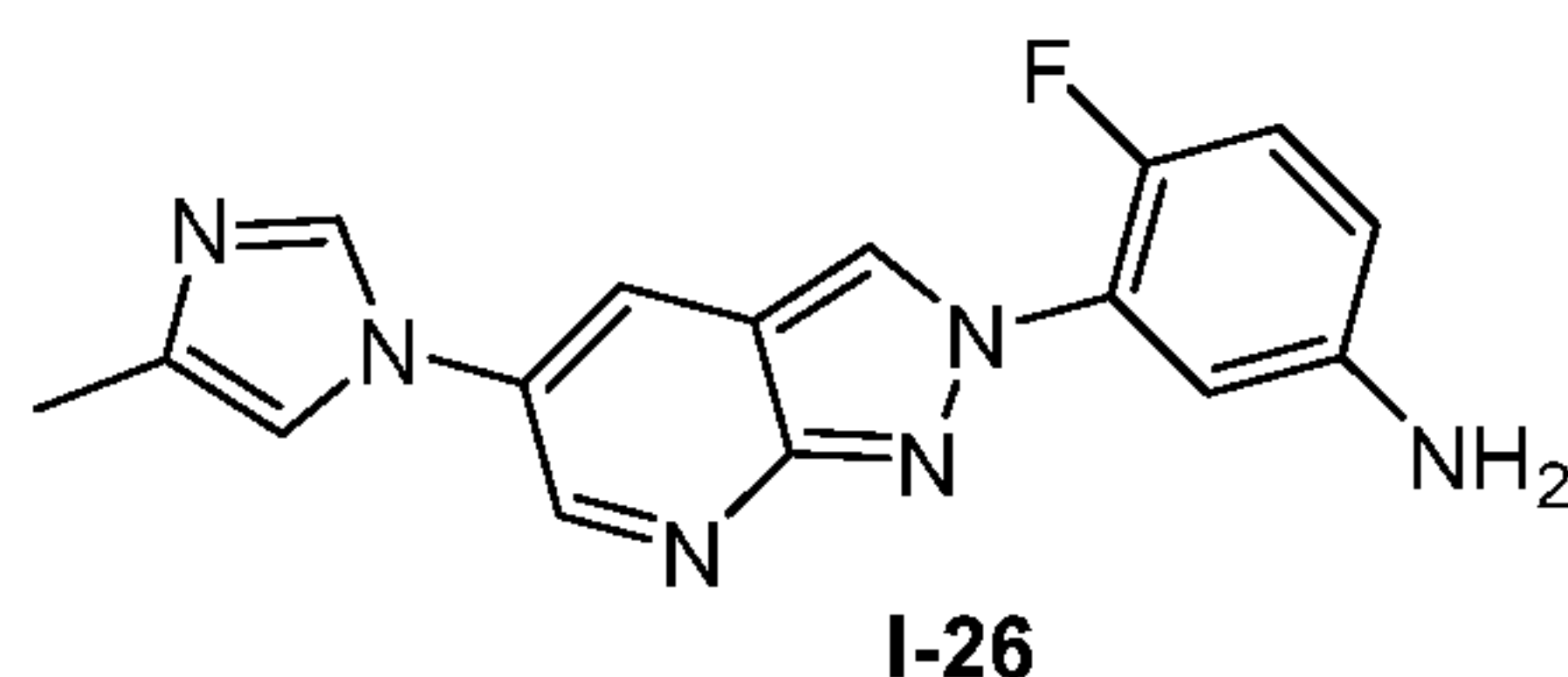


15 **Step A:** The reaction mixture of **I-1** (10 g, 32.6 mmol, 1 eq) and Boc₂O (21.3 g, 97.7 mmol, 22.4 mL, 3 eq) in THF (100 mL) was stirred at 76 °C for 12 hr. The reaction mixture was concentrated and the residue was triturated with petroleum ether (100 mL) to give **I-25a** as a brown solid. M+H = 408.9.

20 **Step B:** The reaction mixture of **I-25a** (0.5 g, 1.2 mmol, 1 eq), 1H-pyrazole (126 mg, 1.8 mmol, 1.5 eq), CuI (35 mg, 184.5 μ mol, 0.15 eq), quinolin-8-ol (27 mg, 184.5 μ mol, 31.9 μ L, 0.15 eq) and K₂CO₃ (221 mg, 1.6 mmol, 1.3 eq) in DMSO (5 mL) was stirred at 120 °C for 12 hr. The reaction mixture was poured into water 20 mL, extracted with DCM (20 mL $\times$ 3). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄ and concentrated to give **I-25b** as a black solid. M+H = 395.3.

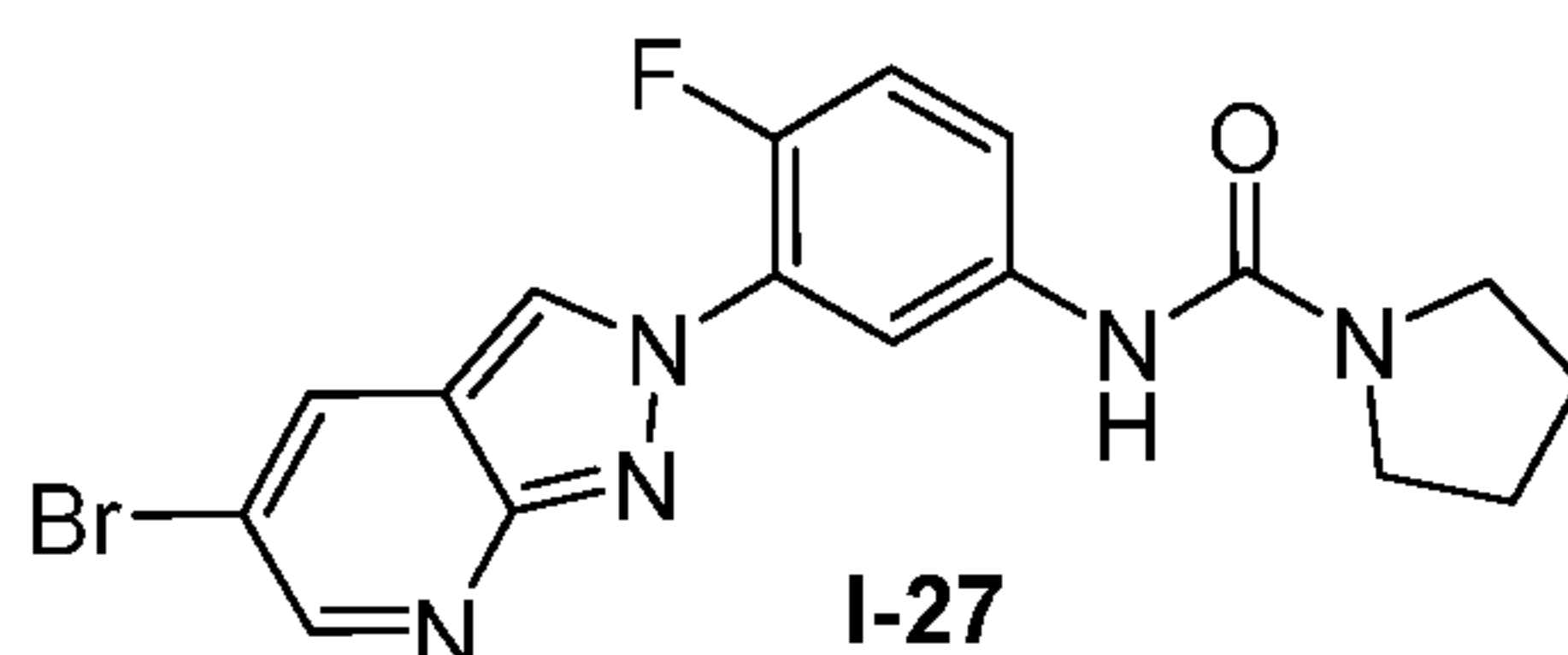
Step C: The reaction mixture of **I-25b** (0.4 g, 1.0 mmol, 1 eq) in HCl/dioxane (10 mL) was stirred at 25 °C for 12 hr. The reaction mixture was concentrated and purified by prep-HPLC (Phenomenex Gemini 150*25 mm*10 um; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 18%-48%, 12 min) to give **I-25** as a yellow solid. ¹H NMR (400 MHz, DMSO) δ ppm 9.28 (d, *J* = 2.69 Hz, 1 H), 8.90 (d, *J* = 2.45 Hz, 1 H), 8.61 (dd, *J* = 10.64, 2.57 Hz, 2 H), 7.84 (d, *J* = 1.47 Hz, 1 H), 7.14 - 7.31 (m, 2 H), 6.66 - 6.75 (m, 1 H), 6.57 - 6.65 (m, 1 H), 5.45 (s, 2 H).

Intermediate 26: 4-fluoro-3-(5-(4-methyl-1H-imidazol-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline (**I-26**)



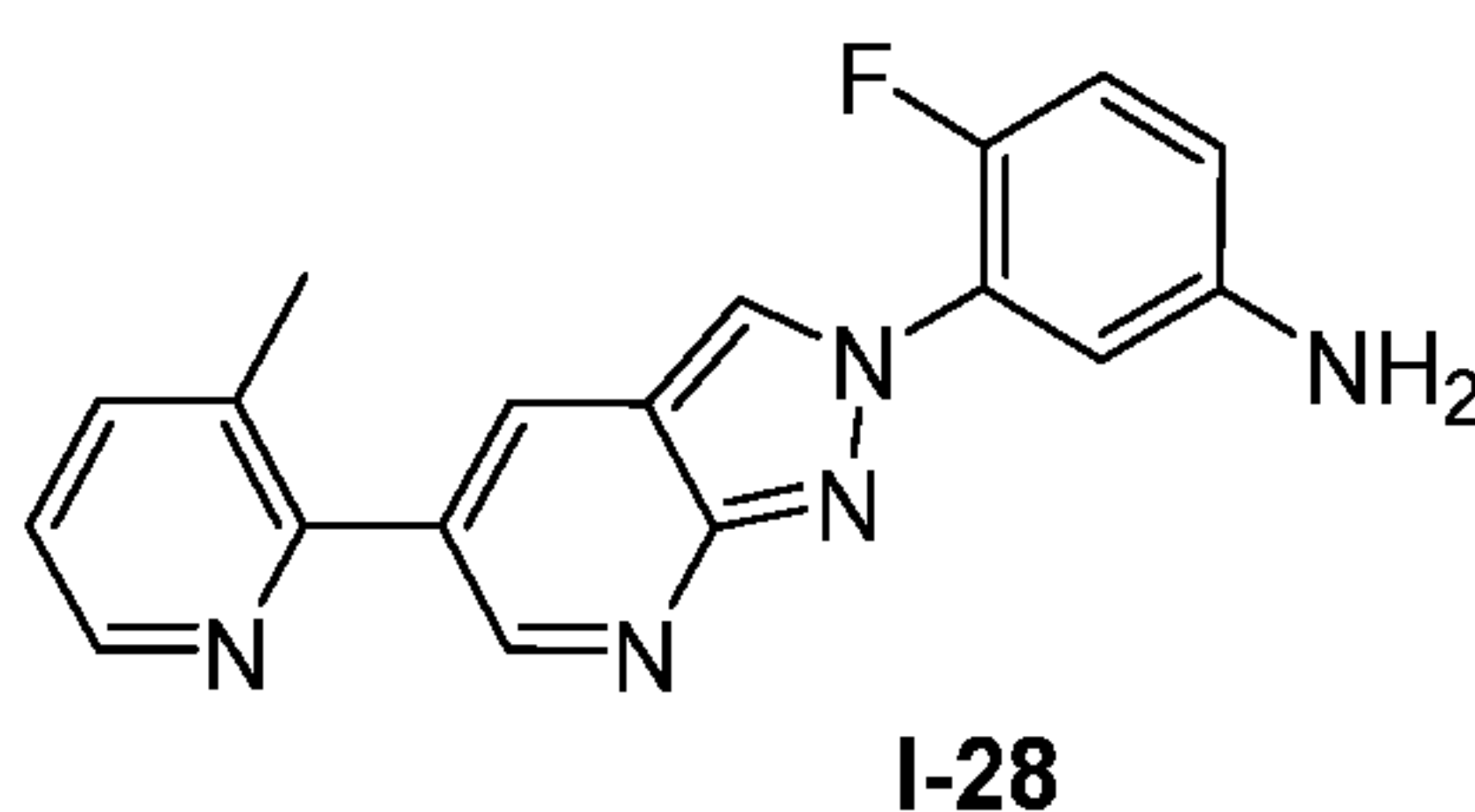
Intermediate **I-26** was prepared in a similar manner as intermediate **I-25** using 4-methyl-1H-imidazole as a starting material in Step B. ¹H NMR: (400 MHz, DMSO) δ ppm 9.00 (d, *J* = 2.69 Hz, 1 H), 8.89 (d, *J* = 2.20 Hz, 1 H), 8.37 - 8.49 (m, 1 H), 8.20 (s, 1 H), 7.53 (s, 1 H), 7.13 - 7.30 (m, 3 H), 6.61 - 6.80 (m, 1 H), 5.45 (s, 2 H), 2.21 (s, 3 H).

Intermediate 27: N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)pyrrolidine-1-carboxamide (**I-27**)



The intermediate **I-27** was prepared in a similar manner as intermediate **I-3** using pyrrolidine as a starting material. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 8.89 (d, *J*=2.26 Hz, 1 H), 8.75 (d, *J*=2.26 Hz, 1 H), 8.62 (d, *J*=2.51 Hz, 1 H), 8.51 (s, 1 H), 8.28 (dd, *J*=7.03, 2.51 Hz, 1 H), 7.74 (dt, *J*=9.10, 3.48 Hz, 1 H), 7.46 (dd, *J*=11.29, 9.29 Hz, 1 H), 3.39 (br s, 4 H), 1.87 (br t, *J*=6.40 Hz, 4 H).

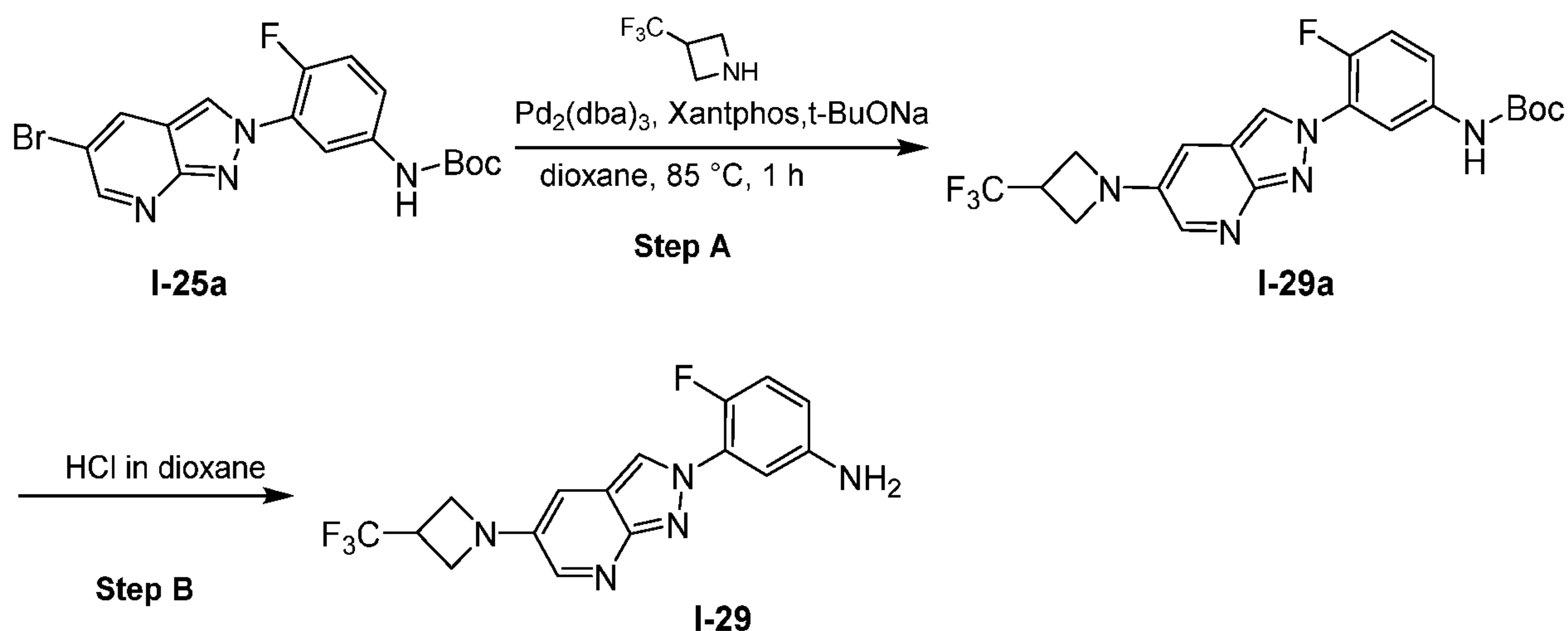
Intermediate 28: 4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline **I-28**



The intermediate **I-28** was prepared in a similar manner as intermediate **I-11** using (3-methylpyridin-2-yl)zinc(II) bromide as a starting material. ¹H NMR (400 MHz, DMSO-*d*₆) 8.89

(dd, $J = 8.2, 2.4$ Hz, 2H), 8.56 (dd, $J = 4.6, 1.7$ Hz, 1H), 8.47 (d, $J = 2.2$ Hz, 1H), 7.80 (ddd, $J = 7.7, 1.7, 0.8$ Hz, 1H), 7.40 - 7.32 (m, 1H), 7.24 - 7.14 (m, 2H), 6.69 (ddd, $J = 9.0, 3.9, 2.8$ Hz, 1H), 5.46 (s, 2H), 2.44 (s, 3H).

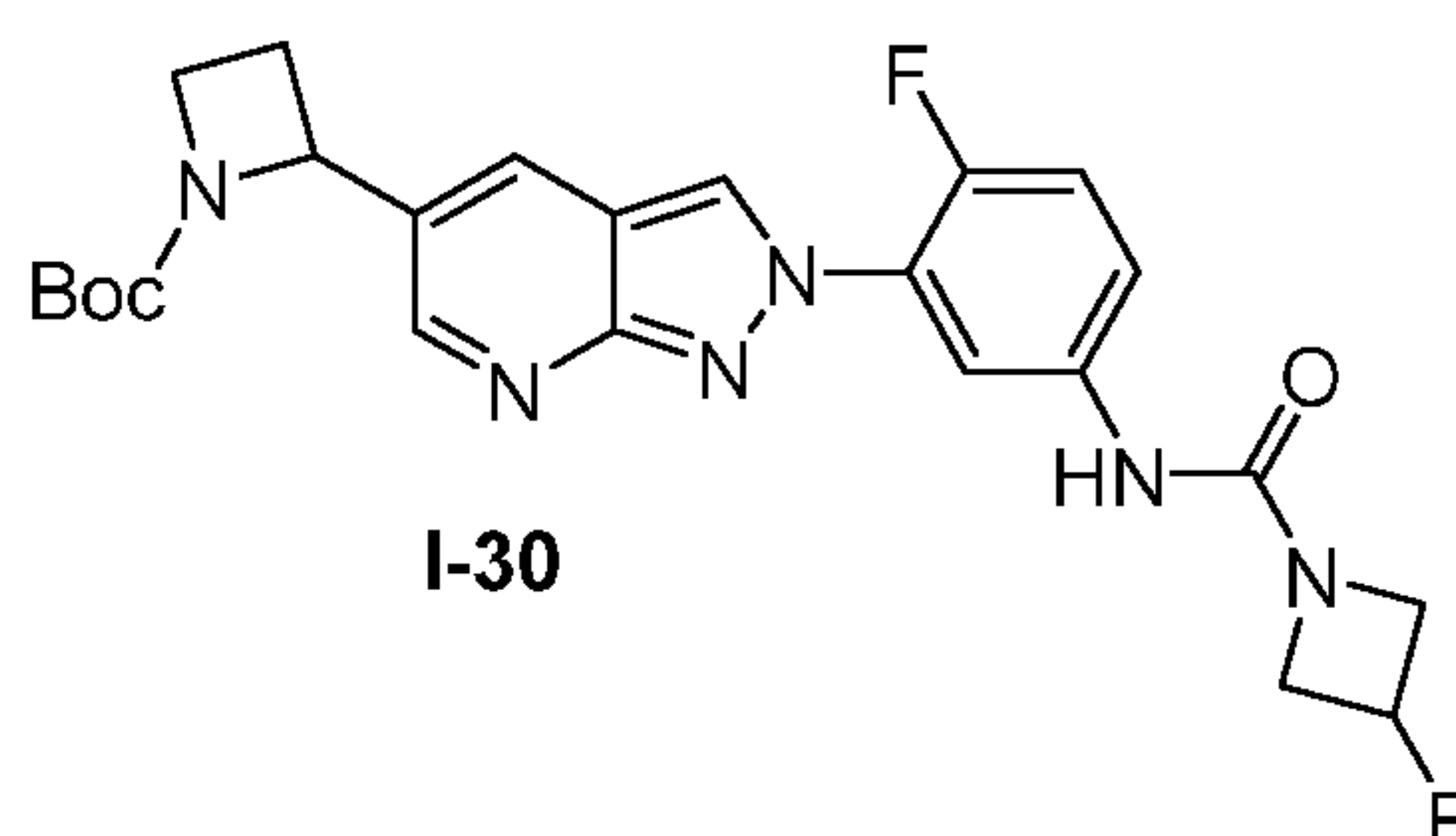
Intermediate 29: 4-fluoro-3-(5-(3-(trifluoromethyl)azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline **I-29**



Step A: A mixture of **I-25a** (100 mg, 245.6 μ mol, 1 eq), 3-(trifluoromethyl)azetidine (48 mg, 294.7 μ mol, 1.2 eq, HCl), NaOBu-t (2 M, 368.3 μ L, 3 eq), XantPhos (28 mg, 49.11 μ mol, 0.2 eq) and $\text{Pd}_2(\text{dba})_3$ (22 mg, 24.6 μ mol, 0.1 eq) in dioxane (2 mL) was de-gassed and then stirred at 80 °C for 1 hour under N_2 . The mixture was quenched and adjusted to pH=7 with 1 M HOAc. The mixture was purified by silica chromatography (Petroleum ether/Ethyl acetate=1/1) to give **I-29a** as a yellow solid. $M+H = 452.3$.

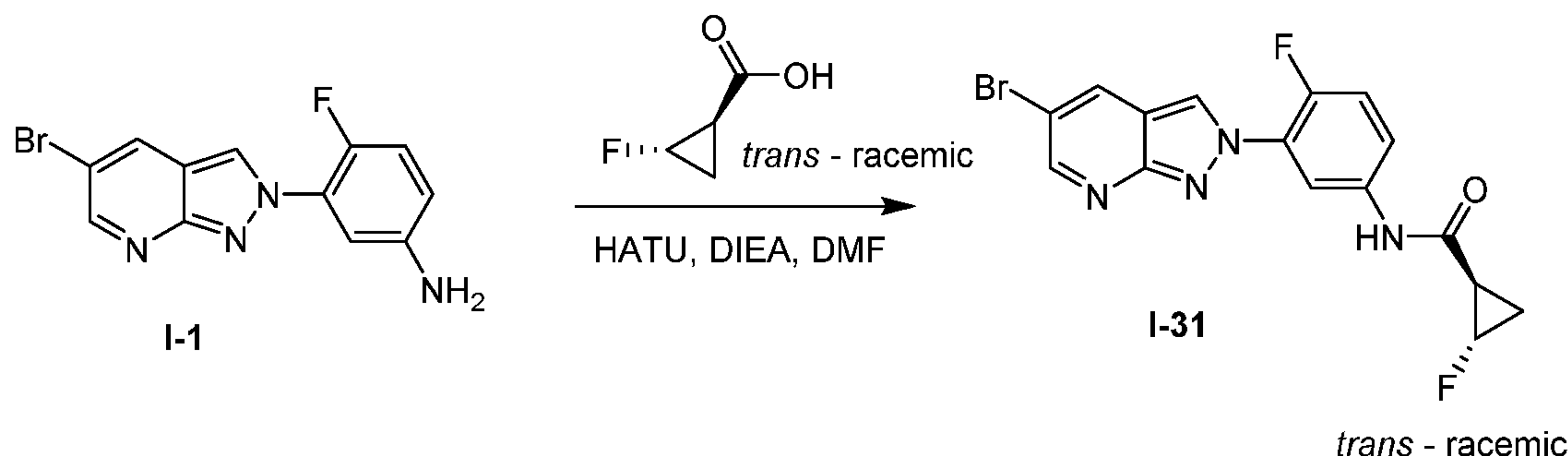
Step B: This step was performed in a similar manner as **I-25** step C to give **I-29**. ^1H NMR (400 MHz, DMSO) δ ppm 8.49 (d, $J = 2.45$ Hz, 1 H), 8.29 (d, $J = 2.81$ Hz, 1 H), 7.09 - 7.22 (m, 2 H), 7.02 (d, $J = 2.69$ Hz, 1 H), 6.63 (dt, $J = 8.74, 3.33$ Hz, 1 H), 5.38 (s, 2 H), 4.07 - 4.23 (m, 2 H), 3.98 (dd, $J = 7.95, 5.38$ Hz, 2 H), 3.66 - 3.83 (m, 1 H).

Intermediate 30: tert-butyl 2-(2-(2-fluoro-5-(3-fluoroazetidine-1-carboxamido)phenyl)-2H-pyrazolo[3,4-b]pyridin-5-yl)azetidine-1-carboxylate (**I-30**)



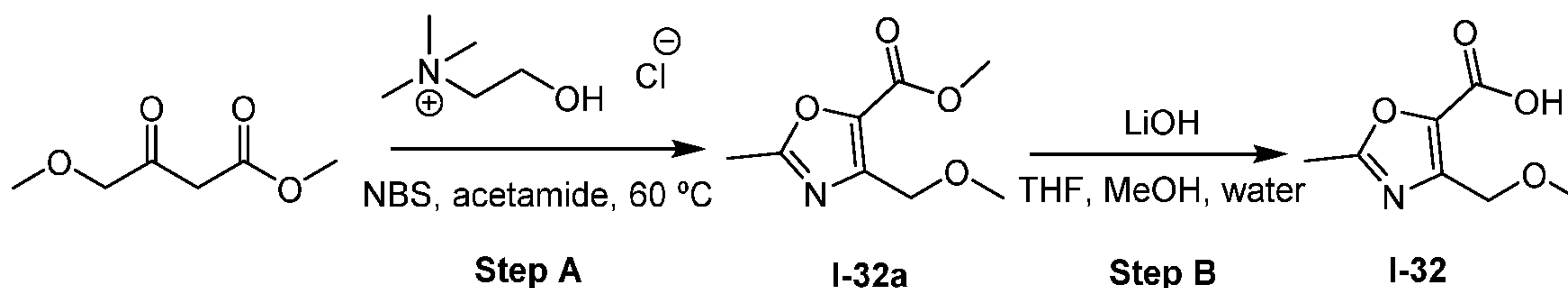
The synthesis of **I-30** is described in Example 24.

Intermediate 31: trans-N-(3-(5-bromo-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-2-fluorocyclopropane-1-carboxamide (**I-31**)



To a solution of **I-1** (2.5 g, 8.1 mmol, 1 eq) and trans-2-fluorocyclopropanecarboxylic acid (1.0 g, 9.8 mmol, 1.2 eq) in DMF (20 mL) was added HATU (3.7 g, 9.8 mmol, 1.2 eq) and DIEA (1.6 g, 12.2 mmol, 2.1 mL, 1.5 eq). The mixture was stirred at 25 °C for 16 hr. The reaction was diluted with ethyl acetate (150 mL) and was washed with saturated NaHCO₃ (50 mL) and brine 100 mL (50 mL * 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was triturated in tert-butyl methyl ether (20 mL) and collected by filtration to give **I-31** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 10.74 (s, 1 H), 8.91 (d, *J*=2.51 Hz, 1 H), 8.75 (d, *J*=2.26 Hz, 1 H), 8.62 (d, *J*=2.26 Hz, 1 H), 8.36 (dd, *J*=7.03, 2.51 Hz, 1 H), 7.60 - 7.74 (m, 1 H), 7.55 (dd, *J*=11.17, 9.16 Hz, 1 H), 4.70 - 5.12 (m, 1 H), 2.89 (s, 1 H), 2.23 - 2.41 (m, 1 H), 1.46 - 1.66 (m, 1 H).

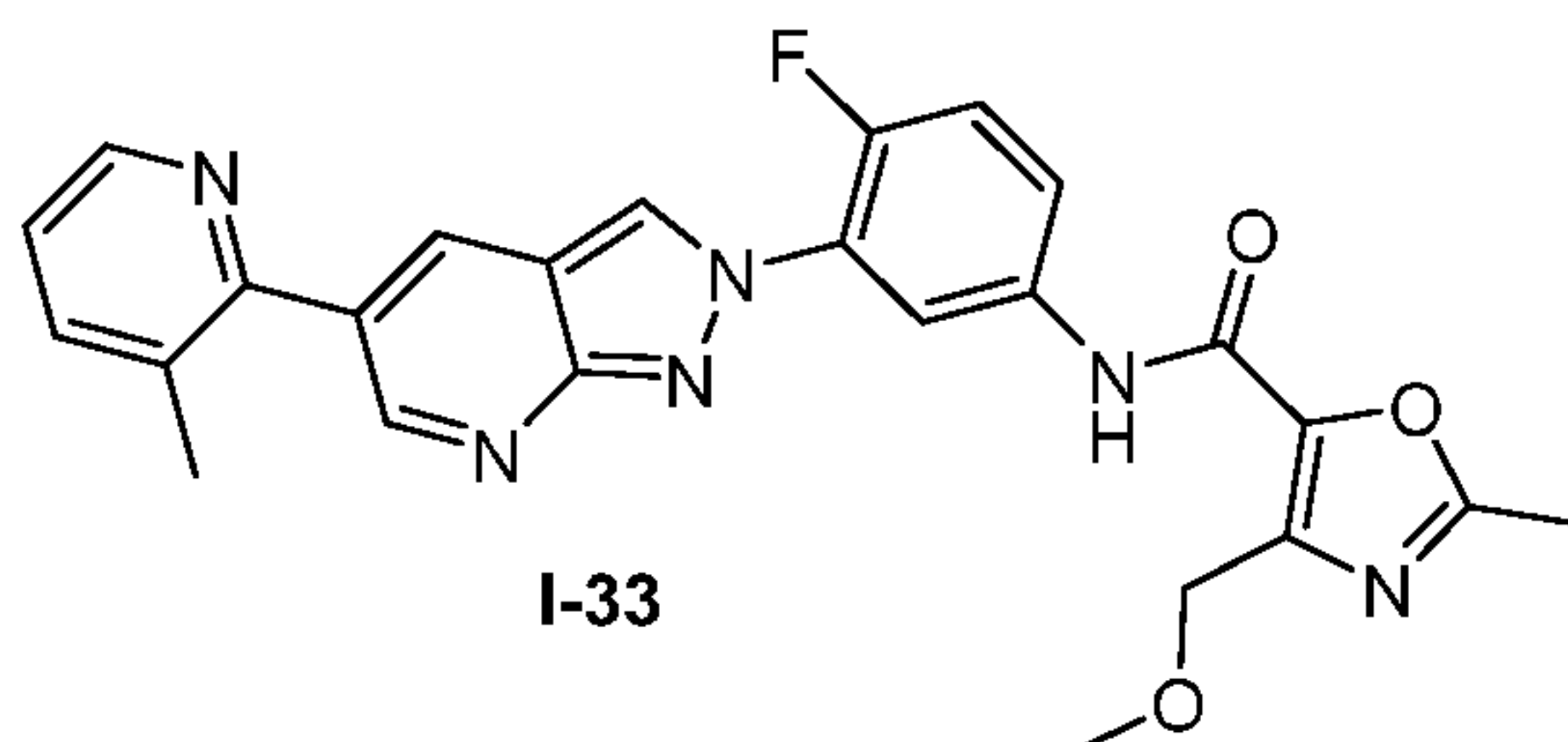
Intermediate 32: 4-(methoxymethyl)-2-methyloxazole-5-carboxylic acid (**I-32**)



Step A: Acetamide (1.7 g, 28.6 mmol, 4 eq) and 2-hydroxy-N,N,N-trimethylethan-1-aminium chloride (1 g, 7.2 mmol, 1 eq) were combined and heated to 60 °C for 30 min. NBS (2.5 g, 14.3 mmol, 2 eq) and methyl 4-methoxy-3-oxobutanoate (2.1 g, 14.3 mmol, 2 eq) were added to the reaction and heated to 60 °C for 1 h. The reaction mixture was purified by prep-TLC eluting with 50% ethyl acetate in petroleum ether to give **I-32a** as a light yellow oil. ¹H NMR: (400 MHz, CDCl₃) δ ppm 4.66 (s, 2 H), 3.94 (s, 3 H), 3.47 (s, 3 H), 2.55 (s, 3 H).

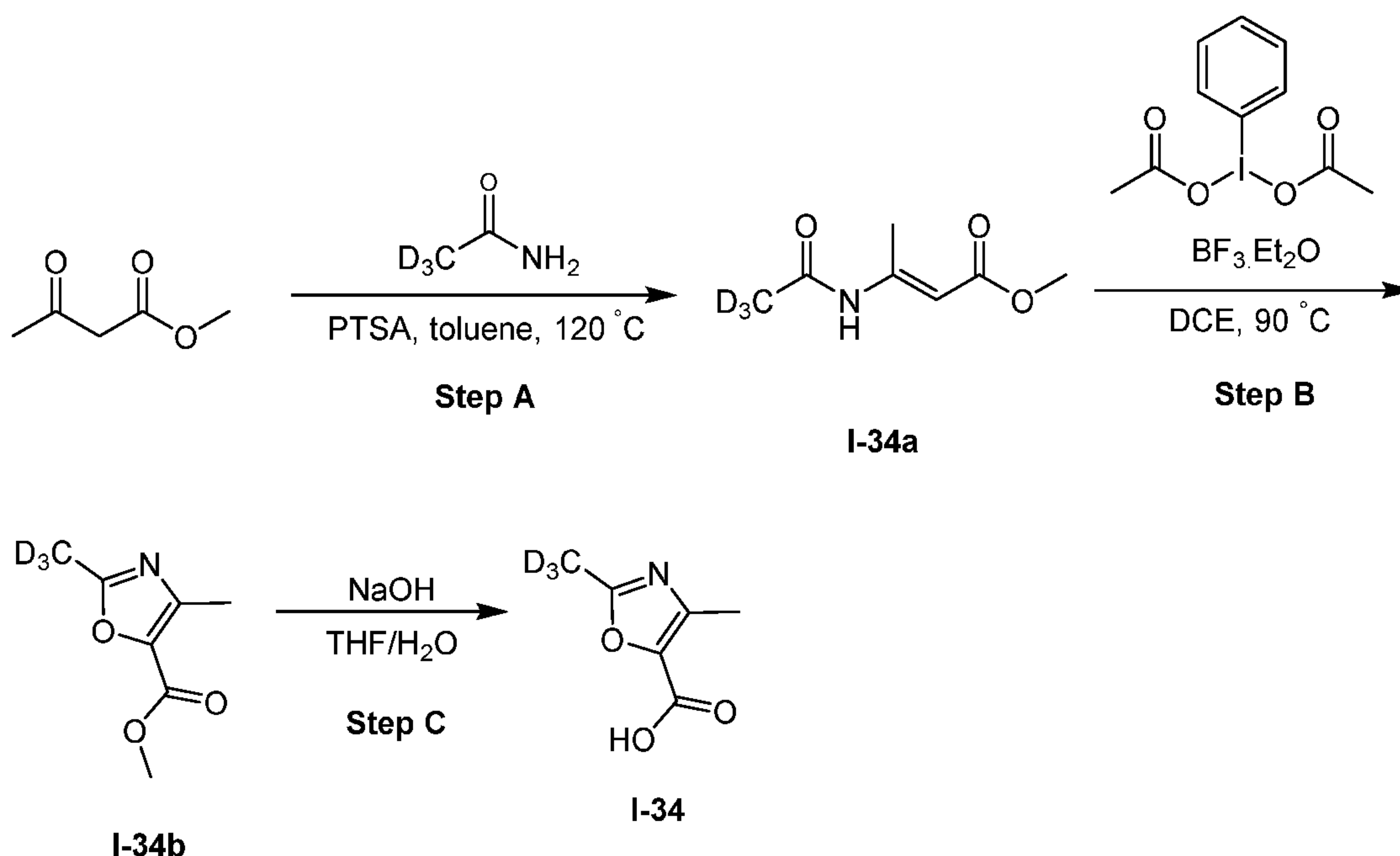
Step B: A mixture of **I-32a** (60 mg, 324.01 μmol, 1 eq) and LiOH·H₂O (27.2 mg, 648.0 μmol, 2 eq) in THF (1 mL), MeOH (1 mL) and H₂O (0.5 mL) was stirred at 25 °C for 16 hr under a N₂ atmosphere. The reaction mixture was concentrated under vacuo to give 60mg of a lithium salt of **I-32** as a yellow solid.

Intermediate 33: N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-4-(methoxymethyl)-2-methyloxazole-5-carboxamide (**I-33**)



The synthesis of **I-33** is described in Example 28.

5 **Intermediate 34:** 4-methyl-2-(methyl-d3)oxazole-5-carboxylic acid (**I-34**)

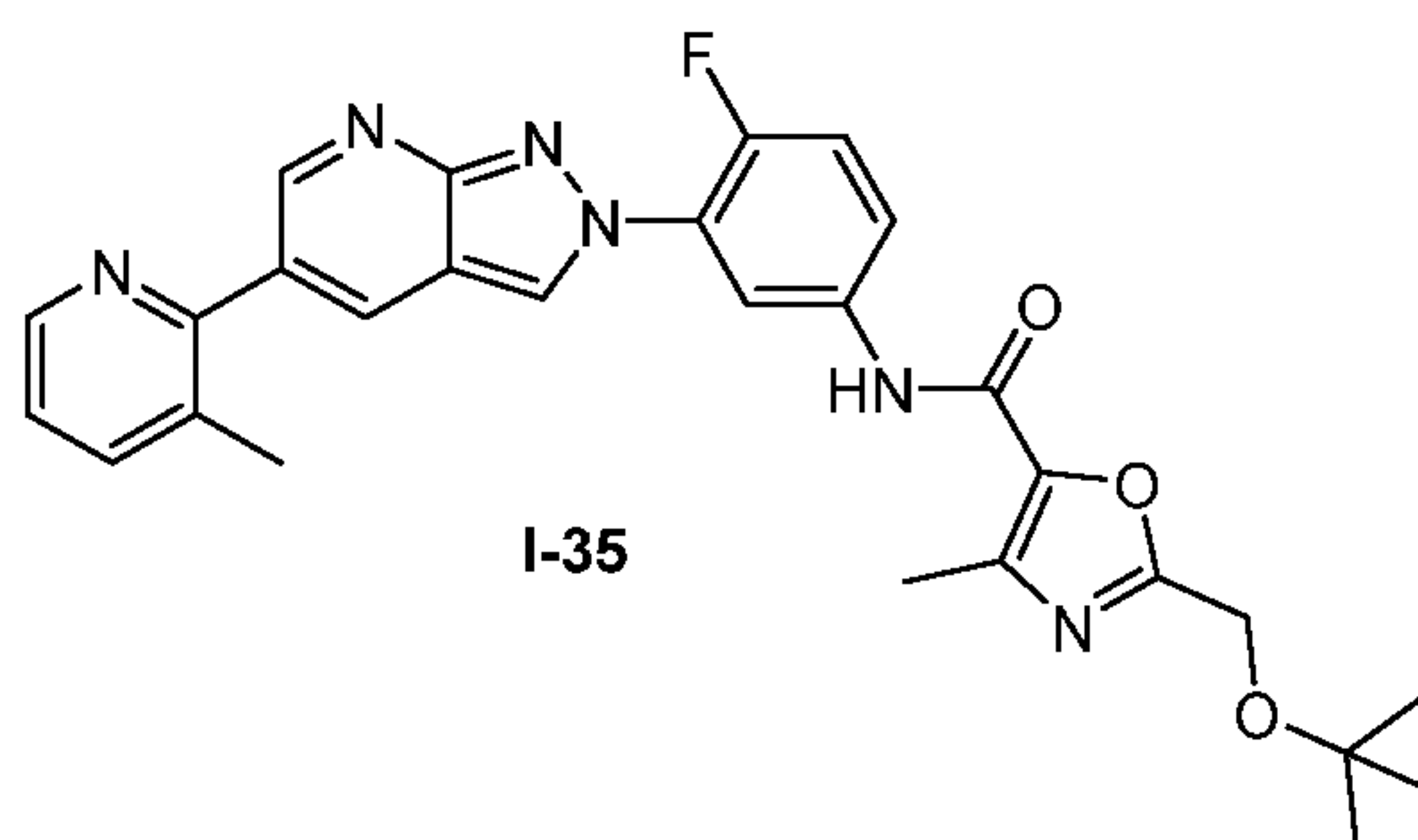


Step A: To a solution of methyl 3-oxobutanoate (900 mg, 7.7 mmol, 833 μ L, 1 *eq*) in toluene (15 mL) was added 2,2,2-trideuteroacetamide (962 mg, 15.5 mmol, 2 *eq*) and TsOH (13.3 mg, 77.5 μ mol, 0.01 *eq*). The mixture was stirred at 120 °C for 12 h. The mixture was concentrated under vacuum to give a residue which was purified by silica chromatography eluting with petroleum ether:ethyl acetate in a 30:1-10:1 gradient to give **I-34a** as a white solid. ^1H NMR (400 MHz, DMSO- d_6) δ ppm 10.88 (br s, 1 H), 5.02 (s, 1 H), 3.63 (s, 3 H), 2.29 (s, 3 H).

Step B: To a solution of **I-34a** (250 mg, 1.6 mmol, 1 *eq*) in DCE (8 mL) was added (diacetoxyiodo)benzene (654 mg, 2.0 mmol, 1.3 *eq*) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (443 mg, 3.1 mmol, 385 μ L, 2 *eq*). The mixture was stirred at 90 °C for 2 h. The mixture was concentrated under vacuum to give a residue which was purified by silica chromatography eluting with petroleum ether:ethyl acetate in a 30:1-10:1 gradient to give **I-34b** as a white solid. ^1H NMR: (400 MHz, DMSO- d_6) δ ppm 3.81 (s, 3 H), 2.33 (s, 3 H).

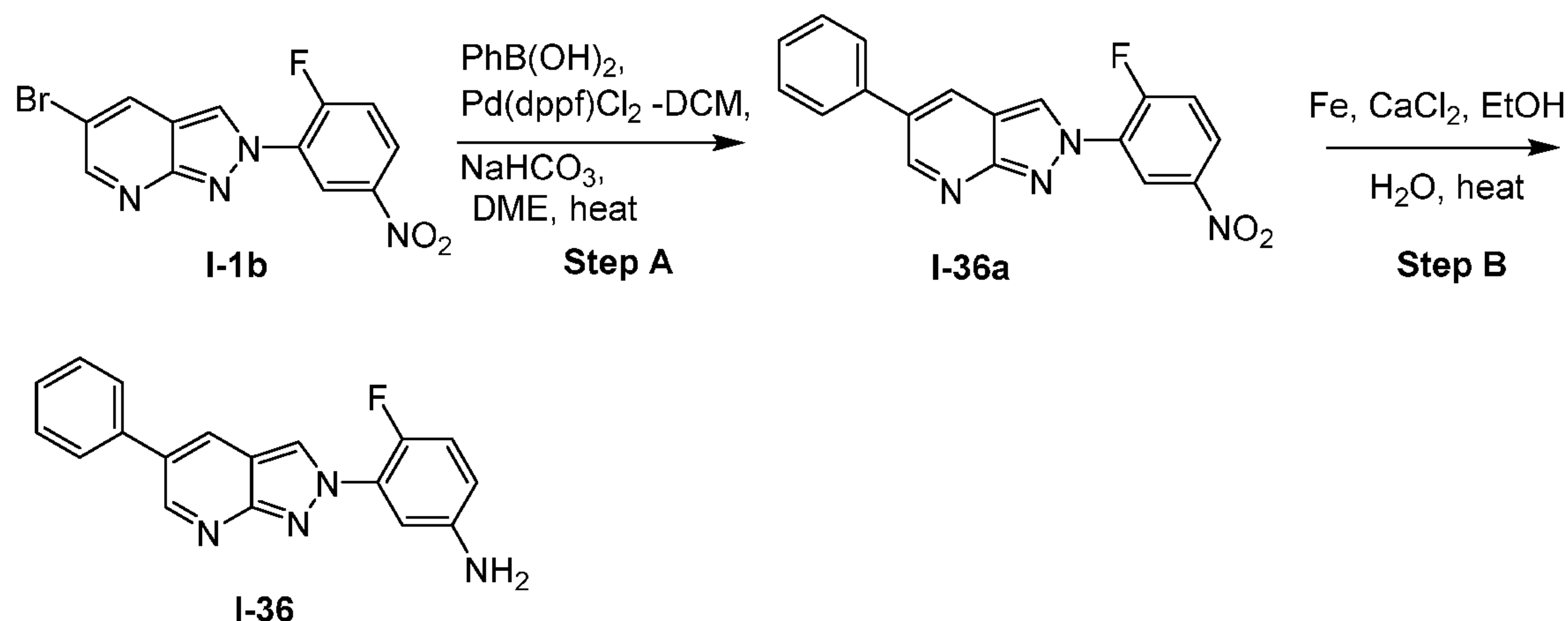
Step C: To a solution of **I-34b** (100 mg, 632 μ mol, 1 eq) in THF (1 mL) and H₂O (1 mL) was added a 15% aqueous NaOH (1 mL) solution. The mixture was stirred at 70 °C for 2 h. The pH was adjusted to 5 by addition of aqueous HCl solution (1 M) and a white solid was formed. The suspension was filtered and the filter cake was washed with H₂O (5 mL). The filter cake
 5 was dried under reduced pressure to give **I-34** as a white solid. ¹H NMR: (400 MHz, DMSO-d₆) δ ppm 13.30 (br s, 1 H), 2.32 (s, 3 H).

Intermediate 35: 2-(tert-butoxymethyl)-N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-4-methyloxazole-5-carboxamide (**I-35**)



10 The synthesis of **I-35** is described in Example 29.

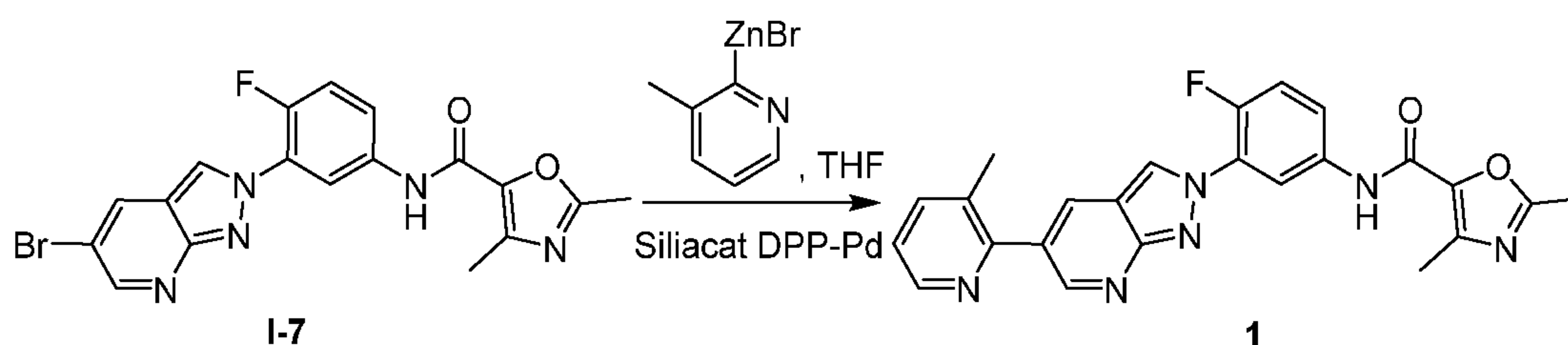
Intermediate 36: 4-fluoro-3-(5-phenyl-2H-pyrazolo[3,4-b]pyridin-2-yl)aniline (**I-36**)



Step A: A 100 ml sealed tube containing **I-1b** (500 mg, 1.483 mmol) and Phenyl boronic acid (181 mg, 1.483 mmol) in DME:H₂O (8:2) (15 mL) was purged with Argon gas for 15 min. NaHCO₃ (249 mg, 2.966 mmol) and Pd(dppf)Cl₂.DCM (61 mg, 0.074 mmol) were added and the
 15 reaction was stirred at 80 °C for 1 h. The reaction mixture was diluted with water, extracted with EtOAc (100 mL X 2). The combined organic layers were washed with 1x with water (150 mL) and 1x with brine (100 mL) and then dried over sodium sulphate and concentrated in vacuo. The crude compound was purified by silica gel chromatography eluting with 25% EtOAc in n-
 20 Hexane to afford **I-36a**. ¹H NMR (300 MHz, CDCl₃): δ 9.32-9.29 (m, 1H), 9.10 (s, 1H), 8.69 (s, 1H), 8.34-8.29 (m, 1H), 8.23 (s, 1H), 7.65 (d, J=6.9 Hz, 2H), 7.55-7.41 (m, 4H).; M+H = 335.2

Step B: To a flask containing **I-36a** (150 mg, 0.449 mmol) in EtOH:H₂O (8:2) (20 mL) was added Iron powder (370 mg, 6.730 mmol) and CaCl₂ (995 mg, 8.973 mmol) and the reaction was stirred at 65 °C for 2 h. The reaction mixture was diluted with water and extracted with EtOAc (100 mL X 2). The combined organic layers were washed 1x with water (100 mL) and 1x
 5 with brine (100 mL) and then dried over sodium sulphate and concentrated invacuo. The crude compound was purified by n-Pentane washings to afford **I-36**. ¹H NMR (300 MHz, CDCl₃): δ 9.04 (s, 1H), 8.61 (s, 1H), 8.22 (s, 1H), 7.70-7.40 (m, 6H), 7.20-7.00 (m, 1H), 6.75-6.60 (m, 1H); M+H = 305.30.

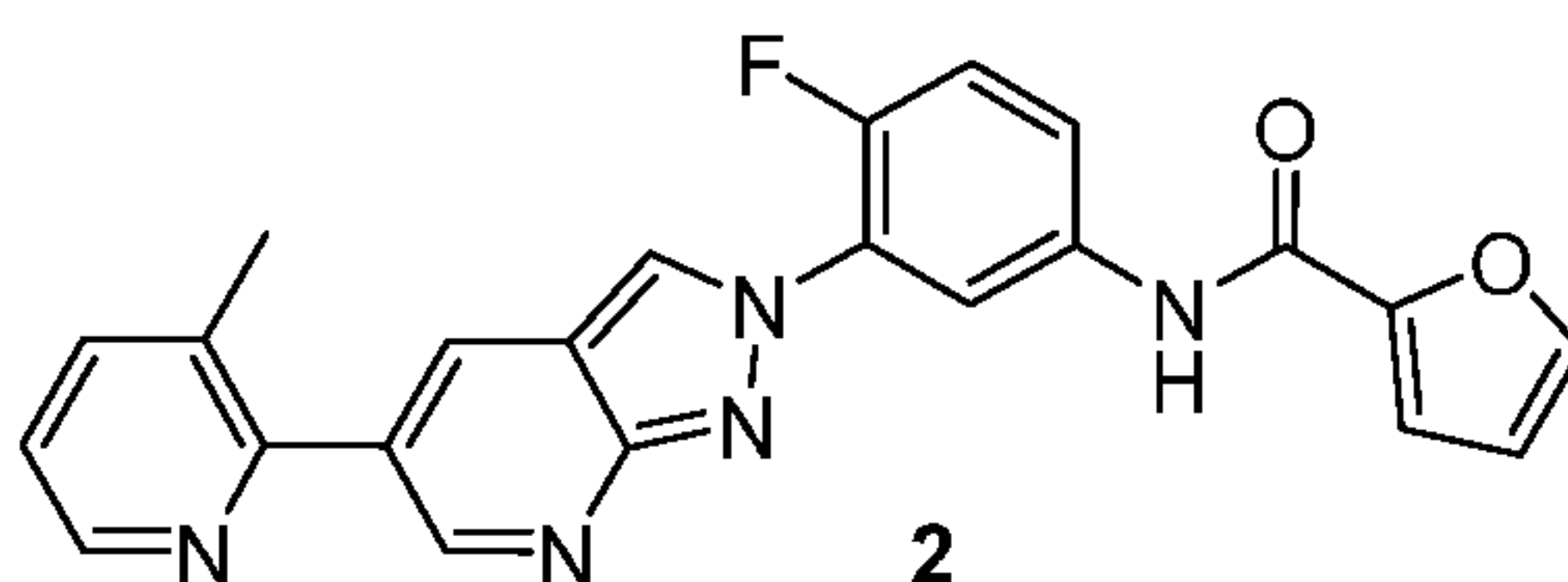
Example 1: N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-2,4-dimethyloxazole-5-carboxamide (Compound 1)



To a mixture of **I-7** (30 mg, 0.070 mmol) and Siliacat DPP-Pd 0.25 mmol/g (0.014 g, 3.52 μmol, 0.05 eq) was added 0.5 mL anhydrous THF. The reaction mixture was placed under a nitrogen atmosphere and (3-methylpyridin-2-yl)zinc(II) bromide (0.5M in THF, 0.56 mL, 0.28
 15 mmol, 4 eq) was added and the reaction was stirred at 65 °C overnight. The reaction was quenched with 0.2 mL water and purified by prep-HPLC (Waters Atlantis T3 C18 19*50mm*10 μm column) eluting with 20-80% acetonitrile (0.035% TFA) in water (0.05% TFA) to give compound **1**. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.90 (dd, *J* = 13.2, 2.3 Hz, 2H), 8.59 – 8.43 (m, 3H), 7.97 – 7.81 (m, 2H), 7.55 – 7.35 (m, 2H), 2.56 (s, 3H), 2.48 – 2.45 (m, 6H). Method 1:
 20 RT = 2.69 min.; M+H = 443.1.

Compounds **16**, **17**, **101**, **102**, **103**, **104**, **105**, **106**, **107** and **108** were synthesized according to the protocol described above using the corresponding zinc(II) bromides.

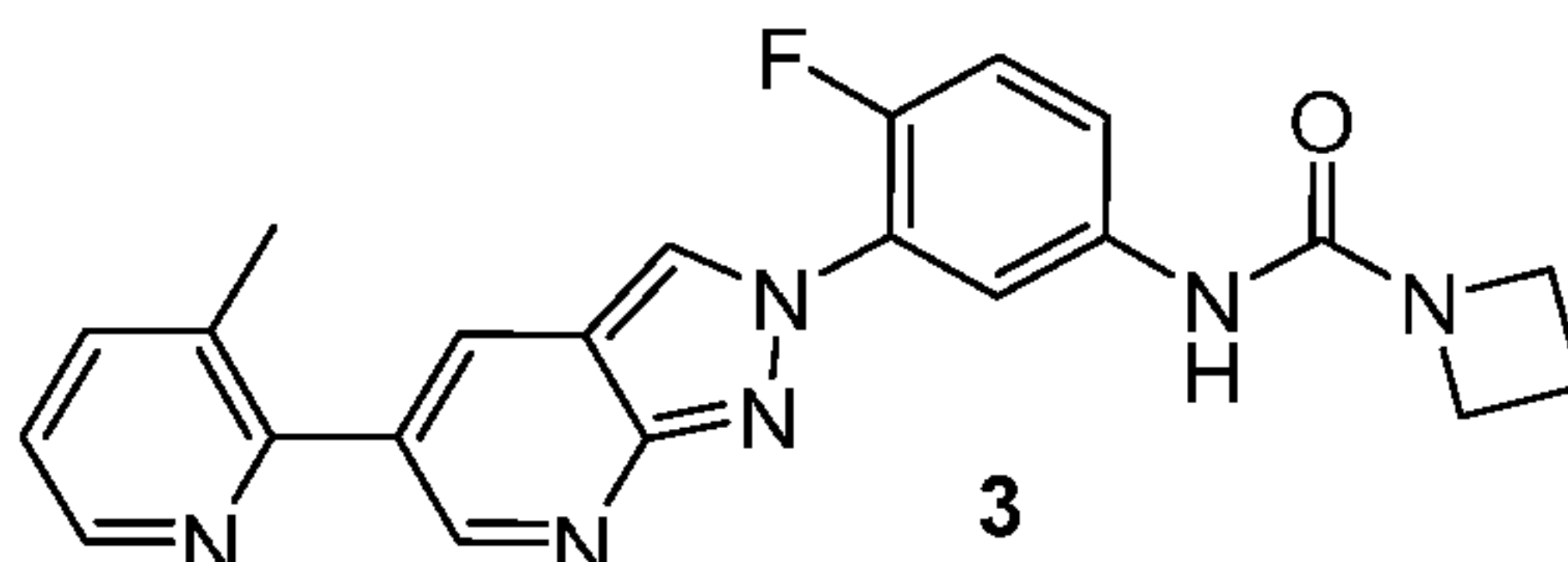
Example 2: N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)furan-2-carboxamide (Compound 2)



Compound **2** was prepared in a similar manner as compound **1** utilizing **I-8** as a starting material. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.92 (d, *J* = 2.4 Hz, 1H), 8.88 (d, *J* = 2.2 Hz, 1H), 8.55 - 8.45 (m, 3H), 7.96 (m, 1H), 7.87 (m, 1H), 7.78 (m, 1H), 7.52 - 7.39 (m, 2H), 7.32 (m, 1H), 6.68 (m, 1H), 2.46 (s, 3H). Method 2: RT = 0.89 min.; M+H = 414.3.

Compounds **54**, **55**, **56**, **57**, **59**, **60**, **61**, **62**, **63** and **64** were synthesized according to the protocol described above using the corresponding zinc(II) bromides.

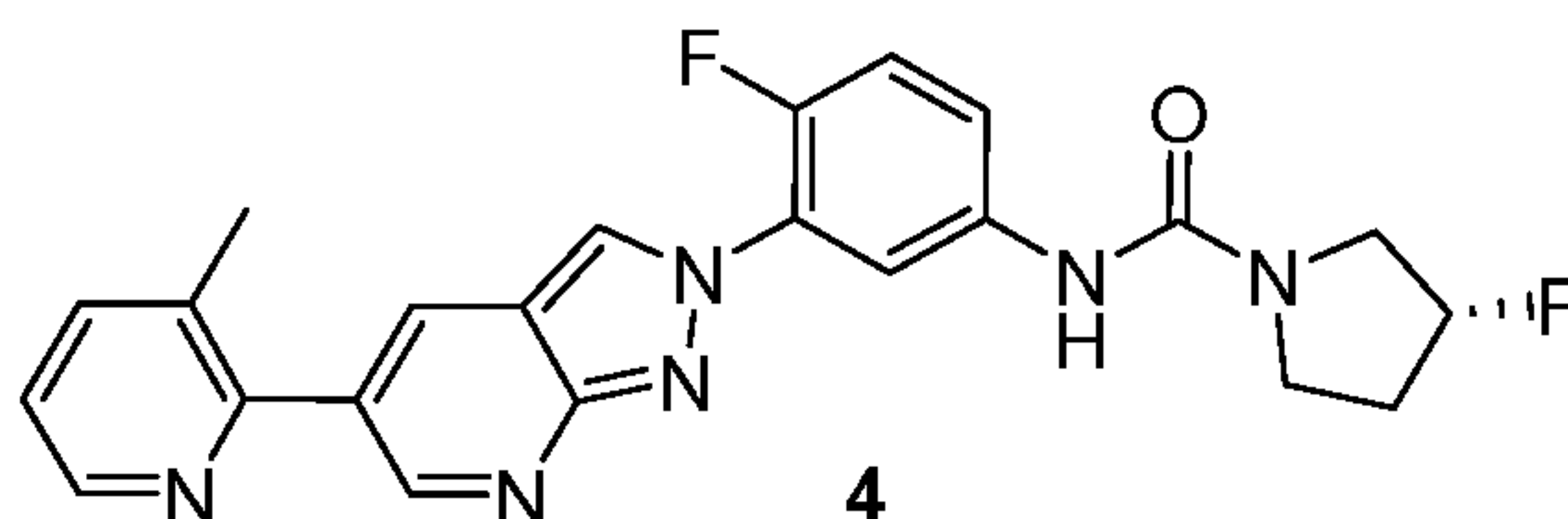
Example 3: N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 3)



Compound **3** was prepared in a similar manner as compound **1** utilizing **I-6** as a starting material. ¹H NMR (400 MHz, Methanol-d₄) δ 8.89 – 8.84 (m, 2H), 8.52 (m, 1H), 8.48 (m, 1H), 8.18 (m, 1H), 7.86 (m, 1H), 7.67 (m, 1H), 7.44 – 7.32 (m, 2H), 4.18 – 4.06 (m, 4H), 2.46 (s, 3H), 2.41 – 2.26 (m, 2H). Method 1: RT = 2.41 min.; M+H = 403.3.

Compound **99** was synthesized according to the protocol described above using the corresponding zinc(II) bromide.

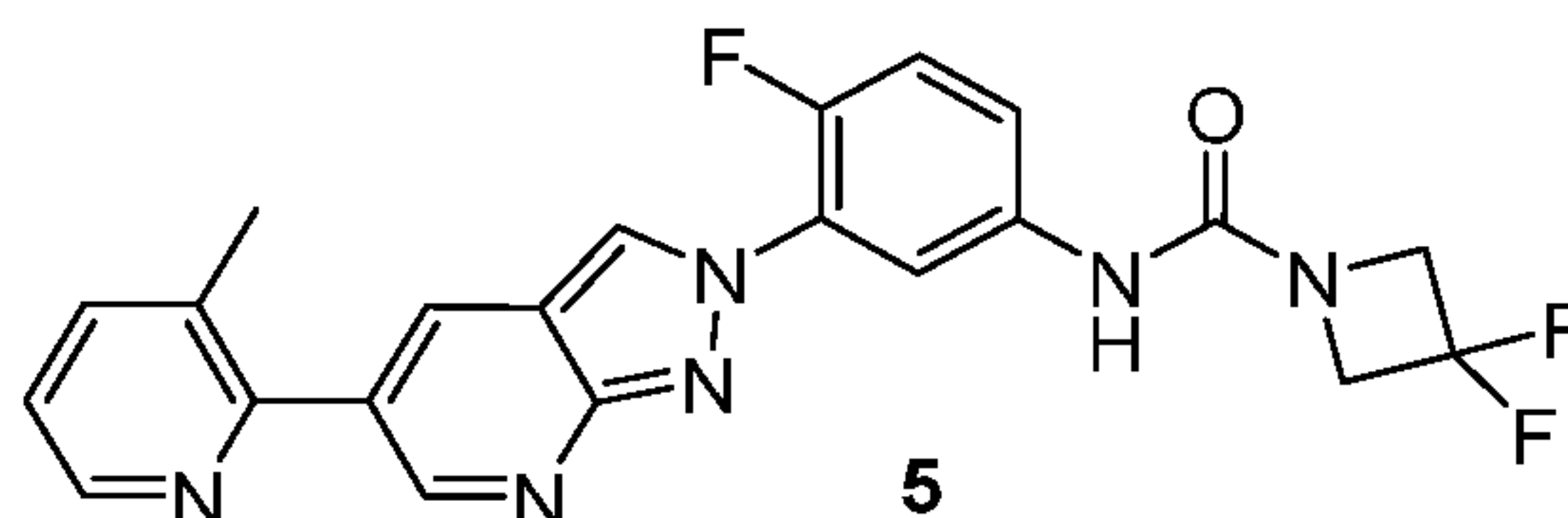
Example 4: (R)-3-fluoro-N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)pyrrolidine-1-carboxamide (Compound 4)



Compound **4** was prepared in a similar manner as compound **1** utilizing **I-5** as a starting material. ¹H NMR (400 MHz, Methanol-d₄) δ 8.87 (dd, J = 4.7, 2.3 Hz, 2H), 8.52 (m, 1H), 8.49 (m, 1H), 8.19 (m, 1H), 7.86 (m, 1H), 7.67 (m, 1H), 7.45 – 7.34 (m, 2H), 5.42 – 5.25 (m, 1H), 3.85 – 3.55 (m, 4H), 2.46 (s, 3H), 2.39 – 2.19 (m, 2H). Method 1: RT = 2.41 min.; M+H = 435.3.

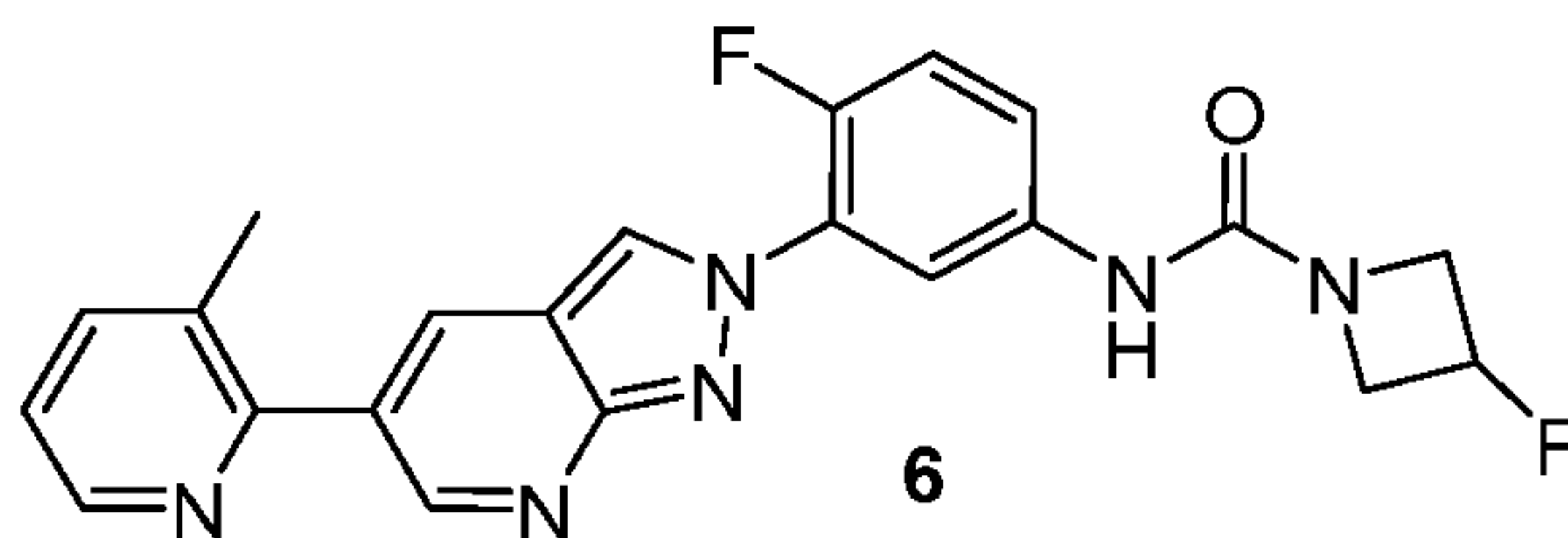
Compounds **41**, **42**, **43**, **44**, **45**, **46**, **47**, **48**, **49**, **50**, **51**, **52** and **53** were synthesized according to the protocol described above using the corresponding zinc(II) bromides.

Example 5: 3,3-difluoro-N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 5)



Compound **5** was prepared in a similar manner as compound **1** utilizing **I-3** as a starting material. ¹H NMR (400 MHz, Methanol-d₄) δ 8.88 (dd, J = 5.4, 2.3 Hz, 2H), 8.52 (m, 1H), 8.48 (m, 1H), 8.22 (m, 1H), 7.86 (m, 1H), 7.69 (m, 1H), 7.45 – 7.36 (m, 2H), 4.44 (m, 4H), 2.46 (s, 3H). Method 2: RT = 0.76 min.; M+H = 439.1.

Example 6: 3-fluoro-N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 6)

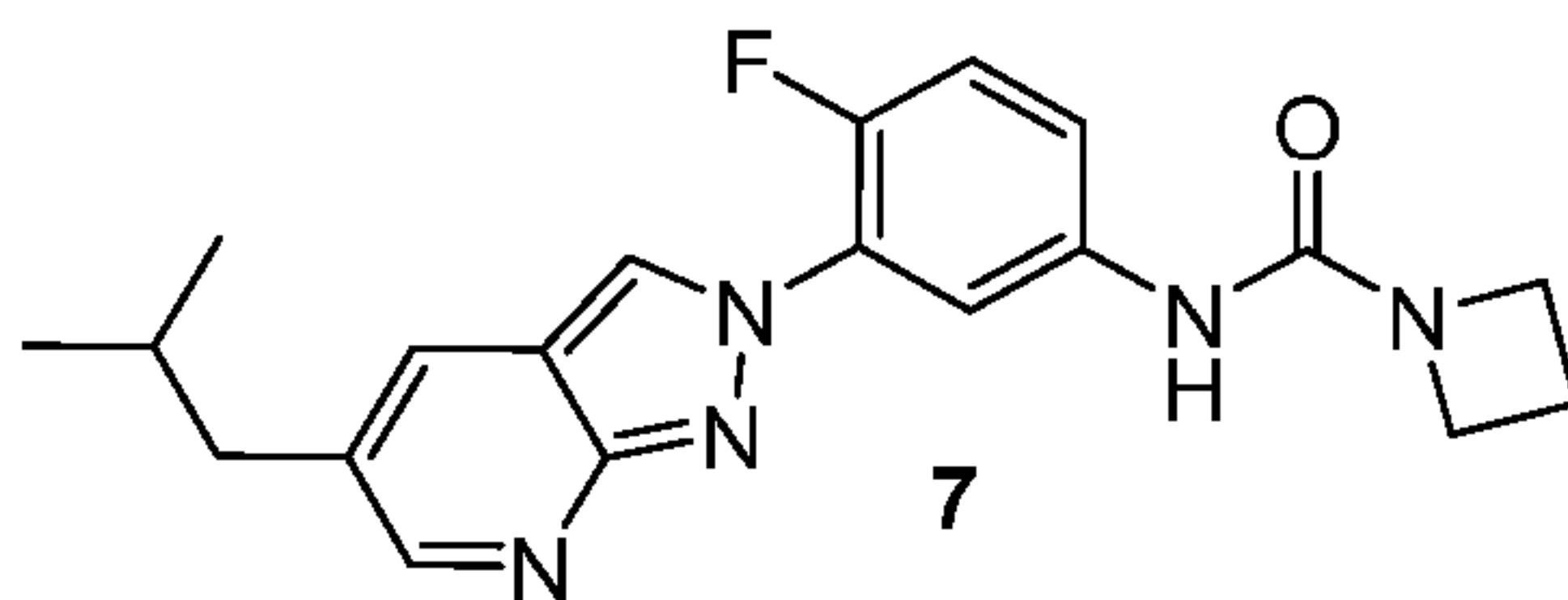


Compound **6** was prepared in a similar manner as compound **1** utilizing **I-4** as a starting material. ¹H NMR (500 MHz, DMSO-d₆) δ 8.98 (s, 1H), 8.94 (dd, J = 16.9, 2.3 Hz, 2H), 8.57 (ddd, J = 4.8, 1.7, 0.7 Hz, 1H), 8.49 (d, J = 2.3 Hz, 1H), 8.28 (dd, J = 7.0, 2.7 Hz, 1H), 7.80 (ddd, J = 7.7, 1.7, 0.8 Hz, 1H), 7.72 (ddd, J = 9.1, 4.1, 2.7 Hz, 1H), 7.49 (dd, J = 11.2, 9.1 Hz, 1H), 7.37 (dd, J = 7.7, 4.7 Hz, 1H), 5.41 (dt, J = 57.5, 6.1, 3.1 Hz, 1H), 4.34 (dddd, J = 21.7, 10.4, 6.0, 1.4 Hz, 2H), 4.04 (dddd, J = 24.9, 10.4, 3.1, 1.4 Hz, 2H), 2.44 (s, 3H). Method 1: RT = 2.39 min.; M+H = 421.1.

Compounds **14**, **15**, **18**, **19**, **20**, **21**, **23**, **24**, **25**, **26**, **27** and **28** were synthesized according to the protocol described above using the corresponding zinc(II) bromides.

Compound **318** was synthesized according to the protocol described above using dimethylzinc.

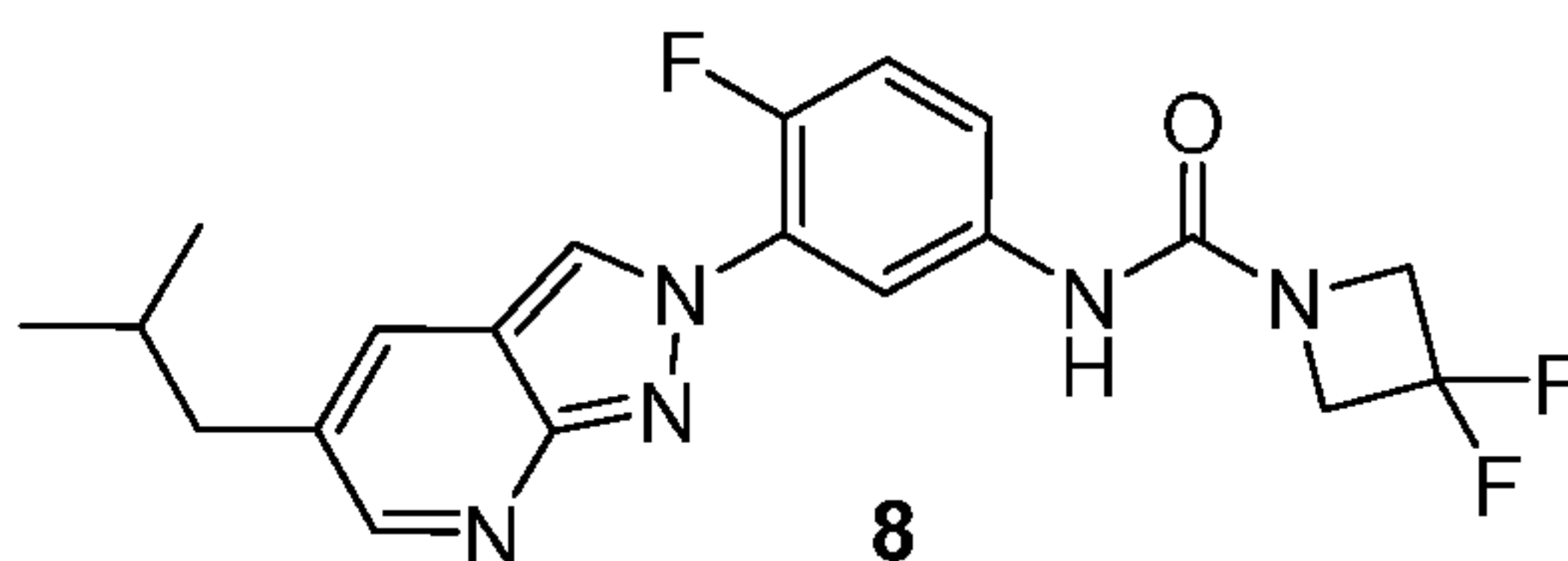
Example 7: N-(4-fluoro-3-(5-isobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 7)



Compound **7** was prepared in a similar manner as compound **1** utilizing **I-6** and isobutylzinc(II) bromide as starting materials. ¹H NMR (400 MHz, Methanol-d₄) δ 8.66 (d, J = 2.4 Hz, 1H), 8.56 (d, J = 2.2 Hz, 1H), 8.12 (m, 1H), 8.07 (m, 1H), 7.64 (m, 1H), 7.34 (m, 1H), 4.19 – 4.01 (m, 4H), 2.67 (m, 2H), 2.41 – 2.24 (m, 2H), 1.97 (m, 1H), 0.99 (m, 6H). Method 1: RT = 3.11 min.; M+H = 368.3.

Compounds **91**, **93**, **94**, **95**, **96**, **97** and **98** were synthesized according to the protocol described above using the corresponding zinc(II) bromides.

Example 8: 3,3-difluoro-N-(4-fluoro-3-(5-isobutyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 8)

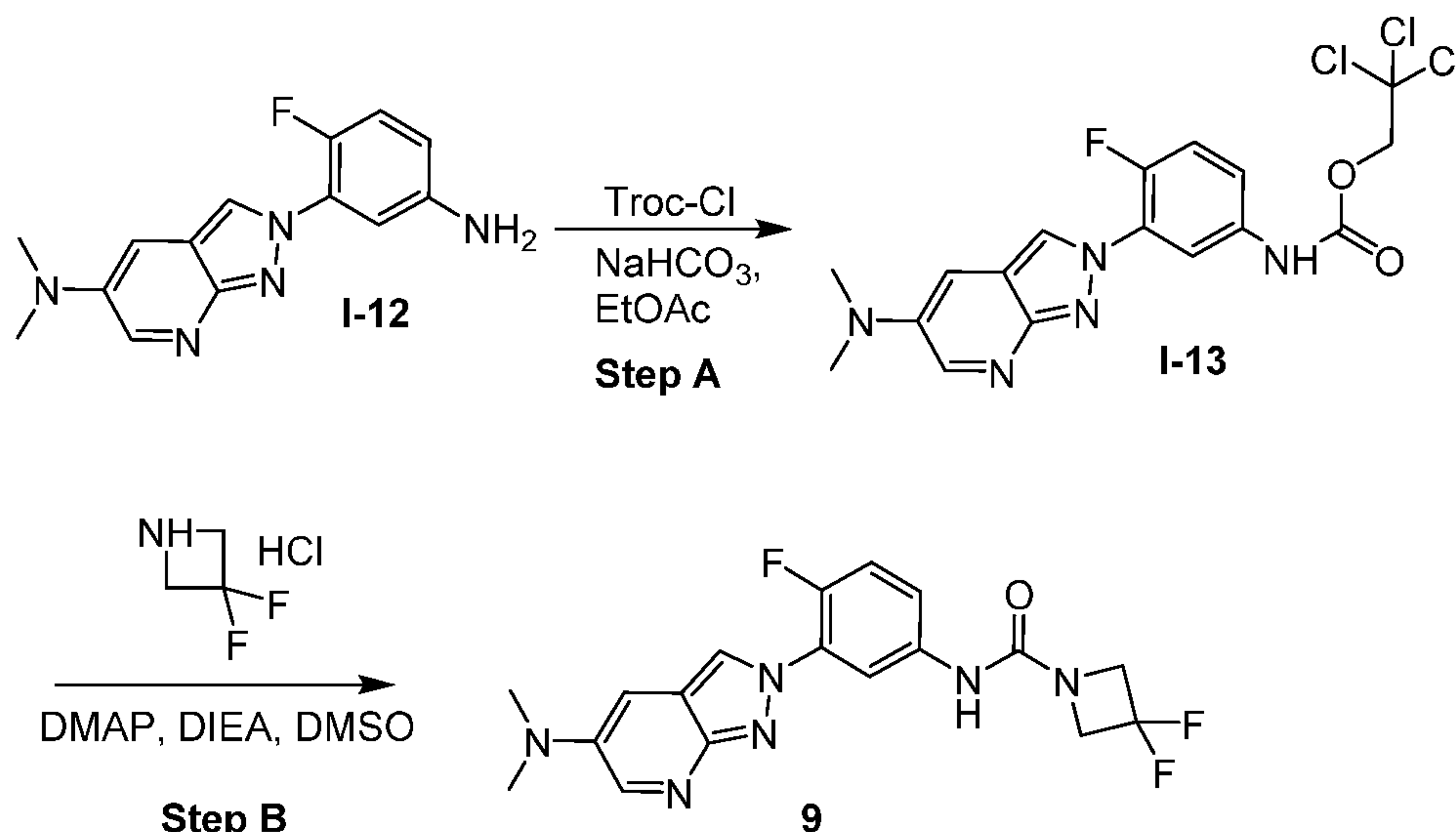


Compound **8** was prepared in a similar manner as compound **1** utilizing **I-3** and isobutylzinc(II) bromide as starting materials. ¹H NMR (400 MHz, Methanol-d₄) δ 8.59 (d, J = 2.5 Hz, 1H), 8.46 (d, J = 2.2 Hz, 1H), 8.06 (m, 1H), 7.97 (m, 1H), 7.56 (m, 1H), 7.30 – 7.24 (m, 1H), 4.33 (m, 4H), 2.57 (m, 2H), 1.92 – 1.81 (m, 1H), 0.89 (m, 6H). Method 2: RT = 1.09 min.

M+H = 404.1.

Compounds **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37** and **38** were synthesized according to the protocol described above using the corresponding zinc(II) bromides.

Example 9: N-(3-(5-(dimethylamino)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-3,3-difluoroazetidine-1-carboxamide (Compound 9)

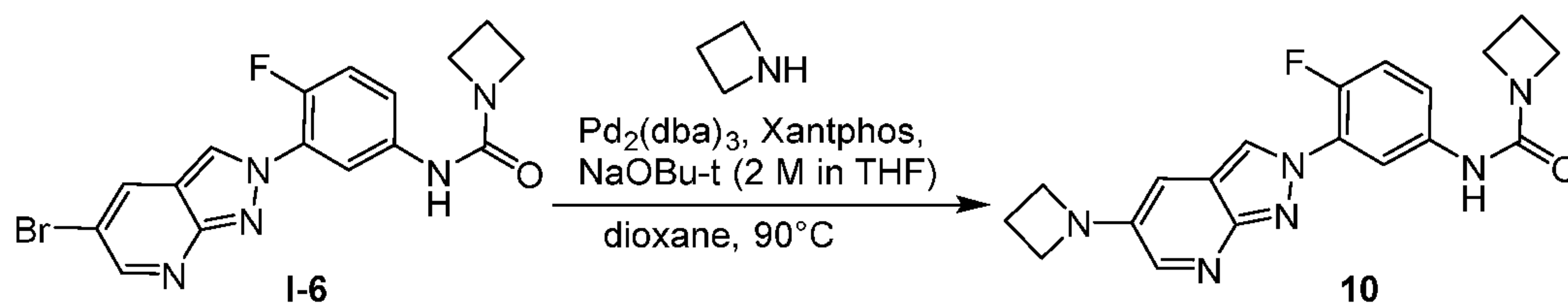


Step A: To a solution of **I-12** (0.5 g, 1.8 mmol, 1 eq) in ethyl acetate (5 mL) and saturated aqueous NaHCO₃ (5 mL) was added 2,2,2-trichloroethyl carbonochloridate (585.7 mg, 2.8 mmol, 370.7 μL, 1.5 eq) at 0°C and the reaction was stirred at 0°C for 1 hr. The reaction mixture was extracted with EtOAc (30 mL*3) and the combined organics were dried over sodium sulfate and concentrated. The resulting residue was purified by silica chromatography eluting with 20% EtOAc and 20% DCM in petroleum ether to give **I-13** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 10.52 (br s, 1 H), 8.71 (d, *J*=2.93 Hz, 1 H), 8.57 (d, *J*=2.69 Hz, 1 H), 8.25 (br d, *J*=5.14 Hz, 1 H), 7.44 - 7.64 (m, 2 H), 7.16 (d, *J*=2.69 Hz, 1 H), 4.99 (s, 2 H), 2.96 (s, 6 H).

Step B: The reaction mixture of **I-13** (60 mg, 134.3 μmol, 1 eq), 3,3-difluoroazetidine HCl (25 mg, 268.6 μmol, 2 eq), DIEA (34.6 mg, 268.6 μmol, 46.7 μL, 2 eq), DMAP (1.6 mg, 13.4 μmol, 0.1 eq) in DMSO (1 mL) was stirred at 60°C for 12 hours and at 70 °C for another 12 hours. The reaction mixture was purified by Prep-HPLC column: Phenomenex Gemini C18 250*50mm*10 μm; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 25%-55%, 12 min to give **9** as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 9.18 (s, 1 H), 8.70 (d, *J*=3.01 Hz, 1 H), 8.55 (d, *J*=2.76 Hz, 1 H), 8.20 (dd, *J*=6.90, 2.64 Hz, 1 H), 7.56 - 7.78 (m, 1 H), 7.45 (dd, *J*=11.42, 9.16 Hz, 1 H), 7.15 (d, *J*=3.01 Hz, 1 H), 4.41 (t, *J*=12.67 Hz, 4 H), 2.95 (s, 6 H). Method 1: RT = 2.84 min.; M+H = 391.1.

Compounds **100**, **124**, **133**, **142**, **143**, **156**, **167**, **170**, **195**, **219**, **220**, **221**, **222**, **223**, **224**, **225**, **226**, **227**, **228**, **229**, **260**, **276**, **319**, **320**, **321**, **322**, **323**, **324**, and **328**, were synthesized according to the protocol described above using intermediates **I-9**, **I-12**, **I-16**, **I-23**, **I-25** or **I-26** and the corresponding amine.

Example 10: N-(3-(5-(azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)azetidine-1-carboxamide (Compound 10)



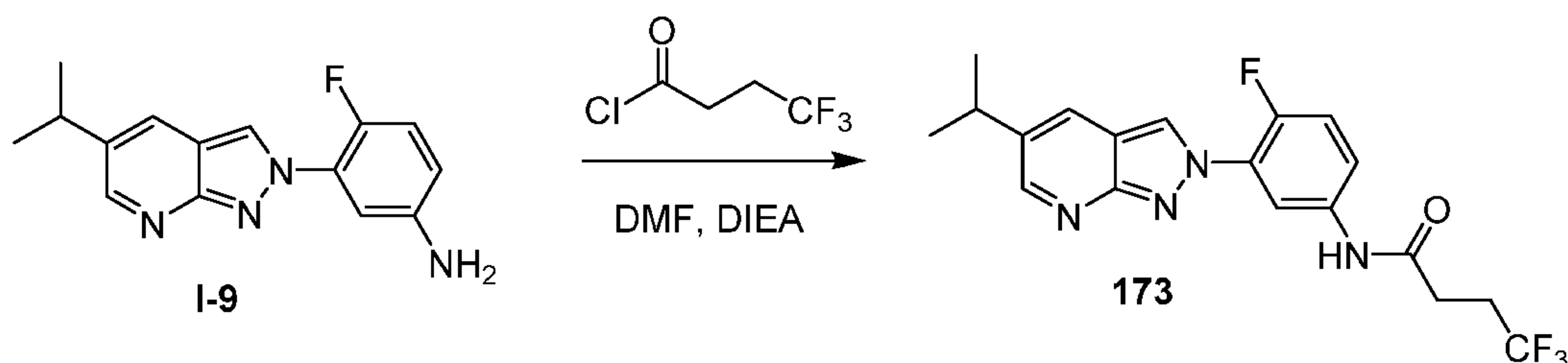
A mixture of **I-6** (80 mg, 205 μ mol, 1 eq), azetidine (17.6 mg, 307.5 μ mol, 20.7 μ L, 1.5 eq), NaOt-Bu (2 M in THF, 307.5 μ L, 3 eq), XantPhos (23.7 mg, 41 μ mol, 0.20 eq) and $\text{Pd}_2(\text{dba})_3$ (18.8 mg, 20.5 μ mol, 0.10 eq) in dioxane (3 mL) was de-gassed with Argon and heated to 90 °C for 4 h. The reaction was quenched with 1 M HOAc and purified by prep-HPLC (column: Phenomenex Gemini C18 250*50mm*10 μ m; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 28%-58%, 12 min) to give **10** as a yellow solid. ^1H NMR (400 MHz, Methanol- d_4), δ ppm, 8.42 (d, J = 2.51 Hz, 1 H), 8.22 (d, J = 2.76 Hz, 1 H), 8.05 (dd, J =6.78, 2.76 Hz, 1 H), 7.58 - 7.62 (m, 1 H), 7.30 (dd, J = 11.04, 9.16 Hz, 1 H), 7.01 (d, J = 2.64 Hz, 1 H), 4.10 (t, J = 7.65 Hz, 4 H), 3.99 (t, J = 7.22 Hz, 4 H), 2.41 - 2.49 (m, 2 H), 2.27 - 2.35 (m, 2 H). Method 1: RT = 2.80 min.; $M+H$ = 367.1.

Compounds **40**, **58**, **92**, **122**, **131**, **132**, **134**, **135**, **137**, **141**, **144**, **145**, **147**, **149**, **151**, **155**, **157**, **158**, **161**, **163**, **171**, **172**, **177**, **178**, **179**, **180**, **181**, **183**, **184**, **185**, **186**, **190**, **191**, **192**, **193**, **194**, **197**, **198**, **199**, **200**, **201**, **202**, **203**, **204**, **205**, **230**, **231**, **232**, **234**, **235**, **236**, **237**, **238**, **239**, **240**, **241**, **243**, **244**, **245**, **248**, **249**, **250**, **251**, **252**, **253**, **255**, **263**, **266**, **272**, **290**, **291**, **292**, **298**, **299**, **300**, **302**, **303**, **306**, **307**, **308**, **314**, **326**, **327**, **338** and **339** were synthesized according to the protocol described above using the corresponding intermediate **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, **I-24**, **I-27** or **I-31** and the corresponding amines.

Compounds **242** was isolated in addition to compound **241** using the above reaction conditions. Similarly compound **246** was isolated in addition to compound **202** using the above reaction conditions.

Compound **270** was synthesized using the protocol described above using Boc-piperidine after which the Boc group was removed using 0.36:1 ratio of TFA in DCM followed by neutralization to pH = 7 with Et_3N and then prep-HPLC purification (column: Phenomenex Synergi C18 150*25*10 μ m; mobile phase: [water(0.225%FA)-acetonitrile]; B%: 3%-30%, 10 min) to give compound **270**.

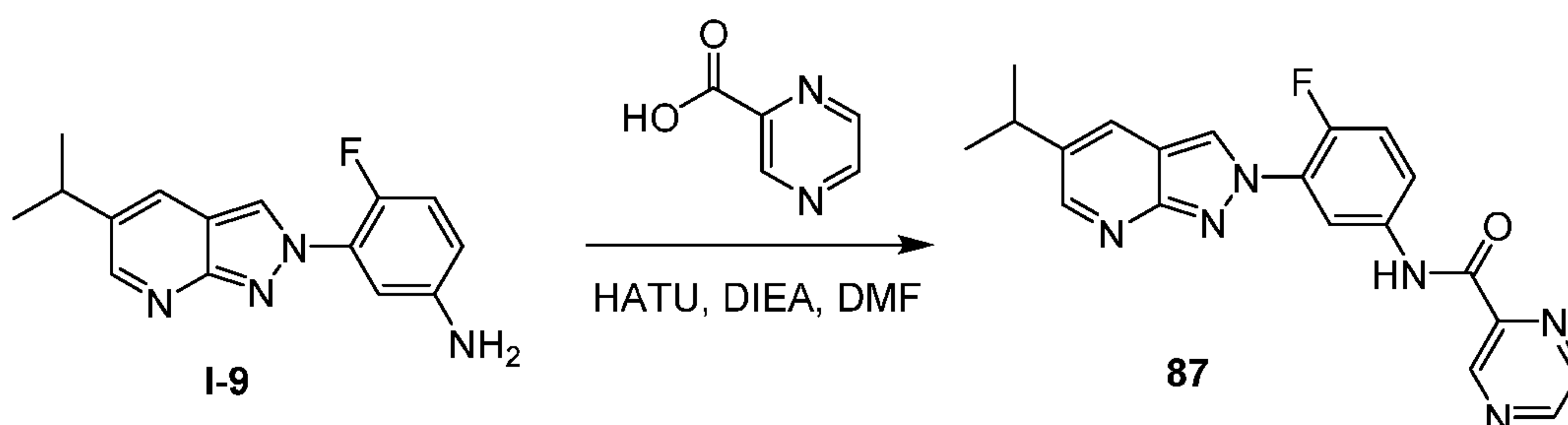
Example 11: 4,4,4-trifluoro-N-(4-fluoro-3-(5-isopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)butanamide (Compound 173)



To a solution of **I-9** (25mg, 0.092 mmol) in DMF (1.5 ml) and DIEA (0.040 ml, 0.23 mmol) was added 4,4,4-trifluorobutanoyl chloride (14.9 mg, 0.092 mmol) and the reaction was stirred for 12 hrs at room temperature. The crude reaction mixture was purified directly on a 15 g C18 flash chromatography column eluting with 20-90% acetonitrile in water to give compound **173** as a white solid. ¹H NMR (400 MHz, DMSO-d₆) δ 10.45 (s, 1H), 8.81 (d, J = 2.7 Hz, 1H), 8.69 (d, J = 2.3 Hz, 1H), 8.36 (dd, J = 7.0, 2.7 Hz, 1H), 8.05 (dd, J = 2.3, 0.8 Hz, 1H), 7.68 (ddd, J = 9.1, 4.2, 2.7 Hz, 1H), 7.54 (dd, J = 11.2, 9.0 Hz, 1H), 3.08 (pd, J = 6.9, 0.8 Hz, 1H), 2.72 - 2.55 (m, 4H), 1.30 (d, J = 6.9 Hz, 6H). Method 1: RT = 3.19 min.; M+H = 395.2.

Compound **174** was synthesized according to the protocol described above using the corresponding chloroformate in place of the acid chloride.

Example 12: N-(4-fluoro-3-(5-isopropyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)pyrazine-2-carboxamide (Compound 87)



Pyrazine-2-carboxylic acid (16.5 mg, 0.13 mmol) was added to a flask followed by **I-9** (30 mg, 0.11 mmol) dissolved in 0.25mL DMF. A solution of DIEA (0.058 mL, 0.33 mmol) and HATU (50.6 mg, 0.13 mmol) in 0.25mL DMF was added to the reaction and the resulting mixture was stirred overnight. The reaction was filtered through a 0.2 micron syringe filter and the material was purified by prep-HPLC (Waters Atlantis T3 C18 19*50mm*10 um column) eluting with 20-80% acetonitrile (0.035% TFA) in water (0.05% TFA) to give compound **87**. ¹H NMR (400 MHz, Methanol-d₄) δ 9.36 (m, 1H), 8.84 (m, 1H), 8.76 (m, 1H), 8.72 (m, 1H), 8.66 (m, 1H), 8.57 (m, 1H), 8.13 (m, 1H), 7.99 (m, 1H), 7.46 (m, 1H), 3.13 (m, 1H), 1.38 (2s, 6H). Method 1: RT = 3.05 min.; M+H = 377.3.

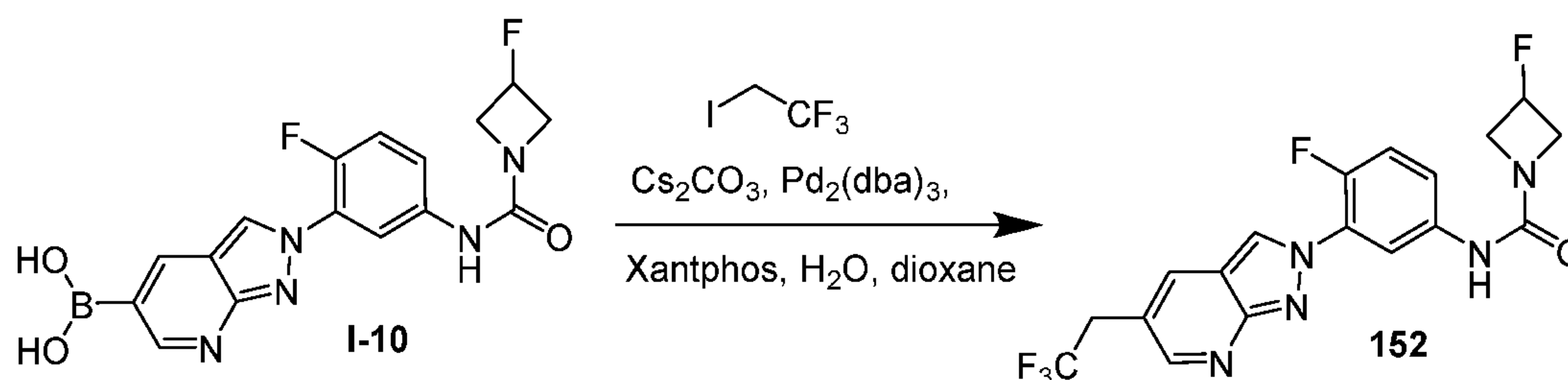
Compounds **65, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 196, 207, 208,**

209, 210, 211, 212, 213, 214, 215, 216, 217, 261, 262 and 351 were synthesized according to the protocol described above using the corresponding carboxylic acids.

Compounds **139, 140, 153, 154, 279, 330 and 352** were synthesized according to the protocol described above using **I-12, I-29 or I-36** and the corresponding carboxylic acids.

5 Compound **278** was synthesized according to the protocol described above using **I-28** and **I-34** as starting materials.

Example 13: 3-fluoro-N-(4-fluoro-3-(5-(2,2,2-trifluoroethyl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 152)



10 To a solution of **I-10** (106 mg, 285.6 μ mol, 1 eq) in dioxane (1 mL) was added 1,1,1-trifluoro-2-iodo-ethane (119.9 mg, 571.10 μ mol, 56.03 μ L, 2 eq), $\text{Pd}_2(\text{dba})_3$ (13.1 mg, 14.3 μ mol, 0.05 eq), XantPhos (28.1 mg, 48.5 μ mol, 0.2 eq) and Cs_2CO_3 (372.15 mg, 1.1 mmol, 4 eq) under a N_2 atmosphere. After 1 min. water (92.6 mg, 5.1 mmol, 92.6 μ L, 18 eq) was added and the mixture was stirred at 80 $^\circ\text{C}$ for 16 hr. The reaction mixture was concentrated under

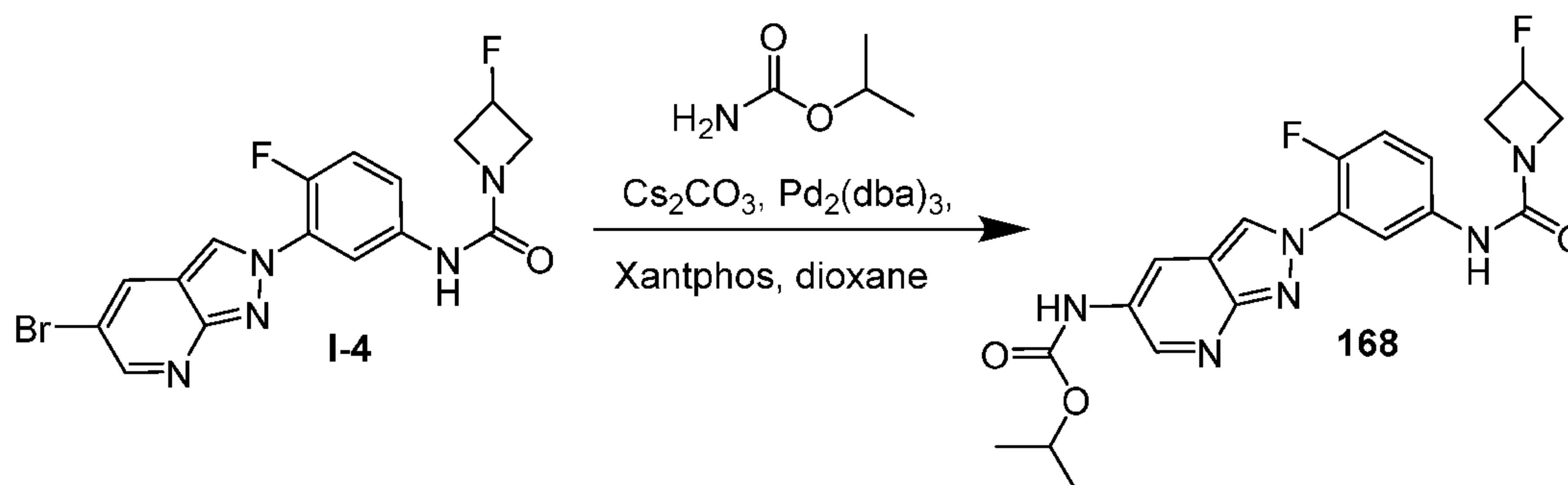
15 reduced pressure. The residue was diluted with DCM (30 mL) and the organic layer was washed with water (10 mL*2), dried over Na_2SO_4 , filtered and concentrated to give a residue. The residue was purified by prep-TLC (SiO_2 , DCM : Methanol=10:1) and further purified by prep-HPLC (column: Phenomenex Gemini C18 250*50mm*10 μ m; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 28%-58%, 12 min) to give compound **152** as a yellow

20 solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$), δ ppm, 8.98 (s, 1 H), 8.95 (d, $J=2.51$ Hz, 1 H), 8.69 (d, $J=2.01$ Hz, 1 H), 8.33 (d, $J=1.76$ Hz, 1 H), 8.24 (dd, $J=6.90, 2.63$ Hz, 1 H), 7.67 - 7.74 (m, 1 H), 7.48 (dd, $J=11.29, 9.29$ Hz, 1 H), 5.30 - 5.52 (m, 1 H), 4.26 - 4.39 (m, 2 H), 3.97 - 4.09 (m, 2 H), 3.87 (q, $J=11.71$ Hz, 2 H). Method 1: RT = 2.76 min.; $M+H = 412.2$.

Compounds **162, 164, 166, 175 and 176** were synthesized according to the protocol described above using the corresponding boronic acid prepared from intermediate **I-3, I-5, I-6, I-7 or I-8** prepared in the same manner as **I-10**.

25

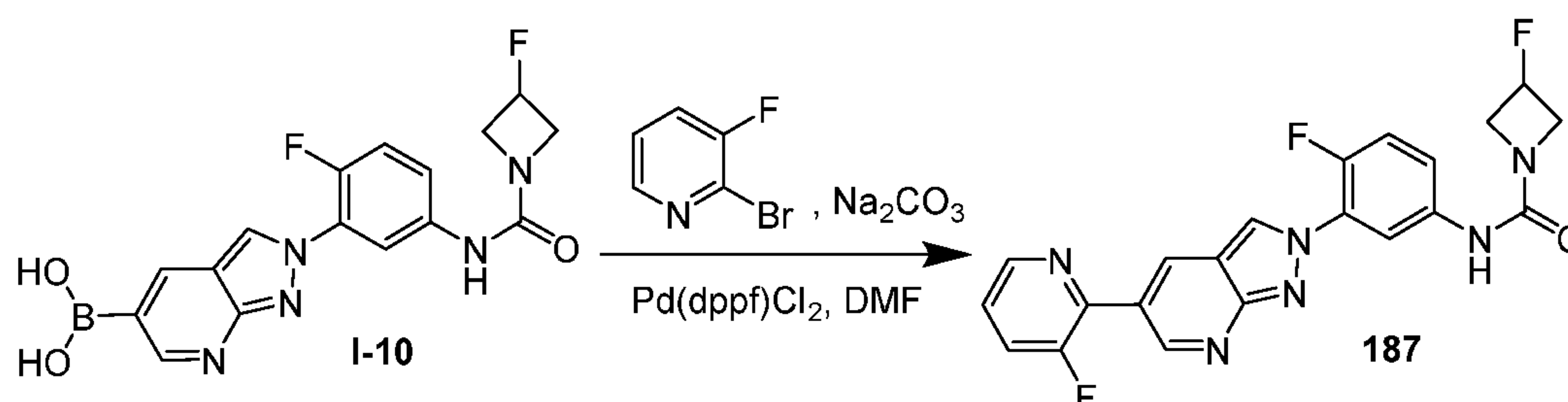
Example 14: Isopropyl (2-(2-fluoro-5-(3-fluoroazetidine-1-carboxamido)phenyl)-2H-pyrazolo[3,4-b]pyridin-5-yl)carbamate (Compound 168)



To a mixture of **I-4** (120 mg, 294 μ mol, 1 eq), isopropyl carbamate (45.5 mg, 441 μ mol, 1.5 eq) and Cs_2CO_3 (287.3 mg, 881.9 μ mol, 3 eq) in dioxane (3 mL) was added XantPhos (34.0 mg, 58.8 μ mol, 0.20 eq) and $\text{Pd}_2(\text{dba})_3$ (26.9 mg, 29.4 μ mol, 0.10 eq) under an Argon atmosphere. The mixture was heated to 90 °C and stirred for 4 hours. The mixture was quenched by addition of 1 M HOAc and purified by prep-HPLC (column: Boston pH-Iex 150*25 10 μ m; mobile phase: [water(0.225%Formic Acid)-acetonitrile]; B%: 33%-63%,10 min followed by further purification on column: Phenomenex Gemini C18 250*50mm*10 μ m; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 28%-58%,12 min). Compound **168** was obtained as a yellow solid. ^1H NMR (400 MHz, Methanol- d_4), δ ppm, 8.64 (br d, J = 2.26 Hz, 1 H), 8.61 (br d, J = 2.64 Hz, 1 H), 8.44 (br s, 1 H), 8.10 (dd, J = 6.71, 2.70 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.33 (dd, J = 10.92, 9.16 Hz, 1 H), 5.25 - 5.47 (m, 1 H), 5.01 (dt, J = 12.52, 6.23 Hz, 1 H), 4.32 - 4.43 (m, 2 H), 4.07 - 4.19 (m, 2 H), 1.33 (d, J = 6.27 Hz, 6 H). Method 1: RT = 2.88 min.; $M+H$ = 431.1.

Compounds **123**, **136**, **138**, **146** and **159** were synthesized according to the protocol described above using the corresponding intermediate **I-3**, **I-5**, **I-6**, **I-7** or **I-8**.

Example 15: 3-fluoro-N-(4-fluoro-3-(5-(3-fluoropyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 187)

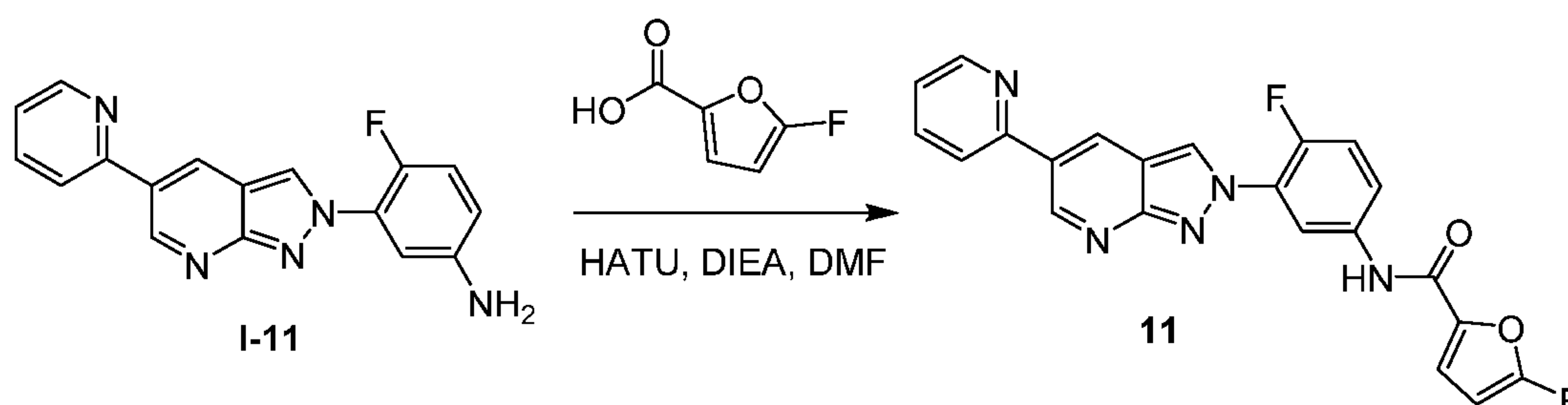


To a solution of intermediate **I-10** (95 mg, 254.6 μ mol, 1 eq) in DMF (3mL) was added $\text{Pd}(\text{dppf})\text{Cl}_2$ (18.6 mg, 25.5 μ mol, 0.1 eq), Na_2CO_3 (81 mg, 763.8 μ mol, 3 eq) and 2-bromo-3-fluoropyridine (89.5 mg, 509.2 μ mol, 2 eq). The mixture was stirred at 90 °C for 16 hr. The reaction mixture was concentrated under reduced pressure and purified by prep-HPLC (column: Boston Green ODS 150*30 5 μ ; mobile phase: [water(0.225%FA)-acetonitrile]; B%:

35%-65%, 10 min) to give compound **187** as a yellow solid. ¹H NMR (400 MHz, DMSO-d₆) δ ppm 9.27 (s, 1 H), 9.00 - 9.09 (m, 2 H), 8.82 (s, 1 H), 8.63 (br d, J=4.39 Hz, 1 H), 8.29 (dd, J=6.90, 2.51 Hz, 1 H), 7.93 (dd, J=10.73, 8.47 Hz, 1 H), 7.72 (dt, J=8.60, 3.48 Hz, 1 H), 7.52 - 7.58 (m, 1 H), 7.46 - 7.51 (m, 1 H), 5.28 - 5.55 (m, 1 H), 4.25 - 4.44 (m, 2 H), 3.93 - 4.14 (m, 2 H). Method 1: RT = 2.74 min.; M+H = 425.1.

Compounds **188**, **294**, **295**, **297**, **301**, **304**, **312**, **325**, **329**, **330**, and **335** were synthesized according to the protocol described above using the corresponding bromides.

Example 16: 5-fluoro-N-(4-fluoro-3-(5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)furan-2-carboxamide (Compound 11)

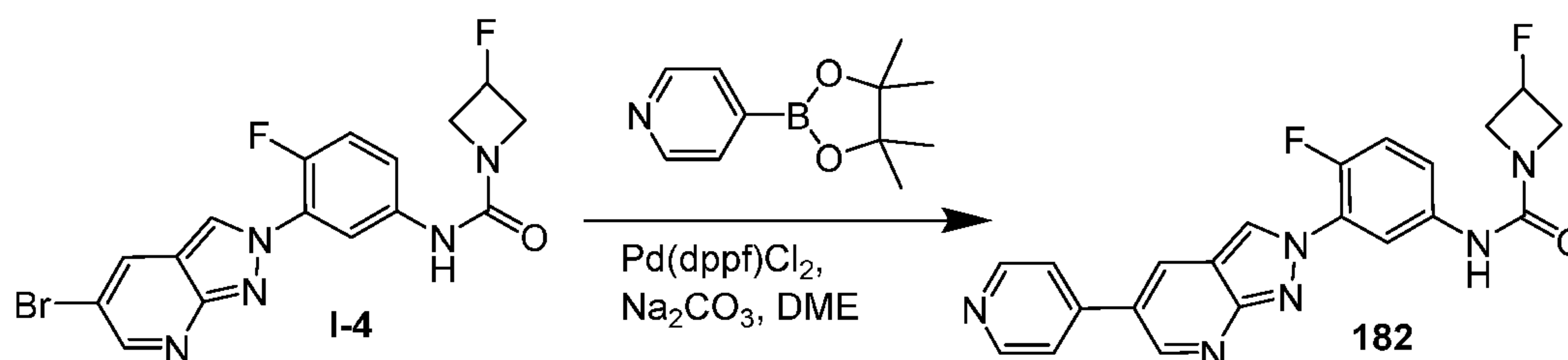


I-11 (40 mg, 0.131 mmol) was dissolved in 2 mL of DMF. 5-fluorofuran-2-carboxylic acid (25.6 mg, 0.20 mmol), DIEA (0.058 mL, 0.33 mmol) and HATU (50.6 mg, 0.13 mmol) were added to the reaction and the resulting mixture was stirred overnight. The reaction was diluted with EtOAc and washed 1x with sat. aq Na₂CO₃ solution and 1x with water. The organics were dried over Na₂SO₄ and concentrated. The crude material was purified on silica chromatography eluting with 0 – 100% 3:1 EtOAc:EtOH in heptanes to give compound **11**. ¹H NMR (400 MHz, DMSO-d₆) δ 10.53 (s, 1H), 9.49 (d, J = 2.3 Hz, 1H), 9.06 (d, J = 2.6 Hz, 1H), 8.96 (d, J = 2.3 Hz, 1H), 8.74 (ddd, J = 4.8, 1.9, 0.9 Hz, 1H), 8.53 (dd, J = 7.0, 2.7 Hz, 1H), 8.14 (dt, J = 8.0, 1.1 Hz, 1H), 8.01 - 7.91 (m, 2H), 7.62 (dd, J = 11.2, 9.1 Hz, 1H), 7.50 - 7.38 (m, 2H), 6.14 (dd, J = 7.0, 3.7 Hz, 1H). Method 2: RT = 0.91 min.; M+H = 418.1.

Compounds **12**, **13**, **206**, **218**, **345**, **346**, **347**, **348**, and **349** were synthesized according to the protocol described above using the corresponding carboxylic acid.

Compound **350** was synthesized according to the protocol described above using the corresponding carboxylic acid and **I-28**.

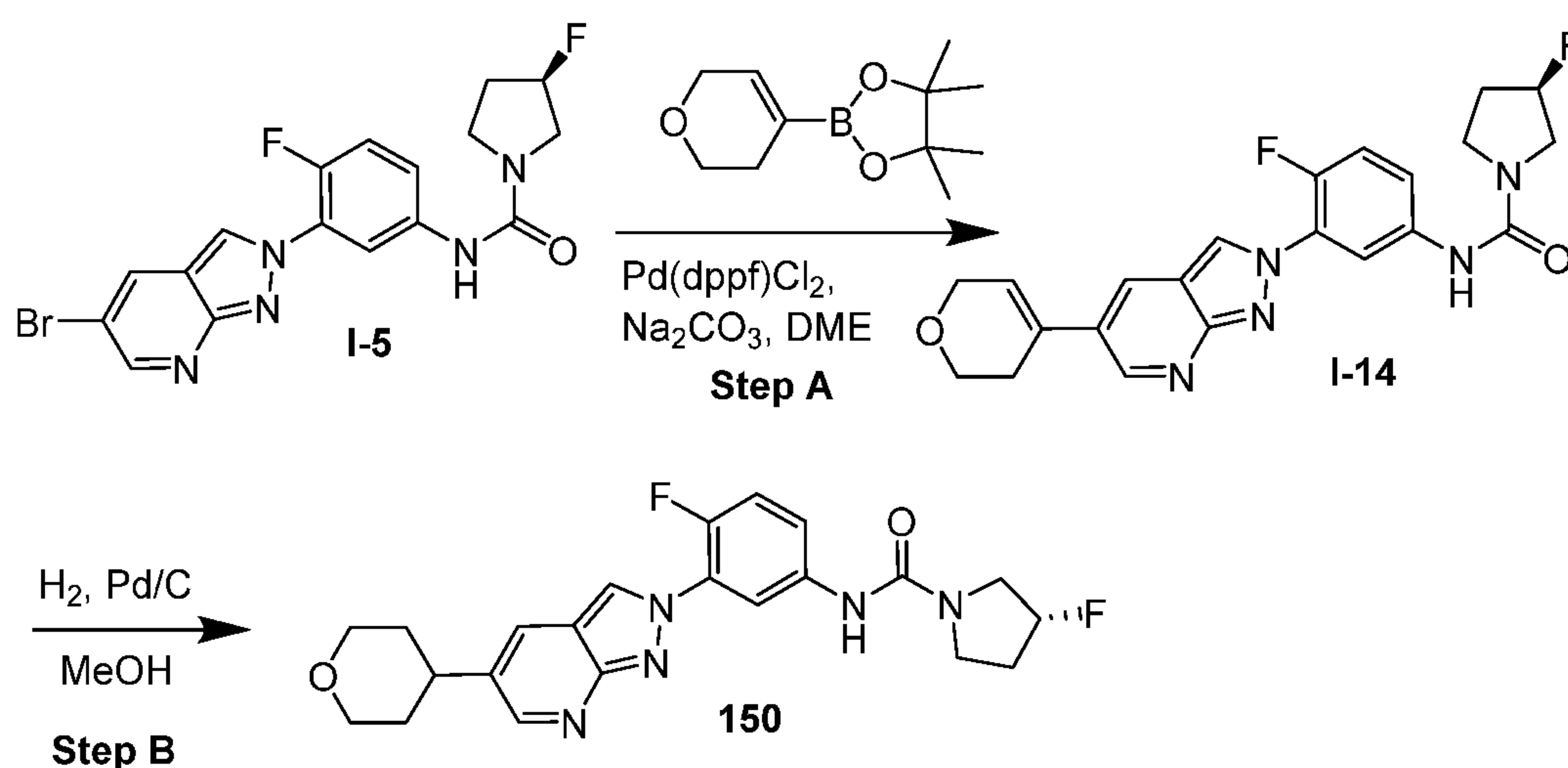
Example 17: 3-fluoro-N-(4-fluoro-3-(5-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 182)



To a solution of **I-4** (80 mg, 196 μ mol, 1 eq) and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (60.3 mg, 294 μ mol, 1.5 eq) in DME (3 mL) was added Pd(dppf)Cl₂ (14.34 mg, 19.6 μ mol, 0.1 eq) and Na₂CO₃ (2 M, 294 μ L, 3 eq) under a N₂ atmosphere. The mixture was stirred at 90 °C for 20 hrs. The reaction mixture was concentrated and the residue was diluted with EtOAc (30 mL). The organic layer was washed with water (10 mL * 2), dried over anhydrous Na₂SO₄, filtered and concentrated. The residue was purified by prep-HPLC (column: Phenomenex Gemini C18 250*50mm*10 μ m; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 18%-48%, 12 min) to give compound **182** as a white solid. ¹H NMR (400 MHz, DMSO-d₆), δ ppm, 9.17 (d, J=2.26 Hz, 1 H), 9.03 (d, J=2.51 Hz, 1 H), 9.00 (s, 1 H), 8.75 (d, J=2.51 Hz, 1 H), 8.67 - 8.73 (m, 2 H), 8.28 (dd, J=6.90, 2.64 Hz, 1 H), 7.84 - 7.90 (m, 2 H), 7.68 - 7.75 (m, 1 H), 7.50 (dd, J=11.29, 9.03 Hz, 1 H), 5.30 - 5.52 (m, 1 H), 4.27 - 4.40 (m, 2 H), 3.97 - 4.10 (m, 2 H). Method 2: RT = 0.58 min.; M+H = 407.1.

Compound **189** was synthesized according to the protocol described above using the corresponding boronic ester.

Example 18: (R)-3-fluoro-N-(4-fluoro-3-(5-(tetrahydro-2H-pyran-4-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)pyrrolidine-1-carboxamide (Compound 150)



Step A: To a mixture of 2-(3,6-dihydro-2H-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (65.7 mg, 312.6 μ mol, 1.1 eq), **I-5** (120 mg, 284.2 μ mol, 1 eq) and Na₂CO₃ (2 M, 426.3 μ L, 3 eq) in DME (3 mL) and water (0.5 mL) under an Argon atmosphere was added Pd(dppf)Cl₂ (20.8 mg, 28.4 μ mol, 0.1 eq). The mixture was heated to 90°C for 4 hrs. The mixture was purified by prep-TLC eluting with 90% EtOAc in petroleum ether to give **I-14** as white solid. M+H = 426.2.

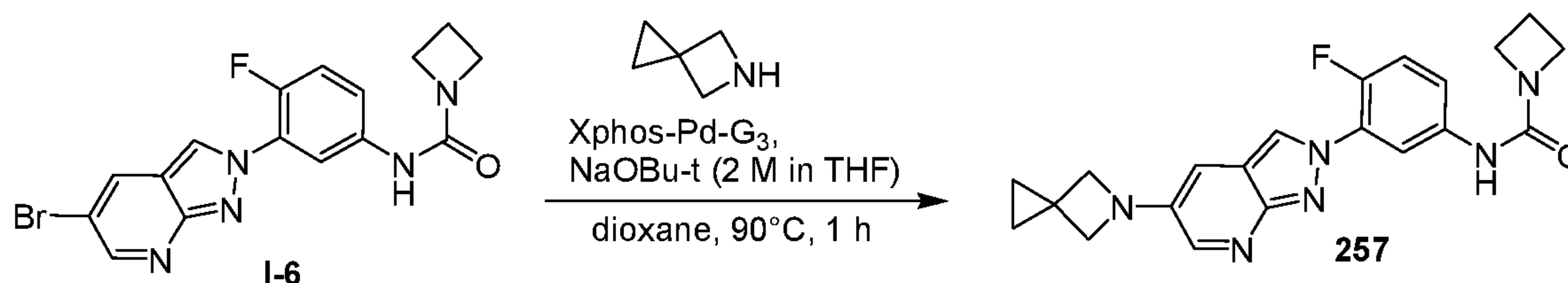
Step B: To a mixture of **I-14** (85 mg, 199.8 μ mol, 1 eq) in methanol (10 mL) was added Pd/C (30 mg, 10% purity). The suspension was degassed under vacuum and purged with H₂ several times. The mixture was stirred under H₂ (15 psi) at 10°C for 1 h. The mixture was filtered and the filtrate was concentrated to give a residue. The residue was purified by prep-HPLC (column: Boston Green ODS 150*30 5 μ ; mobile phase: [water(0.225%FA)-

acetonitrile]; B%: 27%-51%, 10 min) to give compound **150** as a yellow solid. ¹H NMR (400 MHz, Methanol-*d*₄) δ ppm, 9.15 (d, *J* = 2.01 Hz, 1 H), 8.98 (s, 1 H), 8.85 (d, *J* = 1.88 Hz, 1 H), 8.33 (dd, *J* = 6.78, 9.16 Hz, 1 H), 7.61 - 7.65 (m, 1 H), 7.42 (dd, *J* = 11.04, 9.16 Hz, 1 H), 5.28 - 5.41 (m, 1 H), 4.11 - 4.14 (m, 2 H), 3.57 - 3.85 (m, 6 H), 3.14 - 3.20 (m, 1 H), 2.11 - 2.32 (m, 2 H), 1.91 - 1.97 (m, 4 H). Method 1: RT = 2.60 min.; M+H = 428.2.

Compounds **148**, **160**, **165**, **169**, **296**, and **305** were synthesized according to the protocol described above using intermediates **I-3**, **I-4**, **I-6** or **I-7** and the corresponding boronic acid or boronic ester.

Compound **293** was synthesized using the protocol described above using **I-4** and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate after which the Boc group was removed using 1:5 ratio of TFA in DCM followed by concentration and then prep-HPLC purification (column: Phenomenex Synergi C18 150*25*10 μm; mobile phase: [water(0.225%FA)-acetonitrile]; B%: 2%-22%, 10 min) to give compound **293**.

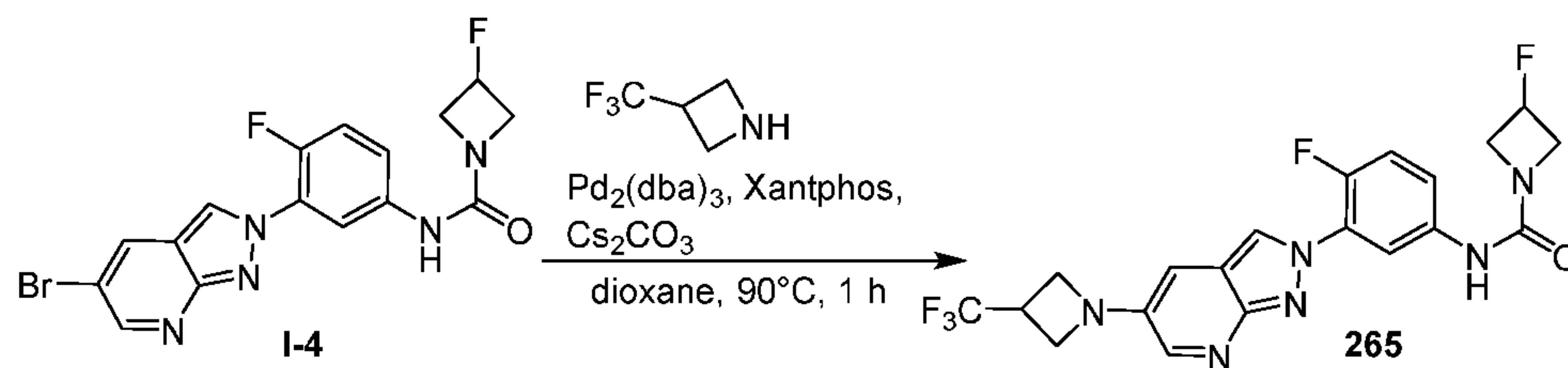
Example 19: N-(3-(5-(5-azaspiro[2.3]hexan-5-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)azetidine-1-carboxamide (Compound 257)



A mixture of **I-6** (400 mg, 1.0 mmol, 1 eq), 5-azaspiro[2.3]hexane hemioxalate (128 mg, 1.0 mmol, 1 eq), NaOBu-t (2 M in THF, 1.5 mL, 3 eq) and Xphos Pd G3 (87 mg, 102.5 μmol, 0.1 eq) in dioxane (10 mL) was de-gassed, placed under an Argon atmosphere and heated to 90°C for 1 hour. The reaction was quenched by addition of saturated NH₄Cl (40 mL). The resulting mixture was extracted by dichloromethane (30 mL×6) and the organic phase was dried over Na₂SO₄ and filtered. The filtrate was concentrated and the residue was purified by silica gel chromatography eluting with 50% MeOH in DCM followed by prep-HPLC purification (column: Phenomenex Synergi C18 150*25*10 μm; mobile phase: [water(0.225%FA)-acetonitrile]; B%: 30%-60%, 10 min) to give compound **257** as a yellow solid. ¹H NMR (400 MHz, DMSO) δ ppm 8.69 (s, 1 H), 8.52 (d, *J* = 2.63 Hz, 1 H), 8.28 (d, *J* = 2.76 Hz, 1 H), 8.20 (dd, *J* = 7.03, 2.63 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.40 (dd, *J* = 11.29, 9.16 Hz, 1 H), 6.91 (d, *J* = 2.76 Hz, 1 H), 4.01 (s, 4 H), 3.97 (t, *J* = 7.53 Hz, 4 H), 2.19 (quin, *J* = 7.56 Hz, 2 H), 0.68 (s, 4 H). Method 1: RT = 2.90 min.; M+H = 393.2.

Compounds **233**, **258**, **259**, and **337** were synthesized according to the protocol described above using the corresponding intermediates **I-3**, **I-4**, **I-5** or **I-27**.

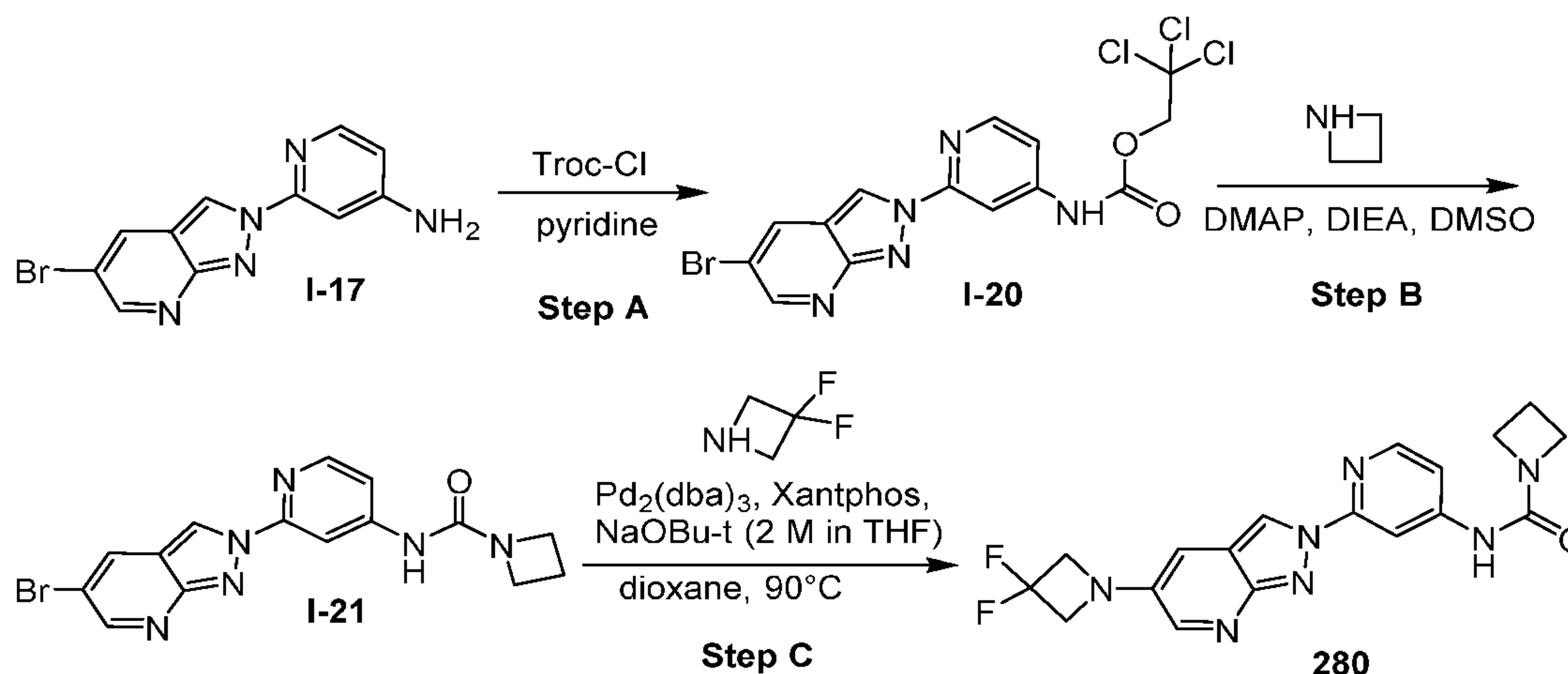
Example 20: 3-fluoro-N-(4-fluoro-3-(5-(3-(trifluoromethyl)azetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 265)



A mixture of **I-4** (3.5 g, 8.6 mmol, 1 eq), 3-(trifluoromethyl)azetidine HCl salt (1.7 g, 10.3 mmol, 1.2 eq), Pd₂(dba)₃ (785 mg, 857.4 μmol, 0.1 eq), XantPhos (992 mg, 1.7 mmol, 0.2 eq) and Cs₂CO₃ (8.4 g, 25.7 mmol, 3 eq) in dioxane (60 mL) was de-gassed and then heated to 85 °C for 1.2 hr under a N₂ atmosphere. The reaction mixture was quenched with sat NH₄Cl solution (400 mL) and extracted with EtOAc (300 mL×2). The combined organic layers were washed with brine (200 mL), dried over Na₂SO₄ and concentrated. The residue was purified by silica chromatography eluting with MeOH/Ethyl acetate/DCM = 0:1:1 to 1:5:1 to give a yellow solid, which was further purified by prep HPLC; column: Phenomenex Synergi Max-RP 250*80mm*10 um; mobile phase: [water(0.225%FA)-acetonitrile]; B%: 30%-60%, 35 min. The pH of the solution was adjusted to pH = 7 by 20 % NH₃ in H₂O and acetonitrile was removed under vacuo at 30 °C. The resulting yellow solid was collected by filtration, washed with water 100 mL×4, and lyophilized to give compound **265** as yellow solid. ¹H NMR (400 MHz, DMSO) δ ppm 8.93 (s, 1 H), 8.58 (d, *J* = 2.76 Hz, 1 H), 8.32 (d, *J* = 2.76 Hz, 1 H), 8.20 (dd, *J* = 7.03, 2.64 Hz, 1 H), 7.65 (dd, *J* = 7.34, 4.58 Hz, 1 H), 7.44 (dd, *J* = 11.17, 9.16 Hz, 1 H), 7.03 (d, *J* = 2.89 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.24 - 4.38 (m, 2 H), 4.18 (t, *J* = 8.34 Hz, 2 H), 3.95 - 4.10 (m, 4 H), 3.65 - 3.85 (m, 1 H). Method 1: RT = 2.86 min.; M+H = 453.1.

Compounds **274** and **275** were synthesized according to the protocol described above using the corresponding intermediates **I-5** or **I-6**.

Example 21: N-(2-(5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-yl)azetidine-1-carboxamide (Compound 280)



Step A: To a solution **I-17** (2.5 g, 8.6 mmol, 1 eq) in pyridine (30 mL) was added 2,2,2-trichloroethyl carbonochloridate (3.6 g, 17.2 mmol, 2.3 mL, 2 eq). The mixture was stirred at 30 °C for 22 hr. The reaction mixture was precipitated by addition water 100 mL, and then filtered. The filter cake was washed with water 50 mL and dried under reduced pressure. The precipitate was then triturated in tert-butyl methyl ether (20 mL) and collected by filtration to give **I-20** as a brown solid. ¹H NMR (400 MHz, DMSO) δ ppm 11.08 (s, 1 H), 9.32 (s, 1 H), 8.77 (d, *J* = 1.71 Hz, 1 H), 8.62 (d, *J* = 1.96 Hz, 1 H), 8.52 (d, *J* = 1.71 Hz, 1 H), 8.49 (d, *J* = 3.91 Hz, 1 H), 7.75 (dd, *J* = 5.38, 1.71 Hz, 1 H), 5.05 (s, 2 H).

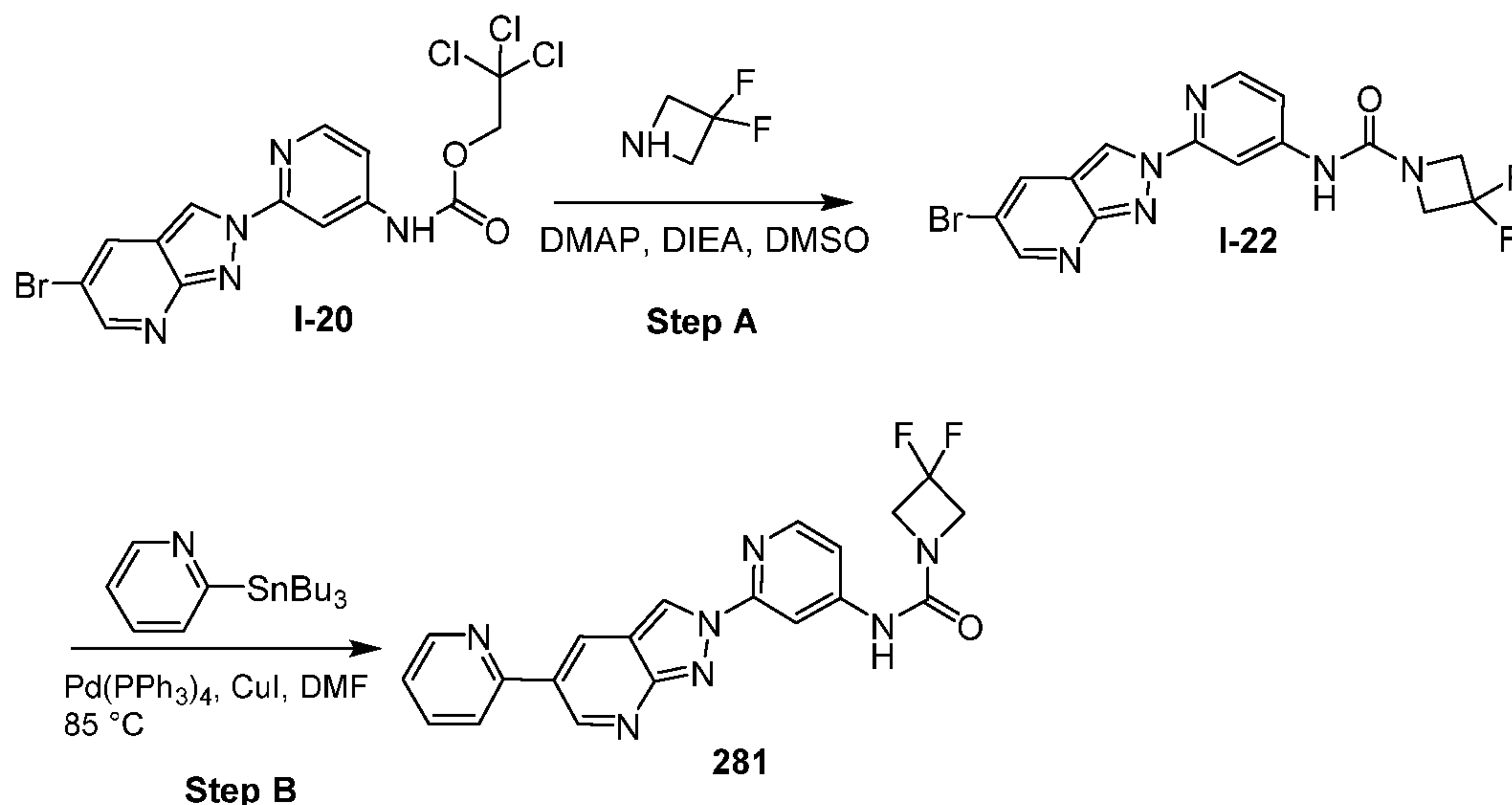
Step B: To a solution of **I-20** (1.2 g, 2.6 mmol, 1 eq) and azetidine hydrochloride (482 mg, 5.2 mmol, 2 eq) in DMSO (12 mL) was added DMAP (31 mg, 257.8 μmol, 0.10 eq) and DIEA (666 mg, 5.2 mmol, 898.0 μL, 2 eq). The mixture was stirred at 60 °C for 144 hr. The reaction mixture was precipitated by addition water 100 mL and then filtered. The filter cake was washed with water 50 mL, dried under reduced pressure to give **I-21** as a brown solid. ¹H NMR (400 MHz, DMSO) δ ppm 9.24 (s, 2 H), 8.75 (d, *J* = 2.45 Hz, 1 H), 8.60 (d, *J* = 2.20 Hz, 1 H), 8.49 (d, *J* = 1.71 Hz, 1 H), 8.35 (d, *J* = 5.62 Hz, 1 H), 7.73 (dd, *J* = 5.75, 1.83 Hz, 1 H), 4.04 (br t, *J* = 7.58 Hz, 4 H), 2.23 (quin, *J* = 7.64 Hz, 2 H).

Step C: A mixture of **I-21** (180 mg, 482.3 μmol, 1 eq), 3,3-difluoroazetidine (125 mg, 964.6 μmol, 2 eq, HCl), XantPhos (56 mg, 96.5 μmol, 0.20 eq), Pd₂(dba)₃ (44 mg, 48.2 μmol, 0.10 eq) and NaOBu-t (2 M, 964.6 μL, 4 eq) in dioxane (3 mL) was stirred at 90 °C for 16 hr under N₂ atmosphere. The reaction mixture was concentrated under reduced pressure to remove solvent. The residue was purified by silica chromatography eluting with 10-100% petroleum ether in Ethyl acetate to give 65 mg of a residue. The residue was triturated in MeOH (3 mL) and the solid collected by filtration to give compound **280** as a yellow solid. ¹H NMR (400 MHz, DMSO-d₆) δ ppm 9.18 (s, 1 H), 8.99 (s, 1 H), 8.44 (d, *J* = 1.76 Hz, 1 H), 8.36 (d, *J* = 2.76 Hz, 1 H), 8.31 (d, *J* = 5.77 Hz, 1 H), 7.67 (dd, *J* = 5.52, 2.01 Hz, 1 H), 7.14 (d, *J* = 2.76 Hz, 1 H), 4.42 (t, *J* = 12.17 Hz, 4 H), 4.04 (t, *J* = 7.53 Hz, 4 H), 2.16 - 2.29 (m, 2 H). Method 1: RT = 2.76 min.; M+H = 386.0.

Compounds **282**, **284**, **286**, **287**, and **343** were synthesized according to the protocol described above using intermediates **I-17**, **I-18**, or **I-19** and the corresponding amines.

Compound **340** was synthesized according to the protocol described in Step A and Step B using (R)-3-fluoropyrrolidine.

Example 22: 3,3-difluoro-N-(2-(5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)pyridin-4-yl)azetidine-1-carboxamide (Compound 281)



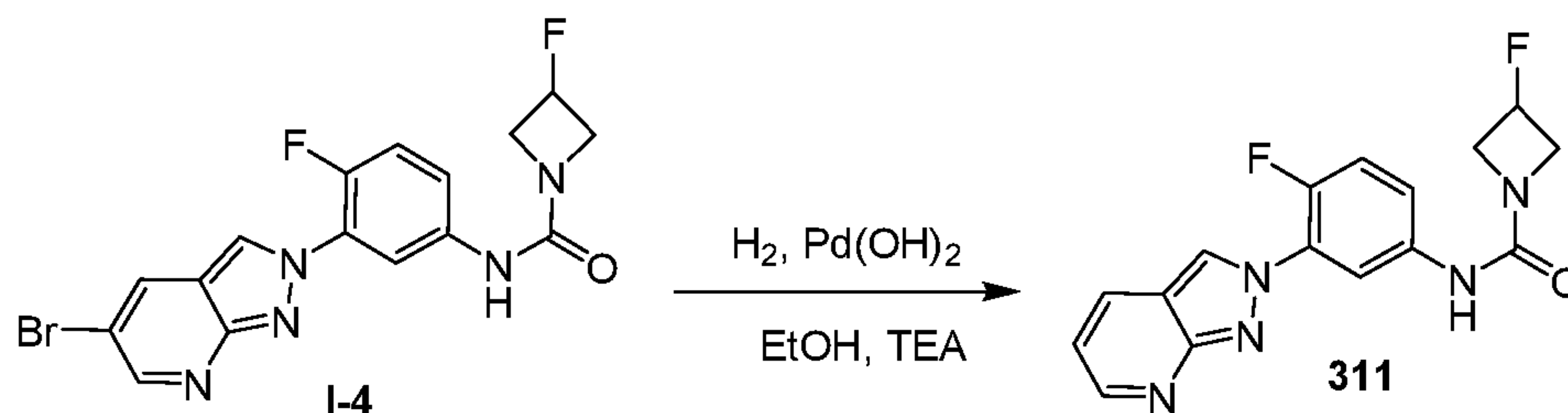
Step A: To a solution of **I-20** (800 mg, 1.7 mmol, 1 eq) and 3,3-difluoroazetidine HCl salt (445 mg, 3.4 mmol, 2 eq) in DMSO (10 mL) was added DMAP (21 mg, 171.8 μ mol, 0.1 eq) and DIEA (444 mg, 3.4 mmol, 598.7 μ L, 2 eq). The mixture was stirred at 60°C for 320 hr. The reaction mixture was precipitated by addition water (100 mL) and then filtered. The filter cake was washed with water 50 mL, dried under reduced pressure to give **I-22** as a brown solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 9.69 (s, 1 H), 9.23 - 9.27 (m, 1 H), 8.75 (d, *J* = 2.45 Hz, 1 H), 8.61 (d, *J* = 2.44 Hz, 1 H), 8.47 (d, *J* = 1.96 Hz, 1 H), 8.41 (d, *J* = 5.62 Hz, 1 H), 7.71 (dd, *J* = 5.62, 1.96 Hz, 1 H), 4.48 (t, *J* = 12.72 Hz, 4 H).

Step B: To a solution of **I-22** (460 mg, 1.12 mmol, 1 eq) and tributyl(2-pyridyl)stannane (497 mg, 1.3 mmol, 1.2 eq) in DMF (10 mL) was added Pd(PPh₃)₄ (130 mg, 112.4 μ mol, 0.1 eq) and CuI (21 mg, 112.4 μ mol, 0.1 eq). The mixture was stirred at 85°C for 16 hr under a N₂ atmosphere. The reaction mixture was concentrated under reduced pressure to remove solvent. The residue was purified by silica eluting with 10-100% petroleum ether in ethyl acetate to give a solid, which was triturated in DCM (3 mL). The resulting solid was collected by filtration to give compound **281** as an off-white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 9.70 (s, 1 H), 9.47 (d, *J*=2.20 Hz, 1 H), 9.38 (s, 1 H), 8.95 (d, *J*=2.20 Hz, 1 H), 8.71 - 8.77 (m, 1 H), 8.49 (d, *J*=1.71 Hz, 1 H), 8.42 (d, *J*=5.62 Hz, 1 H), 8.12 (d, *J*=8.07 Hz, 1 H), 7.96 (td, *J*=7.76, 1.83 Hz, 1 H), 7.72 (dd, *J*=5.62, 1.96 Hz, 1 H), 7.39 - 7.47 (m, 1 H), 4.49 (t, *J*=12.72 Hz, 4 H). Method 1: RT = 2.81 min.; M+H = 408.0.

Compounds **283**, **285**, **309**, **310**, **313**, **315**, **317**, **341**, **342**, and **344** were synthesized according to the protocol described above using intermediate **I-1**, **I-17**, **I-18** or **I-19** and the corresponding amine and corresponding organotin.

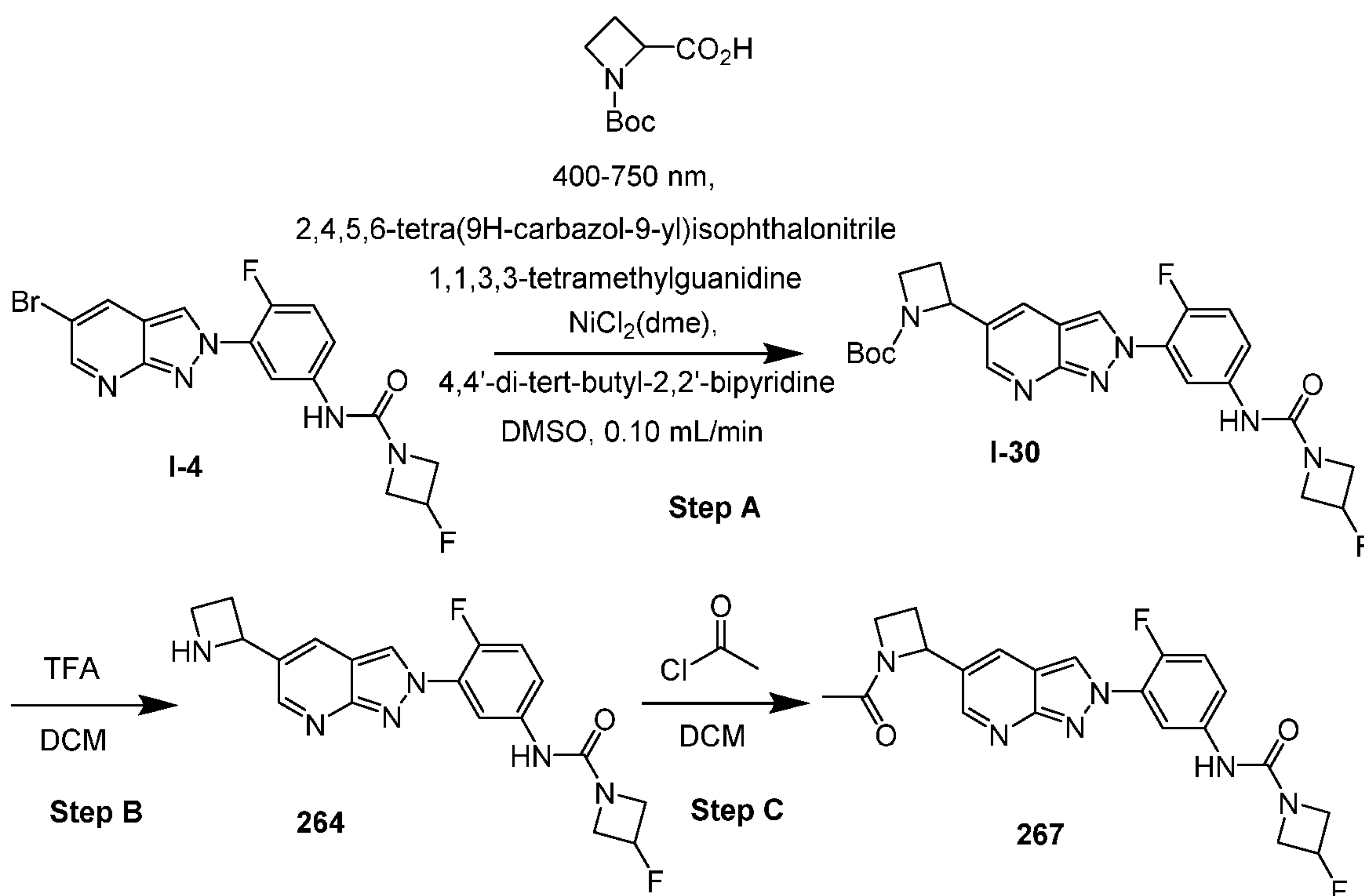
Compounds **256**, **332**, **333**, and **336** was synthesized according the protocol in Step B using **I-24**, **I-27** or **I-31** and the corresponding organotins.

Example 23: 3-fluoro-N-(4-fluoro-3-(2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 311)



To a solution of **I-4** (100 mg, 245 μ mol, 1 eq) in EtOH (2 mL) was added TEA (25 mg, 245 μ mol, 34.1 μ L, 1 eq) and Pd(OH)₂/C (34 mg, 24.5 μ mol, 10% purity, 0.1 eq) under N₂ atmosphere. The suspension was degassed and purged with H₂ 3 times. The mixture was stirred under H₂ (15 Psi) at 25 °C for 3 hrs. The reaction mixture was filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC (column: Luna C18 150*25*5 μ m; mobile phase: [water(0.225%FA)-acetonitrile]; B%: 17%-44%, 10 min) and lyophilized to give compound **311** as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆), ppm, 8.98 (s, 1 H), 8.90 (d, J=2.26 Hz, 1 H), 8.72 (d, J=3.01 Hz, 1 H), 8.31 (d, J=8.28 Hz, 1 H), 8.25 (dd, J=7.03, 2.51 Hz, 1 H), 7.66 - 7.73 (m, 1 H), 7.43 - 7.51 (m, 1 H), 7.20 (dd, J=8.41, 4.14 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.24 - 4.39 (m, 2 H), 3.96 - 4.10 (m, 2 H). Method 1: RT = 2.41 min.; M+H = 330.1.

Example 24: N-(3-(5-(1-acetylazetidin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)-4-fluorophenyl)-3-fluoroazetidine-1-carboxamide (Compound 267)



Step A: 1-(tert-butoxycarbonyl)azetidine-2-carboxylic acid (394 mg, 2 mmol), **I-4** (400 mg, 1 mmol), 1,1,3,3-tetramethylguanidine (226 mg, 1.96 mmol), NiCl₂(dme) (22 mg, 0.1 mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (26 mg, 0.1 mol) and 2,4,5,6-tetra(9H-carbazol-9-yl)isophthalonitrile (23 mg, 0.03 mmol) were dissolved in DMSO (9.8 mL) upon heating and
 5 sonication. The solution was pumped (0.10 mL/min) via photoreactor (reactor volume – 0.9 mL; PFA tubing 0.04" ID, 0.0625" ID; irradiated area 20 cm²; 1 cm distance to LED board; 400-750 nm LED; 8800 lm brightness) and collected in a vial. The reaction was purified by C18 flash chromatography eluting with 15-85% acetonitrile in water and concentrated. The material was further purified by silica chromatography eluting with 40-100% EtOAc in heptane to give **I-30**.

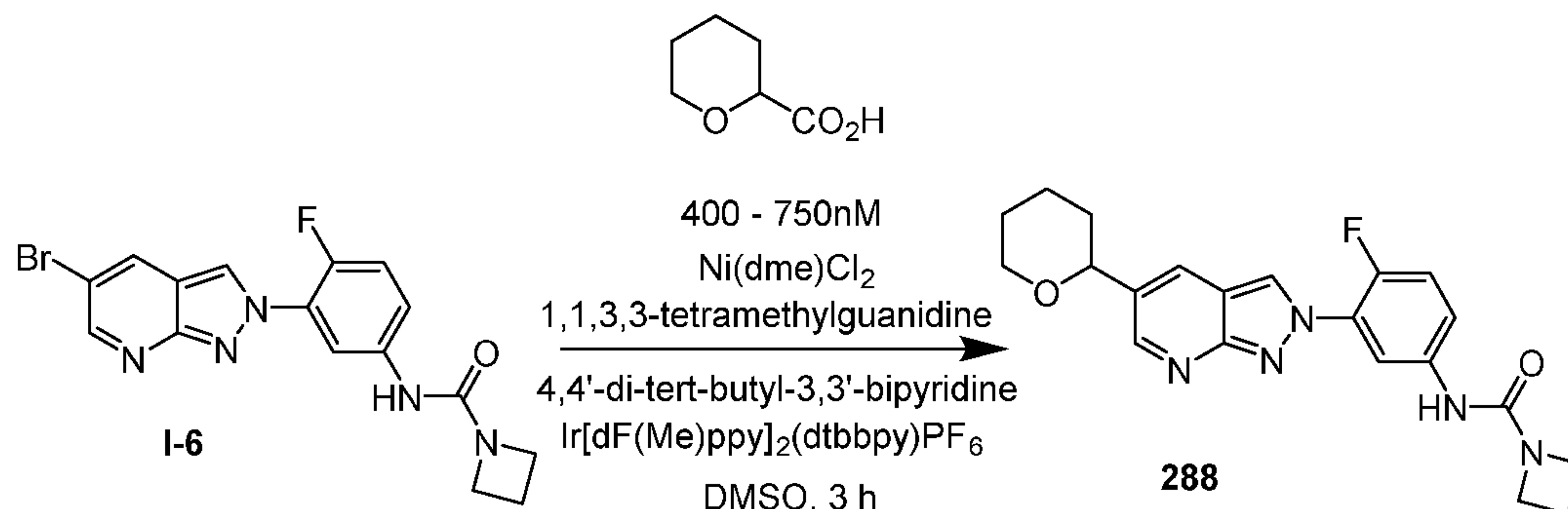
10 ¹H NMR (400 MHz, DMSO-d₆) δ 8.98 (s, 1H), 8.94 (d, J = 2.3 Hz, 1H), 8.71 (d, J = 4.3 Hz, 1H), 8.22 (dd, J = 7.0, 2.7 Hz, 1H), 7.70 (ddd, J = 9.1, 4.1, 2.8 Hz, 1H), 7.48 (dd, J = 11.1, 9.1 Hz, 1H), 7.13 (d, J = 4.4 Hz, 1H), 5.55 (dd, J = 9.0, 6.4 Hz, 1H), 5.48 - 5.30 (m, 1H), 4.32 (dddd, J = 21.7, 10.4, 6.0, 1.4 Hz, 2H), 4.11 - 3.94 (m, 6H), 1.27 (s, 9H).

Step B: **I-30** (83 mg, 0.171 mmol) was dissolved in DCM (1 mL) and TFA (0.5 mL) was
 15 added. The reaction was stirred for 3 hrs and concentrated, dissolved in MeOH and purified by C18 flash chromatography eluting with 5-40% acetonitrile in water. Lyophilization gave compound **264** as a white solid. ¹H NMR (400 MHz, DMSO-d₆) δ 9.38 (s, 1H), 9.07 - 8.96 (m, 2H), 8.84 (d, J = 4.3 Hz, 1H), 8.30 (dd, J = 7.0, 2.7 Hz, 1H), 7.72 - 7.62 (m, 1H), 7.52 (dd, J = 11.2, 9.1 Hz, 1H), 7.33 (dd, J = 4.4, 1.2 Hz, 1H), 6.04 (s, 1H), 5.41 (dt, J = 57.4, 6.1, 3.1 Hz,
 20 1H), 4.40 - 4.25 (m, 2H), 4.27 - 4.16 (m, 1H), 4.10 - 3.94 (m, 2H), 3.90 - 3.77 (m, 1H), 3.06 - 2.94 (m, 1H), 2.86 (dtd, J = 11.7, 8.7, 4.4 Hz, 1H). Method 1: RT = 1.69 min.; M+H = 385.2.

Step C: Compound **264** (20 mg, 0.052 mmol) was dissolved in DCM (Volume: 1 mL) and DIEA (0.027 mL, 0.16 mmol) and acetyl chloride (5.55 μL, 0.078 mmol) were added and stirred for 60 hrs. The reaction was purified by SFC on Princeton PPU 250 x 21.2mm column eluting
 25 with 20-60% MeOH in liquid CO₂ to give compound **267**. ¹H NMR (400 MHz, Methanol-d₄) δ 8.86 (dd, J = 3.4, 2.2 Hz, 1H), 8.74 (d, J = 4.4 Hz, 0.5H), 8.67 (d, J = 4.5 Hz, 0.5H), 8.17 (dd, J = 6.8, 2.7 Hz, 0.5H), 8.13 (dd, J = 6.8, 2.7 Hz, 0.5H), 7.66 (dddd, J = 8.8, 4.3, 2.7, 1.7 Hz, 1H), 7.37 (ddd, J = 10.9, 9.1, 3.7 Hz, 1H), 7.28 (dd, J = 4.4, 0.8 Hz, 0.5H), 7.18 (dd, J = 4.5, 0.9 Hz, 0.5H), 5.93 (dd, J = 9.2, 5.6 Hz, 0.5H), 5.73 (dd, J = 9.3, 6.1 Hz, 0.5H), 5.37 (dt, J = 57.1, 6.1,
 30 3.2 Hz, 1H), 4.48 - 4.32 (m, 3H), 4.24 - 4.15 (m, 2H), 4.11 (ddd, J = 10.3, 3.2, 1.4 Hz, 1H), 3.05 - 2.91 (m, 1H), 2.34 - 2.21 (m, 1H), 2.03 (s, 1.5H), 1.71 (s, 1.5H). Method 2: RT = 0.66 min.; M+H = 427.2.

Compound **247** was synthesized according the above protocol in Step A using 1-(tert-butoxycarbonyl)pyrrolidine-2-carboxylic acid as a starting material.

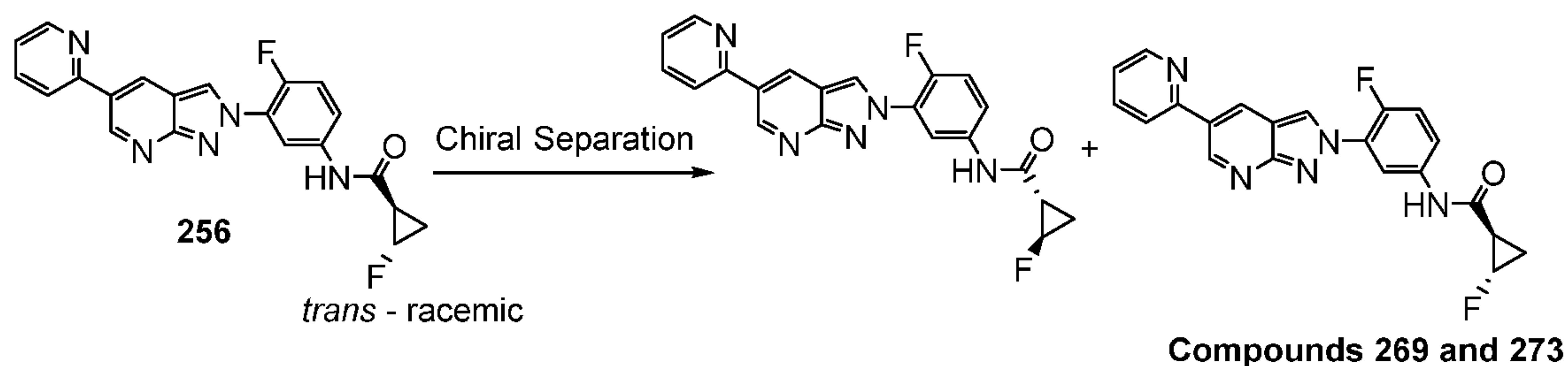
Example 25: N-(4-fluoro-3-(5-(tetrahydro-2H-pyran-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 288)



I-6 (30 mg, 0.077 mmol), Nickel(II) chloride ethylene glycol dimethyl ether complex (1.7 mg, 7.8 μ mol), 1,1,3,3-tetramethylguanidine (53 mg, 0.46 mmol), 4,4'-di-tert-butyl-3,3'-bipyridine (2.1 mg, 7.7 μ mol), tetrahydro-2H-pyran-2-carboxylic acid (60 mg, 0.46 mmol) and [4,4'-bis(tert-butyl)-2,2'-bipyridine]bis[3,5-difluoro-2-[5-methyl-2-pyridinyl]phenyl]iridium(III) hexafluorophosphate (3.90 mg, 3.84 μ mol) were dissolved in DMSO (769 μ L) upon heating and sonication. The solution was added into 0.3 mL well of 96 Teflon well-plate and irradiated for 3 hours (irradiated area 20 cm²; 10 cm distance to LED board; 400-750 nm LED; 7600 lm brightness). The resulting solution was purified by prep-HPLC (Waters Atlantis T3 C18 19*50mm*10 μ m column) eluting with acetonitrile (0.035% TFA) in water (0.05% TFA) to give compound **288**. ¹H NMR (400 MHz, Methanol-d₄) δ 9.03 (d, J = 2.2 Hz, 1H), 8.73 (d, J = 4.9 Hz, 1H), 8.19 (dd, J = 6.8, 2.7 Hz, 1H), 7.63 (ddd, J = 9.1, 4.2, 2.7 Hz, 1H), 7.37 (dd, J = 10.9, 9.1 Hz, 1H), 7.32 (dd, J = 5.0, 0.9 Hz, 1H), 4.92 (ddt, J = 2.7, 1.4, 0.7 Hz, 1H), 4.23 (d, J = 10.3 Hz, 1H), 4.17 – 4.07 (m, 2H), 3.74 (td, J = 11.6, 2.5 Hz, 1H), 3.37 – 3.32 (m, 2H), 2.33 (p, J = 7.6 Hz, 2H), 2.15 – 1.98 (m, 2H), 1.92 – 1.57 (m, 4H). Method 2: RT = 0.89 min.; M+H = 396.0.

Compound **289** was synthesized according the above protocol in using 1,4-dioxane-2-carboxylic acid as a starting material.

Example 26A and B: (1S,2R)-2-fluoro-N-(4-fluoro-3-(5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)cyclopropane-1-carboxamide or (1R,2S)-2-fluoro-N-(4-fluoro-3-(5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)cyclopropane-1-carboxamide (Compounds 269 and 273)

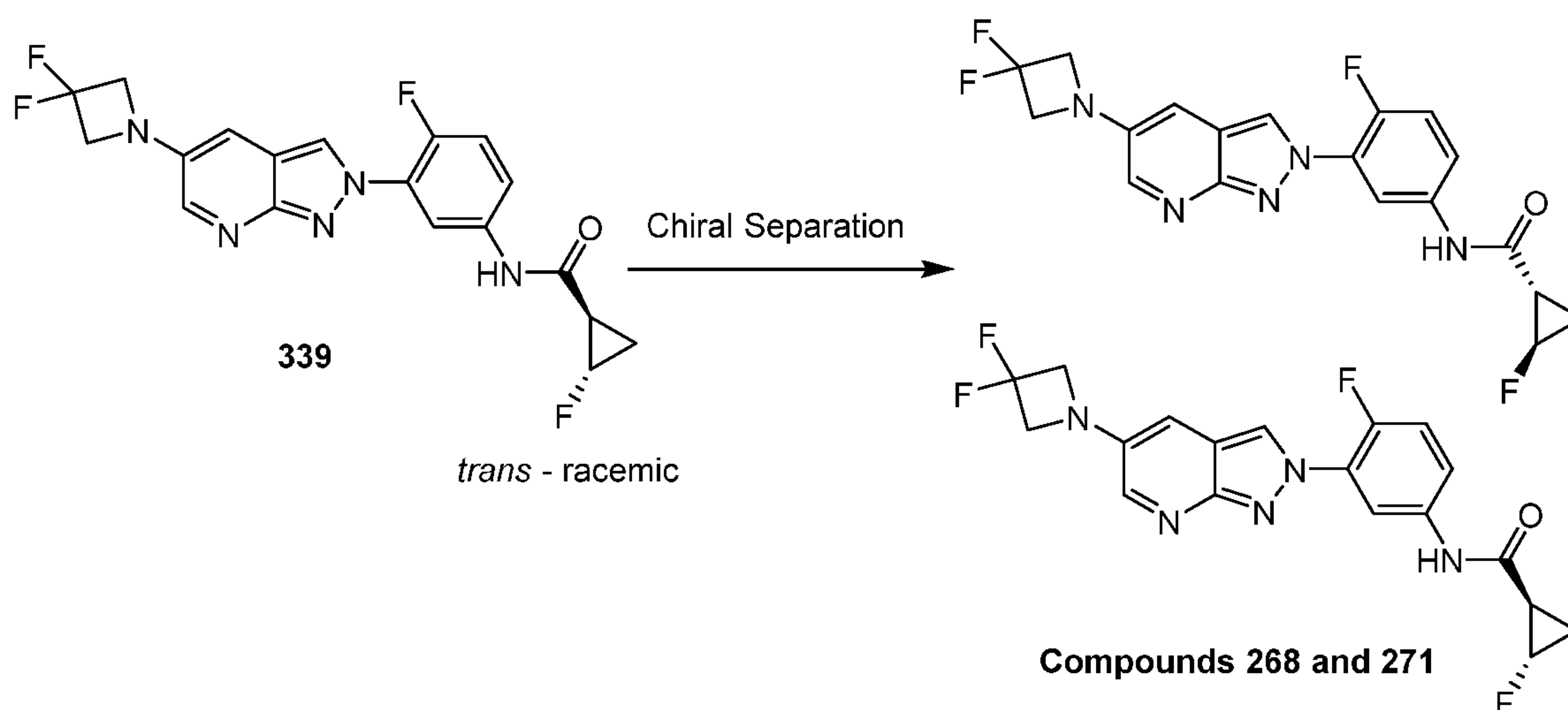


Compound **256** (170 mg) was separated by SFC (column: CHIRALCEL® OJ-H (250mm*25 mm, 10 μ m); mobile phase: [CO₂ – MeOH (0.1%NH₃H₂O)]; B%: 50%) to give compound **269** (peak 1, RT = 5.42 min) as a yellow solid and compound **273** (peak 2, RT = 6.75 min) as an off-white solid.

269 (peak 1): SFC RT: 5.42 min. ¹H NMR (400 MHz, DMSO-d₆) δ ppm 10.75 (s, 1 H), 9.48 (d, J=2.26 Hz, 1 H), 9.03 (d, J=2.38 Hz, 1 H), 8.95 (d, J=2.26 Hz, 1 H), 8.74 (d, J=4.14 Hz, 1 H), 8.39 (dd, J=6.96, 2.57 Hz, 1 H), 8.13 (d, J=8.03 Hz, 1 H), 7.96 (td, J=7.75, 1.69 Hz, 1 H), 7.65 - 7.74 (m, 1 H), 7.57 (dd, J=11.11, 9.10 Hz, 1 H), 7.42 (dd, J=7.22, 5.21 Hz, 1 H), 4.78 - 5.06 (m, 1 H), 2.26 - 2.35 (m, 1 H), 1.49 - 1.66 (m, 1 H), 1.24 - 1.33 (m, 1 H). Method 1: RT = 2.80 min.; M+H = 392.2.

273 (peak 2): SFC RT: 6.75 min. ¹H NMR (400 MHz, DMSO-d₆) δ ppm 10.75 (s, 1 H), 9.48 (d, J=2.08 Hz, 1 H), 9.03 (d, J=2.32 Hz, 1 H), 8.95 (d, J=2.20 Hz, 1 H), 8.74 (d, J=4.52 Hz, 1 H), 8.40 (dd, J=7.03, 2.51 Hz, 1 H), 8.13 (d, J=8.07 Hz, 1 H), 7.96 (td, J=7.79, 1.77 Hz, 1 H), 7.69 (dt, J=8.47, 3.53 Hz, 1 H), 7.57 (dd, J=11.00, 9.17 Hz, 1 H), 7.42 (dd, J=7.09, 5.14 Hz, 1 H), 4.80 - 5.05 (m, 1 H), 2.25 - 2.34 (m, 1 H), 1.48 - 1.67 (m, 1 H), 1.28 (dq, J=13.13, 6.67 Hz, 1 H). Method 1: RT = 2.82 min.; M+H = 392.2.

Example 27A and B: (1*S*,2*R*)-N-(3-(5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-*b*]pyridin-2-yl)-4-fluorophenyl)-2-fluorocyclopropane-1-carboxamide or (1*R*,2*S*)-N-(3-(5-(3,3-difluoroazetidin-1-yl)-2H-pyrazolo[3,4-*b*]pyridin-2-yl)-4-fluorophenyl)-2-fluorocyclopropane-1-carboxamide (Compounds 268 and 271)



Compound **339** (130 mg) was separated by SFC (column: CHIRALCEL® OD-H (250mm*25 mm, 10 μ m); mobile phase: [CO₂ – MeOH (0.1%NH₃H₂O)]; B%: 50%) to give compound **271** (peak 1, RT = 4.58 min) as a yellow solid and compound **268** (peak 2, RT = 8.01 min) as a yellow solid.

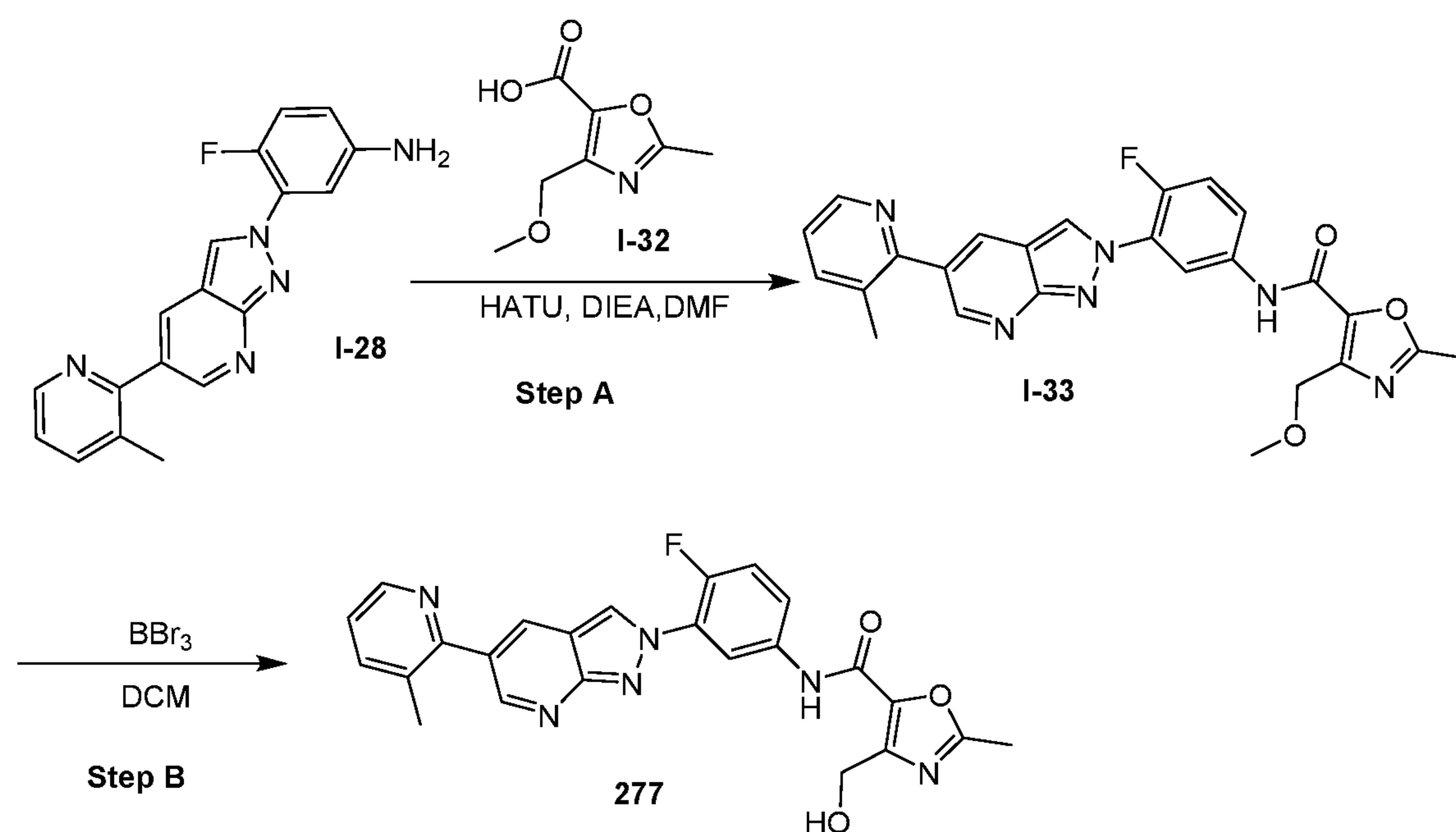
268 (peak 2): SFC RT: 8.01 min. ¹H NMR (400 MHz, DMSO-d₆) δ ppm 10.69 (s, 1 H), 8.64 (d, J=2.69 Hz, 1 H), 8.37 (d, J=2.81 Hz, 1 H), 8.32 (dd, J=7.03, 2.51 Hz, 1 H), 7.61 - 7.67

(m, 1 H), 7.52 (dd, $J=11.19, 9.11$ Hz, 1 H), 7.15 (d, $J=2.81$ Hz, 1 H), 4.80 - 5.03 (m, 1 H), 4.41 (t, $J=12.29$ Hz, 4 H), 2.24 - 2.33 (m, 1 H), 1.46 - 1.67 (m, 1 H), 1.27 (dd, $J=13.27, 6.54$ Hz, 1 H).

Method 1: RT = 2.89 min.; M+H = 406.0.

271 (peak 1): SFC RT: 4.58 min. ^1H NMR (400 MHz, DMSO- d_6) δ ppm 10.75 (s, 1 H),
 5 8.70 (d, $J=2.69$ Hz, 1 H), 8.43 (d, $J=2.81$ Hz, 1 H), 8.38 (dd, $J=6.97, 2.57$ Hz, 1 H), 7.66 - 7.77
 (m, 1 H), 7.52 - 7.63 (m, 1 H), 7.20 (d, $J=2.81$ Hz, 1 H), 4.85 - 5.08 (m, 1 H), 4.47 (t, $J=12.23$
 Hz, 4 H), 2.27 - 2.39 (m, 1 H), 1.52 - 1.72 (m, 1 H), 1.33 (dq, $J=13.11, 6.43$ Hz, 1 H). Method 1:
 RT = 2.89 min.; M+H = 406.0.

Example 28: N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-4-(hydroxymethyl)-2-methyloxazole-5-carboxamide (Compound 277)

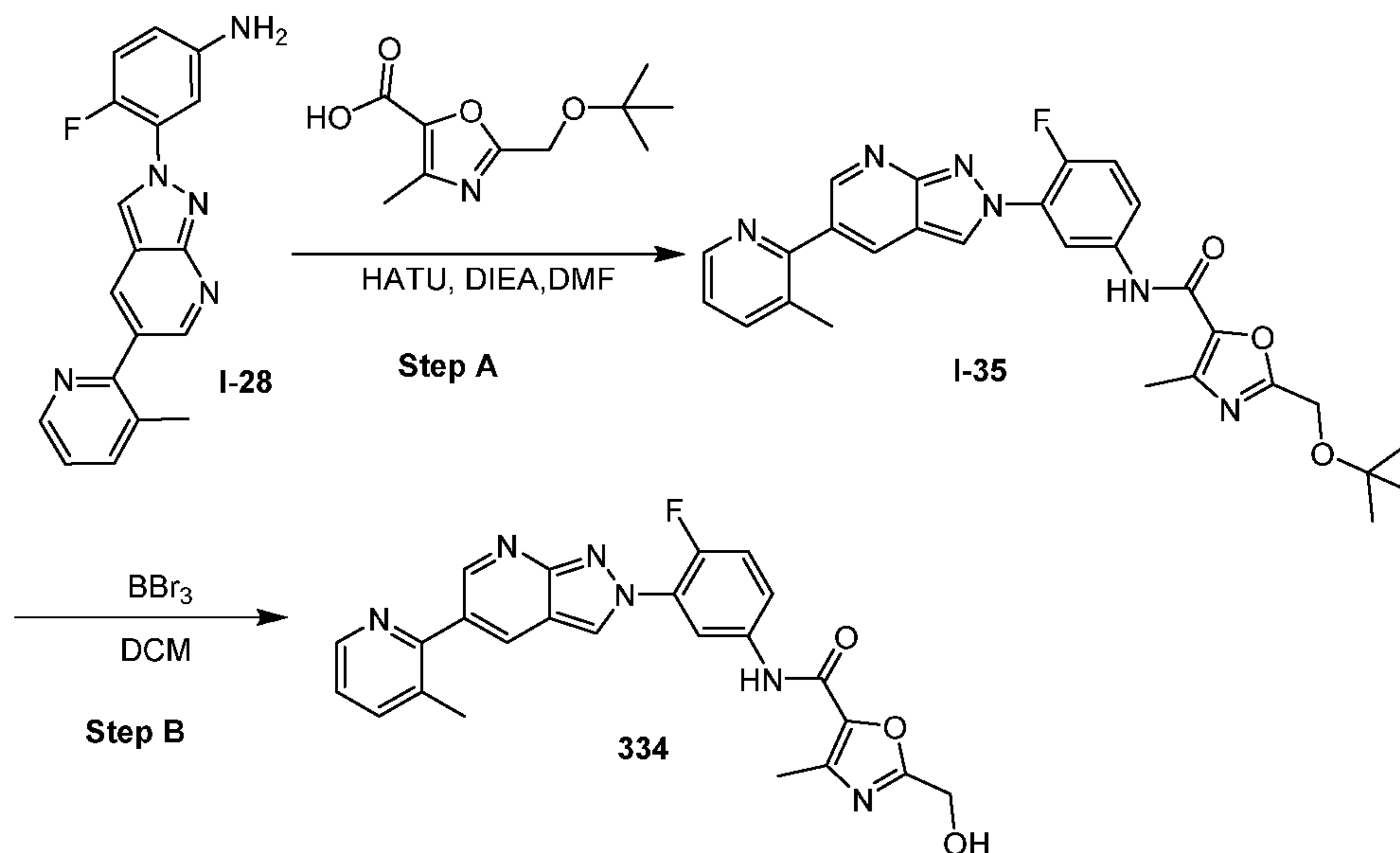


Step A: Intermediate **I-33** was prepared in a similar manner to **Example 12** using **I-28**
 and **I-32** as starting materials. ^1H NMR (400 MHz, DMSO- d_6) δ ppm 10.70 (s, 1 H), 9.04 (d,
 $J=2.45$ Hz, 1 H), 8.95 (d, $J=2.20$ Hz, 1 H), 8.60 - 8.66 (m, 2 H), 8.55 (d, $J=2.20$ Hz, 1 H), 7.89 -
 15 7.96 (m, 2 H), 7.62 (dd, $J=11.00, 9.29$ Hz, 1 H), 7.44 - 7.52 (m, 1 H), 4.64 (s, 2 H), 3.31 (s, 3 H),
 2.57 (s, 3 H), 2.46 (s, 3 H). M+H = 473.0.

Step B: To a solution of **I-33** (15 mg, 28.9 μmol , 1 eq, FA) in DCM (1mL) was added
 dropwise BBr_3 (14.5 mg, 57.9 μmol , 5.6 μL , 2 eq) in DCM (0.5 mL) at -78°C . The mixture was
 stirred at 20°C for 18 hr under a N_2 atmosphere. Saturated NaHCO_3 (3 mL) was added and the
 20 mixture was extracted with DCM (10 mL). The organic layer was dried over Na_2SO_4 , filtered and
 concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC
 (column: Phenomenex Gemini 150*25 mm*10 μm ; mobile phase: [water (0.05% ammonia
 hydroxide v/v)-acetonitrile]; B%: 30%-60%, 12 min) and lyophilized to give compound **277** as a
 white solid. ^1H NMR (400 MHz, DMSO- d_6) δ ppm 9.00 (d, $J=2.20$ Hz, 1 H), 8.94 (d, $J=1.96$ Hz,

1 H), 8.53 - 8.63 (m, 2 H), 8.51 (d, $J=2.20$ Hz, 1 H), 7.85 - 7.95 (m, 1 H), 7.81 (br d, $J=7.34$ Hz, 1 H), 7.55 - 7.67 (m, 1 H), 7.37 (dd, $J=7.46, 4.77$ Hz, 1 H), 4.69 (s, 2 H), 2.55 (s, 3 H), 2.45 (s, 3 H). Method 1: RT = 2.50 min.; M+H = 459.0.

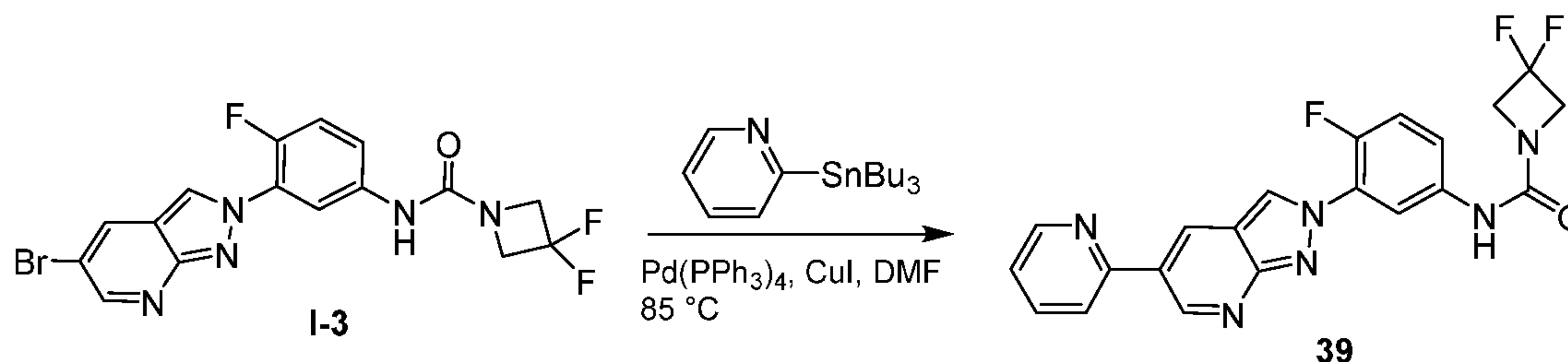
Example 29: N-(4-fluoro-3-(5-(3-methylpyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)-2-(hydroxymethyl)-4-methyloxazole-5-carboxamide (Compound 334)



Step A: Intermediate **I-35** was prepared in a similar manner to **Example 12** using **I-28** and 2-(tert-butoxymethyl)-4-methyloxazole-5-carboxylic acid as starting materials. ^1H NMR (400 MHz, DMSO- d_6) δ ppm 10.55 - 10.67 (m, 1 H) 9.00 (d, $J=2.45$ Hz, 1 H) 8.91 - 8.97 (m, 1 H) 8.54 - 8.65 (m, 2 H) 8.47 - 8.53 (m, 1 H) 7.96 (s, 1 H) 7.80 (dd, $J=7.70, 0.86$ Hz, 1 H) 7.55 - 7.65 (m, 1 H) 7.37 (dd, $J=7.70, 4.77$ Hz, 1 H) 4.54 (s, 2 H) 2.69 (s, 3 H) 2.44 (s, 3 H) 1.24 (s, 9 H).

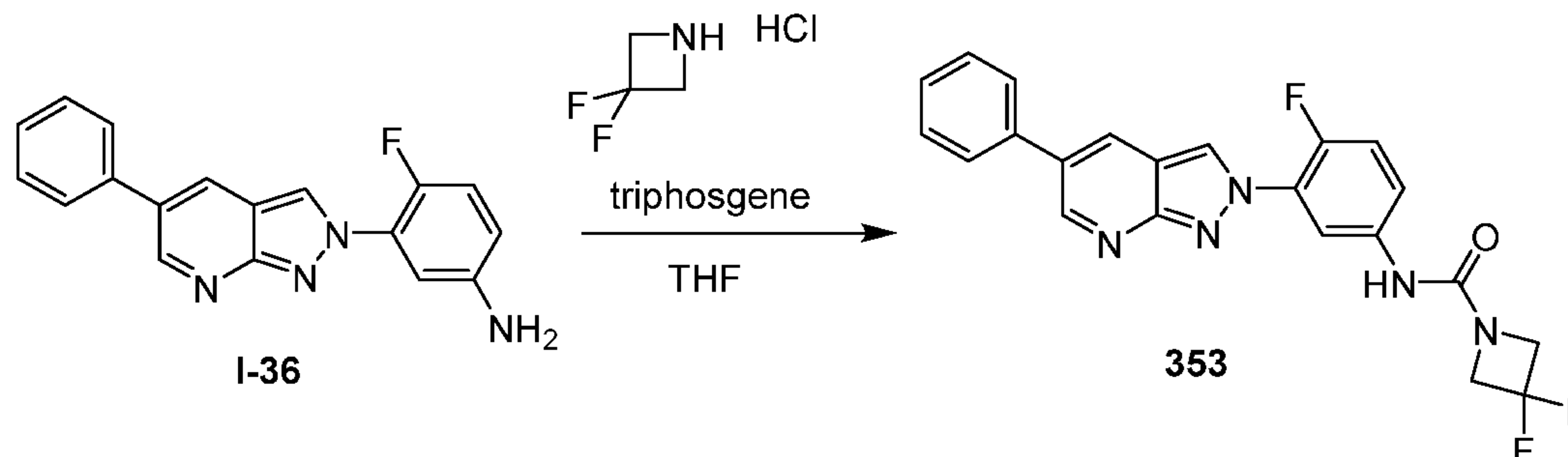
Step B: To a solution of **I-35** (70 mg, 136.04 μmol , 1 eq) in DCM (2 mL) was added TFA (0.5 mL, 6.75 mmol, 49.6 eq). The mixture was stirred at 25 $^\circ\text{C}$ for 3 hr. The reaction mixture was concentrated under reduced pressure to remove solvent. The pH was adjusted to 7 with TEA. The residue was purified by prep-HPLC (column: Phenomenex Gemini 150*25 mm*10 μm ; mobile phase: [water (0.05% ammonia hydroxide v/v)-acetonitrile]; B%: 20%-50%, 12 min) and lyophilized to give compound **334** as a white solid. ^1H NMR (400 MHz, DMSO- d_6) δ ppm, 10.63 (s, 1 H), 9.00 (d, $J=2.20$ Hz, 1 H), 8.94 (d, $J=2.20$ Hz, 1 H), 8.62 (dd, $J=7.09, 2.45$ Hz, 1 H), 8.57 (d, $J=3.67$ Hz, 1 H), 8.51 (d, $J=2.20$ Hz, 1 H), 7.91 - 8.01 (m, 1 H), 7.81 (d, $J=7.34$ Hz, 1 H), 7.60 (dd, $J=11.00, 9.05$ Hz, 1 H), 7.37 (dd, $J=7.70, 4.77$ Hz, 1 H), 5.83 (t, $J=5.99$ Hz, 1 H), 4.60 (d, $J=6.11$ Hz, 2 H), 2.45 (s, 6 H). Method 1: RT = 2.57 min.; M+H = 459.0.

Example 30: 3,3-difluoro-N-(4-fluoro-3-(5-(pyridin-2-yl)-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 39)



To a solution of **I-3** (3.00 g, 7.04 mmol, 1 eq) and tributyl(2-pyridyl)stannane (3.4 g, 9.1 mmol, 1.3 eq) in DMF (40 mL) was added Pd(PPh₃)₄ (813 mg, 703.9 μmol, 0.1 eq) and CuI (134 mg, 703.9 μmol, 0.1 eq) under a N₂ atmosphere. The mixture was stirred at 85 °C for 2 hr. The reaction mixture was concentrated under reduced pressure to remove solvent. The residue was purified by silica chromatography eluting with petroleum ether/ Ethyl acetate = 2:1 to 0:1 to give compound **39** as a white solid. ¹H NMR (400 MHz, Methanol-d₄) δ 9.36 (d, J = 2.3 Hz, 1H), 9.00 – 8.93 (m, 2H), 8.79 – 8.75 (m, 1H), 8.26 (dd, J = 6.8, 2.7 Hz, 1H), 8.19 – 8.14 (m, 2H), 7.70 – 7.64 (m, 1H), 7.64 – 7.56 (m, 1H), 7.46 – 7.35 (m, 1H), 4.44 (td, J = 12.3, 3.0 Hz, 4H). Method 2: RT = 0.99 min.; M+H = 425.0.

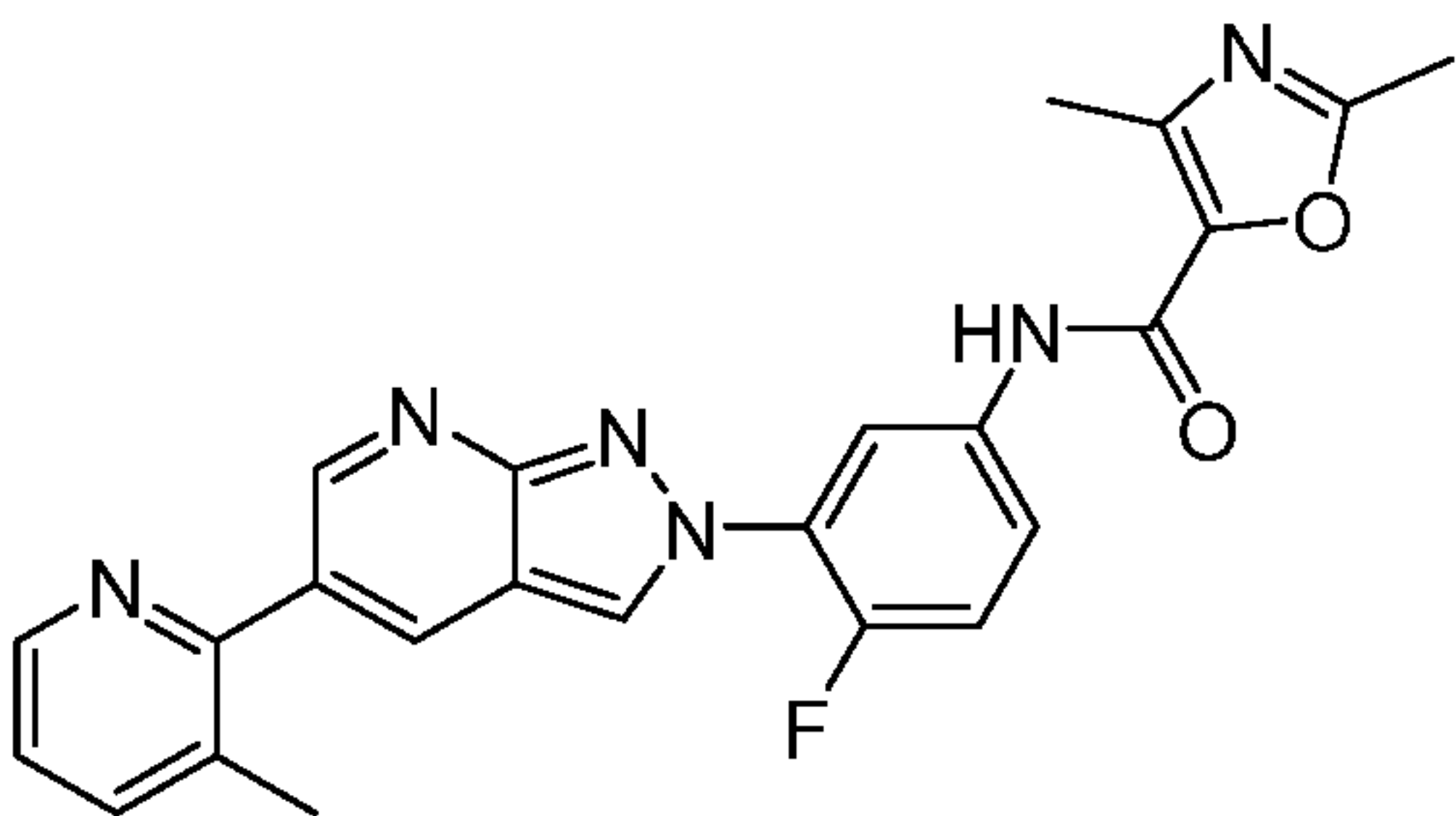
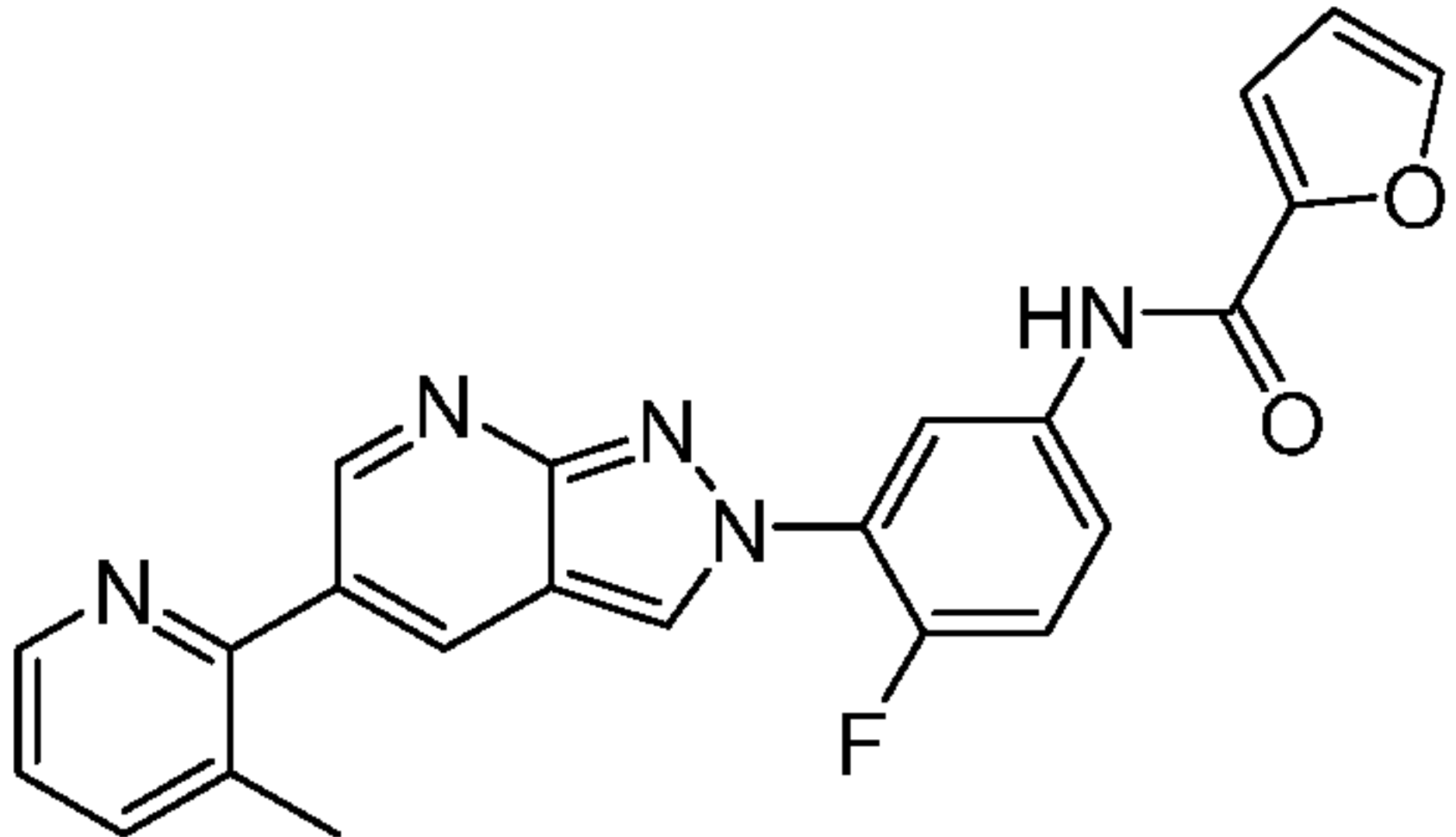
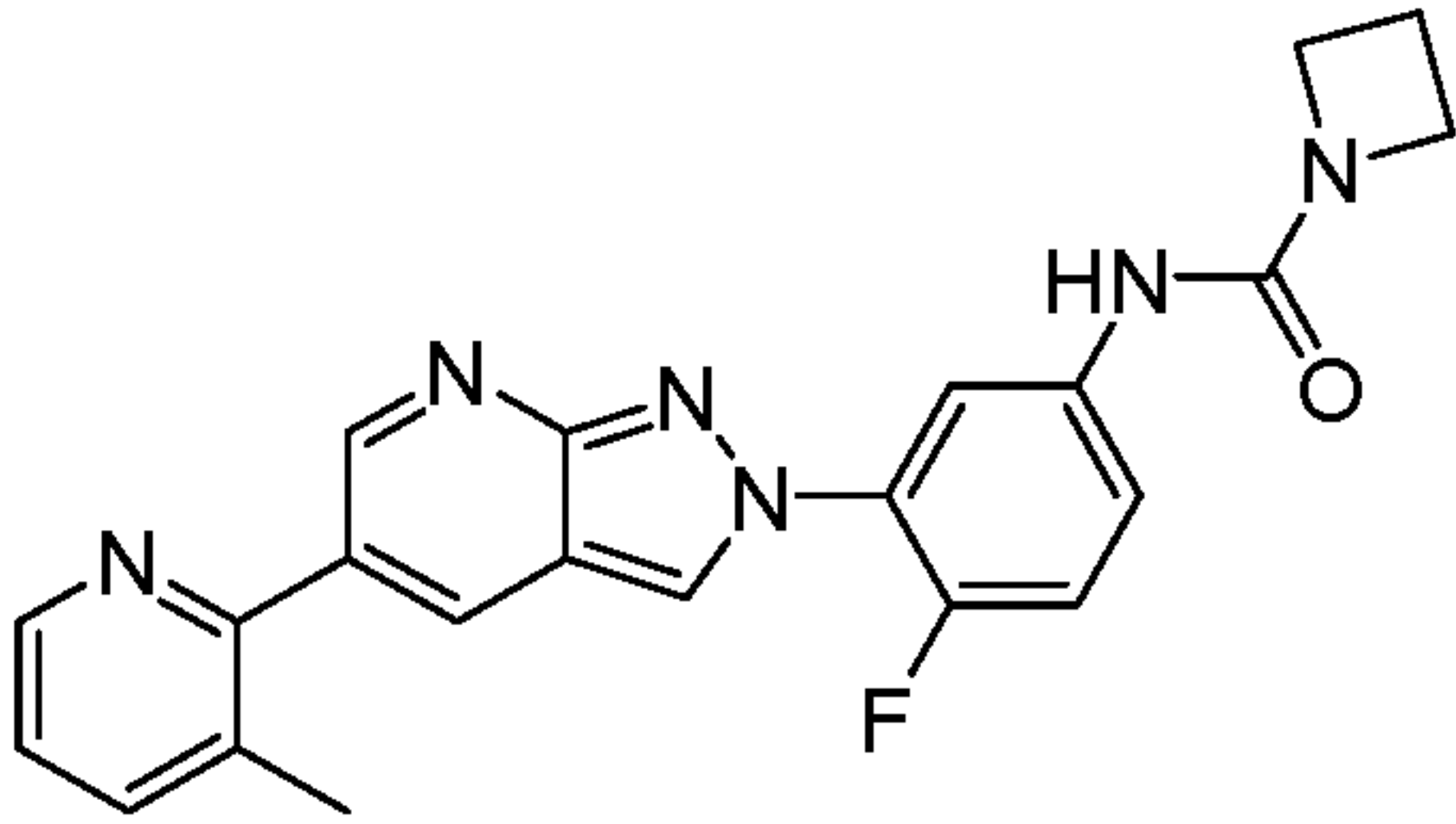
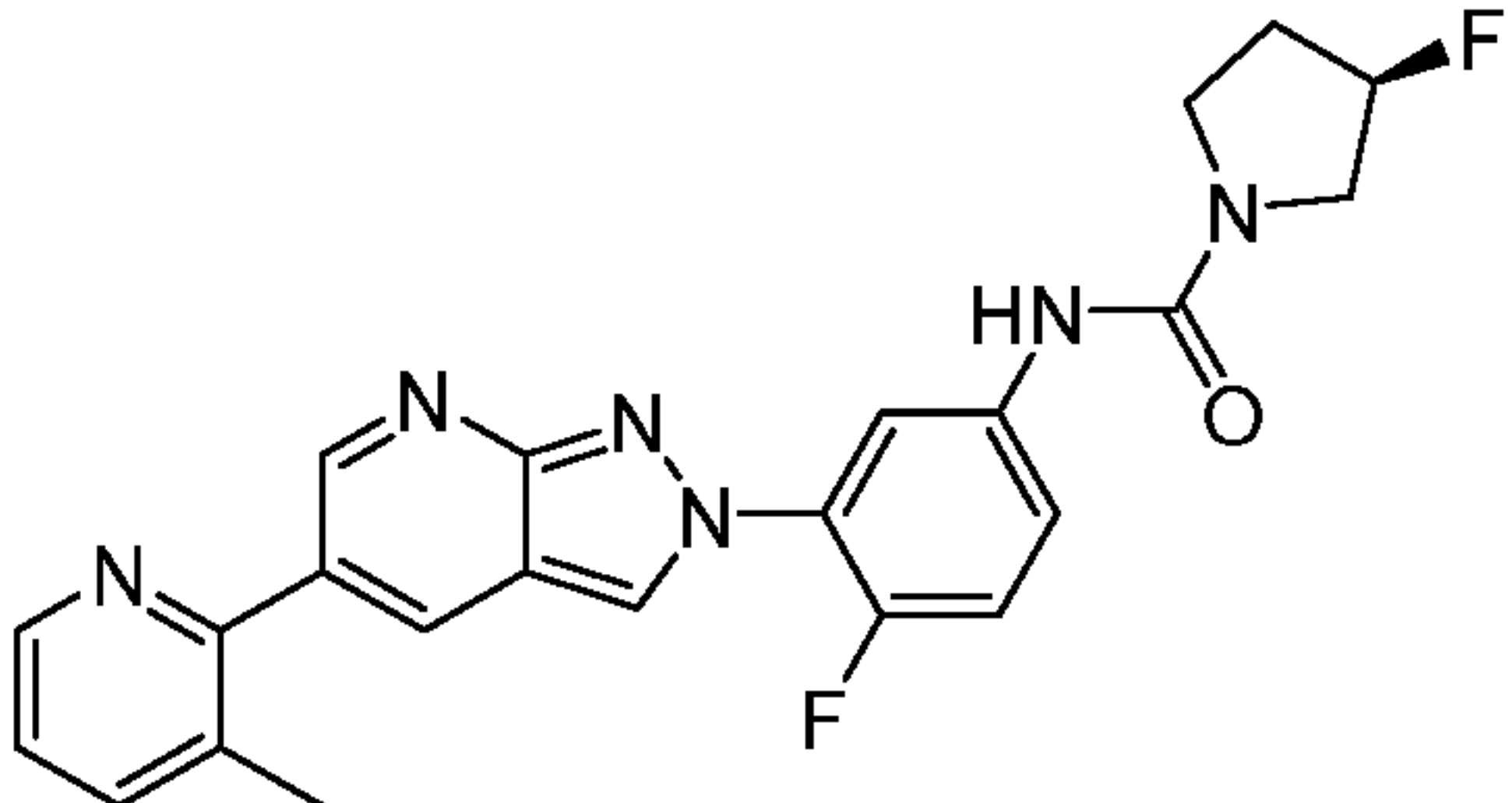
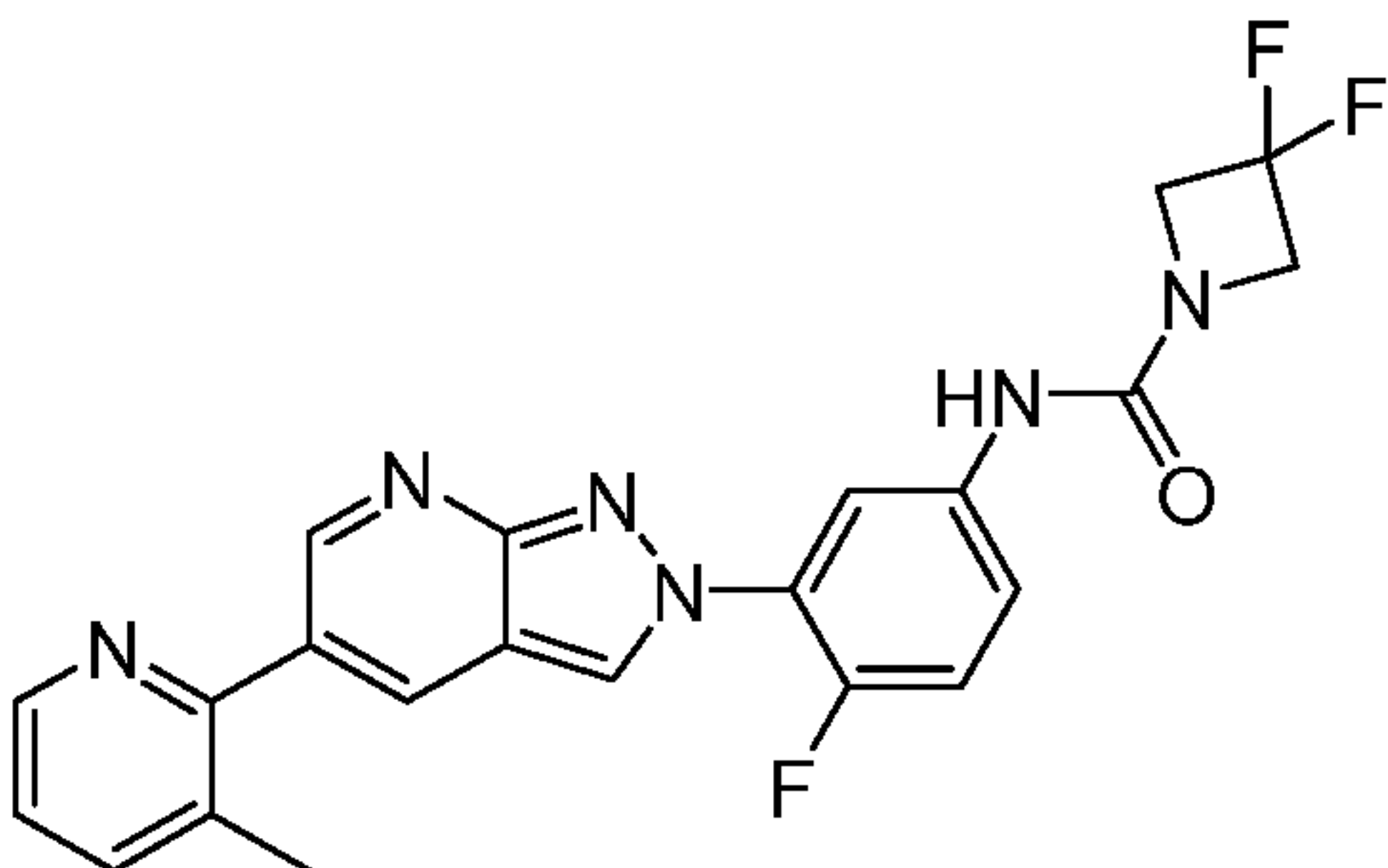
Example 31: 3,3-difluoro-N-(4-fluoro-3-(5-phenyl-2H-pyrazolo[3,4-b]pyridin-2-yl)phenyl)azetidine-1-carboxamide (Compound 353)



To a stirred solution of triphosgene (23 mg, 0.079 mmol) in dry THF (1 mL) was added **I-36** (40 mg, 0.131 mmol) in dry THF (2 mL) at -5 °C – 0 °C and stirred at RT for 10 min. 3,3-difluoroazetidine hydrochloride (34 mg, 0.263 mmol) and DIEA (51 mg, 0.394 mmol) in dry THF (2 mL) were added dropwise at 0 °C and the reaction was stirred at RT for 1 h. The reaction mixture was quenched with saturated NH₄Cl solution and extracted with EtOAc (50 mL X 2). The combined organic layers were washed with water (20 mL), brine (10 mL) and dried over sodium sulphate and concentrated in vacuo. The crude compound was purified by silica gel chromatography eluting with 50% EtOAc in n-Hexane to afford compound **353** as an off-white solid. ¹H NMR (400 MHz, DMSO-d₆) 9.25 (s, 1H), 9.06-9.05 (d, J=2.8, 1H), 8.96-8.95 (d, J=2.0, 1H), 8.52-8.51 (d, J=2.4, 1H), 8.27-8.25 (m, 1H), 7.80-7.78 (d, J=7.2, 2H), 7.72-7.67 (m, 1H), 7.56-7.48 (m, 3H), 7.44-7.41 (m, 1H), 4.44-4.38 (t, J=16.4, 4H).

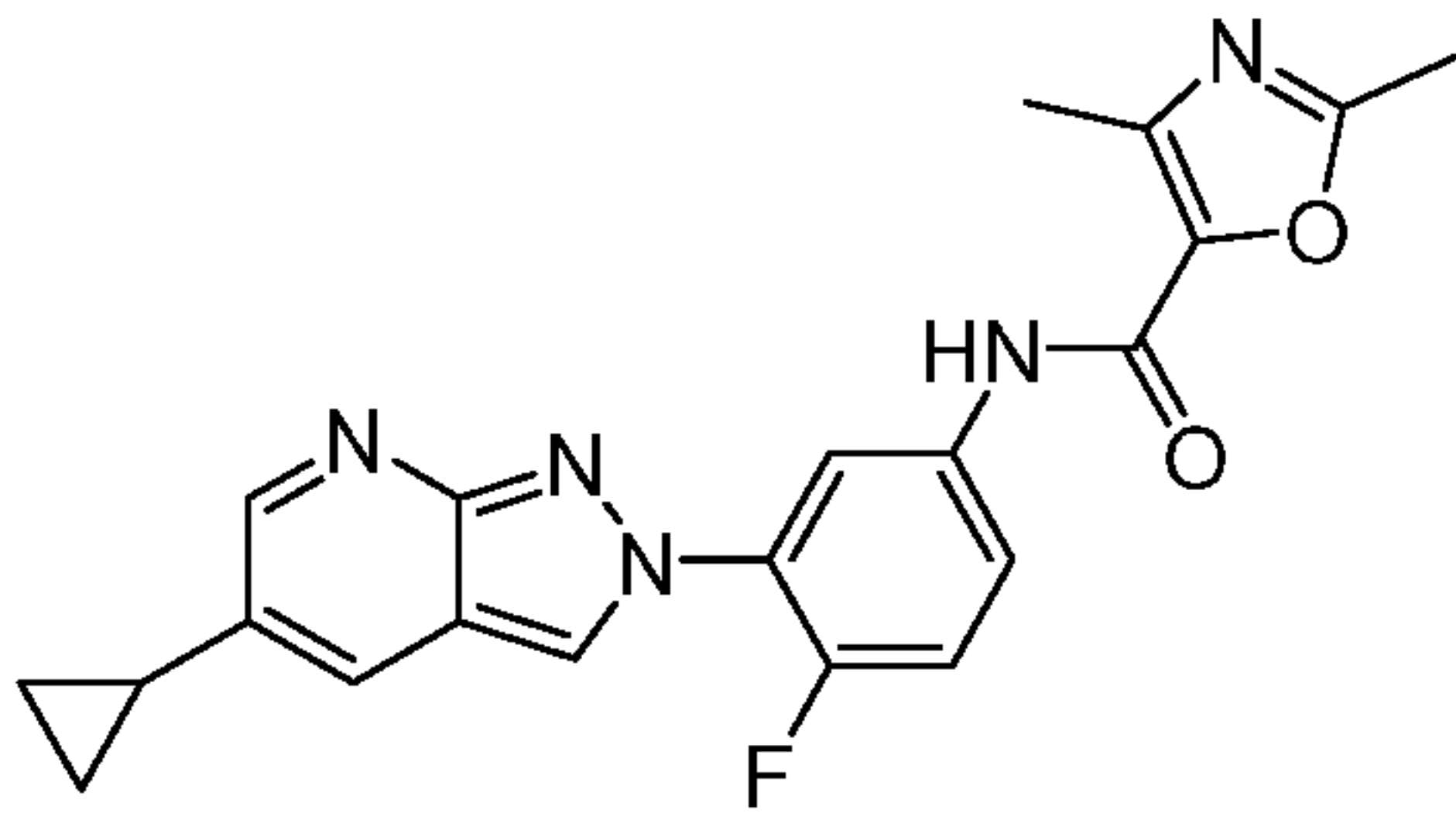
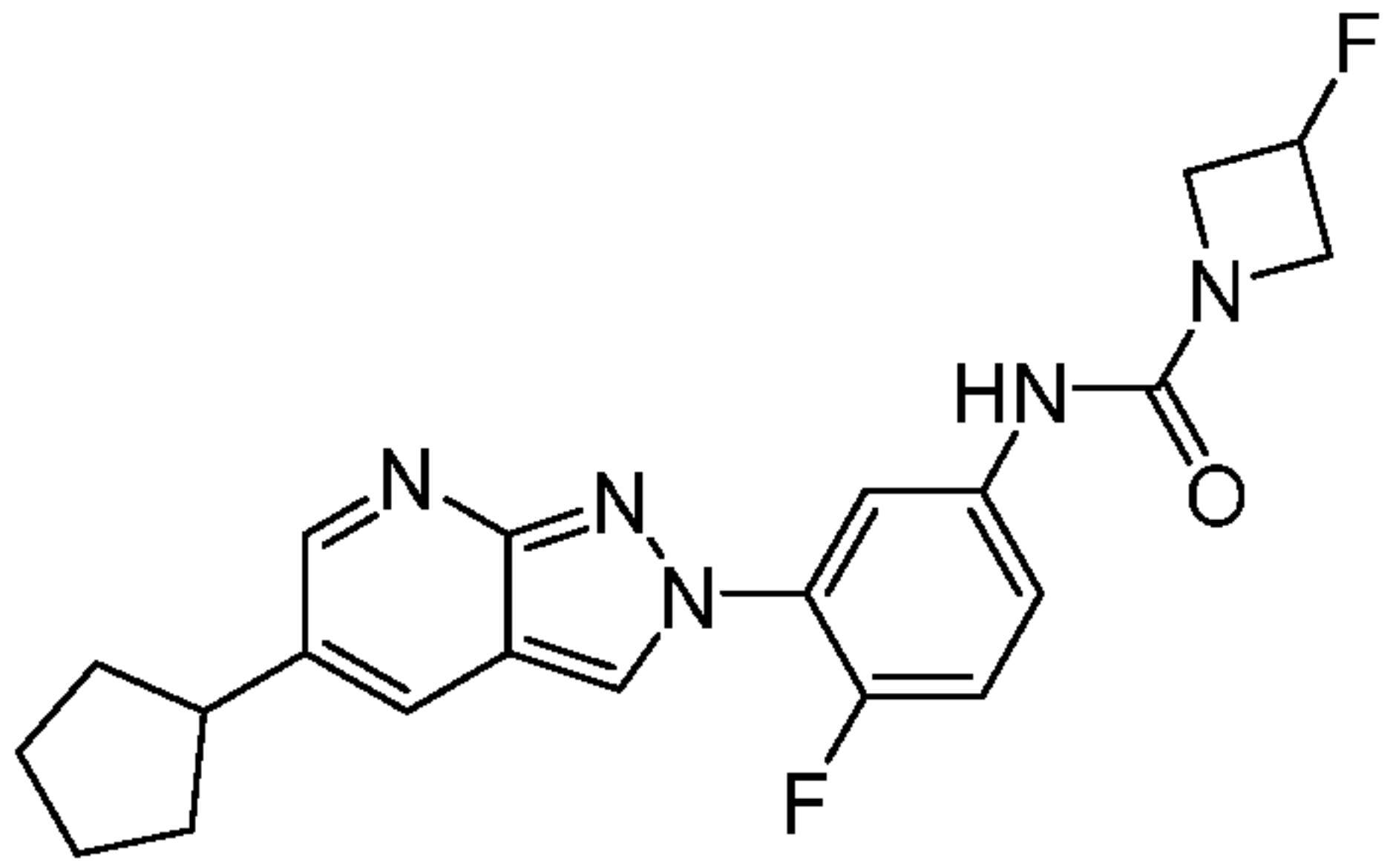
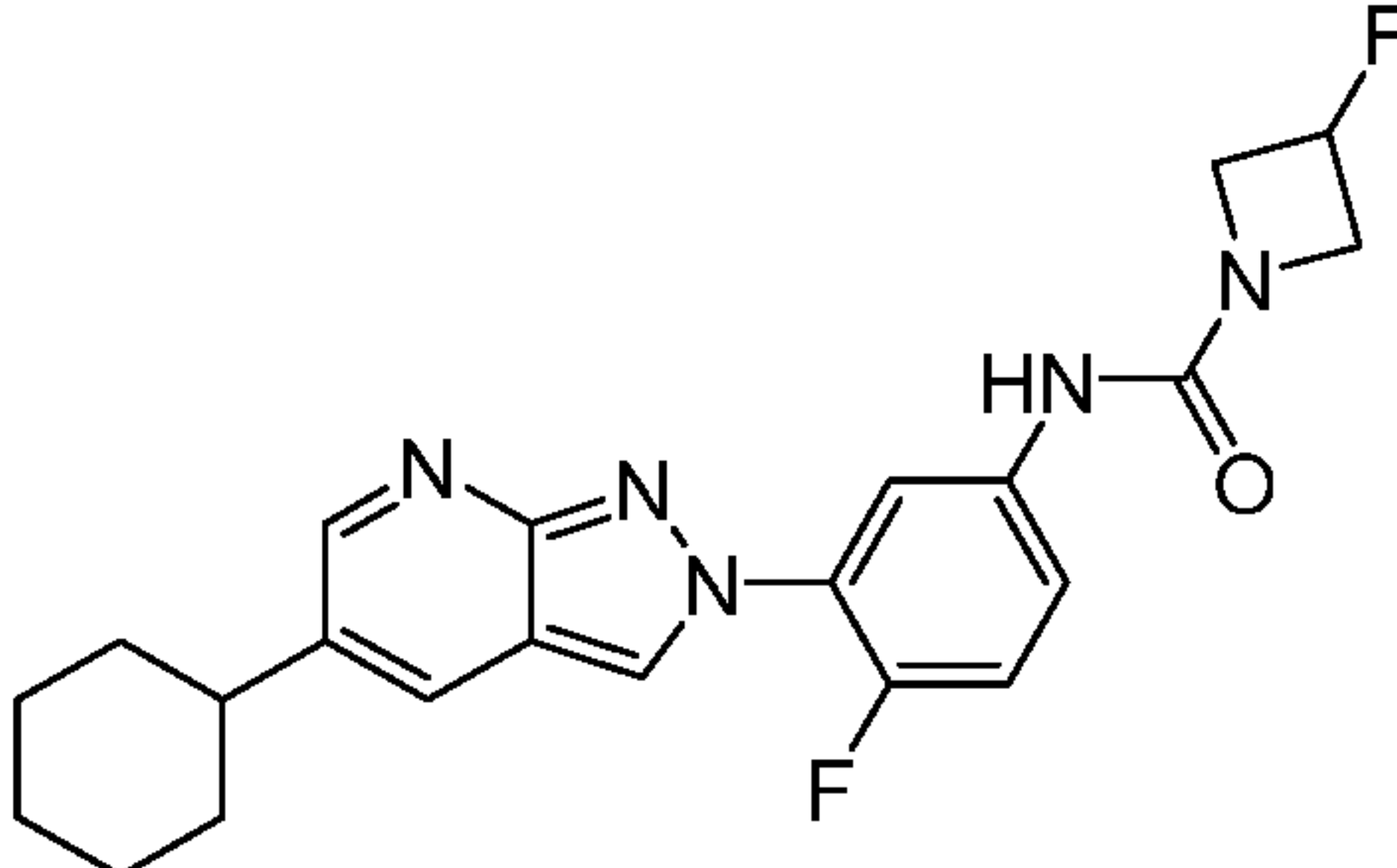
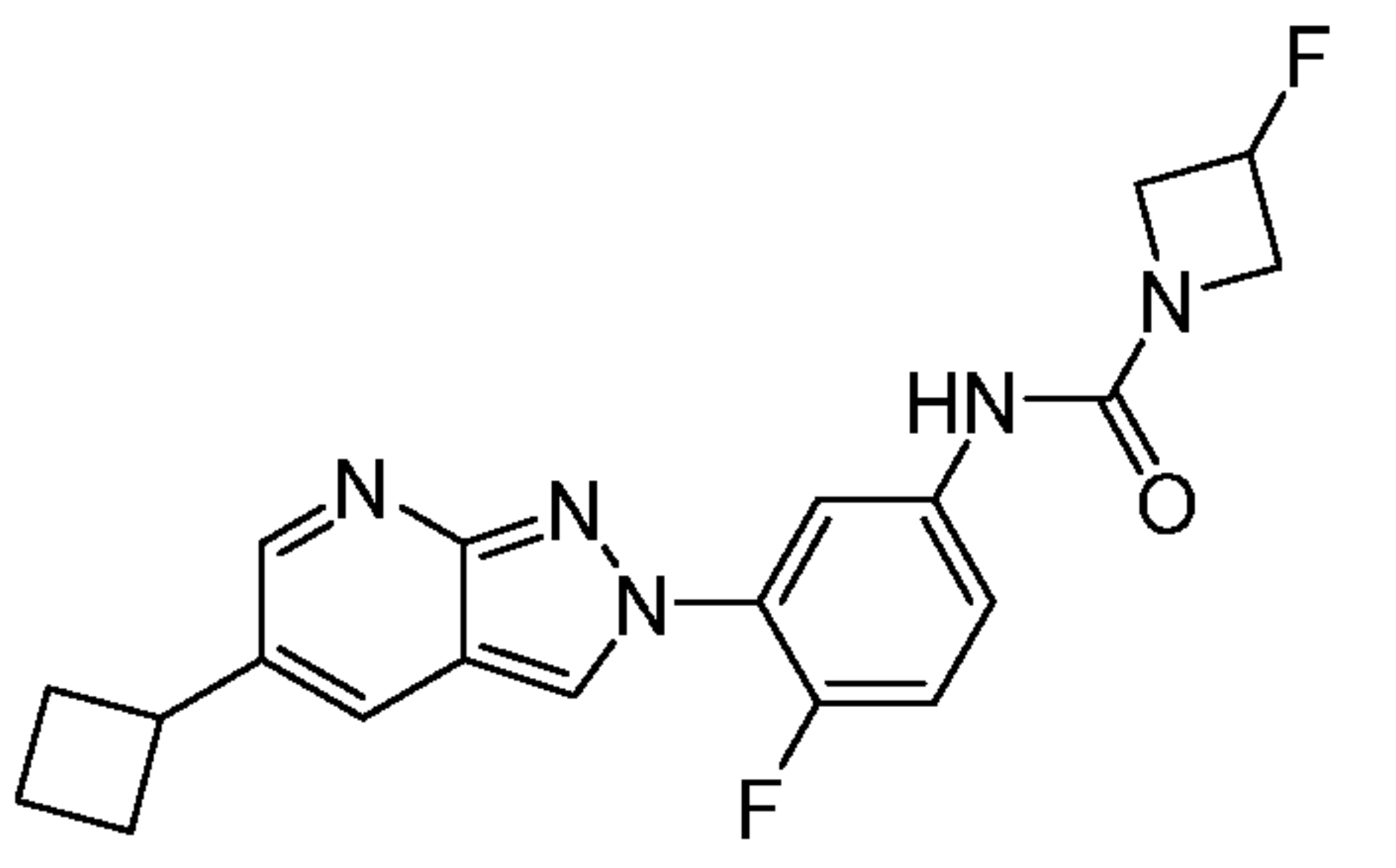
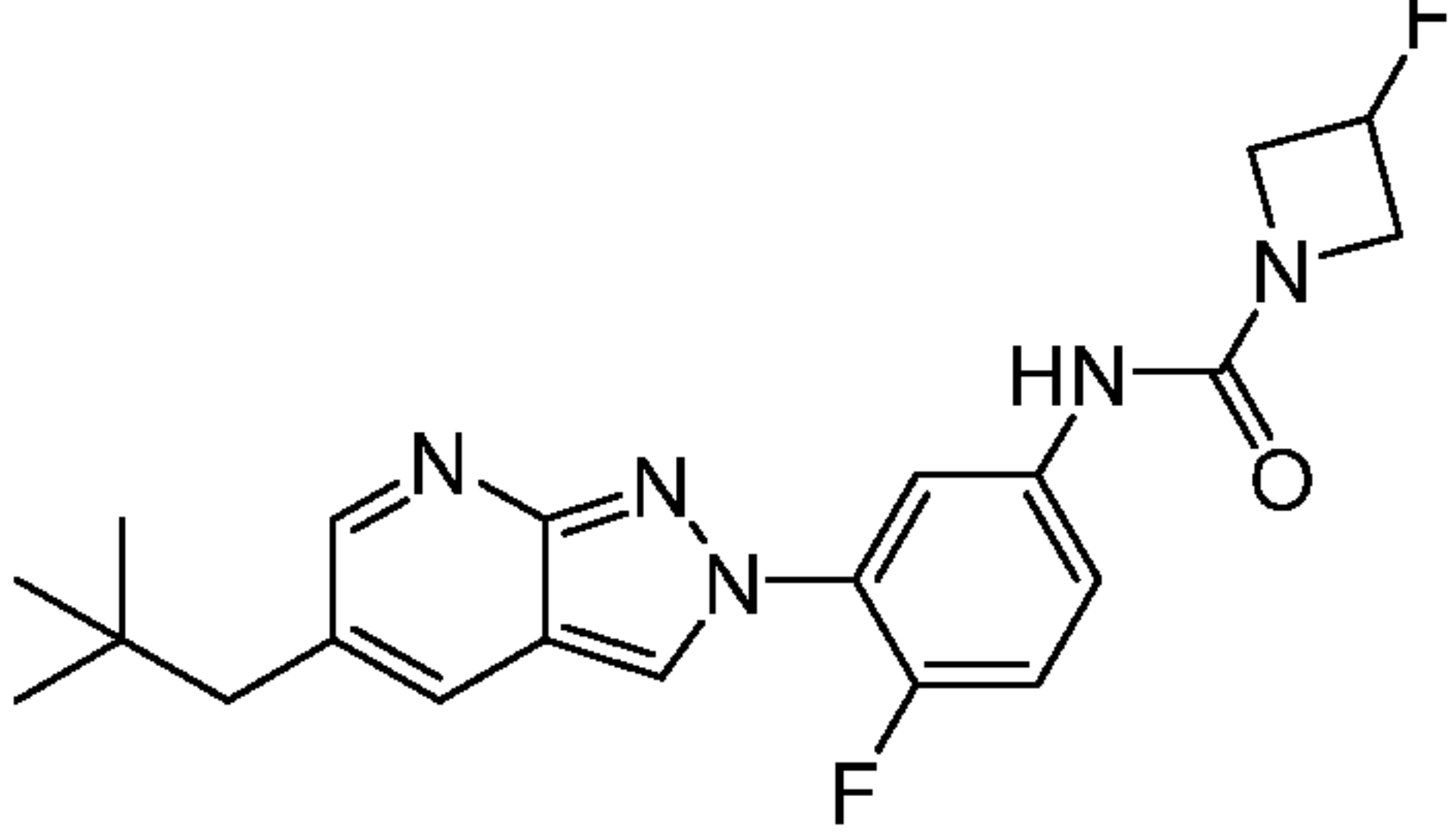
Table 2 lists compounds prepared according to the Examples above.

Table 2

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
1		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.90 (dd, <i>J</i> = 13.2, 2.3 Hz, 2H), 8.59 – 8.43 (m, 3H), 7.97 – 7.81 (m, 2H), 7.55 – 7.35 (m, 2H), 2.56 (s, 3H), 2.48 – 2.45 (m, 6H). Method 1: RT = 2.69 min.; M+H = 443.1
2		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.92 (d, <i>J</i> = 2.4 Hz, 1H), 8.88 (d, <i>J</i> = 2.2 Hz, 1H), 8.55 - 8.45 (m, 3H), 7.96 (m, 1H), 7.87 (m, 1H), 7.78 (m, 1H), 7.52 - 7.39 (m, 2H), 7.32 (m, 1H), 6.68 (m, 1H), 2.46 (s, 3H). Method 2: RT = 0.89 min.; M+H = 414.3
3		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.89 – 8.84 (m, 2H), 8.52 (m, 1H), 8.48 (m, 1H), 8.18 (m, 1H), 7.86 (m, 1H), 7.67 (m, 1H), 7.44 – 7.32 (m, 2H), 4.18 – 4.06 (m, 4H), 2.46 (s, 3H), 2.41 – 2.26 (m, 2H). Method 1: RT = 2.41 min.; M+H = 403.3
4		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.87 (dd, <i>J</i> = 4.7, 2.3 Hz, 2H), 8.52 (m, 1H), 8.49 (m, 1H), 8.19 (m, 1H), 7.86 (m, 1H), 7.67 (m, 1H), 7.45 – 7.34 (m, 2H), 5.42 – 5.25 (m, 1H), 3.85 – 3.55 (m, 4H), 2.46 (s, 3H), 2.39 – 2.19 (m, 2H). Method 1: RT = 2.41 min.; M+H = 435.3
5		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.88 (dd, <i>J</i> = 5.4, 2.3 Hz, 2H), 8.52 (m, 1H), 8.48 (m, 1H), 8.22 (m, 1H), 7.86 (m, 1H), 7.69 (m, 1H), 7.45 – 7.36 (m, 2H), 4.44 (m, 4H), 2.46 (s, 3H). Method 2: RT = 0.76 min.; M+H = 439.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
6		¹ H NMR (500 MHz, DMSO-d ₆) δ 8.98 (s, 1H), 8.94 (dd, <i>J</i> = 16.9, 2.3 Hz, 2H), 8.57 (ddd, <i>J</i> = 4.8, 1.7, 0.7 Hz, 1H), 8.49 (d, <i>J</i> = 2.3 Hz, 1H), 8.28 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 7.80 (ddd, <i>J</i> = 7.7, 1.7, 0.8 Hz, 1H), 7.72 (ddd, <i>J</i> = 9.1, 4.1, 2.7 Hz, 1H), 7.49 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.37 (dd, <i>J</i> = 7.7, 4.7 Hz, 1H), 5.41 (dtt, <i>J</i> = 57.5, 6.1, 3.1 Hz, 1H), 4.34 (dddd, <i>J</i> = 21.7, 10.4, 6.0, 1.4 Hz, 2H), 4.04 (dddd, <i>J</i> = 24.9, 10.4, 3.1, 1.4 Hz, 2H), 2.44 (s, 3H). Method 1: RT = 2.39 min.; M+H = 421.1
7		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.66 (d, <i>J</i> = 2.4 Hz, 1H), 8.56 (d, <i>J</i> = 2.2 Hz, 1H), 8.12 (m, 1H), 8.07 (m, 1H), 7.64 (m, 1H), 7.34 (m, 1H), 4.19 – 4.01 (m, 4H), 2.67 (m, 2H), 2.41 – 2.24 (m, 2H), 1.97 (m, 1H), 0.99 (m, 6H). Method 1: RT = 3.11 min.; M+H = 368.3
8		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.59 (d, <i>J</i> = 2.5 Hz, 1H), 8.46 (d, <i>J</i> = 2.2 Hz, 1H), 8.06 (m, 1H), 7.97 (m, 1H), 7.56 (m, 1H), 7.30 – 7.24 (m, 1H), 4.33 (m, 4H), 2.57 (m, 2H), 1.92 – 1.81 (m, 1H), 0.89 (m, 6H). Method 2: RT = 1.09 min. M+H = 404.1
9		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 9.18 (s, 1 H), 8.70 (d, <i>J</i> =3.01 Hz, 1 H), 8.55 (d, <i>J</i> =2.76 Hz, 1 H), 8.20 (dd, <i>J</i> =6.90, 2.64 Hz, 1 H), 7.56 - 7.78 (m, 1 H), 7.45 (dd, <i>J</i> =11.42, 9.16 Hz, 1 H), 7.15 (d, <i>J</i> =3.01 Hz, 1 H), 4.41 (t, <i>J</i> =12.67 Hz, 4 H), 2.95 (s, 6 H). Method 1: RT = 2.84 min.; M+H = 391.1
10		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.42 (d, <i>J</i> = 2.51 Hz, 1 H), 8.22 (d, <i>J</i> = 2.76 Hz, 1 H), 8.05 (dd, <i>J</i> =6.78, 2.76 Hz, 1 H), 7.58 - 7.62 (m, 1 H), 7.30 (dd, <i>J</i> = 11.04, 9.16 Hz, 1 H), 7.01 (d, <i>J</i> = 2.64 Hz, 1 H), 4.10 (t, <i>J</i> = 7.65 Hz, 4 H), 3.99 (t, <i>J</i> = 7.22 Hz, 4 H), 2.41 - 2.49 (m, 2 H), 2.27 - 2.35 (m, 2 H). Method 1: RT = 2.80 min.; M+H = 367.1
11		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.53 (s, 1H), 9.49 (d, <i>J</i> = 2.3 Hz, 1H), 9.06 (d, <i>J</i> = 2.6 Hz, 1H), 8.96 (d, <i>J</i> = 2.3 Hz, 1H), 8.74 (ddd, <i>J</i> = 4.8, 1.9, 0.9 Hz, 1H), 8.53 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 8.14 (dt, <i>J</i> = 8.0, 1.1 Hz, 1H), 8.01 - 7.91 (m, 2H), 7.62 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.50 - 7.38 (m, 2H), 6.14 (dd, <i>J</i> = 7.0, 3.7 Hz, 1H). Method 2: RT = 0.91 min.; M+H = 418.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
12		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.59 (s, 1H), 9.48 (d, <i>J</i> = 2.3 Hz, 1H), 9.03 (d, <i>J</i> = 2.5 Hz, 1H), 8.95 (d, <i>J</i> = 2.3 Hz, 1H), 8.74 (ddd, <i>J</i> = 4.8, 1.9, 0.9 Hz, 1H), 8.42 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 8.13 (dt, <i>J</i> = 8.1, 1.0 Hz, 1H), 7.96 (td, <i>J</i> = 7.7, 1.9 Hz, 1H), 7.73 (ddd, <i>J</i> = 9.0, 4.2, 2.7 Hz, 1H), 7.55 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.42 (ddd, <i>J</i> = 7.5, 4.8, 1.0 Hz, 1H), 3.17 (d, <i>J</i> = 5.3 Hz, 1H), 0.85 (d, <i>J</i> = 5.9 Hz, 4H). Method 1: RT = 2.74 min.; M+H = 374.1
13		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 9.99 (s, 1H), 9.26 (d, <i>J</i> = 2.3 Hz, 1H), 8.82 (d, <i>J</i> = 2.5 Hz, 1H), 8.73 (d, <i>J</i> = 2.4 Hz, 1H), 8.52 (ddd, <i>J</i> = 4.8, 1.8, 1.0 Hz, 1H), 8.22 (dd, <i>J</i> = 7.1, 2.7 Hz, 1H), 7.91 (dt, <i>J</i> = 8.0, 1.1 Hz, 1H), 7.74 (td, <i>J</i> = 7.7, 1.8 Hz, 1H), 7.52 (ddd, <i>J</i> = 9.0, 4.2, 2.7 Hz, 1H), 7.34 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.21 (ddd, <i>J</i> = 7.5, 4.8, 1.0 Hz, 1H), 2.04 (d, <i>J</i> = 7.0 Hz, 2H), 0.92 - 0.80 (m, 1H), 0.37 - 0.22 (m, 2H), 0.01 (dd, <i>J</i> = 4.8, 1.6 Hz, 2H). Method 1: RT = 2.80 min.; M+H = 388.1
14		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.56 (m, 1H), 8.13 (m, 1H), 8.08 - 8.04 (m, 1H), 7.65 (m, 1H), 7.35 (m, 1H), 5.44 - 5.30 (m, 1H), 4.39 (m, 2H), 4.14 (m, 2H), 2.67 (m, 2H), 1.97 (m, 1H), 0.99 (m, 6H). Method 1: RT = 3.15 min.; M+H = 386.1
15		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.61 (m, 2H), 8.12 (m, 1H), 7.92 (m, 1H), 7.64 (m, 1H), 7.35 (m, 1H), 5.44 - 5.29 (m, 1H), 4.39 (m, 2H), 4.14 (m, 2H), 2.15 - 2.08 (m, 1H), 1.15 - 1.03 (m, 2H), 0.88 - 0.77 (m, 2H). Method 1: RT = 2.79 min.; M+H = 370.1
16		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.57 (m, 1H), 8.43 (m, 1H), 8.13 - 8.06 (m, 1H), 7.89 (m, 1H), 7.45 (m, 1H), 2.67 (m, 2H), 2.55 (s, 3H), 2.47 (s, 3H), 1.98 (dt, <i>J</i> = 13.5, 6.8 Hz, 1H), 1.00 (s, 3H), 0.98 (s, 3H). Method 1: RT = 3.21 min.; M+H = 408.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
17		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.61 (m, 1H), 8.42 (m, 1H), 7.93 (m, 1H), 7.88 (m, 1H), 7.44 (m, 1H), 2.55 (s, 3H), 2.47 (s, 3H), 2.18 – 2.07 (m, 1H), 1.13 – 1.06 (m, 2H), 0.87 – 0.79 (m, 2H). Method 1: RT = 3.03 min.; M+H = 392.1
18		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.77 (m, 1H), 8.49 (m, 1H), 8.02 (m, 1H), 7.56 (m, 1H), 7.29 - 7.24 (m, 1H), 7.01 (m, 1H), 5.35 - 5.20 (m, 1H), 4.30 (m, 2H), 4.04 (m, 2H), 2.16 (m, 1H), 1.85 - 1.67 (m, 4H), 1.56 (m, 2H), 0.81 (m, 2H). Method 1: RT = 3.03 min.; M+H = 398.1
19		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.75 - 8.47 (m, 2H), 8.16 - 8.07 (m, 1H), 7.74 - 7.61 (m, 1H), 7.41 - 7.31 (m, 1H), 7.24 - 7.01 (m, 1H), 5.47 - 5.26 (m, 1H), 4.46 - 4.31 (m, 2H), 4.21 - 4.06 (m, 2H), 2.10 - 1.31 (m, 10H), 0.96 - 0.83 (m, 1H). Method 1: RT = 2.99 min.; M+H = 412.1
20		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.60 (m, 1H), 8.16 – 8.08 (m, 1H), 7.63 (m, 1H), 7.38 – 7.30 (m, 1H), 7.06 (m, 1H), 5.44 - 5.29 (m, 1H), 4.46 – 4.31 (m, 2H), 4.20 – 4.06 (m, 2H), 2.61 – 2.51 (m, 1H), 2.46 (m, 1H), 2.41 – 2.31 (m, 1H), 2.32 – 2.20 (m, 1H), 2.20 – 2.05 (m, 1H), 2.05 – 1.91 (m, 1H), 1.84 – 1.57 (m, 1H). Method 1: RT = 2.92 min.; M+H = 384.1
21		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.54 (m, 1H), 8.16 – 8.10 (m, 1H), 8.07 (m, 1H), 7.68 – 7.61 (m, 1H), 7.39 – 7.32 (m, 1H), 5.44 - 5.30 (m, 1H), 4.39 (m, 2H), 4.14 (m, 2H), 2.70 (s, 2H), 0.99 (s, 9H). Method 1: RT = 2.62 min.; M+H = 400.2

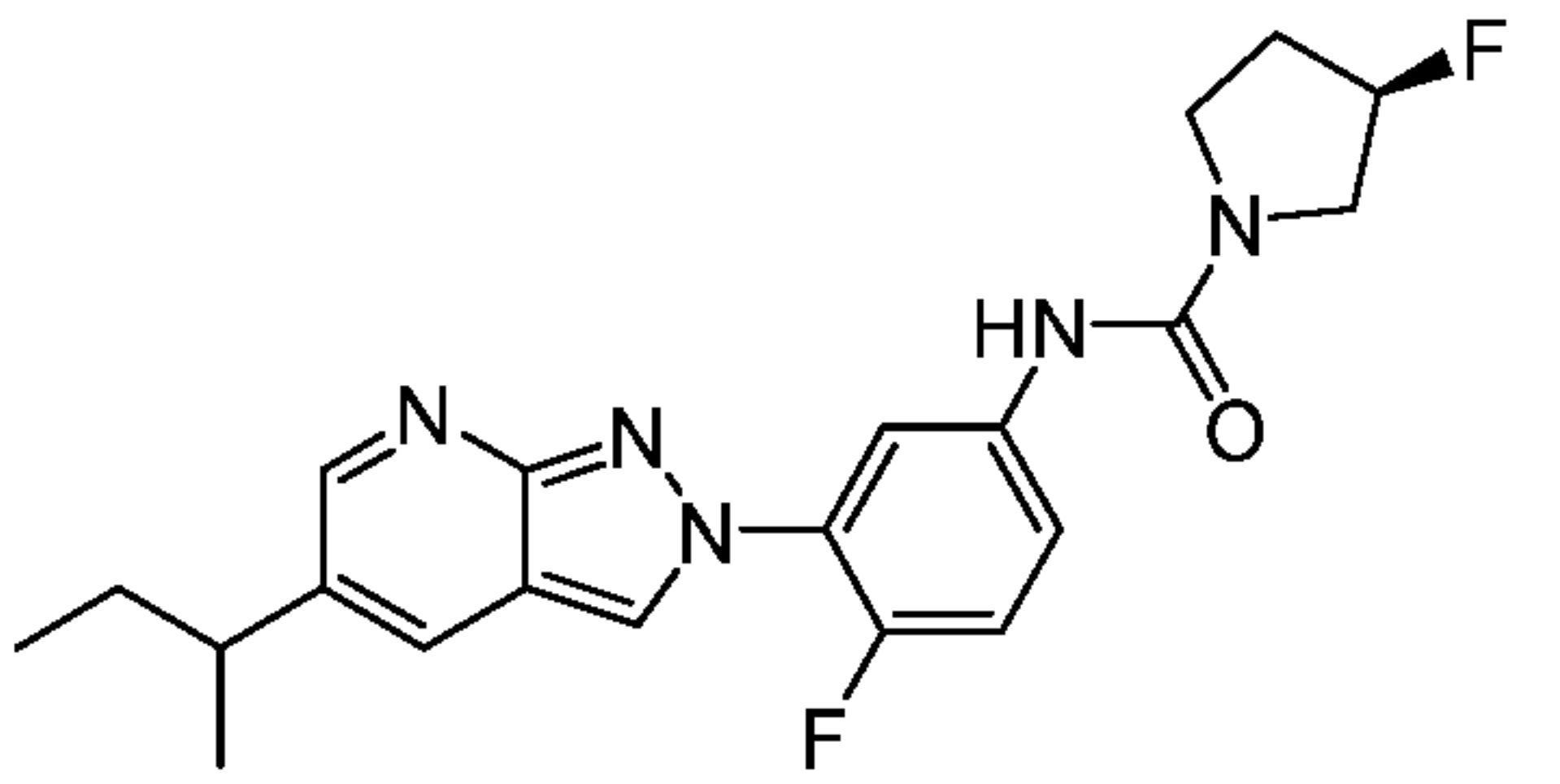
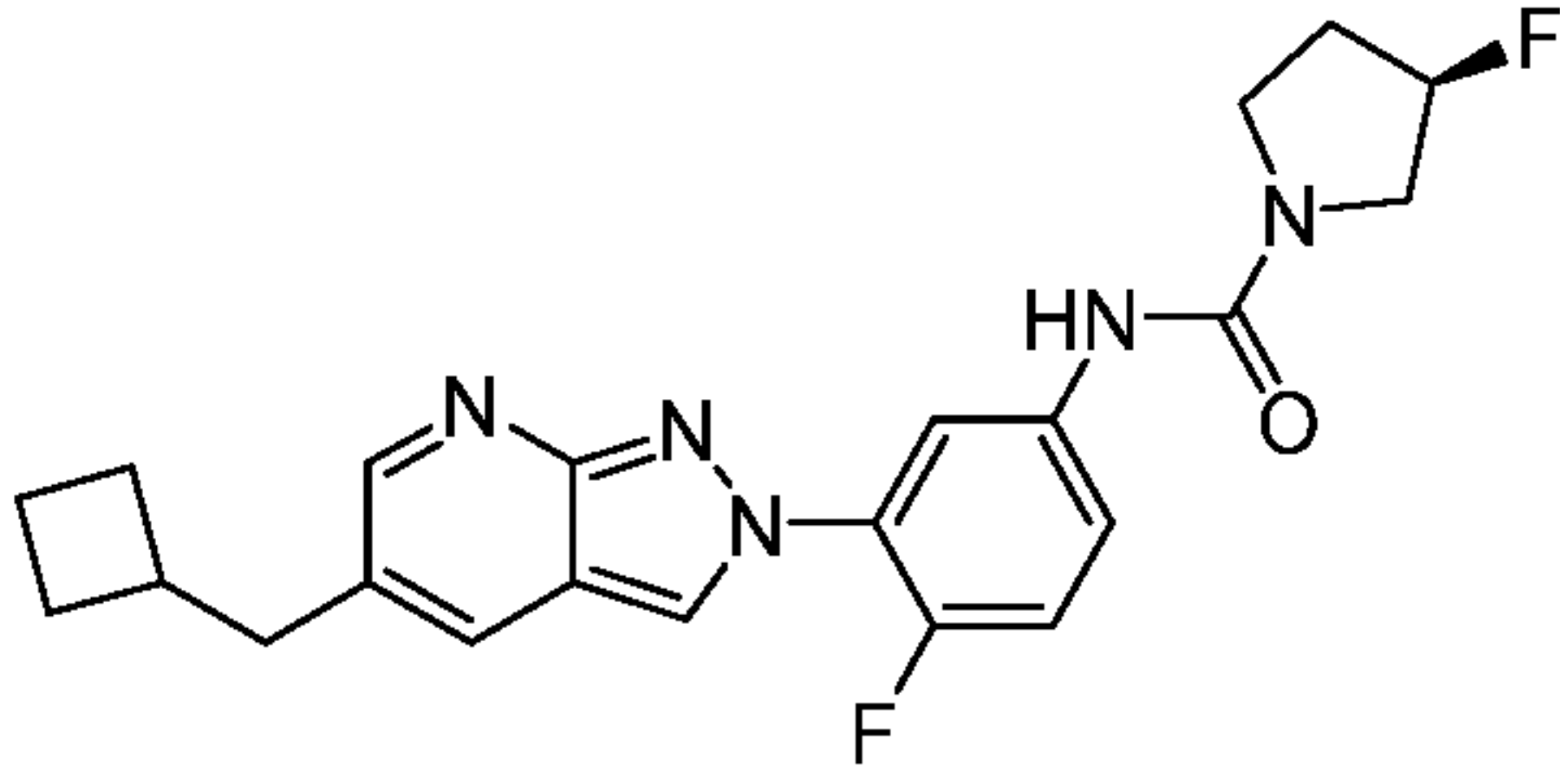
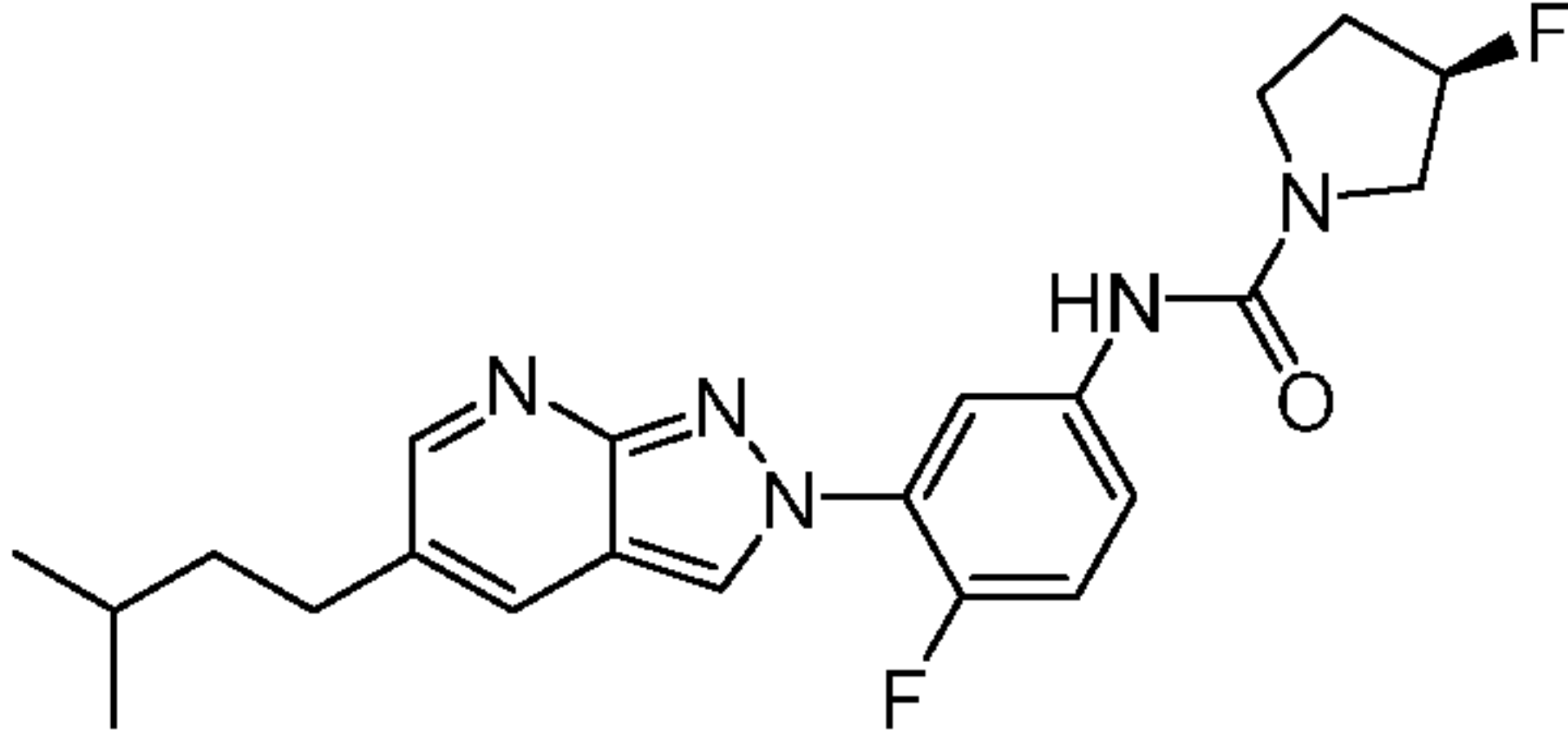
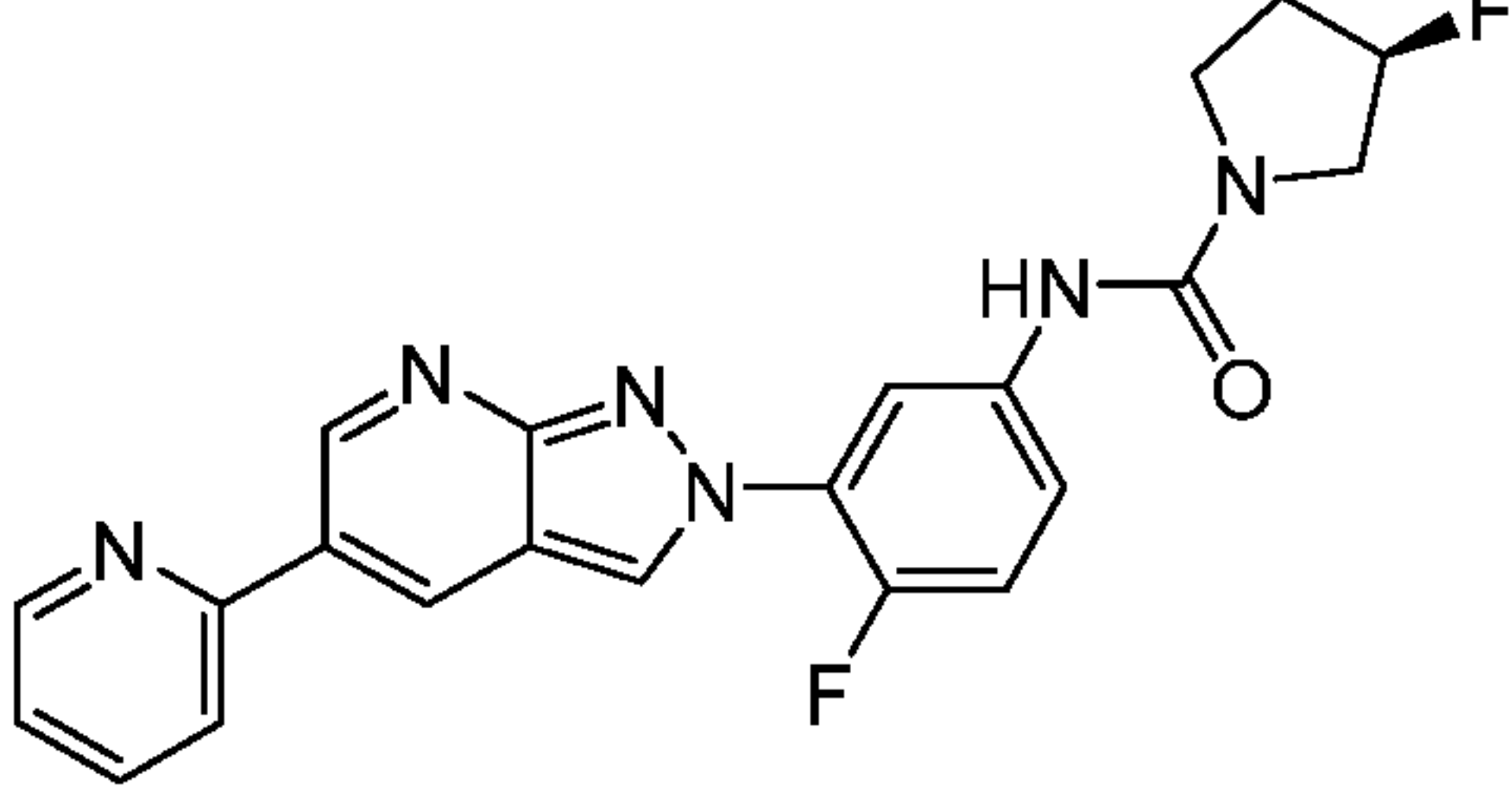
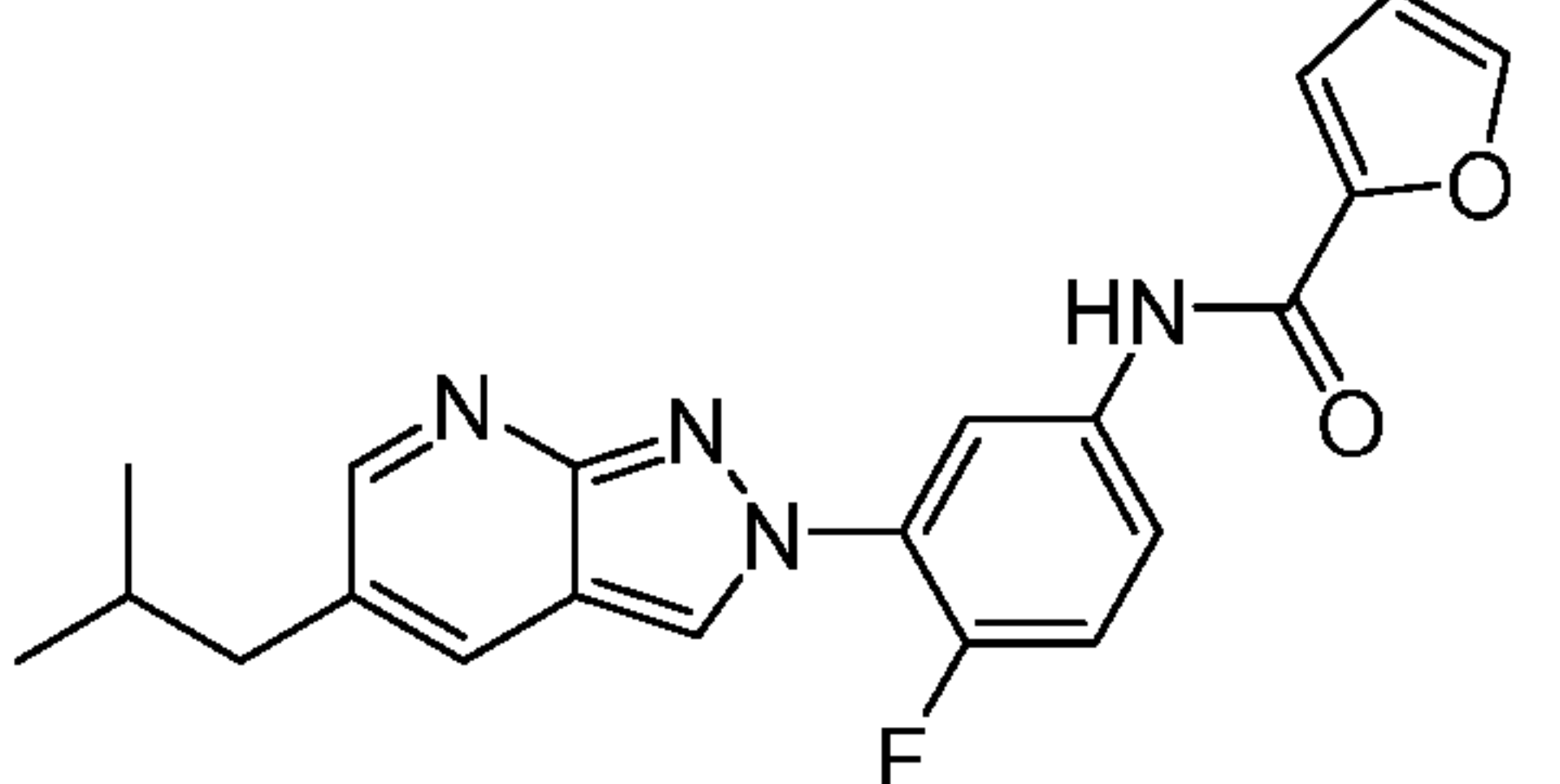
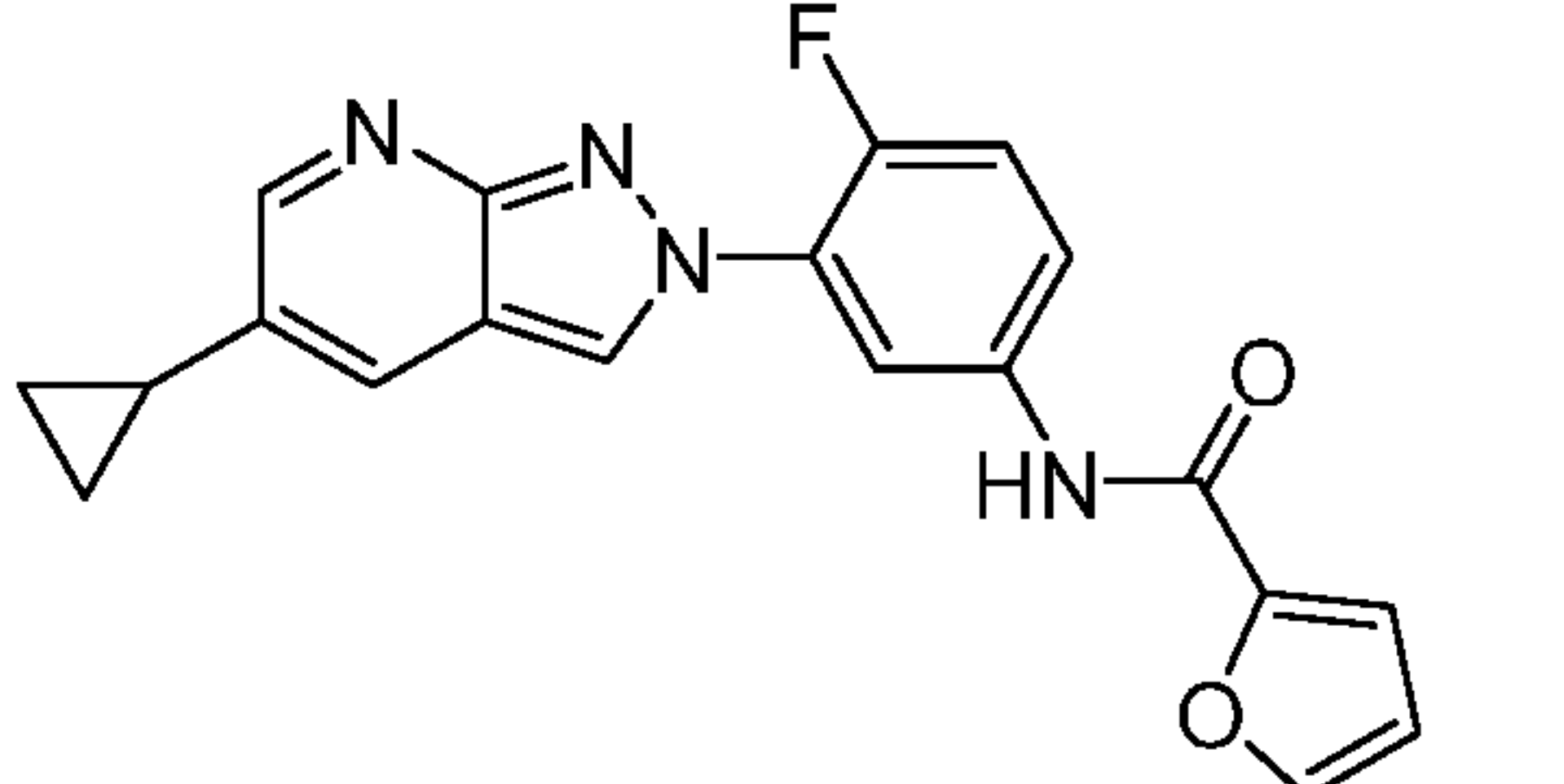
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
22		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 – 8.54 (m, 2H), 7.83 (m, 1H), 7.66 (m, 1H), 7.40 – 7.25 (m, 1H), 7.20 – 7.10 (m, 1H), 5.43 - 5.28 (m, 1H), 4.43 – 4.31 (m, 2H), 4.20 – 4.05 (m, 2H), 1.49 (s, 9H). Method 1: RT = 2.72 min.; M+H = 386.1
23		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.76 – 8.57 (m, 2H), 8.16 – 8.06 (m, 1H), 7.65 (m, 1H), 7.44 – 7.31 (m, 2H), 5.44 - 5.30 (m, 1H), 4.44 – 4.34 (m, 2H), 4.21 – 4.08 (m, 2H), 2.85 – 2.72 (m, 1H), 1.87 – 1.57 (m, 3H), 1.46 – 1.33 (m, 3H), 0.98 – 0.67 (m, 4H). Method 1: RT = 3.13 min.; M+H = 400.1
24		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.55 (m, 1H), 8.45 (m, 1H), 7.73 (m, 1H), 7.56 (m, 1H), 7.19 (m, 1H), 7.07 (m, 1H), 5.33 - 5.18 (m, 1H), 4.33 - 4.21 (m, 2H), 4.10 - 3.96 (m, 2H), 1.90 - 1.67 (m, 2H), 1.39 (s, 3H), 1.27 (s, 3H), 0.66 (t, J = 7.4 Hz, 3H). Method 1: RT = 2.89 min.; M+H = 400.1
25		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.74 - 8.63 (m, 1H), 8.62 - 8.52 (m, 1H), 8.16 - 8.05 (m, 1H), 7.73 - 7.59 (m, 1H), 7.40 - 7.29 (m, 1H), 7.08 (m, 1H), 5.44 - 5.26 (m, 1H), 4.39 (m, 2H), 4.20 - 4.06 (m, 2H), 1.90 - 1.61 (m, 2H), 1.52 - 1.30 (m, 3H), 1.03 - 0.81 (m, 3H), 0.77 (m, 1H). Method 1: RT = 2.78 min.; M+H = 386.1
26		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.58 (m, 1H), 8.16 – 8.08 (m, 1H), 8.05 (m, 1H), 7.64 (m, 1H), 7.38 – 7.31 (m, 1H), 5.44 - 5.30 (m, 1H), 4.39 (m, 2H), 4.14 (m, 2H), 2.87 (m, 1H), 2.68 (m, 1H), 2.19 – 2.04 (m, 2H), 1.98 – 1.66 (m, 4H), 0.91 (m, 1H). Method 1: RT = 3.10 min.; M+H = 398.1
27		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.57 (m, 1H), 8.13 (m, 1H), 8.11 - 8.05 (m, 1H), 7.65 (m, 1H), 7.39 - 7.31 (m, 1H), 5.44 - 5.30 (m, 1H), 4.39 (m, 2H), 4.14 (m, 2H), 2.87 - 2.76 (m, 2H), 1.69 - 1.57 (m, 2H), 1.04 - 0.85 (m, 6H), 0.76 (m, 1H). Method 1: RT = 3.18 min.; M+H = 400.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
28		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.37 (m, 1H), 8.86 (m, 2H), 8.70 (m, 1H), 8.19 (m, 1H), 8.04 - 7.92 (m, 2H), 7.66 (m, 1H), 7.45 - 7.31 (m, 2H), 5.45 - 5.30 (m, 1H), 4.46 - 4.34 (m, 2H), 4.21 - 4.08 (m, 2H). Method 1: RT = 2.67 min.; M+H = 407.1
29		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.53 (m, 1H), 8.49 (m, 1H), 8.04 (m, 1H), 7.85 - 7.79 (m, 1H), 7.54 (m, 1H), 7.29 - 7.22 (m, 1H), 4.32 (t, <i>J</i> = 12.3 Hz, 4H), 2.07 - 1.95 (m, 1H), 0.98 (m, 2H), 0.71 (m, 2H). Method 2: RT = 1.10 min.; M+H = 388.1
30		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 - 8.62 (m, 1H), 8.25 - 8.12 (m, 1H), 7.94 (m, 1H), 7.73 - 7.60 (m, 1H), 7.45 - 7.29 (m, 2H), 4.44 (m, 4H), 2.19 (m, 1H), 1.97 - 1.49 (m, 6H), 0.90 (m, 2H). Method 2: RT = 1.09 min.; M+H = 416.1
31		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.59 (m, 1H), 8.50 (m, 1H), 8.05 (m, 1H), 8.02 (m, 1H), 7.55 (m, 1H), 7.29 - 7.23 (m, 1H), 4.32 (t, <i>J</i> = 12.3 Hz, 4H), 2.37 (m, 2H), 2.27 - 1.98 (m, 4H), 1.91 - 1.83 (m, 1H). Method 1: RT = 3.16 min.; M+H = 402.1
32		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.54 (m, 1H), 8.16 (m, 1H), 8.07 (m, 1H), 7.66 (m, 1H), 7.41 - 7.34 (m, 1H), 4.43 (t, <i>J</i> = 12.3 Hz, 4H), 2.69 (s, 2H), 0.99 (s, 9H). Method 2: RT = 1.27 min.; M+H = 418.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
33		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.64 (m, 1H), 8.61 – 8.55 (m, 1H), 7.84 (m, 1H), 7.71 – 7.64 (m, 1H), 7.37 – 7.28 (m, 1H), 7.17 (m, 1H), 4.42 (m, 4H), 1.52 (m, 9H). Method 2: RT = 1.04 min.; M+H = 404.1
34		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.68 (m, 1H), 8.63 – 8.57 (m, 1H), 8.15 (m, 1H), 7.98 – 7.91 (m, 1H), 7.69 – 7.62 (m, 1H), 7.39 – 7.32 (m, 1H), 4.42 (m, 4H), 1.53 – 1.33 (m, 5H), 1.00 – 0.72 (m, 6H). Method 2: RT = 1.14 min.; M+H = 418.1
35		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.65 (m, 1H), 8.55 (m, 1H), 7.84 (m, 1H), 7.67 (m, 1H), 7.40 – 7.31 (m, 1H), 7.17 (m, 1H), 4.42 (m, 4H), 1.93 – 1.79 (m, 2H), 1.50 (m, 3H), 1.37 (m, 3H), 0.81 – 0.66 (m, 3H). Method 2: RT = 1.10 min.; M+H = 418.1
36		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.68 (m, 1H), 8.46 (m, 1H), 8.14 (m, 1H), 7.70 – 7.63 (m, 1H), 7.39 – 7.33 (m, 1H), 7.18 (m, 1H), 4.43 (m, 4H), 1.91 – 1.79 (m, 2H), 1.54 – 1.36 (m, 4H), 0.92 (m, 3H). Method 2: RT = 1.14 min.; M+H = 404.1
37		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.59 – 8.54 (m, 1H), 8.45 (m, 1H), 8.07 – 8.00 (m, 1H), 7.96 – 7.92 (m, 1H), 7.55 (m, 1H), 7.29 – 7.23 (m, 1H), 4.32 (t, <i>J</i> = 12.3 Hz, 4H), 2.76 (m, 2H), 2.63 – 2.51 (m, 1H), 2.04 – 1.93 (m, 2H), 1.87 – 1.64 (m, 4H). Method 1: RT = 3.26 min.; M+H = 416.1

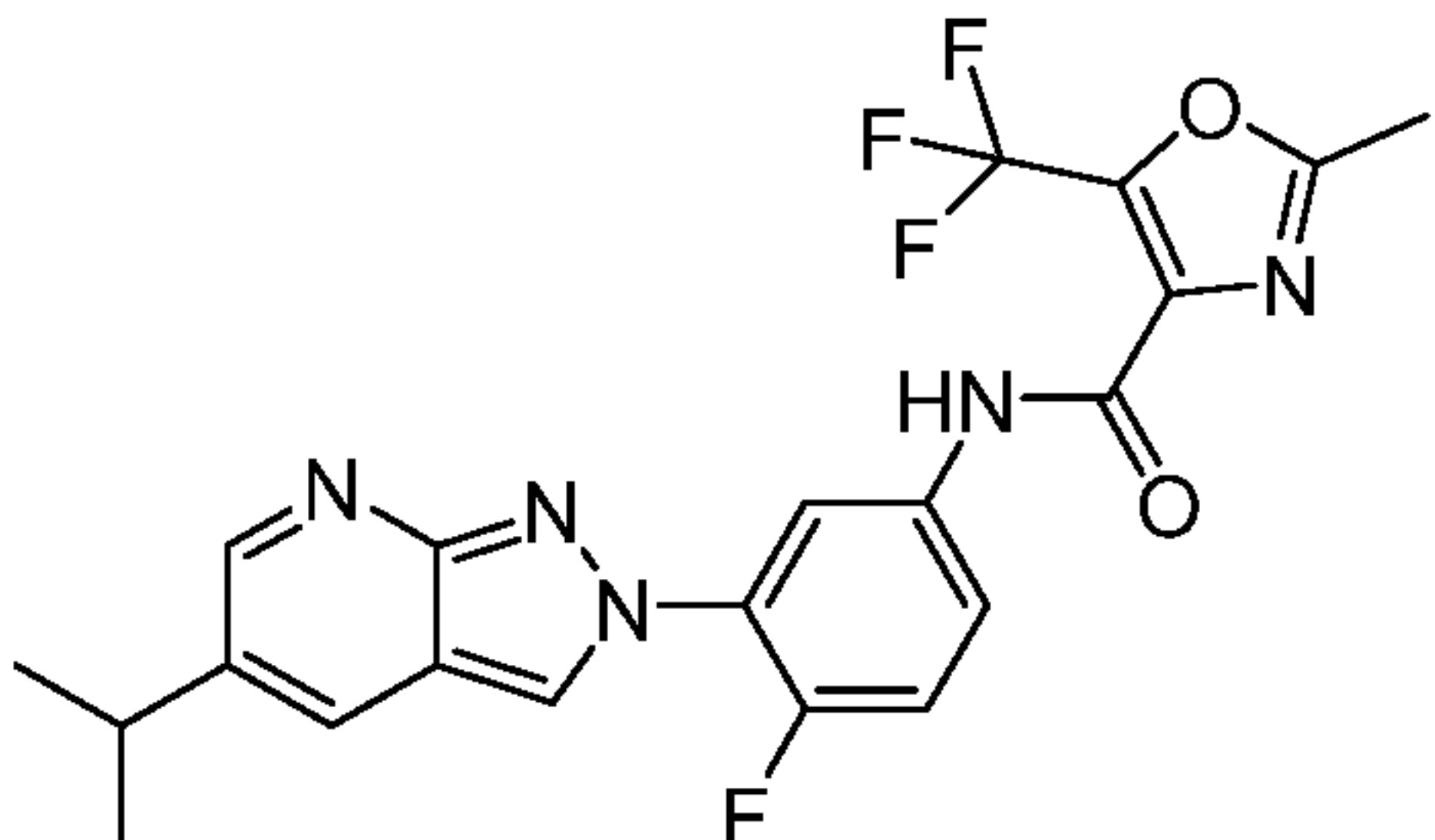
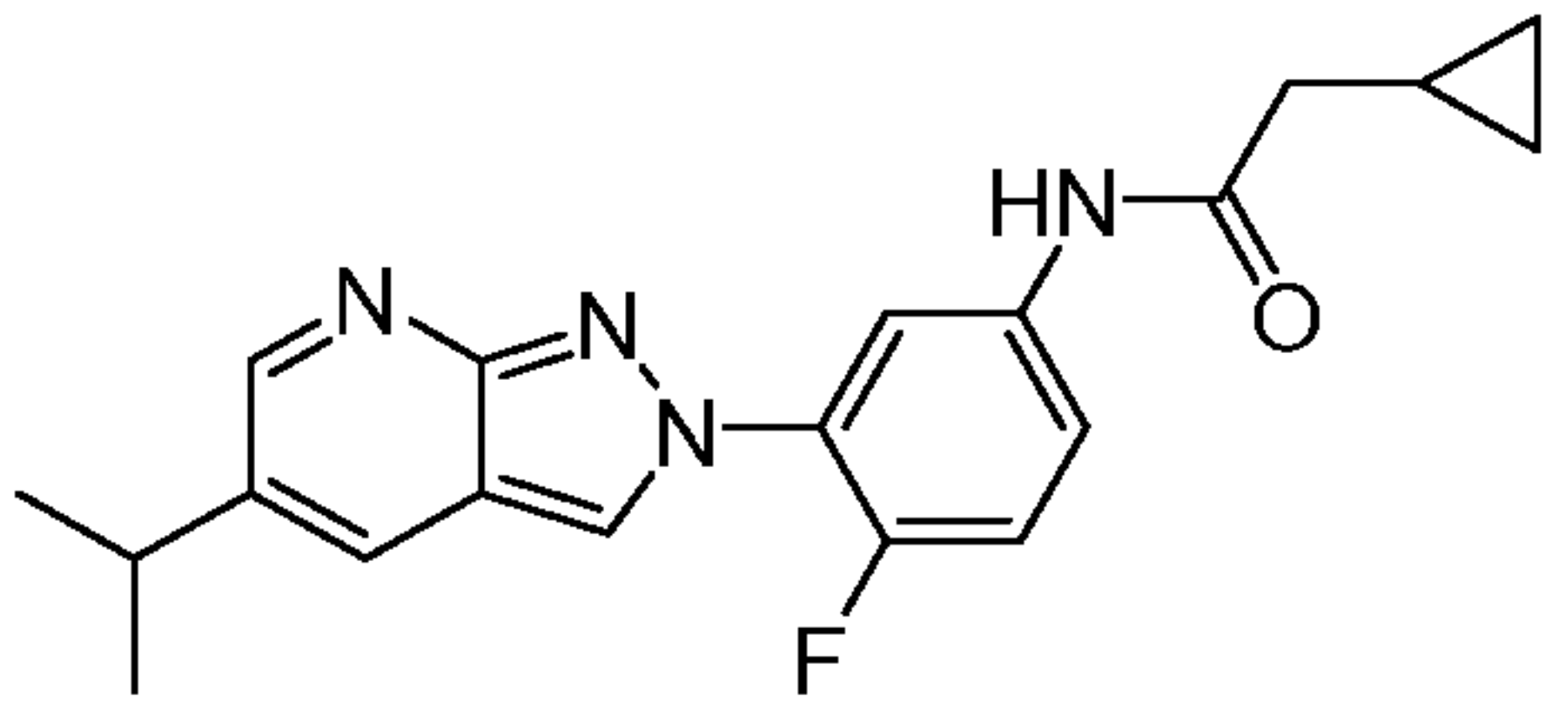
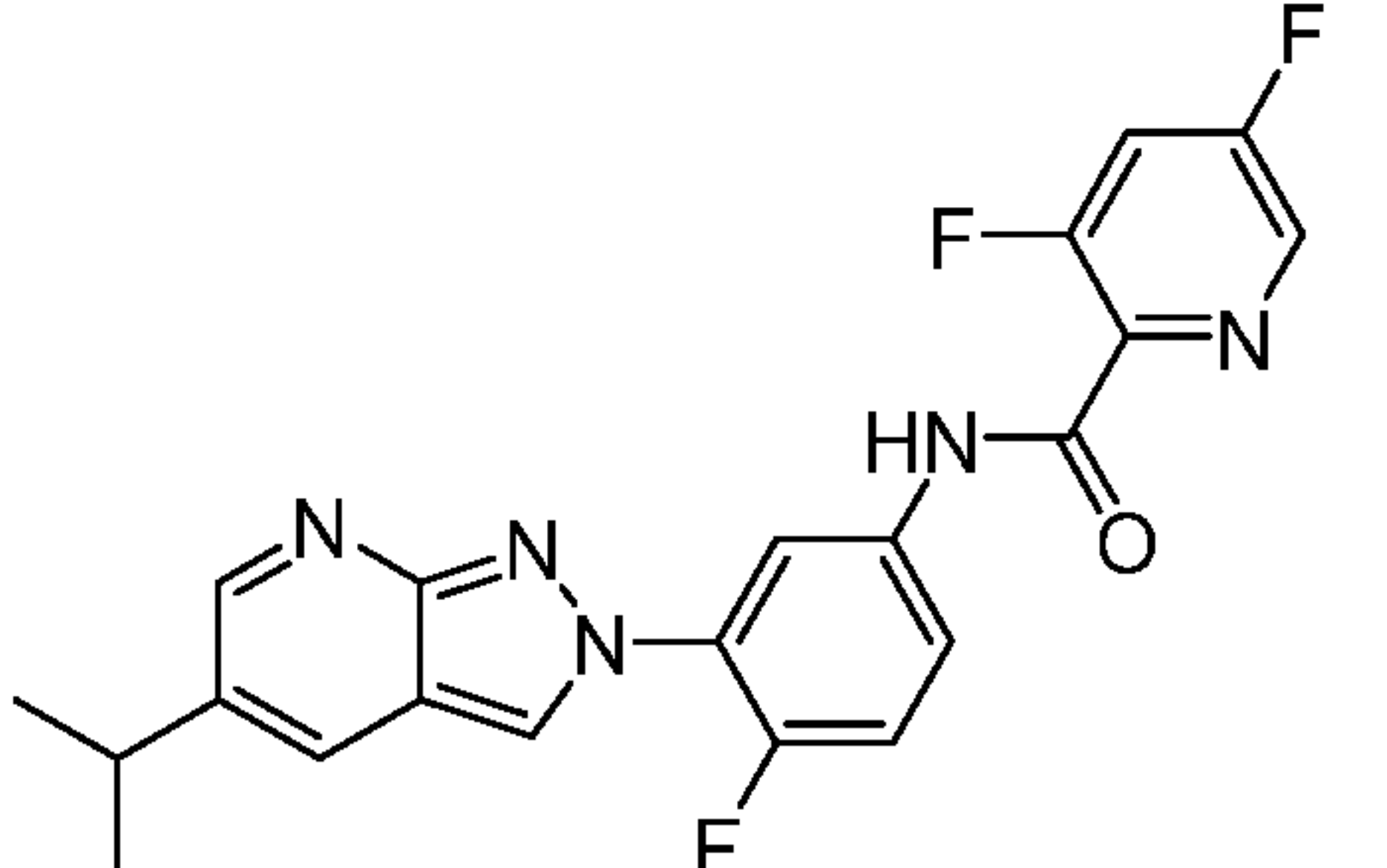
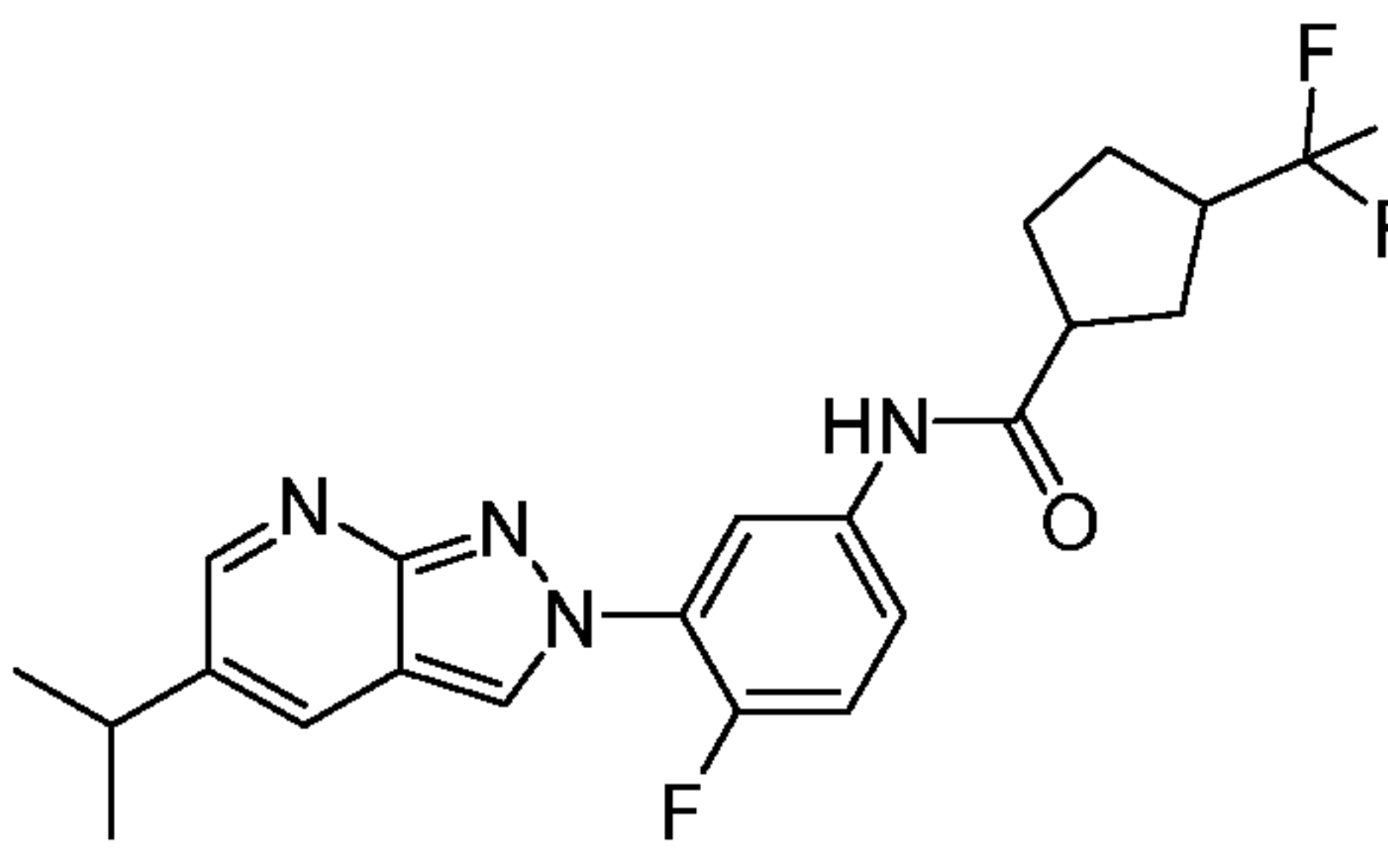
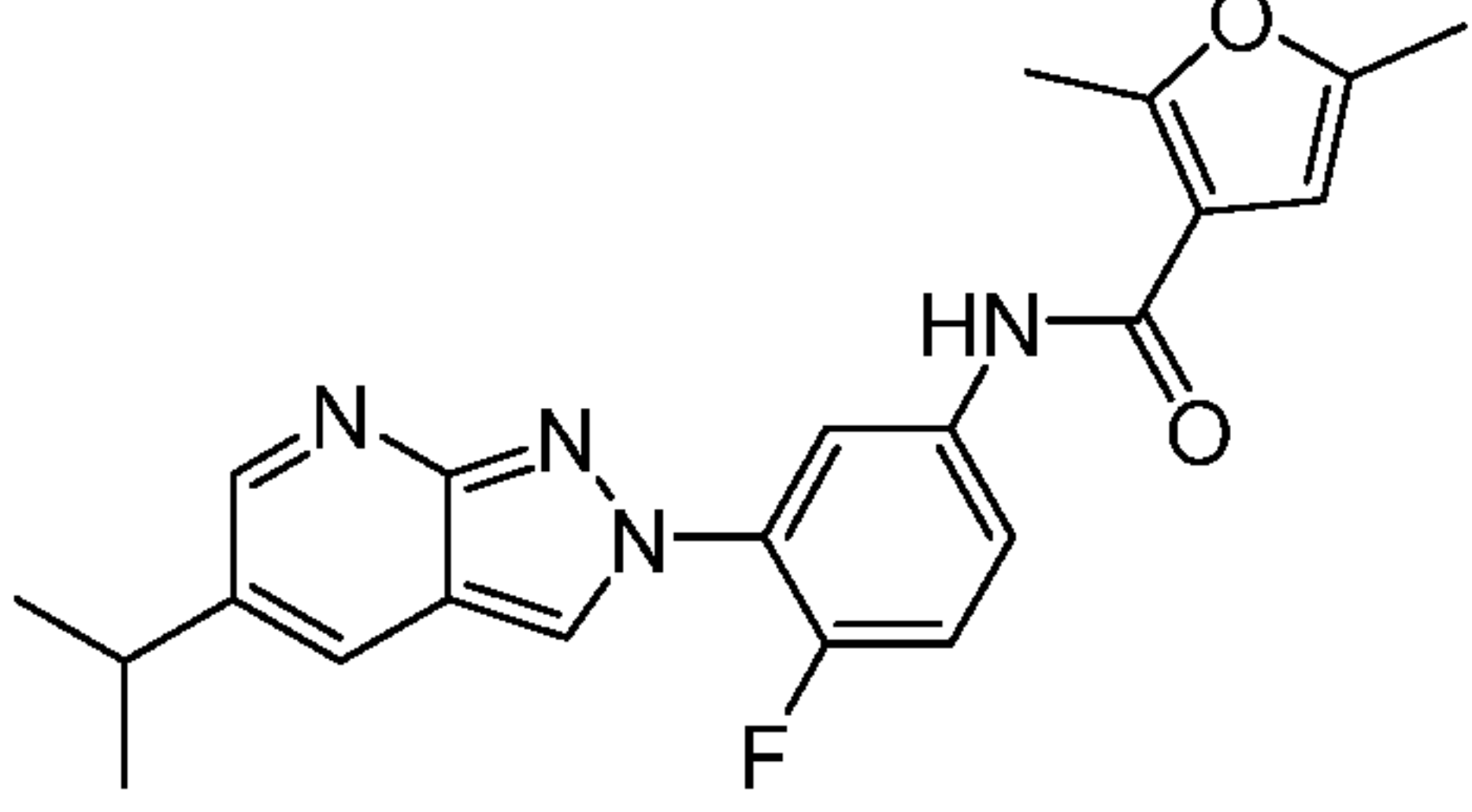
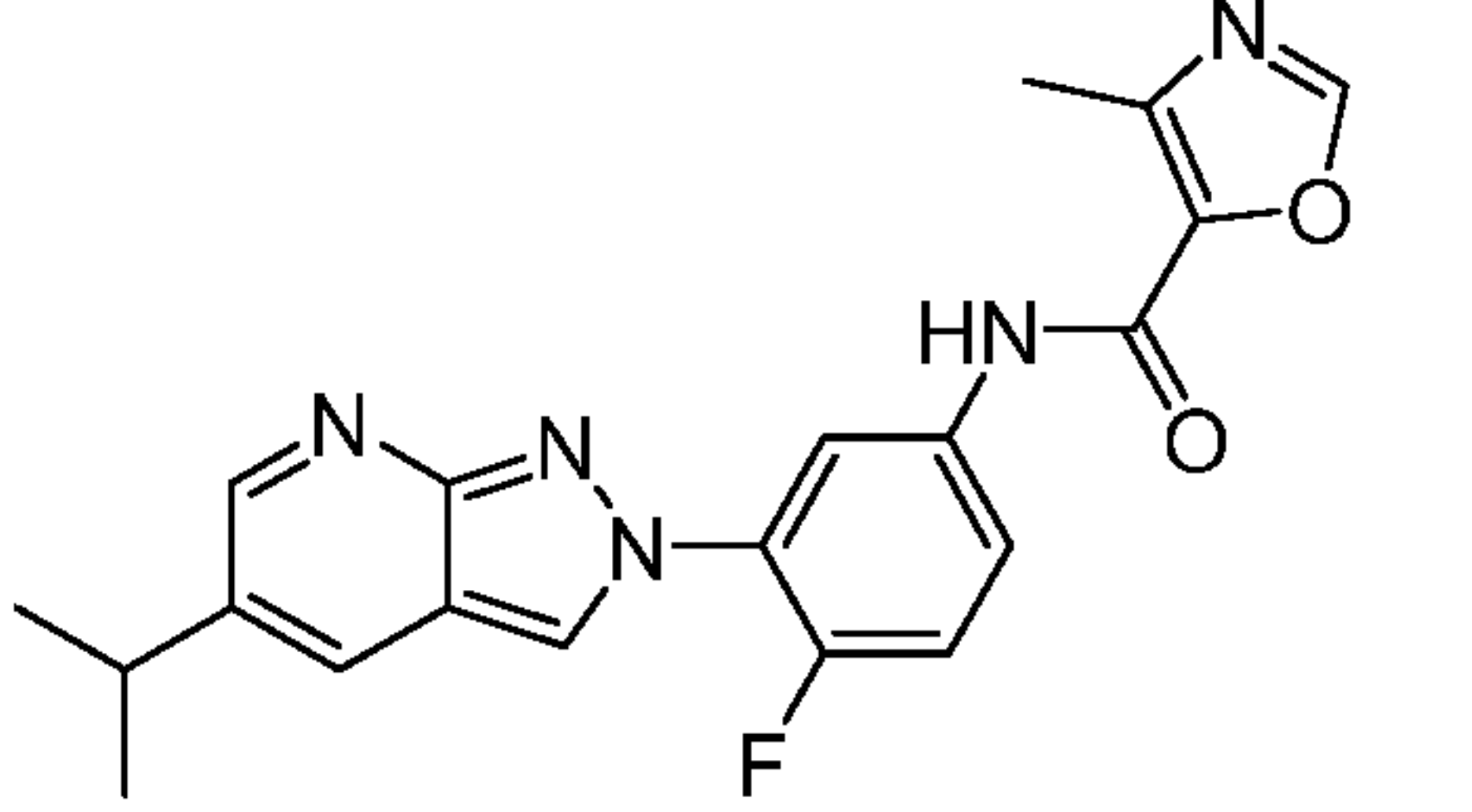
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
38		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.58 (m, 1H), 8.16 (m, 1H), 8.10 – 8.04 (m, 1H), 7.69 – 7.62 (m, 1H), 7.40 – 7.33 (m, 1H), 4.43 (t, <i>J</i> = 12.3 Hz, 4H), 2.89 – 2.78 (m, 2H), 1.72 – 1.53 (m, 3H), 1.04 – 0.86 (m, 6H). Method 2: RT = 1.30 min.; M+H = 418.1
39		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.36 (d, <i>J</i> = 2.3 Hz, 1H), 9.00 – 8.93 (m, 2H), 8.79 – 8.75 (m, 1H), 8.26 (dd, <i>J</i> = 6.8, 2.7 Hz, 1H), 8.19 – 8.14 (m, 2H), 7.70 – 7.64 (m, 1H), 7.64 – 7.56 (m, 1H), 7.46 – 7.35 (m, 1H), 4.44 (td, <i>J</i> = 12.3, 3.0 Hz, 4H). Method 2: RT = 0.99 min.; M+H = 425.0
40		¹ H NMR (400 MHz, DMSO) δ 8.70 (s, 1 H), 8.56 (d, <i>J</i> = 2.76 Hz, 1 H), 8.31 (d, <i>J</i> = 2.76 Hz, 1 H), 8.21 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.59 - 7.72 (m, 1 H), 7.41 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.01 (d, <i>J</i> = 2.76 Hz, 1 H), 5.39 - 5.66 (m, 1 H), 4.20 - 4.36 (m, 2 H), 3.89 - 4.09 (m, 6 H), 2.12 - 2.28 (m, 2 H). Method 1: RT = 2.66 min. M+H = 385.3
41		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.68 (m, 1H), 8.56 (m, 1H), 8.12 (m, 1H), 8.07 (m, 1H), 7.65 (m, 1H), 7.36 (m, 1H), 5.40 - 5.27 (m, 1H), 3.85 - 3.68 (m, 2H), 3.59 (m, 2H), 2.67 (m, 2H), 2.28 (m, 2H), 1.97 (m, 1H), 0.99 (d, <i>J</i> = 6.6 Hz, 6H). M+H = 400.3
42		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.63 (m, 1H), 8.59 (m, 1H), 8.11 (m, 1H), 7.92 (m, 1H), 7.63 (m, 1H), 7.34 (m, 1H), 5.40 - 5.26 (m, 1H), 3.80 - 3.67 (m, 2H), 3.59 (m, 2H), 2.37 - 2.18 (m, 2H), 2.12 (m, 1H), 1.08 (m, 2H), 0.85 - 0.79 (m, 2H). Method 2: RT = 1.03 min.; M+H = 384.3
43		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.77 – 8.54 (m, 2H), 8.27 – 8.07 (m, 2H), 7.64 (m, 1H), 7.36 (m, 1H), 5.40 – 5.23 (m, 1H), 3.87 – 3.51 (m, 4H), 3.20 (m, 1H), 2.46 – 1.96 (m, 5H), 1.98 – 1.56 (m, 5H). Method 2: RT = 1.04 min.; M+H = 412.3

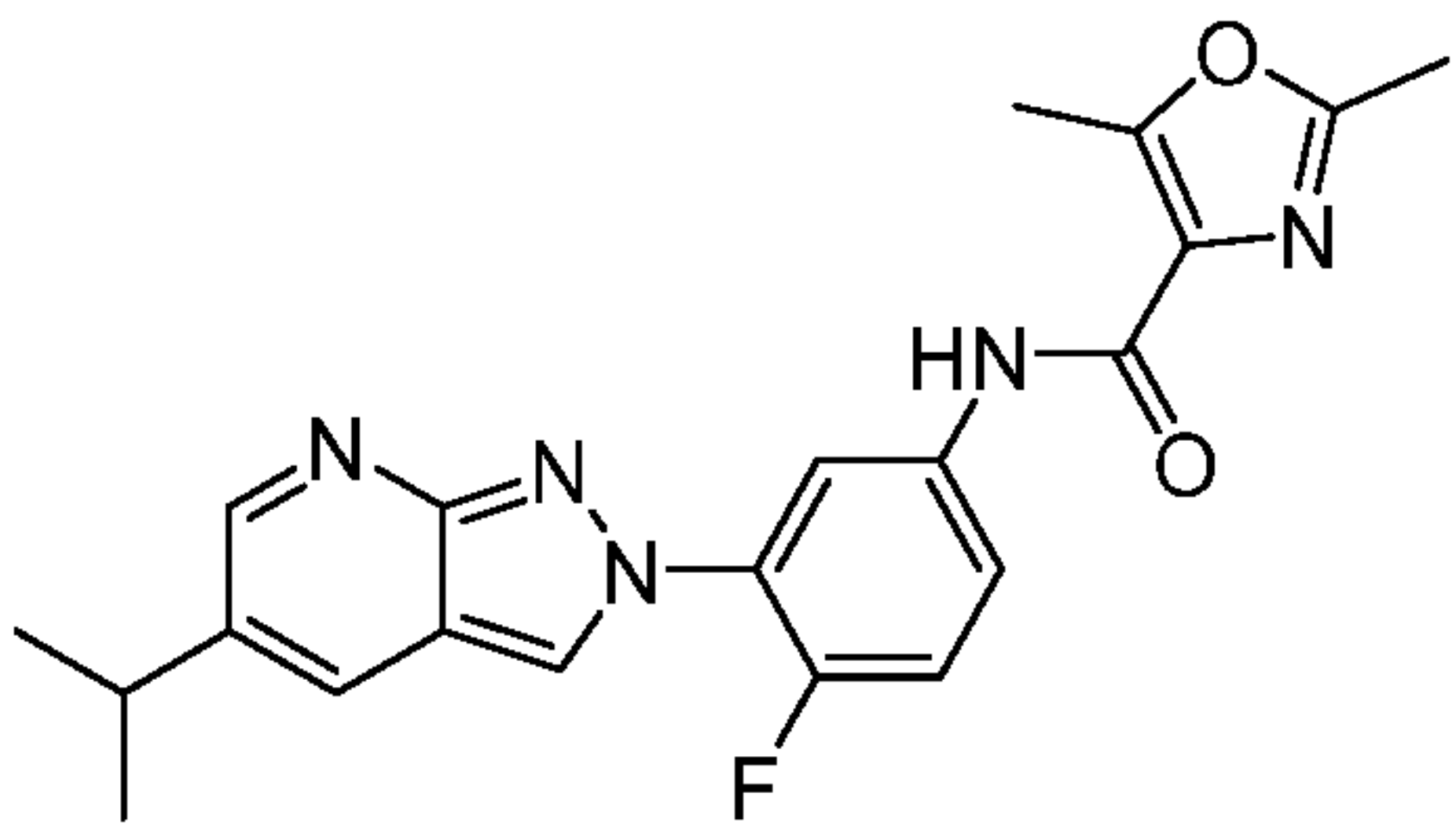
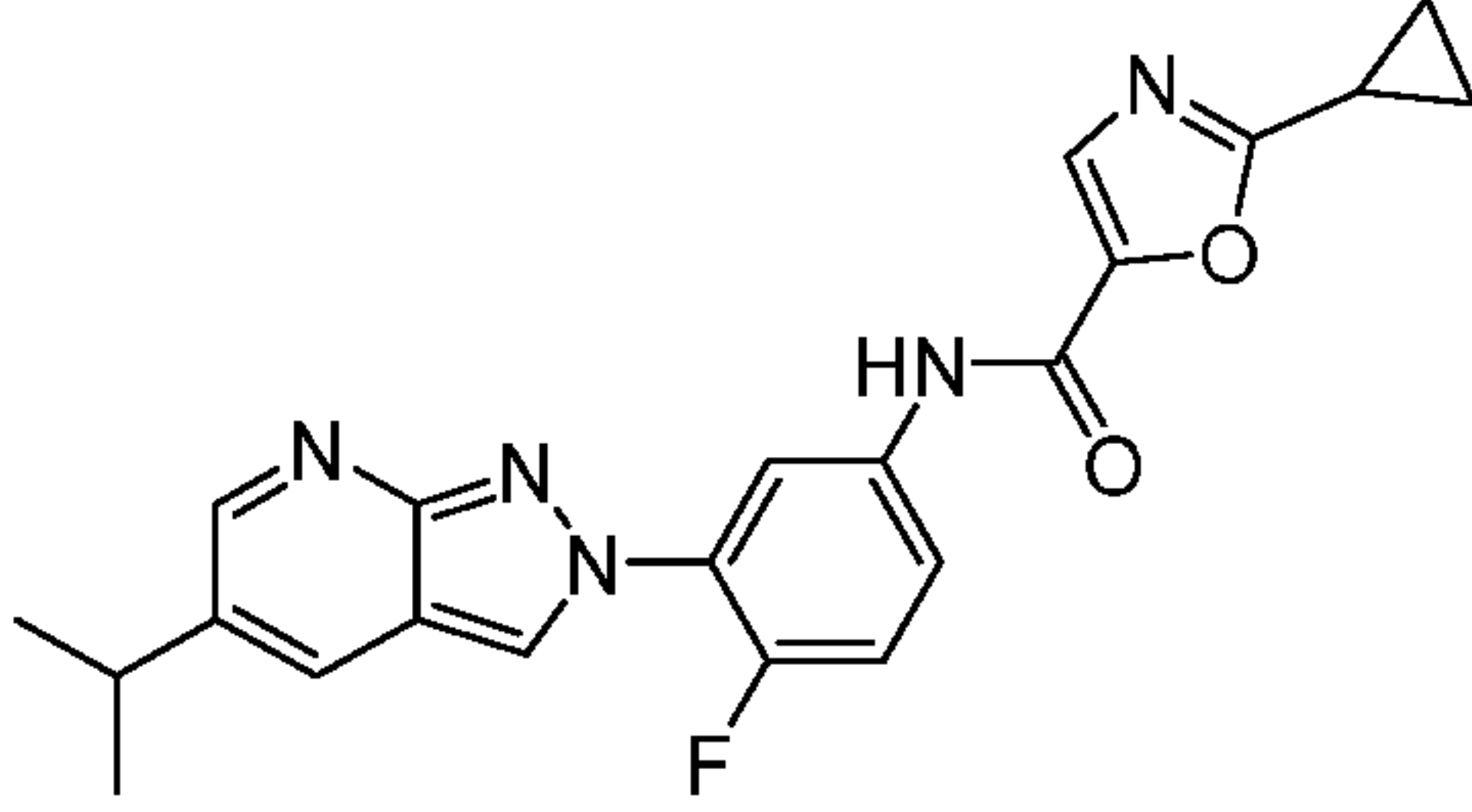
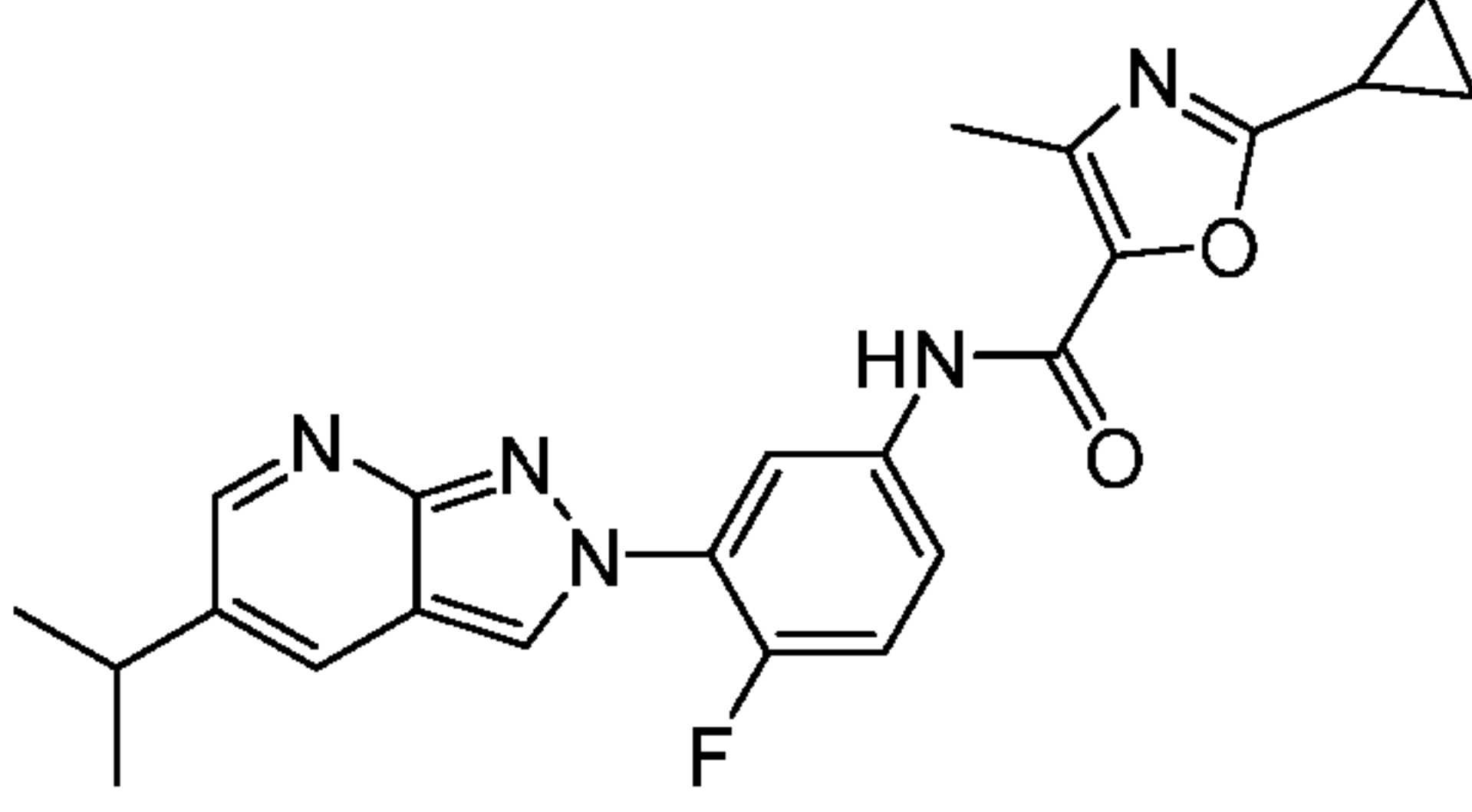
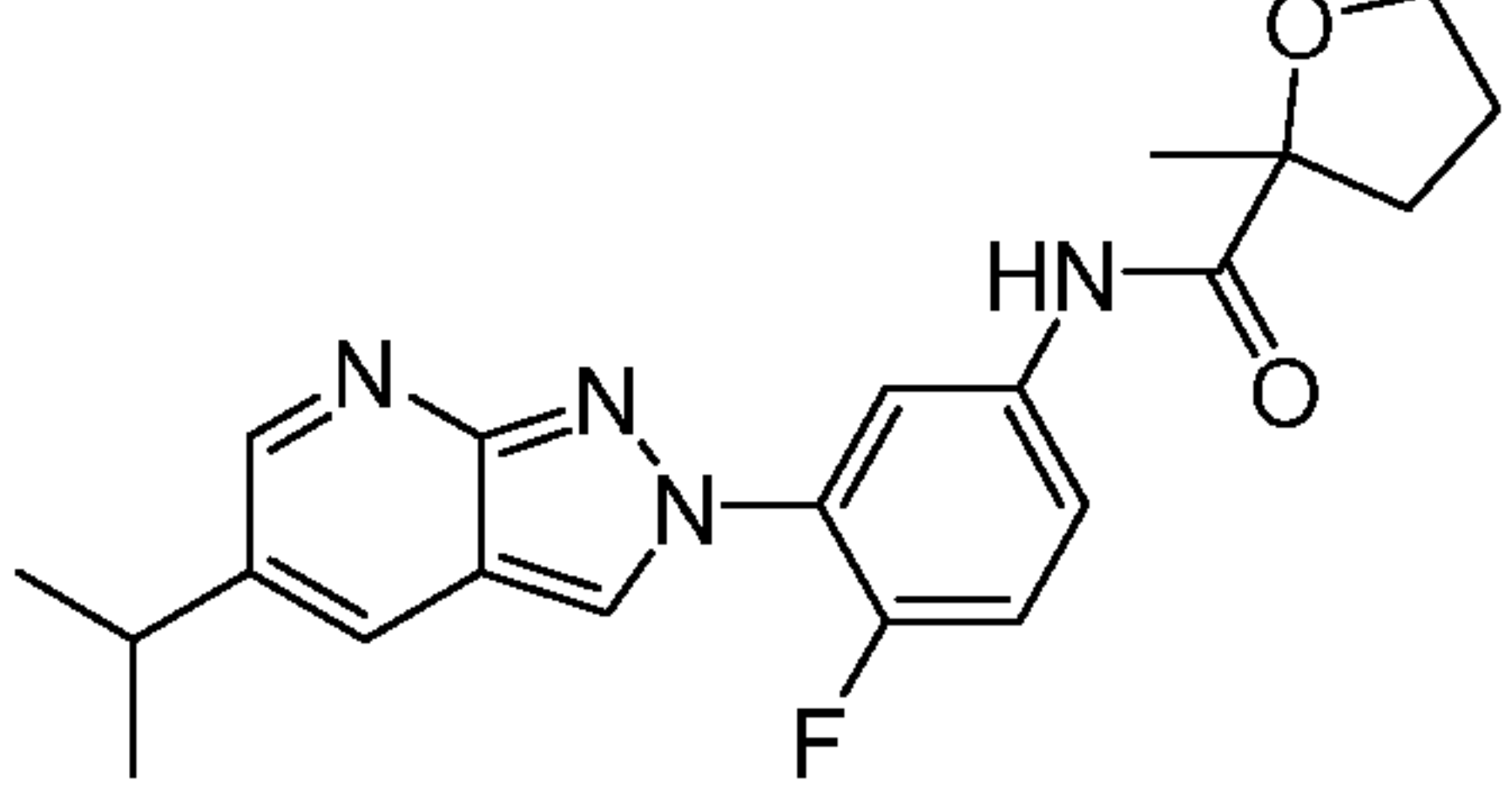
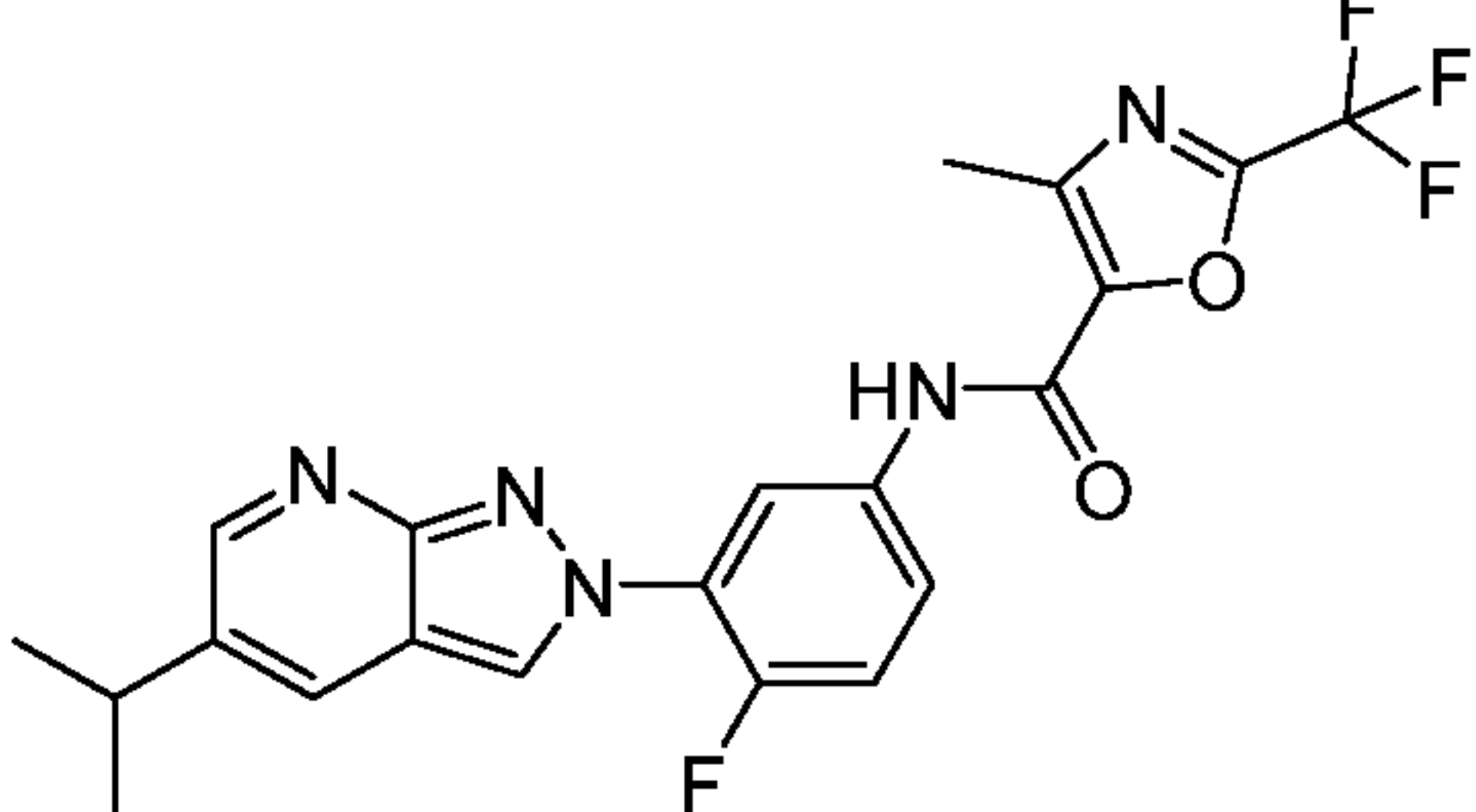
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
44		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.65 – 8.57 (m, 1H), 8.26 – 8.08 (m, 2H), 7.64 (m, 1H), 7.35 (m, 1H), 5.40 - 5.26 (m, 1H), 3.84 – 3.54 (m, 4H), 2.79 – 2.68 (m, 1H), 2.39 – 1.92 (m, 6H), 1.82 (m, 1H), 1.66 – 1.19 (m, 5H). Method 2: RT = 1.26 min.; M+H = 426.4
45		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.77 (m, 1H), 8.69 (m, 1H), 8.61 (m, 1H), 8.17 – 8.09 (m, 1H), 7.63 (m, 1H), 7.40 – 7.32 (m, 1H), 5.42 - 5.25 (m, 1H), 3.82 – 3.53 (m, 4H), 2.63 – 2.07 (m, 6H), 1.90 – 1.89 (m, 3H). Method 1: RT = 2.93 min.; M+H = 398.3
46		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.54 (m, 1H), 8.12 (m, 1H), 8.07 (m, 1H), 7.64 (m, 1H), 7.35 (m, 1H), 5.39 - 5.26 (m, 1H), 3.82 – 3.70 (m, 2H), 3.59 (m, 2H), 2.69 (s, 2H), 2.33 – 2.09 (m, 2H), 0.99 (s, 9H). Method 2: RT = 1.21 min.; M+H = 414.4
47		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 – 8.62 (m, 1H), 8.58 (m, 1H), 7.81 (m, 1H), 7.69 (m, 1H), 7.30 (m, 1H), 7.17 (m, 1H), 5.38 – 5.23 (m, 1H), 3.78 – 3.66 (m, 2H), 3.57 (m, 2H), 2.35 – 2.11 (m, 2H), 1.71 – 1.22 (m, 9H). Method 2: RT = 0.98 min.; M+H = 400.3
48		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 – 8.65 (m, 1H), 8.47 (m, 1H), 8.18 – 8.08 (m, 1H), 7.74 – 7.60 (m, 1H), 7.43 – 7.33 (m, 1H), 7.26 – 7.14 (m, 1H), 5.39 - 5.26 (m, 1H), 3.83 – 3.53 (m, 4H), 3.16 – 3.01 (m, 1H), 2.85 – 2.72 (m, 1H), 2.40 – 2.05 (m, 4H), 1.54 – 1.15 (m, 4H), 1.03 – 0.88 (m, 2H), 0.84 – 0.74 (m, 1H). Method 2: RT = 1.08 min.; M+H = 414.4
49		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.65 (m, 1H), 8.56 (m, 1H), 7.82 (m, 1H), 7.69 (m, 1H), 7.30 (m, 1H), 7.19 (m, 1H), 5.40 - 5.26 (m, 1H), 3.81 – 3.69 (m, 2H), 3.58 (m, 2H), 2.35 – 2.19 (m, 2H), 1.87 – 1.79 (m, 2H), 1.55 – 1.43 (s, 3H), 1.39 (s, 3H), 0.85 – 0.68 (m, 3H). Method 2: RT = 1.04 min.; M+H = 414.3

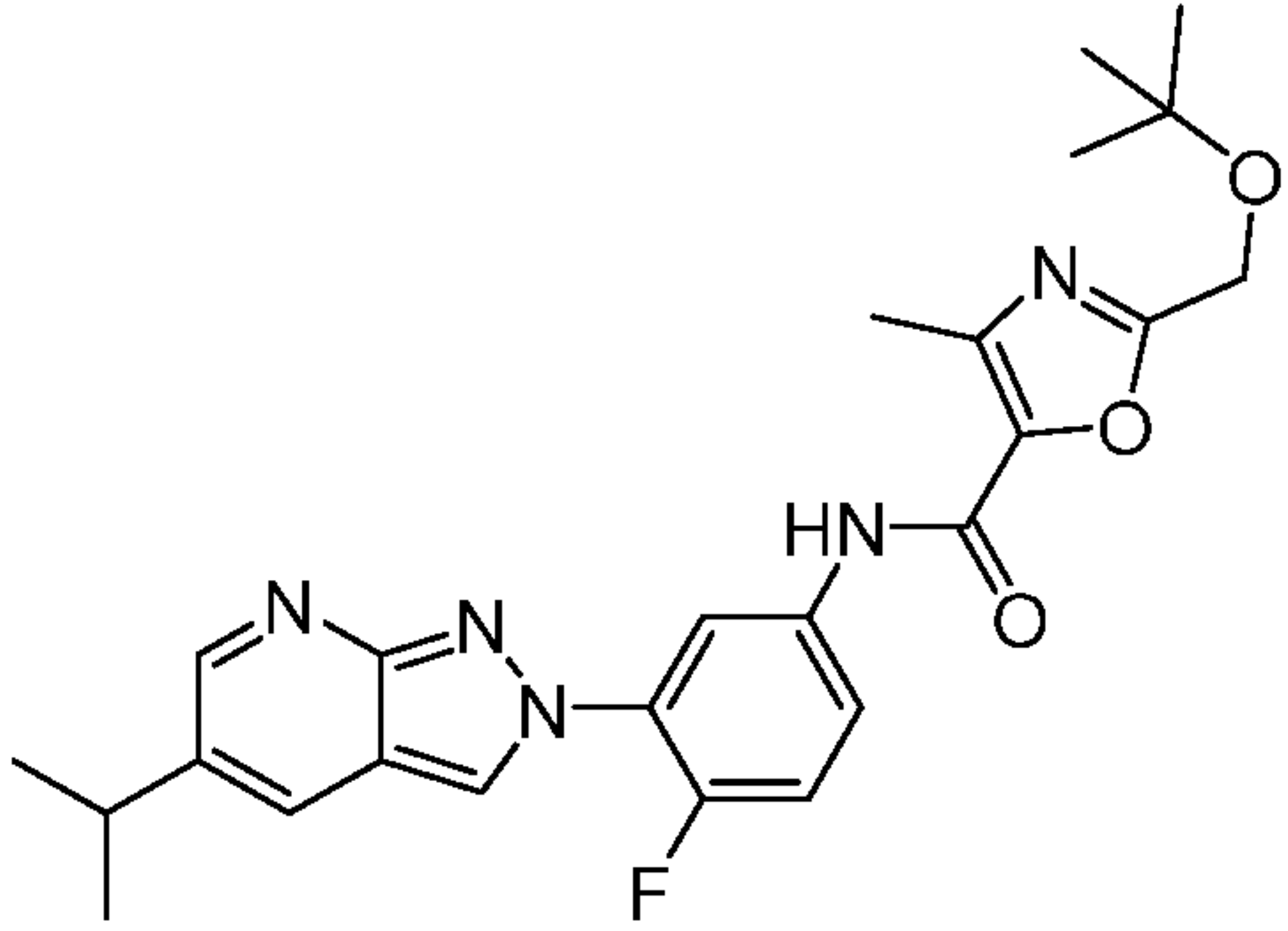
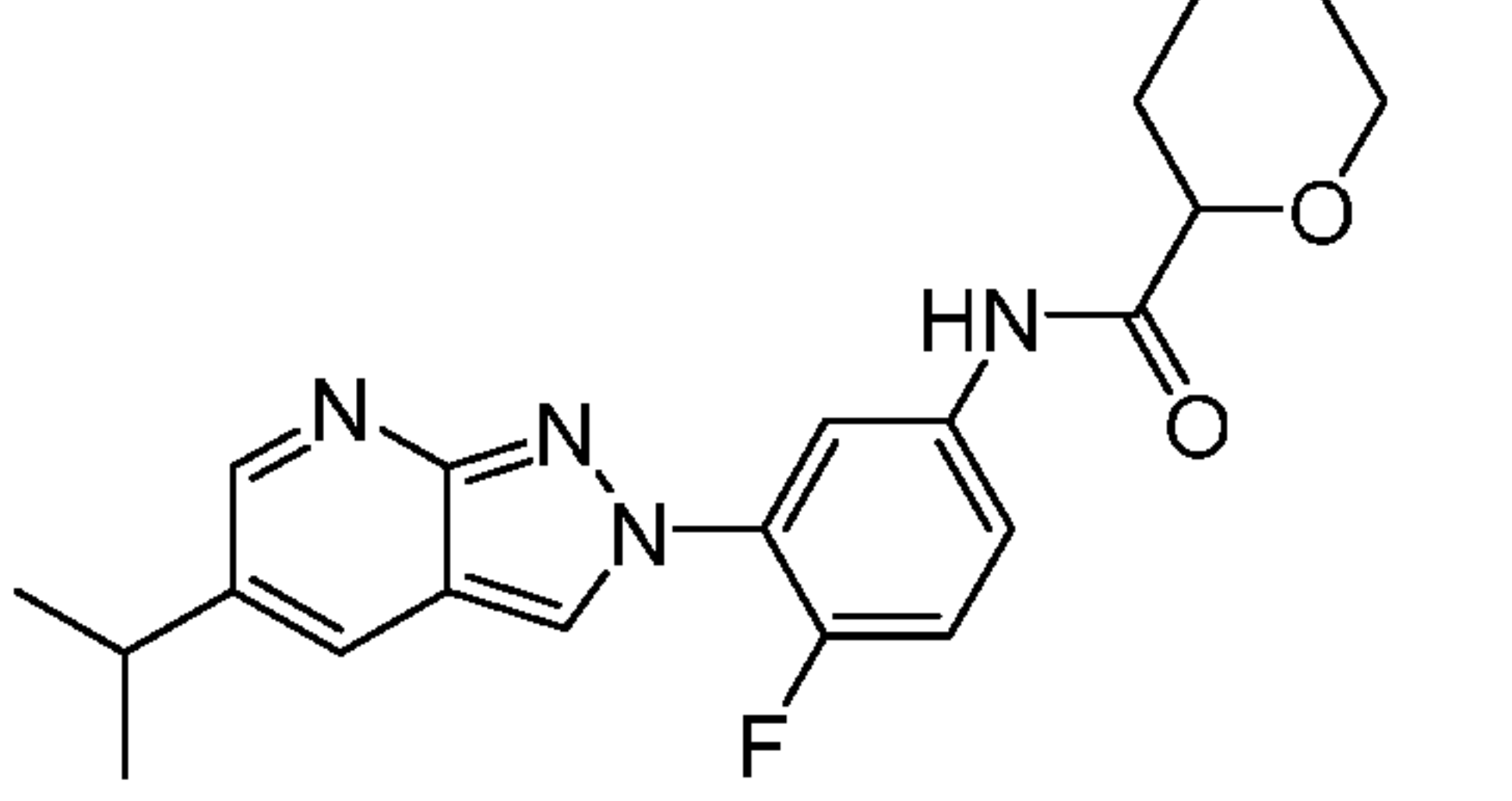
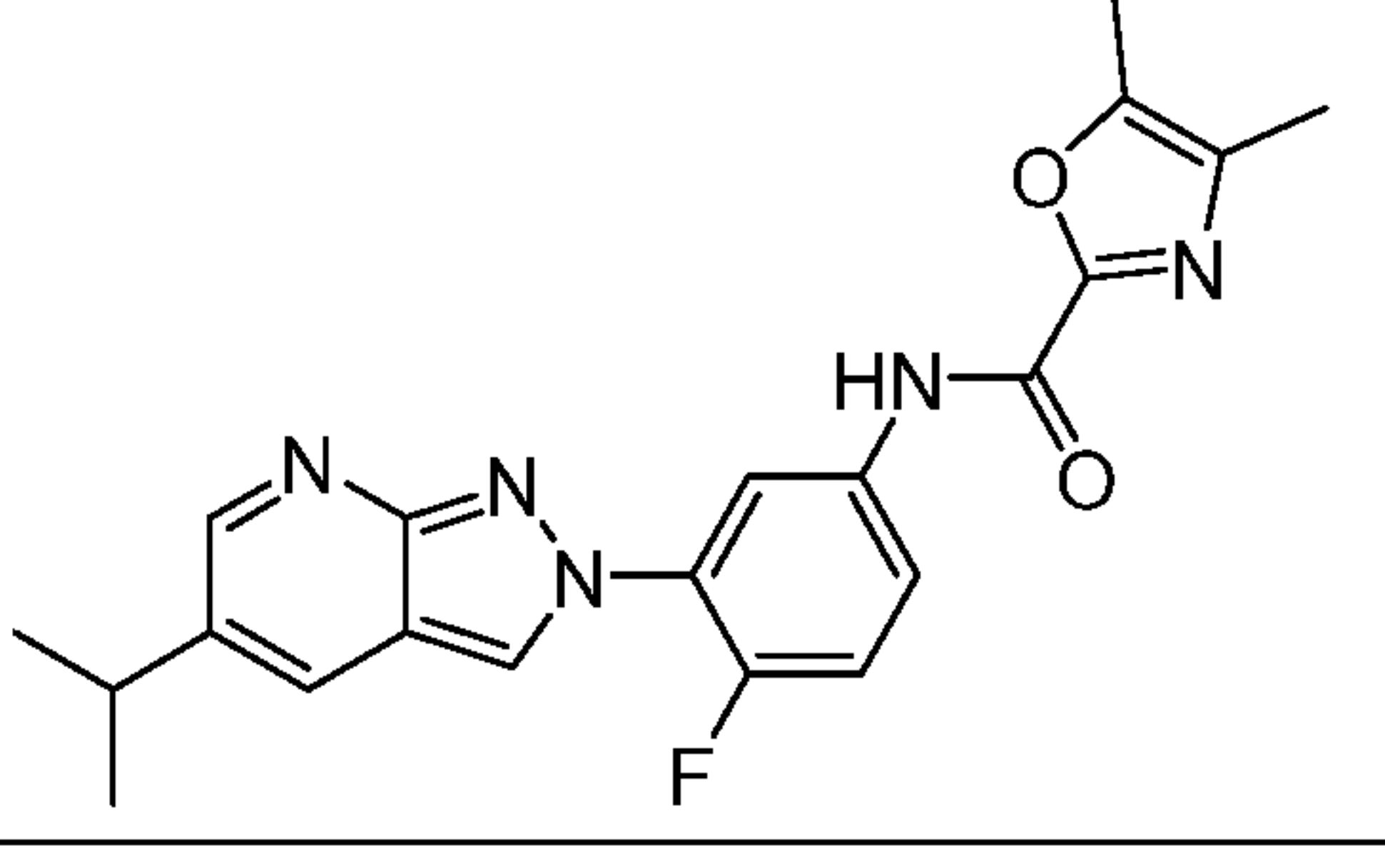
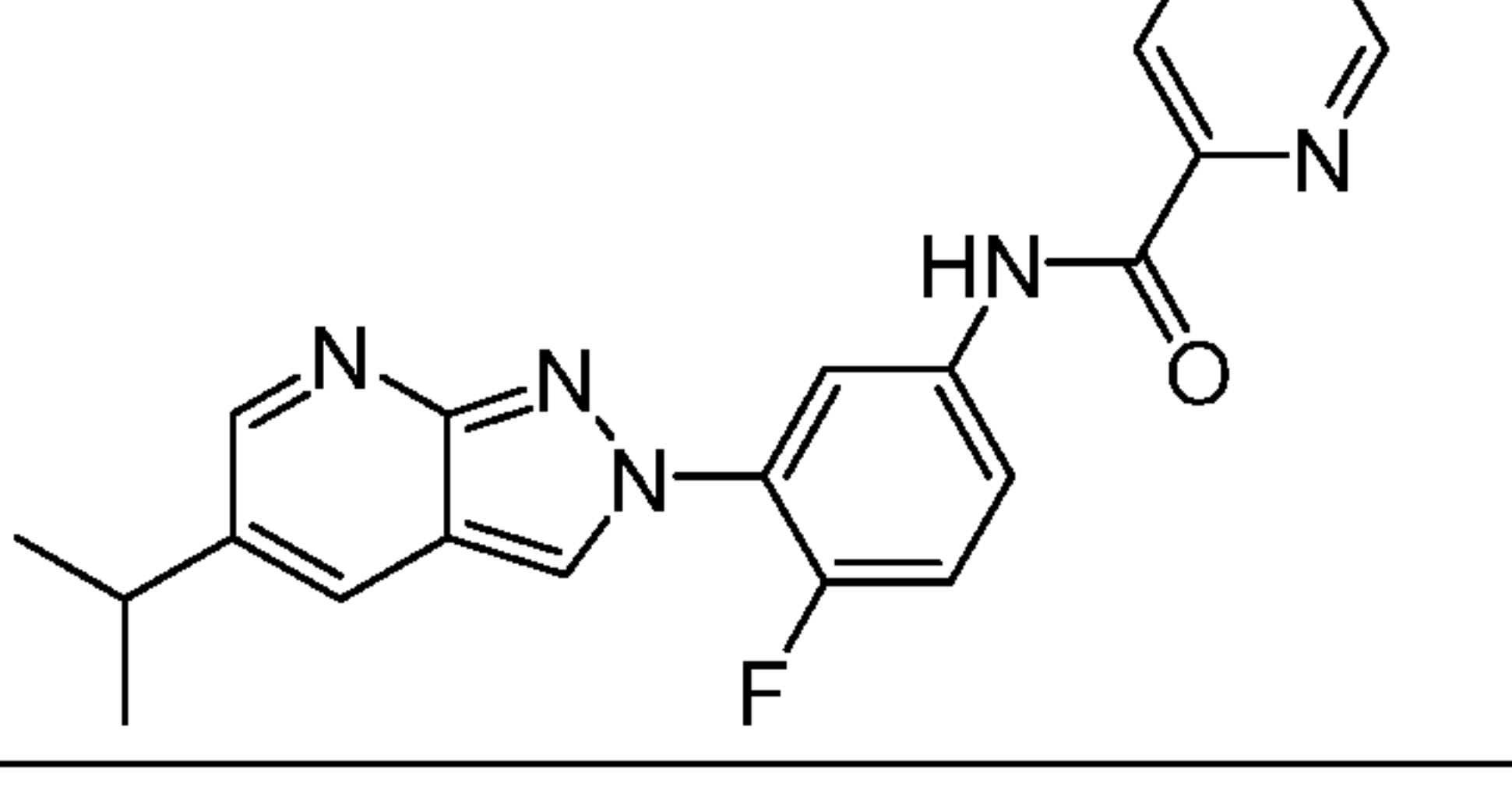
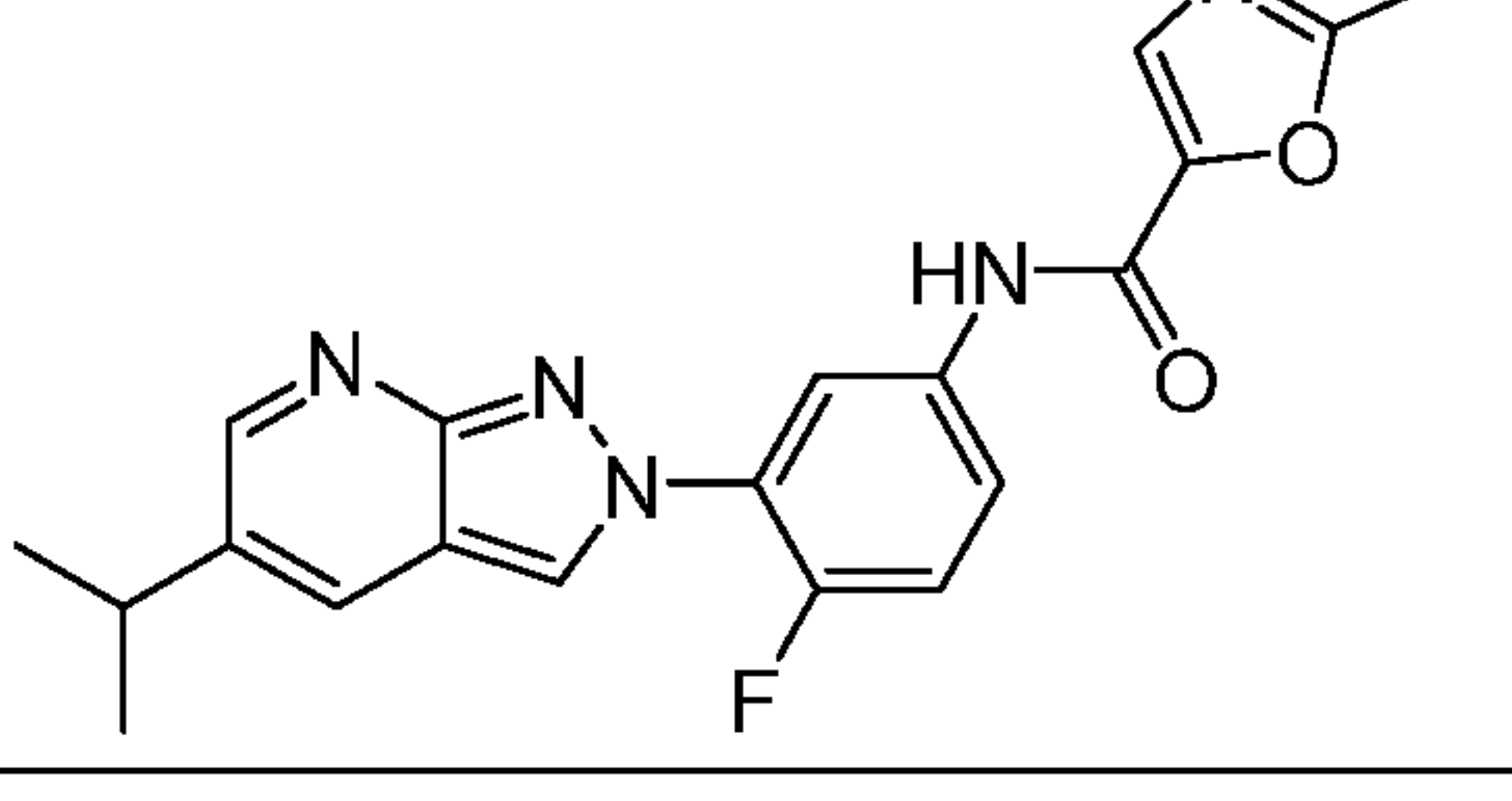
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
50		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.64 – 8.56 (m, 1H), 8.12 (m, 1H), 7.69 – 7.59 (m, 1H), 7.41 – 7.30 (m, 1H), 7.22 – 7.14 (m, 1H), 5.40 – 5.26 (m, 1H), 3.82 – 3.55 (m, 4H), 2.97 – 2.77 (m, 2H), 2.37 – 2.21 (m, 2H), 1.75 – 1.65 (m, 1H), 1.52 – 1.21 (m, 3H), 1.11 – 0.82 (m, 3H). Method 2: RT = 1.18 min.; M+H = 400.3
51		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.66 (m, 1H), 8.55 (m, 1H), 8.13 (m, 1H), 8.07 – 8.03 (m, 1H), 7.62 (m, 1H), 7.35 (m, 1H), 5.40 – 5.25 (m, 1H), 3.83 – 3.69 (m, 2H), 3.66 – 3.50 (m, 2H), 2.90 – 2.78 (m, 2H), 2.73 – 2.62 (m, 1H), 2.59 – 2.45 (m, 1H), 2.39 – 2.18 (m, 2H), 2.15 – 2.04 (m, 2H), 1.89 – 1.78 (m, 3H). Method 1: RT = 3.16 min.; M+H = 412.3
52		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.57 (m, 1H), 8.12 (m, 1H), 8.10 – 8.05 (m, 1H), 7.64 (m, 1H), 7.35 (m, 1H), 5.40 – 5.26 (m, 1H), 3.83 – 3.69 (m, 2H), 3.59 (m, 2H), 2.89 – 2.77 (m, 2H), 2.38 – 2.05 (m, 3H), 1.70 – 1.57 (m, 2H), 1.04 – 0.88 (m, 6H). Method 2: RT = 1.25 min.; M+H = 414.4
53		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.37 (m, 1H), 8.88 (m, 1H), 8.86 (m, 1H), 8.70 (m, 1H), 8.17 (m, 1H), 8.05 – 7.92 (m, 2H), 7.66 (m, 1H), 7.43 (m, 1H), 7.37 (m, 1H), 5.40 – 5.27 (m, 1H), 3.85 – 3.70 (m, 2H), 3.60 (m, 2H), 2.38 – 2.09 (m, 2H). Method 2: RT = 0.93 min.; M+H = 421.3
54		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.58 (m, 1H), 8.43 (m, 1H), 8.08 (m, 1H), 7.93 (m, 1H), 7.78 (m, 1H), 7.46 (m, 1H), 7.31 (m, 1H), 6.71 – 6.63 (m, 1H), 2.68 (d, <i>J</i> = 7.1 Hz, 2H), 1.98 (m, 1H), 0.99 (2s, 6H). Method 1: RT = 3.20 min.; M+H = 379.3
55		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.61 (m, 1H), 8.42 (m, 1H), 7.95 – 7.87 (m, 2H), 7.78 (m, 1H), 7.44 (m, 1H), 7.31 (m, 1H), 6.67 (m, 1H), 2.17 – 2.08 (m, 1H), 1.09 (m, 2H), 0.86 – 0.79 (m, 2H). Method 2: RT = 1.11 min.; M+H = 363.3

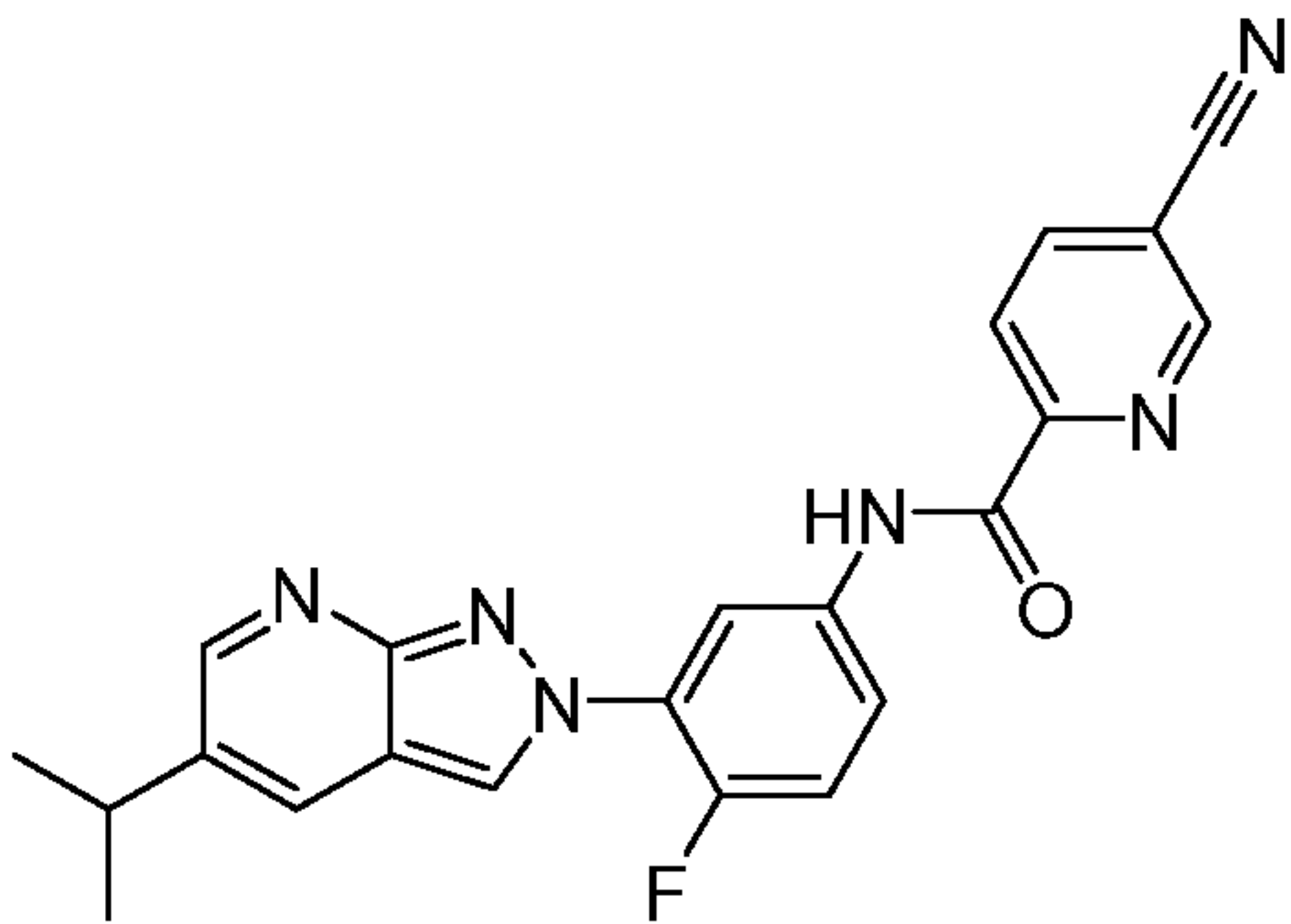
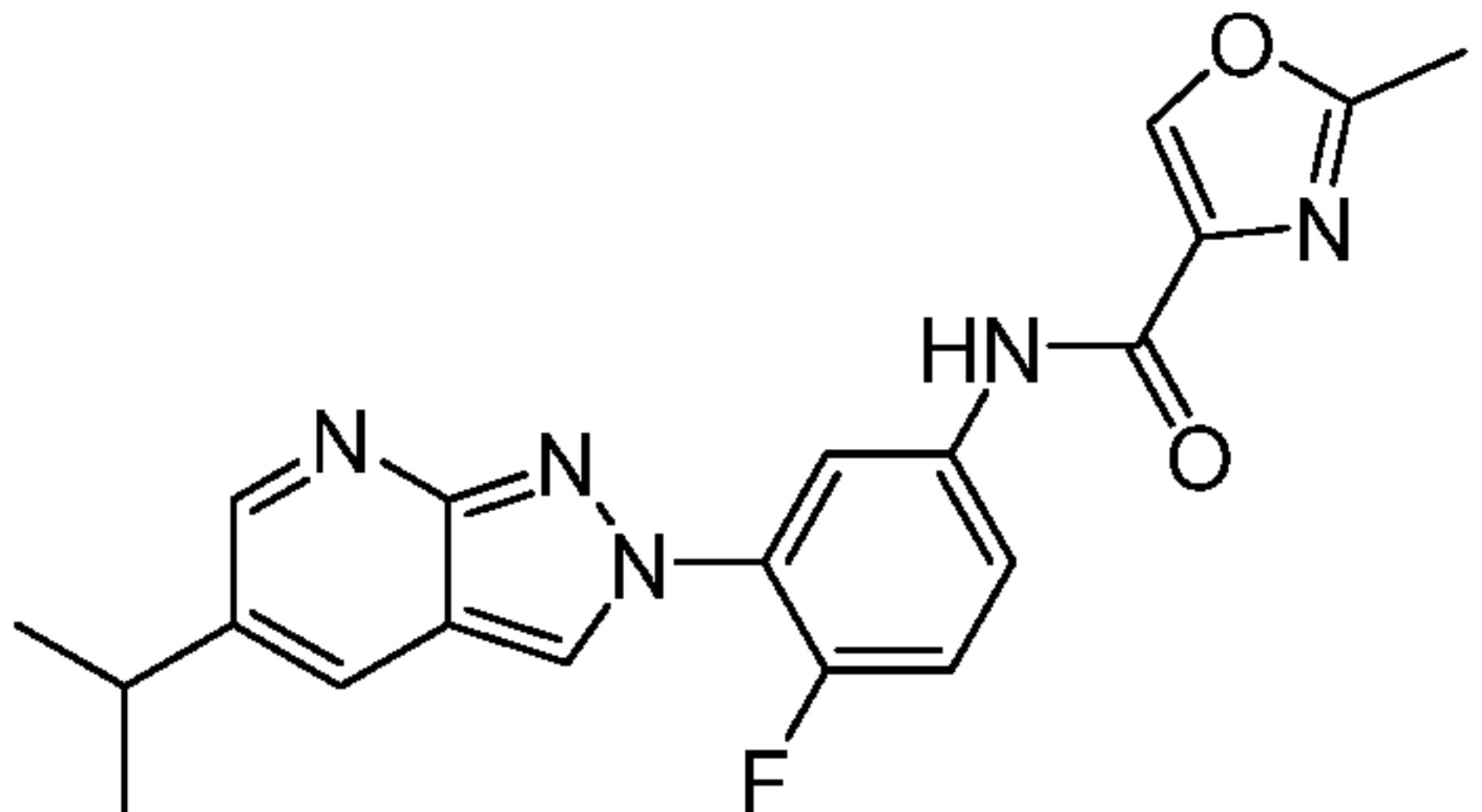
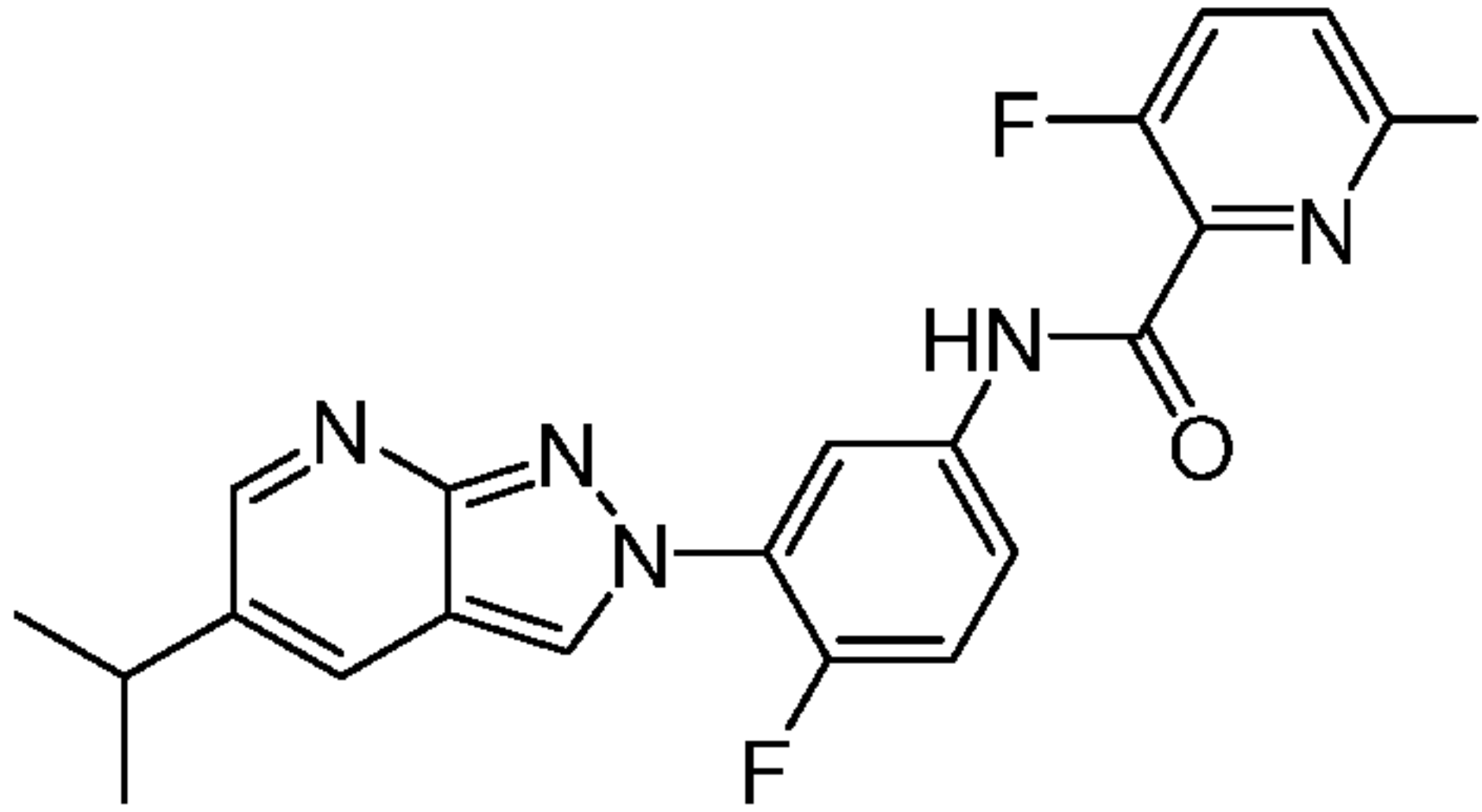
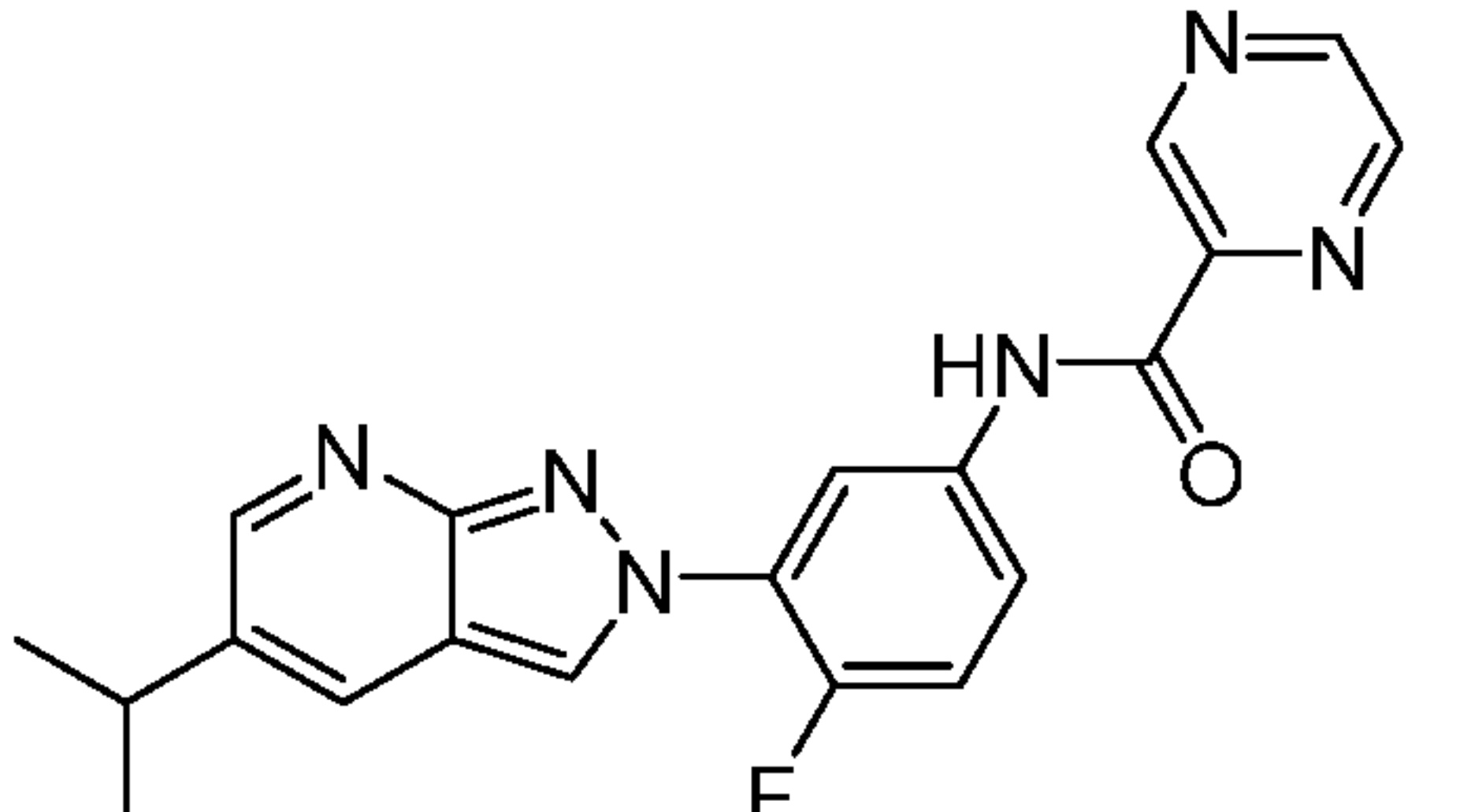
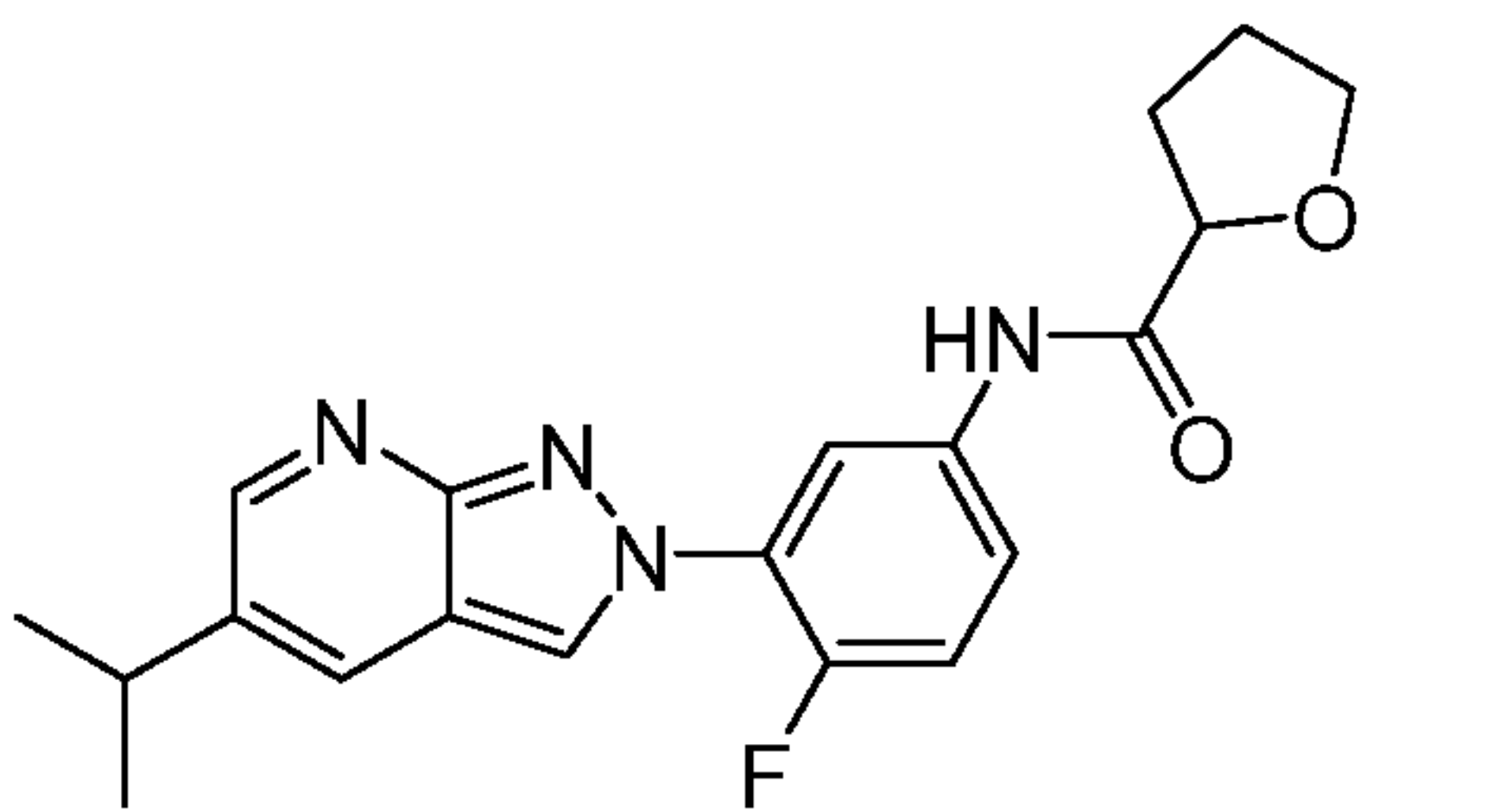
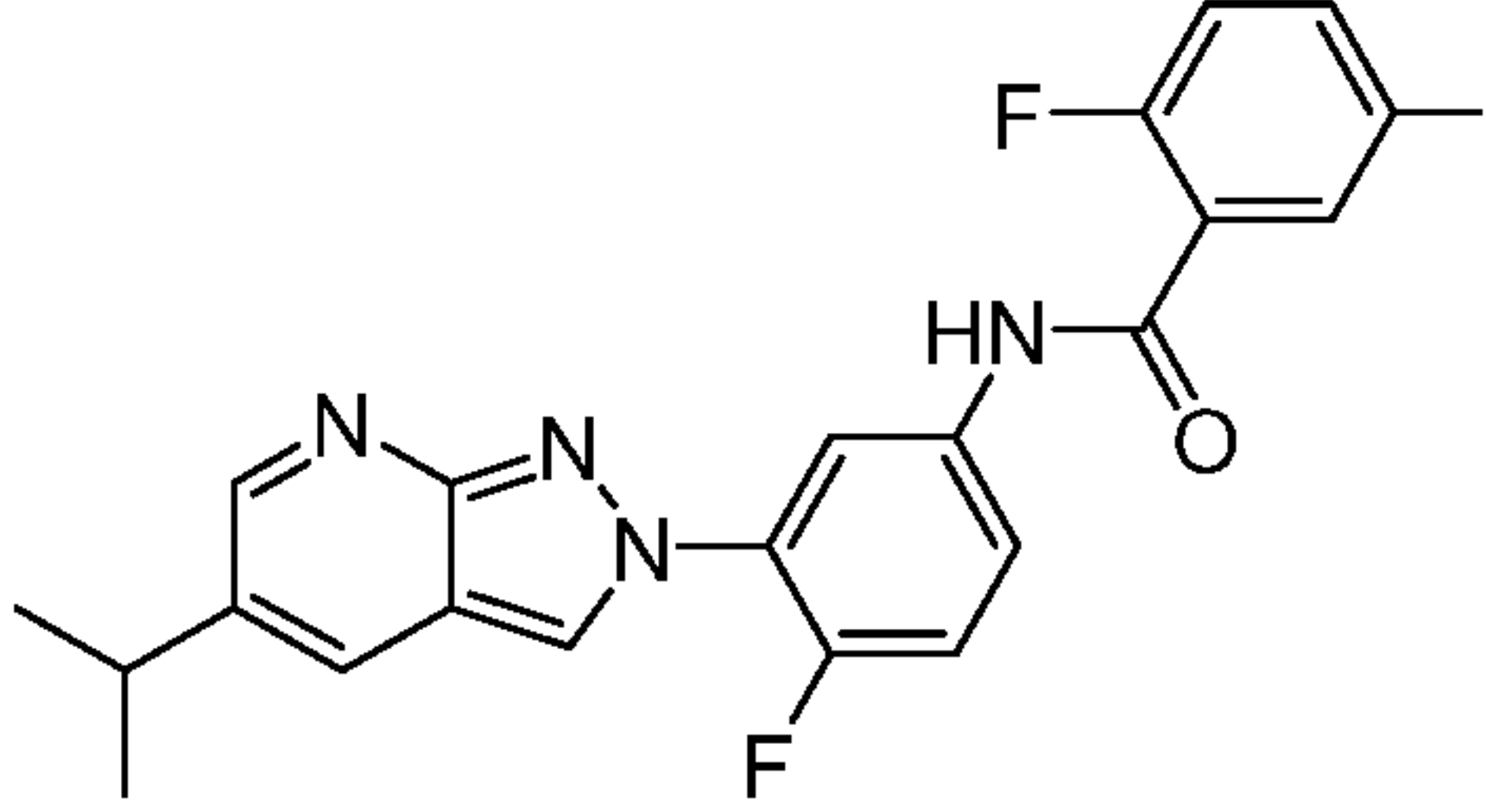
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
56		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.69 – 8.65 (m, 1H), 8.43 (m, 1H), 8.15 (m, 1H), 7.92 (m, 1H), 7.80 – 7.76 (m, 1H), 7.46 (m, 1H), 7.33 – 7.29 (m, 1H), 6.67 (m, 1H), 3.25 – 3.18 (m, 1H), 2.27 – 2.14 (m, 3H), 1.85 – 1.66 (m, 5H). Method 2: RT = 1.27 min.; M+H = 391.3
57		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.67 (m, 1H), 8.53 (m, 1H), 8.07 (m, 1H), 8.00 (m, 1H), 7.77 (m, 1H), 7.47 (m, 1H), 7.34 – 7.29 (m, 1H), 7.19 (m, 1H), 6.67 (m, 1H), 2.88 (m, 2H), 1.98 (m, 3H), 1.88 – 1.72 (m, 3H), 1.40 – 1.28 (m, 3H). M+H = 405.3
58		¹ H NMR (400 MHz, DMSO) δ 8.95 (s, 1 H), 8.56 (d, <i>J</i> = 2.63 Hz, 1 H), 8.30 (d, <i>J</i> = 2.89 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.60 - 7.69 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.00 (d, <i>J</i> = 2.76 Hz, 1 H), 5.28 - 5.63 (m, 2 H), 4.20 - 4.37 (m, 4 H), 3.93 - 4.09 (m, 4 H). Method 1: RT = 2.61 min. M+H = 403.2
59		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.73 (m, 1H), 8.55 (m, 1H), 8.43 (m, 1H), 8.09 (m, 1H), 7.93 (m, 1H), 7.78 (m, 1H), 7.45 (m, 1H), 7.31 (m, 1H), 6.70 – 6.64 (m, 1H), 2.70 (s, 2H), 0.99 (s, 9H). Method 2: RT = 1.29 min.; M+H = 393.3
60		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.66 (m, 1H), 8.64 – 8.54 (m, 1H), 8.12 (m, 1H), 7.94 (m, 1H), 7.77 (m, 1H), 7.40 (m, 1H), 7.30 (m, 1H), 7.18 (m, 1H), 6.67 (m, 1H), 2.03 – 1.79 (m, 2H), 1.51 (s, 3H), 1.39 (s, 3H), 0.75 (m, 3H). Method 2: RT = 1.11 min.; M+H = 393.3
61		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.61 (m, 1H), 8.48 – 8.38 (m, 1H), 8.15 – 8.04 (m, 1H), 7.93 (m, 1H), 7.81 – 7.74 (m, 1H), 7.53 – 7.43 (m, 1H), 7.31 (m, 1H), 7.10 (m, 1H), 6.67 (m, 1H), 2.86 – 2.75 (m, 1H), 1.89 – 1.66 (m, 2H), 1.54 – 1.27 (m, 3H), 1.06 – 0.82 (m, 3H). Method 1: RT = 3.09 min.; M+H = 379.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
62		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.74 – 8.66 (m, 1H), 8.58 (m, 1H), 8.42 (m, 1H), 8.12 – 8.04 (m, 1H), 7.92 (m, 1H), 7.78 (m, 1H), 7.45 (m, 1H), 7.31 (m, 1H), 6.67 (m, 1H), 2.84 (m, 2H), 2.69 (m, 1H), 2.15 – 2.05 (m, 1H), 1.98 – 1.67 (m, 3H), 1.51 – 1.35 (m, 1H), 1.00 (m, 1H). Method 1: RT = 3.26 min.; M+H = 391.3
63		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.59 (m, 1H), 8.42 (m, 1H), 8.12 – 8.05 (m, 1H), 7.95 – 7.88 (m, 1H), 7.78 (m, 1H), 7.45 (m, 1H), 7.31 (m, 1H), 6.70 – 6.64 (m, 1H), 2.87 – 2.75 (m, 2H), 1.82 – 1.56 (m, 3H), 1.05 – 0.82 (m, 6H). Method 2: RT = 1.32 min.; M+H = 393.3
64		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.42 – 9.35 (m, 1H), 8.94 – 8.90 (m, 1H), 8.89 – 8.85 (m, 1H), 8.73 – 8.66 (m, 1H), 8.51 – 8.45 (m, 1H), 8.06 – 7.89 (m, 3H), 7.81 – 7.76 (m, 1H), 7.51 – 7.40 (m, 2H), 7.35 – 7.29 (m, 1H), 6.70 – 6.64 (m, 1H). Method 2: RT = 1.01 min.; M+H = 400.3
65		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.21 (m, 1H), 8.73 (m, 1H), 8.67 (m, 2H), 8.56 (m, 1H), 8.14 (m, 1H), 8.00 (m, 1H), 7.47 (m, 1H), 3.14 (m, 1H), 2.68 (s, 3H), 1.39 (2s, 6H). Method 1: RT = 3.11 min.; M+H = 391.3
66		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.66 (m, 1H), 8.31 – 8.26 (m, 1H), 8.13 (m, 1H), 7.76 (m, 1H), 7.39 (m, 1H), 3.13 (m, 1H), 3.03 – 2.84 (m, 1H), 2.35 – 1.70 (m, 6H), 1.38 (m, 7H), 1.06 (m, 3H). Method 1: RT = 3.36 min.; M+H = 381.4
67		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.74 – 8.69 (m, 1H), 8.69 – 8.64 (m, 1H), 8.64 – 8.59 (m, 1H), 8.59 – 8.53 (m, 1H), 8.33 – 8.26 (m, 1H), 8.16 – 8.10 (m, 1H), 8.01 – 7.94 (m, 1H), 7.86 – 7.77 (m, 1H), 7.51 – 7.41 (m, 1H), 3.14 (m, 1H), 1.39 (2s, 6H). Method 1: RT = 3.22 min.; M+H = 394.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
68		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.73 (m, 1H), 8.67 (m, 1H), 8.48 (m, 1H), 8.14 (m, 1H), 7.91 (m, 1H), 7.47 (m, 1H), 3.19 – 3.09 (m, 1H), 2.62 (s, 3H), 1.39 (2s, 6H). Method 1: RT = 3.29 min.; M+H = 448.3
69		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.45 (m, 1H), 8.41 (m, 1H), 8.05 (m, 1H), 7.88 (m, 1H), 7.52 (m, 1H), 7.15 (m, 1H), 2.89 (m, 1H), 2.09 – 2.01 (m, 2H), 1.13 (2s, 6H), 0.96 – 0.83 (m, 1H), 0.42 – 0.29 (m, 2H), 0.08 – 0.05 (m, 2H). Method 1: RT = 3.06 min.; M+H = 353.3
70		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.67 (m, 1H), 8.56 – 8.48 (m, 2H), 8.14 (m, 1H), 7.96 (m, 1H), 7.80 (m, 1H), 7.47 (m, 1H), 3.14 (m, 1H), 1.39 (2s, 6H). Method 1: RT = 3.12 min.; M+H = 412.3
71		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.66 (m, 1H), 8.30 (m, 1H), 8.15 – 8.09 (m, 1H), 7.76 (m, 1H), 7.40 (m, 1H), 3.18 – 3.07 (m, 1H), 3.07 – 2.74 (m, 2H), 2.27 – 1.73 (m, 6H), 1.56 – 1.17 (2s, 6H). Method 1: RT = 3.35 min.; M+H = 435.3
72		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.66 (m, 1H), 8.36 (m, 1H), 8.14 (m, 1H), 7.84 (m, 1H), 7.46 – 7.38 (m, 1H), 6.53 – 6.45 (m, 1H), 3.14 (m, 1H), 2.54 (s, 3H), 2.29 (s, 3H), 1.39 (2s, 6H). Method 1: RT = 3.31 min.; M+H = 393.3
73		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.67 (m, 1H), 8.44 (m, 1H), 8.28 (m, 1H), 8.14 (m, 1H), 7.90 (m, 1H), 7.45 (m, 1H), 3.14 (m, 1H), 2.53 (s, 3H), 1.39 (2s, 6H). Method 1: RT = 3.00 min.; M+H = 380.3

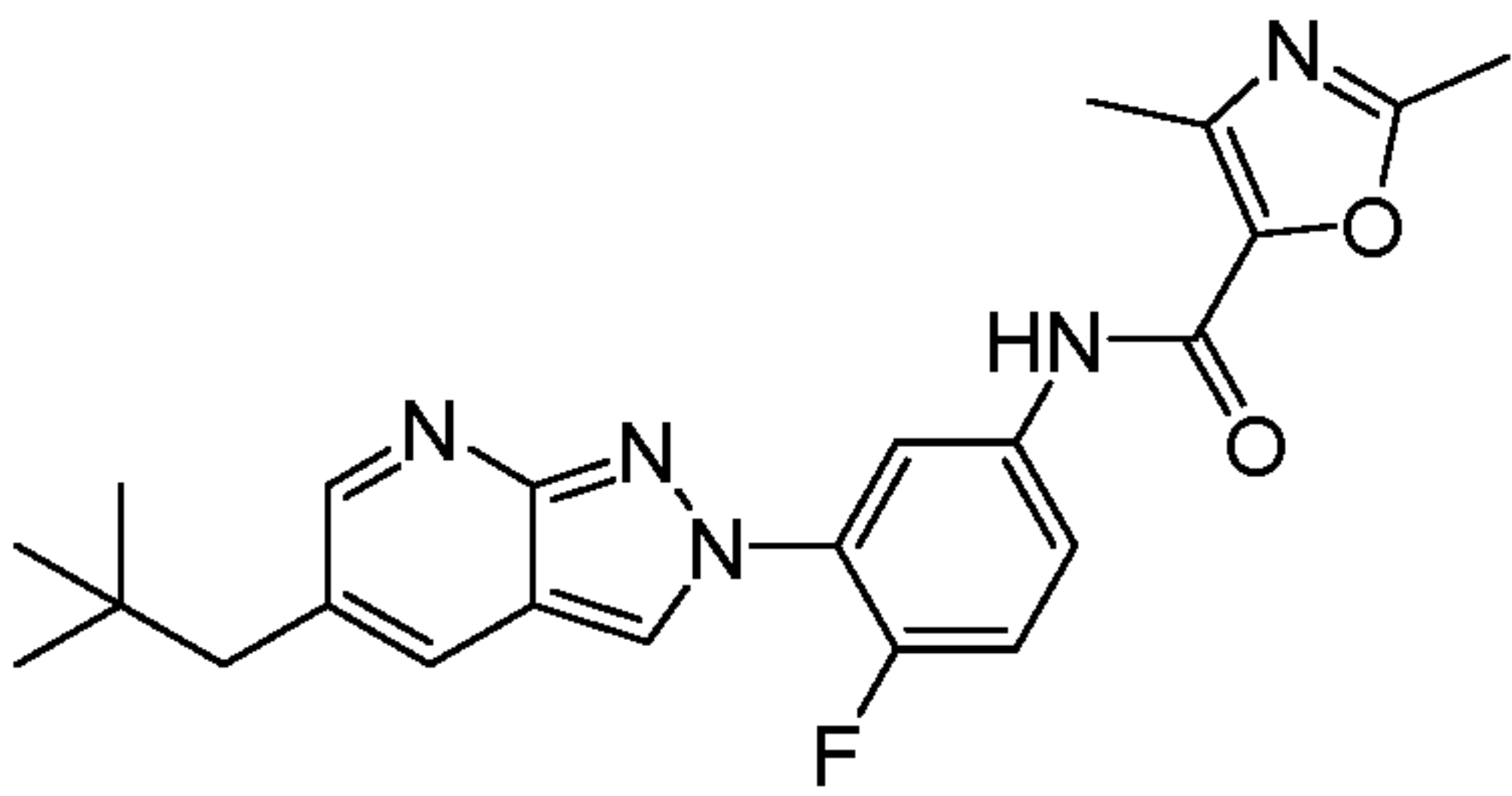
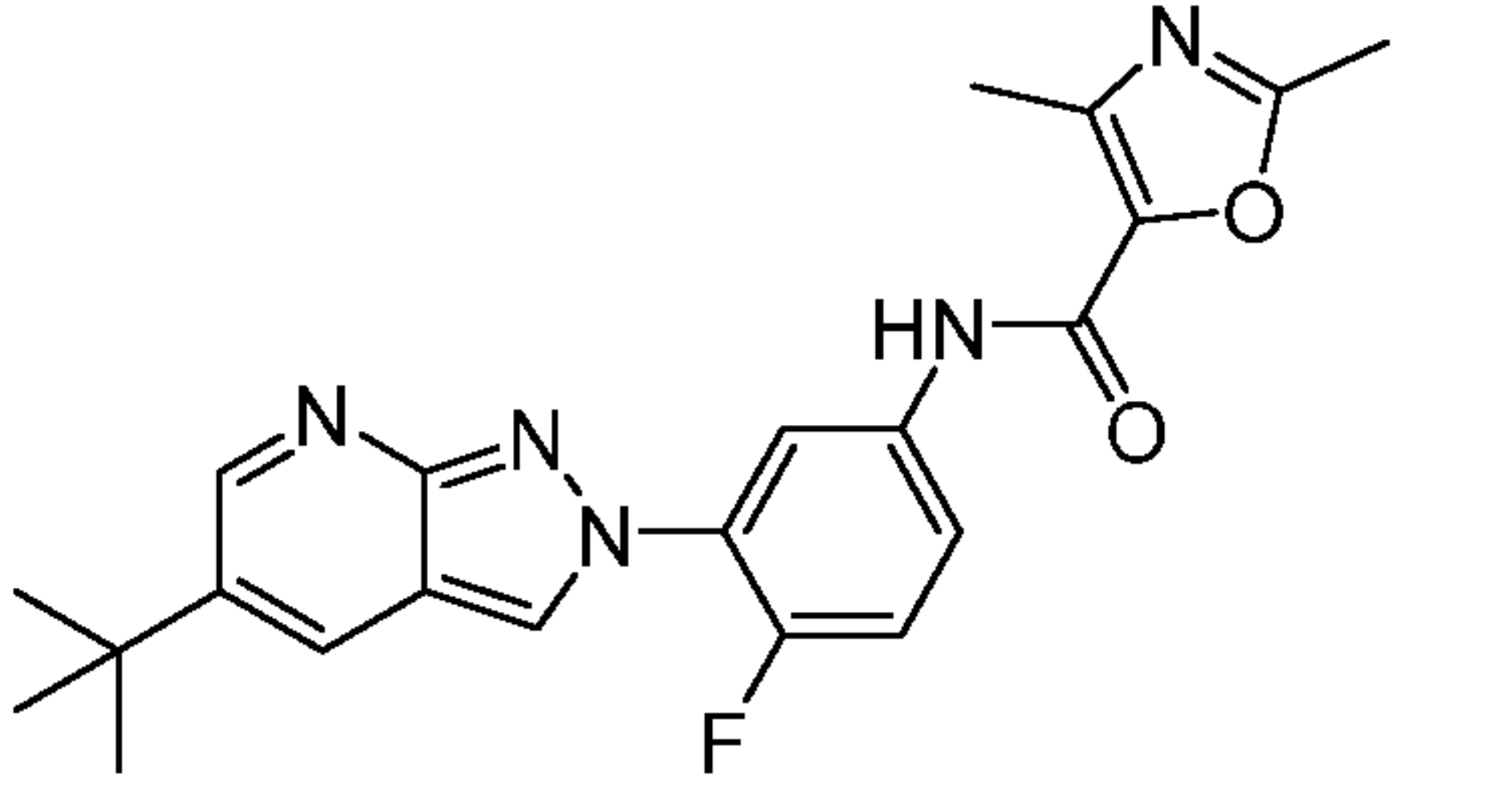
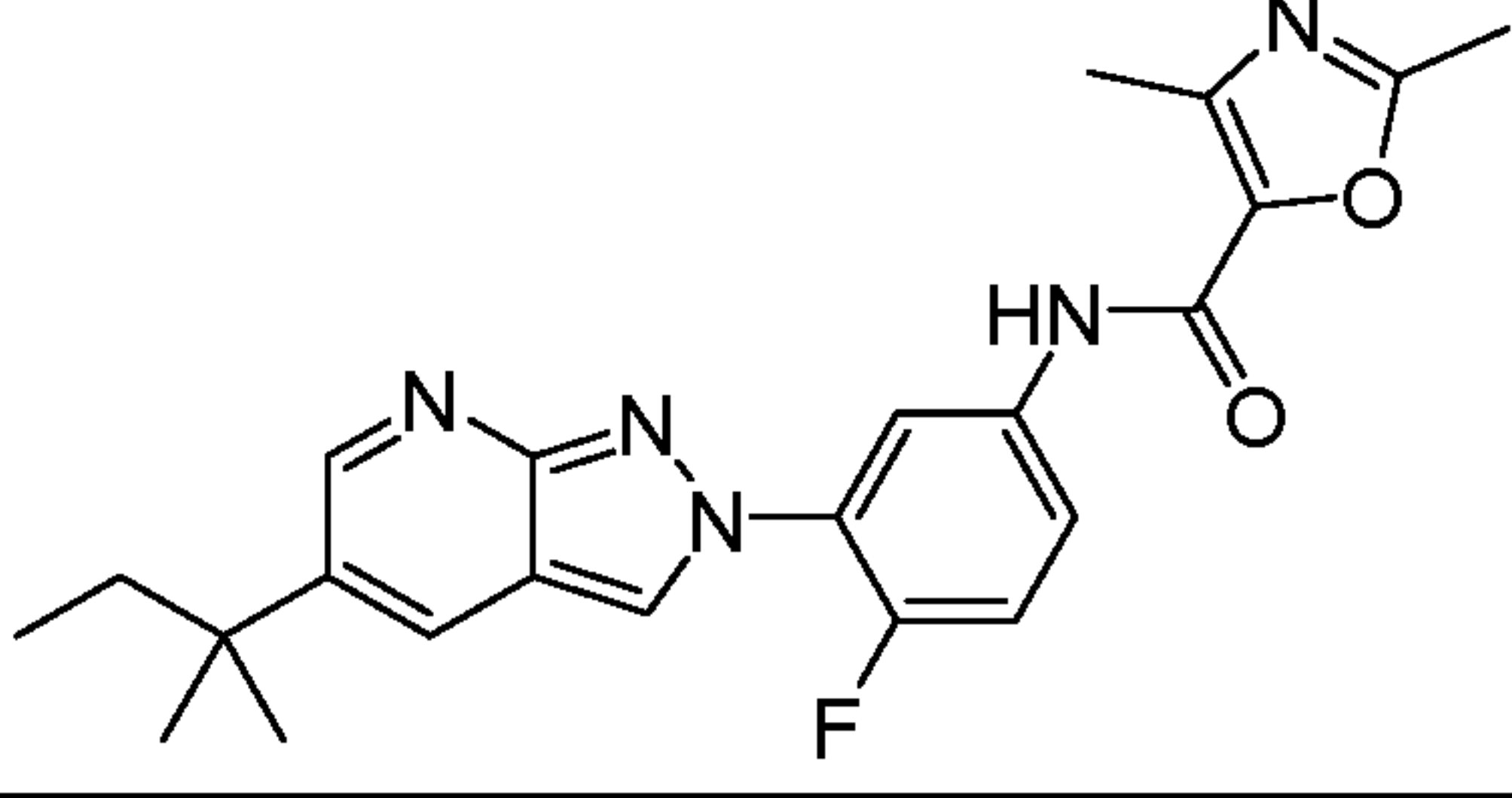
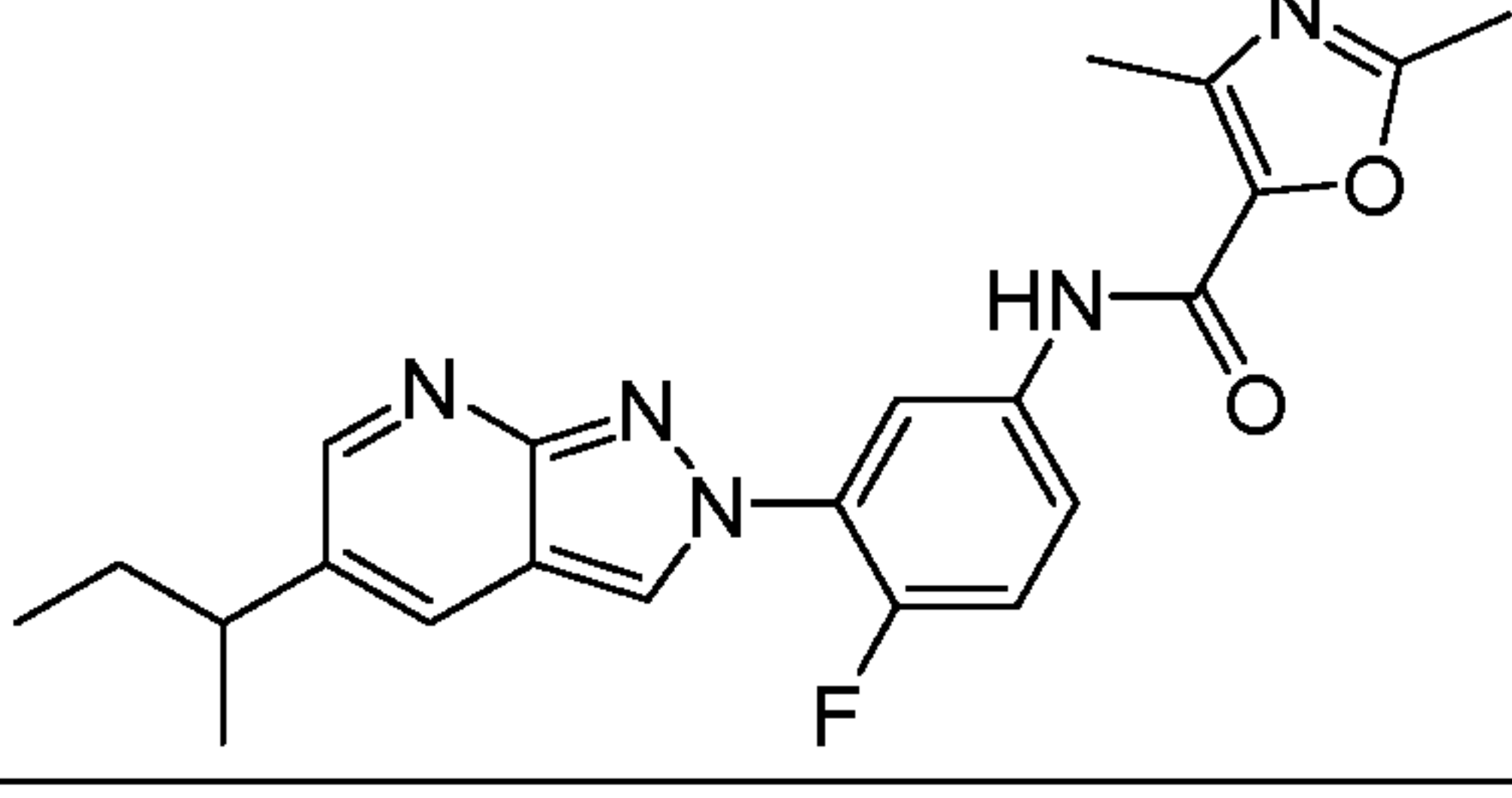
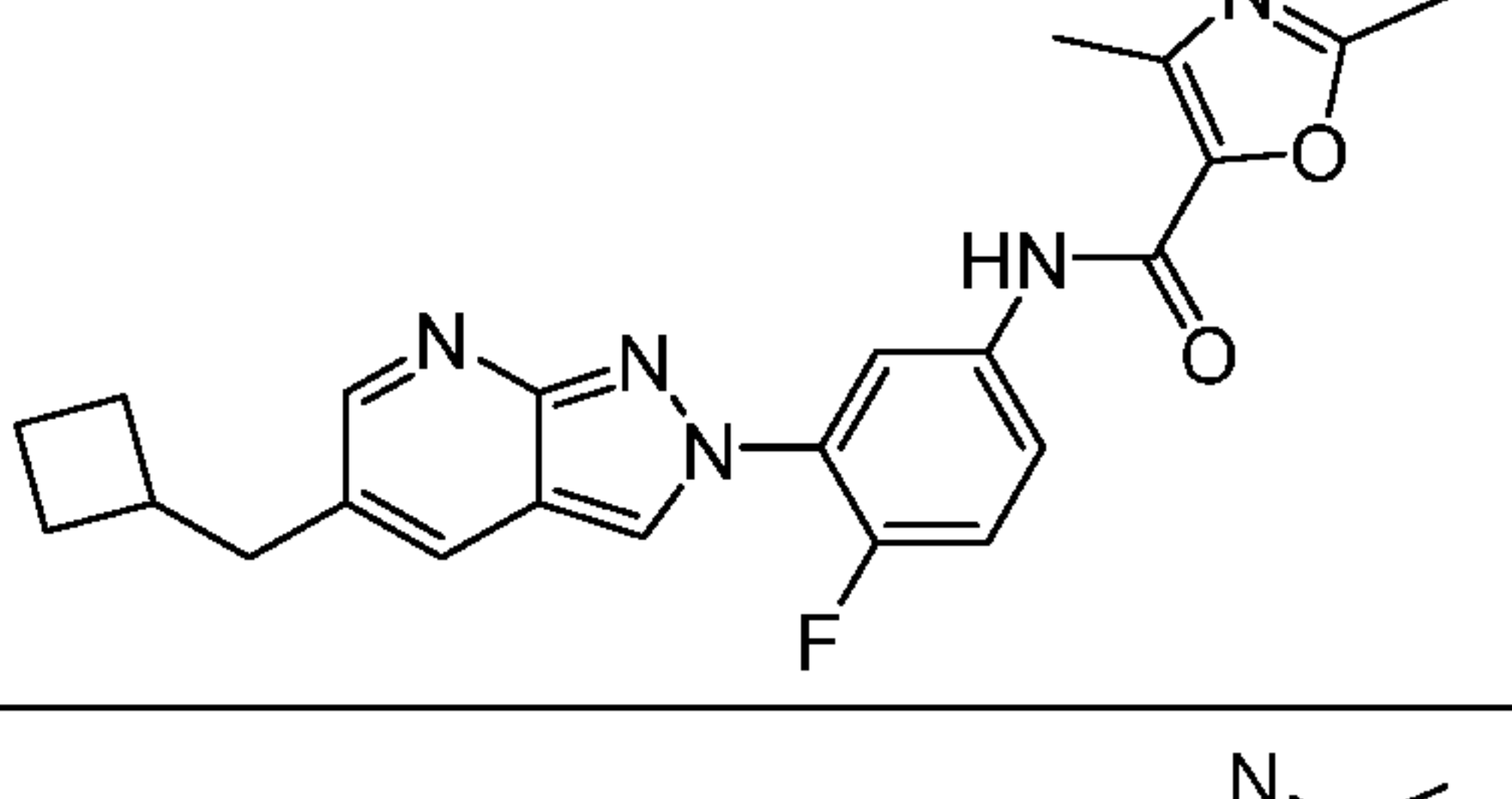
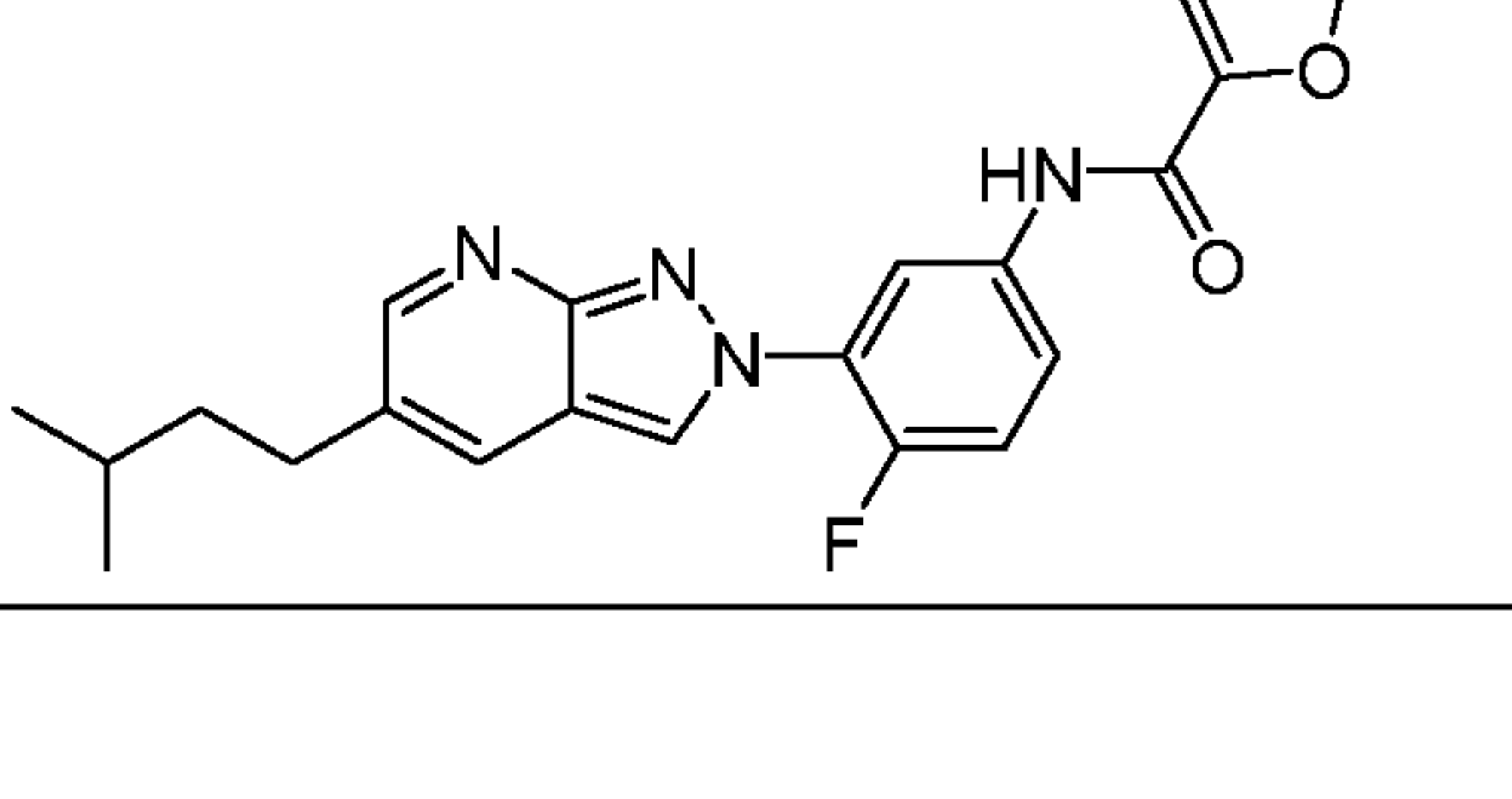
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
74		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.66 (m, 1H), 8.46 (m, 1H), 8.13 (m, 1H), 7.85 (m, 1H), 7.47 – 7.36 (m, 1H), 3.14 (m, 1H), 2.62 (s, 3H), 2.46 (s, 3H), 1.49 – 1.19 (2s, 6H). Method 1: RT = 3.23 min.; M+H = 394.3
75		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.75 – 8.69 (m, 1H), 8.69 – 8.63 (m, 1H), 8.45 – 8.39 (m, 1H), 8.16 – 8.09 (m, 1H), 7.95 – 7.87 (m, 1H), 7.51 – 7.41 (m, 1H), 3.20 – 3.06 (m, 1H), 2.29 – 2.19 (m, 1H), 1.39 (2s, 6H), 1.27 – 1.14 (m, 4H). Method 1: RT = 3.15 min.; M+H = 406.3
76		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.74 – 8.68 (m, 1H), 8.69 – 8.62 (m, 1H), 8.46 – 8.39 (m, 1H), 8.16 – 8.09 (m, 1H), 7.92 – 7.83 (m, 1H), 7.48 – 7.38 (m, 1H), 3.20 – 3.08 (m, 1H), 2.49 – 2.39 (m, 3H), 2.23 – 2.12 (m, 1H), 1.38 (2s, 6H), 1.29 – 1.12 (m, 4H). Method 1: RT = 3.24 min.; M+H = 420.3
77		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 – 8.67 (m, 1H), 8.67 – 8.63 (m, 1H), 8.39 – 8.33 (m, 1H), 8.15 – 8.09 (m, 1H), 7.85 – 7.77 (m, 1H), 7.45 – 7.37 (m, 1H), 4.13 – 3.97 (m, 2H), 3.22 – 3.09 (m, 1H), 2.47 – 2.31 (m, 1H), 2.09 – 1.77 (m, 4H), 1.50 (s, 3H), 1.38 (2s, 6H). Method 1: RT = 3.10 min.; M+H = 383.3
78		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.66 (m, 1H), 8.47 (m, 1H), 8.13 (m, 1H), 7.89 (m, 1H), 7.49 – 7.41 (m, 1H), 3.14 (m, 1H), 2.63 – 2.47 (s, 3H), 1.38 (2s, 6H). Method 1: RT = 3.39 min.; M+H = 448.3

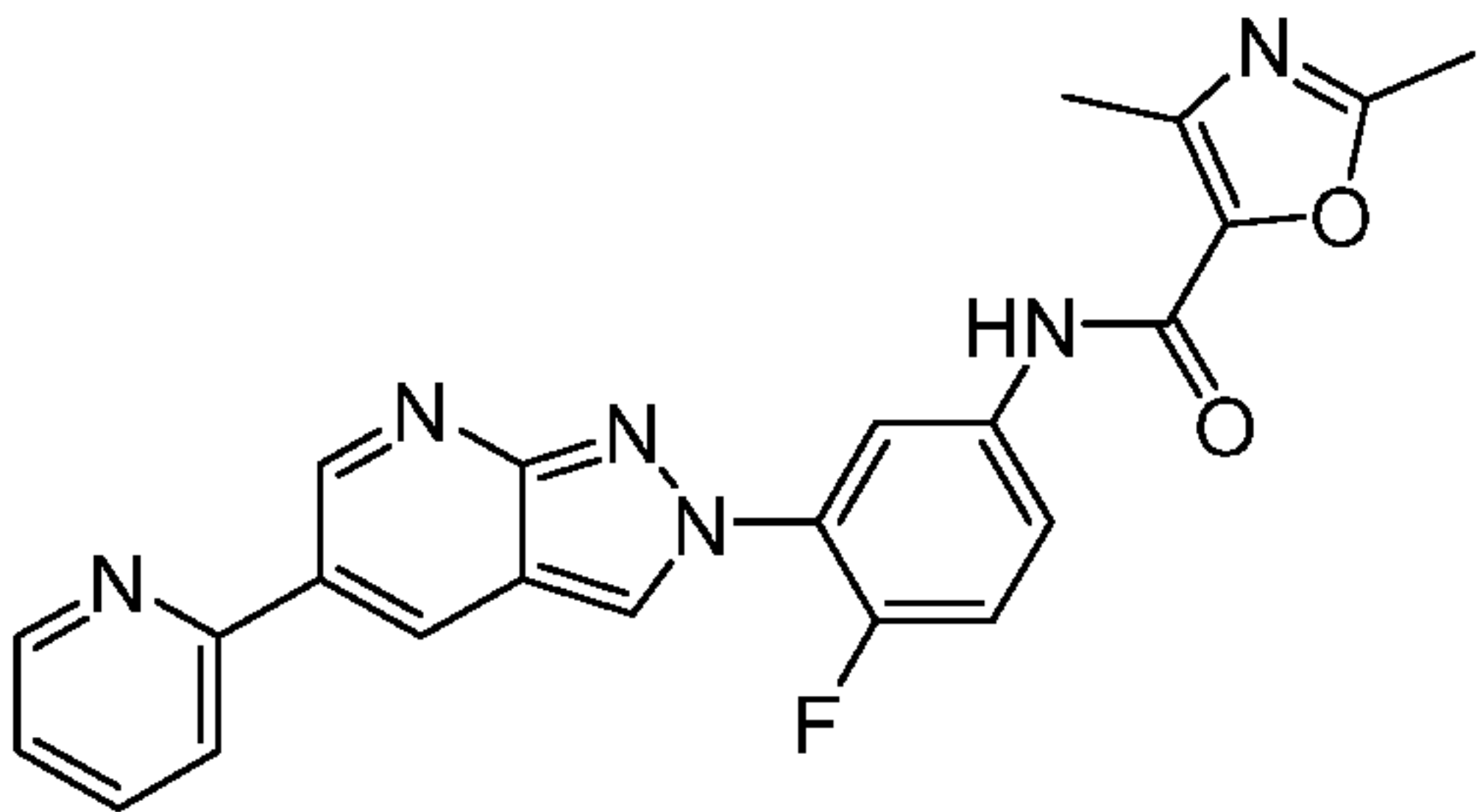
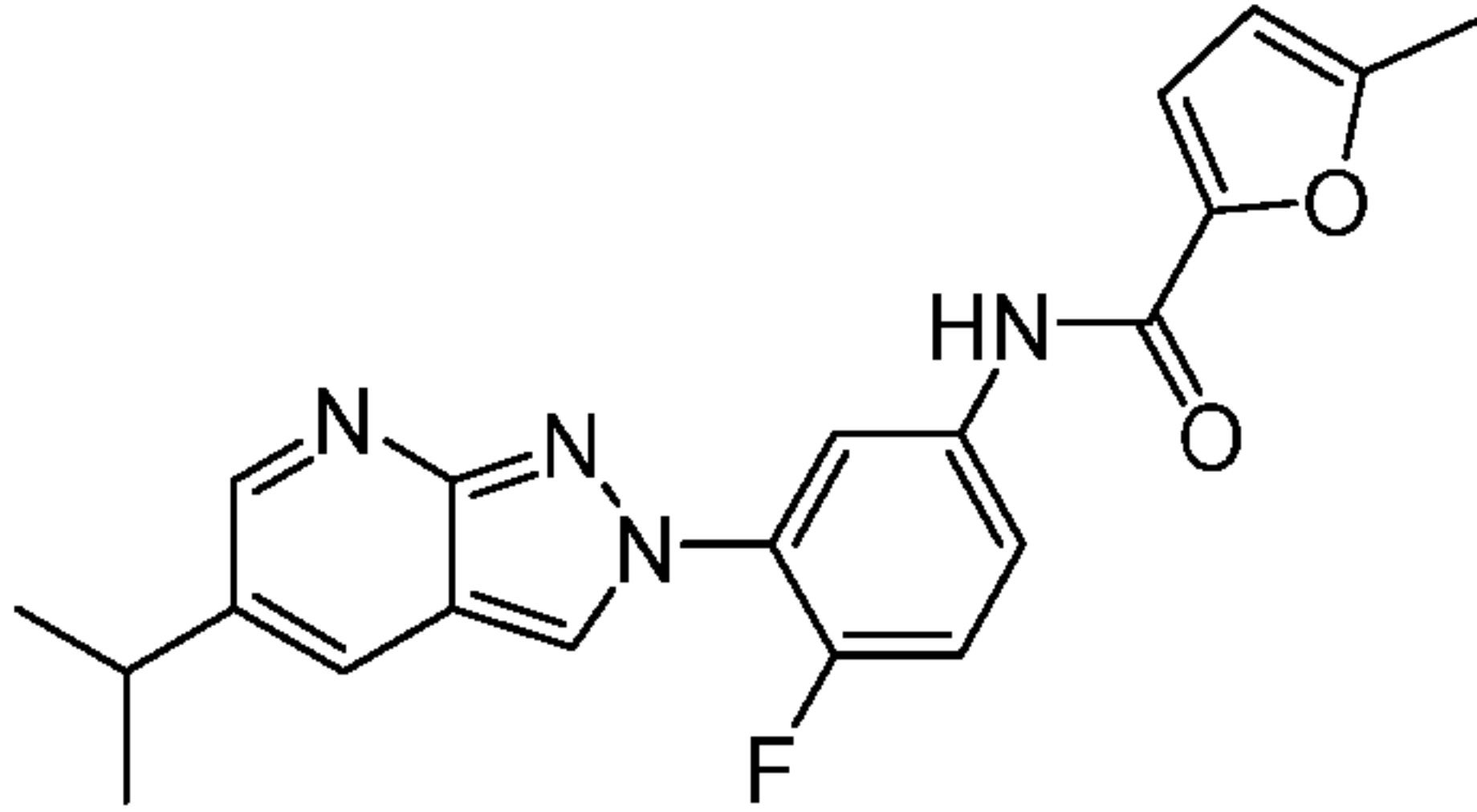
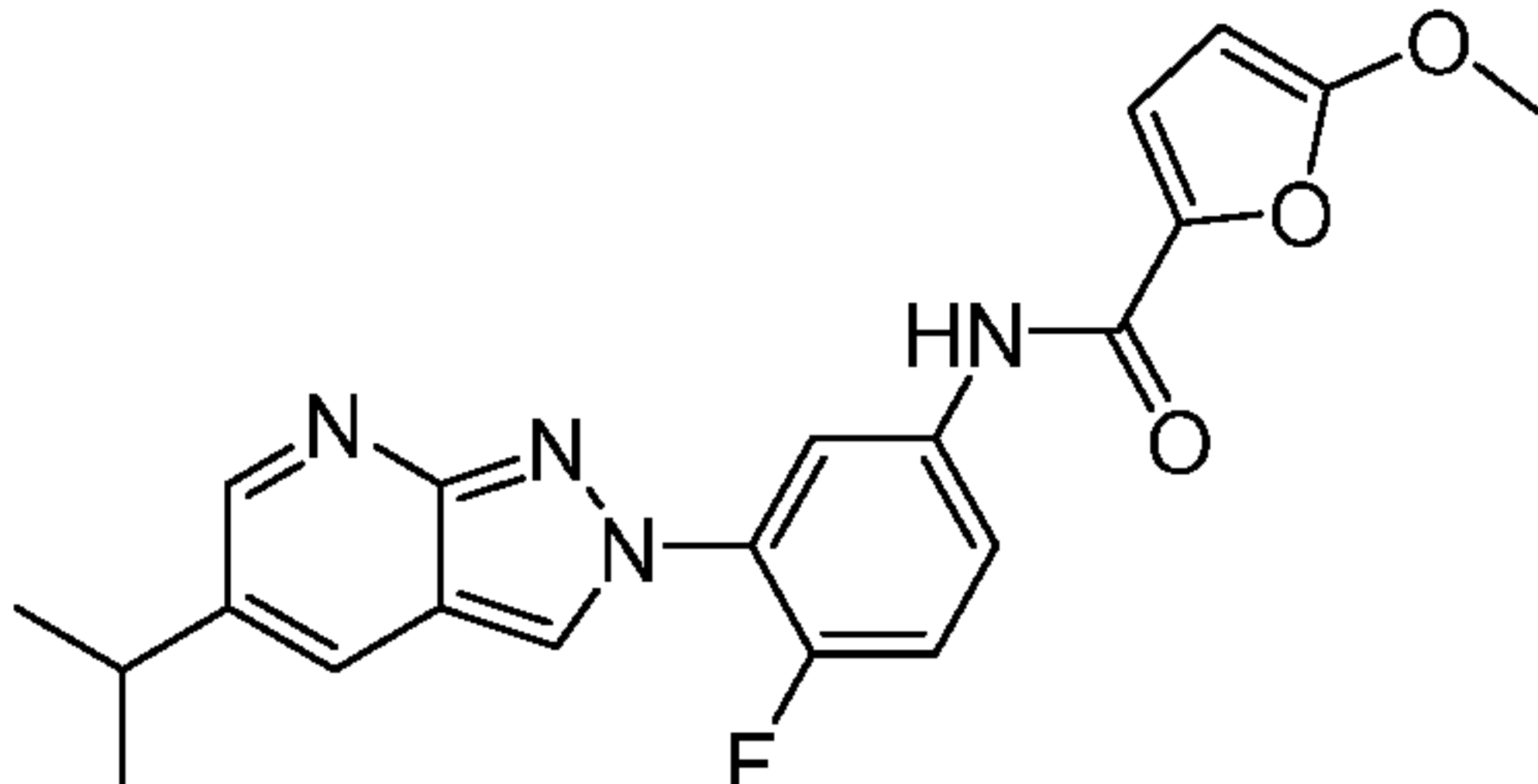
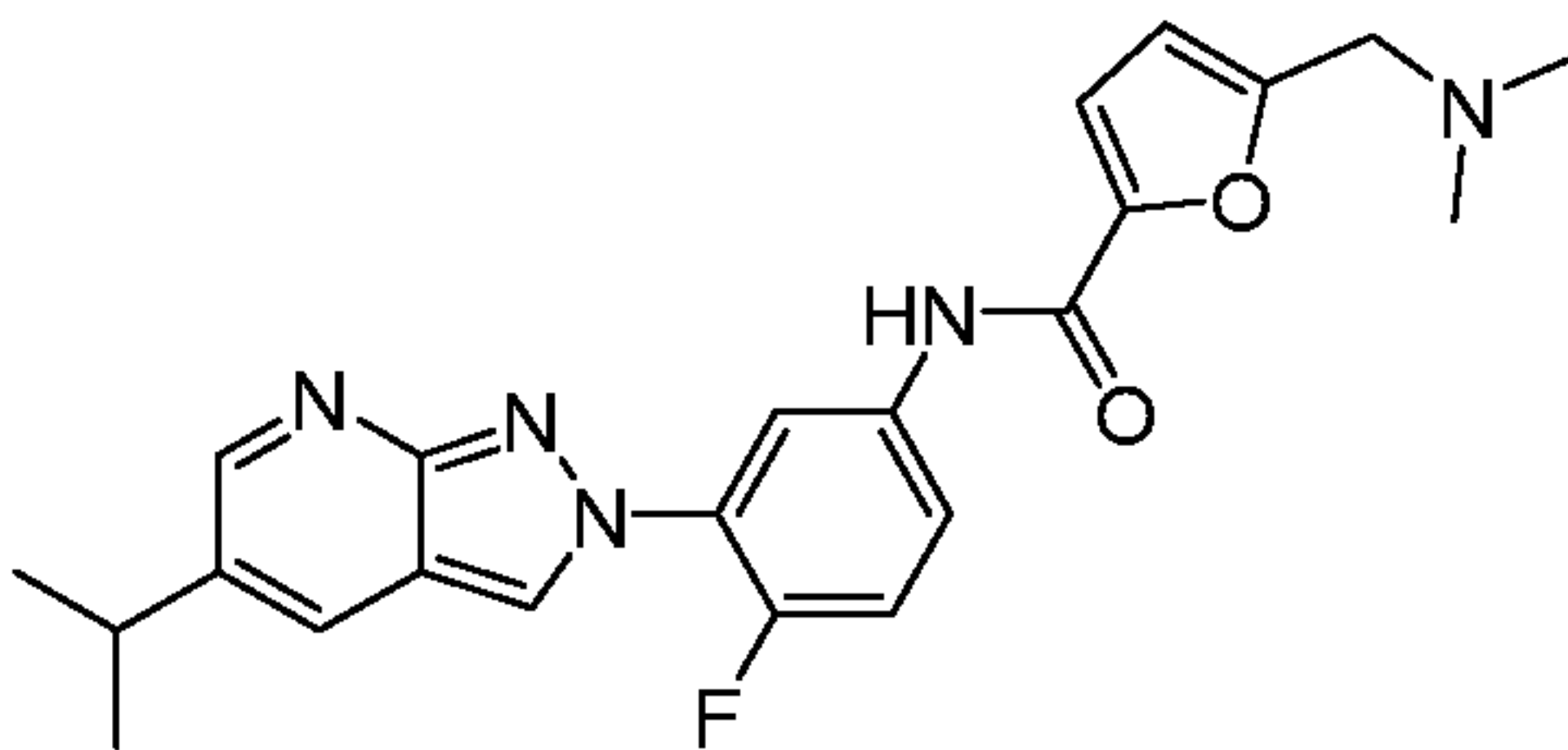
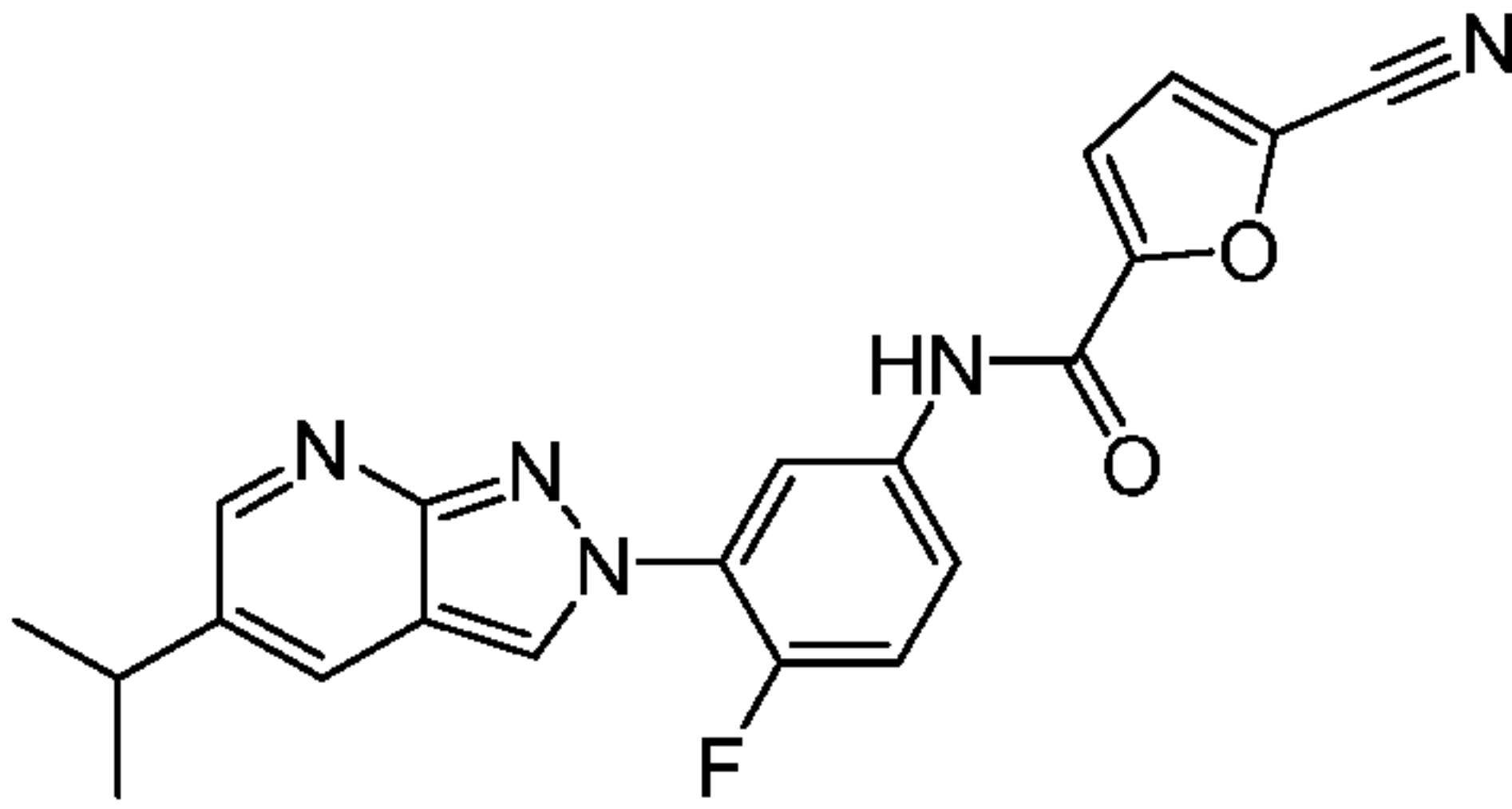
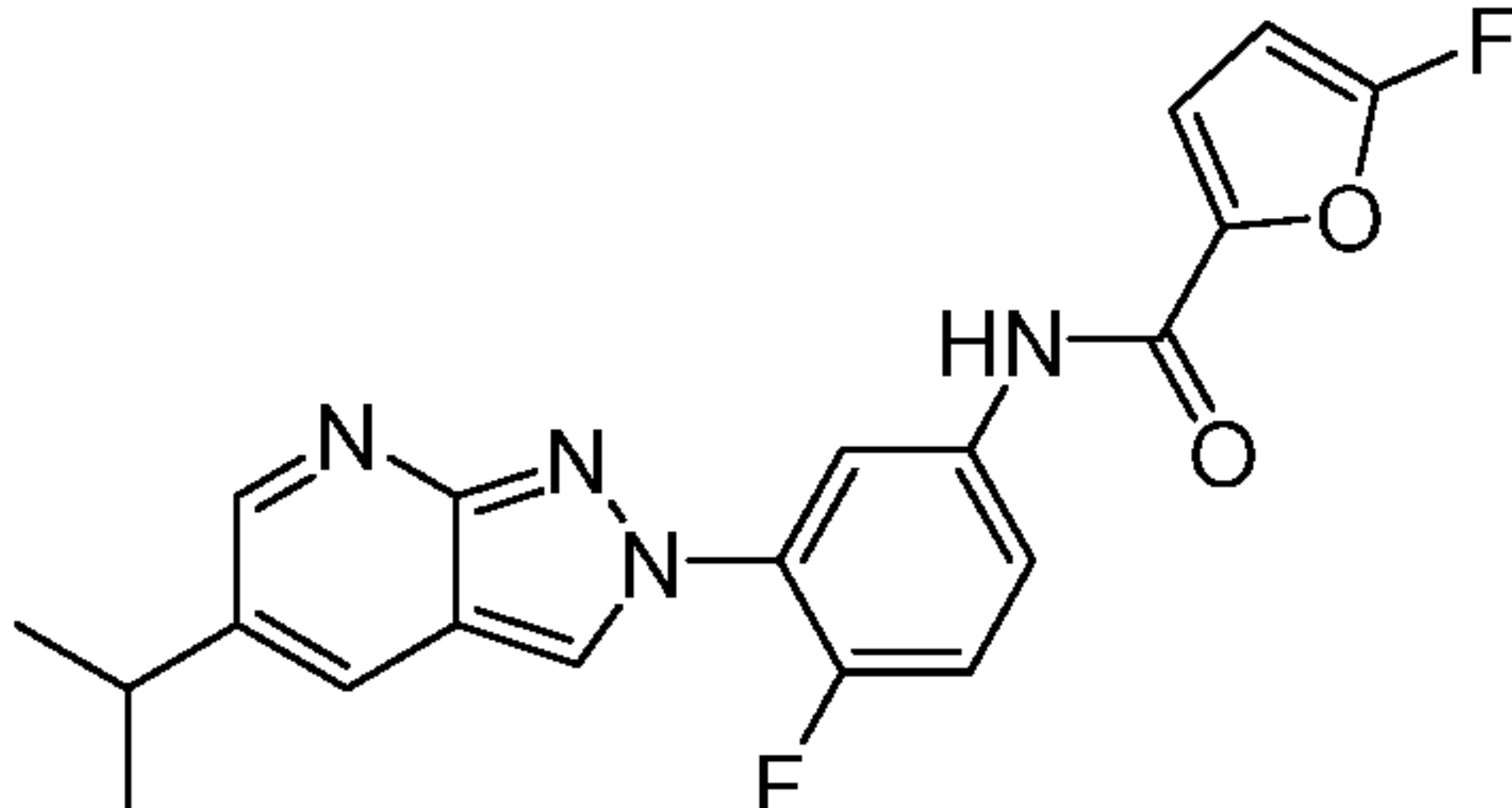
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
79		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.66 (m, 1H), 8.43 (m, 1H), 8.13 (m, 1H), 7.89 (m, 1H), 7.45 (m, 1H), 4.61 (s, 2H), 3.14 (m, 1H), 2.50 (s, 3H), 1.49 – 1.34 (2s, 6H), 1.34 – 1.20 (s, 9H). Method 1: RT = 3.36 min.; M+H = 466.4
80		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.66 (m, 1H), 8.36 (m, 1H), 8.13 (m, 1H), 7.80 (m, 1H), 7.41 (m, 1H), 4.16 (m, 1H), 3.97 (m, 1H), 3.60 (m, 1H), 3.13 (m, 1H), 2.12 – 2.04 (m, 1H), 2.01 – 1.92 (m, 1H), 1.75 – 1.49 (m, 4H), 1.38 (2s, 6H). Method 1: RT = 3.17 min.; M+H = 383.3
81		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.74 – 8.68 (m, 1H), 8.68 – 8.63 (m, 1H), 8.49 – 8.44 (m, 1H), 8.16 – 8.09 (m, 1H), 7.95 – 7.87 (m, 1H), 7.50 – 7.39 (m, 1H), 3.21 – 3.06 (m, 1H), 2.39 (s, 3H), 2.19 (s, 3H), 1.38 (2s, 6H). Method 1: RT = 3.18 min.; M+H = 394.3
82		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.76 – 8.69 (m, 2H), 8.67 (m, 1H), 8.59 (m, 1H), 8.24 (m, 1H), 8.14 (m, 1H), 8.07 – 7.96 (m, 2H), 7.62 (m, 1H), 7.47 (m, 1H), 3.14 (m, 1H), 1.57 – 1.21 (2s, 6H). Method 1: RT = 3.18 min.; M+H = 376.3
83		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.74 – 8.69 (m, 1H), 8.68 – 8.63 (m, 1H), 8.46 – 8.40 (m, 1H), 8.16 – 8.11 (m, 1H), 7.94 – 7.87 (m, 1H), 7.79 – 7.75 (m, 1H), 7.50 – 7.41 (m, 1H), 3.21 – 3.07 (m, 1H), 2.59 (s, 3H), 1.39 (2s, 6H). Method 1: RT = 3.01 min.; M+H = 380.3

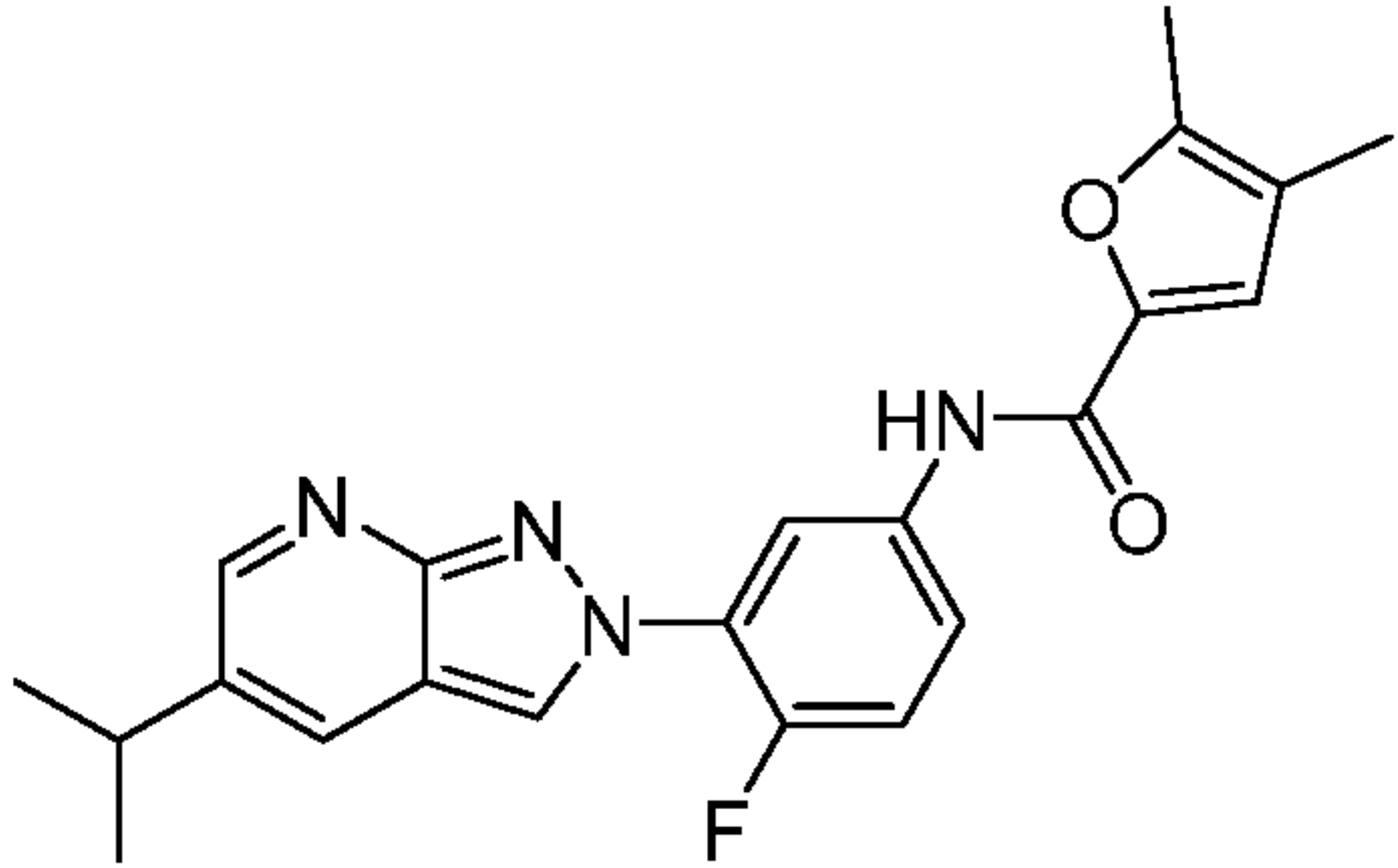
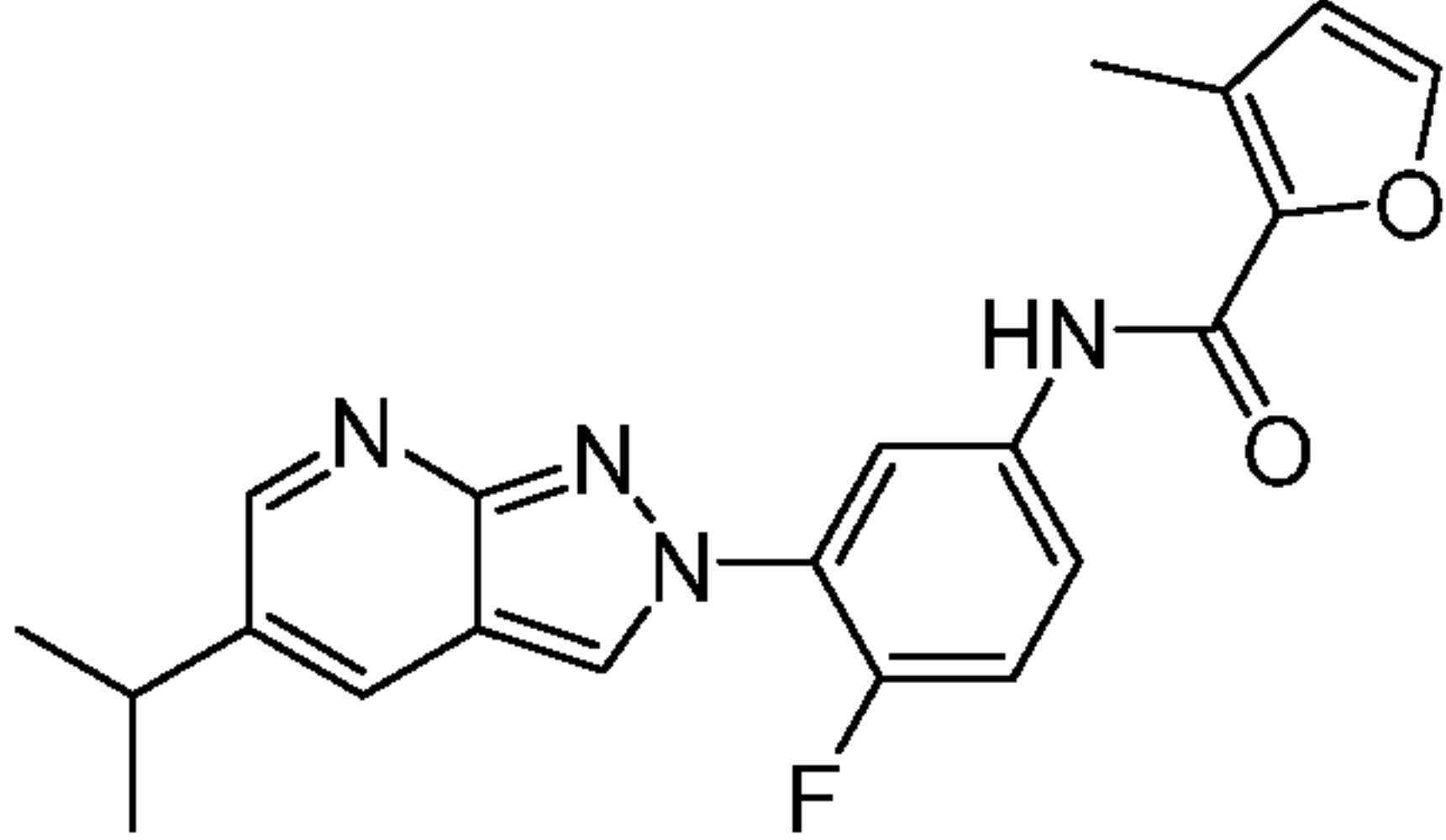
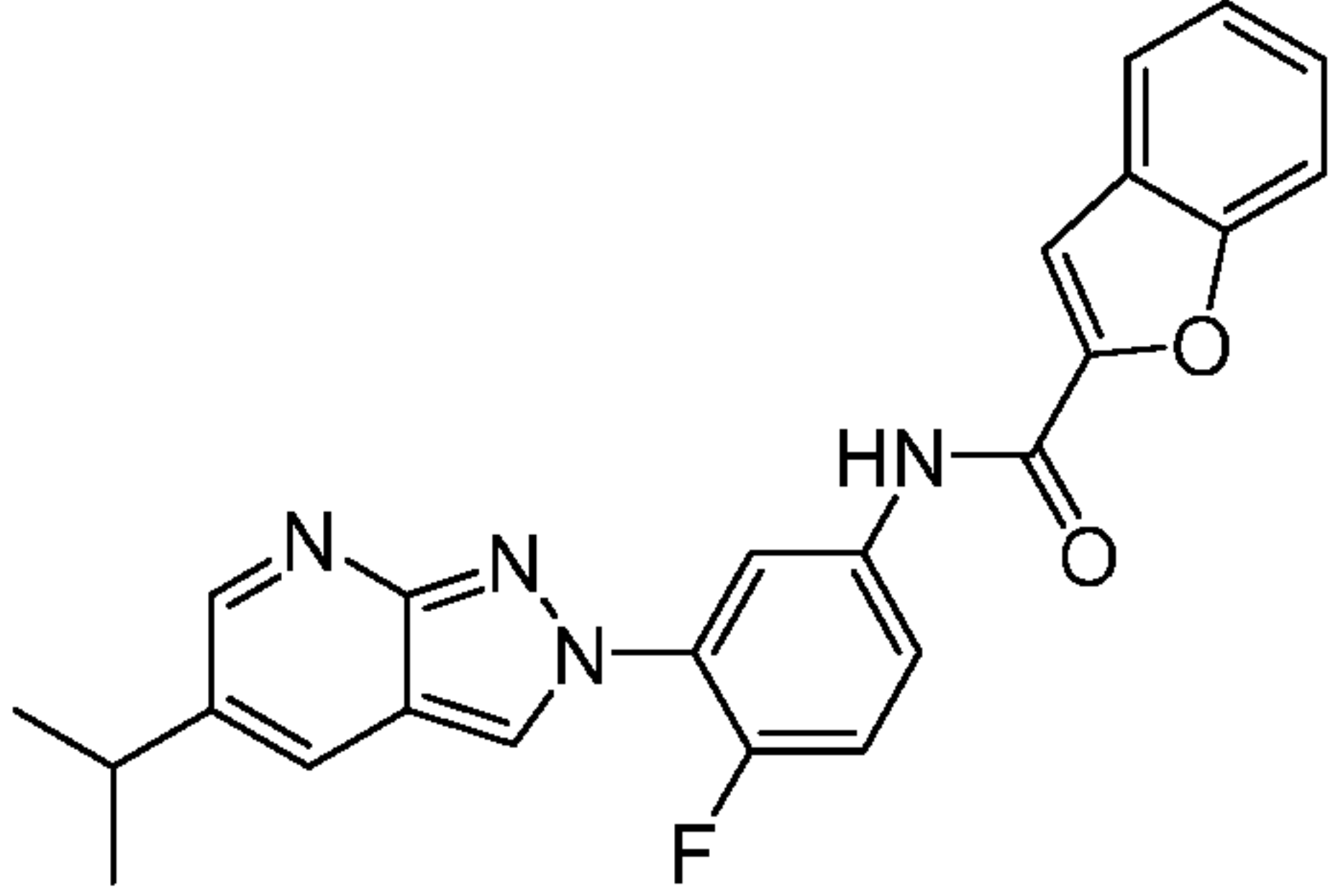
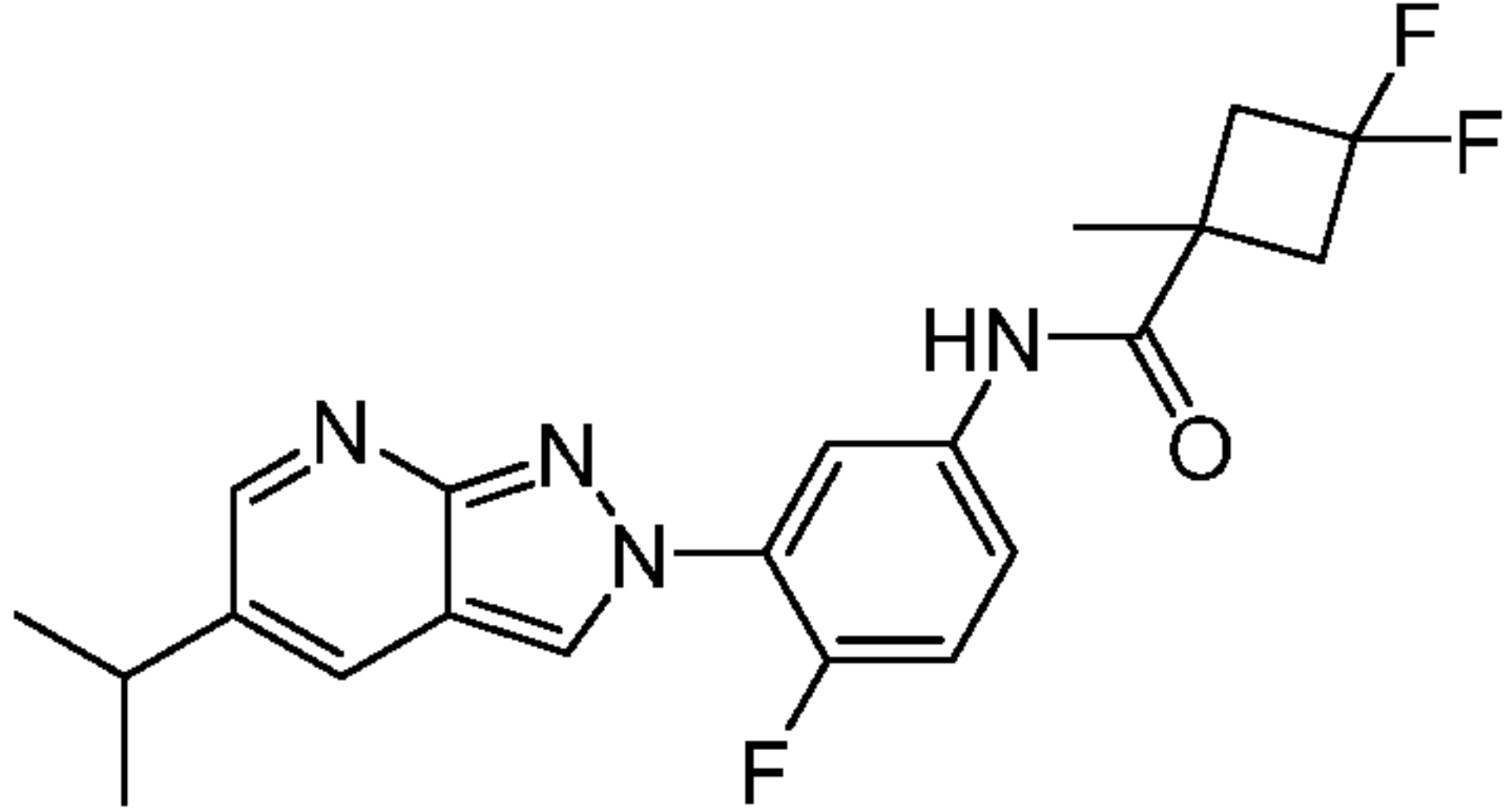
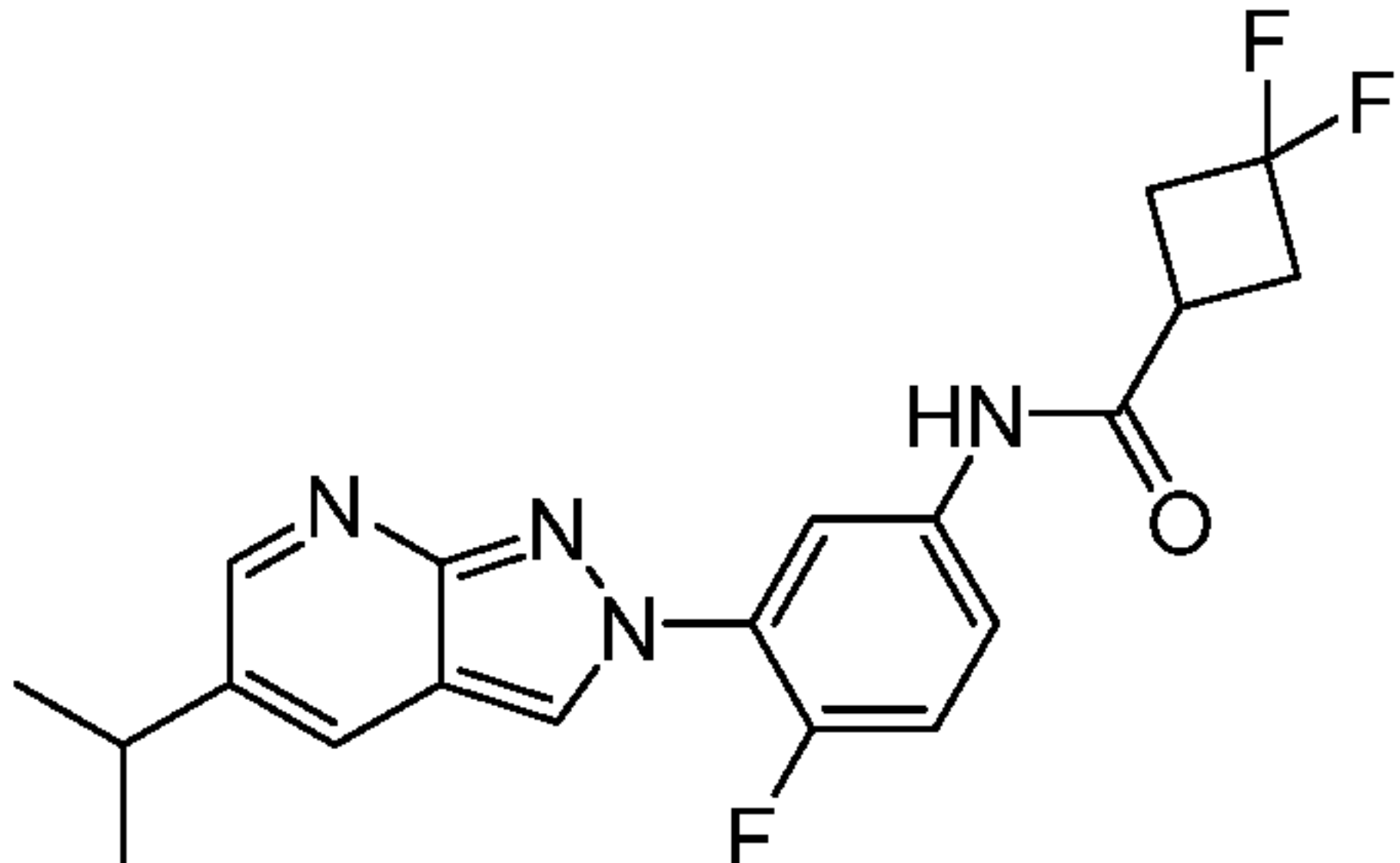
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
84		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.06 (m, 1H), 8.73 (m, 1H), 8.67 (m, 1H), 8.60 (m, 1H), 8.45 – 8.34 (m, 2H), 8.17 – 8.12 (m, 1H), 8.01 (m, 1H), 7.48 (m, 1H), 3.14 (m, 1H), 1.39 (2s, 6H). Method 1: RT = 3.15 min.; M+H = 401.3
85		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.66 (m, 1H), 8.47 (m, 1H), 8.41 (m, 1H), 8.14 (m, 1H), 7.90 (m, 1H), 7.45 (m, 1H), 3.14 (m, 1H), 1.39 (2s, 6H). Method 1: RT = 3.08 min.; M+H = 380.3
86		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.73 (m, 1H), 8.67 (m, 1H), 8.51 (m, 1H), 8.14 (m, 1H), 7.95 (m, 1H), 7.86 (m, 1H), 7.73 (m, 1H), 7.48 (m, 1H), 3.20 – 3.08 (m, 1H), 1.45 – 1.20 (2s, 6H). Method 1: RT = 3.22 min.; M+H = 428.3
87		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.36 (m, 1H), 8.84 (m, 1H), 8.76 (m, 1H), 8.72 (m, 1H), 8.66 (m, 1H), 8.57 (m, 1H), 8.13 (m, 1H), 7.99 (m, 1H), 7.46 (m, 1H), 3.13 (m, 1H), 1.38 (2s, 6H). Method 1: RT = 3.05 min.; M+H = 377.3
88		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.66 (m, 1H), 8.36 (m, 1H), 8.12 (m, 1H), 7.81 (m, 1H), 7.41 (m, 1H), 4.46 (m, 1H), 4.12 (m, 1H), 3.94 (m, 1H), 3.13 (m, 1H), 2.36 (m, 1H), 2.10 (m, 1H), 1.97 (m, 2H), 1.38 (2s, 6H). Method 1: RT = 2.93 min.; M+H = 369.3
89		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.73 (m, 1H), 8.66 (m, 1H), 8.43 (m, 1H), 8.14 (m, 1H), 7.92 - 7.85 (m, 1H), 7.76 (m, 1H), 7.59 (m, 1H), 7.46 (m, 1H), 7.30 (m, 1H), 3.14 (m, 1H), 1.38 (d, J = 6.9 Hz, 6H). Method 1: RT = 3.35 min.; M+H = 427.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
90		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.65 (m, 1H), 8.28 (m, 1H), 8.13 (m, 1H), 7.74 (m, 1H), 7.39 (m, 1H), 3.13 (m, 1H), 1.79 (m, 1H), 1.38 (2s, 6H), 1.01 – 0.84 (m, 4H). Method 1: RT = 3.07 min.; M+H = 339.3
91		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.64 – 8.57 (m, 2H), 8.14 – 8.09 (m, 1H), 7.94 – 7.89 (m, 1H), 7.66 – 7.59 (m, 1H), 7.36 – 7.29 (m, 1H), 4.17 – 4.05 (m, 4H), 2.39 – 2.26 (m, 2H), 2.17 – 2.06 (m, 1H), 1.13 – 1.04 (m, 2H), 0.87 – 0.77 (m, 2H). Method 1: RT = 2.82 min.; M+H = 352.3
92		, ¹ H NMR (400 MHz, DMSO) δ 8.69 (s, 1 H), 8.62 (d, <i>J</i> = 2.64 Hz, 1 H), 8.36 (d, <i>J</i> = 2.76 Hz, 1 H), 8.22 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.65 - 7.72 (m, 1 H), 7.42 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 7.15 (d, <i>J</i> = 2.89 Hz, 1 H), 4.41 (t, <i>J</i> = 12.23 Hz, 4 H), 3.98 (t, <i>J</i> = 7.53 Hz, 4 H), 2.20 (quin, <i>J</i> = 7.56 Hz, 2 H). Method 1: RT = 2.81 min. M+H = 403.2,
93		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.76 – 8.65 (m, 1H), 8.64 – 8.58 (m, 1H), 8.14 – 8.06 (m, 1H), 7.67 – 7.60 (m, 1H), 7.38 – 7.30 (m, 1H), 7.18 – 7.01 (m, 1H), 4.17 – 3.96 (m, 4H), 3.84 – 3.69 (m, 1H), 2.62 – 2.09 (m, 7H), 2.04 – 1.93 (m, 1H). Method 1: RT = 2.94 min.; M+H = 366.3
94		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 – 8.66 (m, 1H), 8.56 – 8.50 (m, 1H), 8.15 – 8.09 (m, 1H), 8.09 – 8.04 (m, 1H), 7.68 – 7.60 (m, 1H), 7.38 – 7.30 (m, 1H), 4.18 – 4.04 (m, 4H), 2.69 (s, 2H), 2.40 – 2.27 (m, 2H), 0.99 (s, 9H). Method 1: RT = 3.19 min.; M+H = 382.4
95		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 – 8.64 (m, 1H), 8.62 – 8.56 (m, 1H), 8.15 – 8.05 (m, 2H), 7.67 – 7.61 (m, 1H), 7.37 – 7.30 (m, 1H), 4.17 – 4.05 (m, 4H), 2.84 – 2.75 (m, 2H), 2.39 – 2.26 (m, 2H), 1.80 – 1.66 (m, 2H), 1.48 – 1.34 (m, 4H), 1.01 – 0.87 (m, 3H). Method 1: RT = 3.22 min.; M+H = 382.4

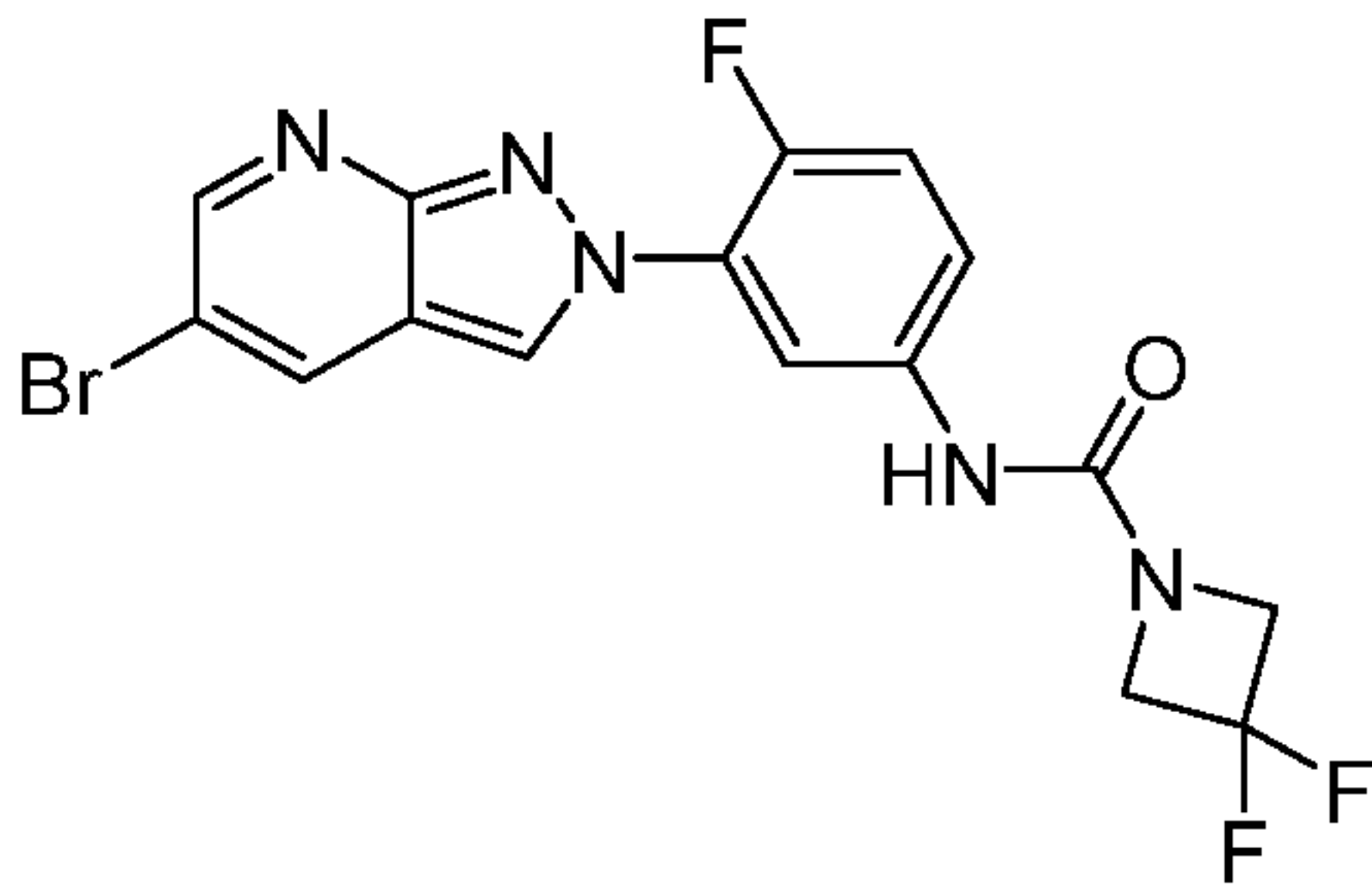
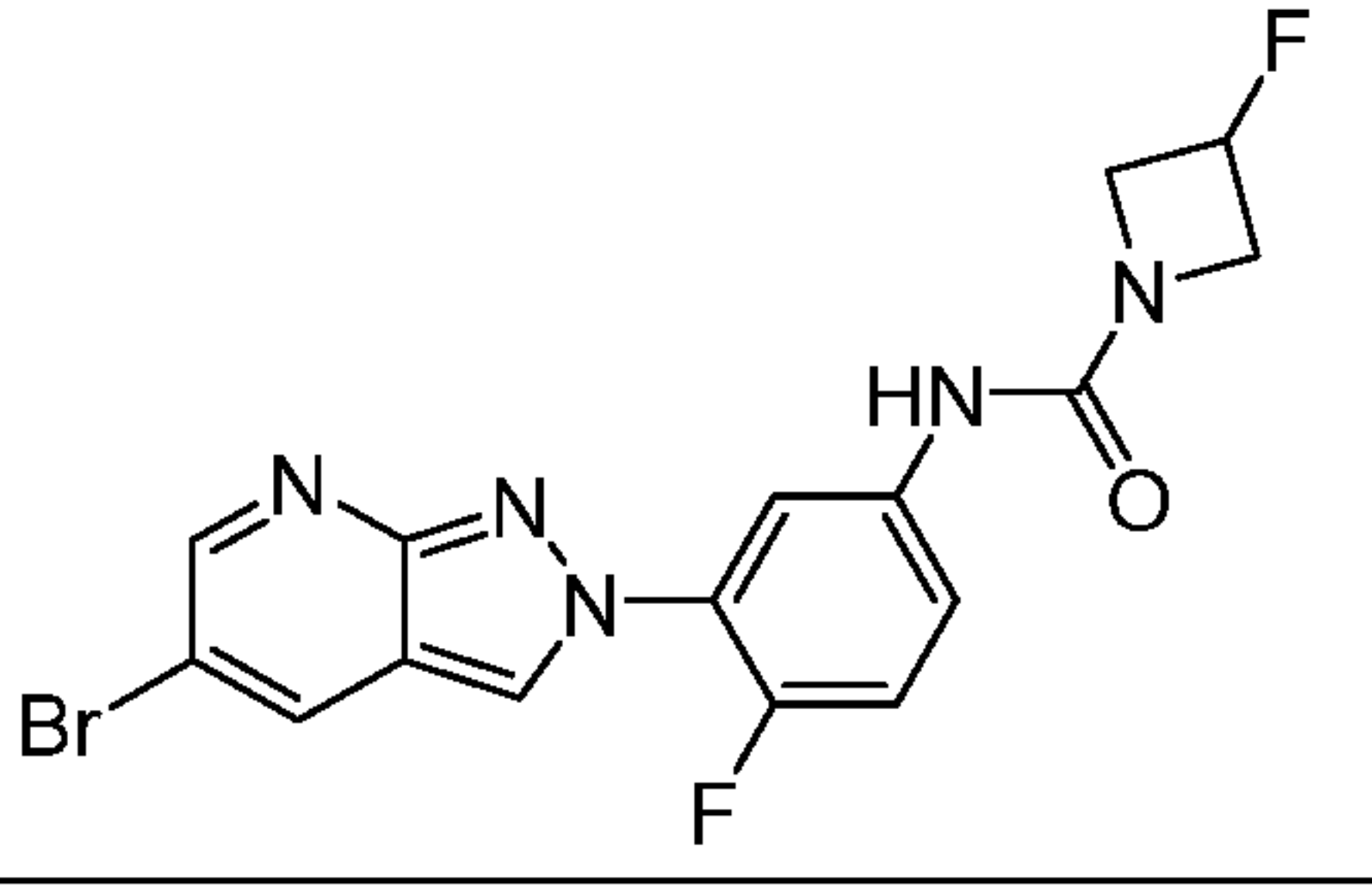
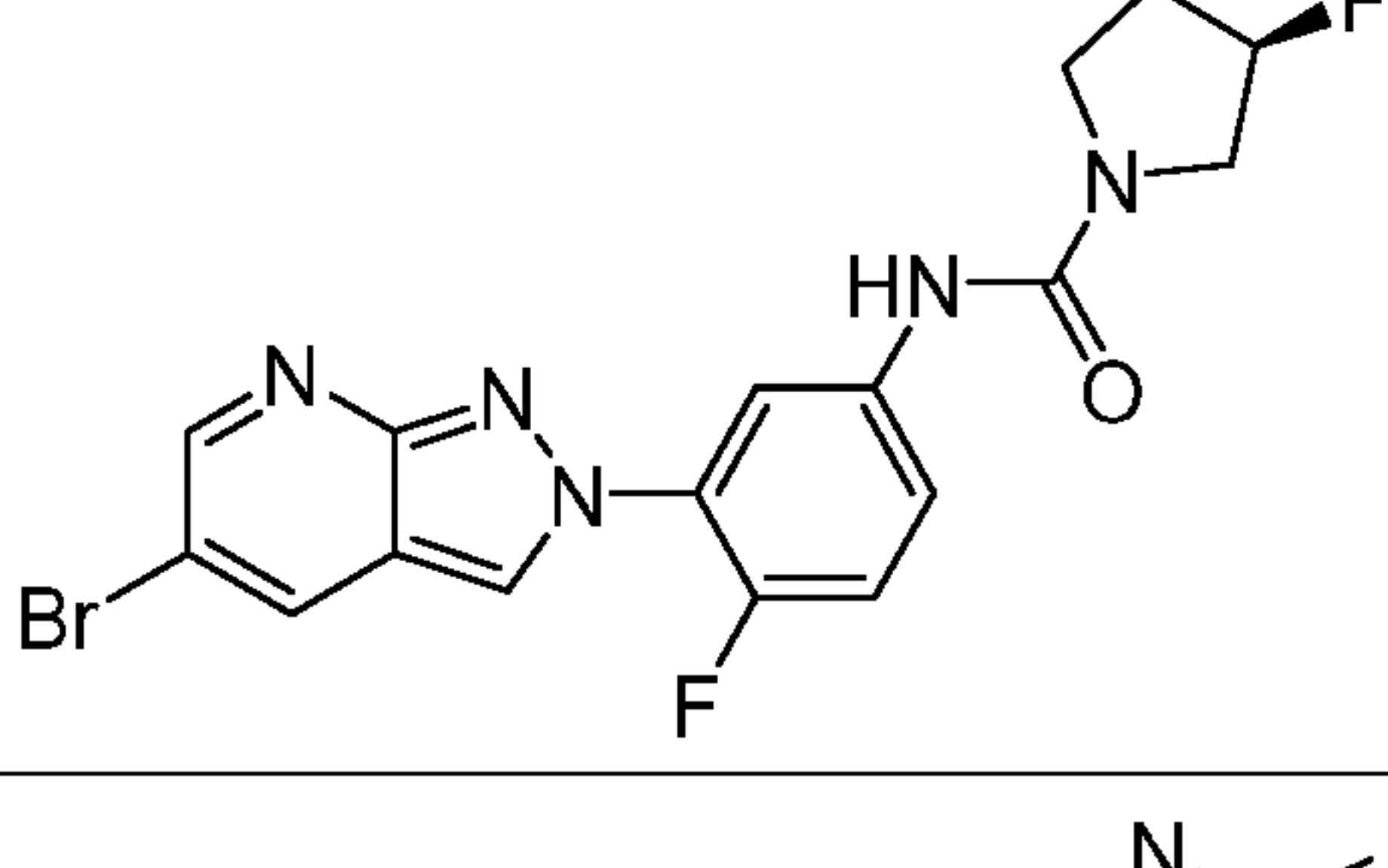
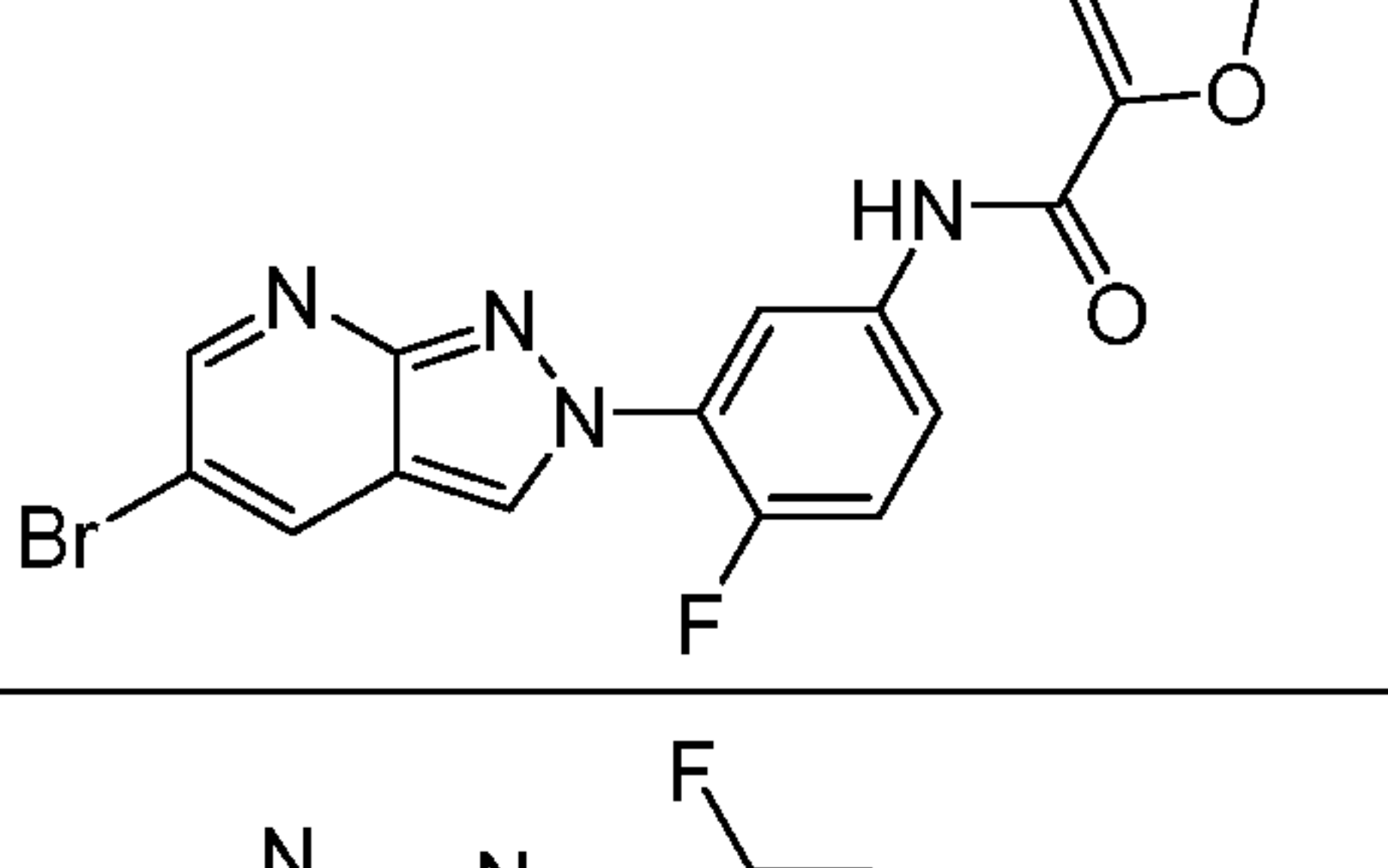
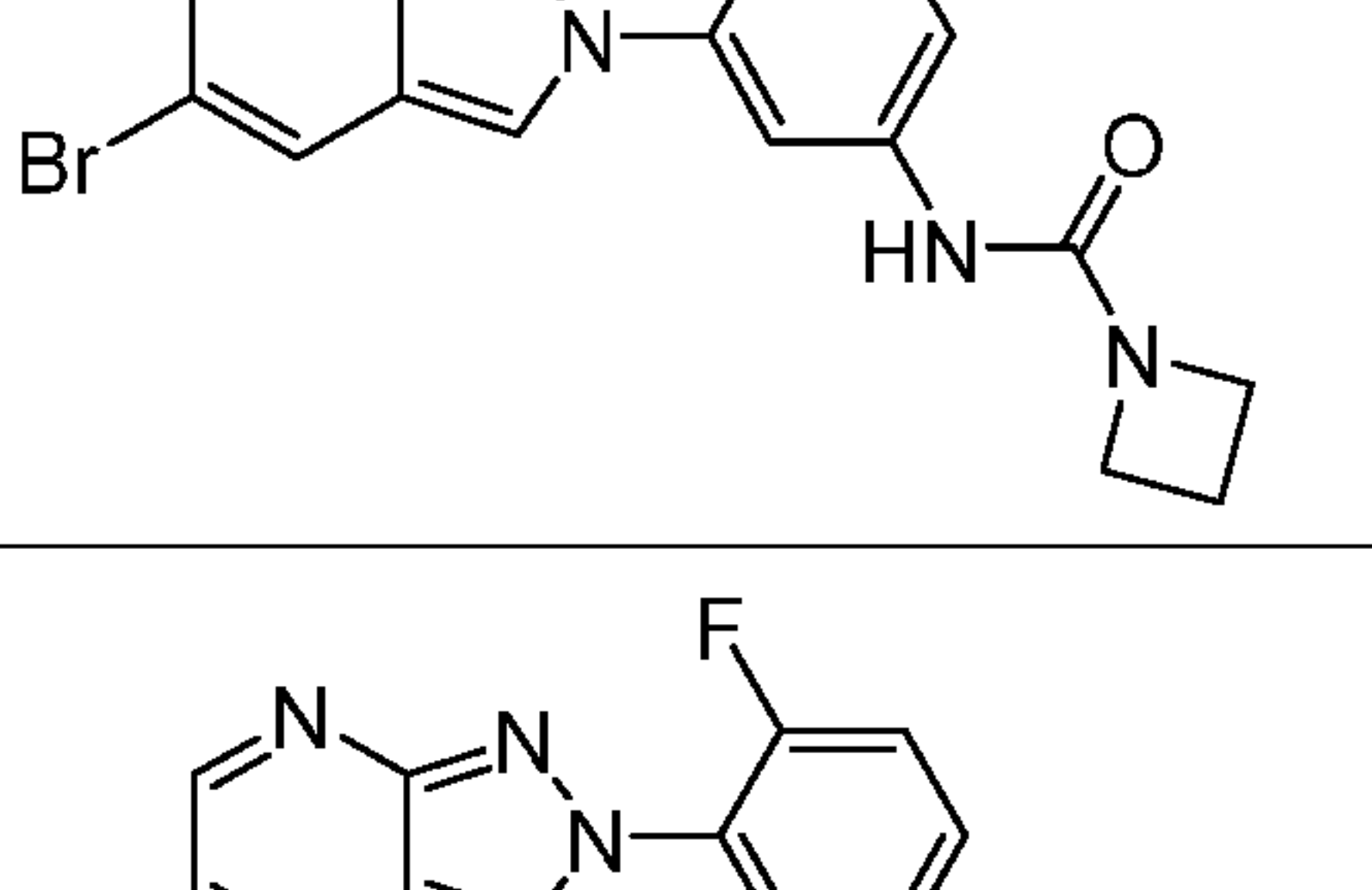
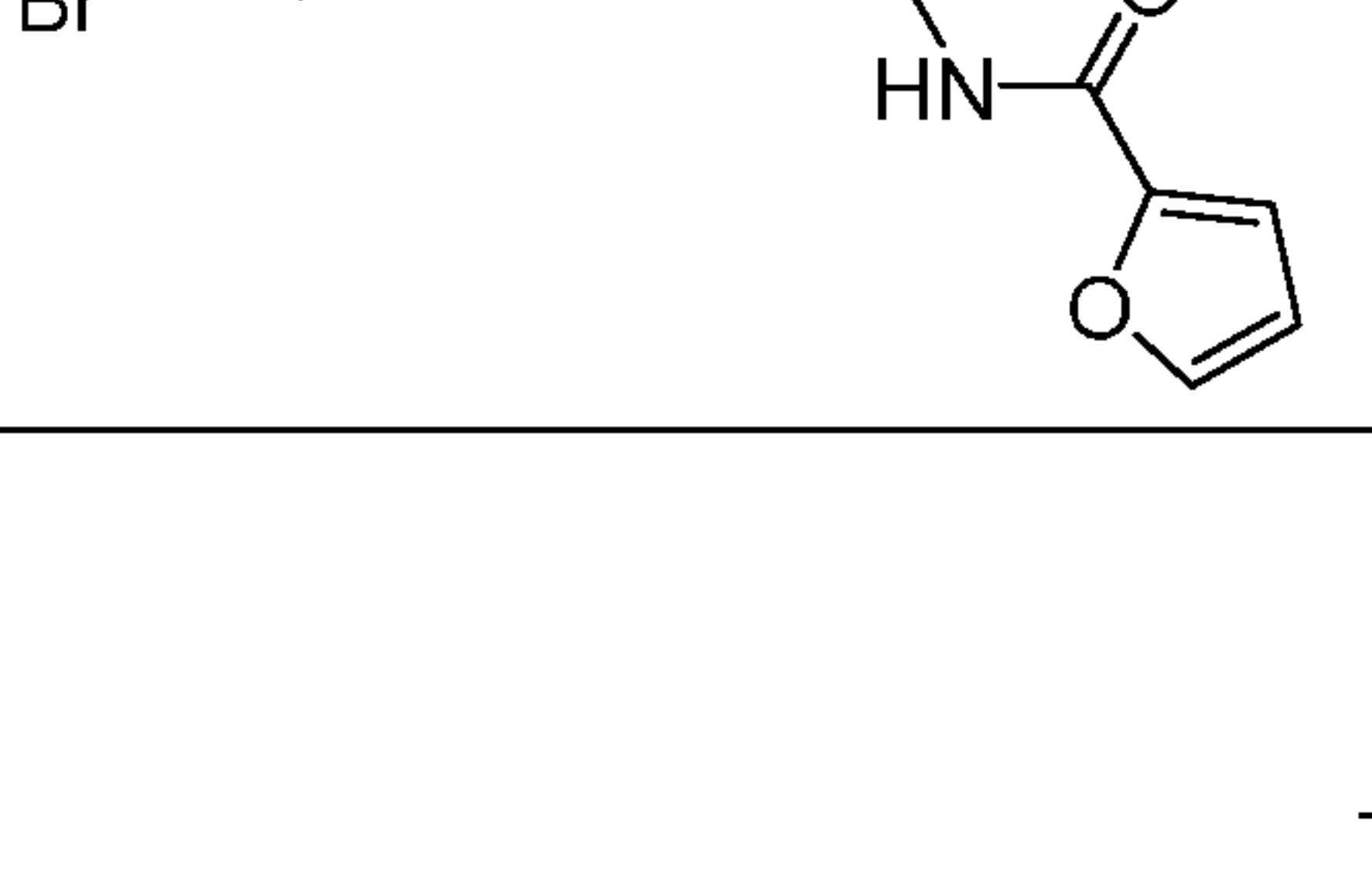
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
96		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.65 (m, 1H), 8.59 (m, 1H), 8.15 – 8.06 (m, 2H), 7.64 (m, 1H), 7.34 (m, 1H), 4.17 – 4.05 (m, 4H), 2.85 – 2.76 (m, 2H), 2.32 (m, 2H), 1.78 – 1.64 (m, 2H), 1.43 (m, 3H), 1.00 (m, 3H). Method 1: RT = 3.13 min.; M+H = 368.3
97		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 – 8.62 (m, 1H), 8.63 – 8.52 (m, 1H), 8.14 – 8.07 (m, 1H), 8.07 – 8.01 (m, 1H), 7.64 (m, 1H), 7.33 (m, 1H), 4.19 – 4.04 (m, 4H), 2.87 (m, 2H), 2.68 (m, 1H), 2.39 – 2.27 (m, 2H), 2.16 – 2.03 (m, 2H), 1.99 – 1.76 (m, 4H). Method 1: RT = 3.11 min.; M+H = 380.3
98		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.65 (m, 1H), 8.57 (m, 1H), 8.15 – 8.02 (m, 2H), 7.64 (m, 1H), 7.33 (m, 1H), 4.18 – 4.01 (m, 4H), 2.92 – 2.69 (m, 2H), 2.32 (m, 2H), 1.84 – 1.53 (m, 3H), 1.06 – 0.89 (m, 6H). Method 1: RT = 3.18 min.; M+H = 382.4
99		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.37 (m, 1H), 8.87 (m, 2H), 8.70 (m, 1H), 8.17 (m, 1H), 8.05 – 7.92 (m, 2H), 7.66 (m, 1H), 7.43 (m, 1H), 7.36 (m, 1H), 4.17 – 4.07 (m, 4H), 2.33 (m, 2H). Method 1: RT = 2.66 min.; M+H = 389.3
100		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.78 (d, J=2.63 Hz, 1 H), 8.73 (s, 1 H), 8.68 (d, J=2.38 Hz, 1 H), 8.24 (dd, J=7.03, 2.76 Hz, 1 H), 8.05 (d, J=1.88 Hz, 1 H), 7.66 - 7.73 (m, 1 H), 7.44 (dd, J=11.29, 9.16 Hz, 1 H), 3.98 (t, J=7.59 Hz, 4 H), 3.02 - 3.14 (m, 1 H), 2.10 - 2.27 (m, 2 H), 1.30 (d, J=6.90 Hz, 6 H). Method 2: RT = 0.94 min.; M+H = 354.1
101		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.07 (m, 1H), 8.79 (m, 1H), 8.49 (m, 1H), 7.87 (m, 1H), 7.52 – 7.43 (m, 1H), 7.36 – 7.29 (m, 1H), 2.69 – 2.56 (m, 2H), 2.55 (m, 3H), 2.46 (m, 3H), 2.34 – 2.12 (m, 3H), 2.07 – 1.93 (m, 2H). Method 1: RT = 3.08 min.; M+H = 406.3

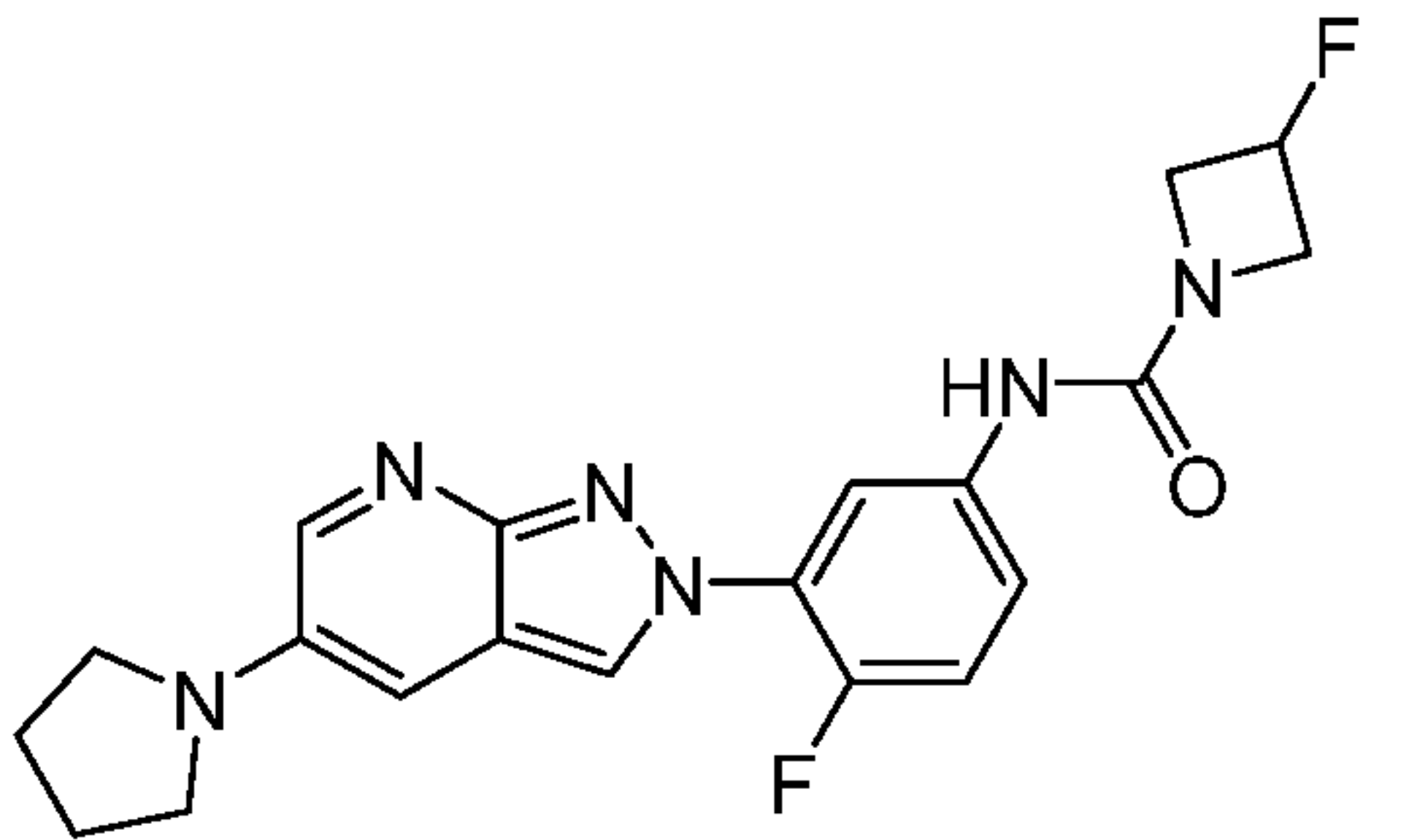
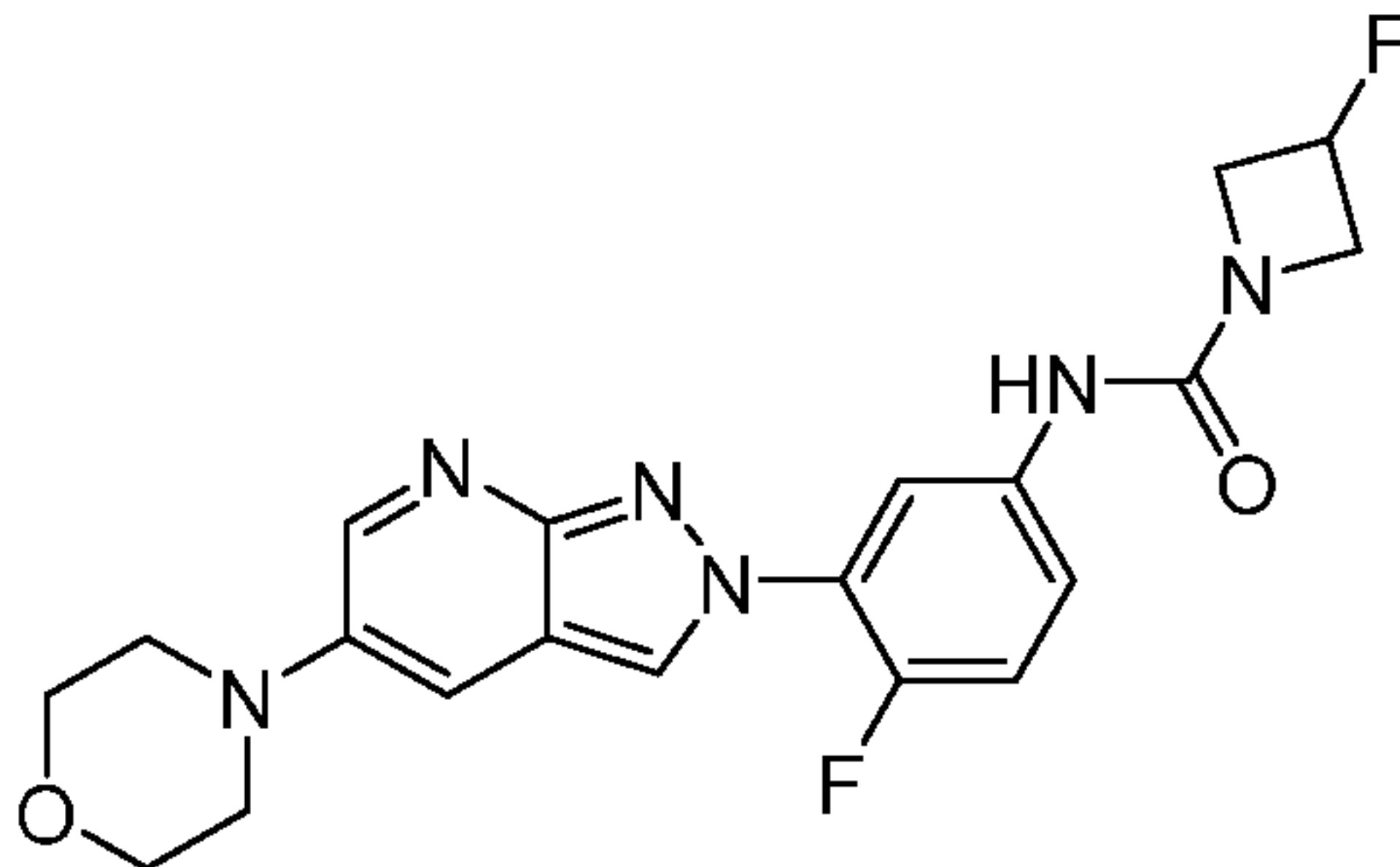
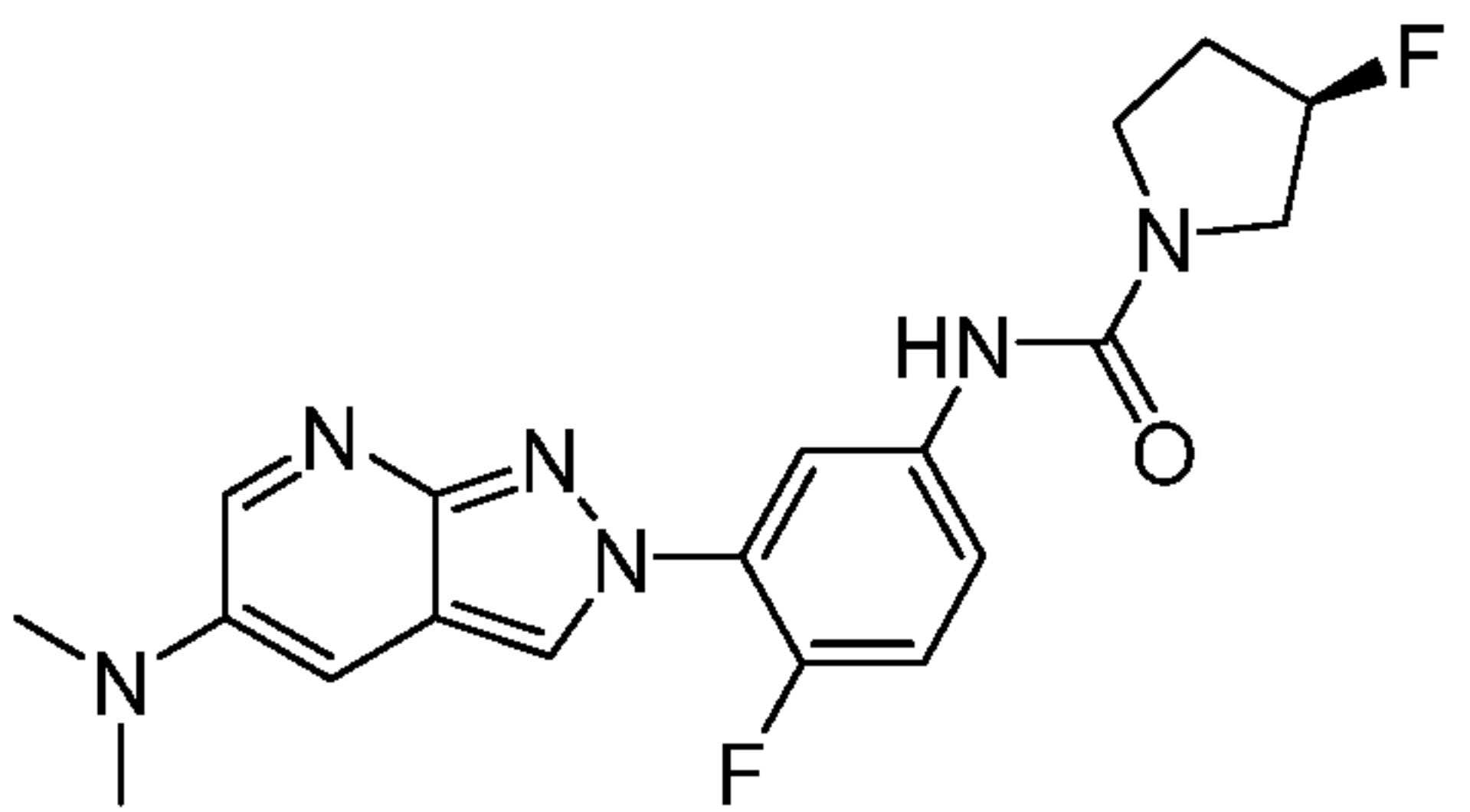
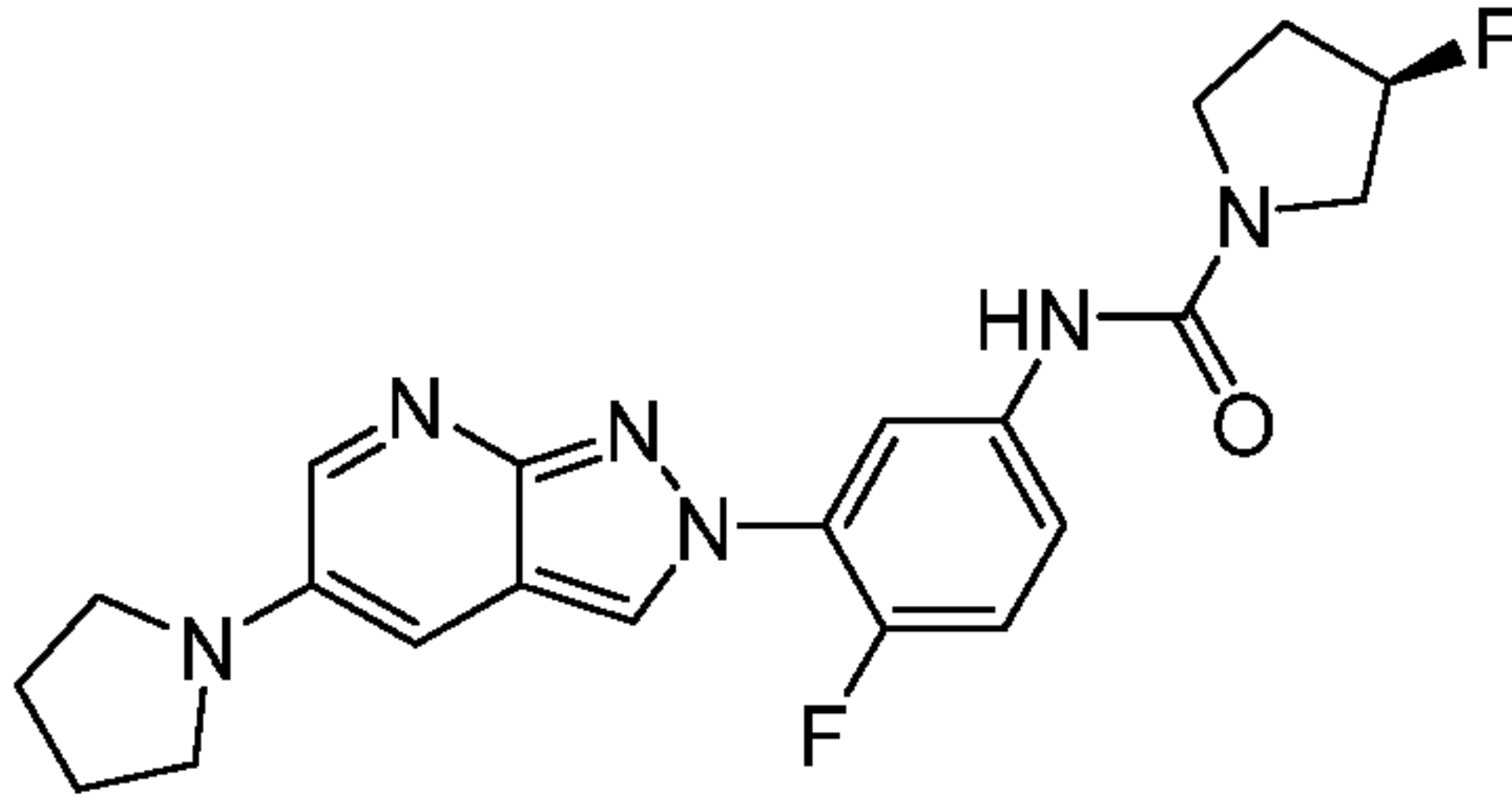
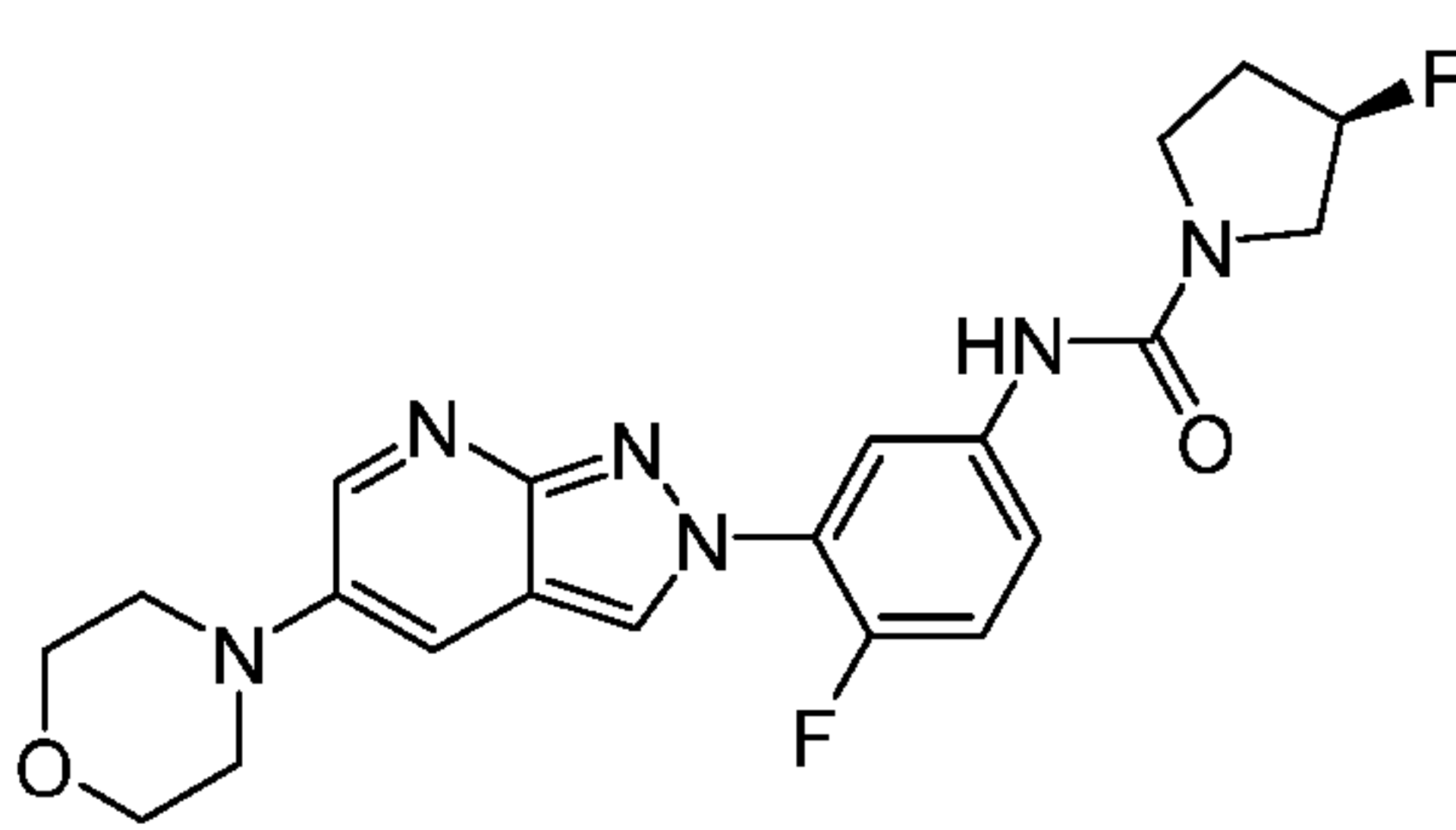
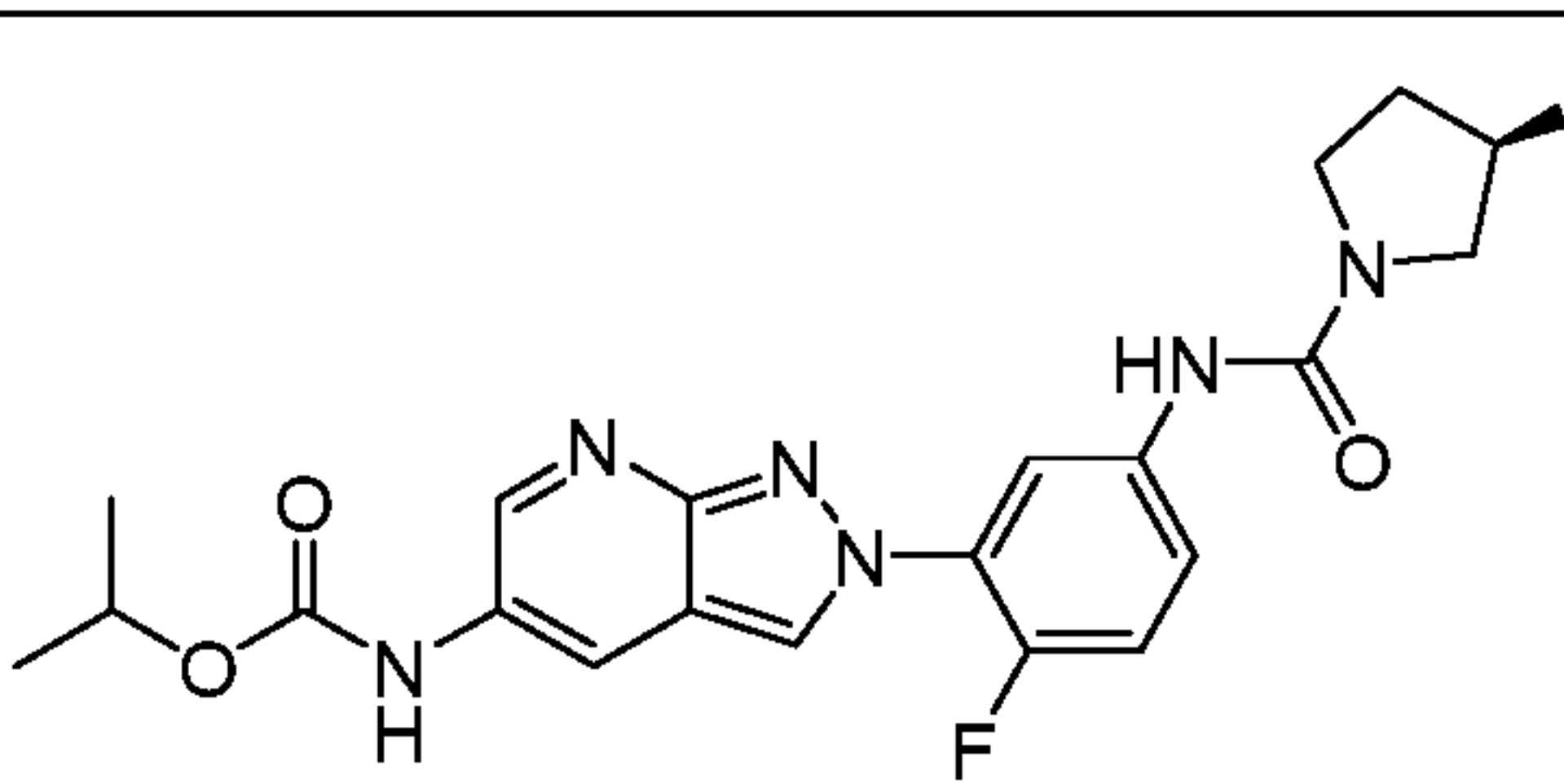
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
102		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.83 (m, 1H), 8.62 (m, 1H), 8.48 (m, 1H), 8.25 – 8.20 (m, 1H), 7.92 – 7.86 (m, 1H), 7.50 – 7.43 (m, 1H), 2.73 (s, 2H), 2.55 (m, 3H), 2.46 (m, 3H), 1.00 (m, 9H). Method 1: RT = 3.28 min.; M+H = 422.3
103		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.79 – 8.68 (m, 2H), 8.13 (m, 1H), 7.98 – 7.91 (m, 1H), 7.47 – 7.38 (m, 1H), 7.31 – 7.24 (m, 1H), 2.55 (m, 3H), 2.46 (m, 3H), 1.55 (m, 9H). Method 1: RT = 2.90 min.; M+H = 408.3
104		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.86 (m, 1H), 8.78 (m, 1H), 8.14 (m, 1H), 7.94 (m, 1H), 7.42 (m, 1H), 7.38 – 7.32 (m, 1H), 2.54 (m, 3H), 2.46 (m, 3H), 1.98 – 1.81 (m, 2H), 1.53 (s, 3H), 1.42 (s, 3H), 0.84 – 0.74 (m, 3H). Method 1: RT = 2.96 min.; M+H = 422.4
105		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.78 – 8.70 (m, 1H), 8.67 – 8.58 (m, 1H), 8.52 – 8.42 (m, 1H), 7.92 – 7.84 (m, 1H), 7.52 – 7.44 (m, 1H), 7.27 (m, 1H), 2.55 (m, 3H), 2.46 (m, 3H), 1.89 (m, 2H), 1.53 – 1.40 (m, 3H), 1.04 – 0.89 (m, 3H), 0.80 (m, 1H). Method 1: RT = 3.13 min.; M+H = 408.3
106		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.77 (m, 1H), 8.62 (m, 1H), 8.45 (m, 1H), 8.17 (m, 1H), 7.88 (m, 1H), 7.45 (m, 1H), 2.90 (m, 2H), 2.74 – 2.65 (m, 1H), 2.55 (s, 3H), 2.46 (s, 3H), 2.10 (m, 2H), 1.96 – 1.80 (m, 4H). Method 1: RT = 3.24 min.; M+H = 420.3
107		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.85 (m, 1H), 8.73 – 8.66 (m, 1H), 8.49 (m, 1H), 8.31 (m, 1H), 7.87 (m, 1H), 7.46 (m, 1H), 2.88 – 2.80 (m, 2H), 2.55 (s, 3H), 2.46 (s, 3H), 1.72 – 1.59 (m, 3H), 1.03 – 0.92 (m, 6H). Method 1: RT = 3.30 min.; M+H = 422.4

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
108		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 9.38 (m, 1H), 8.96 (m, 1H), 8.92 (m, 1H), 8.79 – 8.71 (m, 1H), 8.50 (m, 1H), 8.12 – 8.04 (m, 2H), 7.90 (m, 1H), 7.56 – 7.42 (m, 2H), 2.55 (m, 3H), 2.47 (m, 3H). Method 1: RT = 2.78 min.; M+H = 429.3
109		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.66 (m, 1H), 8.42 (m, 1H), 8.14 (dd, <i>J</i> = 2.2, 0.7 Hz, 1H), 7.91 (ddd, <i>J</i> = 9.1, 4.2, 2.7 Hz, 1H), 7.44 (dd, <i>J</i> = 11.0, 9.1 Hz, 1H), 7.21 (d, <i>J</i> = 3.4 Hz, 1H), 6.31 – 6.24 (m, 1H), 3.14 (p, <i>J</i> = 6.9 Hz, 1H), 2.44 (s, 3H), 1.49 – 1.29 (m, 6H). Method 2: RT = 1.07 min.; M+H = 379.3
110		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.66 (m, 1H), 8.38 (m, 1H), 8.14 (m, 1H), 7.87 (m, 1H), 7.43 (m, 1H), 7.29 (m, 1H), 5.57 (m, 1H), 4.02 – 3.89 (m, 3H), 3.18 – 3.10 (m, 1H), 1.39 (2s, 6H). Method 2: RT = 1.05 min.; M+H = 395.3
111		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.73 (m, 1H), 8.66 (m, 1H), 8.45 (m, 1H), 8.14 (m, 1H), 7.92 (m, 1H), 7.46 (m, 1H), 7.23 (m, 1H), 6.55 (m, 1H), 3.65 (s, 2H), 3.14 (m, 1H), 2.37 (2s, 6H), 1.47 - 1.31 (2s, 6H). Method 2: RT = 0.74 min.; M+H = 422.3
112		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.73 (m, 1H), 8.67 (m, 1H), 8.47 (m, 1H), 8.14 (m, 1H), 7.93 (m, 1H), 7.54 – 7.40 (m, 3H), 3.16 – 3.09 (m, 1H), 1.39 (2s, 6H). Method 2: RT = 1.08 min.; M+H = 390.3
113		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.67 (m, 1H), 8.40 (m, 1H), 8.14 (m, 1H), 7.89 (m, 1H), 7.45 (m, 1H), 7.31 (m, 1H), 5.90 (m, 1H), 3.19 – 3.10 (m, 1H), 1.39 (2s, 6H). Method 2: RT = 1.07 min.; M+H = 383.3

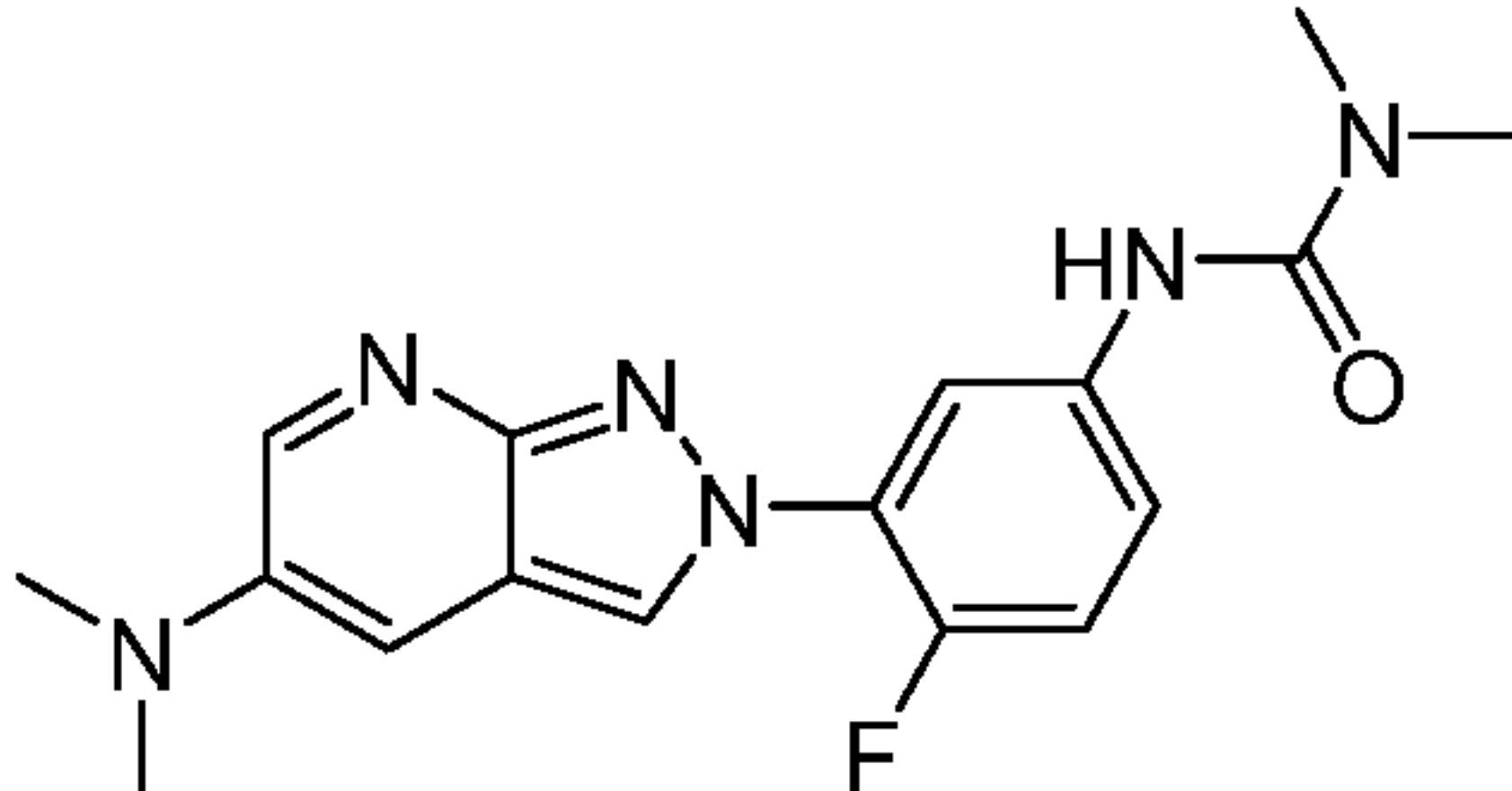
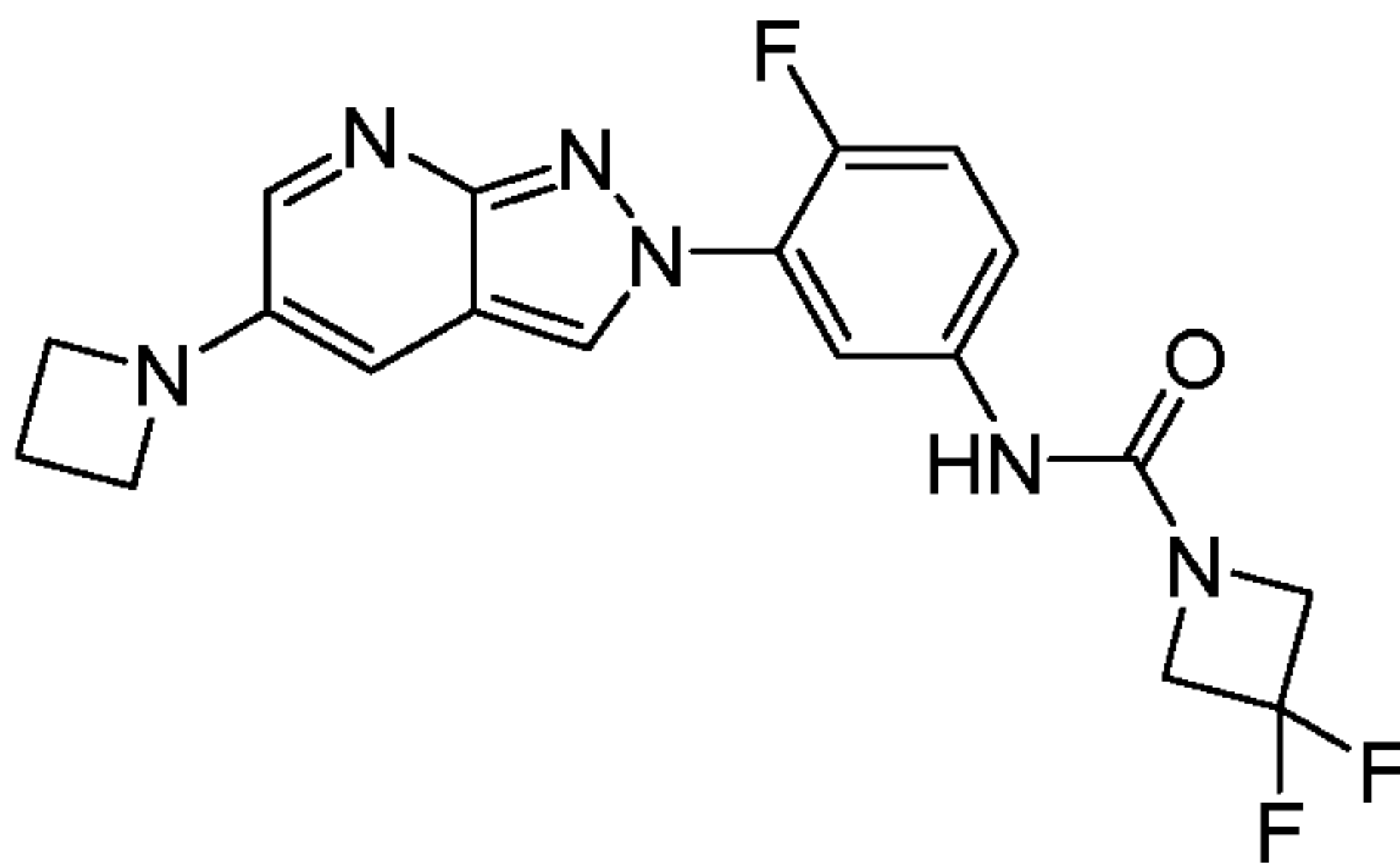
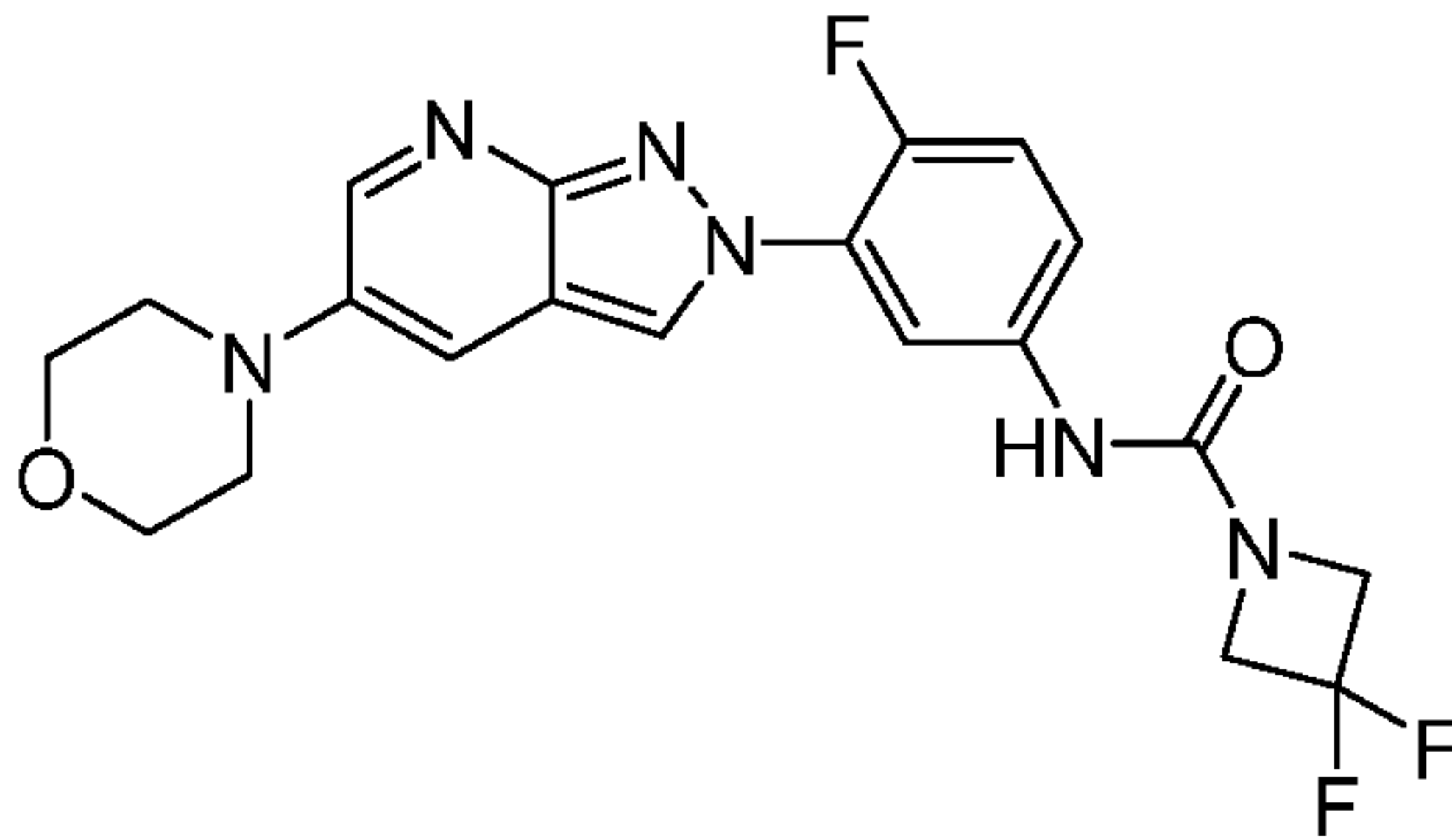
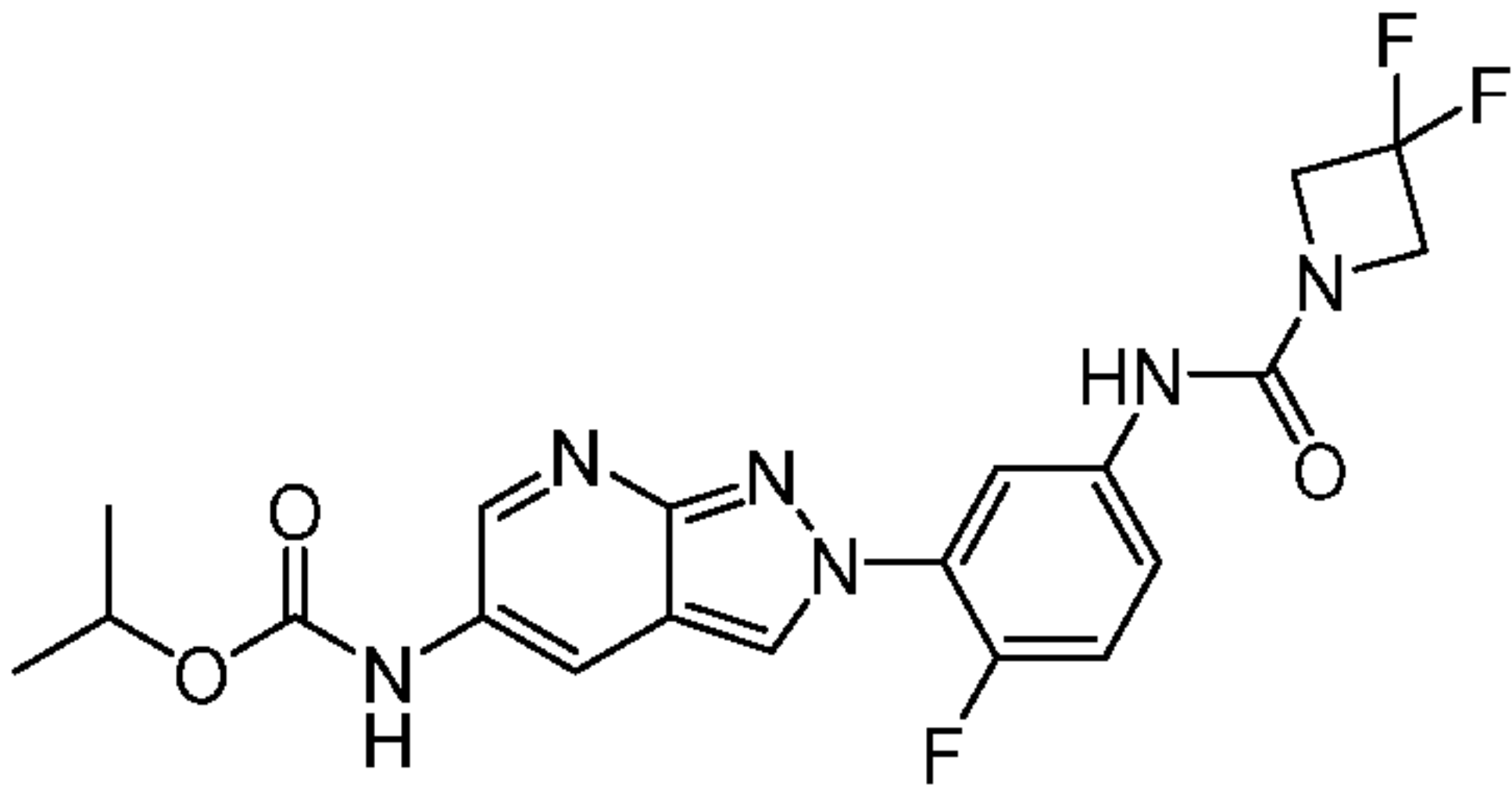
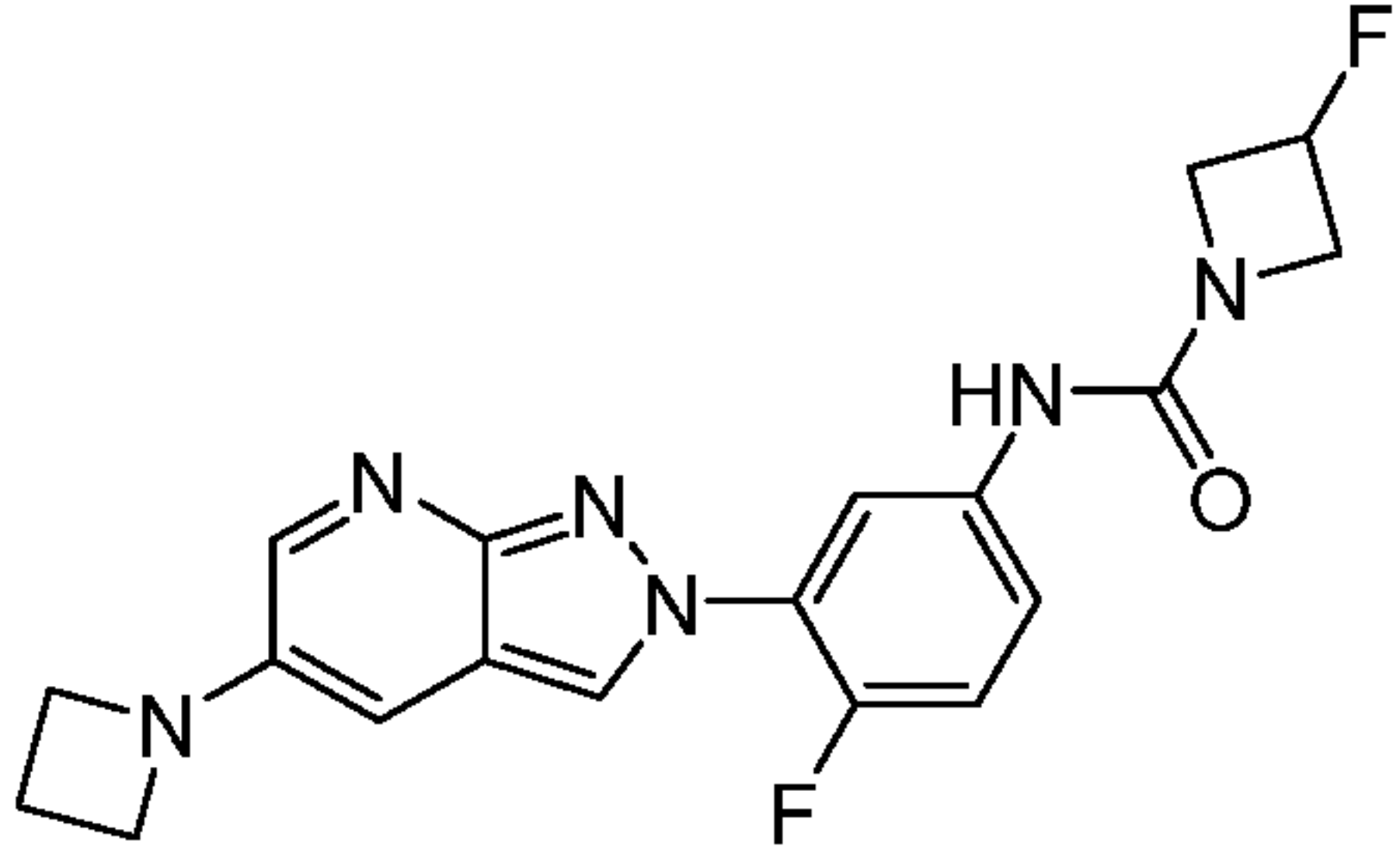
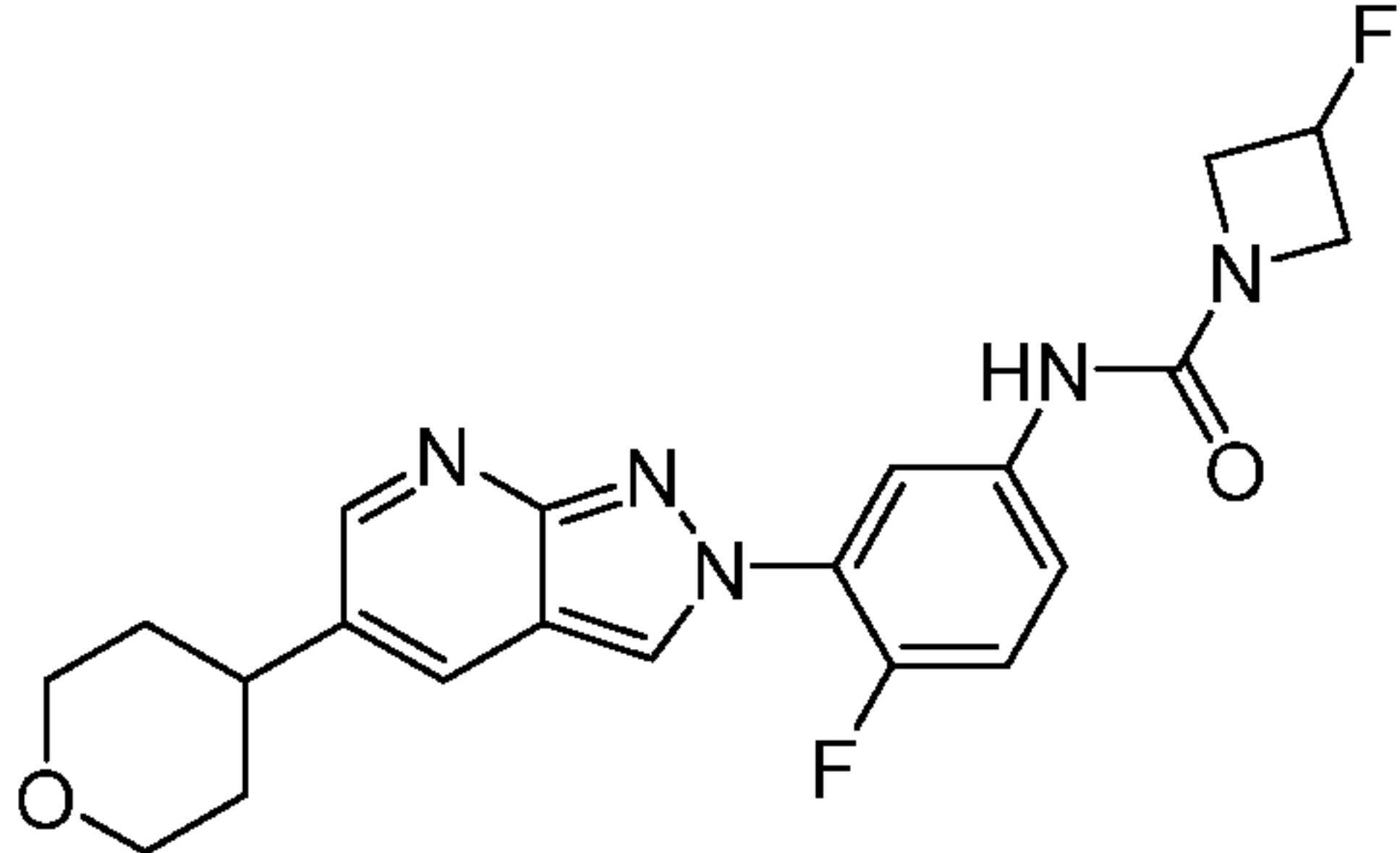
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
114		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.66 (m, 1H), 8.40 (m, 1H), 8.13 (m, 1H), 7.89 (m, 1H), 7.48 – 7.38 (m, 1H), 7.09 (m, 1H), 3.14 (m, 1H), 2.40 – 2.21 (m, 3H), 2.03 (m, 3H), 1.62 – 1.15 (2s, 6H). Method 2: RT = 1.13 min.; M+H = 393.3
115		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.71 (m, 1H), 8.66 (m, 1H), 8.42 (m, 1H), 8.13 (m, 1H), 7.87 (m, 1H), 7.60 (m, 1H), 7.42 (m, 1H), 6.51 (m, 1H), 3.14 (m, 1H), 2.41 (s, 3H), 1.44 – 1.26 (2s, 6H). Method 2: RT = 1.11 min.; M+H = 379.3
116		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.72 (m, 1H), 8.66 (m, 1H), 8.50 (m, 1H), 8.13 (m, 1H), 7.97 (m, 1H), 7.79 – 7.74 (m, 1H), 7.69 – 7.62 (m, 2H), 7.53 – 7.42 (m, 2H), 7.39 – 7.31 (m, 1H), 3.13 (m, 1H), 1.38 (2s, 6H). Method 2: RT = 1.17 min.; M+H = 415.3
117		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.66 (m, 1H), 8.32 (m, 1H), 8.13 (m, 1H), 7.79 (m, 1H), 7.41 (m, 1H), 3.19 – 3.04 (m, 3H), 2.60 – 2.47 (m, 2H), 1.61 (s, 3H), 1.38 (2s, 6H). Method 2: RT = 1.12 min.; M+H = 403.3
118		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.66 (m, 1H), 8.32 (m, 1H), 8.13 (m, 1H), 7.77 (m, 1H), 7.41 (m, 1H), 3.21 – 3.05 (m, 2H), 2.98 – 2.72 (m, 4H), 1.57 – 1.19 (2s, 6H). Method 2: RT = 1.08 min.; M+H = 389.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
119		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.66 (m, 1H), 8.35 (m, 1H), 8.13 (m, 1H), 7.82 (m, 1H), 7.40 (m, 1H), 4.33 (m, 3H), 4.25 (m, 3H), 3.73 (s, 3H), 3.13 (m, 1H), 1.43 – 1.28 (2s, 6H). Method 2: RT = 1.07 min.; M+H = 459.3
120		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.69 (m, 1H), 8.66 (m, 1H), 8.33 (m, 1H), 8.13 (m, 1H), 7.81 (m, 1H), 7.41 (m, 1H), 3.76 – 3.64 (m, 3H), 3.13 (m, 1H), 2.48 – 2.26 (m, 6H), 1.48 – 1.17 (2s, 6H). Method 2: RT = 1.04 min.; M+H = 423.3
121		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.70 (m, 1H), 8.66 (m, 1H), 8.31 (m, 1H), 8.13 (m, 1H), 7.75 (m, 1H), 7.40 (m, 1H), 5.37 – 5.12 (m, 1H), 3.29 – 3.22 (m, 1H), 3.14 (m, 1H), 2.73 – 2.41 (m, 4H), 1.60 – 1.16 (2s, 6H). Method 1: RT = 3.06 min.; M+H = 371.3
122		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.86 (s, 1 H), 8.81 (s, 1 H), 7.63 - 7.67 (m, 1 H), 8.51 (dd, <i>J</i> =6.72, 2.45 Hz, 1 H), 7.92 (brs, 1 H), 7.85 - 7.89 (m, 1 H), 7.77 (s, 1 H), 7.46 (dd, <i>J</i> = 11.07, 9.11 Hz, 1 H), 7.31 (d, <i>J</i> = 3.55 Hz, 1 H), 6.67 (dd, <i>J</i> =3.48, 1.77 Hz, 1 H), 3.90 - 3.93(m, 4 H), 3.25 - 3.28 (m, 4 H).Method 1: RT = 2.65 min.; M+H = 408.1
123		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.91 - 8.94 (m, 2 H), 8.73 (brs, 1 H), 8.54 (dd, <i>J</i> =6.78, 2.64 Hz, 1 H), 7.87 - 7.91 (m, 1 H), 7.78 (s, 1 H),.7.47 (dd, <i>J</i> = 10.85, 9.10 Hz, 1 H), 7.32 (d, <i>J</i> = 3.14 Hz, 1 H), 6.67 (dd, <i>J</i> =3.51, 1.76 Hz, 1 H), 5.01 - 5.09 (m, 1 H), 1.35 (d, <i>J</i> = 6.15 Hz, 6 H). Method 1: RT = 3.03 min.; M+H = 424.1
124		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 9.24 (br s, 1 H), 8.80 (d, <i>J</i> =2.51 Hz, 1 H), 8.69 (d, <i>J</i> =2.13 Hz, 1 H), 8.22 (dd, <i>J</i> =7.03, 2.64 Hz, 1 H), 8.05 (d, <i>J</i> =2.01 Hz, 1 H), 7.63 - 7.74 (m, 1 H), 7.49 (dd, <i>J</i> =11.17, 9.29 Hz, 1 H), 4.41 (t, <i>J</i> =12.74 Hz, 4 H), 3.08 (quin, <i>J</i> =6.81 Hz, 1 H), 1.30 (d, <i>J</i> =6.90 Hz, 6 H). Method 1: RT = 3.07 min.; M+H = 390.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
125		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 9.25 (s, 1 H), 8.91 (br s, 1 H), 8.76 (br s, 1 H), 8.63 (br s, 1 H), 8.25 (br s, 1 H), 7.69 (br s, 1 H), 7.51 (br t, <i>J</i> =10.16 Hz, 1 H), 4.41 (br t, <i>J</i> =12.67 Hz, 4 H). Method 1: RT = 2.98 min.
126		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 8.98 (s, 1 H), 8.90 (d, <i>J</i> =2.51 Hz, 1 H), 8.76 (d, <i>J</i> =2.51 Hz, 1 H), 8.63 (d, <i>J</i> =2.51 Hz, 1 H), 8.24 (dd, <i>J</i> =7.03, 2.76 Hz, 1 H), 7.67 - 7.74 (m, 1 H), 7.49 (dd, <i>J</i> =11.17, 9.16 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.25 - 4.39 (m, 2 H), 3.96 - 4.10 (m, 2 H). Method 1: RT = 2.82 min.
127		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 8.90 (d, <i>J</i> =2.26 Hz, 1 H), 8.76 (d, <i>J</i> =2.51 Hz, 1 H), 8.66 (s, 1 H), 8.63 (d, <i>J</i> =2.26 Hz, 1 H), 8.27 (dd, <i>J</i> =7.03, 2.76 Hz, 1 H), 7.71 - 7.77 (m, 1 H), 7.48 (dd, <i>J</i> =11.17, 9.16 Hz, 1 H), 5.28 - 5.48 (m, 1 H), 3.40 - 3.78 (m, 4 H), 2.01 - 2.27 (m, 2 H). Method 1: RT = 2.89 min.
128		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 10.53 (s, 1 H), 8.94 (d, <i>J</i> =2.51 Hz, 1 H), 8.77 (d, <i>J</i> =2.26 Hz, 1 H), 8.64 (d, <i>J</i> =2.26 Hz, 1 H), 8.58 (dd, <i>J</i> =7.15, 2.64 Hz, 1 H), 7.89 - 7.97 (m, 1 H), 7.59 (dd, <i>J</i> =11.17, 9.16 Hz, 1 H), 2.52 - 2.53 (s, 3 H), 2.40 (s, 3 H). Method 1: RT = 3.03 min
129		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 8.89 (d, <i>J</i> =2.01 Hz, 1 H), 8.70 - 8.80 (m, 2 H), 8.62 (d, <i>J</i> =2.26 Hz, 1 H), 8.25 (dd, <i>J</i> =6.90, 2.38 Hz, 1 H), 7.72 (br d, <i>J</i> =9.03 Hz, 1 H), 7.46 (br t, <i>J</i> =10.16 Hz, 1 H), 3.98 (br t, <i>J</i> =7.53 Hz, 4 H), 2.20 (quin, <i>J</i> =7.59 Hz, 2 H). Method 1: RT = 2.82 min.
130		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 10.58 (br s, 1 H), 8.94 (d, <i>J</i> =2.26 Hz, 1 H), 8.77 (d, <i>J</i> =2.26 Hz, 1 H), 8.64 (d, <i>J</i> =2.26 Hz, 1 H), 8.53 (dd, <i>J</i> =7.03, 2.51 Hz, 1 H), 7.92 - 8.02 (m, 2 H), 7.60 (dd, <i>J</i> =11.04, 9.29 Hz, 1 H), 7.40 (d, <i>J</i> =3.26 Hz, 1 H), 6.74 (dd, <i>J</i> =3.26, 1.51 Hz, 1 H). Method 1: RT = 2.98 min.

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
131		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.47 (d, <i>J</i> = 2.89 Hz, 1 H), 8.38 (d, <i>J</i> = 2.63 Hz, 1 H), 8.07 (dd, <i>J</i> = 6.84, 2.70 Hz, 1 H), 7.58 - 7.62 (m, 1 H), 7.31 (dd, <i>J</i> = 11.11, 9.10 Hz, 1 H), 7.00 (d, <i>J</i> = 2.76 Hz, 1 H), 5.27 - 5.46 (m, 1 H), 4.33 - 4.43 (m, 2H), 4.08 - 4.18 (m, 2H), 3.40 (t, <i>J</i> = 6.53 Hz, 4 H), 2.05 - 2.12 (m, 4 H). Method 1: RT = 3.01 min.; M+H = 399.1
132		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.47 (d, <i>J</i> = 2.89 Hz, 1 H), 8.38 (d, <i>J</i> = 2.63 Hz, 1 H), 8.07 (dd, <i>J</i> = 6.84, 2.70 Hz, 1 H), 7.58 - 7.62 (m, 1 H), 7.31 (dd, <i>J</i> = 11.11, 9.10 Hz, 1 H), 7.00 (d, <i>J</i> = 2.76 Hz, 1 H), 5.27 - 5.46 (m, 1 H), 4.33 - 4.43 (m, 2H), 4.08 - 4.18 (m, 2H), 3.40 (t, <i>J</i> = 6.53 Hz, 4 H), 2.05 - 2.12 (m, 4 H). Method 1: RT = 2.65 min.; M+H = 415.2
133		¹ H NMR (400 MHz, METHANOL- <i>d</i> ₄) δ 8.96 (br s, 1 H), 8.87 (s, 1 H), 8.32 (dd, <i>J</i> = 6.27, 2.01 Hz, 1 H), 8.21 (br d, <i>J</i> = 4.27 Hz, 1 H), 7.54 - 7.71 (m, 1 H), 7.41 (dd, <i>J</i> = 10.92, 9.16 Hz, 1 H), 5.22 - 5.49 (m, 1 H), 3.52 - 3.89 (m, 4 H), 3.21 (d, <i>J</i> = 1.25 Hz, 6 H), 2.03 - 2.46 (m, 2 H). Method 1: RT = 2.75 min.; M+H = 387.1
134		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.69 (d, <i>J</i> = 2.26 Hz, 1 H), 8.58 (d, <i>J</i> = 2.51 Hz, 1 H), 8.21 (dd, <i>J</i> = 6.84, 2.70 Hz, 1 H), 7.57 - 7.61 (m, 1 H), 7.51 (d, <i>J</i> = 2.64 Hz, 1 H), 7.36 (dd, <i>J</i> = 10.98, 9.10 Hz, 1 H), 5.27 - 5.40 (m, 1 H), 3.43 - 3.84 (m, 8H), 1.99 - 2.37 (m, 6 H). Method 1: RT = 2.98 min.; M+H = 413.1
135		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.97 - 9.03 (m, 2 H), 8.26 - 8.31 (m, 2 H), 7.58 - 7.62 (m, 1 H), 7.37 (dd, <i>J</i> = 10.92, 9.16 Hz, 1 H), 5.27 - 5.40 (m, 1 H), 3.90 - 3.93 (m, 4H), 3.55 - 3.84 (m, 4H), 3.31 - 3.33 (m, 4H), 1.97 - 2.36 (m, 2 H). Method 1: RT = 2.58 min.; M+H = 429.1
136		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.62 (dd, <i>J</i> = 9.10, 2.32 Hz, 2 H), 8.44 (brs, 1 H), 8.10 (dd, <i>J</i> = 6.78, 2.64 Hz, 1 H), 7.60 - 7.64 (m, 1 H), 7.34 (dd, <i>J</i> = 10.92, 9.16 Hz, 1 H), 5.26 - 5.39 (m, 1 H), 4.98 - 5.04 (m, 1H), 3.53 - 3.82 (m, 4H), 2.07 - 2.35 (m, 2 H), 1.33 (d, <i>J</i> = 2.67 Hz, 6 H). Method 1: RT = 2.92 min.; M+H = 445.1

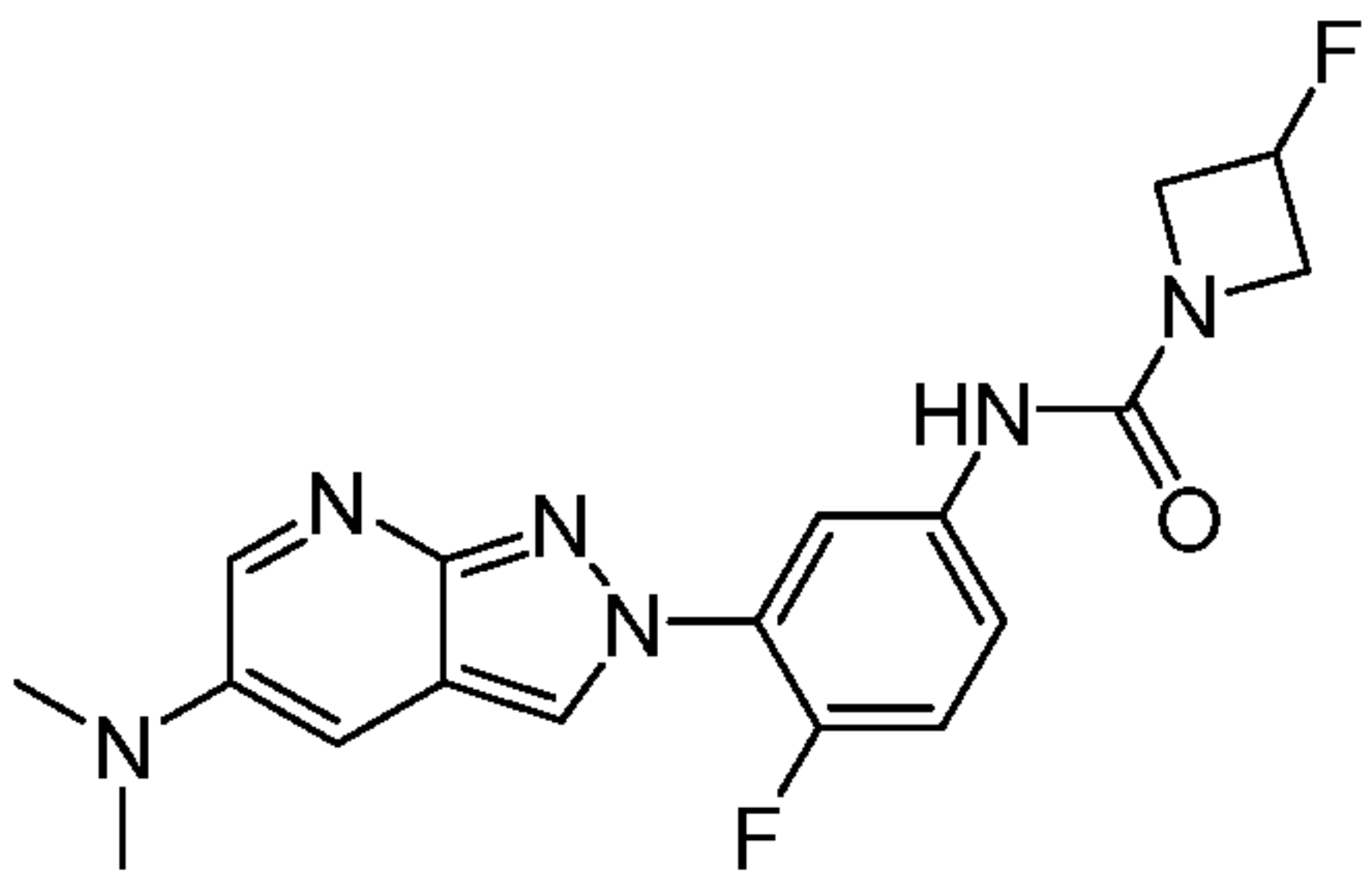
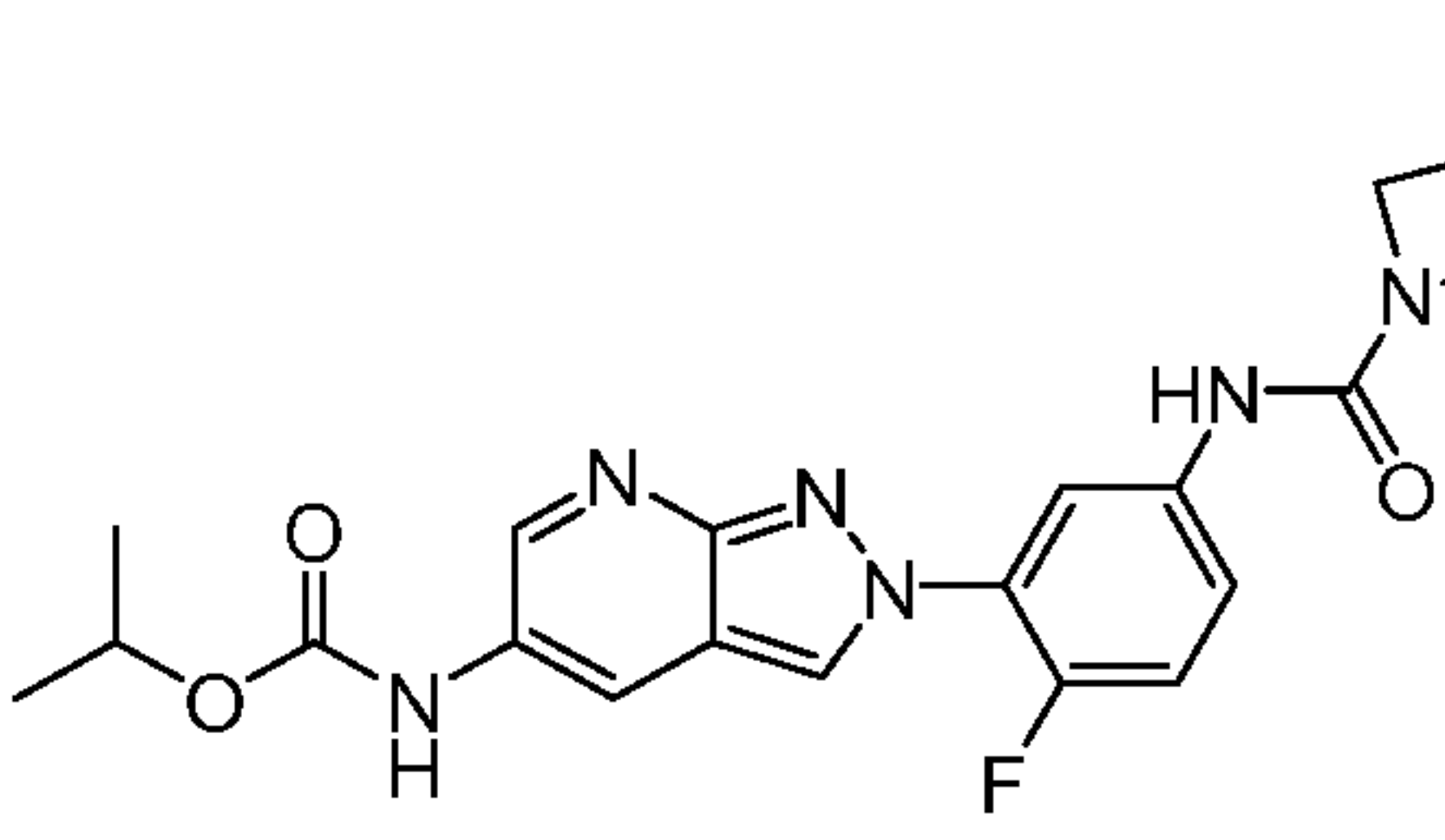
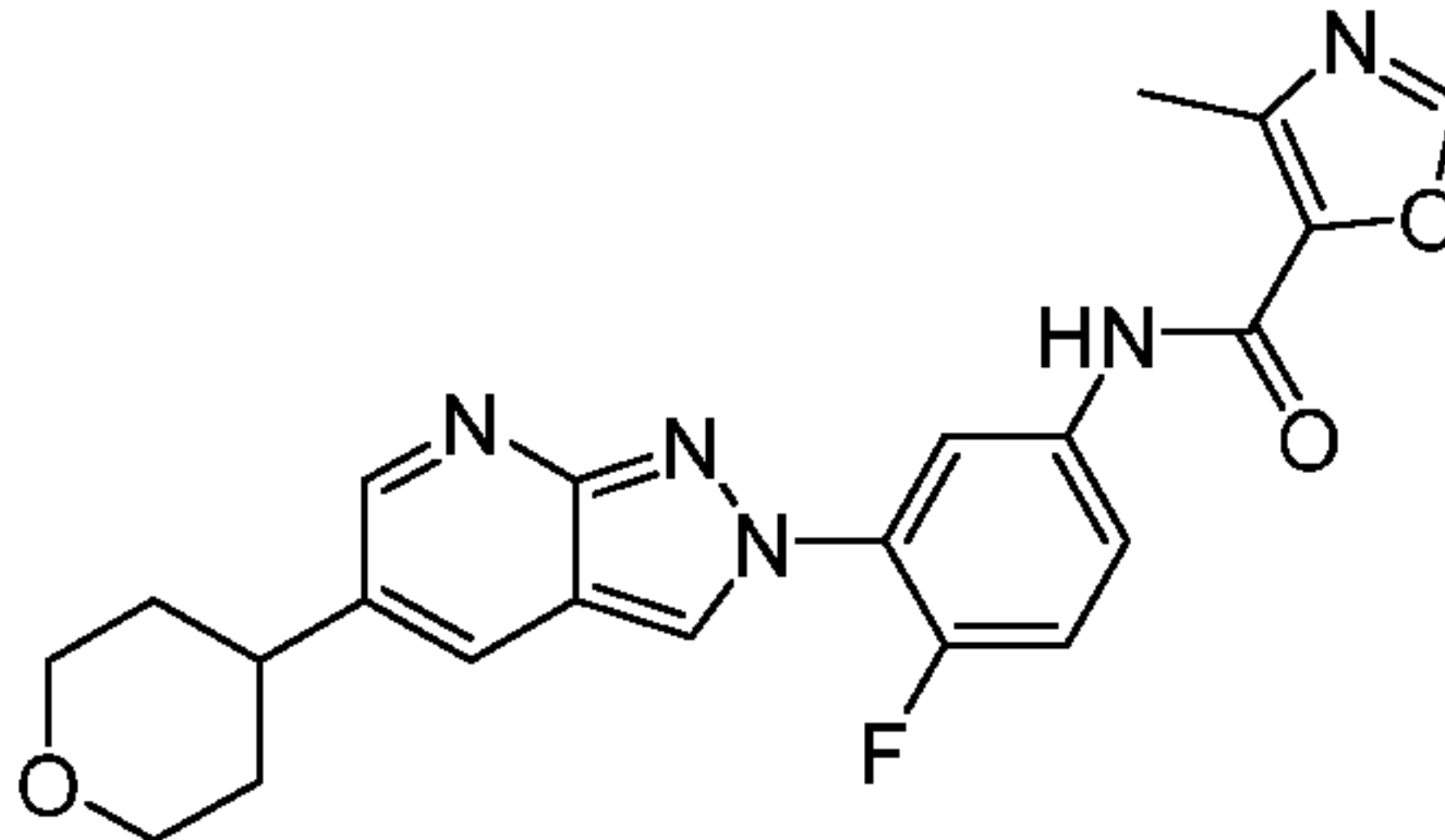
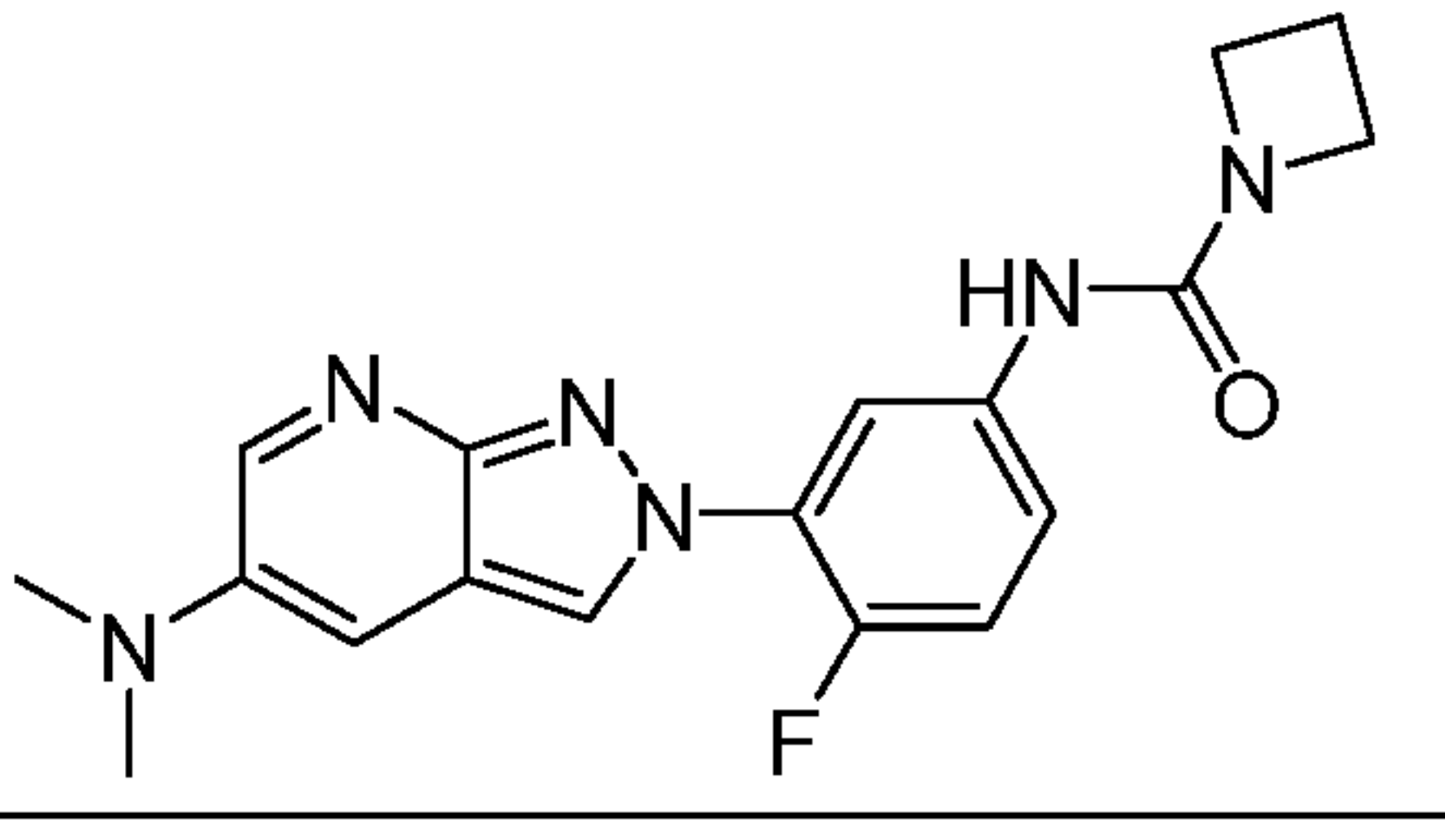
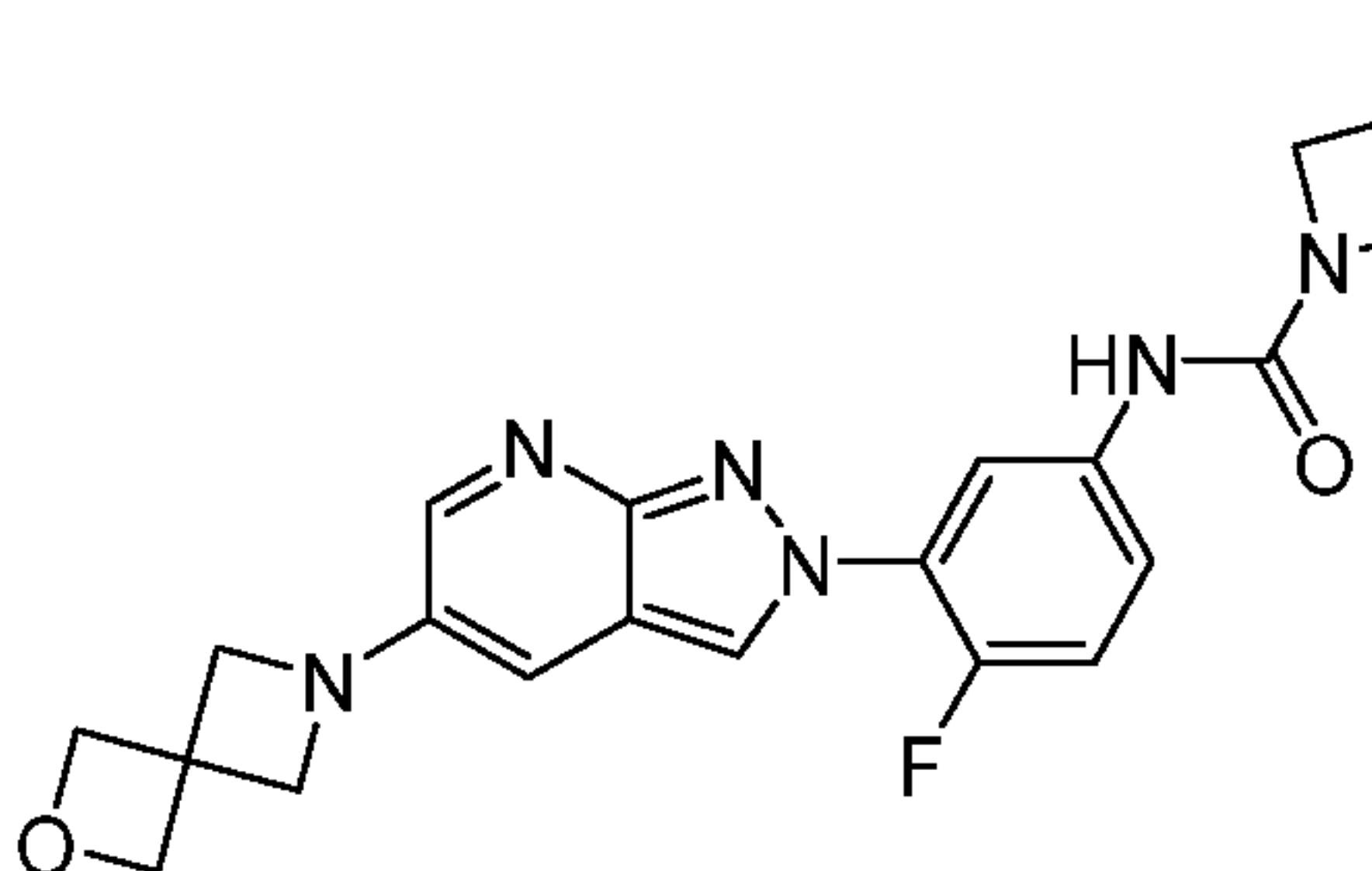
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
137		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.68 (d, <i>J</i> = 2.76 Hz, 1 H), 8.54 (d, <i>J</i> = 2.38 Hz, 1 H), 8.09 (dd, <i>J</i> = 6.84, 2.70 Hz, 1 H), 7.60 - 7.64 (m, 1 H), 7.53 (d, <i>J</i> = 2.64 Hz, 1 H), 7.32 (dd, <i>J</i> = 10.98, 9.10 Hz, 1 H), 4.11 (t, <i>J</i> = 7.65 Hz, 4 H), 3.90 - 3.92 (m, 4 H), 3.19 - 3.21 (m, 4 H), 2.29 - 2.36 (m, 2 H). Method 1: RT = 2.58 min.; M+H = 397.2
138		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.61 - 8.63 (m, 2 H), 8.45 (brs, 1 H), 8.09 (dd, <i>J</i> = 6.78, 2.64 Hz, 1 H), 7.62 - 7.64 (m, 1 H), 7.30 - 7.35 (m, 1 H), 7.30 - 7.35 (m, 1 H), 4.98 - 5.04 (m, 1 H), 4.11 (t, <i>J</i> = 7.65 Hz, 4 H), 2.32 (t, <i>J</i> = 7.62 Hz, 2 H), 1.33 (d, <i>J</i> = 6.15 Hz, 6 H). Method 1: RT = 2.87 min.; M+H = 413.1
139		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.49 (s, 1 H), 8.43 - 8.63 (m, 2 H), 8.35 (d, <i>J</i> = 2.76 Hz, 1 H), 7.98 (d, <i>J</i> = 1.00 Hz, 1 H), 7.82 - 7.94 (m, 1 H), 7.53 (dd, <i>J</i> = 11.29, 9.03 Hz, 1 H), 7.39 (d, <i>J</i> = 3.01 Hz, 1 H), 6.67 - 6.84 (m, 2 H), 6.09 (q, <i>J</i> = 4.77 Hz, 1 H), 2.73 (d, <i>J</i> = 5.02 Hz, 3 H). Method 1: RT = 2.67 min.; M+H = 352.0
140		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.51 (s, 1 H), 8.71 (d, <i>J</i> = 3.01 Hz, 1 H), 8.58 (d, <i>J</i> = 2.76 Hz, 1 H), 8.49 (dd, <i>J</i> = 7.15, 2.64 Hz, 1 H), 7.98 (d, <i>J</i> = 1.00 Hz, 1 H), 7.86 - 7.94 (m, 1 H), 7.54 (dd, <i>J</i> = 11.42, 9.16 Hz, 1 H), 7.39 (d, <i>J</i> = 3.51 Hz, 1 H), 7.16 (d, <i>J</i> = 2.76 Hz, 1 H), 6.73 (dd, <i>J</i> = 3.39, 1.63 Hz, 1 H), 2.96 (s, 6 H). Method 1: RT = 2.82 min.; M+H = 366.1
141		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.48 (d, <i>J</i> = 2.89 Hz, 1 H), 8.42 (d, <i>J</i> = 2.51 Hz, 1 H), 8.35 (dd, <i>J</i> = 6.90, 2.64 Hz, 1 H), 7.76 - 7.89 (m, 1 H), 7.76 (d, <i>J</i> = 0.88 Hz, 1 H), 7.40 (dd, <i>J</i> = 11.04, 9.03 Hz, 1 H), 7.30 (d, <i>J</i> = 3.26 Hz, 1 H), 7.01 (d, <i>J</i> = 2.76 Hz, 1 H), 6.66 (dd, <i>J</i> = 3.45, 1.69 Hz, 1 H), 3.39 - 3.42 (m, 4 H), 2.07 - 2.10 (m, 4 H). Method 1: RT = 3.18 min.; M+H = 392.2
142		¹ H NMR (400 MHz, METHANOL- <i>d</i> ₄) δ 8.68 (d, <i>J</i> = 2.45 Hz, 1 H), 8.52 (br s, 1 H), 8.17 (dd, <i>J</i> = 6.85, 2.69 Hz, 1 H), 7.54 (d, <i>J</i> = 2.45 Hz, 1 H), 7.42 - 7.50 (m, 1 H), 7.35 (dd, <i>J</i> = 11.00, 9.05 Hz, 1 H), 2.95 (s, 3 H), 2.80 (s, 3 H). Method 1: RT = 2.56 min.; M+H = 315.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
143		¹ H NMR (400 MHz, METHANOL-d ₄) δ 9.00 (d, J=2.01 Hz, 1 H), 8.91 (d, J=2.76 Hz, 1 H), 8.31 (d, J=2.76 Hz, 1 H), 8.25 (dd, J=6.78, 2.51 Hz, 1 H), 7.54 - 7.62 (m, 1 H), 7.40 (dd, J=10.92, 9.16 Hz, 1 H), 3.24 (s, 6 H), 3.07 (s, 6 H). Method 1: RT = 2.60 min.; M+H = 343.1
144		¹ H NMR (400 MHz, DMSO), δ 9.19 (s, 1 H), 8.53 (d, J = 2.69 Hz, 1 H), 8.26 (d, J = 2.69 Hz, 1 H), 8.19 (dd, J = 6.97, 2.69 Hz, 1 H), 7.61 - 7.65 (m, 1 H), 7.45 (dd, J = 11.37, 9.17 Hz, 1 H), 6.88 (d, J = 2.81 Hz, 1 H), 4.40 (t, J = 12.65 Hz, 4 H), 3.91 (d, J = 7.15 Hz, 4 H), 2.32 - 2.39 (m, 2 H). Method 1: RT = 2.82 min.; M+H = 403.1
145		¹ H NMR (400 MHz, DMSO), δ 9.20 (s, 1 H), 8.74 (d, J = 2.81 Hz, 1 H), 8.65 (d, J = 2.69 Hz, 1 H), 8.21 (dd, J = 7.09, 2.69 Hz, 1 H), 7.64 - 7.68 (m, 1 H), 7.47 (dd, J = 11.31, 9.11 Hz, 1 H), 7.40 (d, J = 2.81 Hz, 1 H), 4.41 (t, J = 12.65 Hz, 4 H), 3.79 - 3.82 (m, 4 H), 3.14 - 3.16 (m, 4 H). Method 1: RT = 2.65 min.; M+H = 433.1
146		¹ H NMR (400 MHz, DMSO), δ 9.89 (s, 1 H), 9.20 (s, 1 H), 8.79 (d, J = 2.57 Hz, 1 H), 8.65 (d, J = 2.45 Hz, 1 H), 8.36 (s, 1 H), 8.20 (dd, J = 7.03, 2.75 Hz, 1 H), 7.63 - 7.67 (m, 1 H), 7.47 (dd, J = 11.25, 9.05 Hz, 1 H), 4.92 - 4.96 (m, 1H), 4.40 (t, J = 12.72 Hz, 4 H), 1.28 (d, J = 6.36 Hz, 6 H). Method 1: RT = 2.89 min.; M+H = 449.1
147		¹ H NMR (400 MHz, DMSO), δ 8.92 (s, 1 H), 8.52 (d, J = 2.76 Hz, 1 H), 8.25 (d, J = 2.76 Hz, 1 H), 8.19 (dd, J = 7.09, 2.70 Hz, 1 H), 7.61 - 7.69 (m, 1 H), 7.42 (dd, J = 11.36, 9.10 Hz, 1 H), 6.88 (d, J = 2.76 Hz, 1 H), 5.28 - 5.49 (m, 1 H), 4.24 - 4.38 (m, 2 H), 3.95 - 4.08 (m, 2 H), 3.91 (t, J = 7.15 Hz, 4 H), 2.33 - 2.41 (m, 2 H). Method 1: RT = 2.75 min.; M+H = 385.2
148		¹ H NMR (400 MHz, DMSO-d ₆), δ 8.98 (s, 1 H), 8.81 (d, J=2.76 Hz, 1 H), 8.70 (d, J=2.26 Hz, 1 H), 8.23 (dd, J=7.03, 2.76 Hz, 1 H), 8.07 (d, J=1.76 Hz, 1 H), 7.65 - 7.72 (m, 1 H), 7.47 (dd, J=11.29, 9.29 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.25 - 4.39 (m, 2 H), 3.96 - 4.09 (m, 4 H), 3.44 - 3.54 (m, 2 H), 2.91 - 3.02 (m, 1 H), 1.68 - 1.86 (m, 4 H). Method 1: RT = 2.65 min.; M+H = 414.2

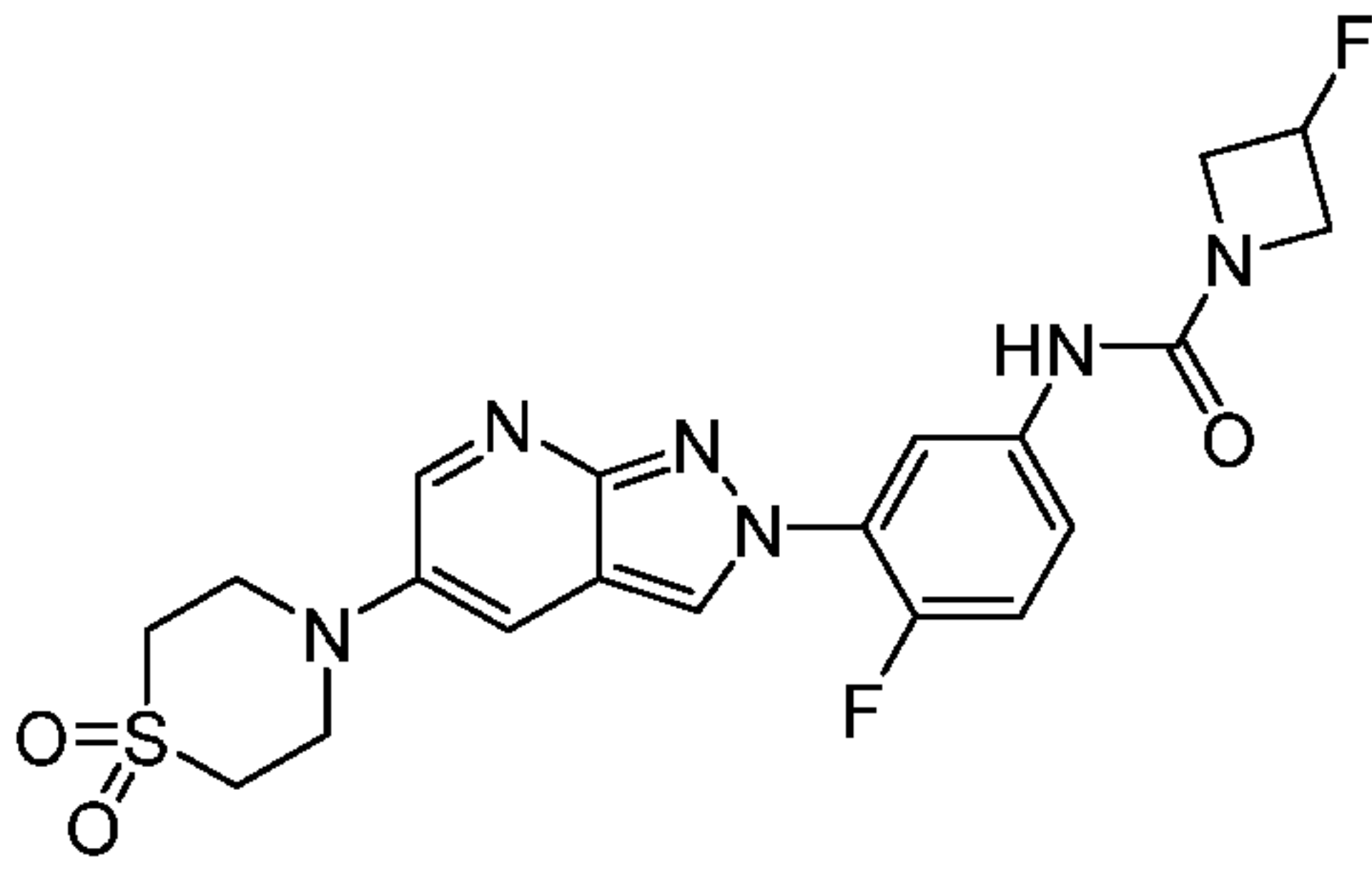
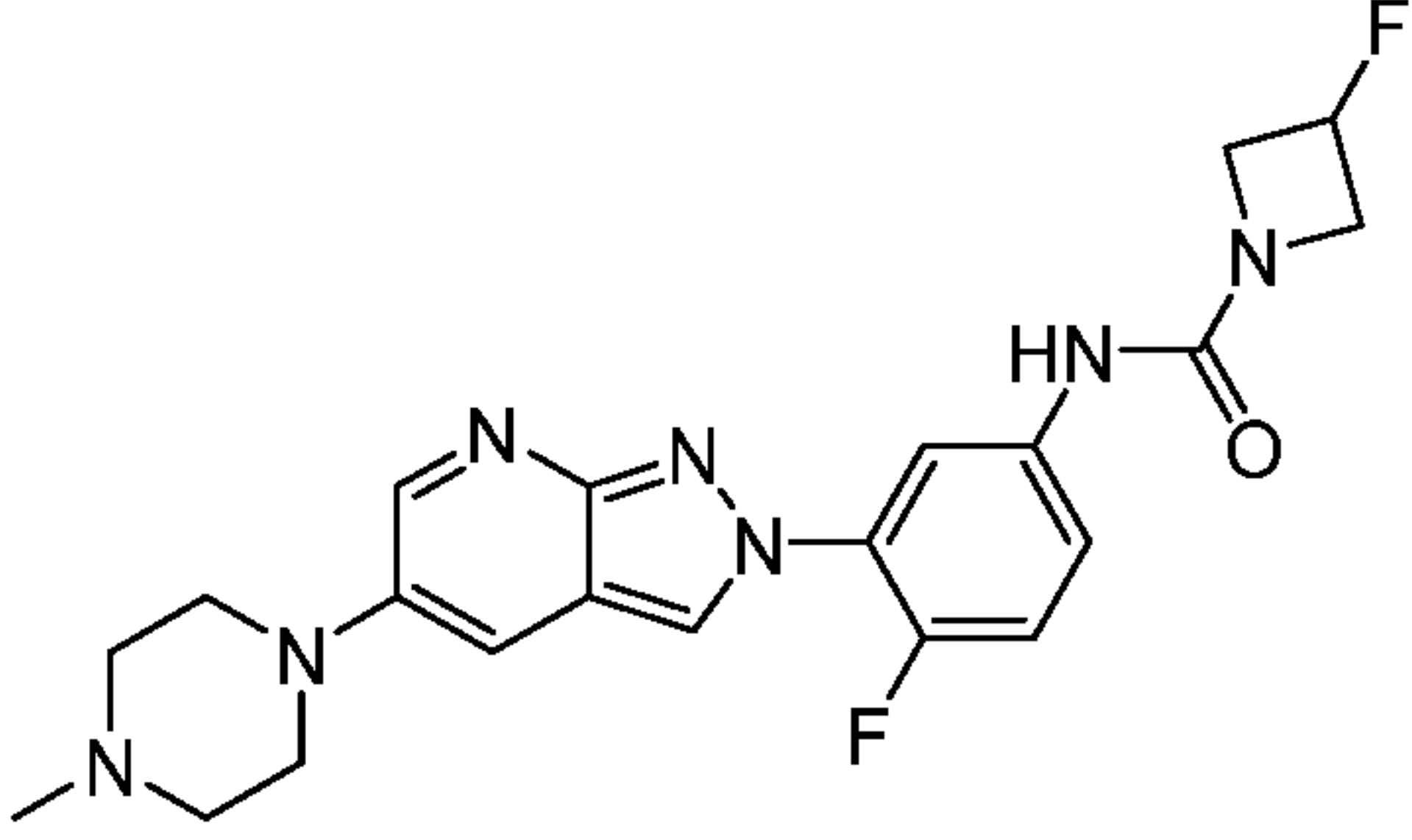
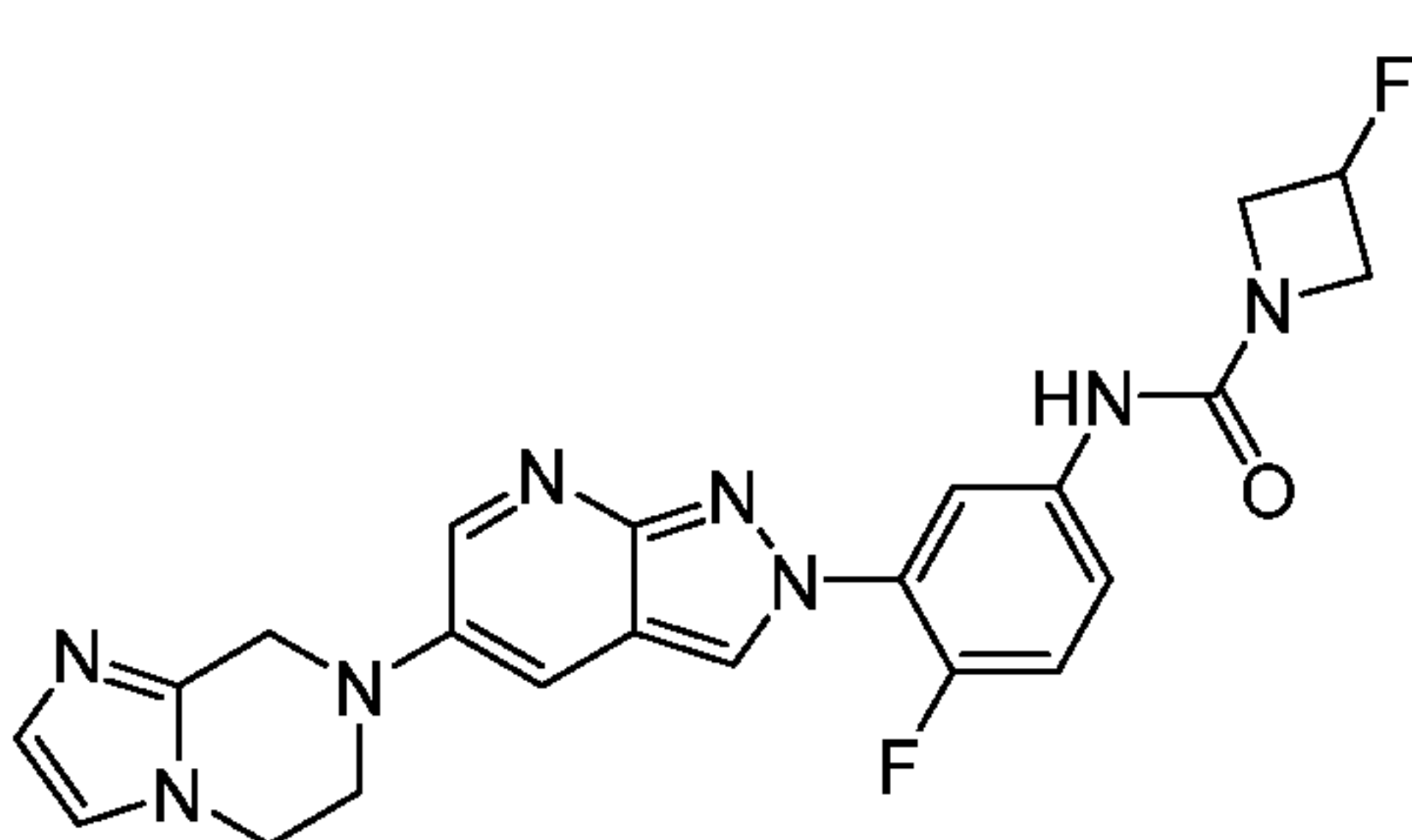
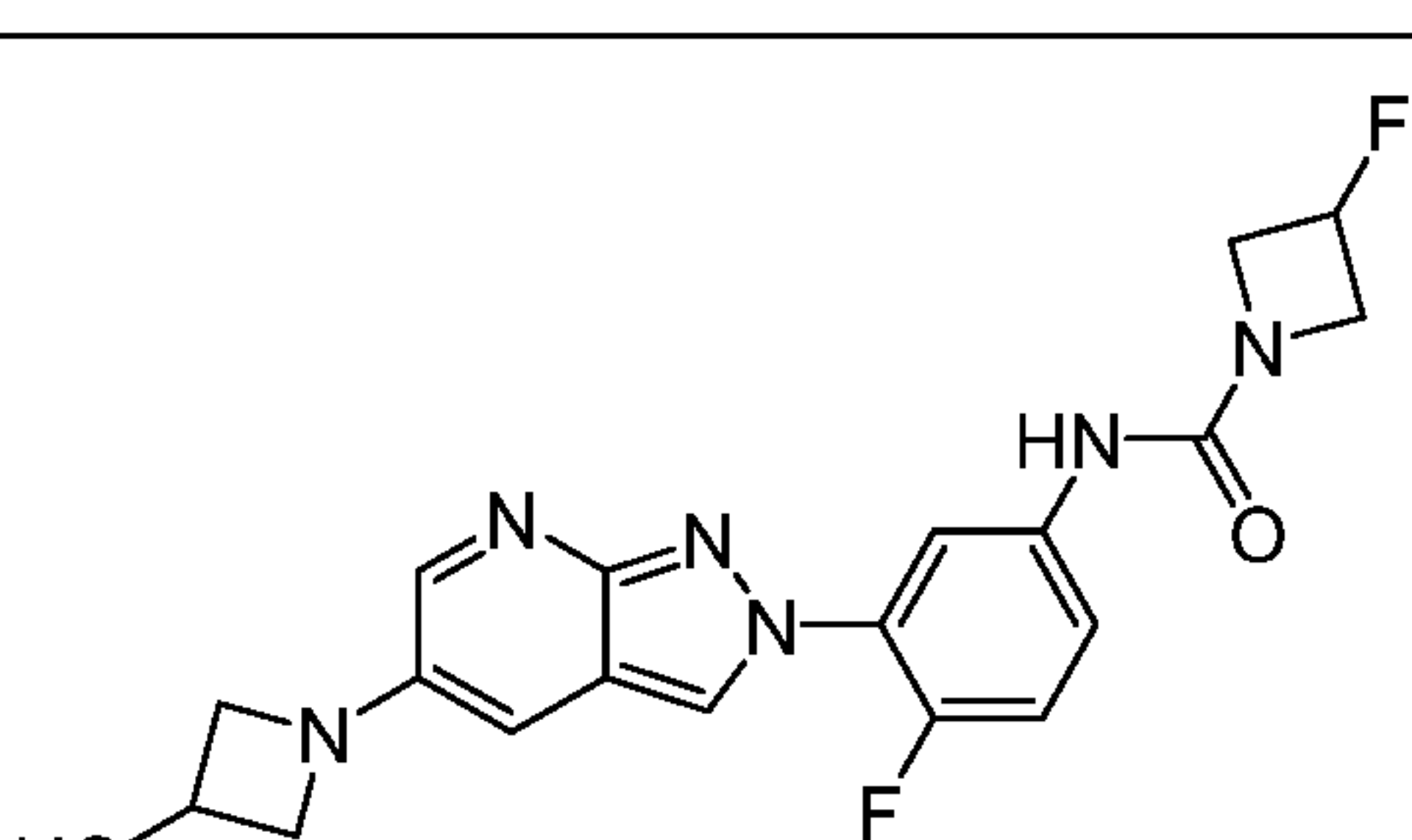
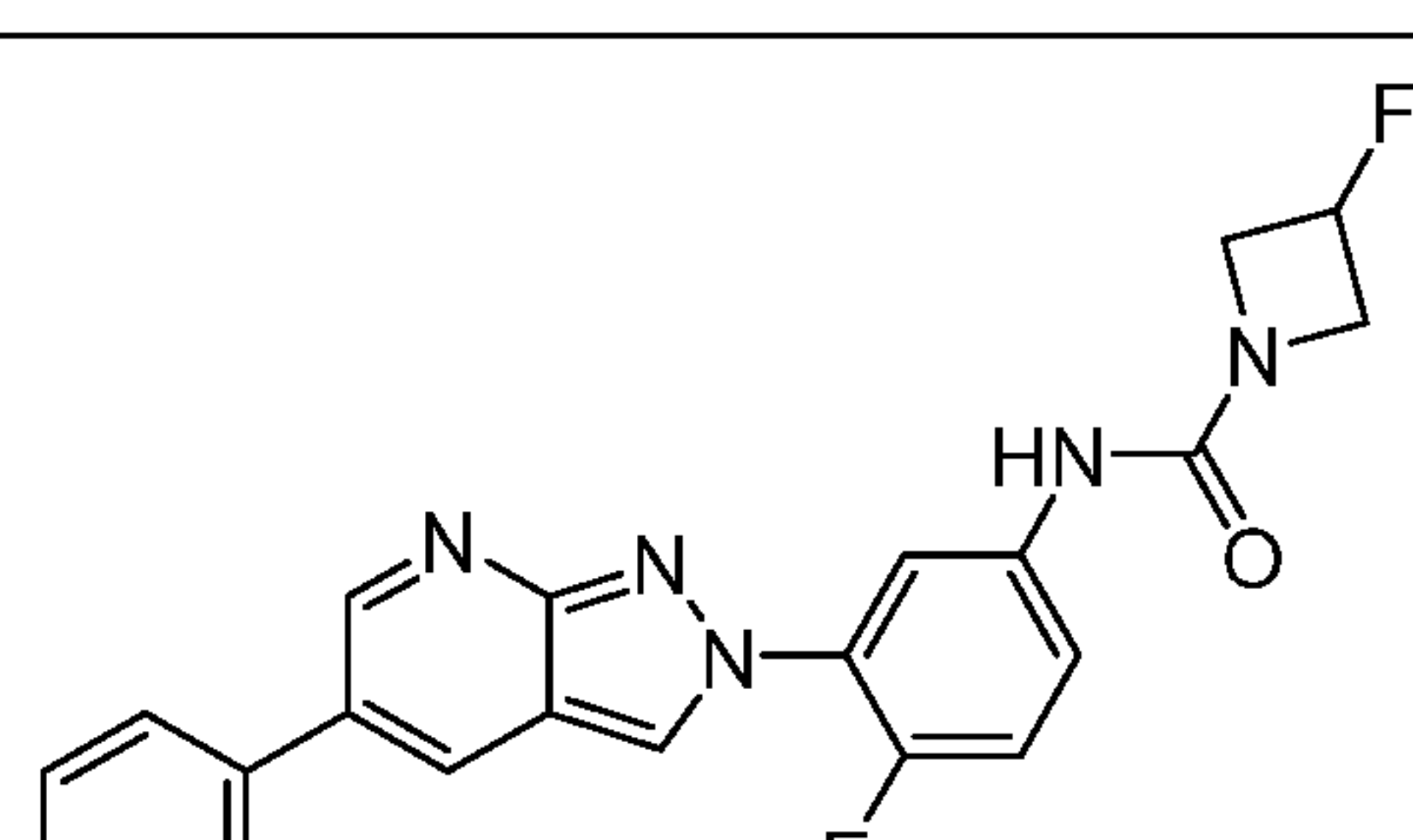
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
149		¹ H NMR (400 MHz, DMSO), δ 8.60 (s, 1 H), 8.53 (d, <i>J</i> = 2.76 Hz, 1 H), 8.25 (d, <i>J</i> = 2.76 Hz, 1 H), 8.21 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.64 - 7.71 (m, 1 H), 7.41 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 6.88 (d, <i>J</i> = 2.76 Hz, 1 H), 5.28 - 5.46 (m, 1 H), 3.91 (t, <i>J</i> = 7.22 Hz, 4 H), 3.62 - 3.73 (m, 2 H), 3.39 - 3.55 (m, 2 H), 2.32 - 2.40 (m, 2 H), 1.99 - 2.22 (m, 2 H). Method 1: RT = 2.76 min.; M+H = 399.2
150		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 9.15 (d, <i>J</i> = 2.01 Hz, 1 H), 8.98 (s, 1 H), 8.85 (d, <i>J</i> = 1.88 Hz, 1 H), 8.33 (dd, <i>J</i> = 6.78, 9.16 Hz, 1 H), 7.61 - 7.65 (m, 1 H), 7.42 (dd, <i>J</i> = 11.04, 9.16 Hz, 1 H), 5.28 - 5.41 (m, 1 H), 4.11 - 4.14 (m, 2 H), 3.57 - 3.85 (m, 6 H), 3.14 - 3.20 (m, 1 H), 2.11 - 2.32 (m, 2 H), 1.91 - 1.97 (m, 4 H). Method 1: RT = 2.60 min.; M+H = 428.2
151		¹ H NMR (400 MHz, DMSO), δ 10.52 (s, 1 H), 8.56 (d, <i>J</i> = 2.76 Hz, 1 H), 8.48 (dd, <i>J</i> = 7.03, 2.63 Hz, 1 H), 8.27 (d, <i>J</i> = 2.76 Hz, 1 H), 7.97 (dd, <i>J</i> = 1.69, 0.82 Hz, 1 H), 7.86 - 7.91 (m, 1 H), 7.54 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.38 (dd, <i>J</i> = 3.51, 0.75 Hz, 1 H), 6.89 (d, <i>J</i> = 2.76 Hz, 1 H), 6.73 (dd, <i>J</i> = 3.51, 1.76 Hz, 1 H), 3.91 (t, <i>J</i> = 7.22 Hz, 4 H), 2.33 - 2.39 (m, 2 H). Method 1: RT = 2.90 min.; M+H = 378.2
152		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 8.98 (s, 1 H), 8.95 (d, <i>J</i> = 2.51 Hz, 1 H), 8.69 (d, <i>J</i> = 2.01 Hz, 1 H), 8.33 (d, <i>J</i> = 1.76 Hz, 1 H), 8.24 (dd, <i>J</i> = 6.90, 2.63 Hz, 1 H), 7.67 - 7.74 (m, 1 H), 7.48 (dd, <i>J</i> = 11.29, 9.29 Hz, 1 H), 5.30 - 5.52 (m, 1 H), 4.26 - 4.39 (m, 2 H), 3.97 - 4.09 (m, 2 H), 3.87 (q, <i>J</i> = 11.71 Hz, 2 H). Method 1: RT = 2.76 min.; M+H = 412.2
153		¹ H NMR (400 MHz, METHANOL- <i>d</i> ₄), δ 8.99 (d, <i>J</i> = 2.20 Hz, 1 H), 8.71 (d, <i>J</i> = 2.69 Hz, 1 H), 8.62 (dd, <i>J</i> = 6.85, 2.69 Hz, 1 H), 8.07 (d, <i>J</i> = 2.44 Hz, 1 H), 7.82 - 7.88 (m, 1 H), 7.51 (dd, <i>J</i> = 10.88, 9.17 Hz, 1 H), 3.04 (s, 3 H), 2.58 (s, 3 H), 2.49 (s, 3 H). Method 1: RT = 2.76 min.; M+H = 381.1
154		¹ H NMR (400 MHz, METHANOL- <i>d</i> ₄), δ 8.92 (d, <i>J</i> = 2.20 Hz, 1 H), 8.80 (d, <i>J</i> = 2.69 Hz, 1 H), 8.53 (dd, <i>J</i> = 6.85, 2.69 Hz, 1 H), 8.17 (d, <i>J</i> = 2.93 Hz, 1 H), 7.69 - 7.77 (m, 1 H), 7.40 (dd, <i>J</i> = 11.00, 9.29 Hz, 1 H), 3.12 (s, 6 H), 2.46 (s, 3 H), 2.37 (s, 3 H). Method 1: RT = 2.84 min.; M+H = 395.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
155		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.48 (s, 1 H), 8.57 (d, J=2.64 Hz, 1 H), 8.54 (dd, J=7.15, 2.64 Hz, 1 H), 8.28 (d, J=2.76 Hz, 1 H), 7.84 - 7.90 (m, 1 H), 7.54 (dd, J=11.29, 9.03 Hz, 1 H), 6.90 (d, J=2.76 Hz, 1 H), 3.93 (t, J=7.15 Hz, 4 H), 2.50 - 2.50 (m, 3 H), 2.40 (s, 3 H), 2.33 - 2.39 (m, 2 H). Method 1: RT = 2.89 min.; M+H = 407.1
156		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.96 (br s, 1 H), 8.79 (d, J=2.57 Hz, 1 H), 8.69 (d, J=2.32 Hz, 1 H), 8.23 (dd, J=6.97, 2.69 Hz, 1 H), 8.05 (d, J=1.96 Hz, 1 H), 7.64 - 7.73 (m, 1 H), 7.46 (dd, J=11.25, 9.17 Hz, 1 H), 5.28 - 5.52 (m, 1 H), 4.26 - 4.39 (m, 2 H), 3.96 - 4.10 (m, 2 H), 3.03 - 3.14 (m, 1 H), 1.30 (d, J=6.97 Hz, 6 H). Method 2: RT = 0.95 min.; M+H = 372.2
157		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.51 (s, 1 H), 8.65 (d, J=2.64 Hz, 1 H), 8.59 (d, J=2.89 Hz, 1 H), 8.55 - 8.58 (m, 1 H), 7.83 - 7.90 (m, 1 H), 7.55 (dd, J=11.29, 9.16 Hz, 1 H), 7.12 (br s, 1 H), 3.38 (br t, J=6.40 Hz, 4 H), 2.50 (br s, 3 H), 2.40 (s, 3 H), 1.97 - 2.06 (m, 4 H). Method 1: RT = 3.12 min.; M+H = 421.1
158		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.52 (s, 1 H), 8.81 (d, J=2.76 Hz, 1 H), 8.73 (d, J=2.64 Hz, 1 H), 8.55 (dd, J=7.03, 2.64 Hz, 1 H), 7.86 - 7.92 (m, 1 H), 7.54 - 7.59 (m, 1 H), 7.50 - 7.54 (m, 1 H), 3.79 - 3.84 (m, 4 H), 3.15 - 3.21 (m, 4 H), 2.49 - 2.50 (m, 3 H), 2.40 (s, 3 H). Method 1: RT = 2.79 min.; M+H = 437.1
159		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.52 (s, 1 H), 9.95 (br s, 1 H), 8.85 (d, J=2.38 Hz, 1 H), 8.69 (d, J=2.51 Hz, 1 H), 8.56 (dd, J=7.03, 2.63 Hz, 1 H), 8.40 (br s, 1 H), 7.86 - 7.93 (m, 1 H), 7.57 (dd, J=11.04, 9.16 Hz, 1 H), 4.95 (dt, J=12.55, 6.27 Hz, 1 H), 2.50 - 2.50 (m, 3 H), 2.40 (s, 3 H), 1.30 (d, J=6.27 Hz, 6 H). Method 1: RT = 2.97 min.; M+H = 453.2
160		¹ H NMR (400 MHz, METHANOL-d ₄) δ 8.71 (d, J=2.26 Hz, 1 H), 8.68 (d, J=2.26 Hz, 1 H), 8.17 (d, J=2.01 Hz, 1 H), 8.14 (dd, J=7.03, 2.51 Hz, 1 H), 7.65 (dt, J=9.29, 3.39 Hz, 1 H), 7.32 - 7.39 (m, 1 H), 4.09 - 4.16 (m, 6 H), 3.61 - 3.69 (m, 2 H), 3.05 (br s, 1 H), 2.34 (quin, J=7.65 Hz, 2 H), 1.86 - 1.95 (m, 4 H). Method 1: RT = 2.68 min.; M+H = 396.2

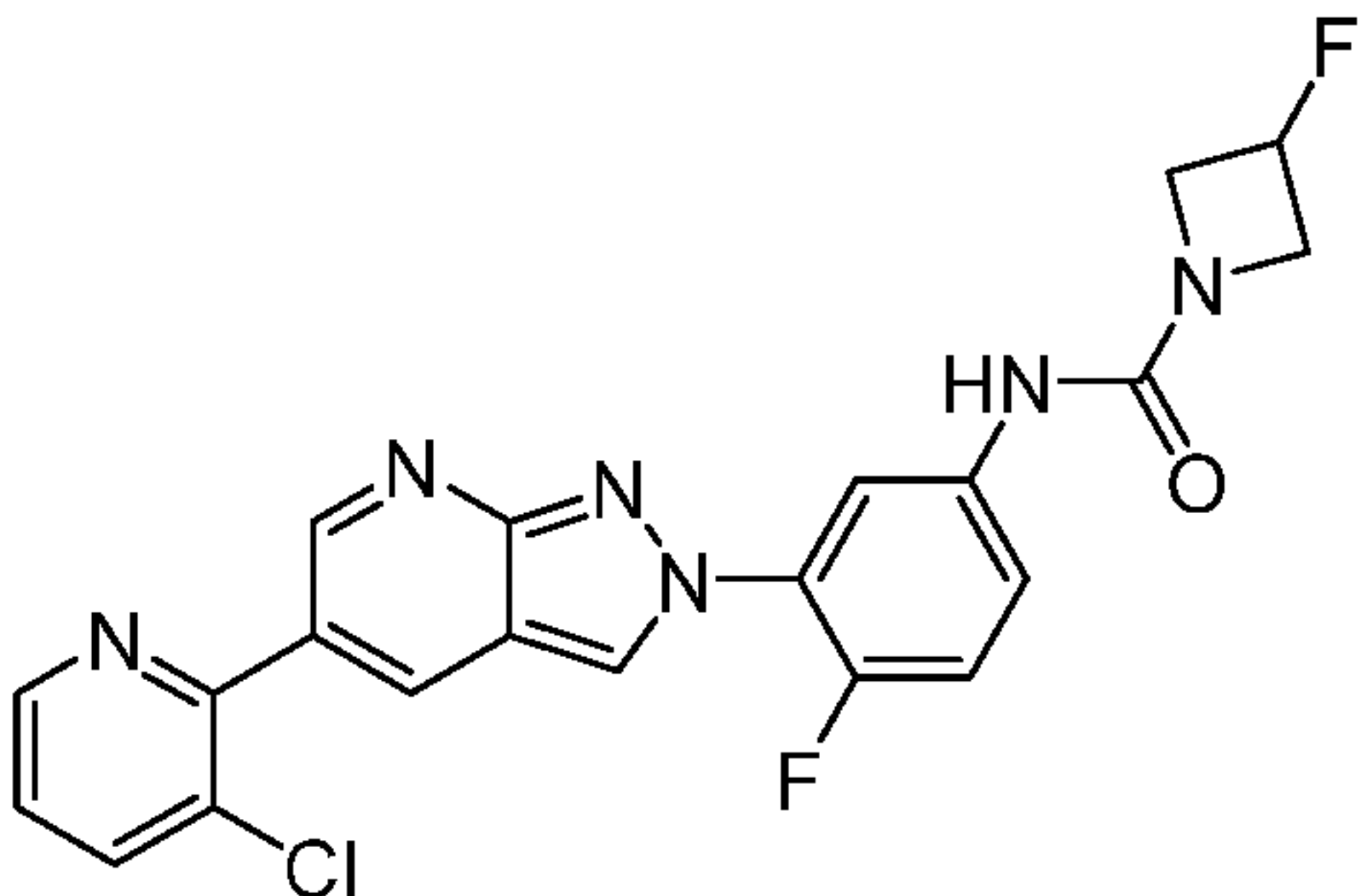
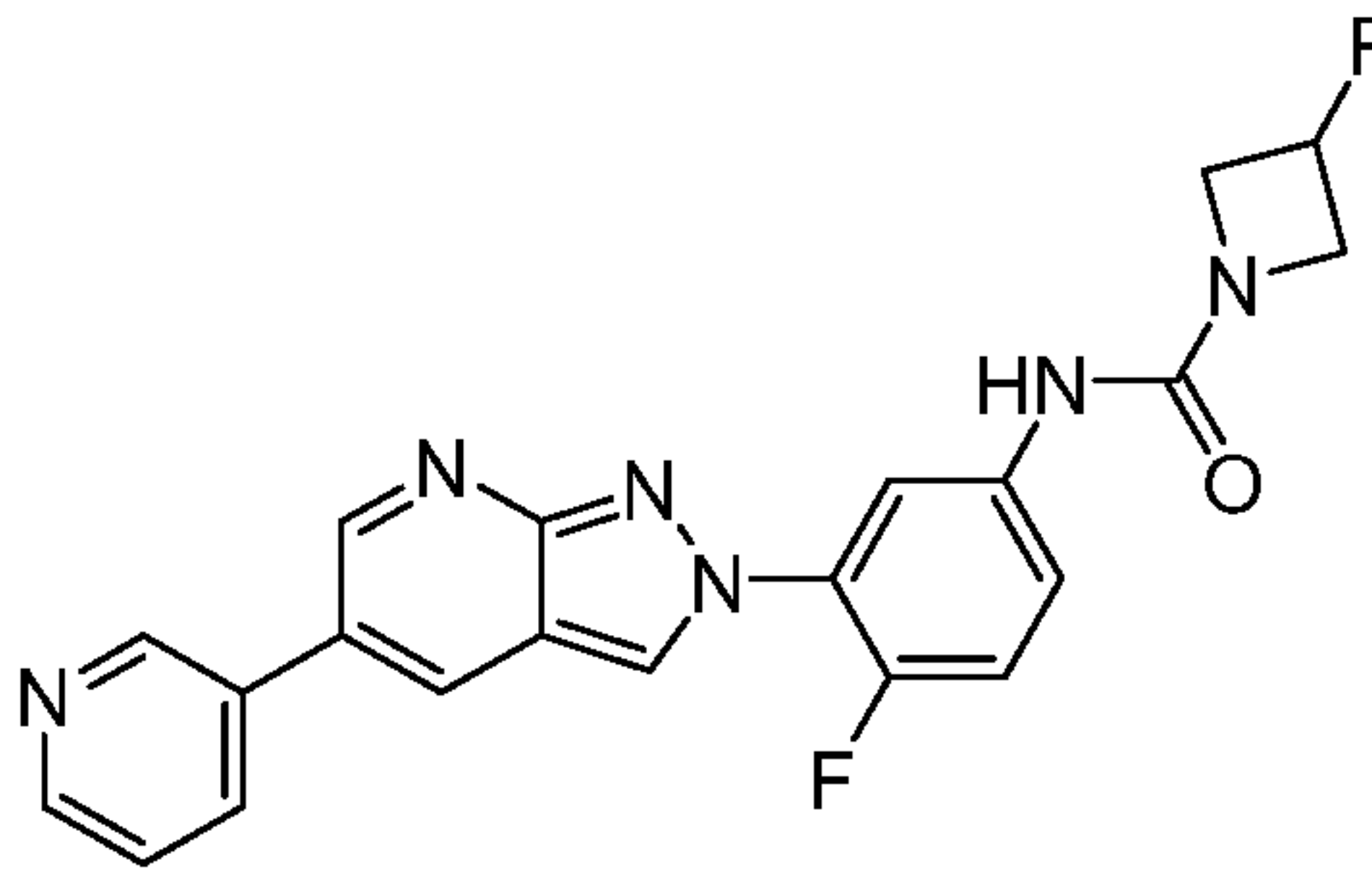
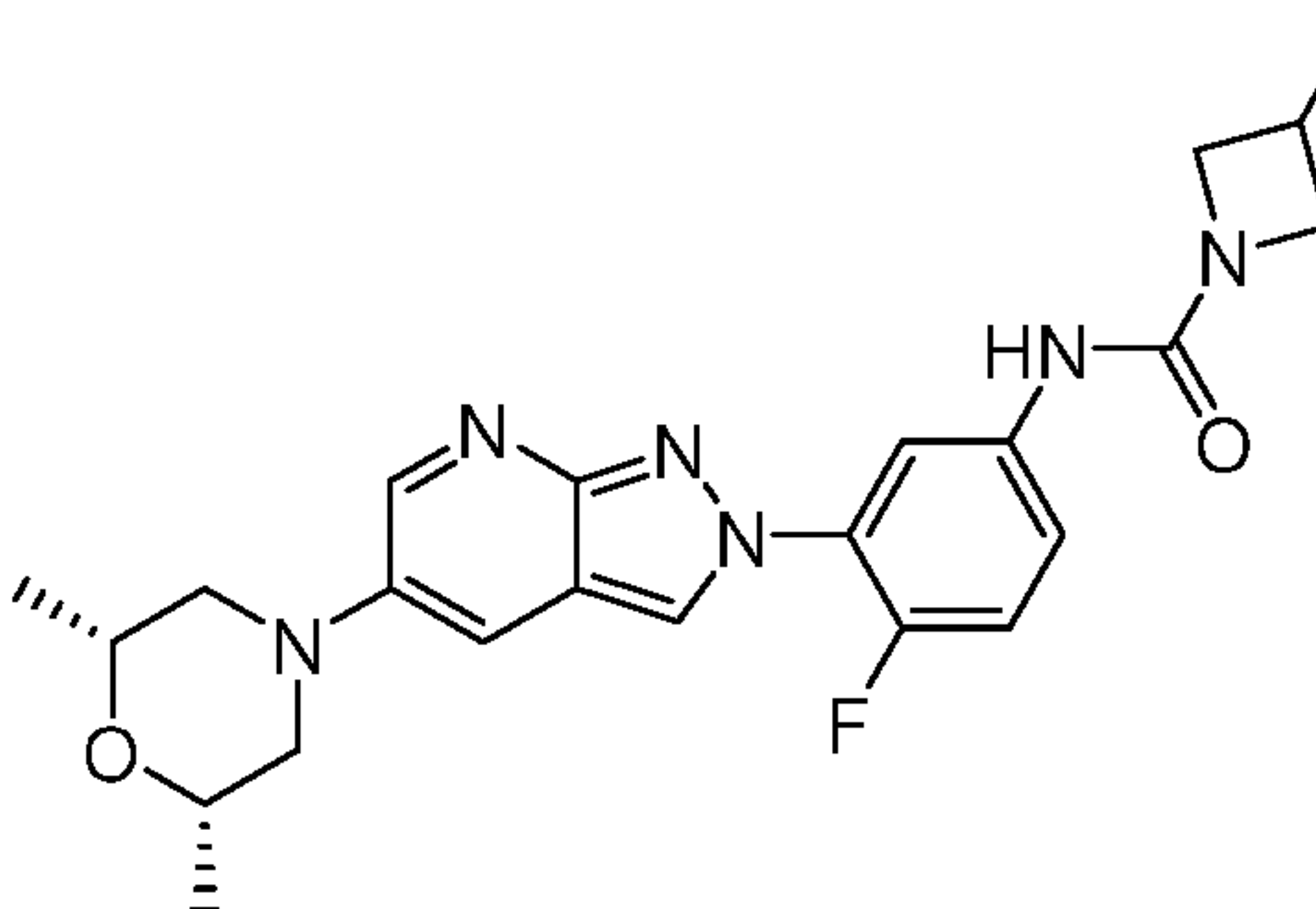
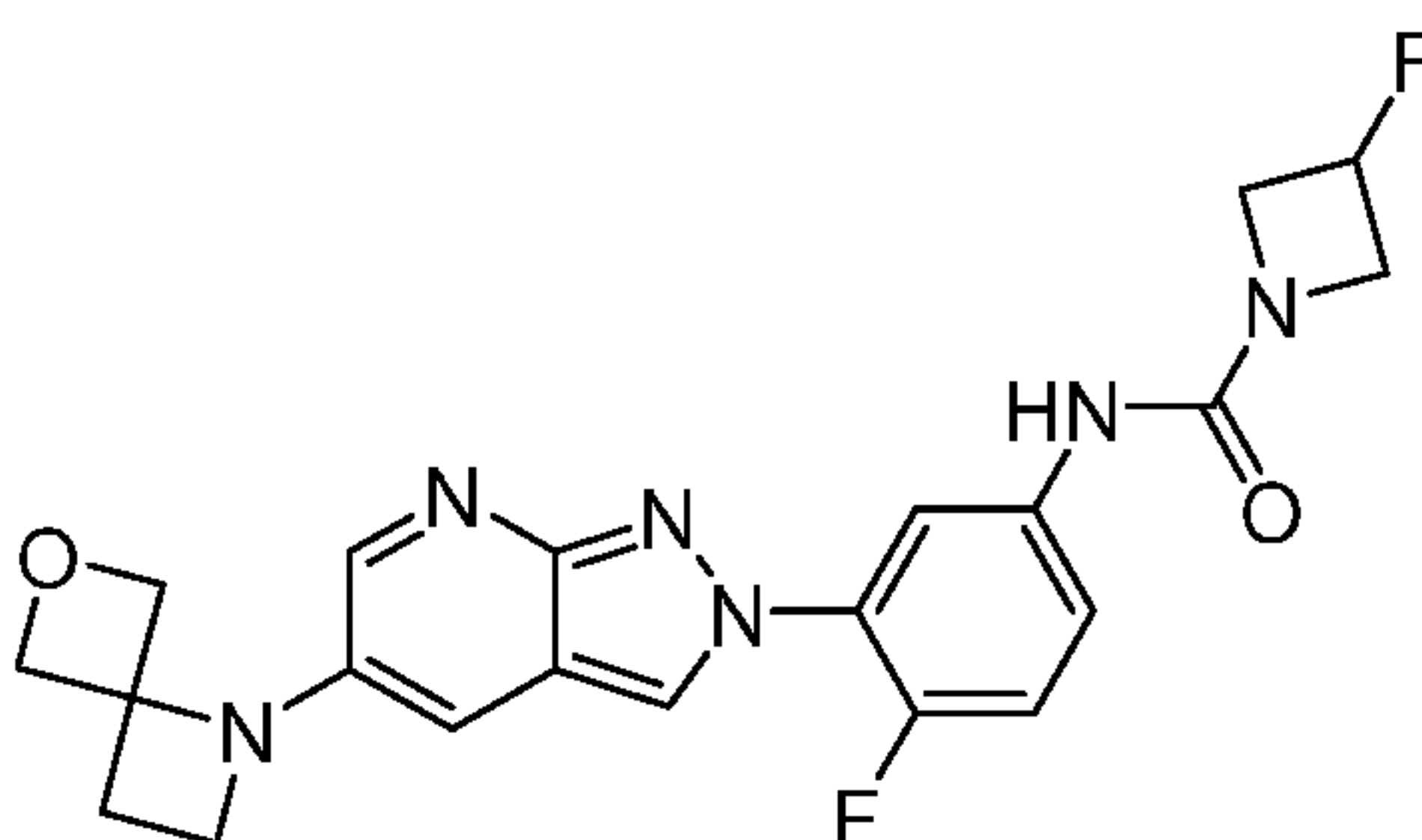
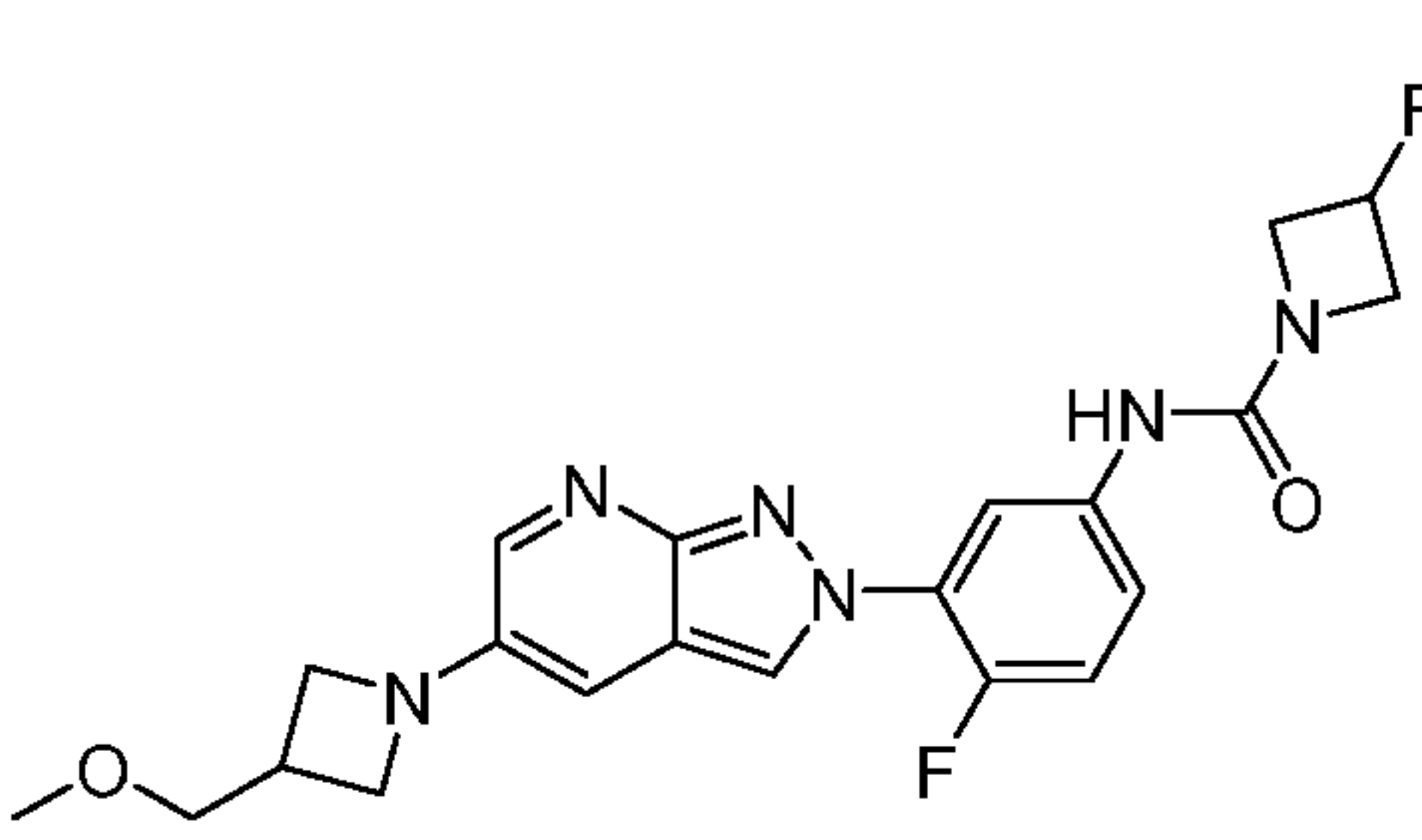
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
161		¹ H NMR (400 MHz, DMSO), δ 9.19 (s, 1 H), 8.50 (dd, <i>J</i> = 6.59, 2.82 Hz, 2 H), 8.20 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.58 - 7.66 (m, 1 H), 7.44 (dd, <i>J</i> = 11.42, 9.16 Hz, 1 H), 6.88 (d, <i>J</i> = 2.76 Hz, 1 H), 4.40 (t, <i>J</i> = 12.67 Hz, 4 H), 3.35 (br s, 4 H), 1.93 - 2.03 (m, 4 H), Method 1: RT = 3.16 min.; M+H = 417.2
162		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 9.09 (d, <i>J</i> = 2.01 Hz, 1 H), 8.91 (s, 1 H), 8.78 (s, 1 H), 8.27 (dd, <i>J</i> = 6.78, 2.76 Hz, 1 H), 7.65 (ddd, <i>J</i> = 9.07, 4.11, 2.76 Hz, 1 H), 7.41 (dd, <i>J</i> = 10.92, 9.03 Hz, 1 H), 5.24 - 5.43 (m, 1 H), 3.54 - 3.91 (m, 6 H), 2.07 - 2.37 (m, 2 H) Method 1: RT = 2.82 min.; M+H = 426.2
163		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄), δ 8.68 (s, 1 H), 8.50 (dd, <i>J</i> = 12.61, 2.82 Hz, 2 H), 8.21 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.61 - 7.67 (m, 1 H), 7.40 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.89 (d, <i>J</i> = 2.76 Hz, 1 H), 3.97 (t, <i>J</i> = 7.53 Hz, 4 H), 3.36 (br s, 4 H), 2.19 (quin, <i>J</i> = 7.56 Hz, 2 H), 1.95 - 2.04 (m, 4 H) Method 1: RT = 2.95 min.; M+H = 381.2
164		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.79 (d, <i>J</i> = 2.26 Hz, 1 H) 8.68 (d, <i>J</i> = 2.01 Hz, 1 H) 8.36 (d, <i>J</i> = 1.51 Hz, 1 H) 8.15 (dd, <i>J</i> = 6.65, 2.64 Hz, 1 H) 7.67 (ddd, <i>J</i> = 9.10, 4.20, 2.76 Hz, 1 H) 7.35 - 7.36 (m, 1 H) 7.26 - 7.47 (m, 1 H) 4.13 (t, <i>J</i> = 7.65 Hz, 4 H) 3.74 (q, <i>J</i> = 10.88 Hz, 2 H) 2.34 (quin, <i>J</i> = 7.65 Hz, 2 H) Method 1: RT = 2.75 min.; M+H = 394.2
165		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 9.24 (s, 1 H), 8.82 (d, <i>J</i> = 2.51 Hz, 1 H), 8.70 (d, <i>J</i> = 2.26 Hz, 1 H), 8.23 (dd, <i>J</i> = 6.90, 2.89 Hz, 1 H), 8.07 (d, <i>J</i> = 2.01 Hz, 1 H), 7.65 - 7.71 (m, 1 H), 7.49 (dd, <i>J</i> = 11.29, 9.03 Hz, 1 H), 4.41 (t, <i>J</i> = 12.67 Hz, 4 H), 4.00 (dd, <i>J</i> = 10.54, 3.76 Hz, 2 H), 3.45 - 3.54 (m, 2 H), 2.92 - 3.01 (m, 1 H), 1.69 - 1.86 (m, 4 H). Method 1: RT = 2.81 min.; M+H = 432.2
166		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆), δ 9.24 (s, 1 H), 8.96 (d, <i>J</i> = 2.51 Hz, 1 H), 8.69 (d, <i>J</i> = 2.01 Hz, 1 H), 8.34 (s, 1 H), 8.24 (dd, <i>J</i> = 7.03, 2.51 Hz, 1 H), 7.66 - 7.73 (m, 1 H), 7.51 (dd, <i>J</i> = 11.29, 9.29 Hz, 1 H), 4.42 (t, <i>J</i> = 12.80 Hz, 4 H), 3.87 (q, <i>J</i> = 11.46 Hz, 2 H). Method 1: RT = 2.85 min.; M+H = 430.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
167		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.92 (s, 1 H), 8.70 (d, J=2.93 Hz, 1 H), 8.55 (d, J=2.93 Hz, 1 H), 8.21 (dd, J=6.97, 2.57 Hz, 1 H), 7.56 - 7.74 (m, 1 H), 7.43 (dd, J=11.49, 9.05 Hz, 1 H), 7.16 (d, J=2.93 Hz, 1 H), 5.25 - 5.57 (m, 1 H), 4.22 - 4.40 (m, 2 H), 3.87 - 4.12 (m, 2 H), 2.96 (s, 6 H) Method 1: RT = 2.69 min.; M+H = 373.1
168		¹ H NMR (400 MHz, Methanol-d ₄) δ 8.64 (br d, J = 2.26 Hz, 1 H), 8.61 (br d, J = 2.64 Hz, 1 H), 8.44 (br s, 1 H), 8.10 (dd, J = 6.71, 2.70 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.33 (dd, J = 10.92, 9.16 Hz, 1 H), 5.25 - 5.47 (m, 1 H), 5.01 (dt, J = 12.52, 6.23 Hz, 1 H), 4.32 - 4.43 (m, 2 H), 4.07 - 4.19 (m, 2 H), 1.33 (d, J = 6.27 Hz, 6 H). Method 1: RT = 2.88 min.; M+H = 431.1
169		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.57 (s, 1 H), 9.05 (d, J=2.51 Hz, 1 H), 8.88 (d, J=2.01 Hz, 1 H), 8.59 (dd, J=7.03, 2.51 Hz, 1 H), 8.43 (d, J=1.76 Hz, 1 H), 7.89 - 7.99 (m, 1 H), 7.59 (dd, J=11.04, 9.03 Hz, 1 H), 4.00 (br dd, J=10.79, 3.26 Hz, 2 H), 3.48 (td, J=11.36, 2.38 Hz, 2 H), 2.98 - 3.10 (m, 1 H), 2.50 (br s, 3 H), 2.39 (s, 3 H), 1.70 - 1.89 (m, 4 H). Method 1: RT = 2.77 min.; M+H = 436.2
170		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.69 (d, J=3.01 Hz, 1 H), 8.66 - 8.68 (m, 1 H), 8.53 (d, J=2.76 Hz, 1 H), 8.21 (dd, J=7.03, 2.76 Hz, 1 H), 7.57 - 7.77 (m, 1 H), 7.40 (dd, J=11.29, 9.03 Hz, 1 H), 7.15 (d, J=2.76 Hz, 1 H), 3.98 (t, J=7.53 Hz, 4 H), 2.95 (s, 6H), 2.20 (quin, J=7.59 Hz, 2 H). Method 1: RT = 2.62 min.; M+H = 355.2
171		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.93 (s, 1H), 8.55 (d, J = 2.7 Hz, 1H), 8.27 (d, J = 2.8 Hz, 1H), 8.20 (dd, J = 7.1, 2.7 Hz, 1H), 7.64 (ddd, J = 9.1, 4.1, 2.7 Hz, 1H), 7.43 (dd, J = 11.4, 9.1 Hz, 1H), 6.94 (d, J = 2.8 Hz, 1H), 5.40 (dtt, J = 57.5, 6.1, 3.1 Hz, 1H), 4.75 (s, 4H), 4.31 (dddd, J = 21.8, 10.4, 6.0, 1.4 Hz, 2H), 4.10 (s, 4H), 4.08 - 3.96 (m, 2H). Method 1: RT = 2.55 min.; M+H = 427.2

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
172		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.93 (s, 1H), 8.54 (d, J = 2.9 Hz, 1H), 8.51 (d, J = 2.8 Hz, 1H), 8.20 (dd, J = 7.1, 2.7 Hz, 1H), 7.64 (ddd, J = 9.0, 4.1, 2.7 Hz, 1H), 7.43 (dd, J = 11.4, 9.1 Hz, 1H), 7.07 (d, J = 2.9 Hz, 1H), 5.40 (ddq, J = 57.5, 6.1, 3.0 Hz, 1H), 4.69 (d, J = 23.8 Hz, 2H), 4.40 - 4.23 (m, 2H), 4.09 - 4.05 (m, 1H), 4.04 - 3.95 (m, 1H), 3.82 - 3.70 (m, 2H), 3.70 - 3.58 (m, 1H), 3.08 (ddd, J = 9.6, 1.4, 0.7 Hz, 1H), 1.99 - 1.84 (m, 2H). Method 2: RT = 0.90 min.; M+H = 427.2
173		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.45 (s, 1H), 8.81 (d, J = 2.7 Hz, 1H), 8.69 (d, J = 2.3 Hz, 1H), 8.36 (dd, J = 7.0, 2.7 Hz, 1H), 8.05 (dd, J = 2.3, 0.8 Hz, 1H), 7.68 (ddd, J = 9.1, 4.2, 2.7 Hz, 1H), 7.54 (dd, J = 11.2, 9.0 Hz, 1H), 3.08 (pd, J = 6.9, 0.8 Hz, 1H), 2.72 - 2.55 (m, 4H), 1.30 (d, J = 6.9 Hz, 6H). Method 1: RT = 3.19 min.; M+H = 395.2
174		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.13 (s, 1H), 8.80 (d, J = 2.7 Hz, 1H), 8.69 (d, J = 2.3 Hz, 1H), 8.26 - 8.15 (m, 1H), 8.05 (dd, J = 2.3, 0.8 Hz, 1H), 7.65 - 7.45 (m, 2H), 4.35 (t, J = 6.0 Hz, 2H), 3.18 - 3.00 (m, 1H), 2.74 (qt, J = 11.5, 5.9 Hz, 2H), 1.30 (d, J = 6.9 Hz, 6H). Method 1: RT = 3.25 min.; M+H = 411.2
175		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.54 (s, 1H), 9.00 (d, J=2.51 Hz, 1H), 8.71 (d, J=2.01 Hz, 1H), 8.58 (dd, J=7.03, 2.51 Hz, 1H), 8.36 (s, 1H), 7.86 - 7.97 (m, 1H), 7.52 - 7.67 (m, 1H), 3.88 (q, J=11.13 Hz, 2H), 2.40 (s, 6H). Method 1: RT = 2.88 min.; M+H = 434.1
176		¹ H NMR (400 MHz, Methanol-d ₄) δ 8.91 (d, J = 1.88 Hz, 1H), 8.74 (s, 1H), 8.44 - 8.51 (m, 2H), 7.93 (dt, J = 7.18, 4.44 Hz, 1H), 7.78 (d, J = 1.13 Hz, 1H), 7.48 (dd, J = 11.11, 9.22 Hz, 1H), 7.32 (d, J = 3.51 Hz, 1H), 6.68 (dd, J = 3.58, 1.69 Hz, 1H), 3.77 (q, J = 10.75 Hz, 2H). Method 1: RT = 2.86 min.; M+H = 405.1
177		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.94 (s, 1H), 8.71 (d, J=2.76 Hz, 1H), 8.61 (d, J=2.51 Hz, 1H), 8.21 (dd, J=7.03, 2.51 Hz, 1H), 7.65 (dt, J=8.60, 3.61 Hz, 1H), 7.44 (dd, J=11.17, 9.16 Hz, 1H), 7.37 (d, J=2.51 Hz, 1H), 5.28 - 5.54 (m, 1H), 4.24 - 4.40 (m, 2H), 3.93 - 4.19 (m, 4H), 3.18 (dd, J=11.67, 2.89 Hz, 2H), 2.87 (dd, J=11.67, 5.90 Hz, 2H), 1.26 (d, J=6.27 Hz, 6H). Method 2: RT = 0.92 min.; M+H = 443.2

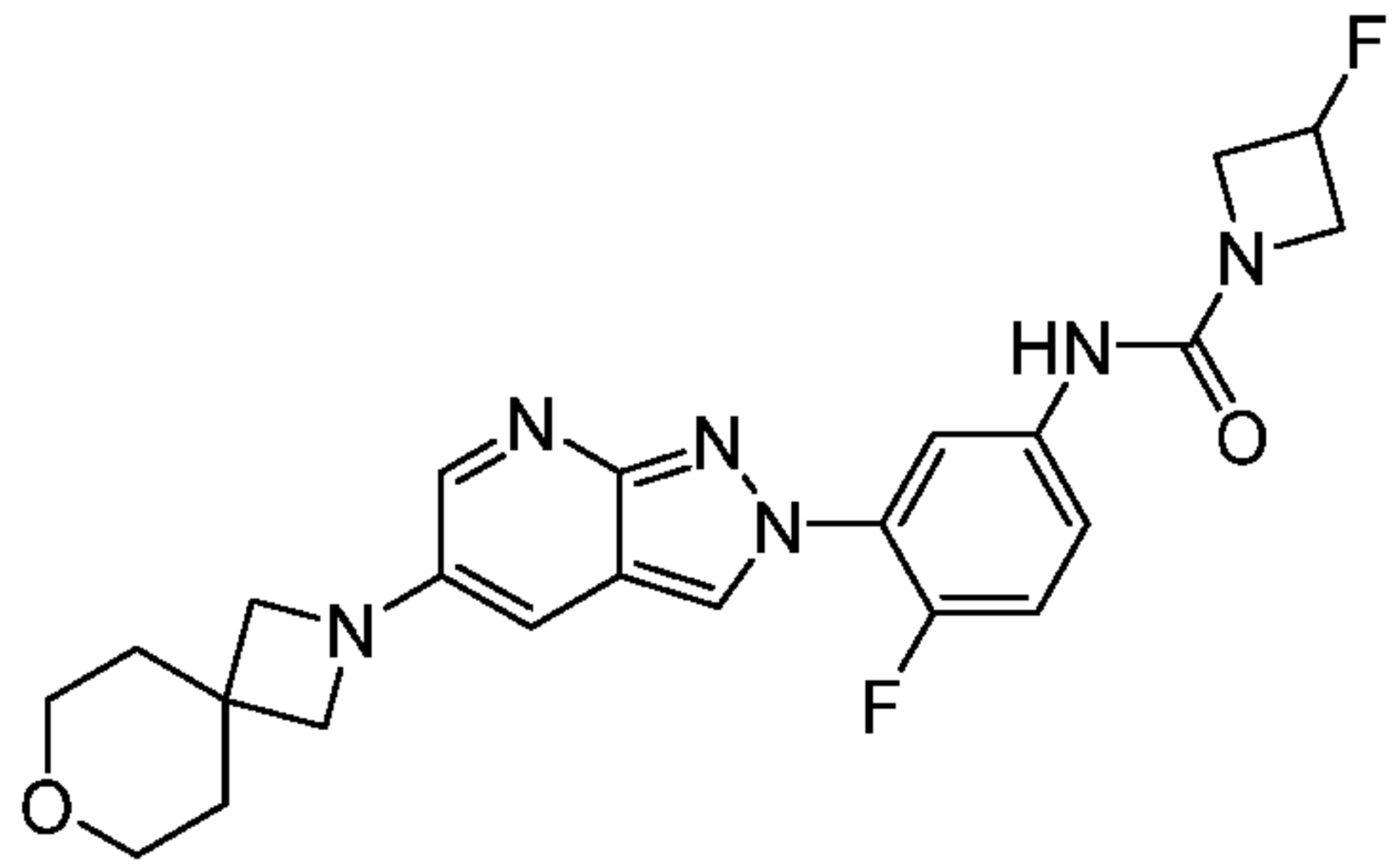
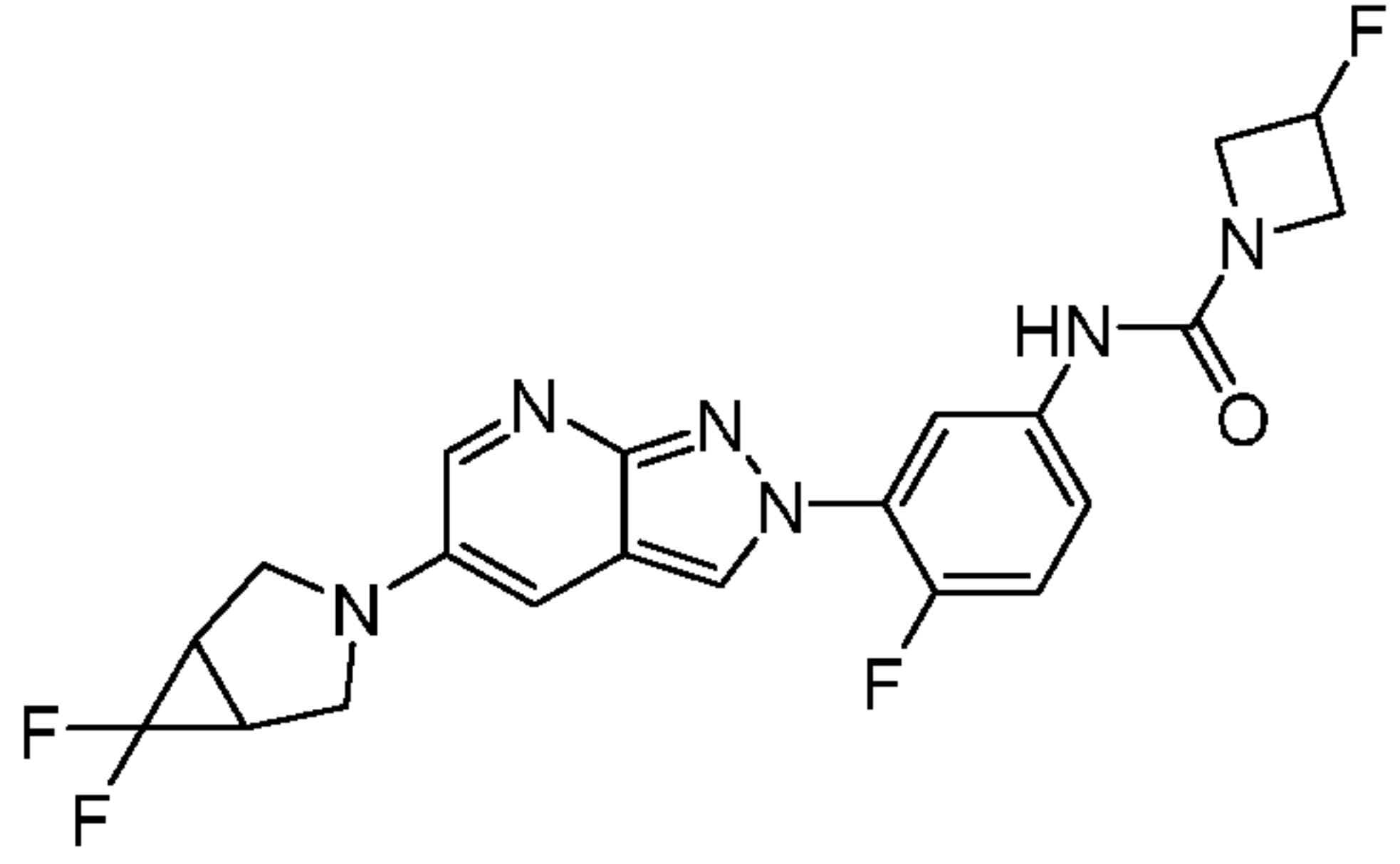
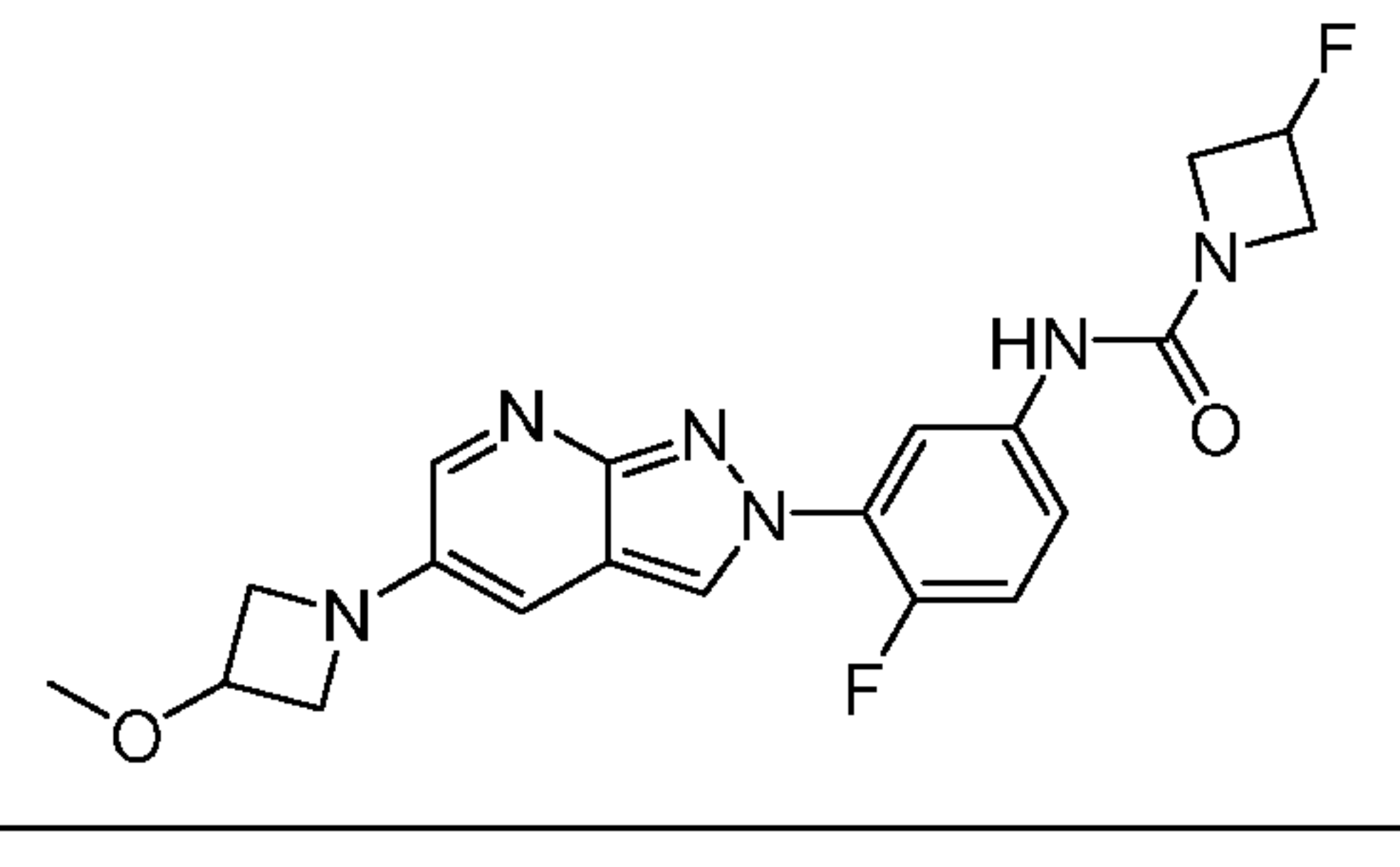
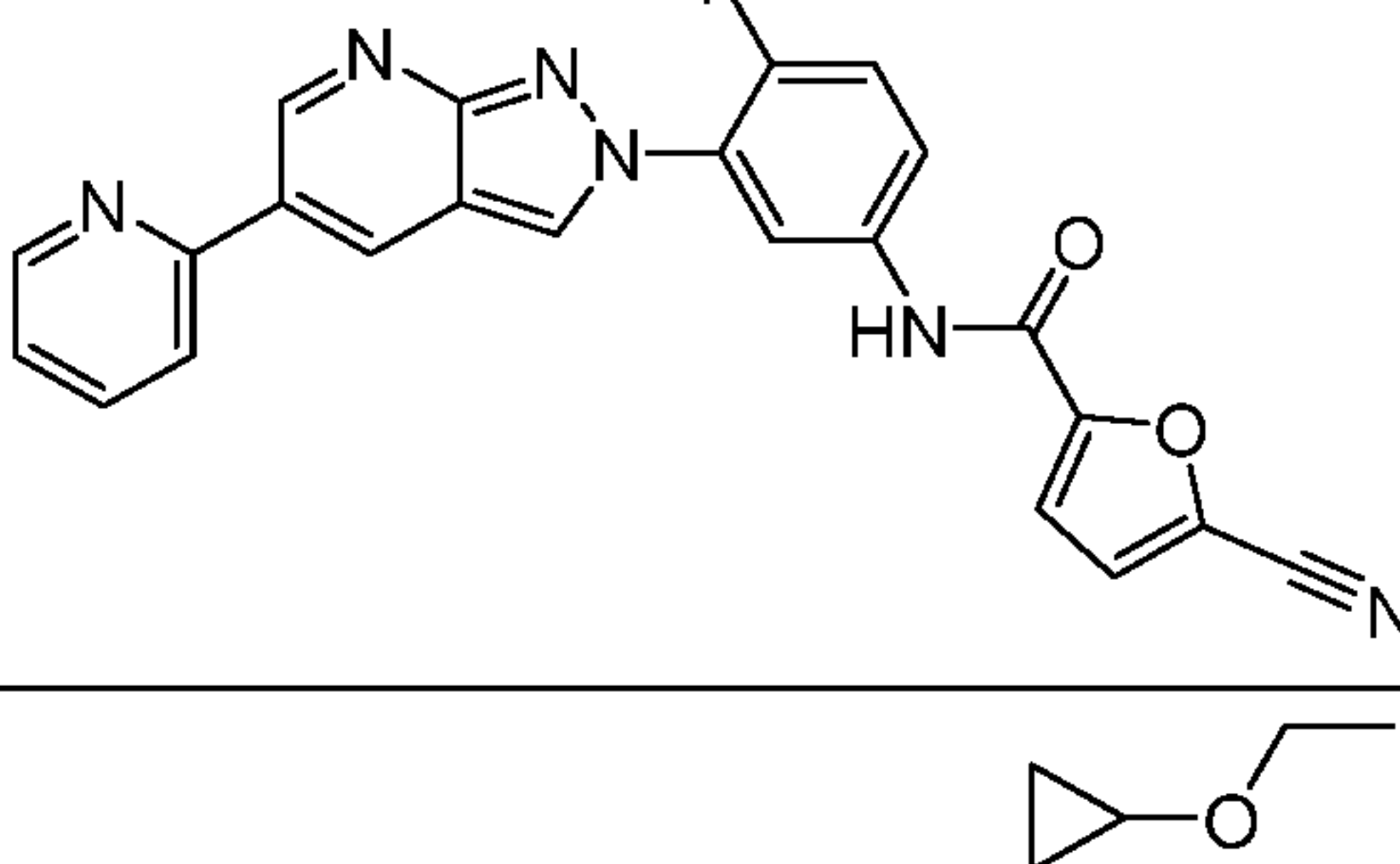
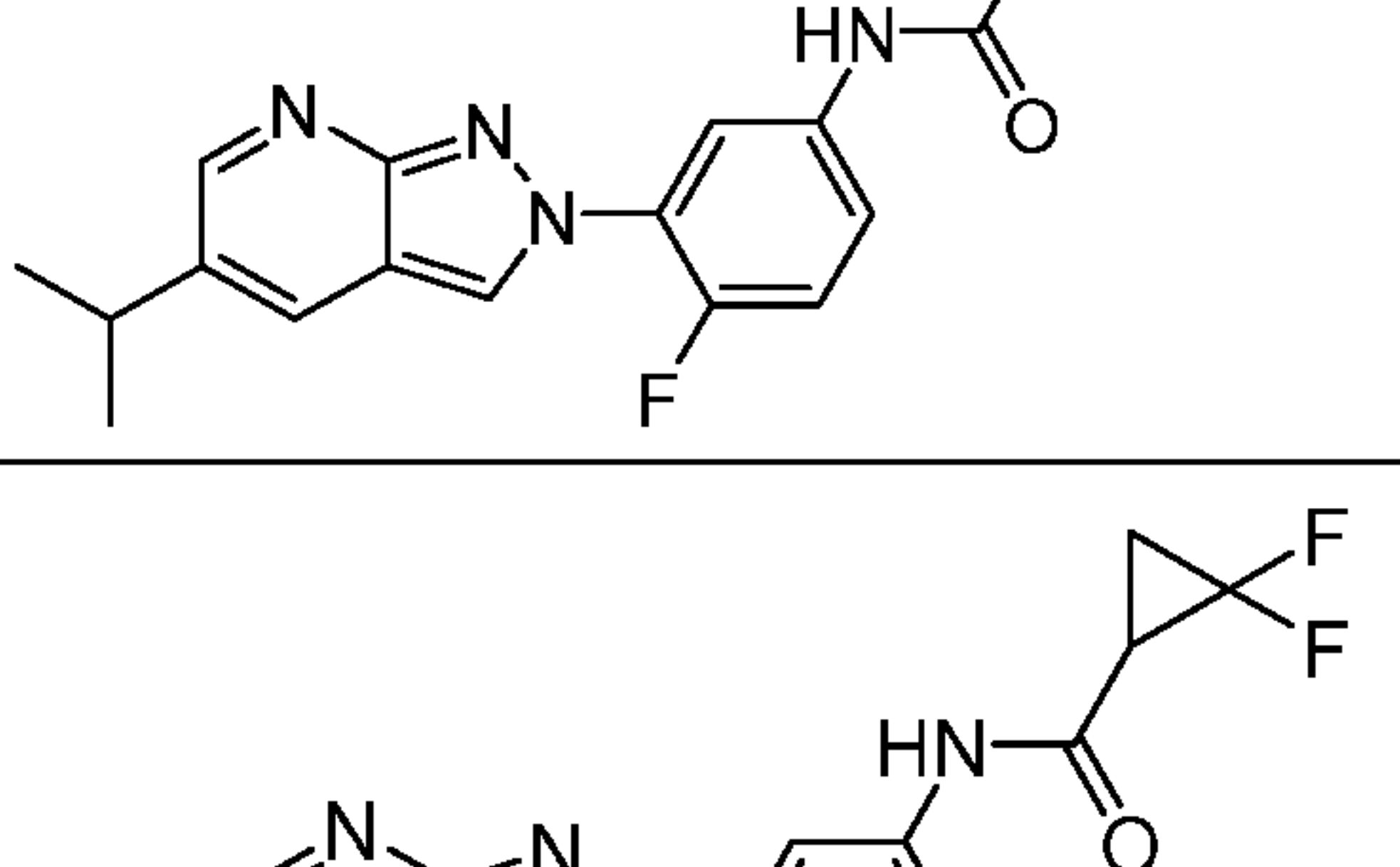
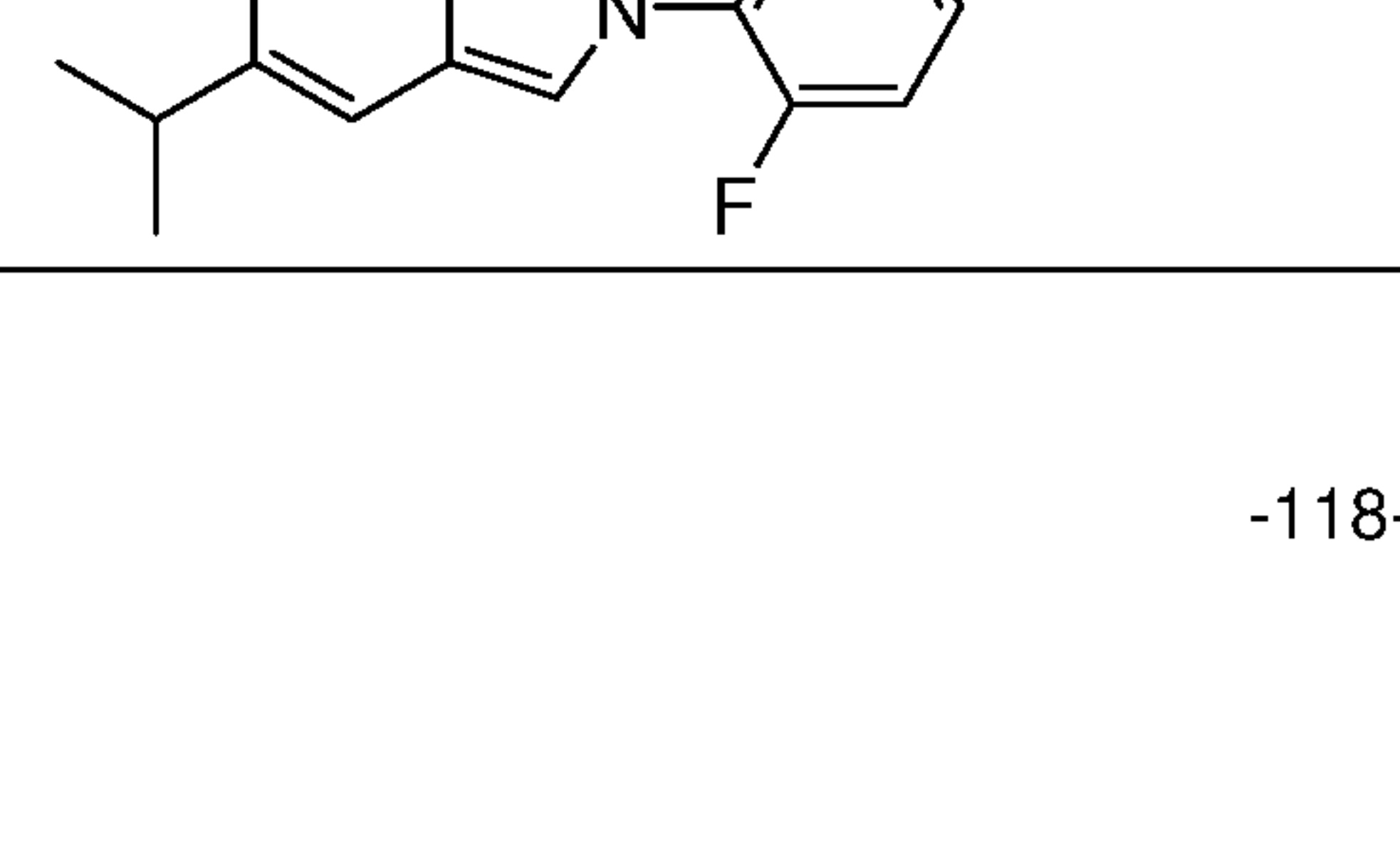
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
178		¹ H NMR (400 MHz, DMSO-d ₆), δ 8.95 (s, 1 H), 8.76 (d, J=2.76 Hz, 1 H), 8.64 (d, J=2.76 Hz, 1 H), 8.20 (dd, J=7.03, 2.51 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.60 (d, J=3.01 Hz, 1 H), 7.45 (dd, J=11.29, 9.03 Hz, 1 H), 5.28 - 5.55 (m, 1 H), 4.24 - 4.41 (m, 2 H), 3.94 - 4.10 (m, 2 H), 3.67 - 3.82 (m, 4 H), 3.25 - 3.31 (m, 4 H). Method 2: RT = 0.72 min.; M+H = 463.1
179		¹ H NMR (400 MHz, METHANOL-d ₄), δ 8.68 (d, J=2.76 Hz, 1 H), 8.55 (d, J=2.26 Hz, 1 H), 8.11 (dd, J=6.78, 2.76 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.55 (d, J=2.76 Hz, 1 H), 7.35 (dd, J=10.92, 9.16 Hz, 1 H), 5.27 - 5.49 (m, 1 H), 4.34 - 4.47 (m, 2 H), 4.08 - 4.21 (m, 2 H), 3.22 - 3.31 (m, 4 H), 2.68 - 2.76 (m, 4 H), 2.41 (s, 3 H). Method 2: RT = 0.51 min.; M+H = 428.2
180		¹ H NMR (400 MHz, DMSO-d ₆), δ 8.95 (s, 1 H), 8.87 (d, J=3.01 Hz, 1 H), 8.66 (d, J=2.76 Hz, 1 H), 8.21 (dd, J=7.15, 2.64 Hz, 1 H), 7.66 (dt, J=8.85, 3.48 Hz, 1 H), 7.54 (d, J=3.01 Hz, 1 H), 7.45 (dd, J=11.29, 9.29 Hz, 1 H), 7.14 (d, J=1.00 Hz, 1 H), 6.92 (d, J=1.00 Hz, 1 H), 5.30 - 5.51 (m, 1 H), 4.40 (s, 2 H), 4.26 - 4.38 (m, 2 H), 4.15 (t, J=5.40 Hz, 2 H), 3.97 - 4.09 (m, 2 H), 3.76 (t, J=5.40 Hz, 2 H). Method 2: RT = 0.53 min.; M+H = 451.2
181		¹ H NMR (400 MHz, DMSO-d ₆), δ 8.93 (s, 1 H), 8.54 (d, J=2.76 Hz, 1 H), 8.28 (d, J=2.76 Hz, 1 H), 8.20 (dd, J=7.15, 2.64 Hz, 1 H), 7.61 - 7.70 (m, 1 H), 7.43 (dd, J=11.42, 9.16 Hz, 1 H), 6.92 (d, J=2.76 Hz, 1 H), 5.68 (d, J=6.78 Hz, 1 H), 5.28 - 5.51 (m, 1 H), 4.57 - 4.67 (m, 1 H), 4.25 - 4.40 (m, 2 H), 4.20 (t, J=7.15 Hz, 2 H), 3.94 - 4.11 (m, 2 H), 3.56 - 3.65 (m, 2 H). Method 2: RT = 0.70 min.; M+H = 401.1
182		¹ H NMR (400 MHz, DMSO-d ₆), δ 9.17 (d, J=2.26 Hz, 1 H), 9.03 (d, J=2.51 Hz, 1 H), 9.00 (s, 1 H), 8.75 (d, J=2.51 Hz, 1 H), 8.67 - 8.73 (m, 2 H), 8.28 (dd, J=6.90, 2.64 Hz, 1 H), 7.84 - 7.90 (m, 2 H), 7.68 - 7.75 (m, 1 H), 7.50 (dd, J=11.29, 9.03 Hz, 1 H), 5.30 - 5.52 (m, 1 H), 4.27 - 4.40 (m, 2 H), 3.97 - 4.10 (m, 2 H). Method 2: RT = 0.58 min.; M+H = 407.1

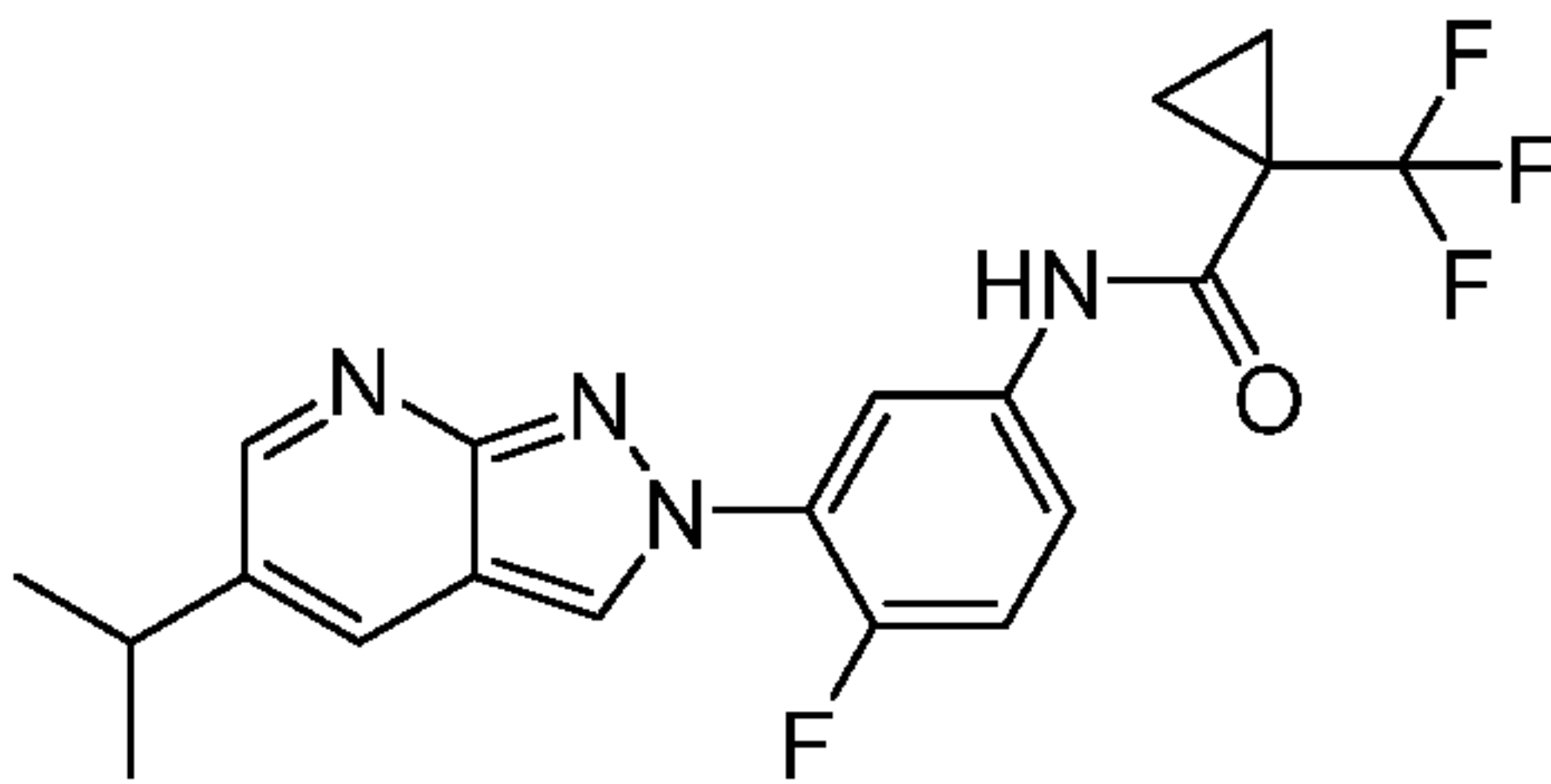
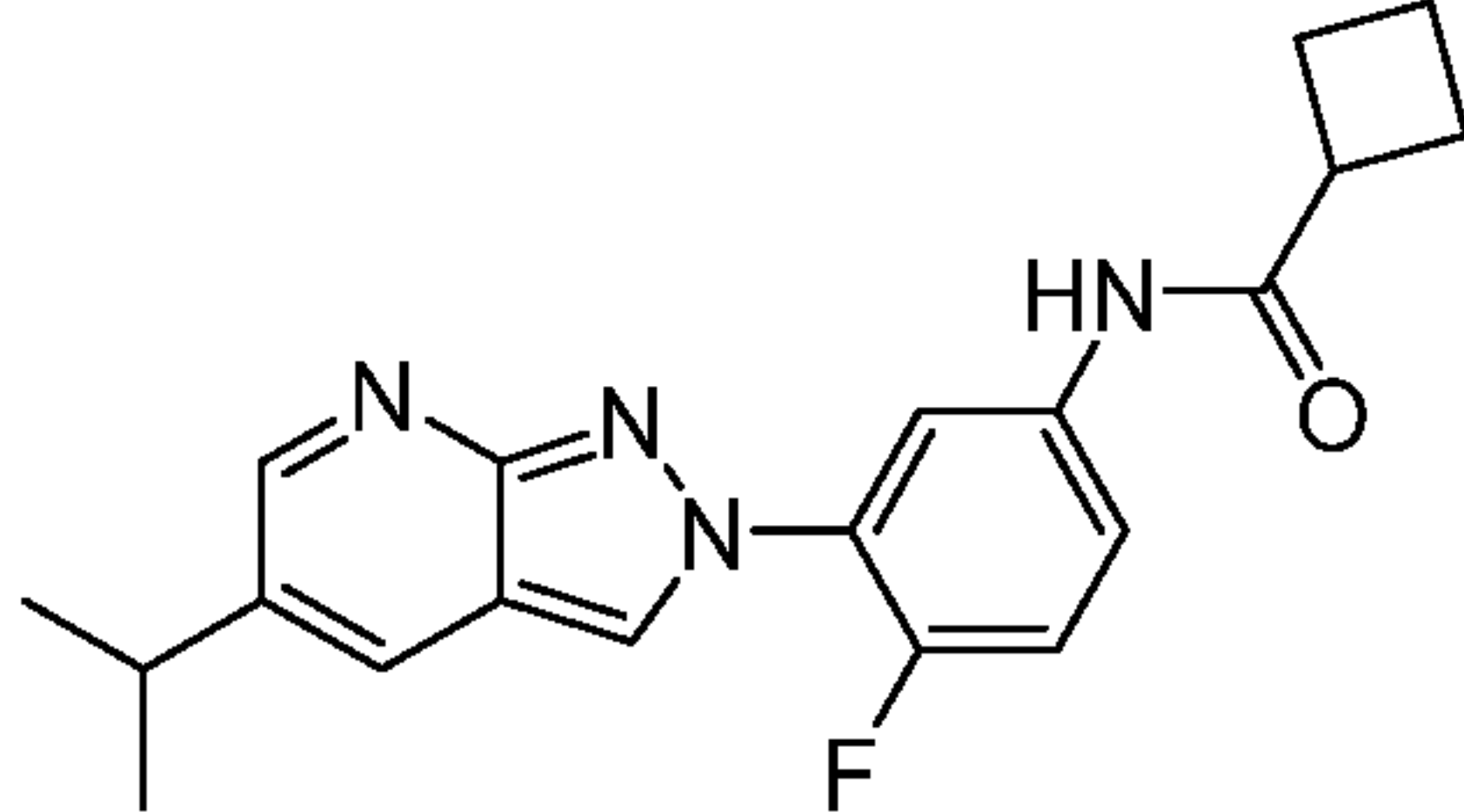
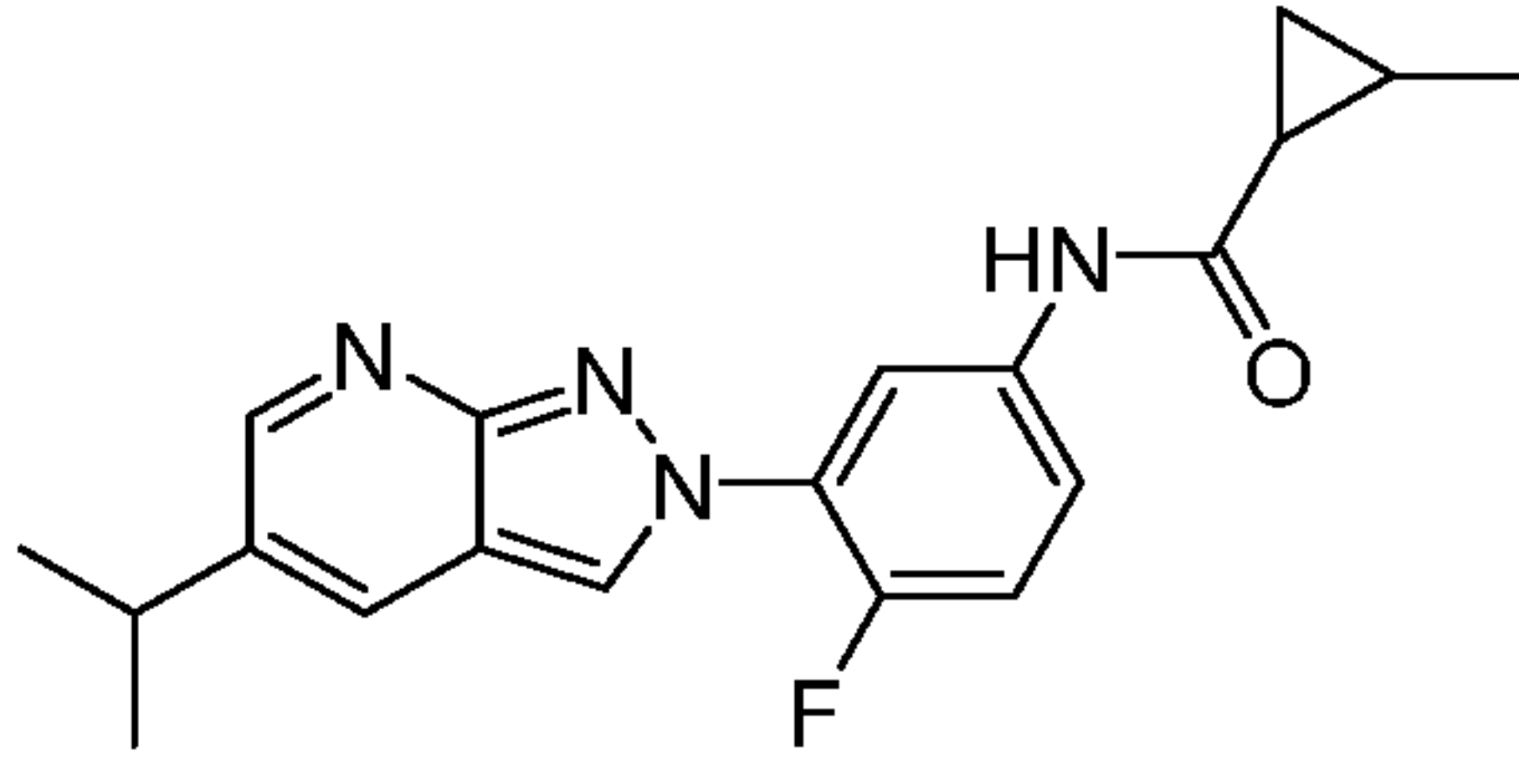
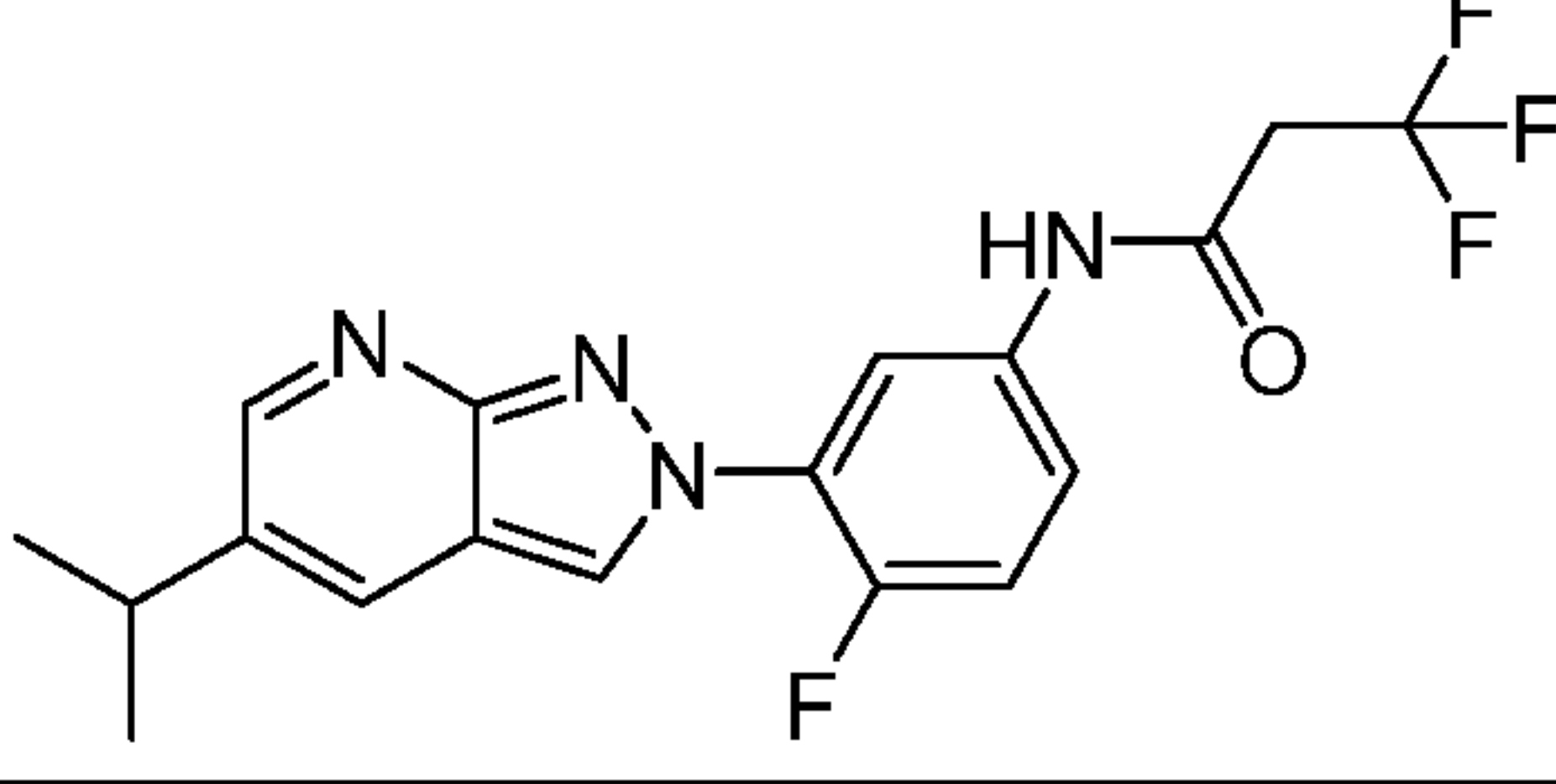
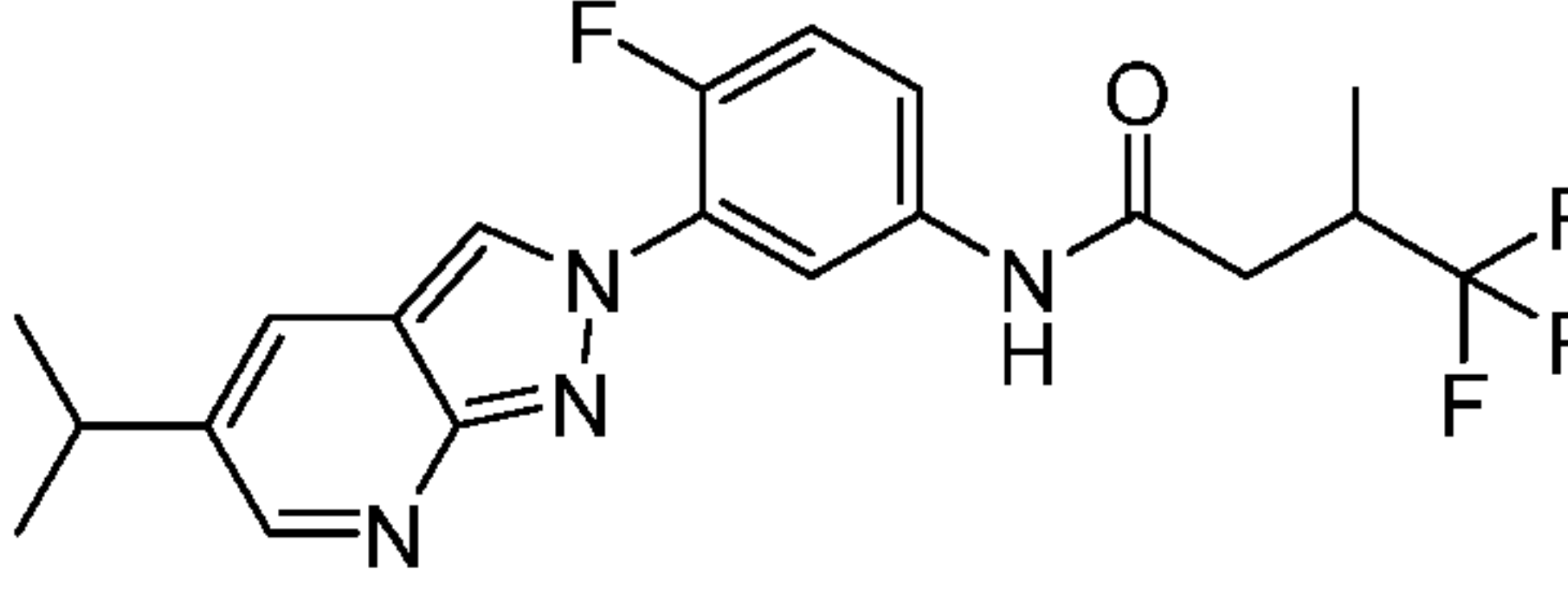
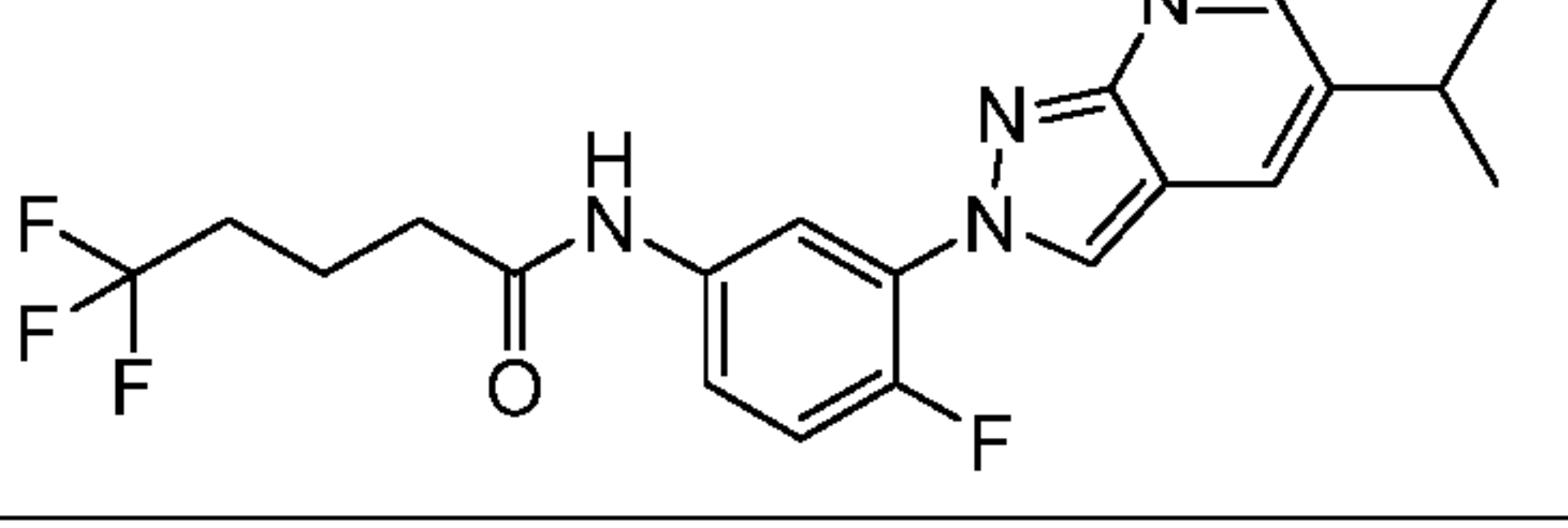
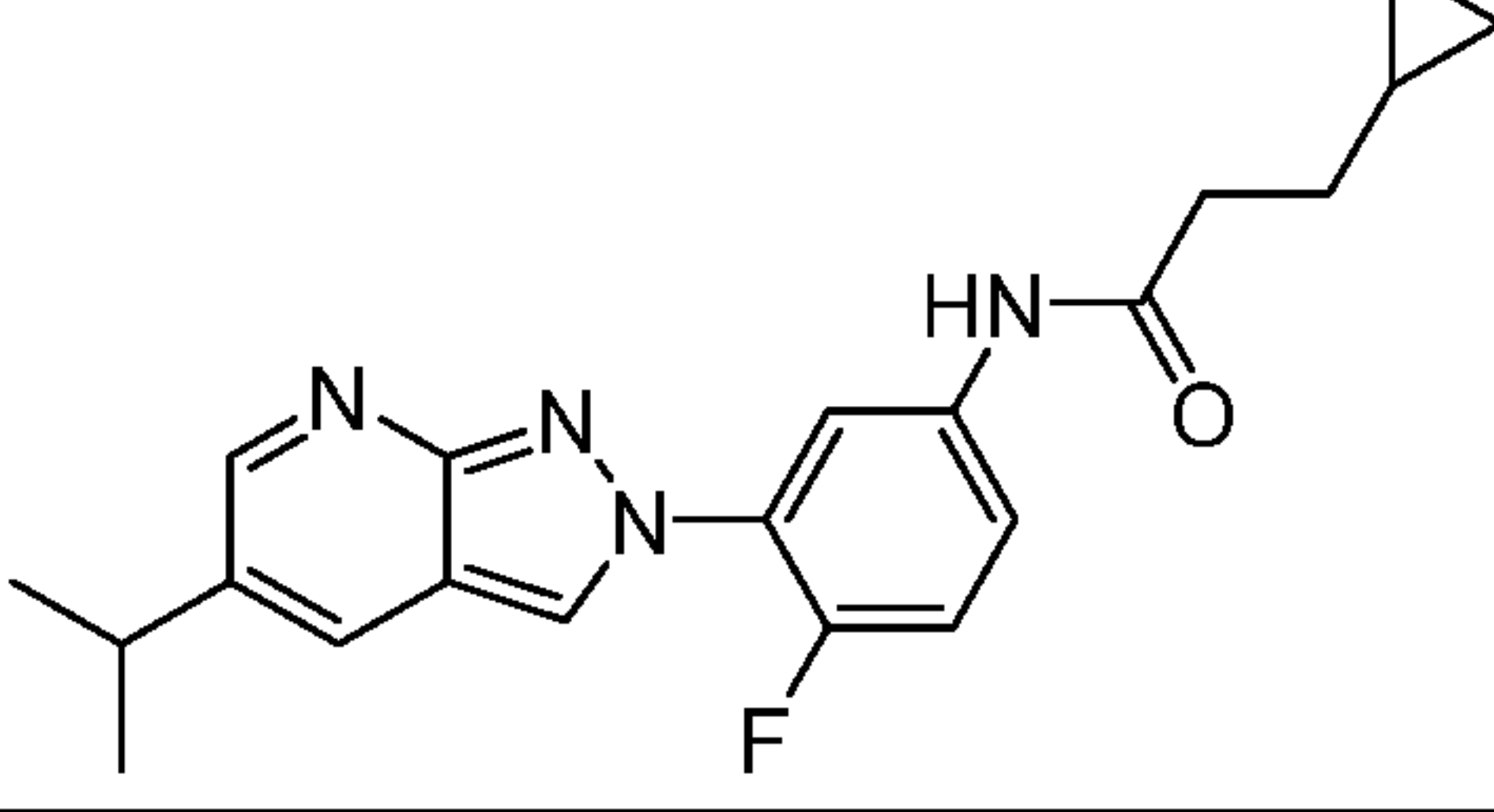
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Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
188		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.02 - 9.05 (m, 2 H), 9.00 (d, J=2.38 Hz, 1 H), 8.72 (dd, J=4.64, 1.38 Hz, 1 H), 8.69 (d, J=2.26 Hz, 1 H), 8.29 (dd, J=6.96, 2.70 Hz, 1 H), 8.14 (dd, J=8.16, 1.38 Hz, 1 H), 7.69 - 7.76 (m, 1 H), 7.52 - 7.55 (m, 1 H), 7.47 - 7.51 (m, 1 H), 5.28 - 5.53 (m, 1 H), 4.28 - 4.39 (m, 2 H), 3.97 - 4.10 (m, 2 H). Method 1: RT = 2.76 min.; M+H = 441.0
189		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.11 (d, J=2.38 Hz, 1 H), 9.03 (d, J=1.88 Hz, 1 H), 9.01 (s, 1 H), 8.99 (d, J=2.51 Hz, 1 H), 8.62 - 8.66 (m, 2 H), 8.28 (dd, J=6.90, 2.64 Hz, 1 H), 8.24 (dt, J=8.22, 1.79 Hz, 1 H), 7.69 - 7.75 (m, 1 H), 7.56 (dd, J=7.40, 4.77 Hz, 1 H), 7.50 (dd, J=11.17, 9.16 Hz, 1 H), 5.23 - 5.56 (m, 1 H), 4.27 - 4.41 (m, 2 H), 3.97 - 4.11 (m, 2 H). Method 1: RT = 2.40 min.; M+H = 407.1
190		¹ H NMR (400 MHz, DMSO) δ 8.91 (s, 1 H), 8.73 (d, J = 2.76 Hz, 1 H), 8.58 (d, J = 2.64 Hz, 1 H), 8.18 (dd, J=7.03, 2.64 Hz, 1 H), 7.57 - 7.68 (m, 1 H), 7.41 (dd, J=11.29, 9.03 Hz, 1 H), 7.35 (d, J = 2.76 Hz, 1 H), 5.25 - 5.49 (m, 1 H), 4.23 - 4.36 (m, 2 H), 3.93 - 4.07 (m, 2 H), 3.69 - 3.84 (m, 2 H), 3.56 (br d, J = 10.92 Hz, 2 H), 2.24 - 2.32 (m, 2 H), 1.15 (d, J = 6.15 Hz, 6 H). Method 1: RT = 2.77 min. M+H = 443.3
191		¹ H NMR (400 MHz, DMSO) δ 8.94 (s, 1 H), 8.60 (d, J = 2.76 Hz, 1 H), 8.56 (d, J = 2.76 Hz, 1 H), 8.22 (dd, J = 7.09, 2.70 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.44 (dd, J = 11.29, 9.16 Hz, 1 H), 7.18 (d, J = 2.76 Hz, 1 H), 5.30 - 5.51 (m, 1 H), 5.10 (d, J = 8.28 Hz, 2 H), 4.75 (d, J = 8.28 Hz, 2 H), 4.26 - 4.38 (m, 2 H), 3.96 - 4.09 (m, 2 H), 3.74 (t, J = 6.96 Hz, 2 H), 2.58 (br s, 2 H). Method 1: RT = 2.65 min. M+H = 427.2
192		¹ H NMR (400 MHz, DMSO) δ 8.94 (s, 1 H), 8.52 (d, J = 2.69 Hz, 1 H), 8.26 (d, J = 2.81 Hz, 1 H), 8.19 (dd, J = 7.03, 2.63 Hz, 1 H), 7.60 - 7.68 (m, 1 H), 7.42 (dd, J = 11.37, 9.17 Hz, 1 H), 6.88 (d, J = 2.69 Hz, 1 H), 5.28 - 5.50 (m, 1 H), 4.24 - 4.37 (m, 2 H), 4.02 - 4.08 (m, 1 H), 3.98 (t, J = 7.64 Hz, 3 H), 3.65 (dd, J = 7.15, 5.69 Hz, 2 H), 3.56 (d, J=6.60 Hz, 2 H), 3.29 (s, 3 H), 2.96 (m, 1 H). Method 1: RT = 2.76 min. M+H = 429.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
193		¹ H NMR (400 MHz, DMSO) δ 8.92 (s, 1 H), 8.52 (d, <i>J</i> = 2.76 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.59 - 7.67 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.91 (d, <i>J</i> = 2.89 Hz, 1 H), 5.27 - 5.50 (m, 1 H), 4.23 - 4.38 (m, 2 H), 3.94 - 4.10 (m, 6 H), 0.68 (s, 4 H). Method 1: RT = 2.92 min. M+H = 411.3 +
194		¹ H NMR (400 MHz, DMSO) δ 8.88 (s, 1 H), 8.48 - 8.59 (m, 2 H), 8.17 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.54 - 7.67 (m, 1 H), 7.39 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.03 (d, <i>J</i> = 2.89 Hz, 1 H), 5.19 - 5.63 (m, 3 H), 4.19 - 4.40 (m, 2 H), 3.93 - 4.06 (m, 2 H), 3.57 - 3.87 (m, 4 H). Method 1: RT = 2.77 min. M+H = 435.1
195		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.79 (d, <i>J</i> = 2.51 Hz, 1 H), 8.69 (d, <i>J</i> = 2.13 Hz, 1 H), 8.64 (s, 1 H), 8.26 (dd, <i>J</i> = 6.96, 2.57 Hz, 1 H), 8.05 (d, <i>J</i> = 2.01 Hz, 1 H), 7.68 - 7.76 (m, 1 H), 7.46 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 5.27 - 5.49 (m, 1 H), 3.62 - 3.77 (m, 2 H), 3.40 - 3.59 (m, 2 H), 3.08 (dt, <i>J</i> = 13.61, 6.74 Hz, 1 H), 2.02 - 2.25 (m, 2 H), 1.31 (d, <i>J</i> = 6.90 Hz, 6 H). Method 1: RT = 2.95 min.; M+H = 386.1,
196		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.54 (br s, 1 H), 8.83 (d, <i>J</i> = 2.51 Hz, 1 H), 8.70 (d, <i>J</i> = 2.26 Hz, 1 H), 8.51 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 8.07 (d, <i>J</i> = 2.01 Hz, 1 H), 7.98 (d, <i>J</i> = 0.88 Hz, 1 H), 7.91 - 7.96 (m, 1 H), 7.57 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 7.40 (d, <i>J</i> = 3.14 Hz, 1 H), 6.74 (dd, <i>J</i> = 3.45, 1.69 Hz, 1 H), 3.04 - 3.14 (m, 1 H), 1.31 (d, <i>J</i> = 6.90 Hz, 6 H). Method 1: RT = 3.04 min.; M+H = 365.0
197		¹ H NMR (400 MHz, DMSO) δ 8.87 - 8.98 (m, 1 H), 8.60 (d, <i>J</i> = 2.89 Hz, 1 H), 8.48 (d, <i>J</i> = 2.76 Hz, 1 H), 8.18 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.58 - 7.65 (m, 1 H), 7.41 (dd, <i>J</i> = 11.42, 9.16 Hz, 1 H), 7.04 (d, <i>J</i> = 3.01 Hz, 1 H), 5.26 - 5.49 (m, 1 H), 4.23 - 4.36 (m, 2 H), 3.91 - 4.10 (m, 5 H), 3.73 (br d, <i>J</i> = 10.42 Hz, 1 H), 3.40 (br d, <i>J</i> = 9.66 Hz, 2 H), 1.65 - 2.09 (m, 4 H). Method 1: RT = 2.69 min.; M+H = 441.3

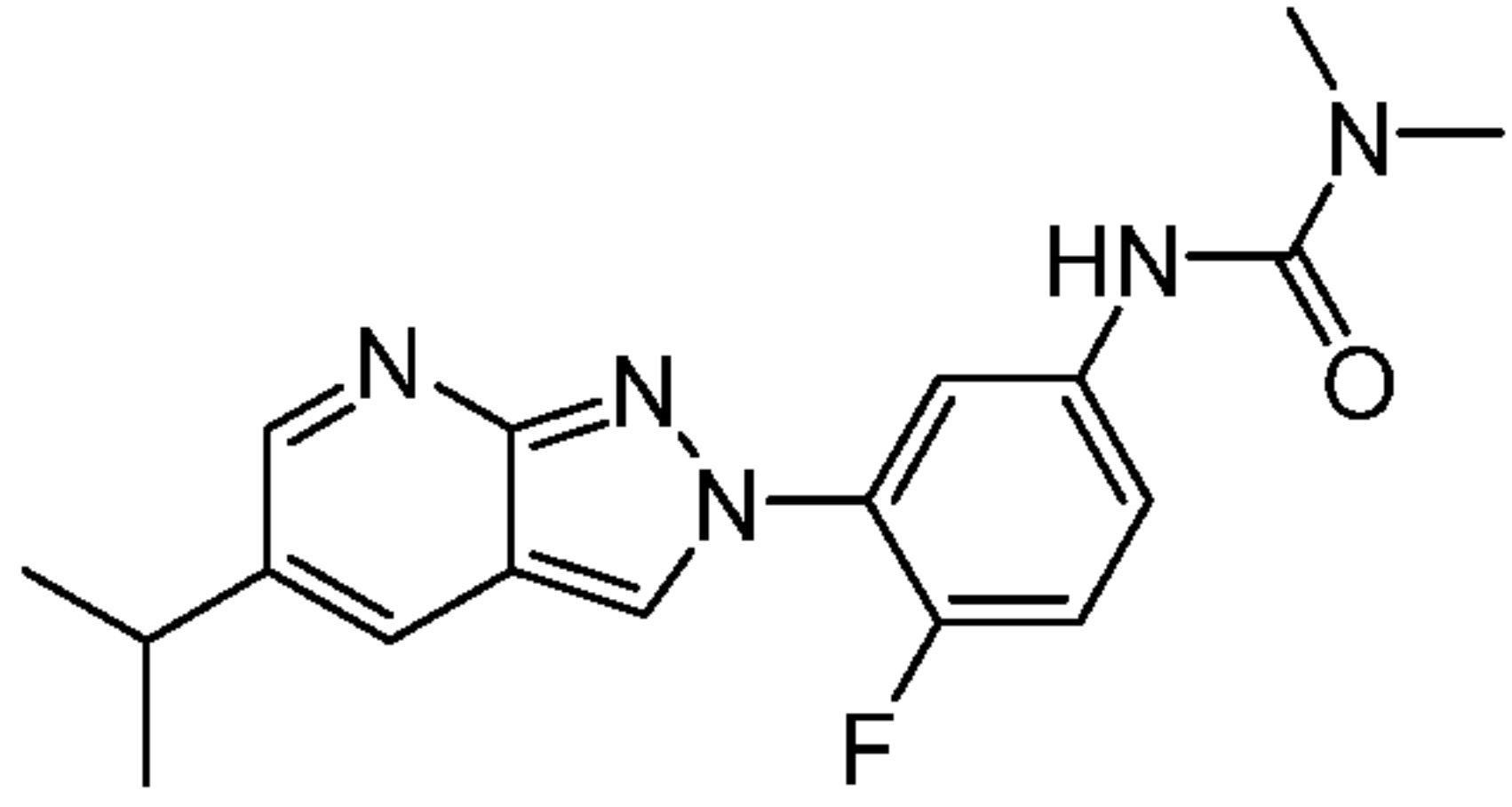
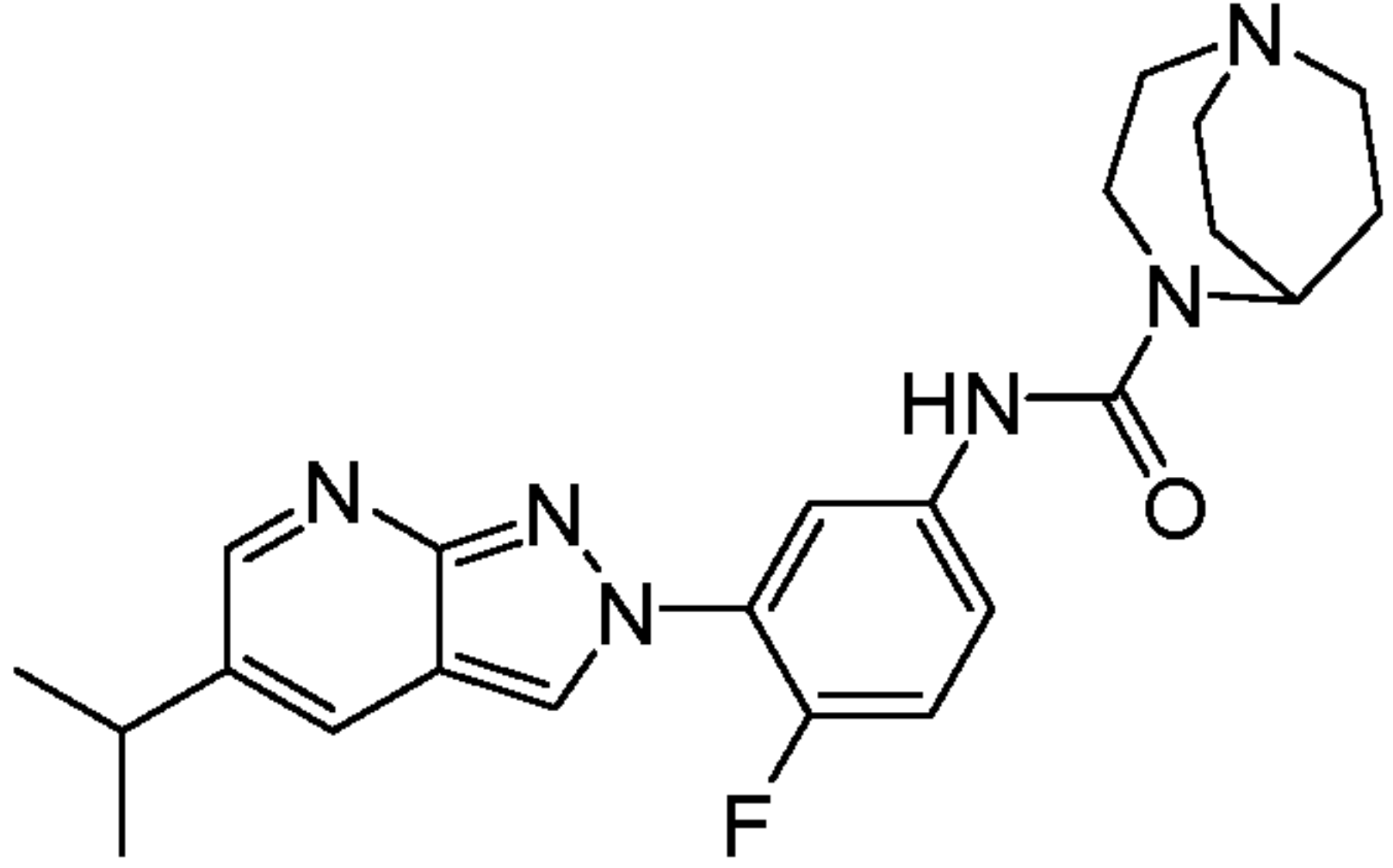
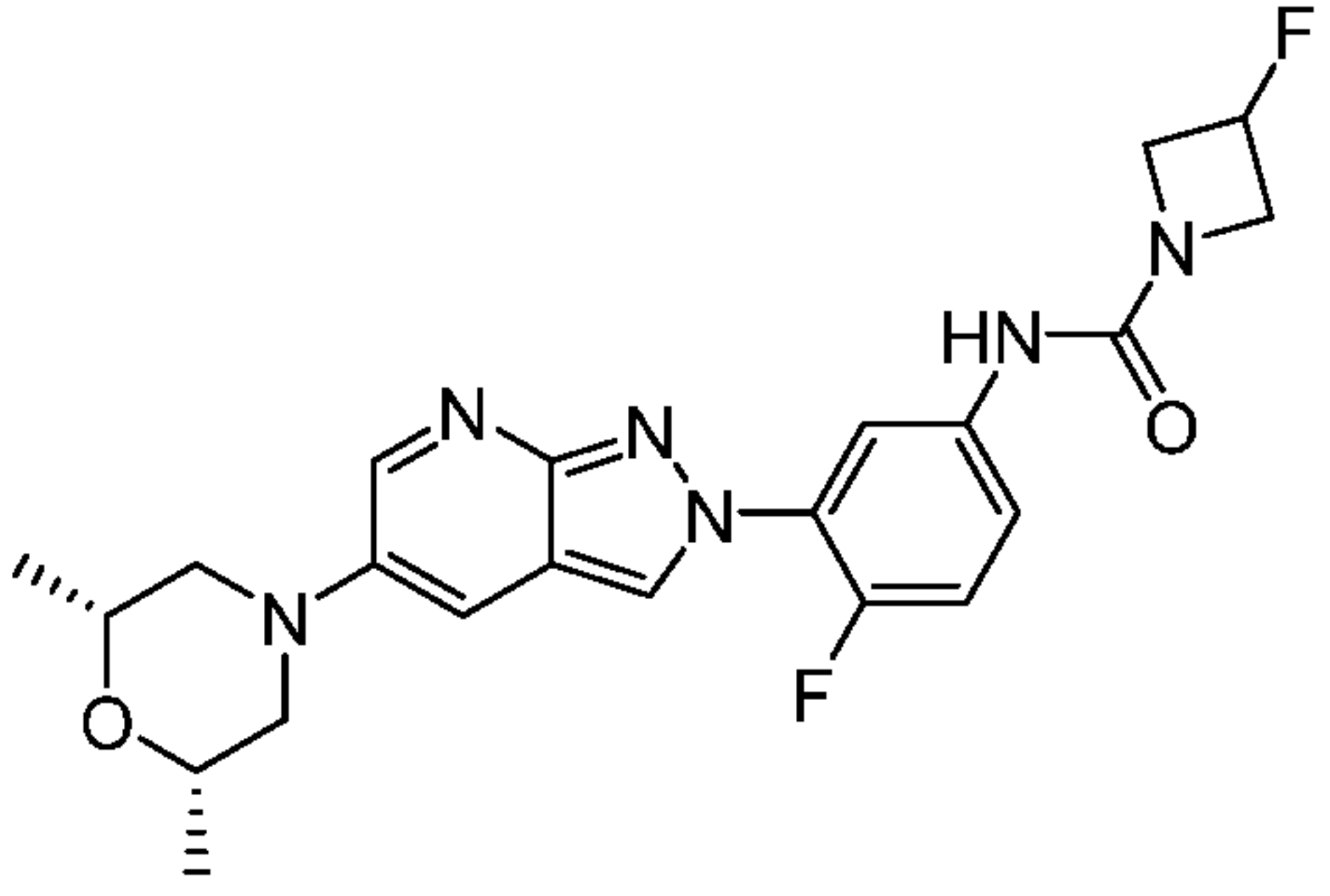
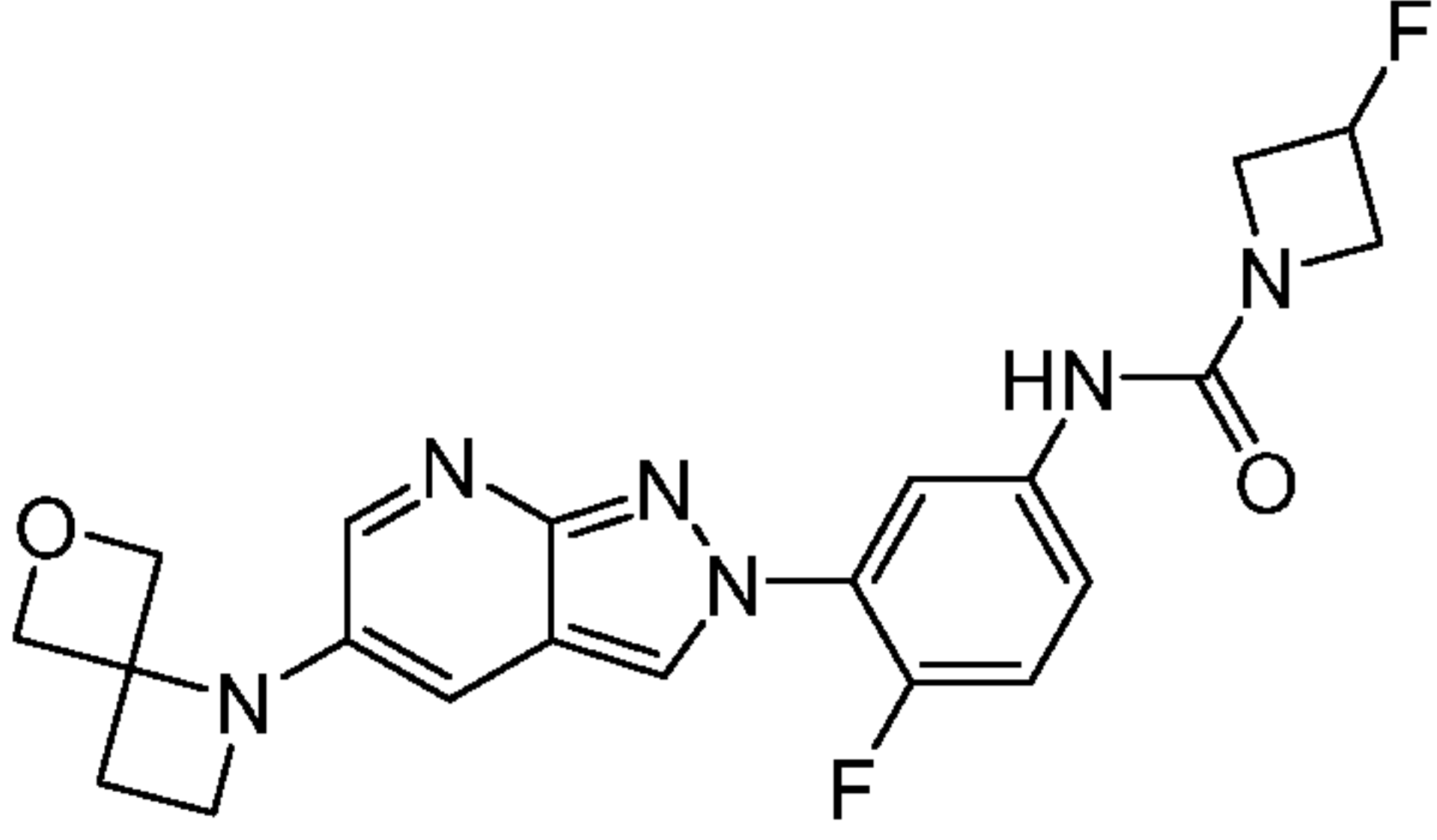
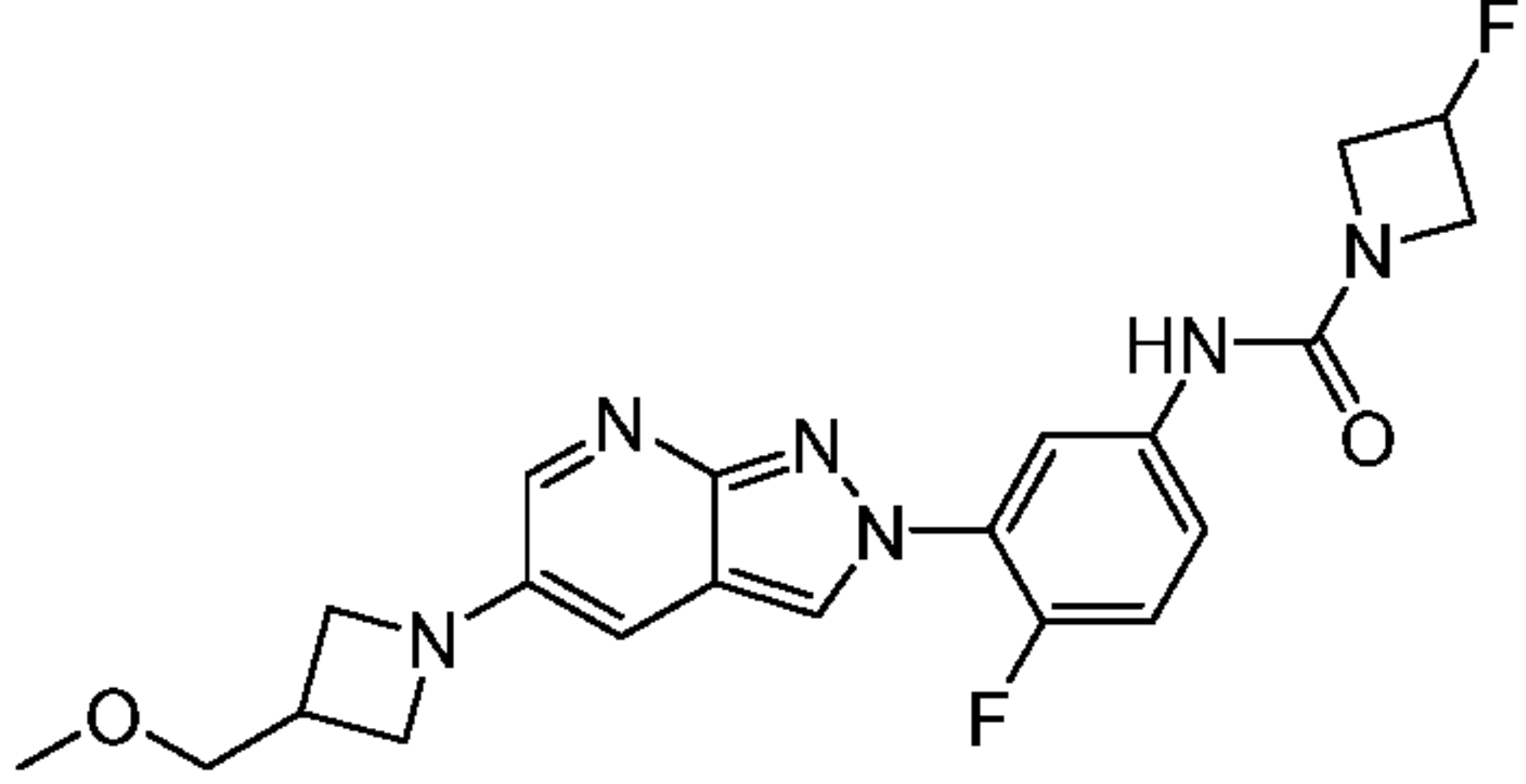
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
198		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.92 (s, 1 H), 8.40 (dd, <i>J</i> =2.64, 1.88 Hz, 2 H), 8.17 (dd, <i>J</i> =7.03, 2.76 Hz, 1 H), 7.57 - 7.72 (m, 1 H), 7.37 - 7.46 (m, 1 H), 6.76 (d, <i>J</i> =2.76 Hz, 1 H), 6.05 (t, <i>J</i> =5.52 Hz, 1 H), 5.29 - 5.57 (m, 1 H), 4.24 - 4.40 (m, 2 H), 3.94 - 4.11 (m, 2 H), 2.85 (t, <i>J</i> =6.02 Hz, 2 H), 1.93 (dq, <i>J</i> =13.35, 6.58, 6.58, 6.58 Hz, 1 H), 0.99 (d, <i>J</i> =6.53 Hz, 6 H) Method 1: RT = 3.00 min.; M+H = 401.4
199		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.93 (s, 1 H), 8.34 - 8.43 (m, 2 H), 8.17 (dd, <i>J</i> =7.03, 2.51 Hz, 1 H), 7.59 - 7.68 (m, 1 H), 7.41 (dd, <i>J</i> =11.42, 9.16 Hz, 1 H), 6.77 (d, <i>J</i> =2.76 Hz, 1 H), 5.97 (t, <i>J</i> =5.02 Hz, 1 H), 5.27 - 5.53 (m, 1 H), 4.24 - 4.40 (m, 2 H), 3.93 - 4.10 (m, 2 H), 3.01 - 3.10 (m, 2 H), 1.24 (t, <i>J</i> =7.15 Hz, 3 H). Method 2: RT = 0.80 min.; M+H = 373.4
200		¹ H NMR (400 MHz, DMSO) δ 8.93 (s, 1 H), 8.40 (d, <i>J</i> = 2.81 Hz, 1 H), 8.33 (d, <i>J</i> = 2.81 Hz, 1 H), 8.15 - 8.21 (m, 1 H), 7.60 - 7.71 (m, 1 H), 7.37 - 7.48 (m, 1 H), 6.79 (d, <i>J</i> = 2.69 Hz, 1 H), 5.84 (br d, <i>J</i> = 7.58 Hz, 1 H), 5.27 - 5.52 (m, 1 H), 4.26 - 4.38 (m, 2 H), 3.96 - 4.09 (m, 2 H), 3.44 - 3.57 (m, 1 H), 1.19 (d, <i>J</i> =6.24 Hz, 6 H). Method 1: RT = 2.78 min.; M+H = 387.2
201		¹ H NMR (400 MHz, DMSO) δ 8.94 (s, 1 H), 8.55 (d, <i>J</i> = 2.64 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.62 - 7.70 (m, 1 H), 7.43 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 6.95 (d, <i>J</i> = 2.76 Hz, 1 H), 5.26 - 5.51 (m, 1 H), 4.47 (t, <i>J</i> = 7.53 Hz, 2 H), 4.18 - 4.37 (m, 4 H), 3.92 - 4.08 (m, 4 H), 2.91 (t, <i>J</i> =7.53 Hz, 2 H). Method 2: RT = 0.78 min.; M+H = 427.3
202		¹ H NMR (400 MHz, DMSO) δ 8.92 (s, 1 H), 8.54 (d, <i>J</i> = 2.64 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.61 - 7.69 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.93 (d, <i>J</i> = 2.76 Hz, 1 H), 5.24 - 5.50 (m, 1 H), 4.23 - 4.38 (m, 2 H), 3.86 - 4.06 (m, 6 H), 3.83 (s, 2 H), 3.74 (t, <i>J</i> = 6.96 Hz, 2 H), 2.16 (t, <i>J</i> = 6.96 Hz, 2 H). Method 2: RT = 0.80 min.; M+H = 441.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
203		¹ H NMR (400 MHz, DMSO) δ 8.93 (s, 1 H), 8.53 (d, <i>J</i> = 2.64 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.15 - 8.24 (m, 1 H), 7.60 - 7.67 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.89 (d, <i>J</i> = 2.76 Hz, 1 H), 5.28 - 5.50 (m, 1 H), 4.24 - 4.37 (m, 2 H), 3.89 - 4.08 (m, 2 H), 3.72 (s, 4 H), 3.43 - 3.62 (m, 4 H), 1.73 - 1.84 (m, 4 H). Method 2: RT = 0.85 min.; M+H = 455.3
204		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.92 (s, 1 H), 8.53 (br d, <i>J</i> = 2.76 Hz, 1 H), 8.50 (br d, <i>J</i> = 2.76 Hz, 1 H), 8.19 - 8.28 (m, 1 H), 7.62 - 7.71 (m, 1 H), 7.43 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 6.96 (d, <i>J</i> = 2.76 Hz, 1 H), 5.29 - 5.50 (m, 1 H), 4.21 - 4.45 (m, 2 H), 3.89 - 4.13 (m, 2 H), 3.77 (d, <i>J</i> = 10.04 Hz, 2 H), 3.65 (br d, <i>J</i> = 8.91 Hz, 2 H), 2.68 - 2.80 (m, 2 H). Method 1: RT = 2.84 min.; M+H = 447.3
205		¹ H NMR (400 MHz, DMSO) δ 8.92 (s, 1 H), 8.51 (d, <i>J</i> = 2.76 Hz, 1 H), 8.26 (d, <i>J</i> = 2.76 Hz, 1 H), 8.17 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.58 - 7.65 (m, 1 H), 7.40 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.91 (d, <i>J</i> = 2.76 Hz, 1 H), 5.23 - 5.50 (m, 1 H), 4.23 - 4.37 (m, 3 H), 4.10 - 4.19 (m, 2 H), 3.93 - 4.07 (m, 2 H), 3.68 (dd, <i>J</i> = 8.22, 4.33 Hz, 2 H), 3.20 - 3.27 (m, 3 H). Method 1: RT = 2.59 min.; M+H = 415.2
206		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.94 (s, 1H), 9.49 (d, <i>J</i> = 2.3 Hz, 1H), 9.08 (d, <i>J</i> = 2.5 Hz, 1H), 8.97 (d, <i>J</i> = 2.3 Hz, 1H), 8.75 (ddd, <i>J</i> = 0.9, 1.9, 4.8 Hz, 1H), 8.56 (dd, <i>J</i> = 2.7, 7.0 Hz, 1H), 8.15 (dt, <i>J</i> = 1.1, 8.1 Hz, 1H), 8.07 - 7.92 (m, 2H), 7.82 (d, <i>J</i> = 3.8 Hz, 1H), 7.65 (dd, <i>J</i> = 9.1, 11.2 Hz, 1H), 7.59 (d, <i>J</i> = 3.8 Hz, 1H), 7.45 (ddd, <i>J</i> = 1.1, 4.8, 7.5 Hz, 1H). Method 1: RT = 2.83 min.; M+H = 425.4
207		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 8.67 (m, 1H), 8.48 (m, 1H), 8.19 (m, 1H), 7.93 - 7.83 (m, 2H), 7.26 (m, 1H), 3.68 - 3.49 (m, 3H), 3.08 (m, 1H), 1.90 - 1.76 (m, 2H), 1.37 - 1.32 (m, 6H), 1.28 - 1.07 (m, 4H). Method 1: RT = 3.08 min.; M+H = 383.3
208		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 9.91 (s, 1H), 8.68 (m, 1H), 8.47 (m, 1H), 8.19 (m, 1H), 8.11 - 8.02 (m, 1H), 7.97 (m, 1H), 7.27 (m, 1H), 3.09 (m, 1H), 2.63 (m, 1H), 2.16 (m, 1H), 1.70 (m, 1H), 1.33 (m, 6H). Method 1: RT = 3.04 min.; M+H = 375.3

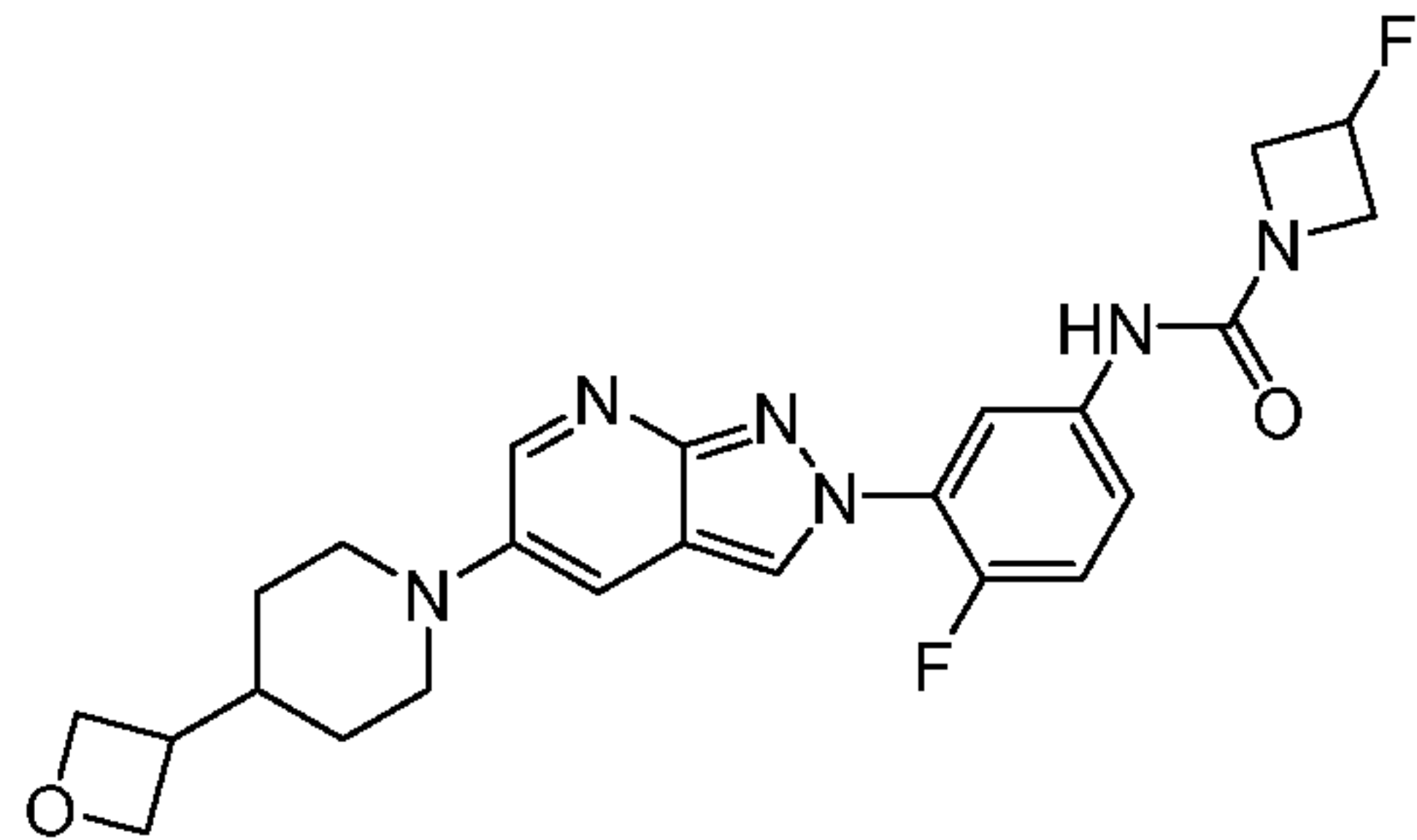
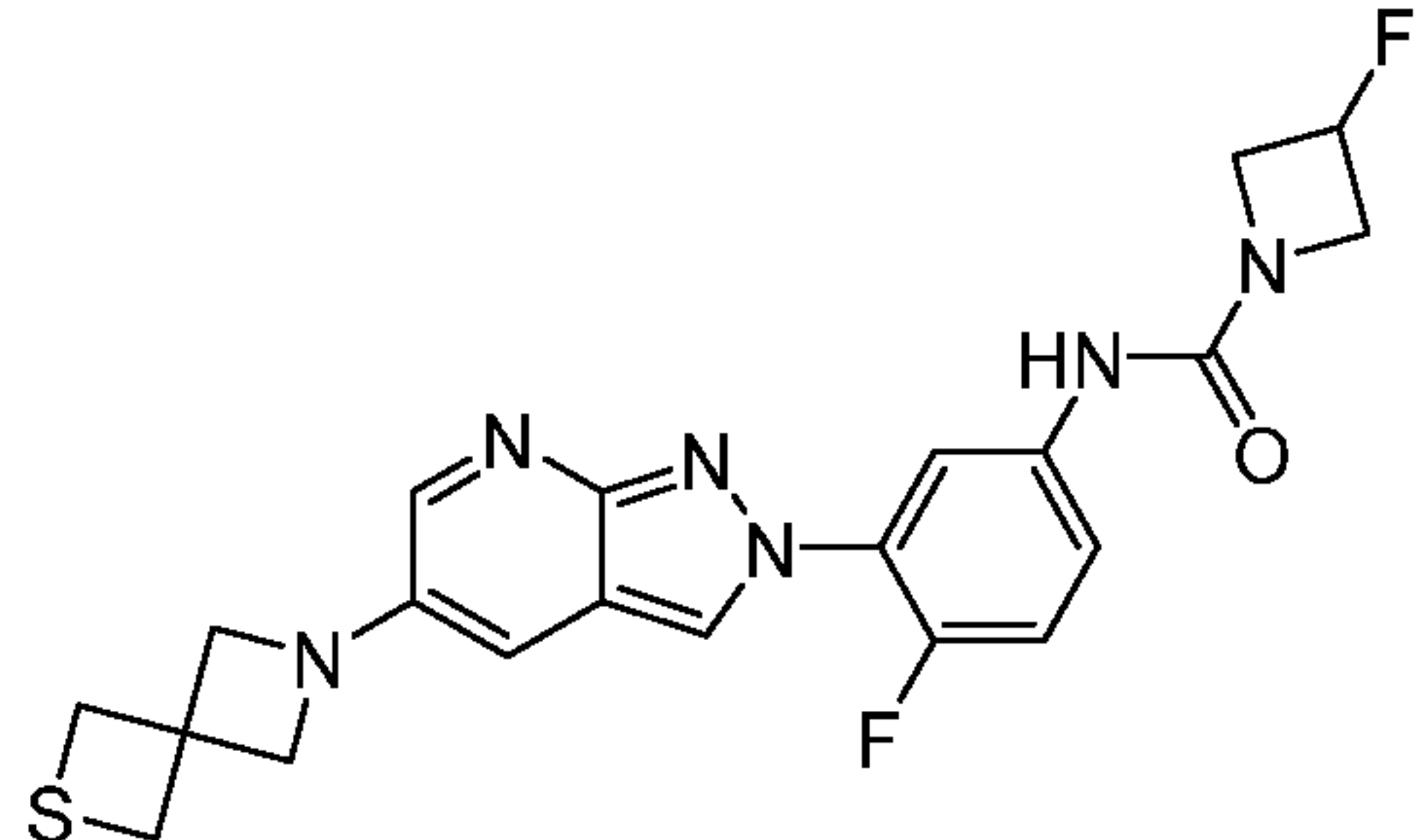
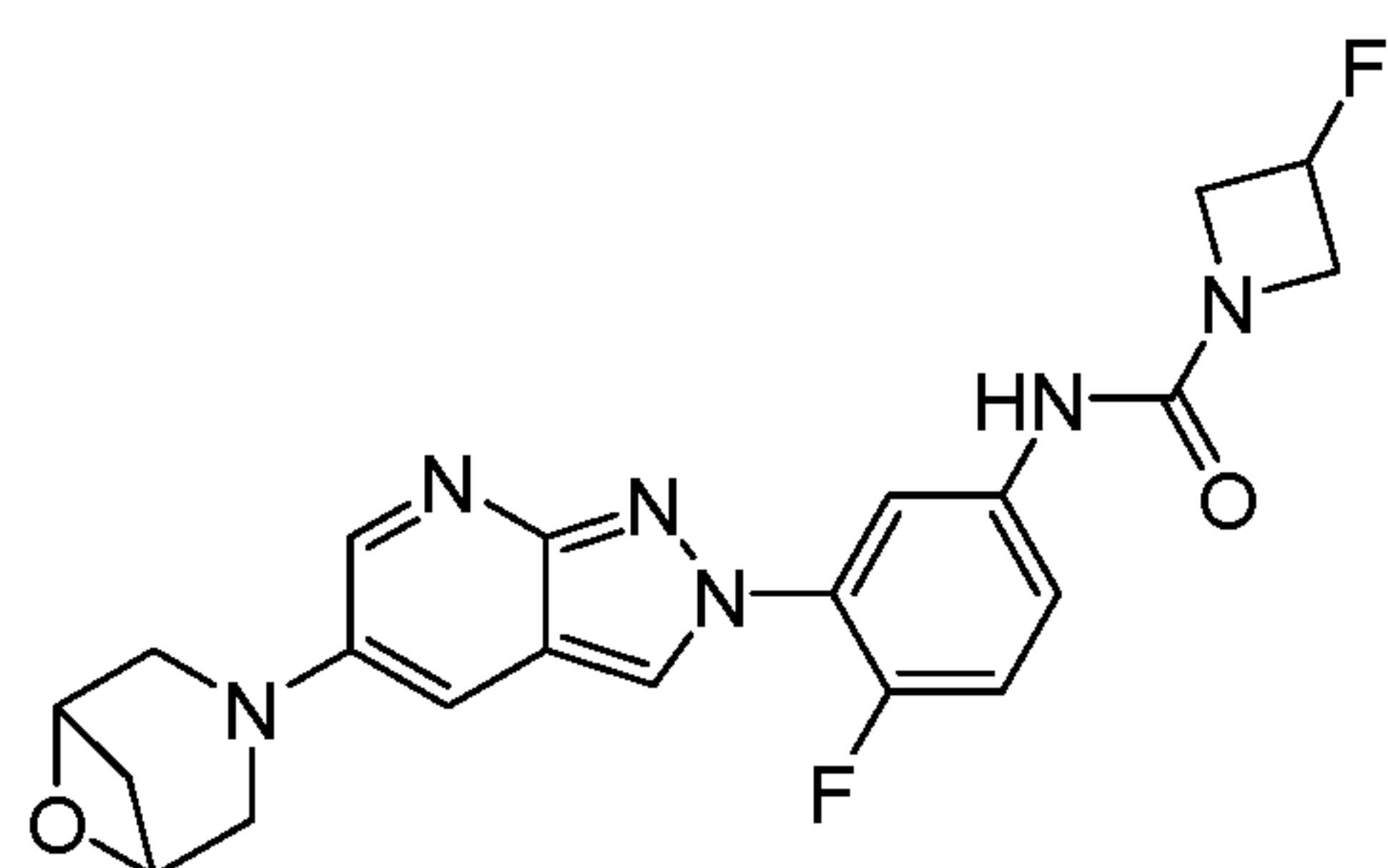
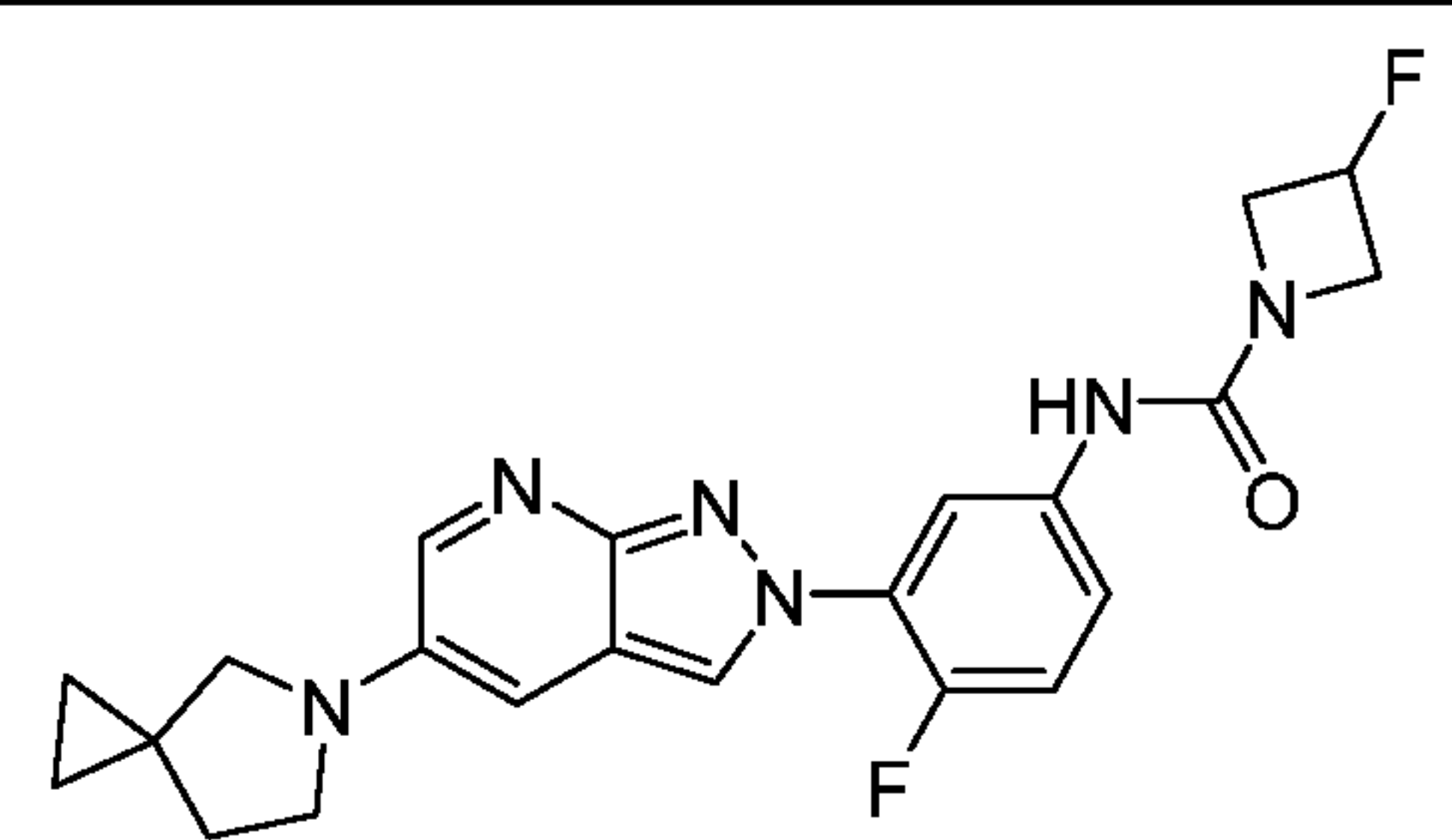
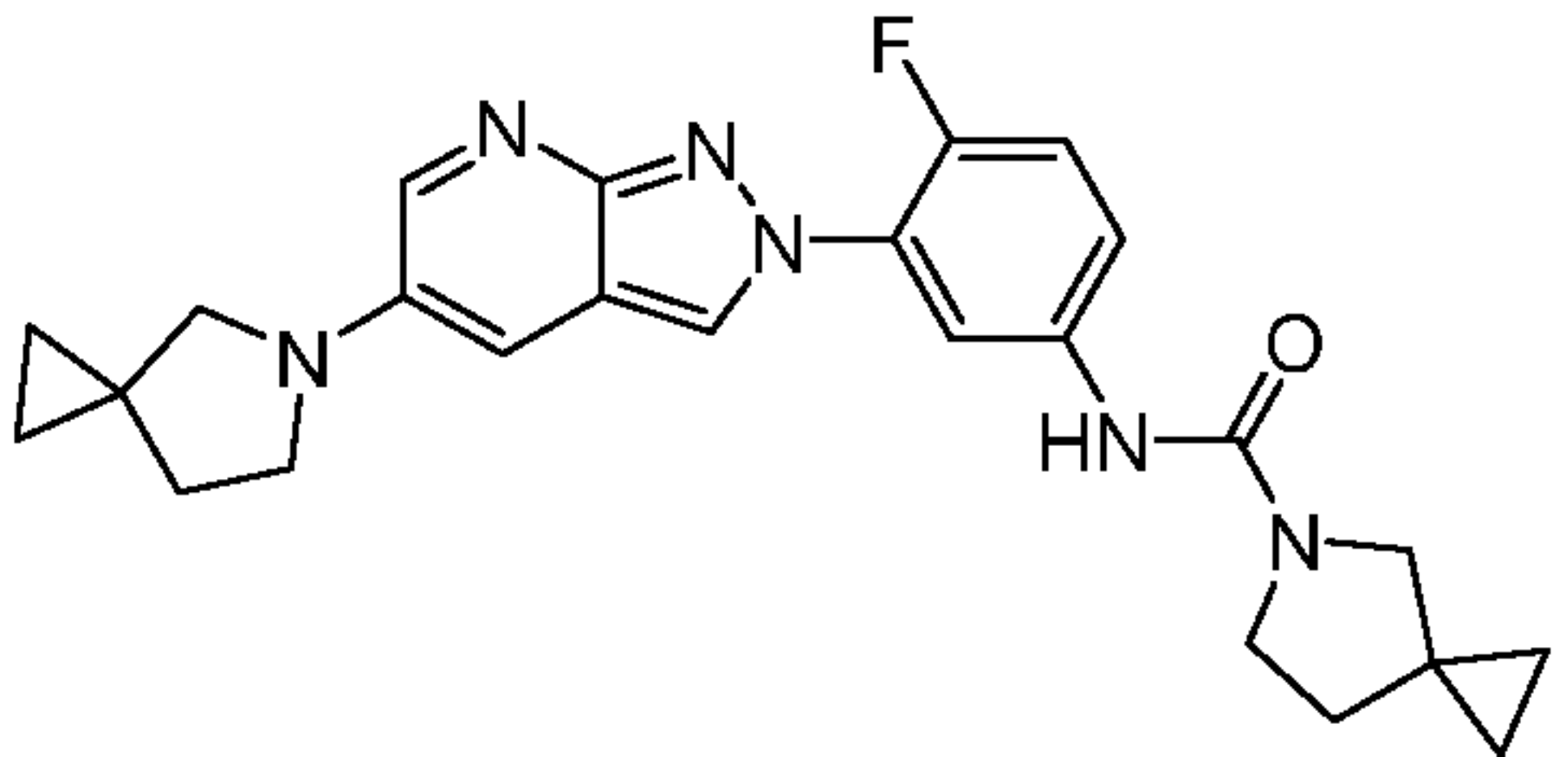
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
209		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 8.78 (m, 2H), 8.35 (m, 1H), 8.30 (m, 1H), 7.99 (m, 1H), 7.81 (m, 1H), 7.36 (m, 1H), 3.19 (m, 1H), 2.30 – 2.18 (m, 2H), 2.03 – 1.95 (m, 2H), 1.42 – 1.34 (m, 6H). Method 1: RT = 3.14 min.; M+H = 407.2
210		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 8.66 (m, 1H), 8.48 (m, 1H), 8.18 (m, 1H), 7.92 - 7.88 (m, 2H), 7.27 (m, 1H), 3.24 - 3.13 (m, 1H), 3.08 (m, 1H), 2.41 - 2.29 (m, 2H), 2.25 - 2.12 (m, 2H), 2.05 - 1.89 (m, 2H), 1.37 - 1.31 (m, 6H). Method 1: RT = 3.14 min.; M+H = 353.3
211		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 8.66 (m, 1H), 8.49 - 8.40 (m, 2H), 8.17 (m, 1H), 7.92 - 7.84 (m, 2H), 7.24 (m, 1H), 3.07 (m, 1H), 1.46 - 1.36 (m, 1H), 1.36 - 1.30 (m, 6H), 1.30 - 1.24 (m, 1H), 1.24 - 1.15 (m, 1H), 1.10 (m, 3H), 0.65 (m, 1H). Method 1: RT = 3.16 min.; M+H = 353.3
212		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 9.74 (m, 1H), 8.64 (m, 1H), 8.44 (m, 1H), 8.15 (m, 1H), 8.05 (m, 1H), 7.93 (m, 1H), 7.31 (m, 1H), 3.30 (m, 2H), 3.08 (m, 1H), 1.46 - 1.17 (m, 6H). Method 1: RT = 3.08 min.; M+H = 381.2
213		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 9.14 (m, 1H), 8.64 (m, 1H), 8.45 (m, 1H), 8.22 (m, 1H), 8.00 (m, 1H), 7.91 (m, 1H), 7.28 (m, 1H), 3.07 (m, 1H), 2.96 - 2.84 (m, 1H), 2.71 (m, 1H), 2.27 (m, 1H), 1.33 (m, 6H), 1.15 (m, 3H). Method 1: RT = 3.27 min.; M+H = 409.3
214		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 8.88 (m, 1H), 8.64 (m, 1H), 8.45 (m, 1H), 8.19 (m, 1H), 7.99 - 7.92 (m, 1H), 7.90 (m, 1H), 7.27 (m, 1H), 3.07 (m, 1H), 2.43 (m, 2H), 2.24 - 2.07 (m, 2H), 1.97 - 1.86 (m, 2H), 1.33 (m, 6H). Method 1: RT = 3.23 min.; M+H = 409.3
215		¹ H NMR (400 MHz, Methylene Chloride- <i>d</i> ₂) δ 8.66 (m, 1H), 8.47 (m, 1H), 8.19 (m, 2H), 7.92 - 7.86 (m, 2H), 7.27 (m, 1H), 3.08 (m, 1H), 2.47 - 2.39 (m, 2H), 1.58 (m, 2H), 1.38 - 1.29 (m, 6H), 0.78 - 0.66 (m, 1H), 0.45 - 0.38 (m, 2H), 0.07 - 0.01 (m, 2H). Method 1: RT = 3.23 min.; M+H = 367.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
216		¹ H NMR (400 MHz, Methylene Chloride-d ₂) δ 8.66 (m, 1H), 8.47 (m, 1H), 8.18 (m, 1H), 8.05 (m, 1H), 7.91 - 7.83 (m, 2H), 7.26 (m, 1H), 3.08 (m, 1H), 2.74 (m, 1H), 2.44 (m, 2H), 2.17 - 2.10 (m, 2H), 1.94 - 1.78 (m, 2H), 1.78 - 1.66 (m, 2H), 1.37 - 1.30 (m, 6H). Method 1: RT = 3.19 min.; M+H = 367.3
217		¹ H NMR (400 MHz, Methylene Chloride-d ₂) δ 8.66 (m, 1H), 8.48 (m, 1H), 8.21 (m, 1H), 7.89 (m, 1H), 7.84 (m, 1H), 7.79 (m, 1H), 7.27 (m, 1H), 3.08 (m, 1H), 2.20 (m, 2H), 1.38 - 1.21 (m, 6H), 1.11 - 0.89 (m, 9H). Method 1: RT = 3.29 min.; M+H = 369.3
218		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.13 (s, 1H), 9.48 (d, <i>J</i> = 2.3 Hz, 1H), 9.04 (d, <i>J</i> = 2.5 Hz, 1H), 8.95 (d, <i>J</i> = 2.3 Hz, 1H), 8.77 - 8.70 (m, 1H), 8.64 - 8.58 (m, 1H), 8.40 (d, <i>J</i> = 8.4 Hz, 1H), 7.58 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.46 - 7.37 (m, 3H), 6.86 (d, <i>J</i> = 1.3 Hz, 1H), 2.77 - 2.72 (m, 2H), 2.48 - 2.42 (m, 2H). Method 1: RT = 2.80 min.; M+H = 386.1
219		¹ H NMR (400 MHz, Chloroform-d) δ 8.70 (m, 1H), 8.51 (m, 1H), 7.96 (m, 1H), 7.90 - 7.81 (m, 2H), 7.27 - 7.19 (m, 1H), 6.73 (m, 1H), 3.08 (m, 1H), 1.43 - 1.28 (m, 6H). Method 2: RT = 0.90 min.; M+H = 348.3
220		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.52 (m, 1H), 8.14 - 7.90 (m, 2H), 7.87 (m, 1H), 7.28 - 7.20 (m, 1H), 6.44 (m, 1H), 3.76 - 3.57 (m, 2H), 3.46 - 3.31 (m, 2H), 3.08 (m, 1H), 1.98 - 1.78 (m, 2H), 1.54 - 1.18 (m, 6H), 0.74 - 0.54 (m, 4H). Method 2: RT = 1.05 min.; M+H = 394.3
221		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.49 (m, 1H), 8.15 - 7.89 (m, 2H), 7.89 - 7.84 (m, 1H), 7.24 (m, 1H), 6.50 (m, 1H), 3.63 (m, 2H), 3.50 - 3.38 (m, 1H), 3.16 - 2.93 (m, 2H), 2.46 - 2.04 (m, 2H), 1.68 - 1.56 (m, 1H), 1.51 - 1.20 (m, 6H), 1.12 (m, 3H). Method 2: RT = 1.02 min.; M+H = 382.3

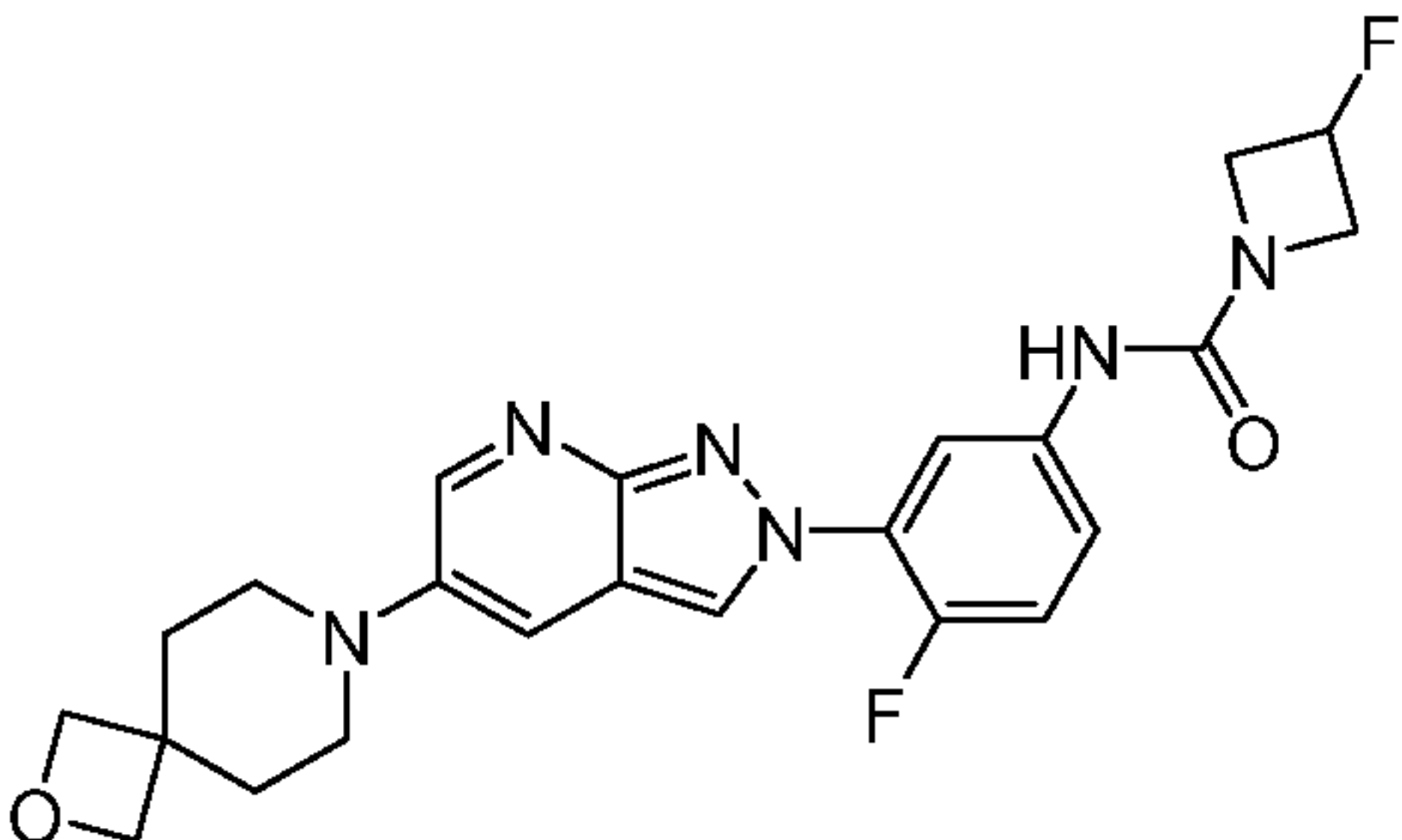
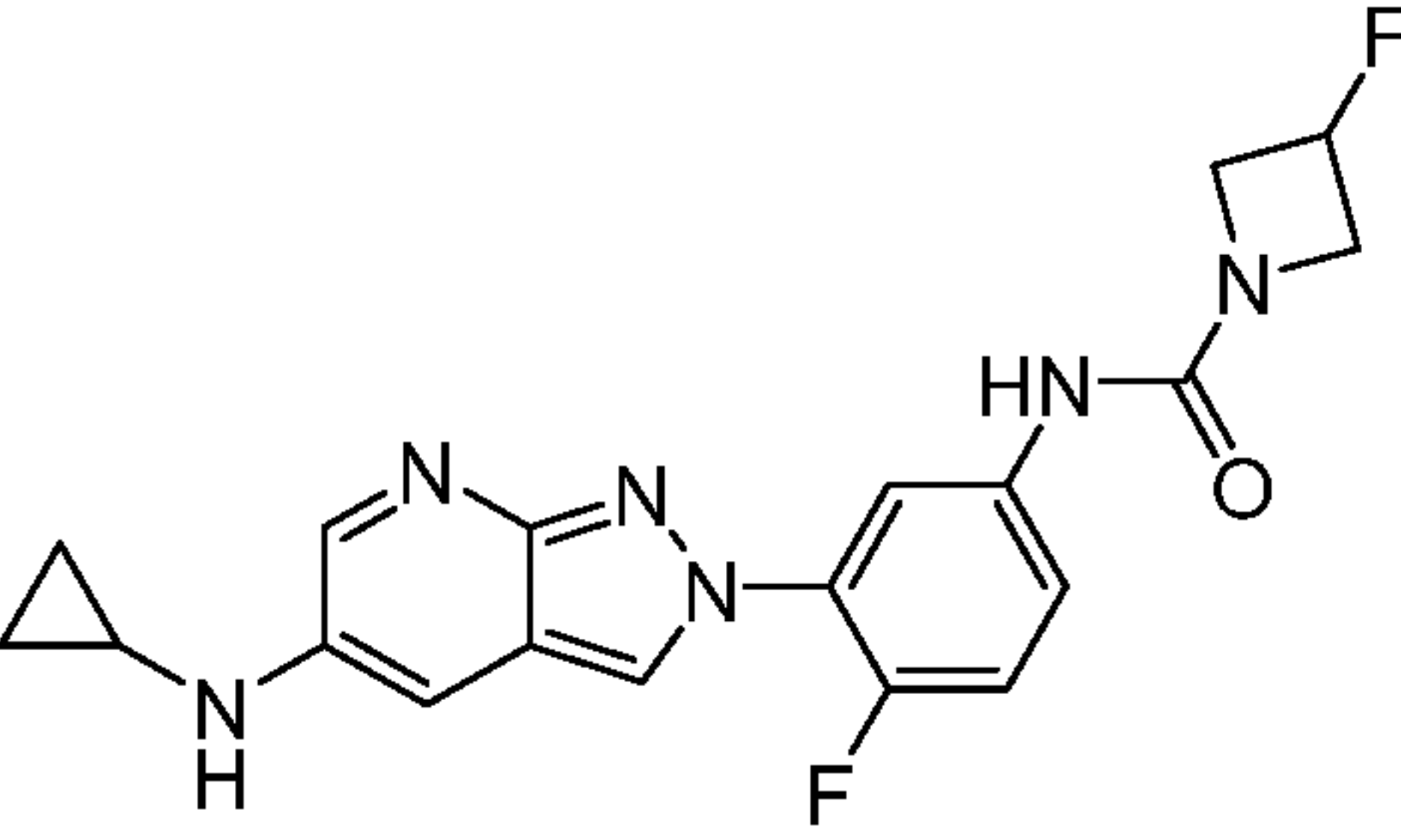
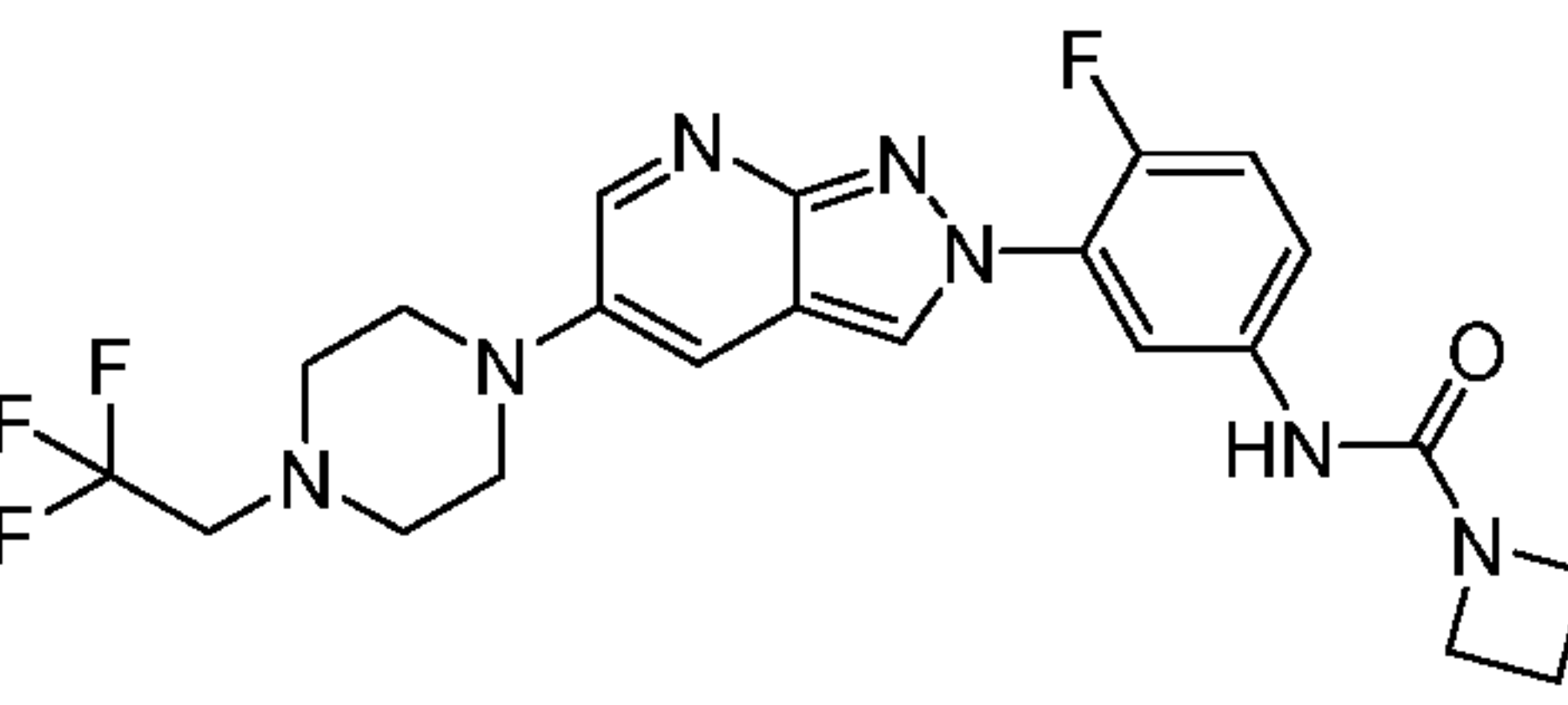
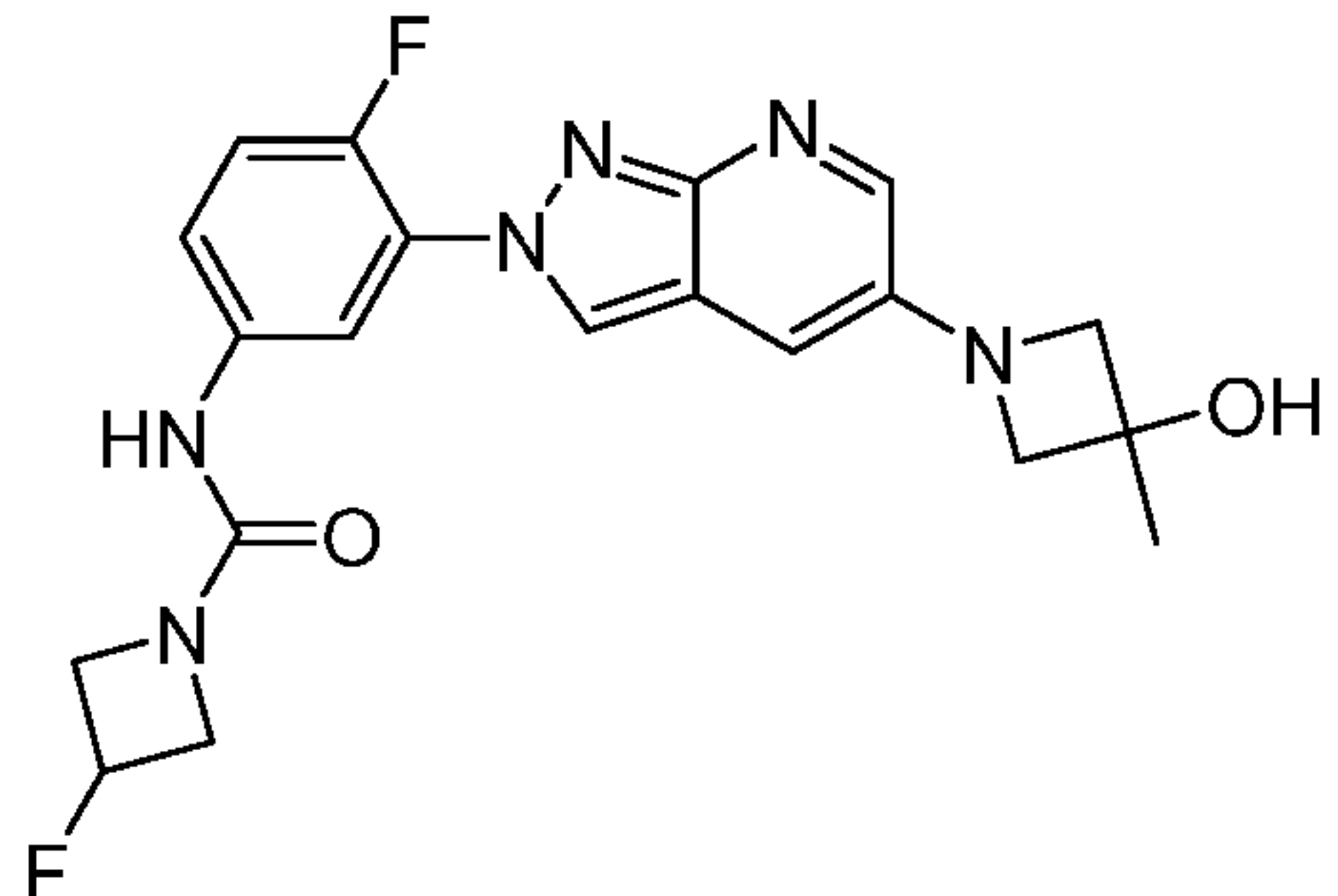
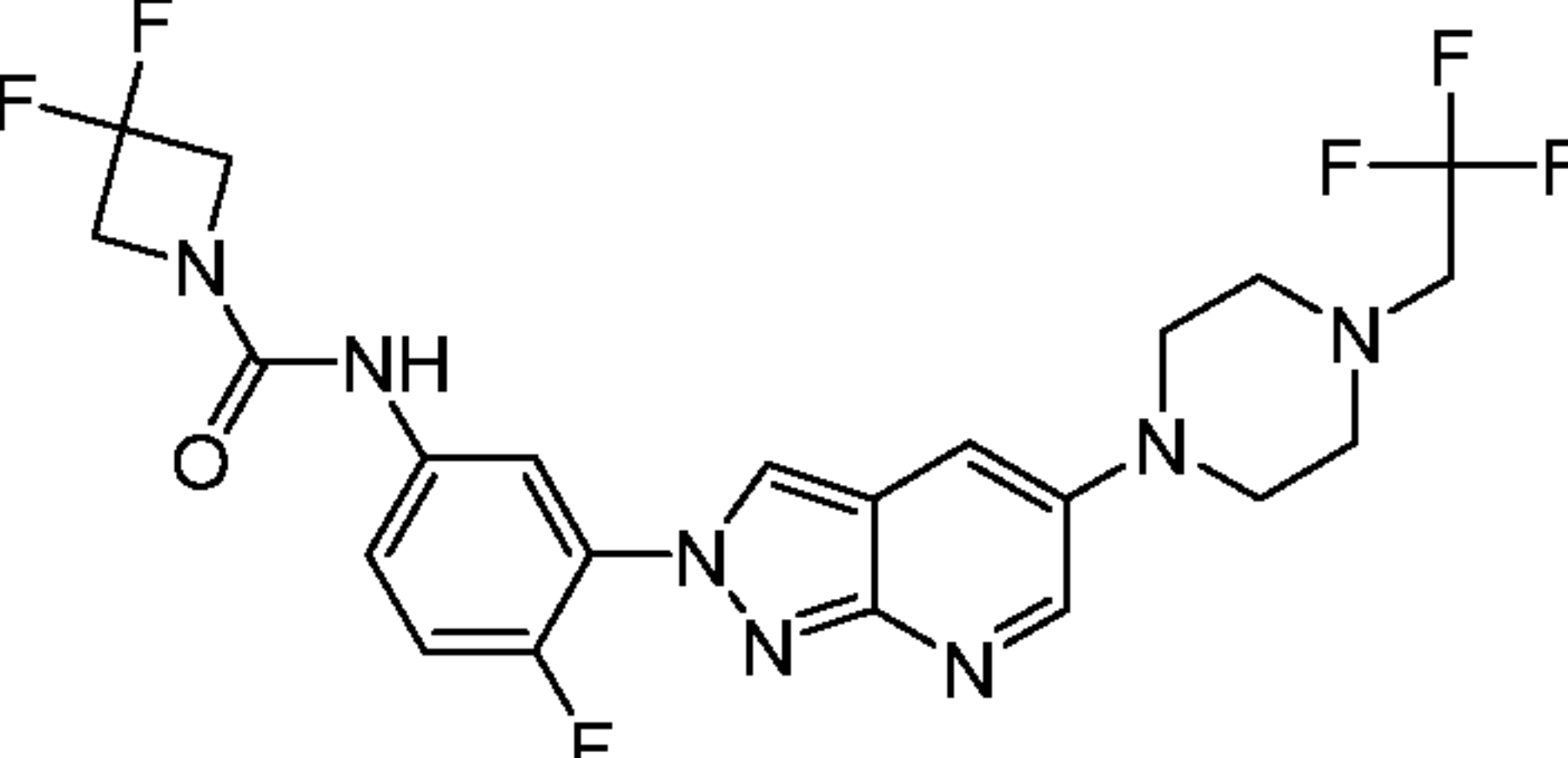
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
222		¹ H NMR (400 MHz, Chloroform-d) δ 8.70 (m, 1H), 8.51 (m, 1H), 7.99 - 7.91 (m, 2H), 7.87 (m, 1H), 7.28 - 7.21 (m, 1H), 6.52 (m, 1H), 4.15 (m, 4H), 3.08 (m, 1H), 1.53 - 1.18 (m, 6H), 0.70 (m, 4H). Method 2: RT = 1.01 min.; M+H = 380.3
223		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.51 (m, 1H), 8.13 - 7.80 (m, 3H), 7.27 - 7.19 (m, 1H), 6.38 (m, 1H), 3.71 - 3.51 (m, 4H), 3.08 (m, 1H), 1.61 - 1.31 (m, 6H), 1.24 (m, 2H), 0.81 (m, 1H), 0.31 (m, 1H). Method 2: RT = 0.99 min.; M+H = 380.3
224		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.53 (m, 1H), 7.96 (m, 1H), 7.92 - 7.83 (m, 2H), 7.27 - 7.21 (m, 1H), 6.55 (m, 1H), 3.45 (m, 2H), 3.10 (m, 1H), 3.06 - 2.98 (m, 3H), 1.37 (m, 6H), 1.26 - 1.22 (m, 3H). Method 2: RT = 0.96 min.; M+H = 356.3
225		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.53 - 8.45 (m, 1H), 8.17 - 7.84 (m, 3H), 7.27 - 7.19 (m, 1H), 6.60 (m, 1H), 4.12 - 3.95 (m, 1H), 3.69 - 3.50 (m, 4H), 3.44 - 3.29 (m, 3H), 3.09 (m, 1H), 2.24 - 2.01 (m, 2H), 1.54 - 1.18 (m, 6H). Method 2: RT = 0.92 min.; M+H = 398.3
226		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.51 (m, 1H), 7.97 - 7.89 (m, 2H), 7.87 (m, 1H), 7.28 - 7.19 (m, 1H), 6.28 (m, 1H), 4.04 (m, 4H), 3.09 (m, 1H), 2.22 (m, 4H), 1.94 - 1.83 (m, 2H), 1.49 - 1.14 (m, 6H). Method 2: RT = 1.06 min.; M+H = 394.3
227		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.49 (m, 1H), 8.09 (m, 1H), 7.87 (m, 1H), 7.81 (m, 1H), 7.28 - 7.20 (m, 1H), 7.09 (m, 1H), 4.08 (m, 2H), 3.19 (m, 3H), 3.09 (m, 1H), 1.37 (m, 6H). Method 2: RT = 1.04 min.; M+H = 410.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
228		¹ H NMR (400 MHz, Chloroform-d) δ 8.71 (m, 1H), 8.51 (m, 1H), 7.96 (m, 1H), 7.89 - 7.81 (m, 2H), 7.24 (m, 1H), 6.71 (m, 1H), 3.51 (m, 1H), 3.09 - 3.03 (m, 6H), 1.42 - 1.28 (m, 6H). Method 2: RT = 0.90 min.; M+H = 342.3
229		¹ H NMR (400 MHz, Chloroform-d) δ 8.62 (m, 1H), 8.44 (m, 1H), 7.89 (m, 1H), 7.81 - 7.77 (m, 1H), 7.75 (m, 1H), 7.18 - 7.12 (m, 1H), 6.61 (m, 1H), 4.13 (m, 1H), 3.73 - 3.62 (m, 2H), 3.13 - 2.90 (m, 6H), 2.06 - 1.97 (m, 3H), 1.77 - 1.74 (m, 2H), 1.28 (m, 6H). Method 1: RT = 2.42 min.; M+H = 423.3
230		¹ H NMR (400 MHz, DMSO) δ ppm 8.91 (s, 1 H), 8.73 (d, <i>J</i> = 2.76 Hz, 1 H), 8.58 (d, <i>J</i> = 2.64 Hz, 1 H), 8.18 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.57 - 7.68 (m, 1 H), 7.41 (dd, <i>J</i> = 11.29, 9.03 Hz, 1 H), 7.35 (d, <i>J</i> = 2.76 Hz, 1 H), 5.25 - 5.49 (m, 1 H), 4.23 - 4.36 (m, 2 H), 3.93 - 4.07 (m, 2 H), 3.69 - 3.84 (m, 2 H), 3.56 (br d, <i>J</i> = 10.92 Hz, 2 H), 2.24 - 2.32 (m, 2 H), 1.15 (d, <i>J</i> = 6.15 Hz, 6 H). Method 1: RT = 2.79 min.; M+H = 433.3
231		¹ H NMR (400 MHz, DMSO) δ ppm 8.94 (s, 1 H), 8.60 (d, <i>J</i> = 2.76 Hz, 1 H), 8.56 (d, <i>J</i> = 2.76 Hz, 1 H), 8.22 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.44 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 7.18 (d, <i>J</i> = 2.76 Hz, 1 H), 5.30 - 5.51 (m, 1 H), 5.10 (d, <i>J</i> = 8.28 Hz, 2 H), 4.75 (d, <i>J</i> = 8.28 Hz, 2 H), 4.26 - 4.38 (m, 2 H), 3.96 - 4.09 (m, 2 H), 3.74 (t, <i>J</i> = 6.96 Hz, 2 H), 2.58 (br s, 2 H). Method 1: RT = 2.65 min.; M+H = 427.2
232		¹ H NMR (400 MHz, DMSO) δ ppm 8.94 (s, 1 H), 8.52 (d, <i>J</i> = 2.69 Hz, 1 H), 8.26 (d, <i>J</i> = 2.81 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.63 Hz, 1 H), 7.60 - 7.68 (m, 1 H), 7.42 (dd, <i>J</i> = 11.37, 9.17 Hz, 1 H), 6.88 (d, <i>J</i> = 2.69 Hz, 1 H), 5.28 - 5.50 (m, 1 H), 4.24 - 4.37 (m, 2 H), 4.02 - 4.08 (m, 1 H), 3.98 (t, <i>J</i> = 7.64 Hz, 3 H), 3.65 (dd, <i>J</i> = 7.15, 5.69 Hz, 2 H), 3.56 (d, <i>J</i> = 6.60 Hz, 2 H), 3.29 (s, 3 H), 2.96 (m, 1 H). Method 1: RT = 2.70 min.; M+H = 429.3

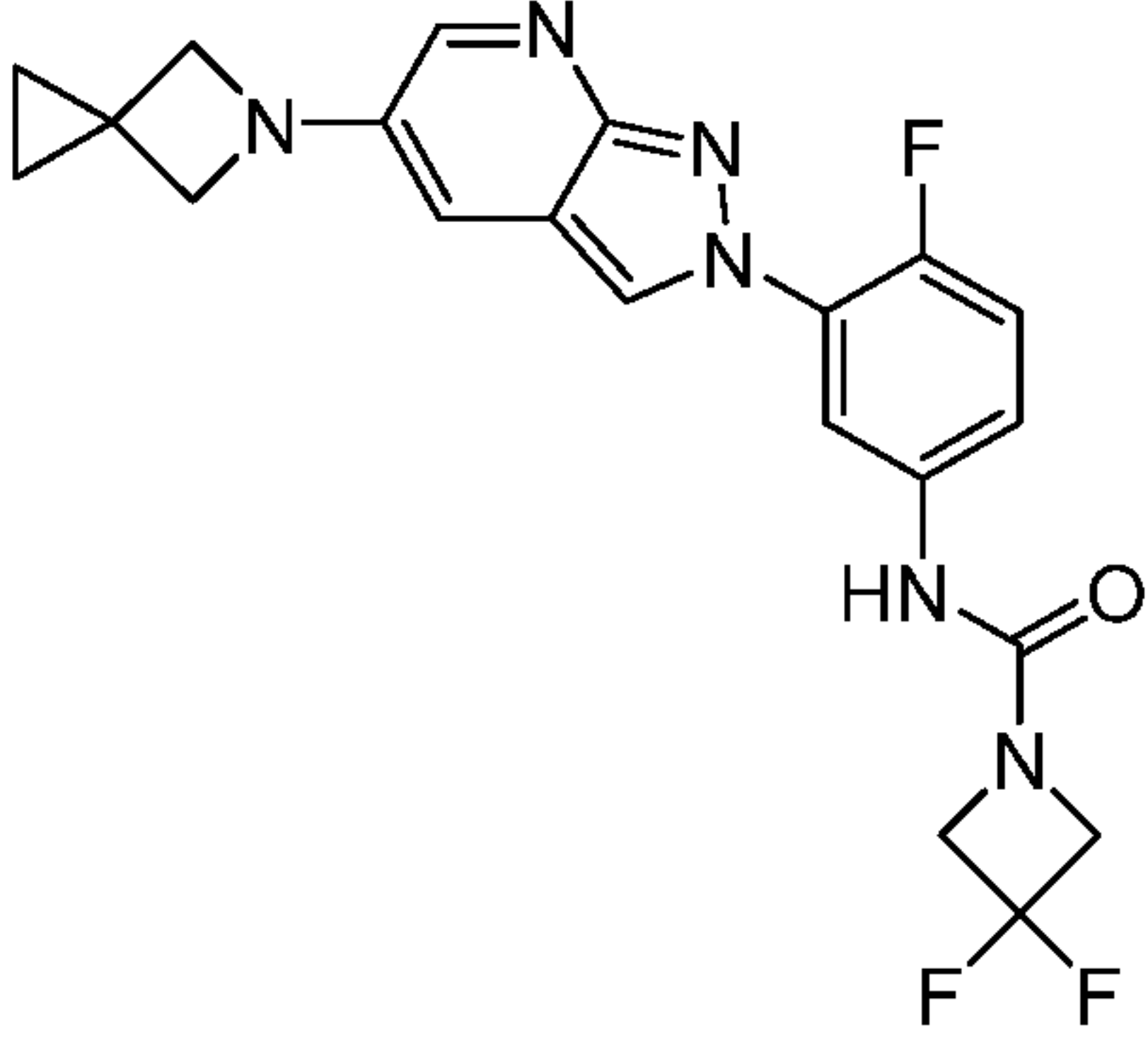
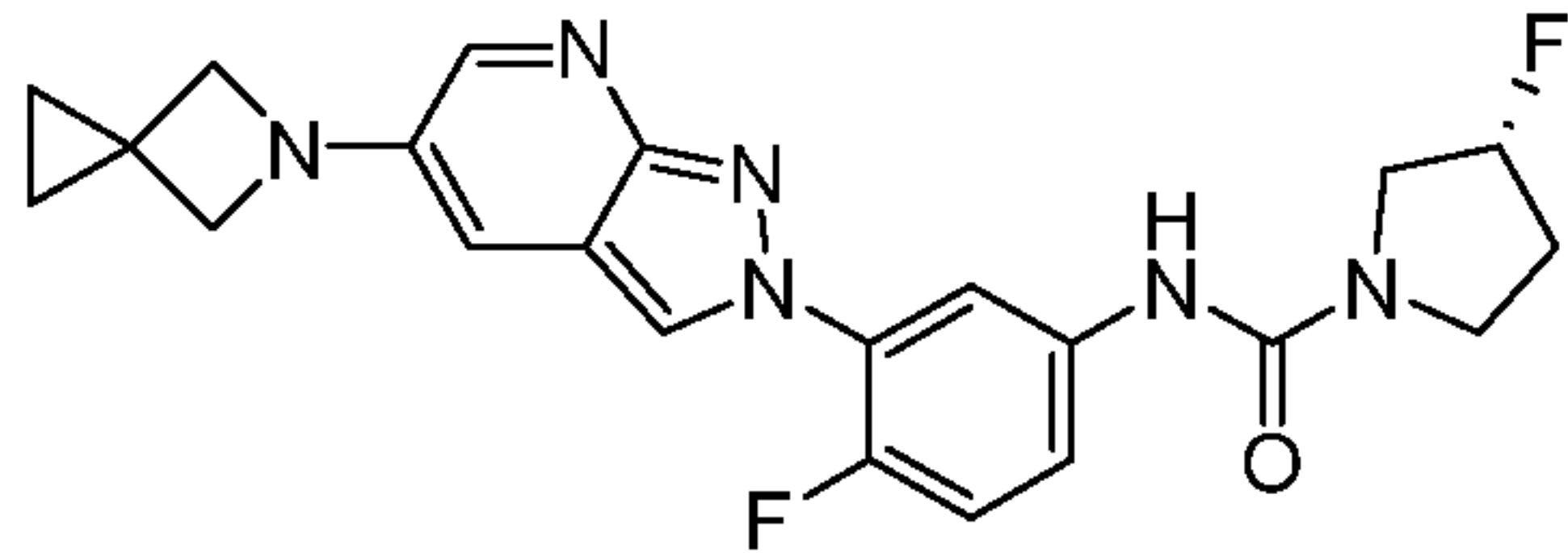
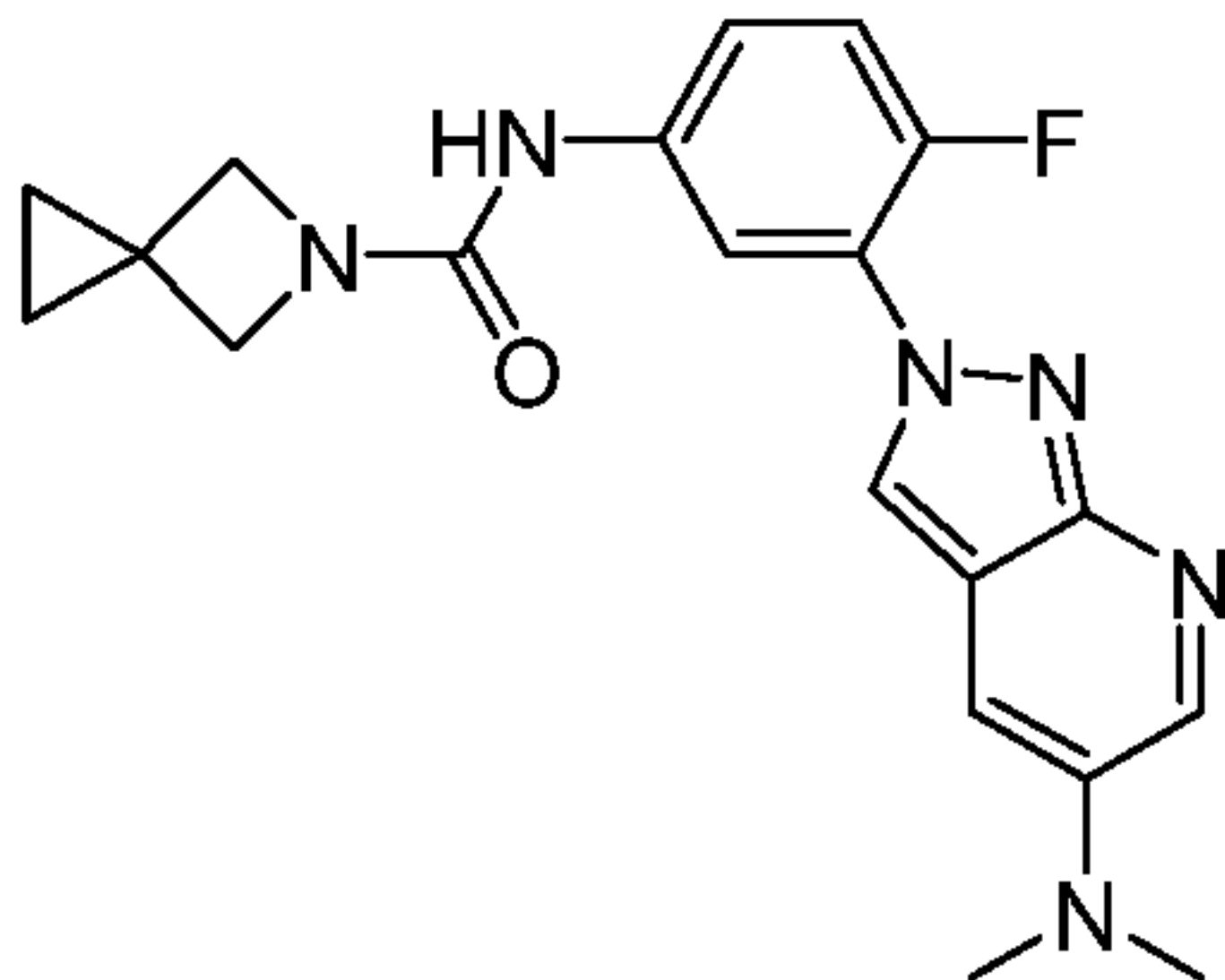
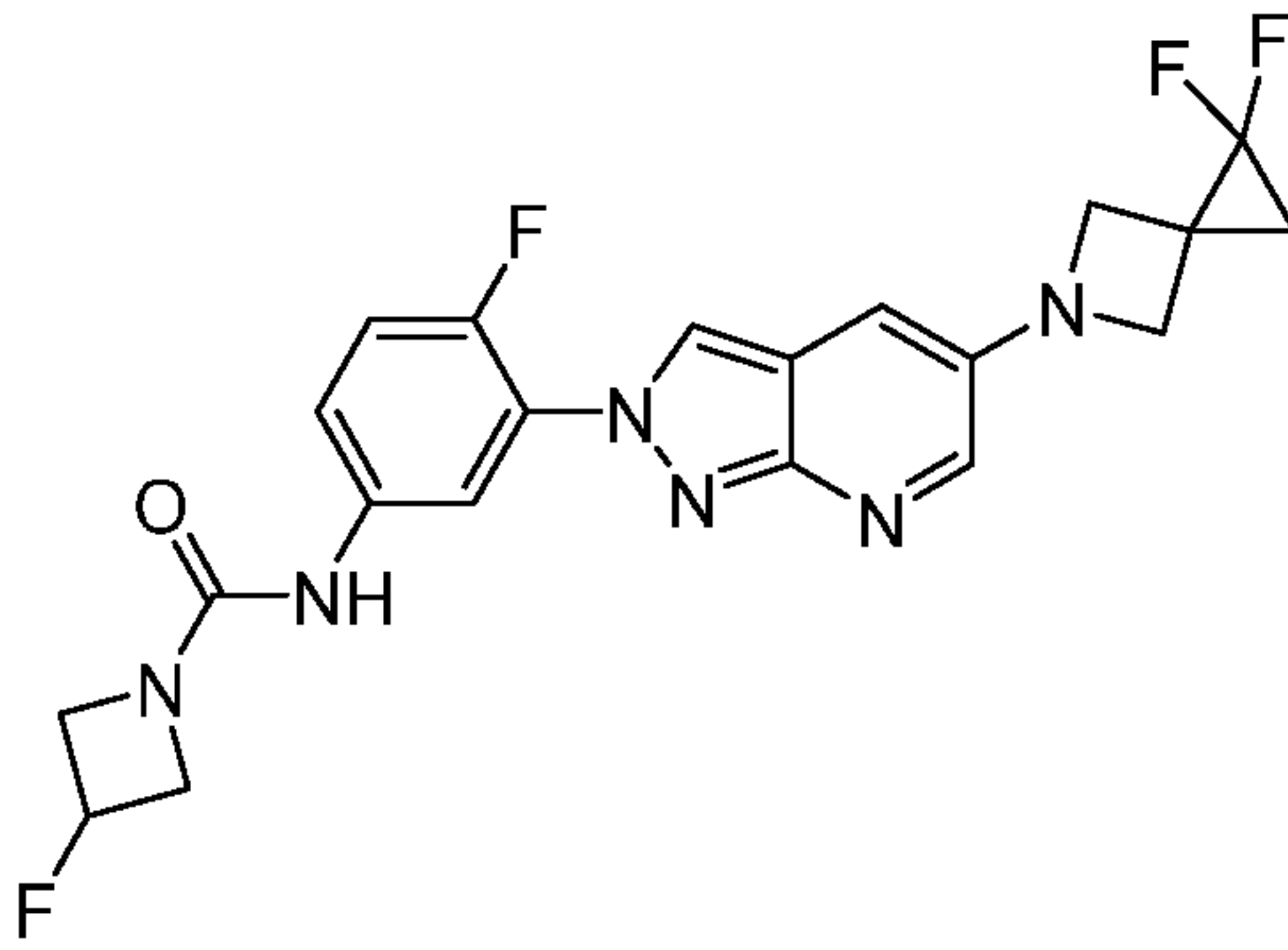
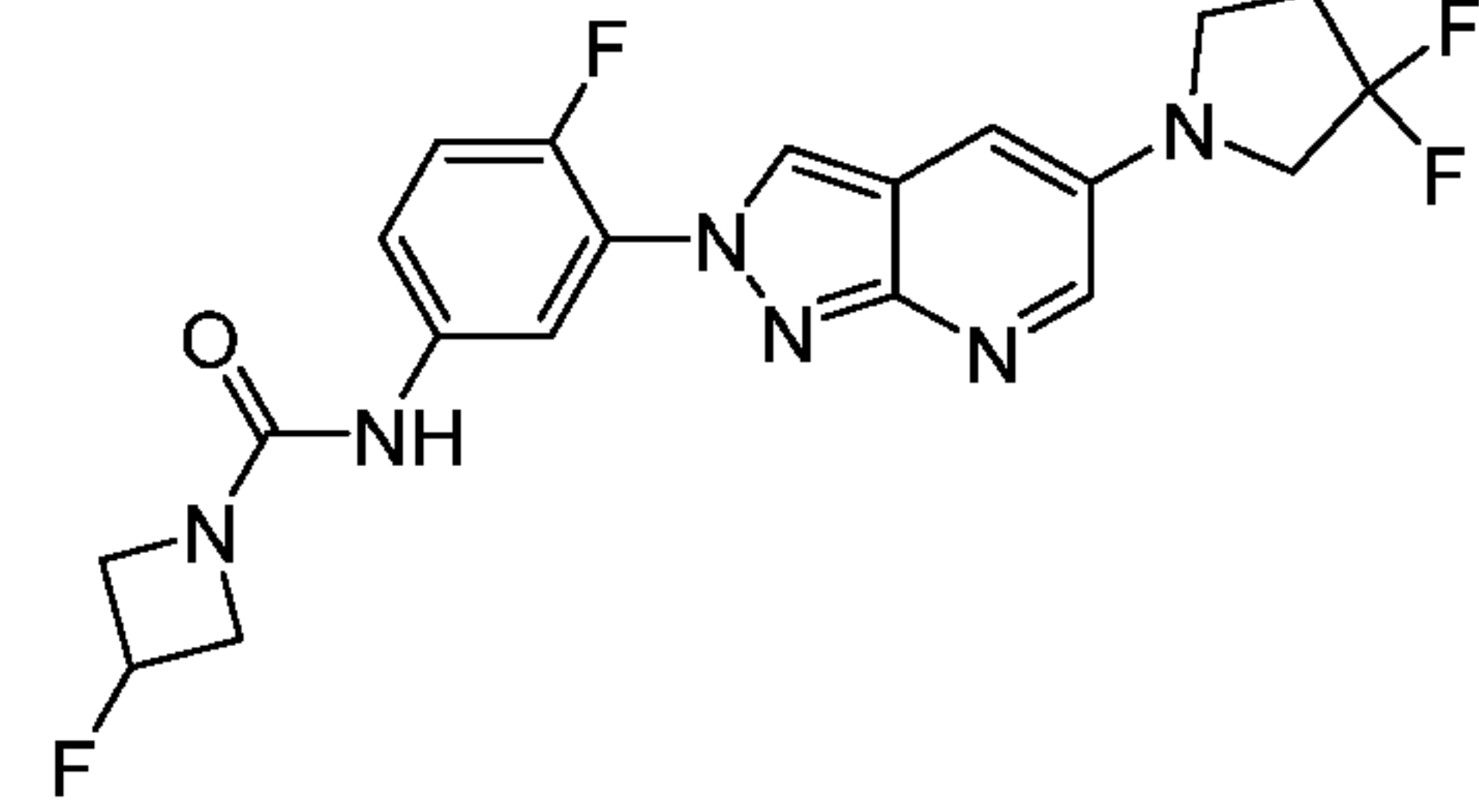
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
233		¹ H NMR (400 MHz, DMSO) δ ppm 8.92 (s, 1 H), 8.52 (d, <i>J</i> = 2.76 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.59 - 7.67 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.91 (d, <i>J</i> = 2.89 Hz, 1 H), 5.27 - 5.50 (m, 1 H), 4.23 - 4.38 (m, 2 H), 3.94 - 4.10 (m, 6 H), 0.68 (s, 4 H). Method 1: RT = 2.92 min.; M+H = 411.3
234		¹ H NMR (400 MHz, DMSO) δ 8.88 (s, 1 H), 8.48 - 8.59 (m, 2 H), 8.17 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.54 - 7.67 (m, 1 H), 7.39 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.03 (d, <i>J</i> = 2.89 Hz, 1 H), 5.19 - 5.63 (m, 3 H), 4.19 - 4.40 (m, 2 H), 3.93 - 4.06 (m, 2 H), 3.57 - 3.87 (m, 4 H). Method 1: RT = 2.77 min.; M+H = 435.1
235		¹ H NMR (400 MHz, DMSO) δ 8.93 - 9.02 (m, 1 H), 8.68 (d, <i>J</i> = 2.76 Hz, 1 H), 8.53 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.43 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.35 (d, <i>J</i> = 2.76 Hz, 1 H), 5.28 - 5.51 (m, 1 H), 4.20 - 4.38 (m, 4 H), 3.94 - 4.14 (m, 2 H), 3.79 (d, <i>J</i> = 10.79 Hz, 2 H), 3.50 (br d, <i>J</i> = 10.67 Hz, 2 H), 1.88 - 2.01 (m, 4 H). Method 1: RT = 2.63 min.; M+H = 441.3
236		¹ H NMR (400 MHz, DMSO) δ 8.96 (s, 1 H), 8.69 (d, <i>J</i> = 2.69 Hz, 1 H), 8.59 (d, <i>J</i> = 2.57 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.63 Hz, 1 H), 7.61 - 7.70 (m, 1 H), 7.31 - 7.47 (m, 2 H), 5.27 - 5.50 (m, 1 H), 4.23 - 4.39 (m, 2 H), 3.93 - 4.08 (m, 2 H), 3.56 (br d, <i>J</i> = 11.98 Hz, 2 H), 2.74 (br t, <i>J</i> = 10.45 Hz, 2 H), 2.23 - 2.33 (m, 1 H), 1.94 (br d, <i>J</i> = 10.76 Hz, 2 H), 1.65 - 1.80 (m, 2 H). Method 1: RT = 2.55 min.; M+H = 457.3
237		¹ H NMR (400 MHz, DMSO) δ 8.96 (s, 1 H), 8.72 (d, <i>J</i> = 2.76 Hz, 1 H), 8.62 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.59 - 7.72 (m, 1 H), 7.44 (t, <i>J</i> = 10.41 Hz, 1 H), 7.38 (s, 1 H), 5.26 - 5.52 (m, 1 H), 4.25 - 4.39 (m, 2 H), 3.96 - 4.10 (m, 2 H), 3.23 - 3.31 (m, 2 H), 3.12 - 3.21 (m, 4 H), 2.76 - 2.90 (m, 4 H). Method 1: RT = 2.88 min.; M+H = 496.4

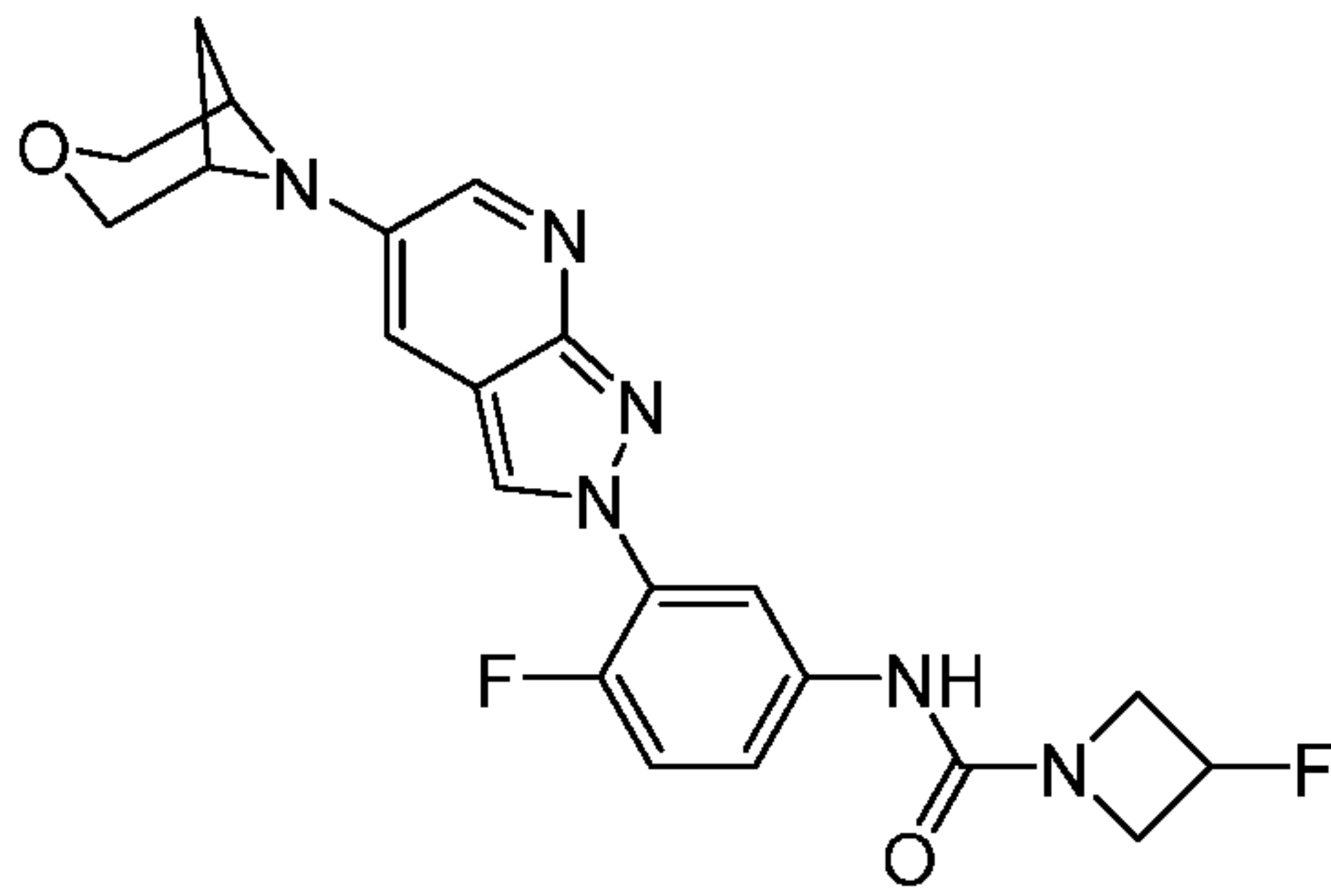
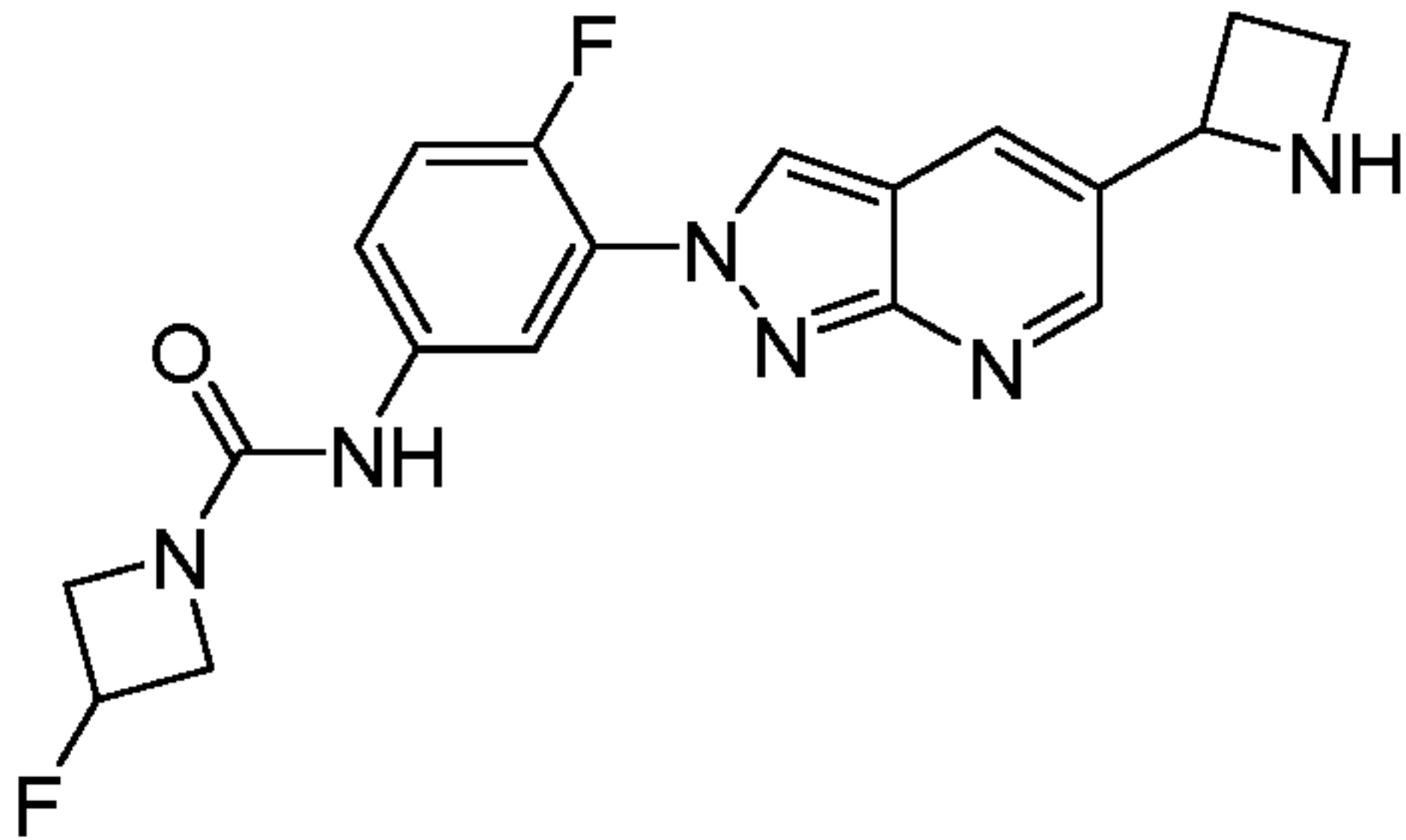
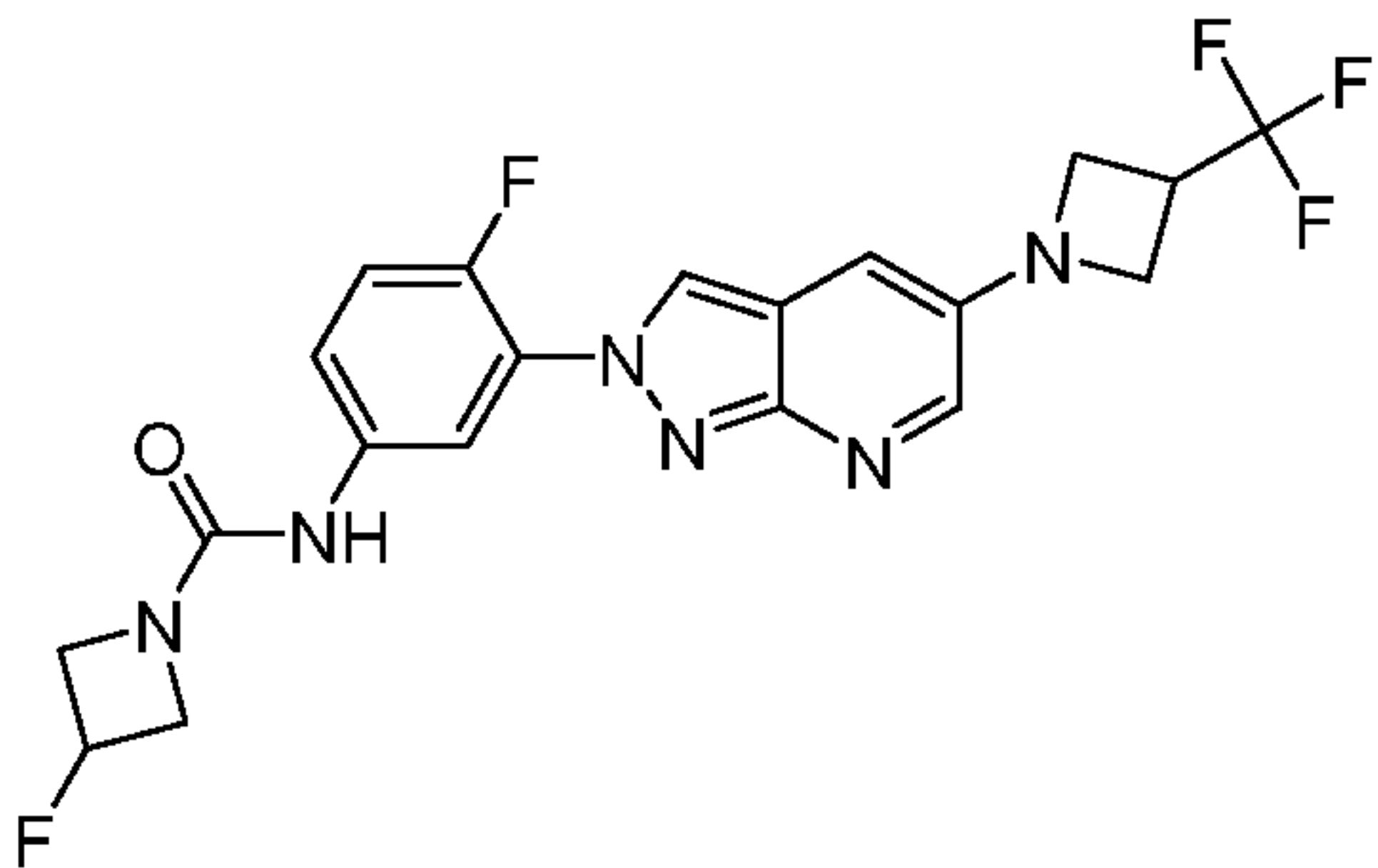
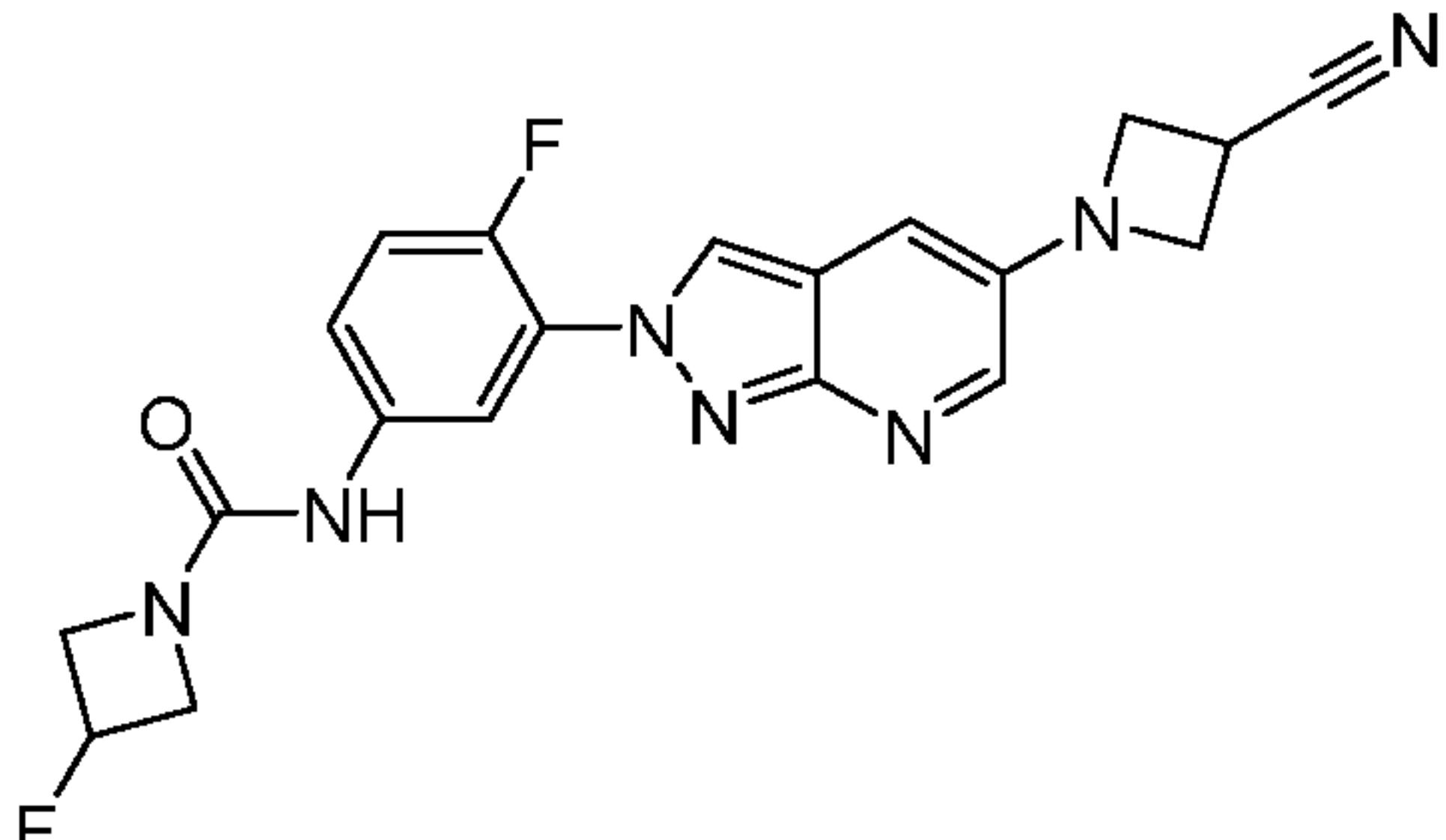
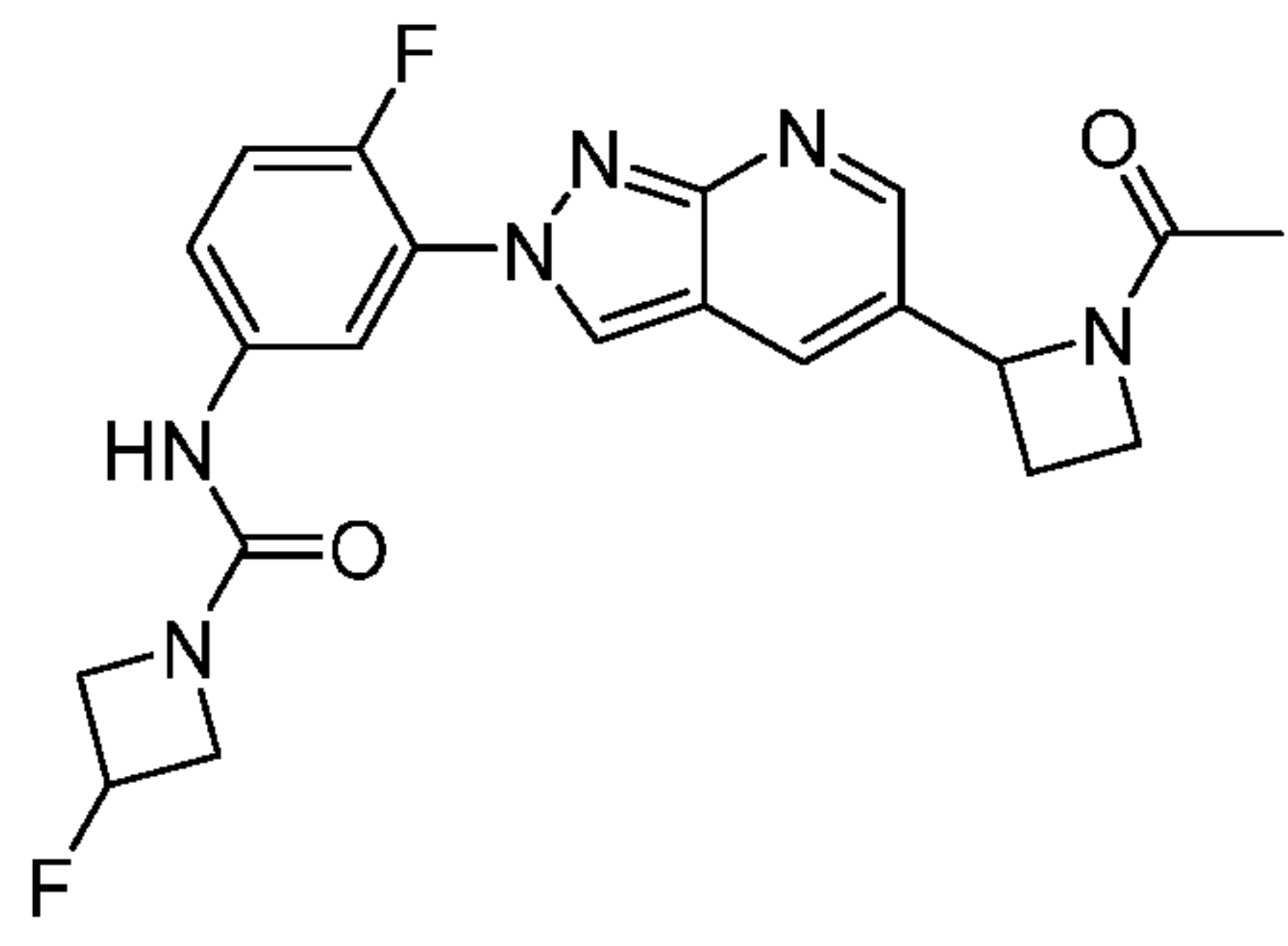
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
238		¹ H NMR (400 MHz, DMSO) δ 8.89 - 8.98 (m, 1 H), 8.71 (d, <i>J</i> = 2.89 Hz, 1 H), 8.62 (d, <i>J</i> = 2.64 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.58 - 7.70 (m, 1 H), 7.36 - 7.51 (m, 2 H), 5.22 - 5.54 (m, 1 H), 4.63 (dd, <i>J</i> = 7.84, 5.96 Hz, 2 H), 4.22 - 4.46 (m, 4 H), 3.92 - 4.11 (m, 2 H), 3.58 - 3.76 (m, 2 H), 2.60 - 2.84 (m, 3 H), 1.65 - 1.85 (m, 3 H), 1.17 - 1.32 (m, 2 H). Method 1: RT = 2.74 min.; M+H = 469.3
239		¹ H NMR (400 MHz, DMSO) δ 8.93 (s, 1 H), 8.54 (d, <i>J</i> = 2.76 Hz, 1 H), 8.26 (d, <i>J</i> = 2.76 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.93 (d, <i>J</i> = 2.76 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.23 - 4.38 (m, 2 H), 3.92 - 4.09 (m, 6 H), 3.41 (s, 4 H). Method 1: RT = 2.84 min.; M+H = 443.3
240		¹ H NMR (400 MHz, DMSO) δ 8.93 (s, 1 H), 8.68 (d, <i>J</i> = 2.89 Hz, 1 H), 8.53 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.59 - 7.65 (m, 1 H), 7.41 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.11 (d, <i>J</i> = 3.01 Hz, 1 H), 5.27 - 5.48 (m, 1 H), 4.73 (d, <i>J</i> = 6.27 Hz, 2 H), 4.23 - 4.36 (m, 2 H), 3.93 - 4.06 (m, 2 H), 3.70 (d, <i>J</i> = 11.29 Hz, 2 H), 3.48 (br d, <i>J</i> = 10.92 Hz, 2 H), 3.08 - 3.16 (m, 1 H), 1.99 (d, <i>J</i> = 8.53 Hz, 1 H). Method 1: RT = 2.52 min.; M+H = 427.3
241		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.91 (s, 1 H), 8.49 (dd, <i>J</i> = 7.09, 2.82 Hz, 2 H), 8.20 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.42 (dd, <i>J</i> = 11.48, 9.10 Hz, 1 H), 6.88 (d, <i>J</i> = 2.89 Hz, 1 H), 5.28 - 5.50 (m, 1 H), 4.24 - 4.39 (m, 2 H), 3.97 - 4.08 (m, 2 H), 3.51 (t, <i>J</i> = 6.78 Hz, 2 H), 3.30 (s, 2 H), 1.96 (t, <i>J</i> = 6.78 Hz, 2 H), 0.60 - 0.71 (m, 4 H). Method 1: RT = 3.16 min.; M+H = 425.3
242		¹ H NMR (400 MHz, DMSO) δ 8.41 - 8.52 (m, 3 H), 8.23 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.60 - 7.69 (m, 1 H), 7.38 (dd, <i>J</i> = 11.42, 9.16 Hz, 1 H), 6.86 (d, <i>J</i> = 2.89 Hz, 1 H), 3.52 (dt, <i>J</i> = 15.34, 6.89 Hz, 3 H), 3.28 (s, 5 H), 1.95 (t, <i>J</i> = 6.78 Hz, 2 H), 1.81 (t, <i>J</i> = 6.78 Hz, 2 H), 0.52 - 0.71 (m, 8 H). Method 1: RT = 3.26 min.; M+H = 447.3

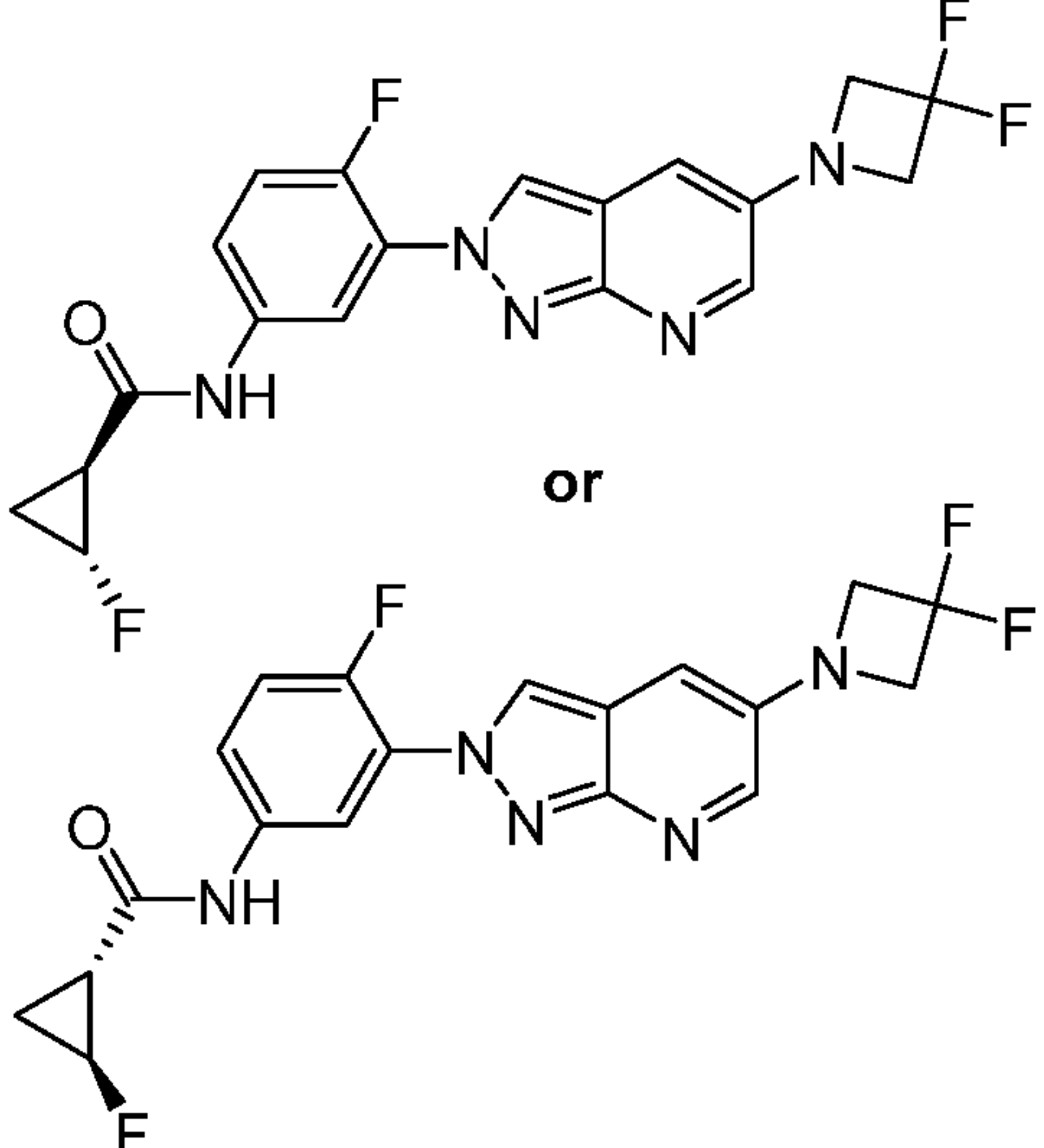
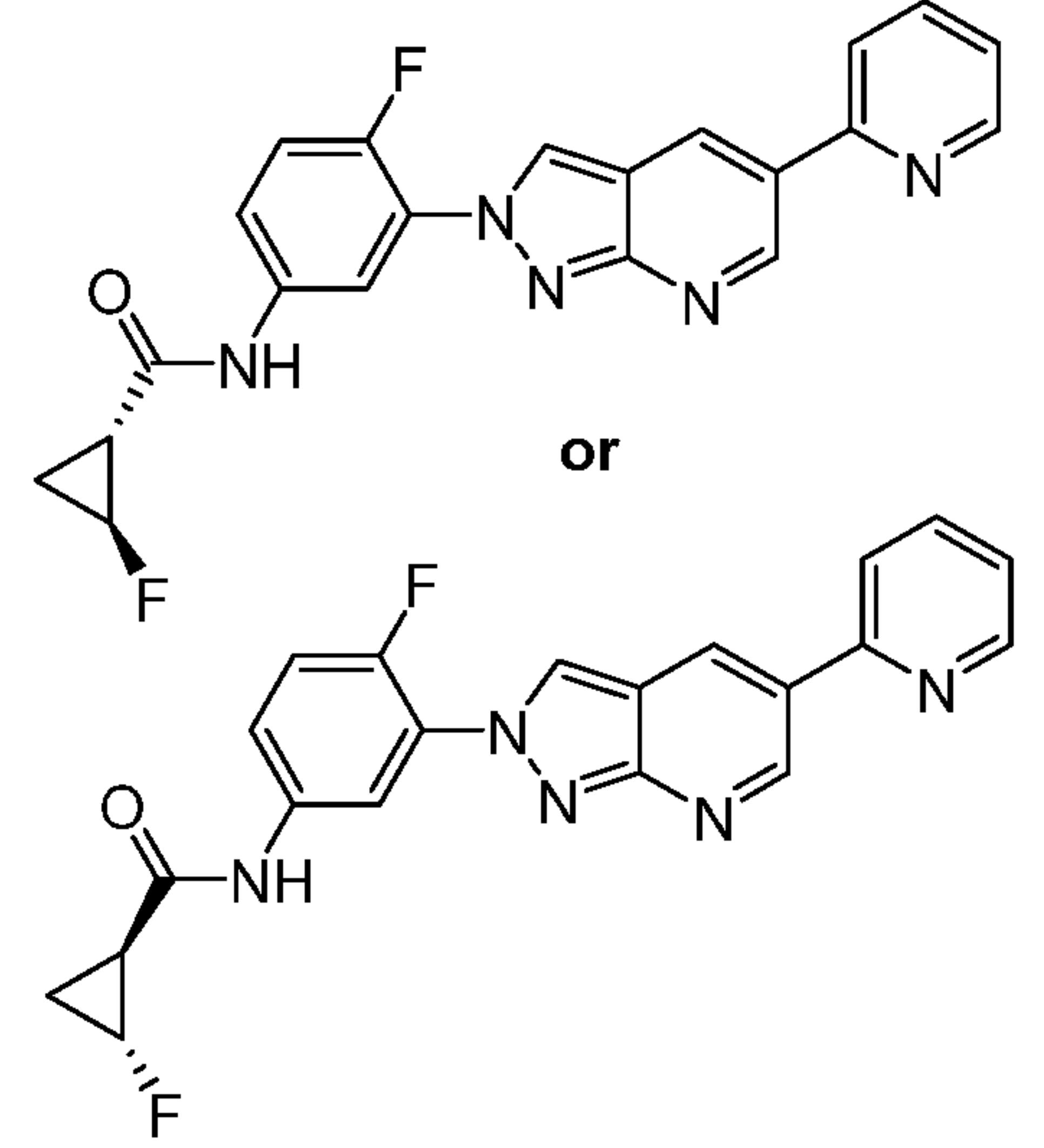
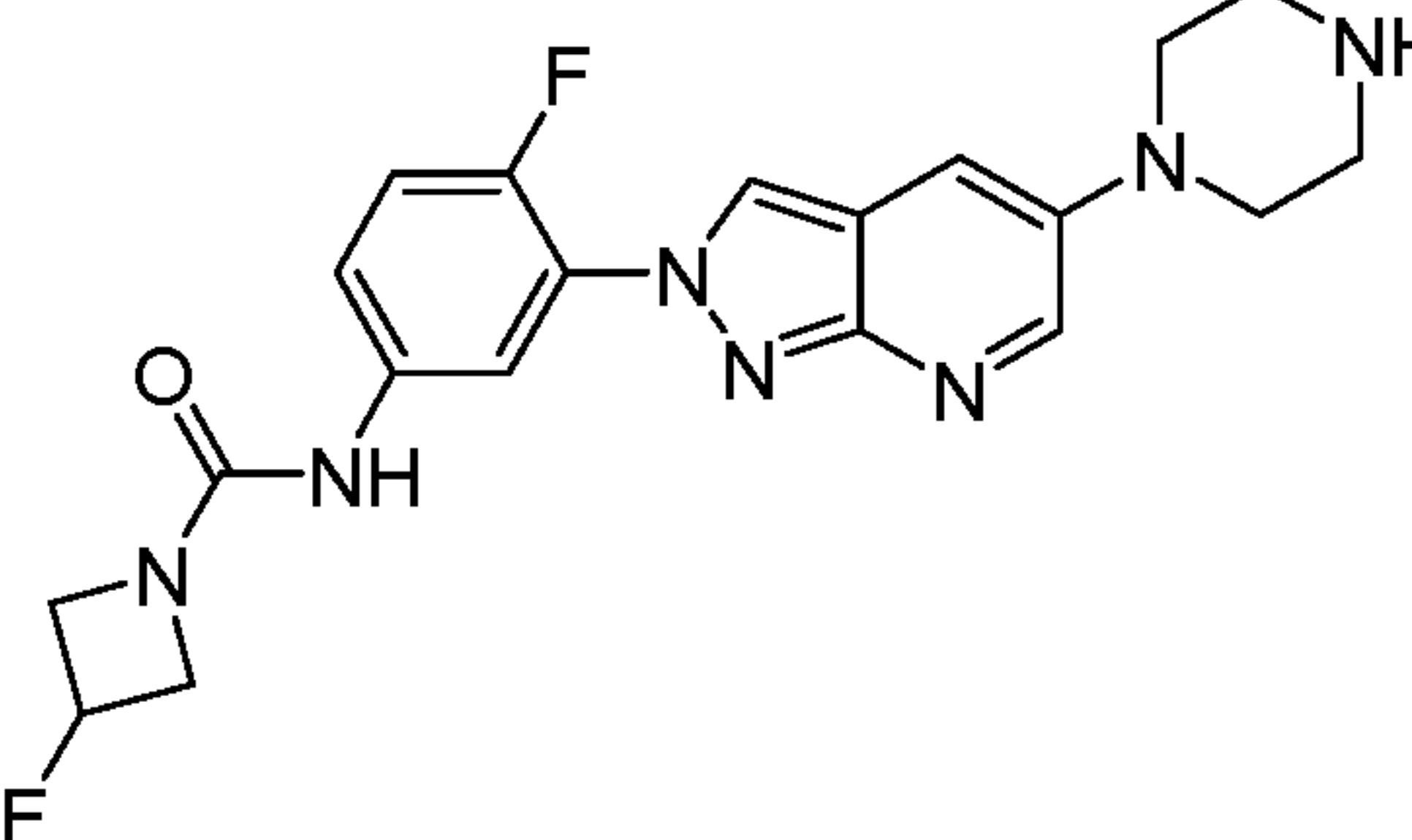
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
243		¹ H NMR (400 MHz, DMSO) δ 8.89 (s, 1 H), 8.50 (d, <i>J</i> = 2.76 Hz, 1 H), 8.22 (s, 1 H), 8.16 (d, <i>J</i> = 6.68 Hz, 1 H), 7.59 - 7.64 (m, 1 H), 7.40 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.85 (d, <i>J</i> = 2.76 Hz, 1 H), 5.25 - 5.49 (m, 1 H), 4.14 - 4.36 (m, 2 H), 3.93 - 4.05 (m, 2 H), 3.86 (s, 4 H), 2.18 (t, <i>J</i> = 7.59 Hz, 4 H), 1.82 (quin, <i>J</i> = 7.53 Hz, 2 H). Method 1: RT = 3.06 min.; M+H = 425.3
244		¹ H NMR (400 MHz, DMSO) δ 8.92 (s, 1 H), 8.49 (dd, <i>J</i> = 9.47, 2.82 Hz, 2 H), 8.20 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.60 - 7.67 (m, 1 H), 7.41 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.88 (d, <i>J</i> = 2.89 Hz, 1 H), 5.27 - 5.50 (m, 1 H), 4.24 - 4.37 (m, 2 H), 3.94 - 4.08 (m, 2 H), 3.55 - 3.69 (m, 4 H), 3.41 - 3.46 (m, 2 H), 3.28 (s, 2 H), 1.92 (t, <i>J</i> = 6.96 Hz, 2 H), 1.46 - 1.63 (m, 4 H). Method 1: RT = 2.86 min.; M+H = 469.3
245		¹ H NMR (400 MHz, DMSO) δ 8.91 (s, 1 H), 8.55 (d, <i>J</i> = 2.64 Hz, 1 H), 8.29 (d, <i>J</i> = 2.89 Hz, 2 H), 8.19 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.60 - 7.66 (m, 1 H), 7.42 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 6.98 (d, <i>J</i> = 2.76 Hz, 1 H), 5.27 - 5.49 (m, 1 H), 4.23 - 4.36 (m, 2 H), 3.94 - 4.09 (m, 4 H), 3.86 (d, <i>J</i> = 7.78 Hz, 2 H), 2.38 (br d, <i>J</i> = 7.78 Hz, 2 H), 2.21 - 2.28 (m, 2 H). Method 1: RT = 2.41 min.; M+H = 454.3
246		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.78 (s, 1 H), 8.53 (d, <i>J</i> = 2.76 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.21 (dd, <i>J</i> = 7.15, 2.64 Hz, 1 H), 7.60 - 7.71 (m, 1 H), 7.41 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 6.94 (d, <i>J</i> = 2.76 Hz, 1 H), 3.93 (d, <i>J</i> = 12.05 Hz, 8 H), 3.84 (s, 2 H), 3.67 - 3.80 (m, 6 H), 2.09 - 2.21 (m, 4 H). Method 1: RT = 2.64 min.; M+H = 479.4
247		¹ H NMR (400 MHz, Methanol-d ₄) δ 8.83 - 8.71 (m, 1H), 8.64 (d, <i>J</i> = 4.8 Hz, 1H), 8.12 (dd, <i>J</i> = 6.8, 2.7 Hz, 1H), 7.65 (dt, <i>J</i> = 9.3, 3.6 Hz, 1H), 7.35 (dd, <i>J</i> = 10.9, 9.1 Hz, 1H), 7.09 - 6.97 (m, 1H), 5.32 - 5.14 (m, 1H), 4.17 - 4.01 (m, 4H), 3.83 - 3.56 (m, 2H), 2.63 - 2.44 (m, 1H), 2.39 - 2.25 (m, 2H), 2.09 - 1.93 (m, 3H), 1.47 (s, 3H), 1.07 (s, 6H). Method 2: RT = 0.93 min.; M+H = 481.3

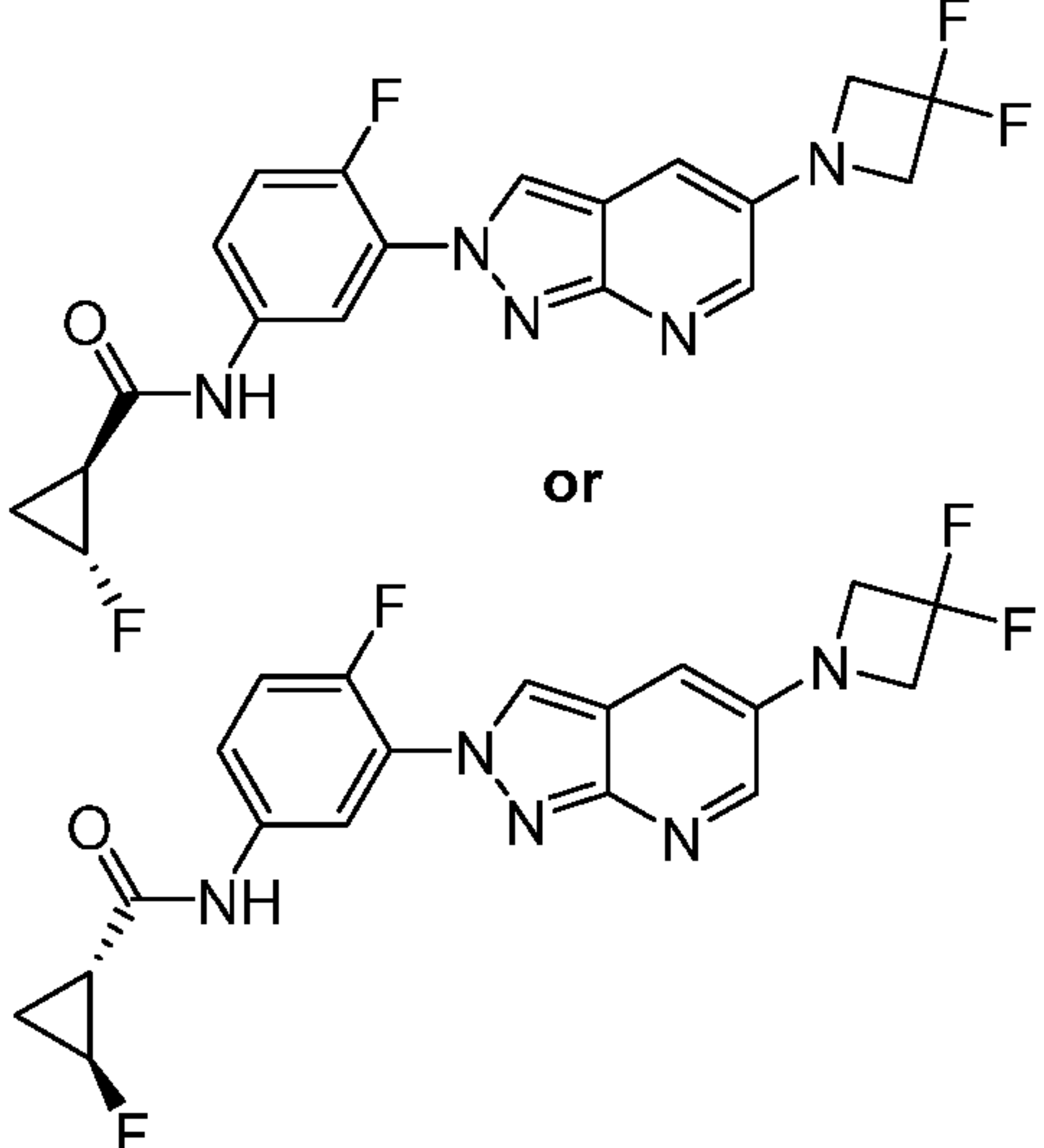
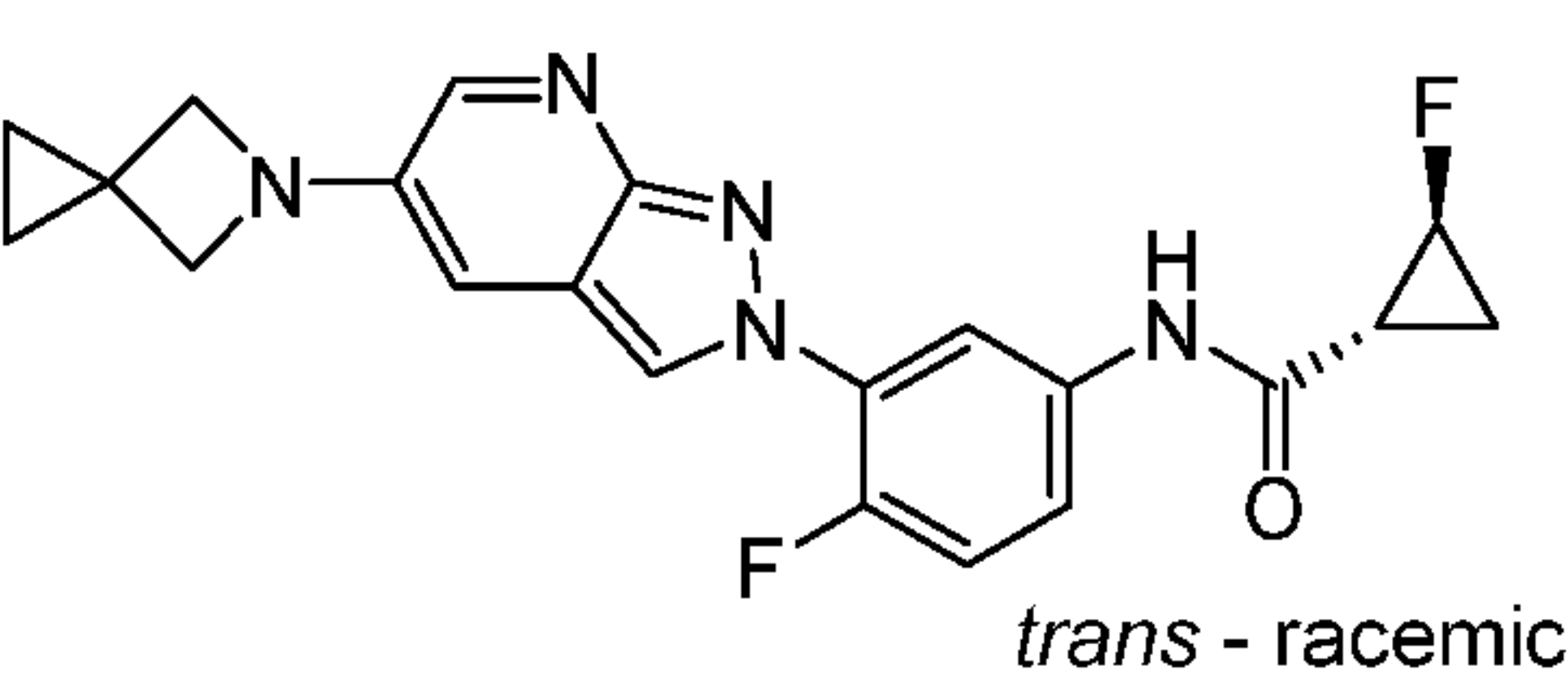
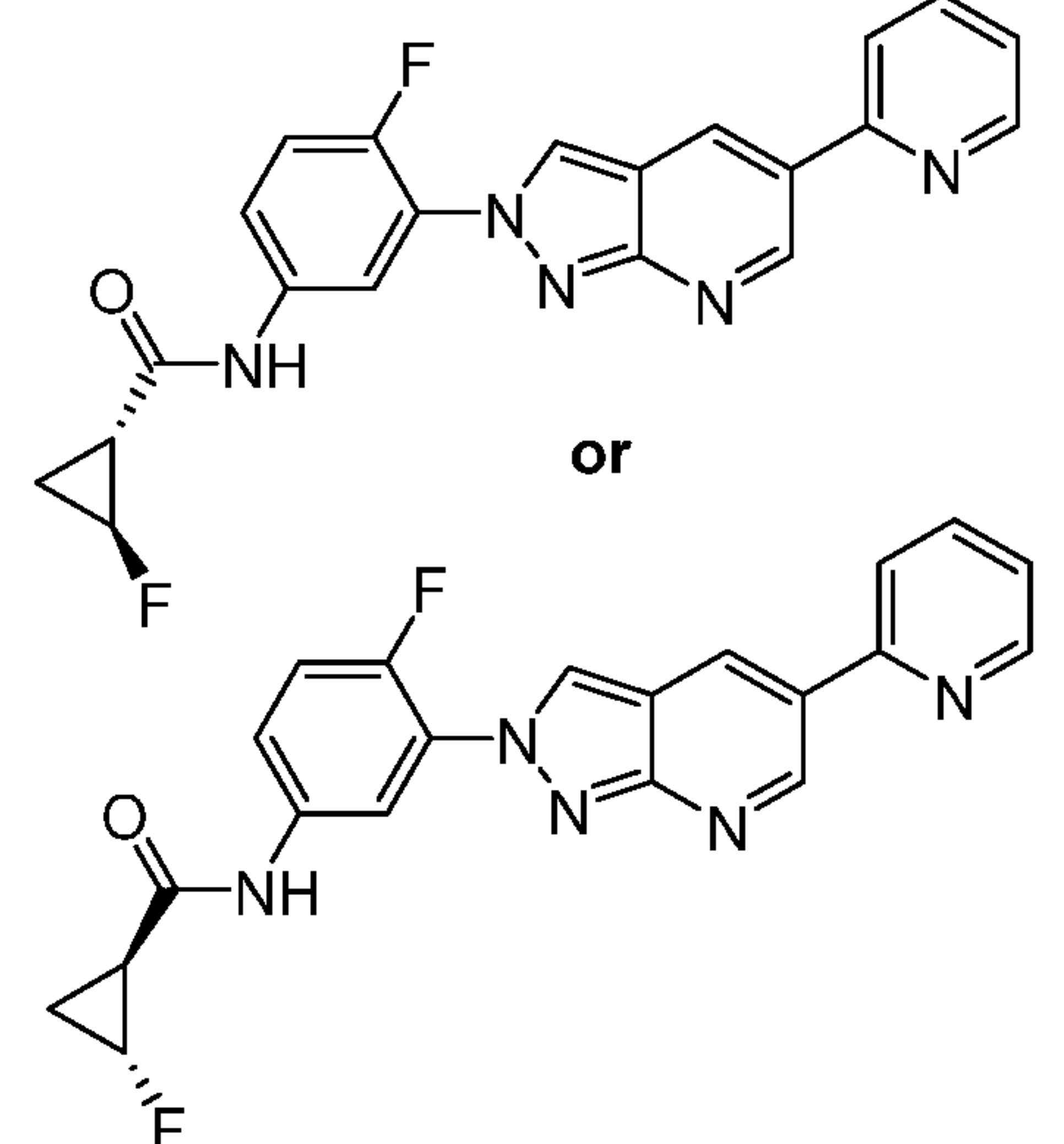
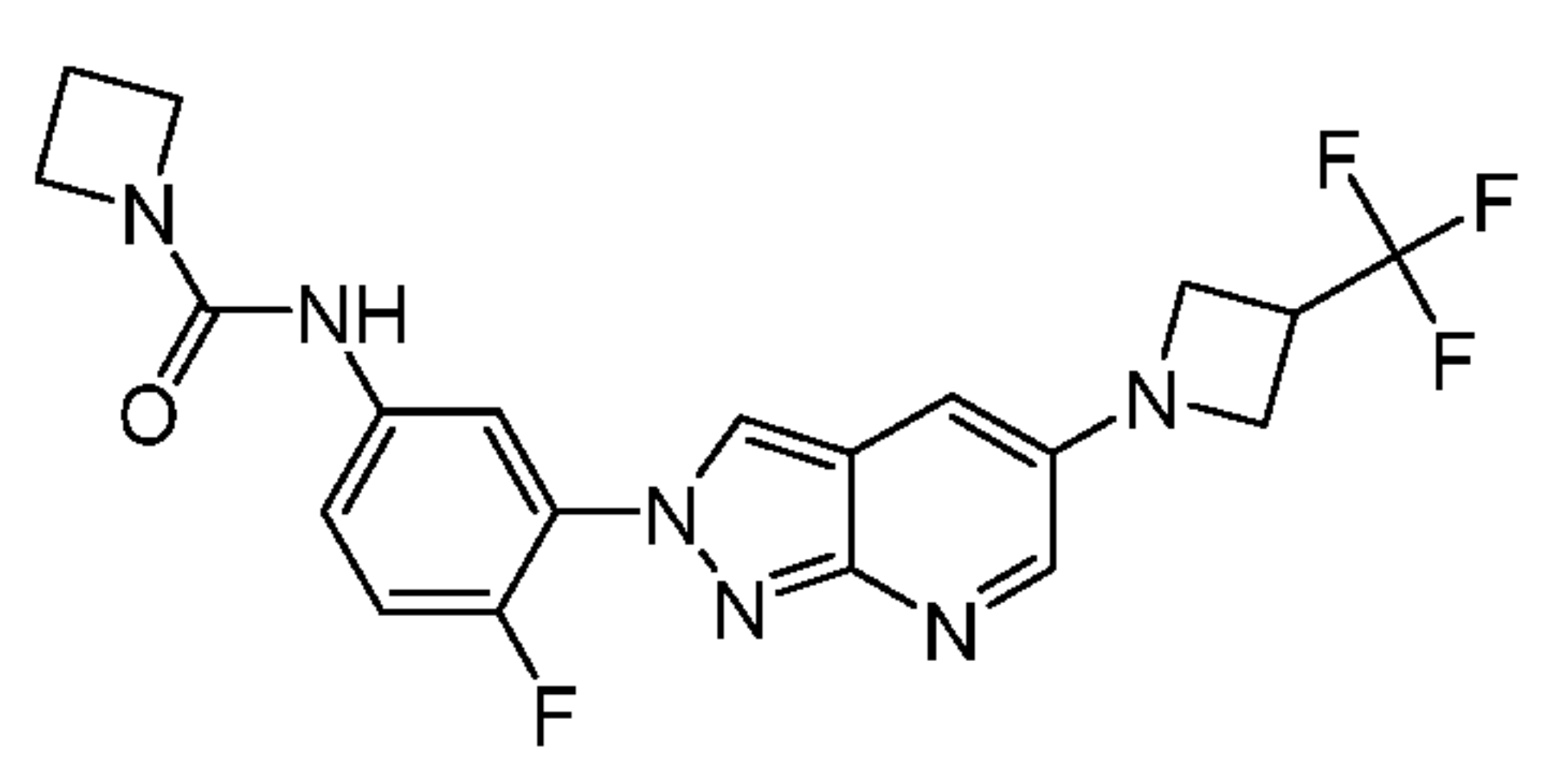
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
248		¹ H NMR (400 MHz, DMSO) δ 8.95 (s, 1 H), 8.70 (d, <i>J</i> = 2.76 Hz, 1 H), 8.60 (d, <i>J</i> = 2.76 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.61 - 7.69 (m, 1 H), 7.44 (dd, <i>J</i> = 11.23, 9.10 Hz, 1 H), 7.37 (d, <i>J</i> = 2.76 Hz, 1 H), 5.27 - 5.51 (m, 1 H), 4.25 - 4.40 (m, 6 H), 3.96 - 4.09 (m, 2 H), 3.02 - 3.10 (m, 4 H), 1.91 - 2.00 (m, 4 H). Method 1: RT = 2.65 min.; M+H = 455.3
249		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.93 (s, 1 H), 8.48 (d, <i>J</i> = 2.89 Hz, 1 H), 8.29 (d, <i>J</i> = 2.76 Hz, 1 H), 8.17 (dd, <i>J</i> = 7.15, 2.64 Hz, 1 H), 7.59 - 7.66 (m, 1 H), 7.41 (dd, <i>J</i> = 11.42, 9.16 Hz, 1 H), 7.09 (d, <i>J</i> = 2.64 Hz, 1 H), 6.47 (s, 1 H), 5.28 - 5.50 (m, 1 H), 4.24 - 4.38 (m, 2 H), 3.94 - 4.08 (m, 2 H), 2.37 (br s, 1 H), 0.70 - 0.77 (m, 2 H), 0.39 - 0.47 (m, 2 H). Method 1: RT = 2.78 min.; M+H = 385.1
250		¹ H NMR (400 MHz, DMSO) δ 8.66 - 8.73 (m, 2 H), 8.60 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.35 - 7.45 (m, 2 H), 3.96 (t, <i>J</i> = 7.53 Hz, 4 H), 3.22 - 3.30 (m, 2 H), 3.11 - 3.19 (m, 4 H), 2.78 - 2.86 (m, 4 H), 2.19 (quin, <i>J</i> = 7.56 Hz, 2 H). Method 1: RT = 2.95 min.; M+H = 478.1
251		¹ H NMR (400 MHz, DMSO) δ 8.87 - 8.99 (m, 1 H), 8.52 (d, <i>J</i> = 2.51 Hz, 1 H), 8.28 (d, <i>J</i> = 2.64 Hz, 1 H), 8.20 (dd, <i>J</i> = 6.96, 2.45 Hz, 1 H), 7.64 (dt, <i>J</i> = 8.72, 3.36 Hz, 1 H), 7.42 (dd, <i>J</i> = 11.17, 9.29 Hz, 1 H), 6.92 (d, <i>J</i> = 2.64 Hz, 1 H), 5.28 - 5.69 (m, 2 H), 4.22 - 4.42 (m, 2 H), 3.94 - 4.10 (m, 2 H), 3.87 (d, <i>J</i> = 7.40 Hz, 2 H), 3.69 (d, <i>J</i> = 7.28 Hz, 2 H), 1.49 (s, 3 H). Method 1: RT = 2.53 min.; M+H = 415.3
252		¹ H NMR (400 MHz, DMSO) δ 9.20 (s, 1 H), 8.72 (d, <i>J</i> = 2.76 Hz, 1 H), 8.62 (d, <i>J</i> = 2.64 Hz, 1 H), 8.30 (d, <i>J</i> = 2.38 Hz, 1 H), 7.59 - 7.68 (m, 1 H), 7.46 (dd, <i>J</i> = 11.23, 9.22 Hz, 1 H), 7.38 (d, <i>J</i> = 2.13 Hz, 1 H), 4.40 (t, <i>J</i> = 12.74 Hz, 4 H), 3.21 - 3.27 (m, 2 H), 3.12 - 3.18 (m, 4 H), 2.78 - 2.86 (m, 4 H). Method 1: RT = 2.99 min.; M+H = 514.3

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
253		¹ H NMR (400 MHz, DMSO) δ 8.72 (d, <i>J</i> = 2.76 Hz, 1 H), 8.54 - 8.64 (m, 2 H), 8.22 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.68 (dt, <i>J</i> = 8.97, 3.48 Hz, 1 H), 7.33 - 7.49 (m, 2 H), 5.25 - 5.49 (m, 1 H), 3.38 - 3.79 (m, 6 H), 3.16 (br d, <i>J</i> = 4.89 Hz, 4 H), 2.83 (br d, <i>J</i> = 4.27 Hz, 4 H), 2.00 - 2.26 (m, 2 H). Method 1: RT = 2.95 min.; M+H = 510.3
254		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.90 (d, <i>J</i> = 2.45 Hz, 1 H), 8.85 (s, 1 H), 8.74 - 8.78 (m, 1 H), 8.61 - 8.65 (m, 1 H), 8.26 (dd, <i>J</i> = 7.09, 2.69 Hz, 1 H), 7.69 - 7.76 (m, 1 H), 7.47 (dd, <i>J</i> = 11.25, 9.29 Hz, 1 H), 4.05 (s, 4 H), 0.66 (s, 4 H). Method 1: RT = 2.95 min.; M+H = 416.0, 418.0
255		¹ H NMR (500 MHz, DMSO-d ₆) δ 8.91 (s, 1H), 8.52 (d, <i>J</i> = 2.7 Hz, 1H), 8.26 (d, <i>J</i> = 2.8 Hz, 1H), 8.20 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 7.65 (ddd, <i>J</i> = 9.1, 4.1, 2.7 Hz, 1H), 7.43 (dd, <i>J</i> = 11.4, 9.1 Hz, 1H), 6.87 (d, <i>J</i> = 2.8 Hz, 1H), 5.51 - 5.26 (m, 1H), 4.39 - 4.23 (m, 2H), 4.09 - 3.94 (m, 2H), 3.65 (s, 4H), 1.32 (s, 6H). Method 1: RT = 3.08 min.; M+H = 413.2
256		¹ H NMR (500 MHz, DMSO-d ₆) δ 10.74 (s, 1H), 9.48 (d, <i>J</i> = 2.3 Hz, 1H), 9.03 (d, <i>J</i> = 2.4 Hz, 1H), 8.94 (d, <i>J</i> = 2.3 Hz, 1H), 8.74 (ddd, <i>J</i> = 4.8, 1.9, 0.9 Hz, 1H), 8.39 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 8.21 - 8.10 (m, 1H), 7.96 (td, <i>J</i> = 7.7, 1.8 Hz, 1H), 7.75 - 7.62 (m, 1H), 7.57 (dd, <i>J</i> = 11.1, 9.0 Hz, 1H), 7.42 (ddd, <i>J</i> = 7.5, 4.8, 1.1 Hz, 1H), 4.92 (dddd, <i>J</i> = 64.6, 6.3, 3.3, 1.6 Hz, 1H), 2.41 - 2.24 (m, 1H), 1.57 (dddd, <i>J</i> = 22.4, 10.3, 6.6, 3.3 Hz, 1H), 1.28 (dq, <i>J</i> = 13.0, 6.5 Hz, 1H). Method 1: RT = 2.79 min.; M+H = 392.1
257		¹ H NMR (400 MHz, DMSO) δ 8.69 (s, 1 H), 8.52 (d, <i>J</i> = 2.63 Hz, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.03, 2.63 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.40 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 6.91 (d, <i>J</i> = 2.76 Hz, 1 H), 4.01 (s, 4 H), 3.97 (t, <i>J</i> = 7.53 Hz, 4 H), 2.19 (quin, <i>J</i> = 7.56 Hz, 2 H), 0.68 (s, 4 H). Method 1: RT = 2.90 min.; M+H = 393.2

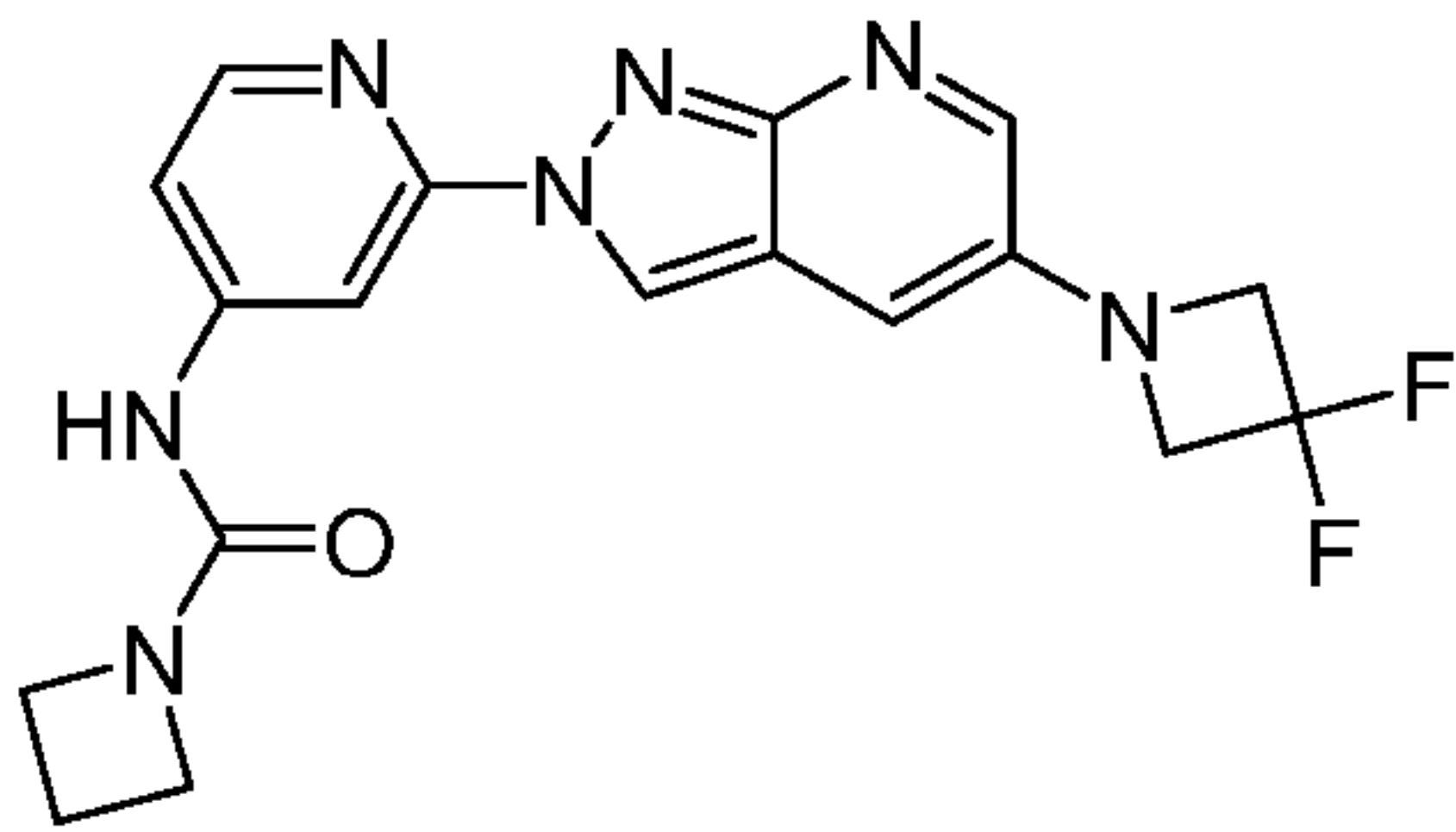
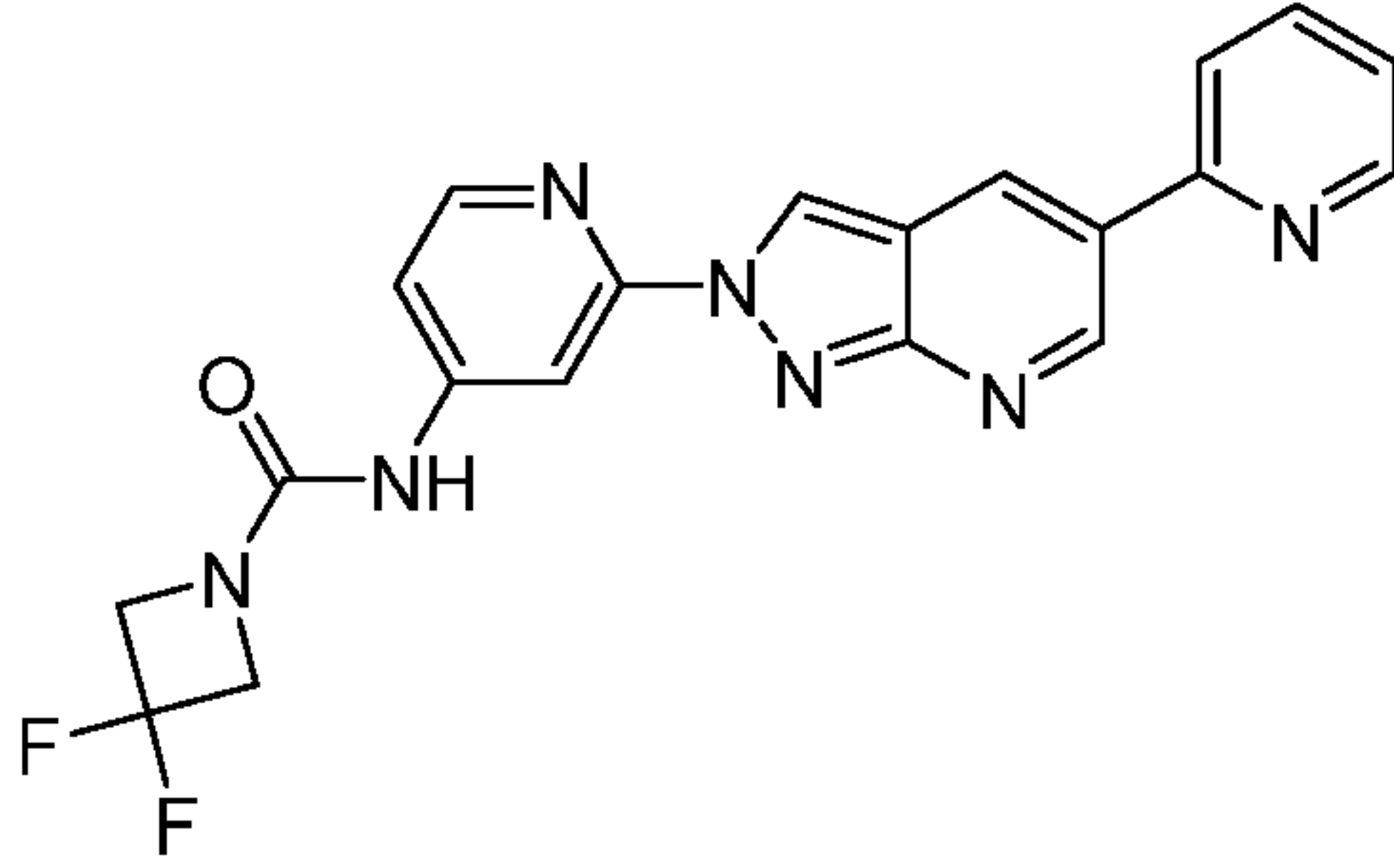
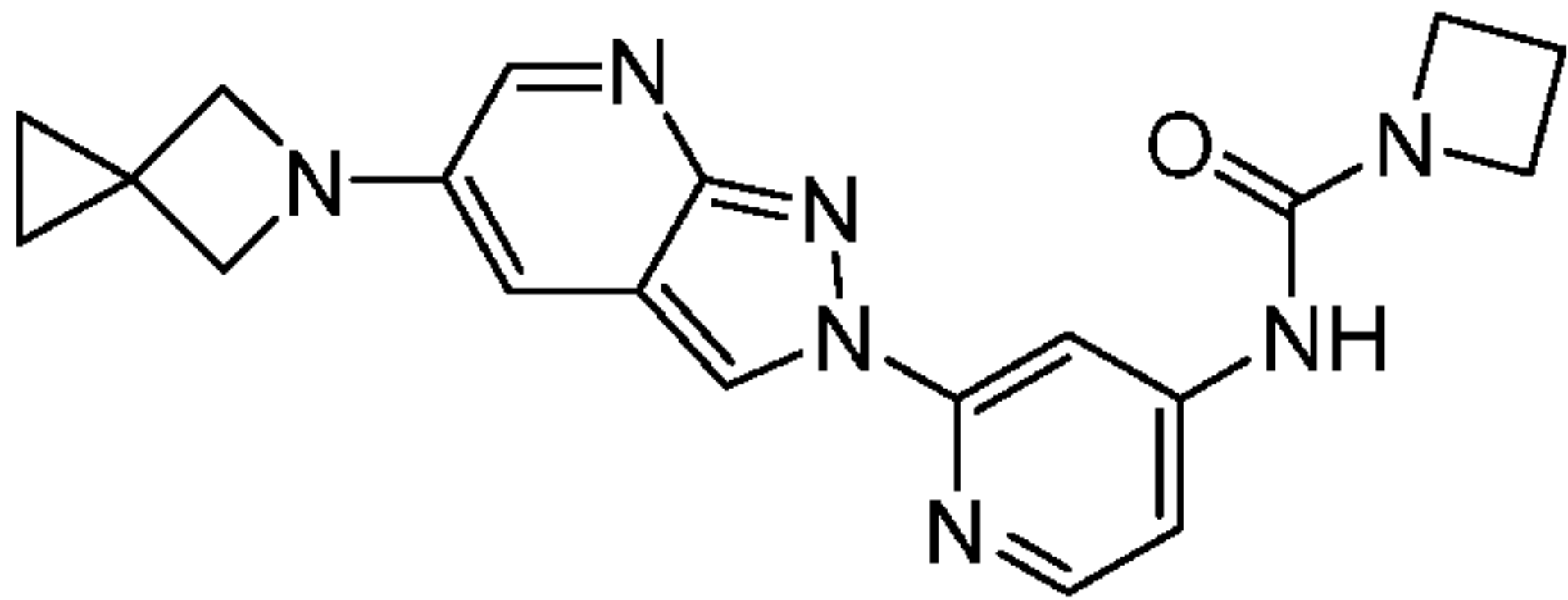
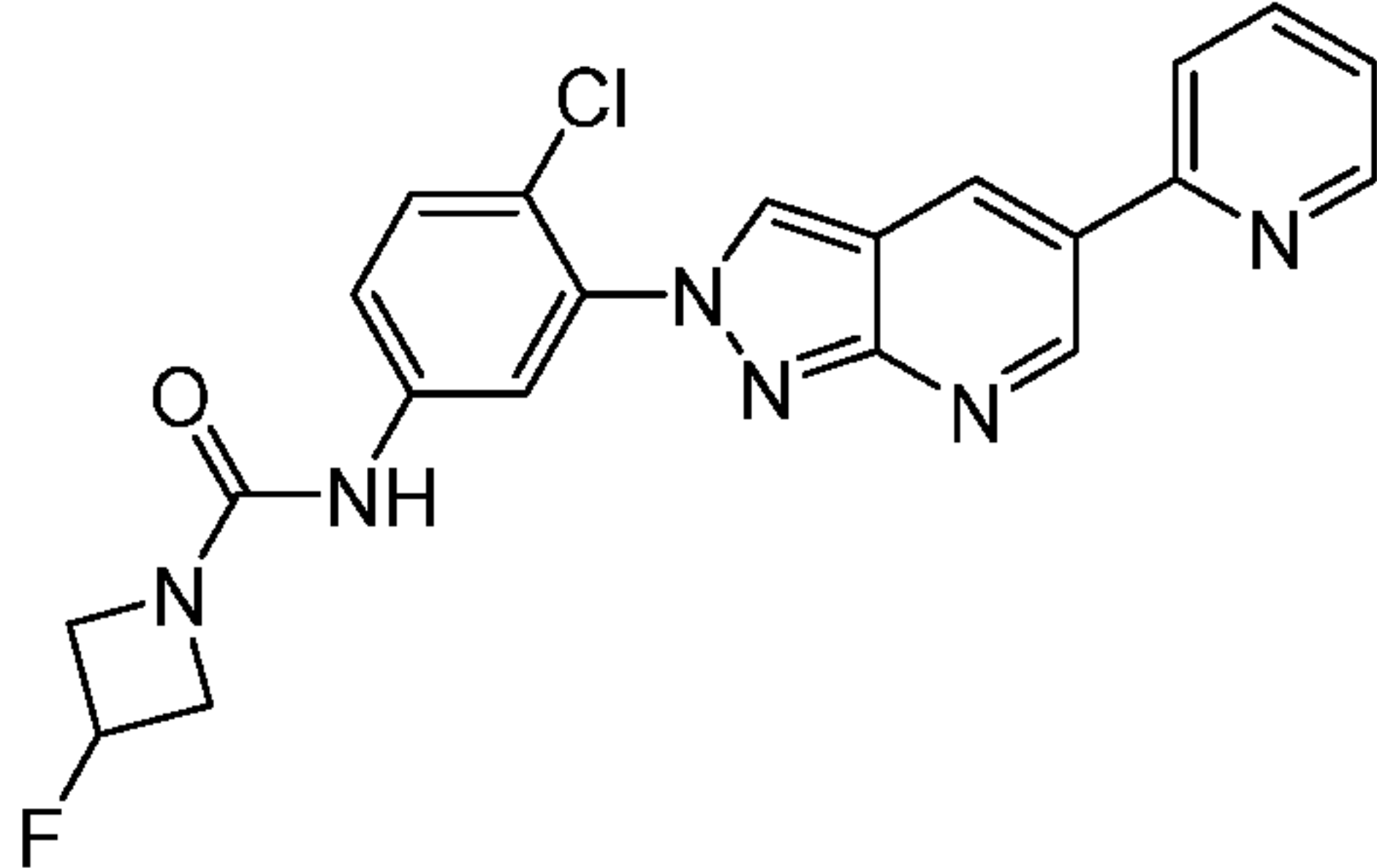
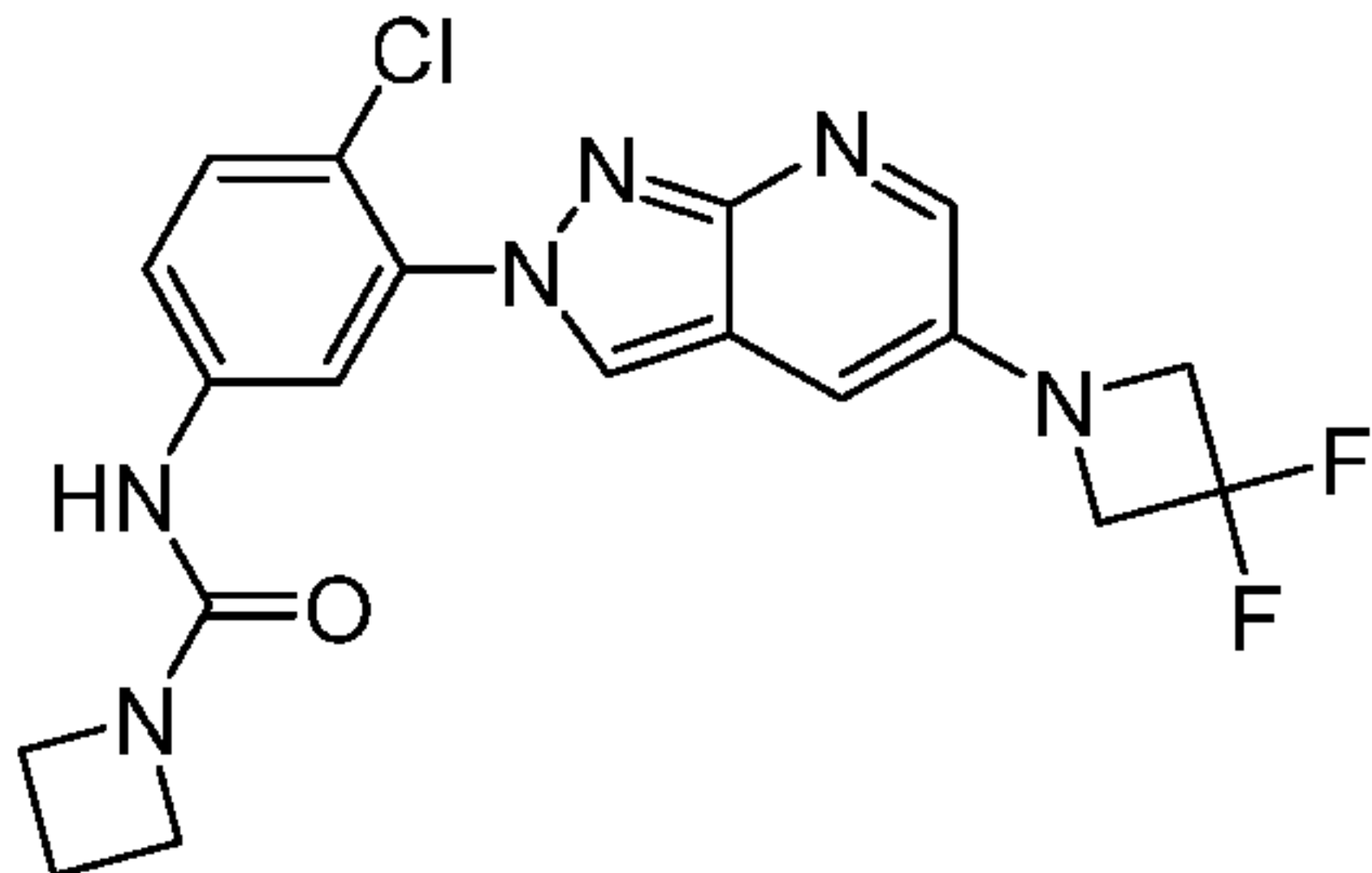
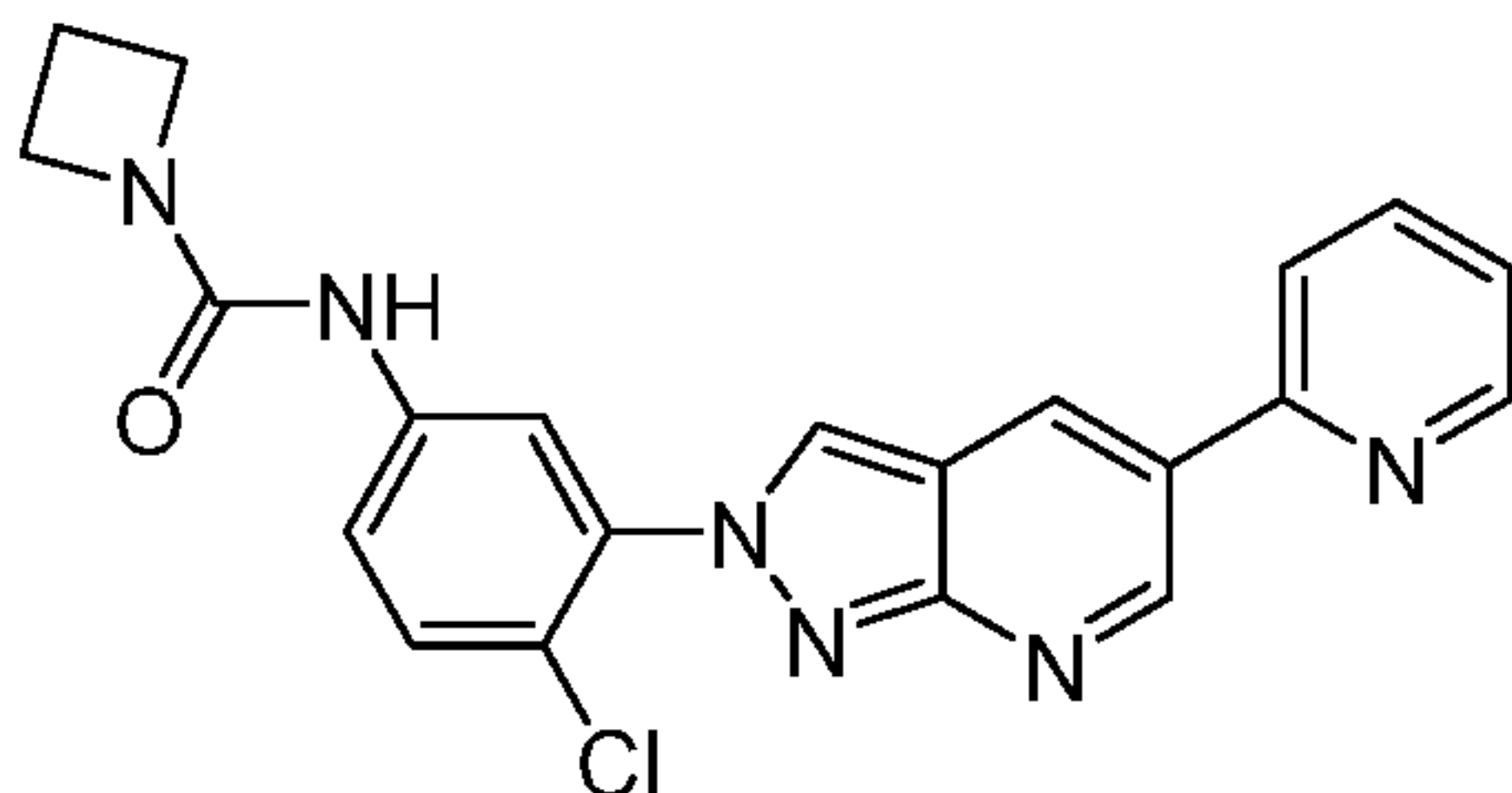
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
258		¹ H NMR (400 MHz, DMSO) δ 9.21 (br s, 1 H), 8.54 (s, 1 H), 8.28 (d, <i>J</i> = 1.63 Hz, 1 H), 8.20 (br d, <i>J</i> = 6.65 Hz, 1 H), 7.63 (br d, <i>J</i> = 8.41 Hz, 1 H), 7.45 (t, <i>J</i> = 9.91 Hz, 1 H), 6.92 (d, <i>J</i> = 2.01 Hz, 1 H), 4.40 (t, <i>J</i> = 12.86 Hz, 4 H), 4.02 (s, 4 H), 0.68 (s, 4 H). Method 1: RT = 3.03 min.; M+H = 429.2
259		¹ H NMR (400 MHz, DMSO) δ 8.60 (s, 1 H), 8.54 (br s, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.22 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.64 - 7.72 (m, 1 H), 7.41 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 6.92 (d, <i>J</i> = 2.76 Hz, 1 H), 5.27 - 5.48 (m, 1 H), 4.02 (s, 4 H), 3.57 - 3.77 (m, 4 H), 2.03 - 2.24 (m, 2 H), 0.68 (s, 4 H). Method 1: RT = 2.93 min.; M+H = 425.2
260		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.81 (s, 1 H), 8.70 (d, <i>J</i> = 2.93 Hz, 1 H), 8.55 (d, <i>J</i> = 2.69 Hz, 1 H), 8.22 (dd, <i>J</i> = 7.09, 2.69 Hz, 1 H), 7.63 - 7.72 (m, 1 H), 7.42 (dd, <i>J</i> = 11.37, 9.17 Hz, 1 H), 7.15 (d, <i>J</i> = 2.93 Hz, 1 H), 3.97 - 4.14 (m, 4 H), 2.95 (s, 6 H), 0.65 (s, 4 H). Method 1: RT = 2.87 min.; M+H = 381.0
261		¹ H NMR (400 MHz, DMSO) δ 8.94 (s, 1 H), 8.56 (dd, <i>J</i> = 8.28, 2.38 Hz, 2 H), 8.21 (dd, <i>J</i> = 6.96, 2.57 Hz, 1 H), 7.64 (dt, <i>J</i> = 8.91, 3.26 Hz, 1 H), 7.43 (dd, <i>J</i> = 10.79, 9.54 Hz, 1 H), 7.08 (d, <i>J</i> = 2.51 Hz, 1 H), 5.27 - 5.50 (m, 1 H), 4.24 - 4.39 (m, 2 H), 3.92 - 4.11 (m, 2 H), 3.83 (br t, <i>J</i> = 13.30 Hz, 2 H), 3.59 (br t, <i>J</i> = 7.15 Hz, 2 H), 2.60 (br d, <i>J</i> = 7.53 Hz, 2 H). Method 1: RT = 2.67 min.; M+H = 447.2
262		¹ H NMR (400 MHz, DMSO) δ 8.95 (s, 1 H), 8.58 (d, <i>J</i> = 2.76 Hz, 1 H), 8.35 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.60 - 7.68 (m, 1 H), 7.44 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.05 (d, <i>J</i> = 2.76 Hz, 1 H), 5.28 - 5.51 (m, 1 H), 4.24 - 4.38 (m, 2 H), 4.10 - 4.17 (m, 2 H), 3.95 - 4.10 (m, 4 H), 1.79 (t, <i>J</i> = 8.91 Hz, 2 H). Method 1: RT = 2.84 min.; M+H = 434.9

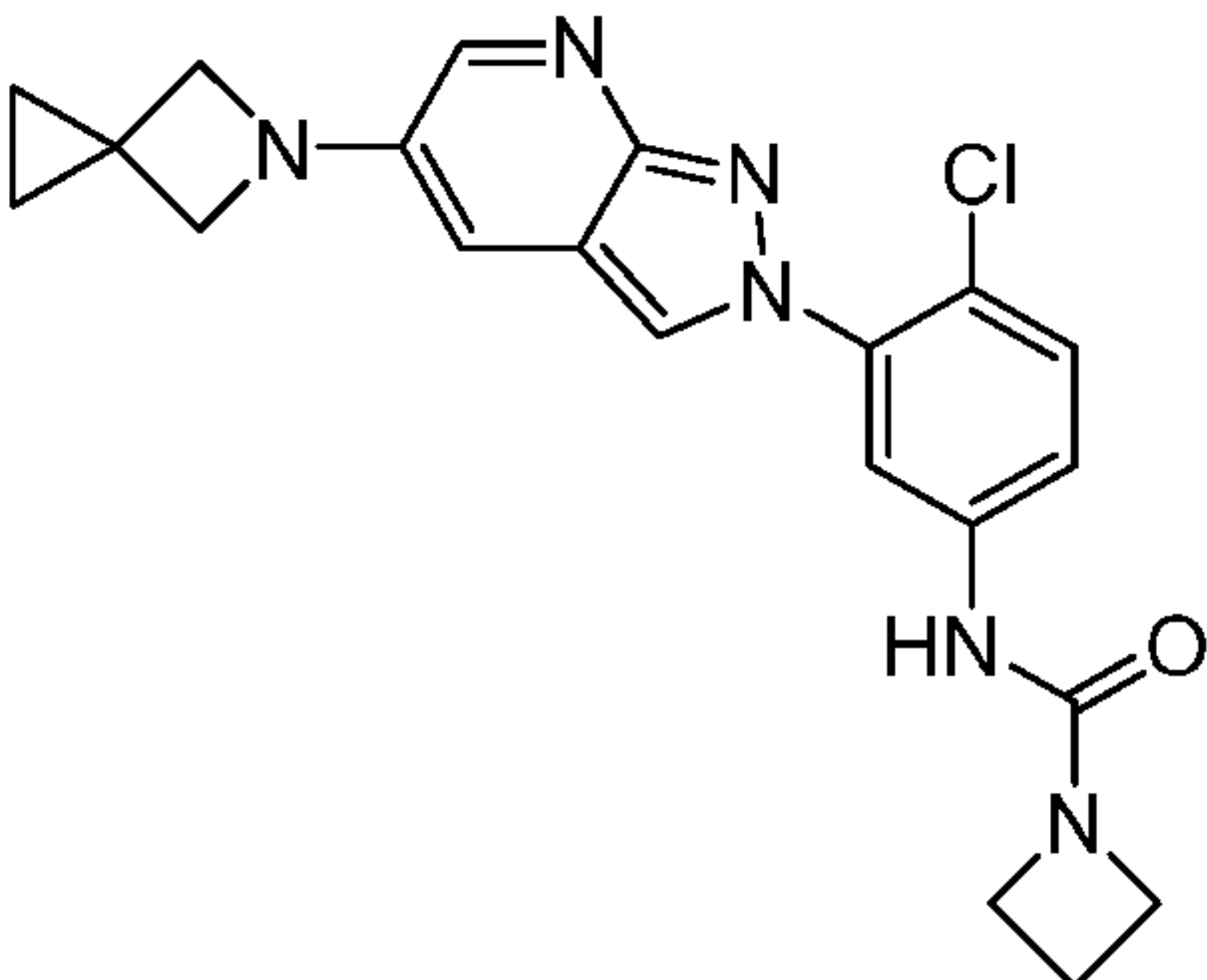
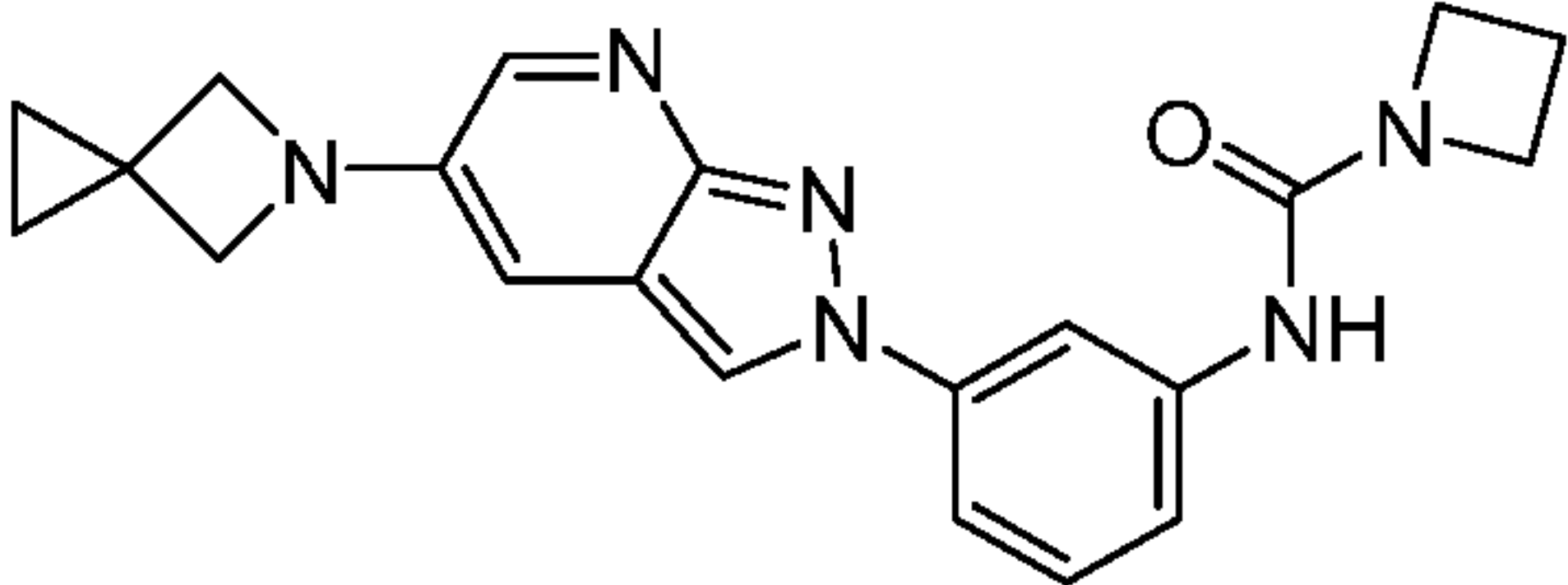
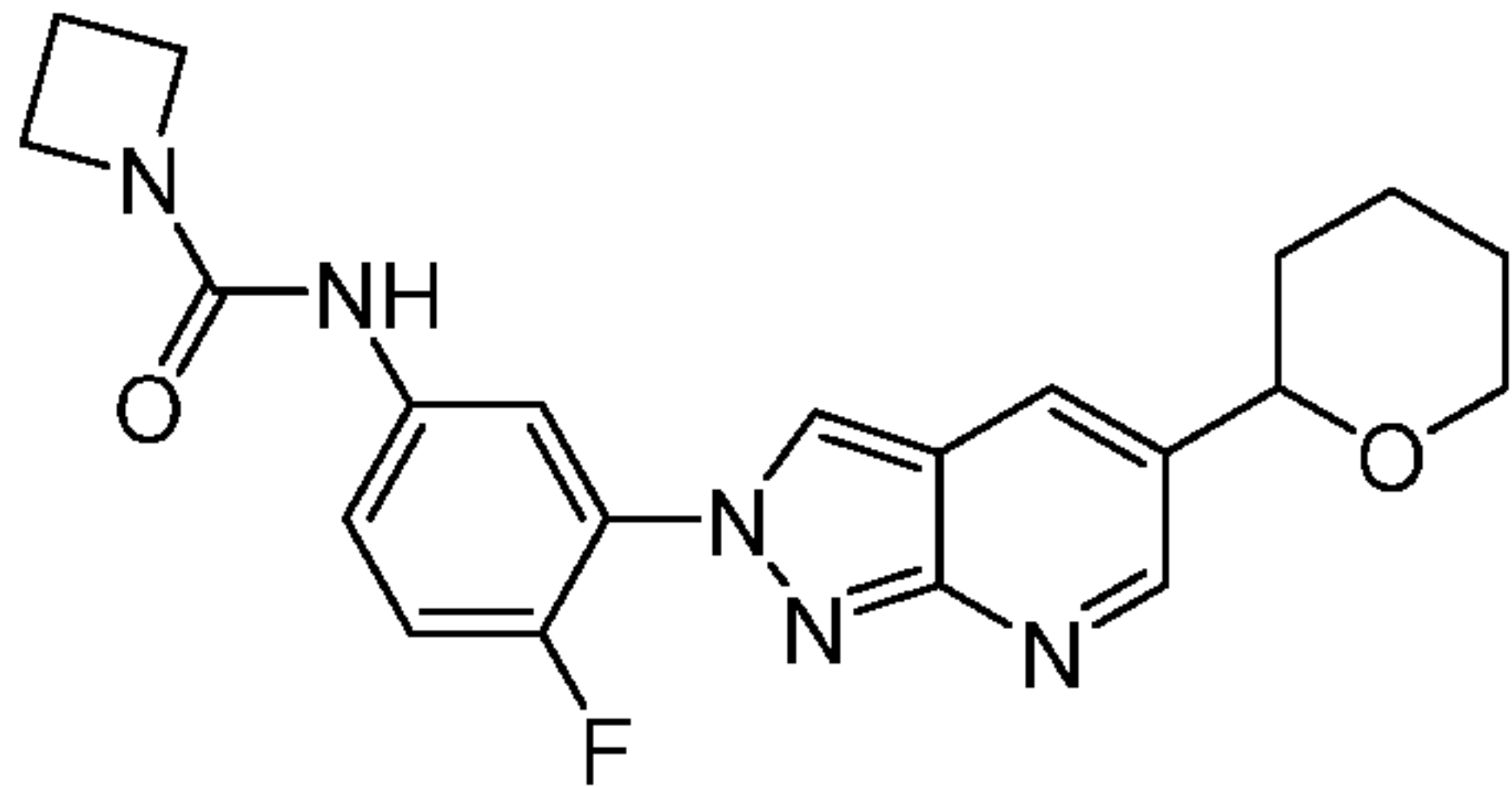
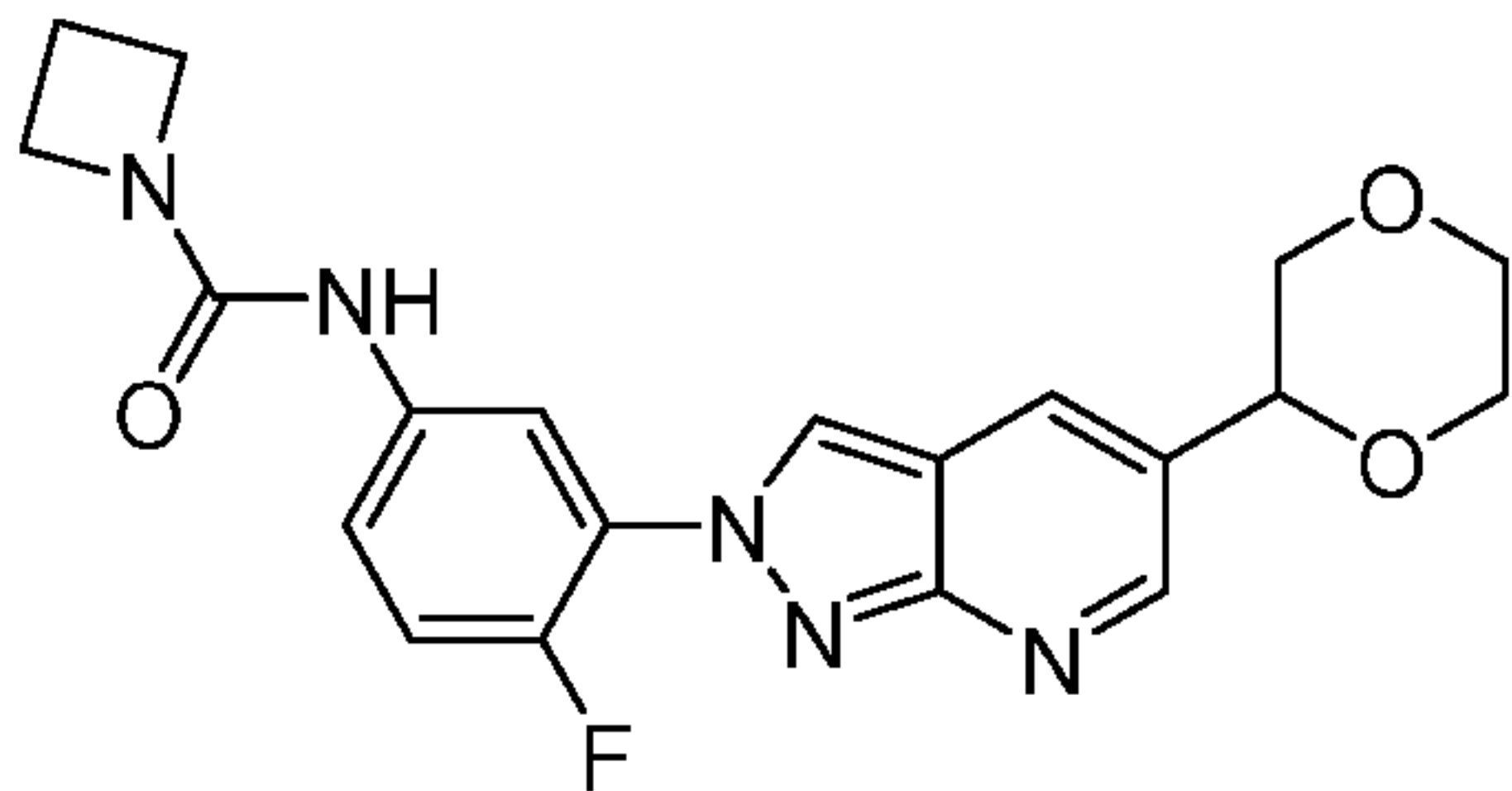
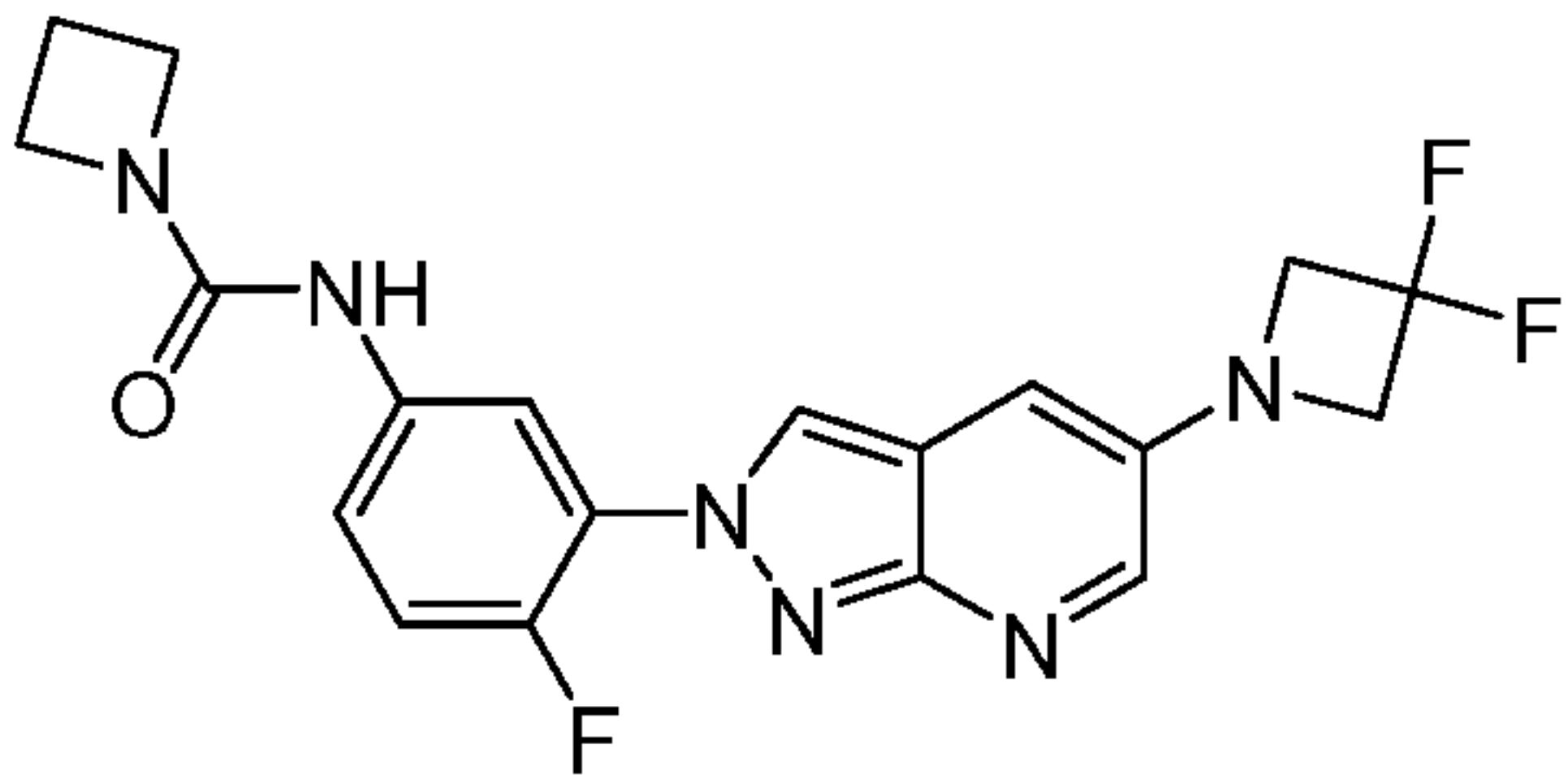
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
263		¹ H NMR (400 MHz, DMSO) δ 8.96 (s, 1 H), 8.53 (d, <i>J</i> = 1.88 Hz, 1 H), 8.37 (d, <i>J</i> = 1.88 Hz, 1 H), 8.19 (dd, <i>J</i> = 6.96, 2.45 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.39 - 7.50 (m, 1 H), 7.14 (d, <i>J</i> = 2.01 Hz, 1 H), 5.28 - 5.52 (m, 1 H), 4.41 (br d, <i>J</i> = 6.02 Hz, 2 H), 4.26 - 4.38 (m, 2 H), 4.21 (br d, <i>J</i> = 10.92 Hz, 2 H), 3.96 - 4.10 (m, 2 H), 3.70 (br d, <i>J</i> = 10.92 Hz, 2 H), 2.72 - 2.76 (m, 1 H), 1.88 (d, <i>J</i> = 8.03 Hz, 1 H). Method 1: RT = 2.49 min.; M+H = 427.3
264		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.38 (s, 1H), 9.07 - 8.96 (m, 2H), 8.84 (d, <i>J</i> = 4.3 Hz, 1H), 8.30 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 7.72 - 7.62 (m, 1H), 7.52 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.33 (dd, <i>J</i> = 4.4, 1.2 Hz, 1H), 6.04 (s, 1H), 5.41 (dtt, <i>J</i> = 57.4, 6.1, 3.1 Hz, 1H), 4.40 - 4.25 (m, 2H), 4.27 - 4.16 (m, 1H), 4.10 - 3.94 (m, 2H), 3.90 - 3.77 (m, 1H), 3.06 - 2.94 (m, 1H), 2.86 (dtd, <i>J</i> = 11.7, 8.7, 4.4 Hz, 1H). Method 1: RT = 1.69 min.; M+H = 385.2
265		¹ H NMR (400 MHz, DMSO) δ 8.93 (s, 1 H), 8.58 (d, <i>J</i> = 2.76 Hz, 1 H), 8.32 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.65 (dd, <i>J</i> = 7.34, 4.58 Hz, 1 H), 7.44 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 7.03 (d, <i>J</i> = 2.89 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.24 - 4.38 (m, 2 H), 4.18 (t, <i>J</i> = 8.34 Hz, 2 H), 3.95 - 4.10 (m, 4 H), 3.65 - 3.85 (m, 1 H). Method 1: RT = 2.86 min.; M+H = 453.1
266		¹ H NMR (400 MHz, DMSO) δ 8.93 (s, 1 H), 8.60 (d, <i>J</i> = 2.76 Hz, 1 H), 8.31 (d, <i>J</i> = 2.76 Hz, 1 H), 8.20 (dd, <i>J</i> = 6.96, 2.57 Hz, 1 H), 7.60 - 7.69 (m, 1 H), 7.44 (dd, <i>J</i> = 11.04, 9.16 Hz, 1 H), 7.04 (d, <i>J</i> = 2.76 Hz, 1 H), 5.27 - 5.54 (m, 1 H), 4.26 - 4.38 (m, 2 H), 4.17 - 4.24 (m, 2 H), 3.95 - 4.13 (m, 4 H), 3.85 - 3.94 (m, 1 H). Method 1: RT = 2.44 min.; M+H = 410.3
267		¹ H NMR (400 MHz, Methanol-d ₄) δ 8.86 (dd, <i>J</i> = 3.4, 2.2 Hz, 1H), 8.74 (d, <i>J</i> = 4.4 Hz, 0.5H), 8.67 (d, <i>J</i> = 4.5 Hz, 0.5H), 8.17 (dd, <i>J</i> = 6.8, 2.7 Hz, 0.5H), 8.13 (dd, <i>J</i> = 6.8, 2.7 Hz, 0.5H), 7.66 (dddd, <i>J</i> = 8.8, 4.3, 2.7, 1.7 Hz, 1H), 7.37 (ddd, <i>J</i> = 10.9, 9.1, 3.7 Hz, 1H), 7.28 (dd, <i>J</i> = 4.4, 0.8 Hz, 0.5H), 7.18 (dd, <i>J</i> = 4.5, 0.9 Hz, 0.5H), 5.93 (dd, <i>J</i> = 9.2, 5.6 Hz, 0.5H), 5.73 (dd, <i>J</i> = 9.3, 6.1 Hz, 0.5H), 5.37 (dtt, <i>J</i> = 57.1, 6.1, 3.2 Hz, 1H), 4.48 - 4.32 (m, 3H), 4.24 - 4.15 (m, 2H), 4.11 (ddd, <i>J</i> = 10.3, 3.2, 1.4 Hz, 1H), 3.05 - 2.91 (m, 1H), 2.34 - 2.21 (m, 1H), 2.03 (s, 1.5H), 1.71 (s, 1.5H). Method 2: RT = 0.66 min.; M+H = 427.2

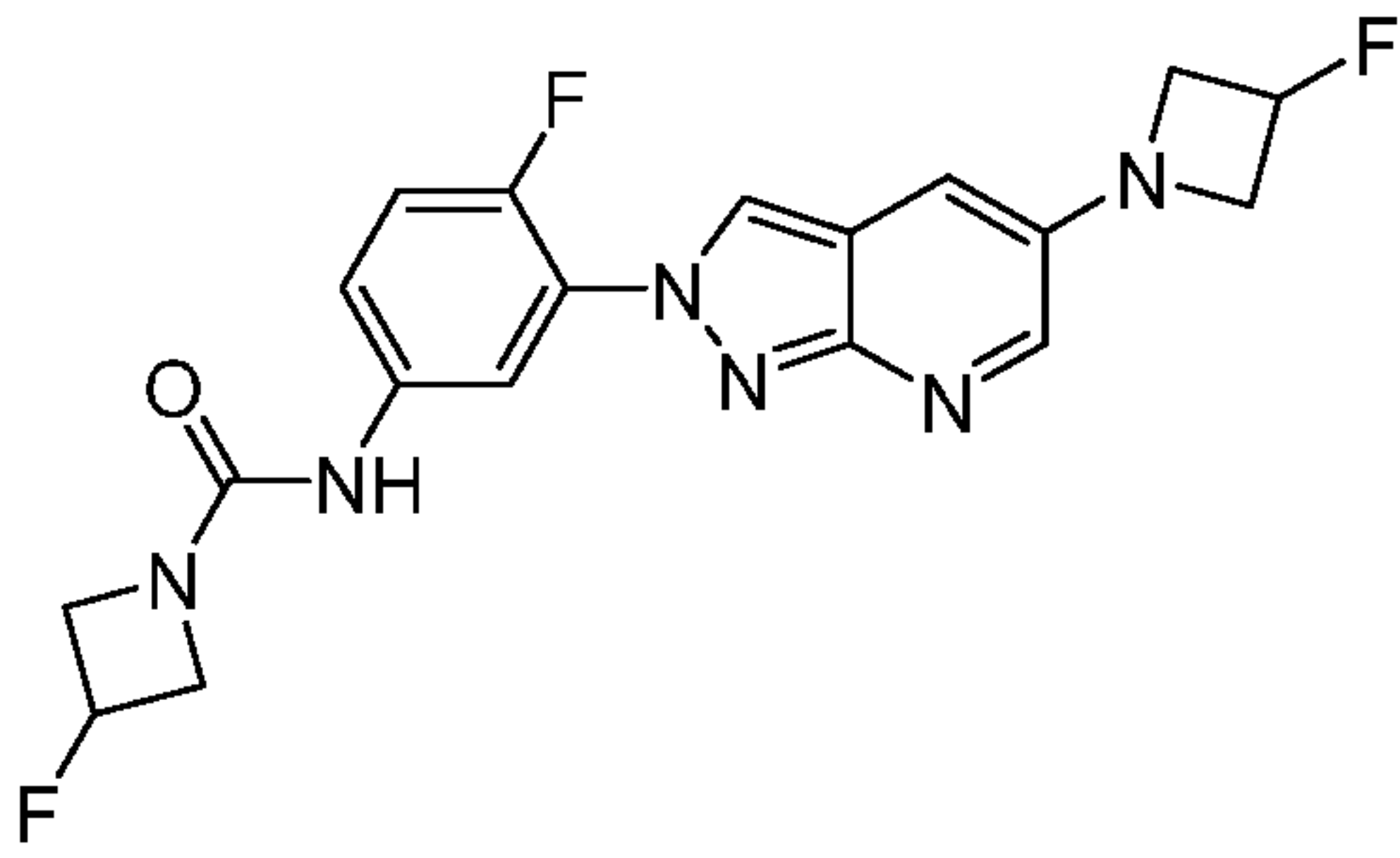
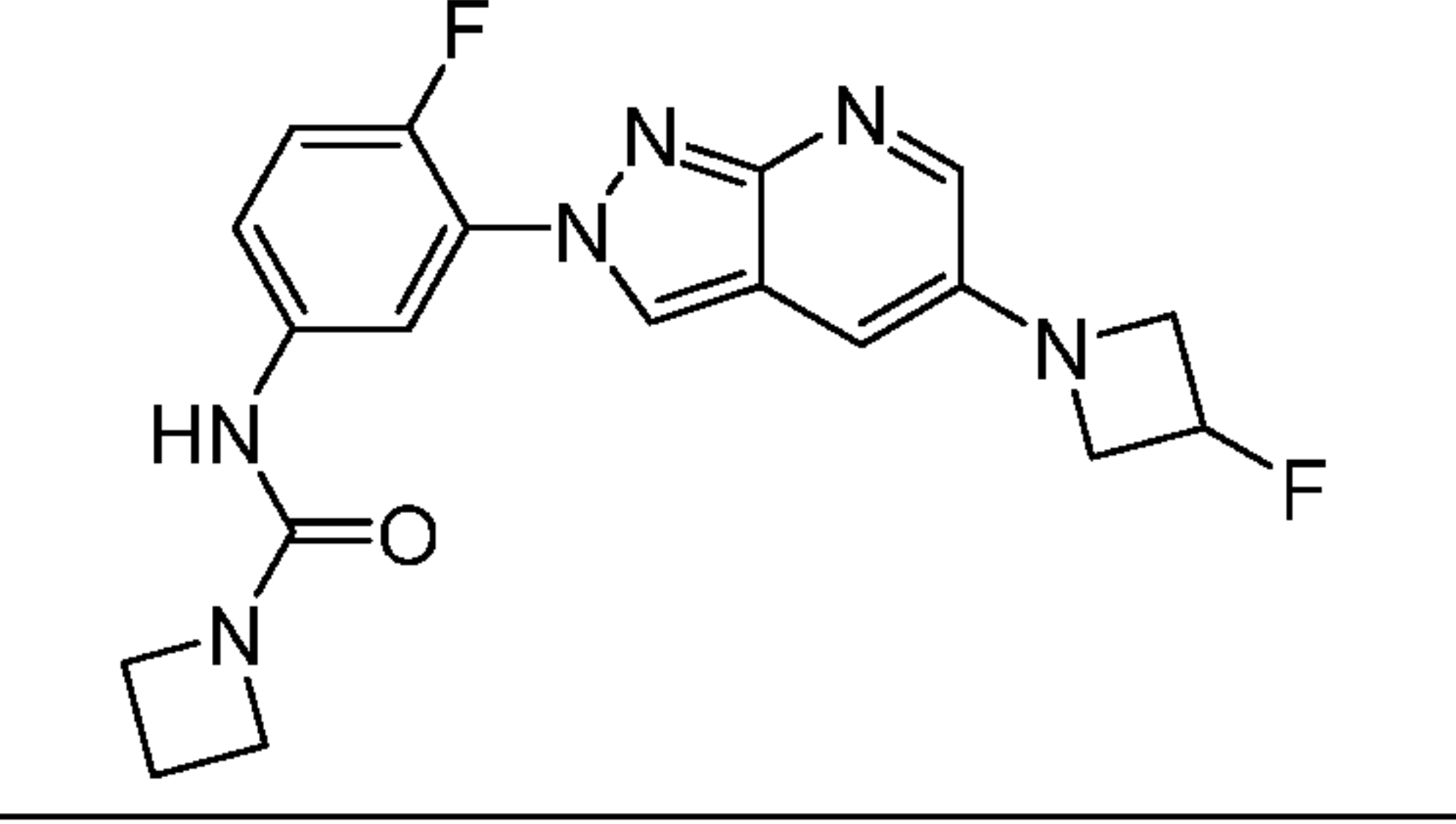
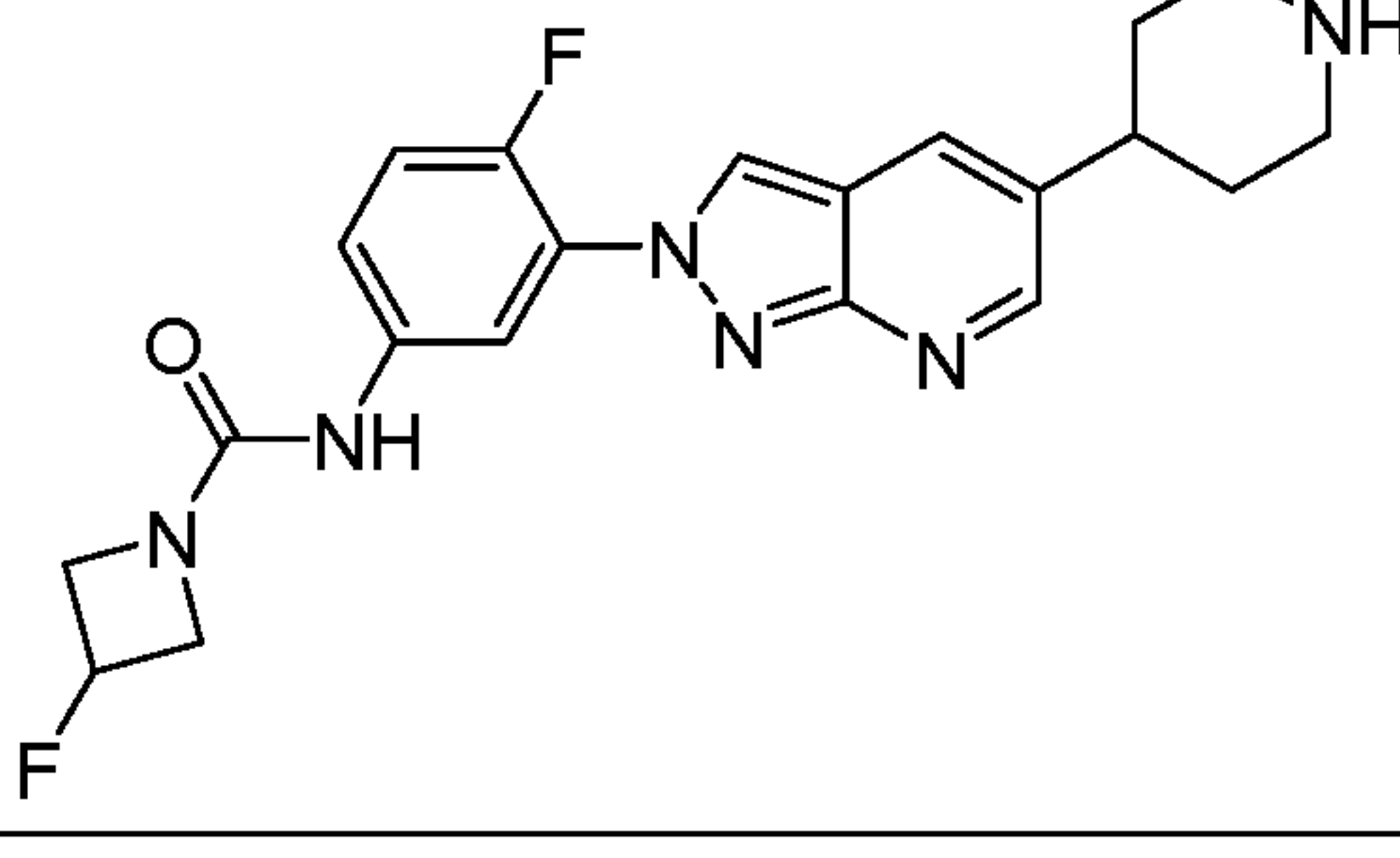
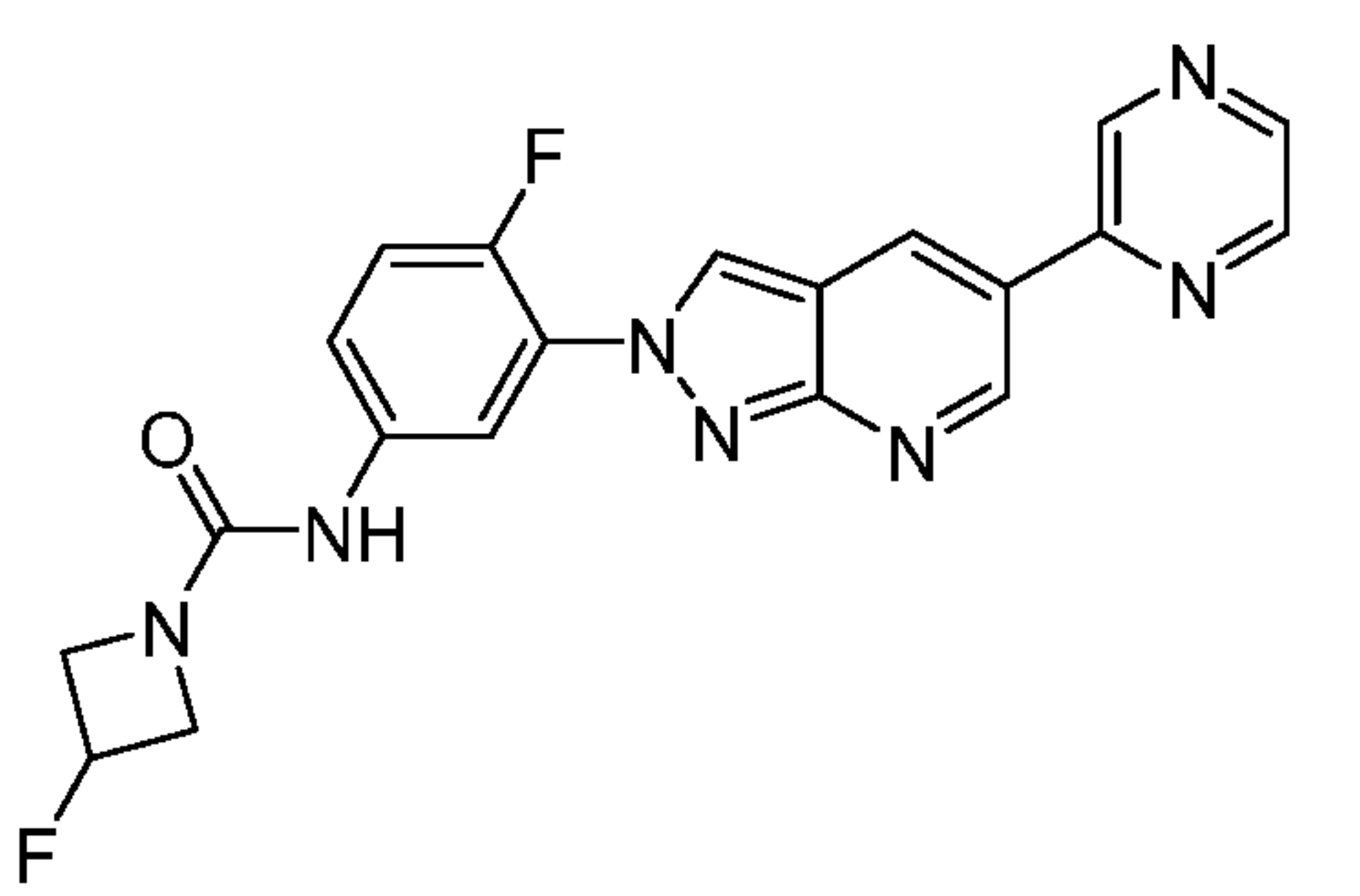
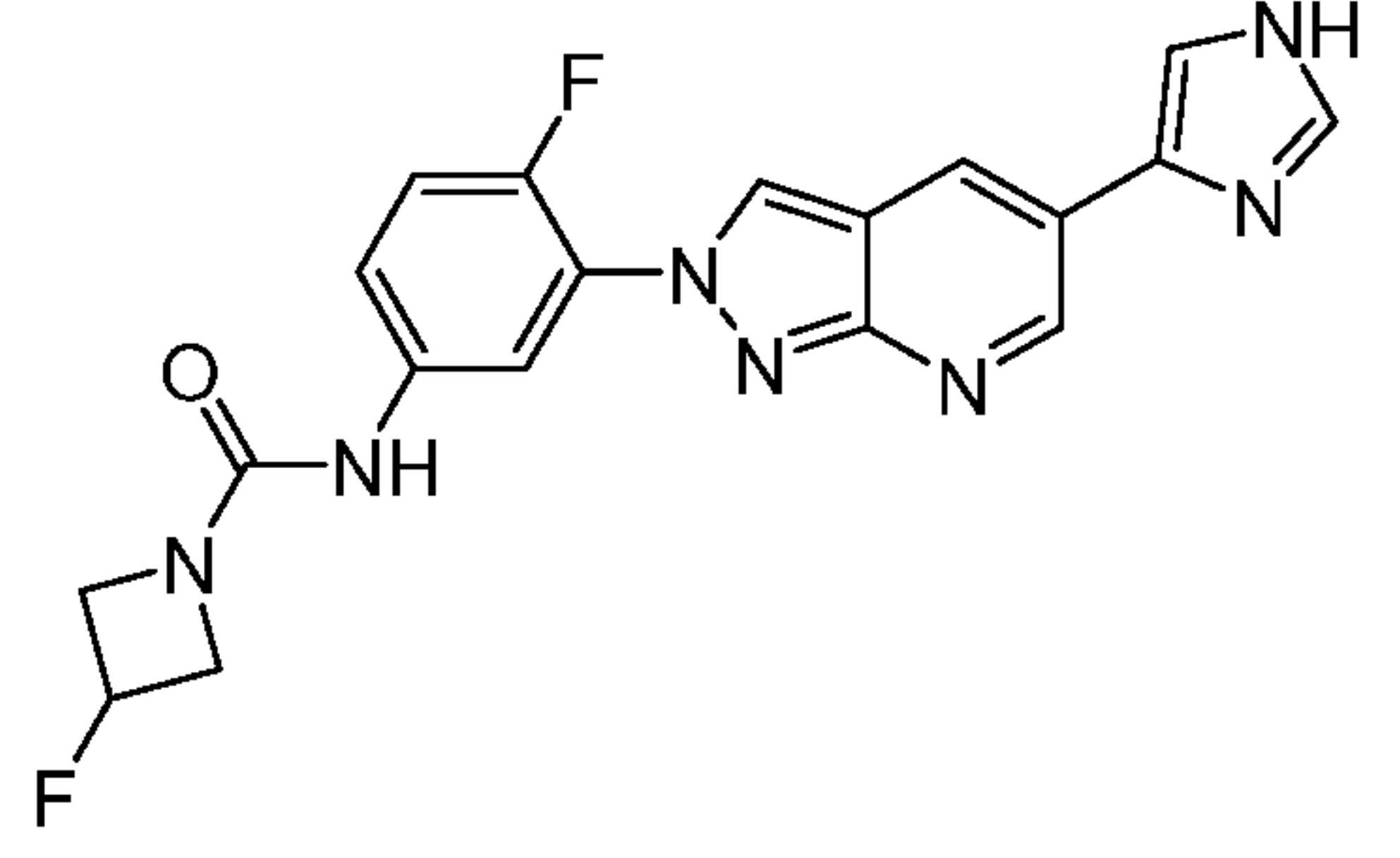
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
268		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.69 (s, 1 H), 8.64 (d, J=2.69 Hz, 1 H), 8.37 (d, J=2.81 Hz, 1 H), 8.32 (dd, J=7.03, 2.51 Hz, 1 H), 7.61 - 7.67 (m, 1 H), 7.52 (dd, J=11.19, 9.11 Hz, 1 H), 7.15 (d, J=2.81 Hz, 1 H), 4.80 - 5.03 (m, 1 H), 4.41 (t, J=12.29 Hz, 4 H), 2.24 - 2.33 (m, 1 H), 1.46 - 1.67 (m, 1 H), 1.27 (dd, J=13.27, 6.54 Hz, 1 H). Method 1: RT = 2.89 min.; M+H = 406.0
269		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.75 (s, 1 H), 9.48 (d, J=2.26 Hz, 1 H), 9.03 (d, J=2.38 Hz, 1 H), 8.95 (d, J=2.26 Hz, 1 H), 8.74 (d, J=4.14 Hz, 1 H), 8.39 (dd, J=6.96, 2.57 Hz, 1 H), 8.13 (d, J=8.03 Hz, 1 H), 7.96 (td, J=7.75, 1.69 Hz, 1 H), 7.65 - 7.74 (m, 1 H), 7.57 (dd, J=11.11, 9.10 Hz, 1 H), 7.42 (dd, J=7.22, 5.21 Hz, 1 H), 4.78 - 5.06 (m, 1 H), 2.26 - 2.35 (m, 1 H), 1.49 - 1.66 (m, 1 H), 1.24 - 1.33 (m, 1 H). Method 1: RT = 2.80 min.; M+H = 392.2
270		¹ H NMR (400 MHz, DMSO) δ 8.94 (s, 1 H), 8.72 (d, J = 2.81 Hz, 1 H), 8.63 (d, J = 2.57 Hz, 1 H), 8.16 - 8.27 (m, 1 H), 7.61 - 7.67 (m, 1 H), 7.40 - 7.47 (m, 2 H), 5.26 - 5.54 (m, 1 H), 4.24 - 4.40 (m, 2 H), 3.96 - 4.08 (m, 2 H), 3.29 - 3.33 (m, 1 H), 3.21 (br d, J = 5.01 Hz, 4 H), 3.11 (br d, J = 4.40 Hz, 4 H). Method 1: RT = 1.86 min.; M+H = 414.3

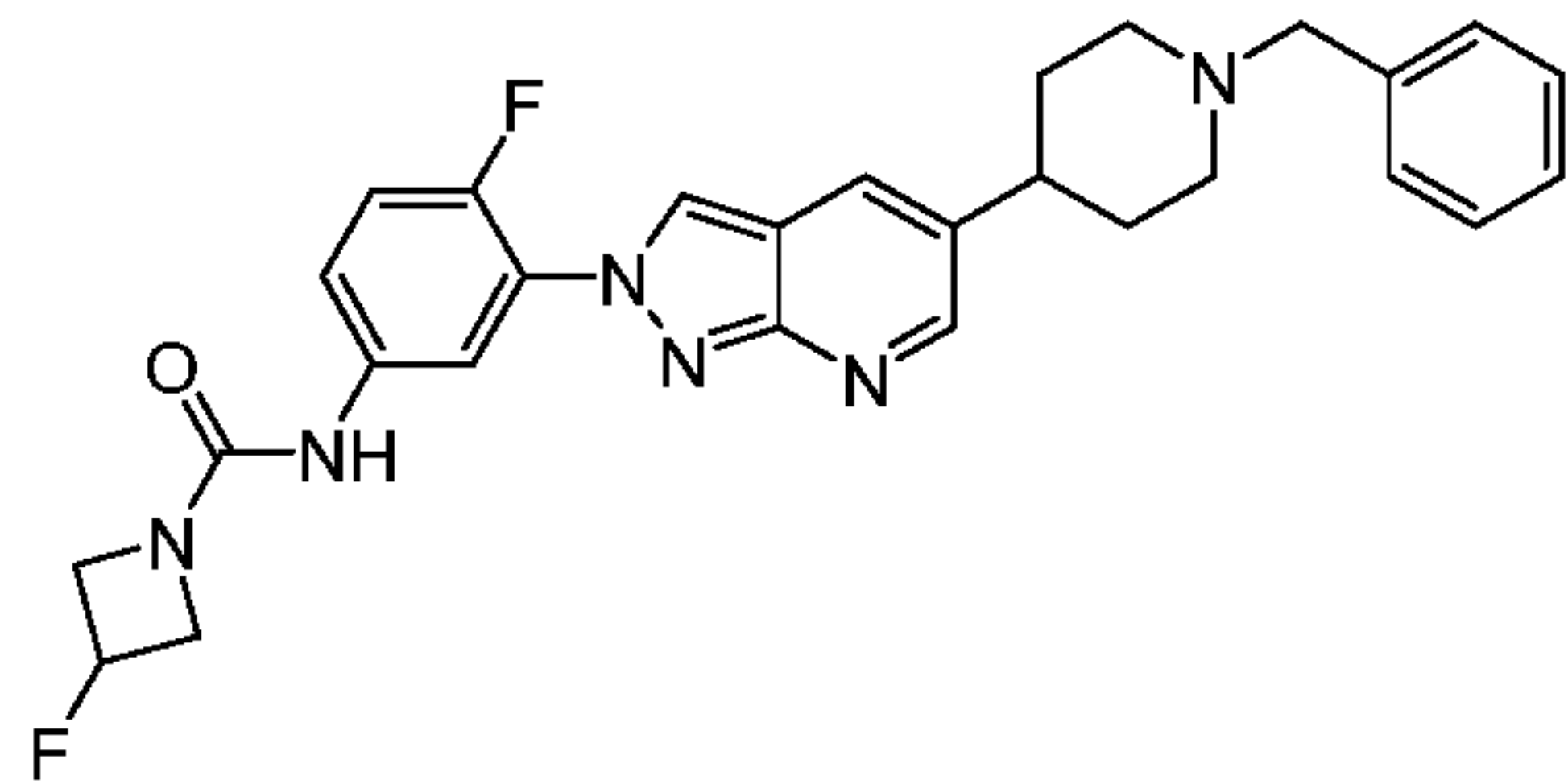
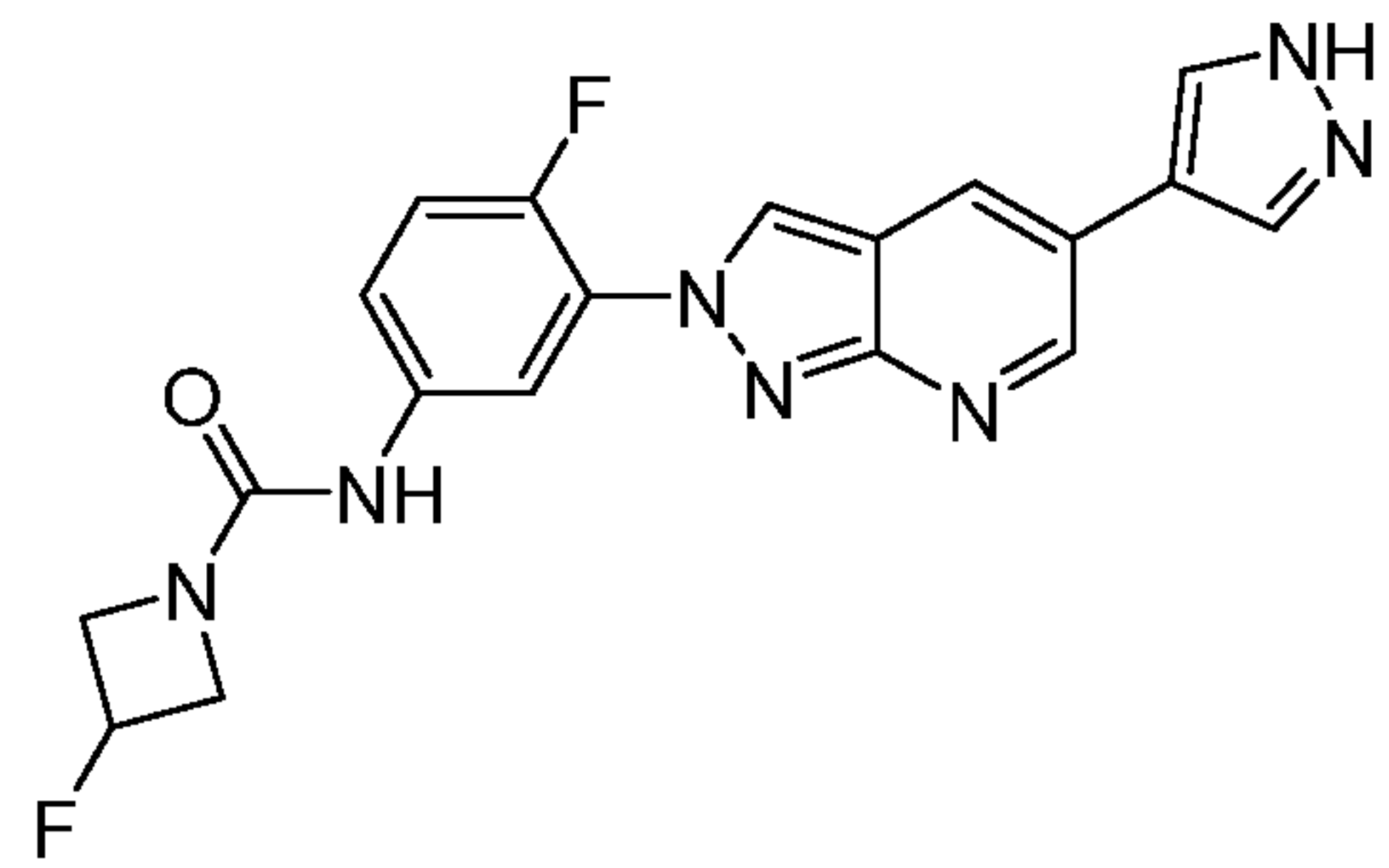
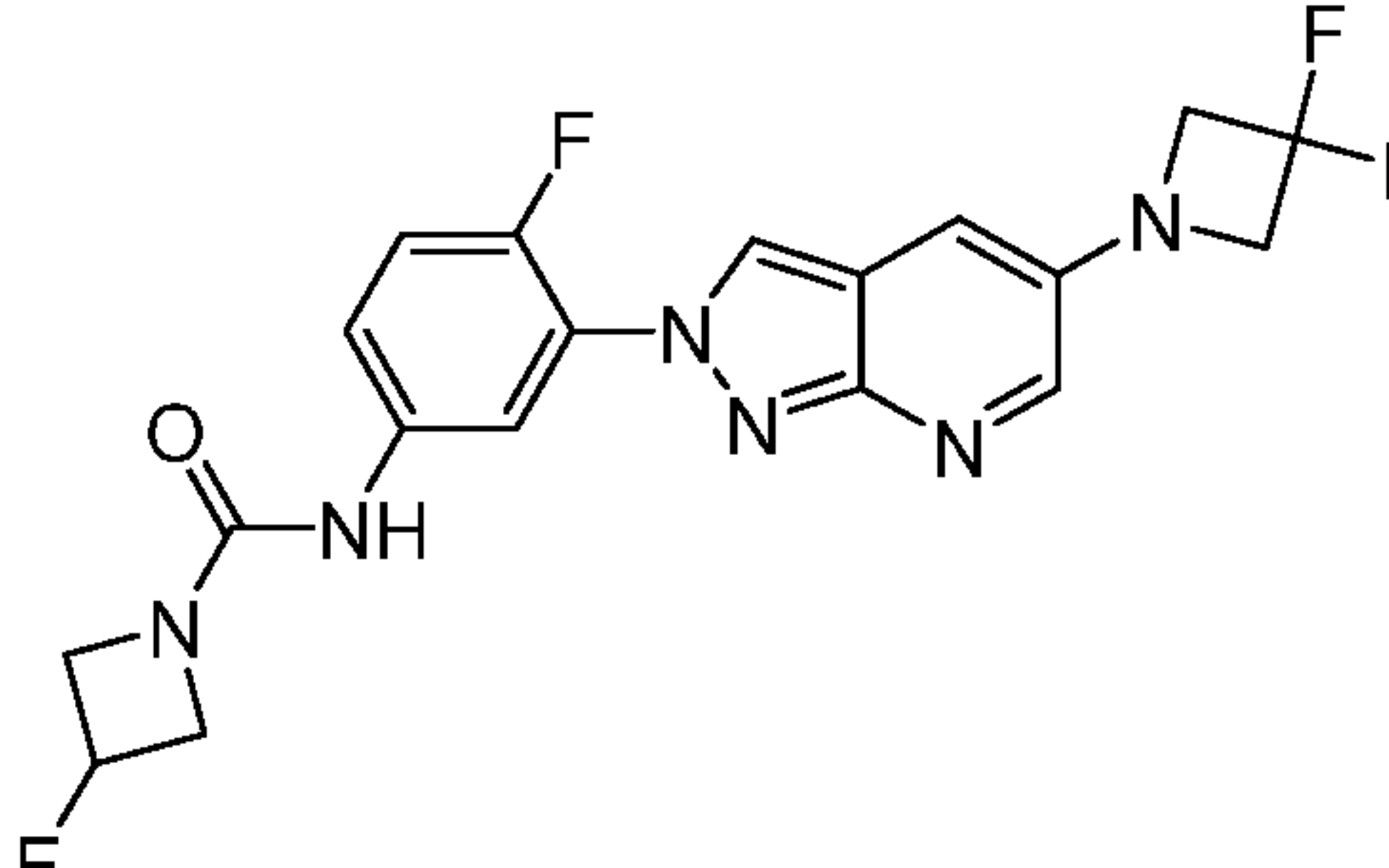
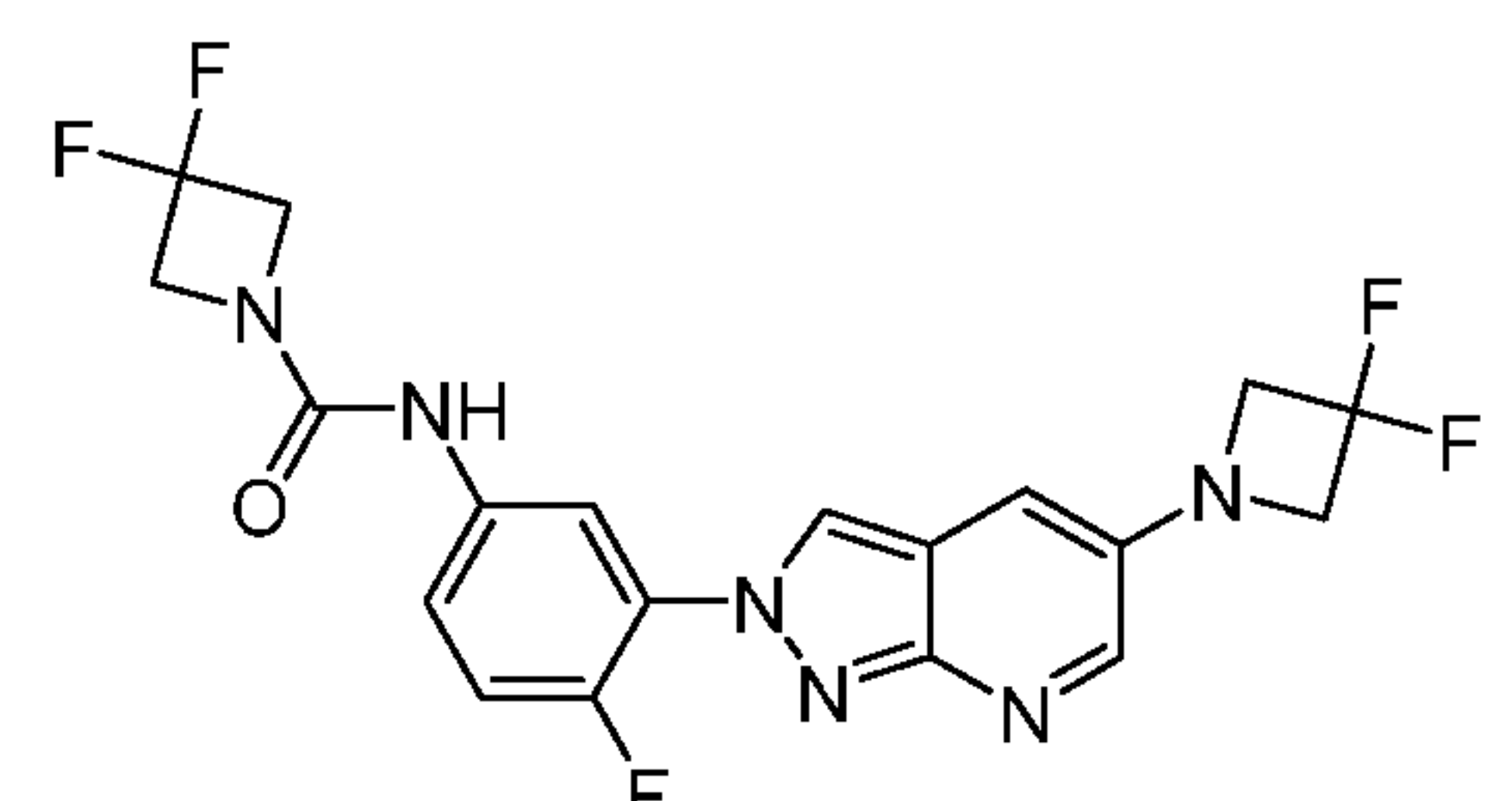
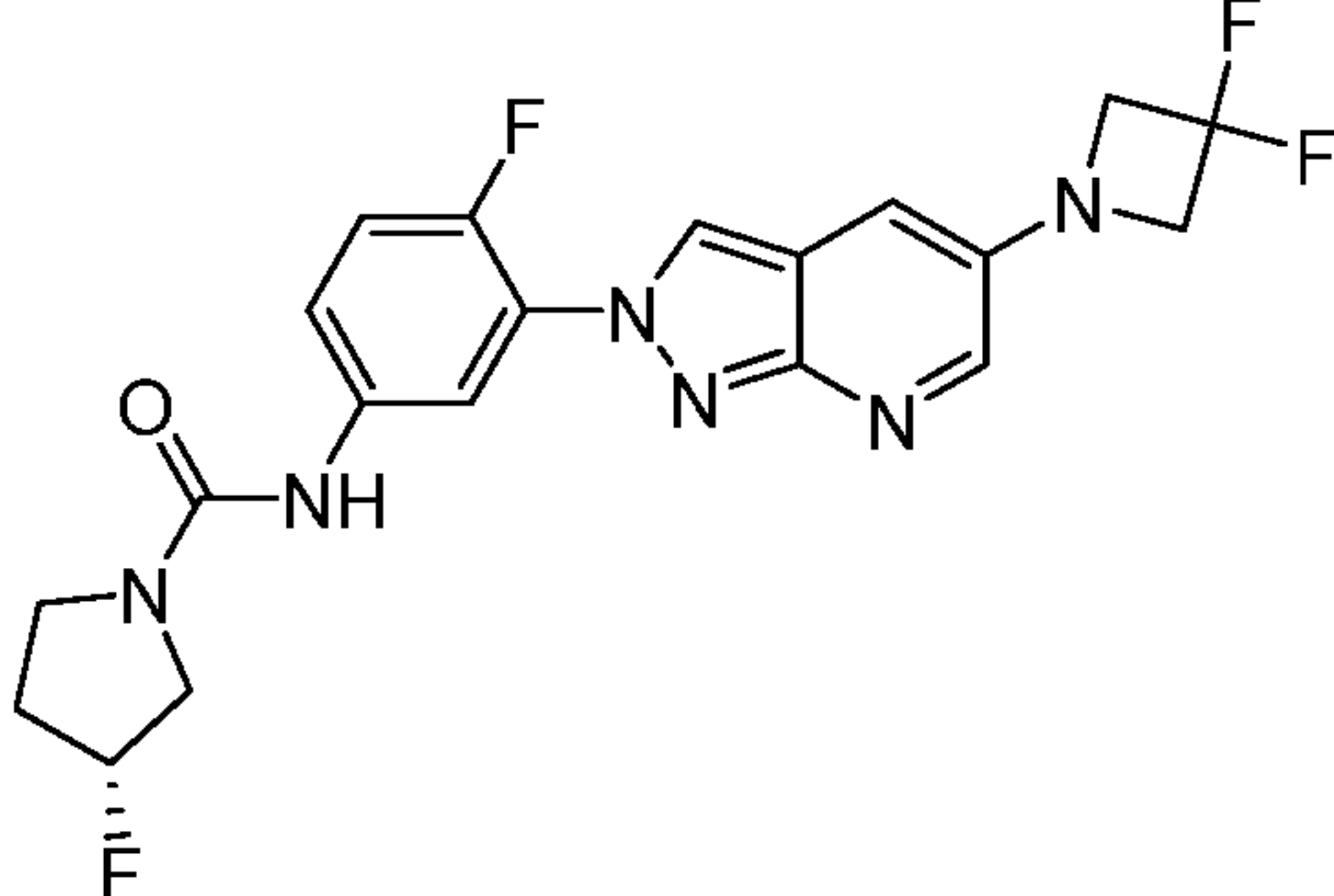
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
271	 or	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.75 (s, 1 H), 8.70 (d, J=2.69 Hz, 1 H), 8.43 (d, J=2.81 Hz, 1 H), 8.38 (dd, J=6.97, 2.57 Hz, 1 H), 7.66 - 7.77 (m, 1 H), 7.52 - 7.63 (m, 1 H), 7.20 (d, J=2.81 Hz, 1 H), 4.85 - 5.08 (m, 1 H), 4.47 (t, J=12.23 Hz, 4 H), 2.27 - 2.39 (m, 1 H), 1.52 - 1.72 (m, 1 H), 1.33 (dq, J=13.11, 6.43 Hz, 1 H). Method 1: RT = 2.89 min.; M+H = 406.0
272	 <i>trans</i> - racemic	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.74 (s, 1 H), 8.56 (d, J=2.57 Hz, 1 H), 8.25 - 8.37 (m, 2 H), 7.58 - 7.68 (m, 1 H), 7.45 - 7.56 (m, 1 H), 6.92 (d, J=2.69 Hz, 1 H), 4.78 - 5.05 (m, 1 H), 4.03 (s, 4 H), 2.23 - 2.33 (m, 1 H), 1.48 - 1.63 (m, 1 H), 1.23 - 1.33 (m, 1 H), 0.69 (s, 4 H). Method 1: RT = 3.13 min.; M+H = 396.3
273	 or	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.75 (s, 1 H), 9.48 (d, J=2.08 Hz, 1 H), 9.03 (d, J=2.32 Hz, 1 H), 8.95 (d, J=2.20 Hz, 1 H), 8.74 (d, J=4.52 Hz, 1 H), 8.40 (dd, J=7.03, 2.51 Hz, 1 H), 8.13 (d, J=8.07 Hz, 1 H), 7.96 (td, J=7.79, 1.77 Hz, 1 H), 7.69 (dt, J=8.47, 3.53 Hz, 1 H), 7.57 (dd, J=11.00, 9.17 Hz, 1 H), 7.42 (dd, J=7.09, 5.14 Hz, 1 H), 4.80 - 5.05 (m, 1 H), 2.25 - 2.34 (m, 1 H), 1.48 - 1.67 (m, 1 H), 1.28 (dq, J=13.13, 6.67 Hz, 1 H). Method 1: RT = 2.82 min.; M+H = 392.2
274		¹ H NMR (400 MHz, DMSO) δ 8.68 (s, 1 H), 8.57 (d, J = 2.57 Hz, 1 H), 8.32 (d, J = 2.69 Hz, 1 H), 8.20 (dd, J = 7.09, 2.69 Hz, 1 H), 7.62 - 7.69 (m, 1 H), 7.41 (dd, J = 11.25, 9.17 Hz, 1 H), 7.03 (d, J = 2.81 Hz, 1 H), 4.13 - 4.22 (m, 2 H), 3.98 (q, J = 7.78 Hz, 6 H), 3.76 (br dd, J = 9.54, 4.77 Hz, 1 H), 2.19 (quin, J = 7.55 Hz, 2 H). Method 1: RT = 2.87 min.; M+H = 435.3

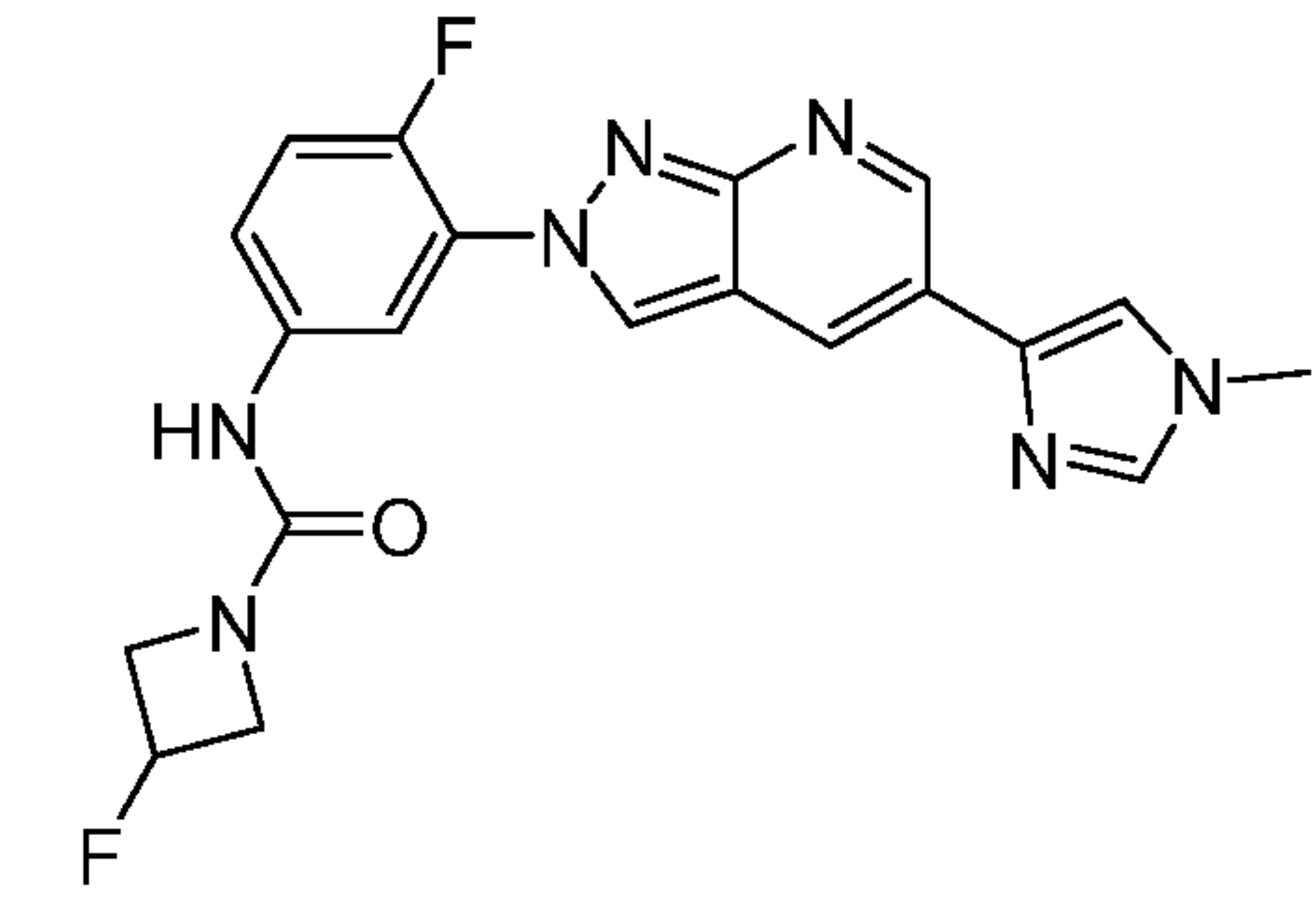
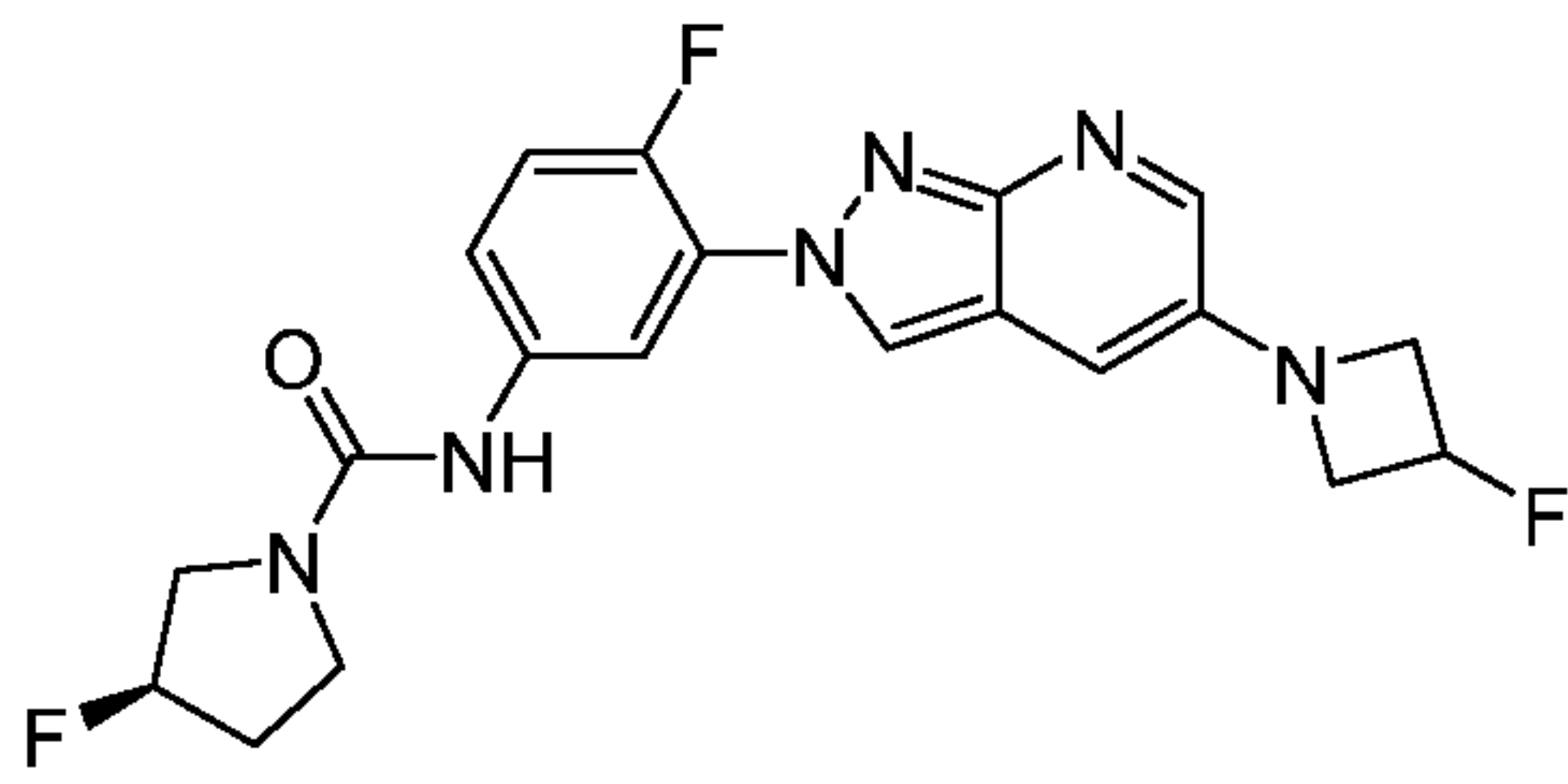
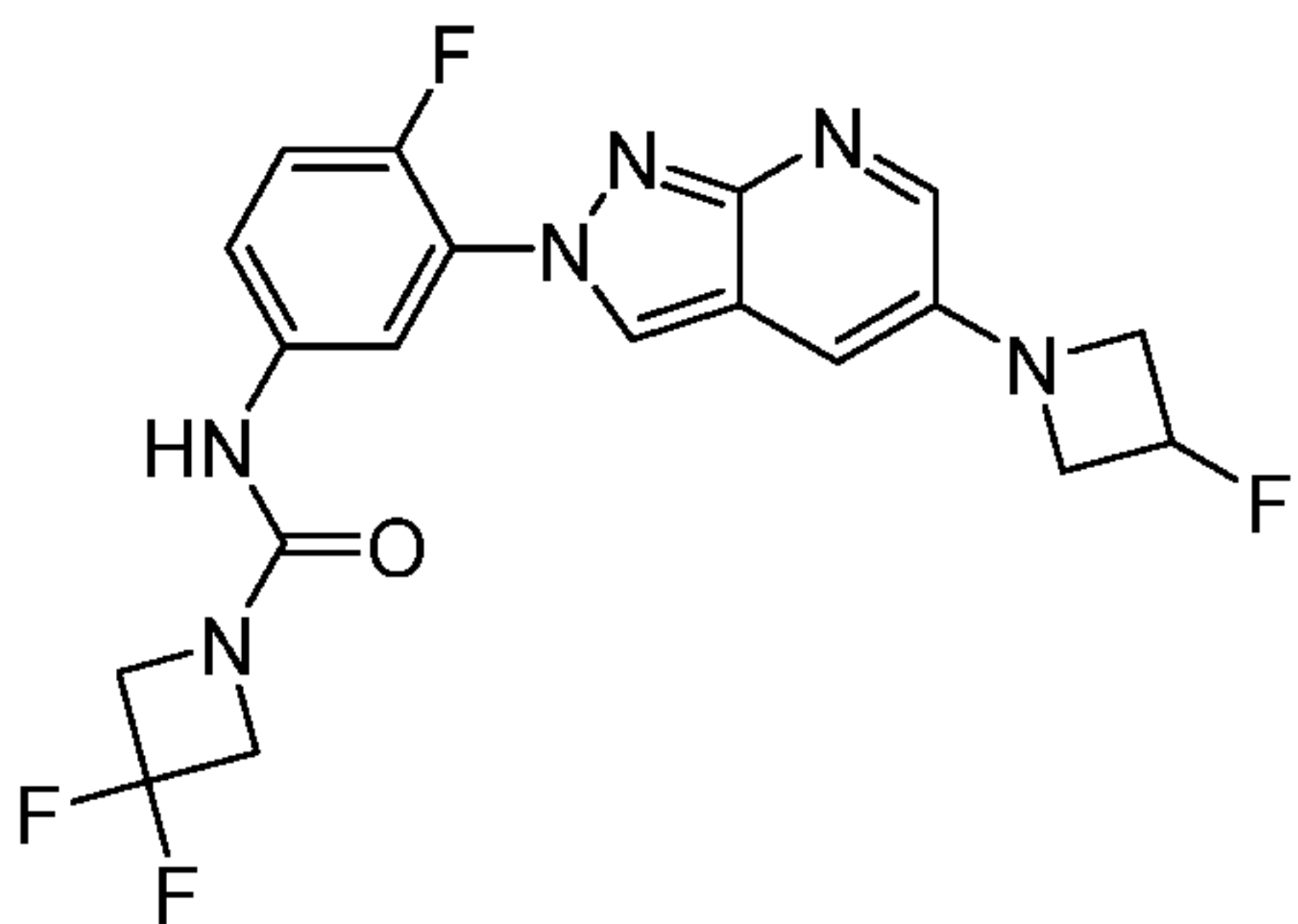
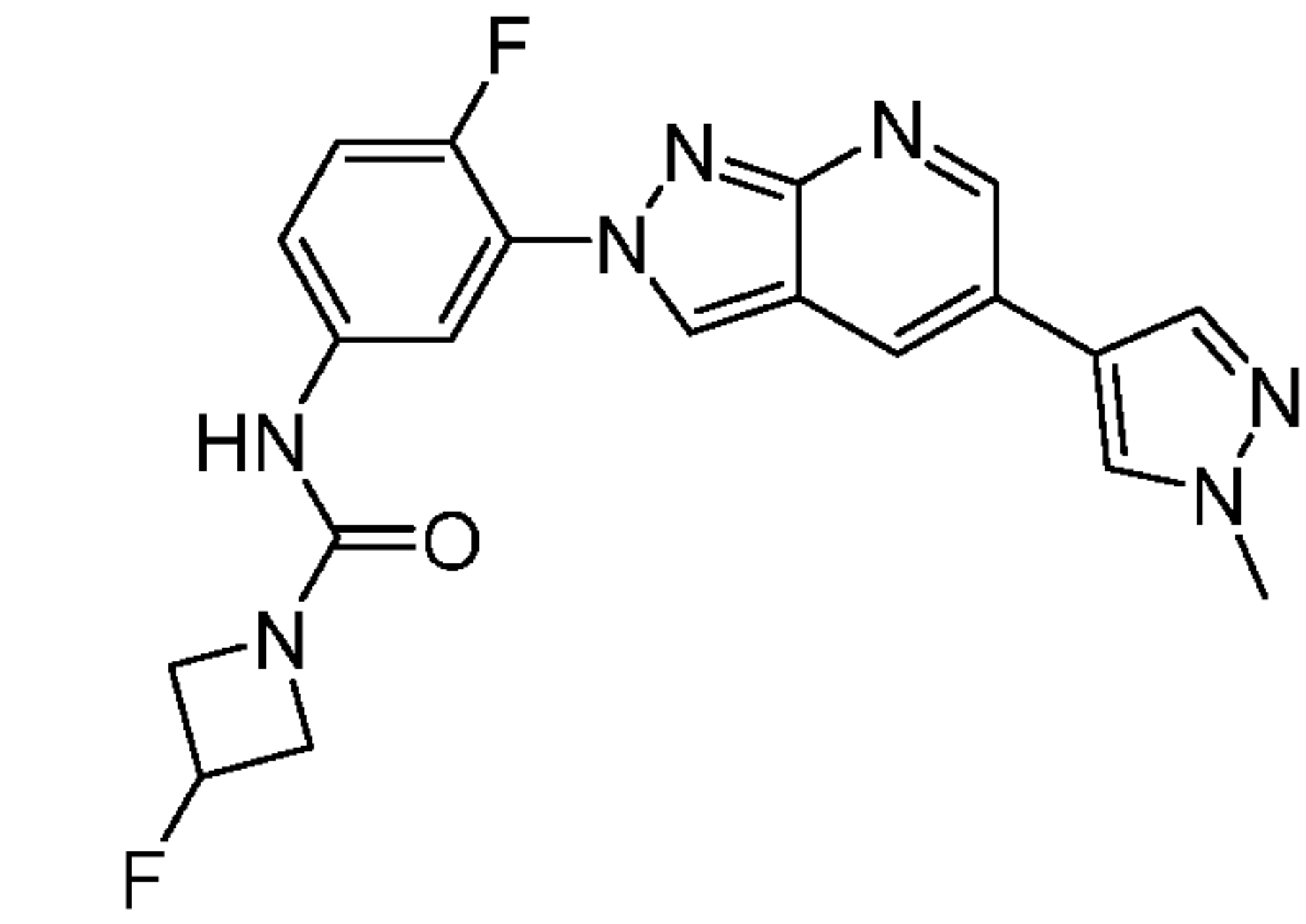
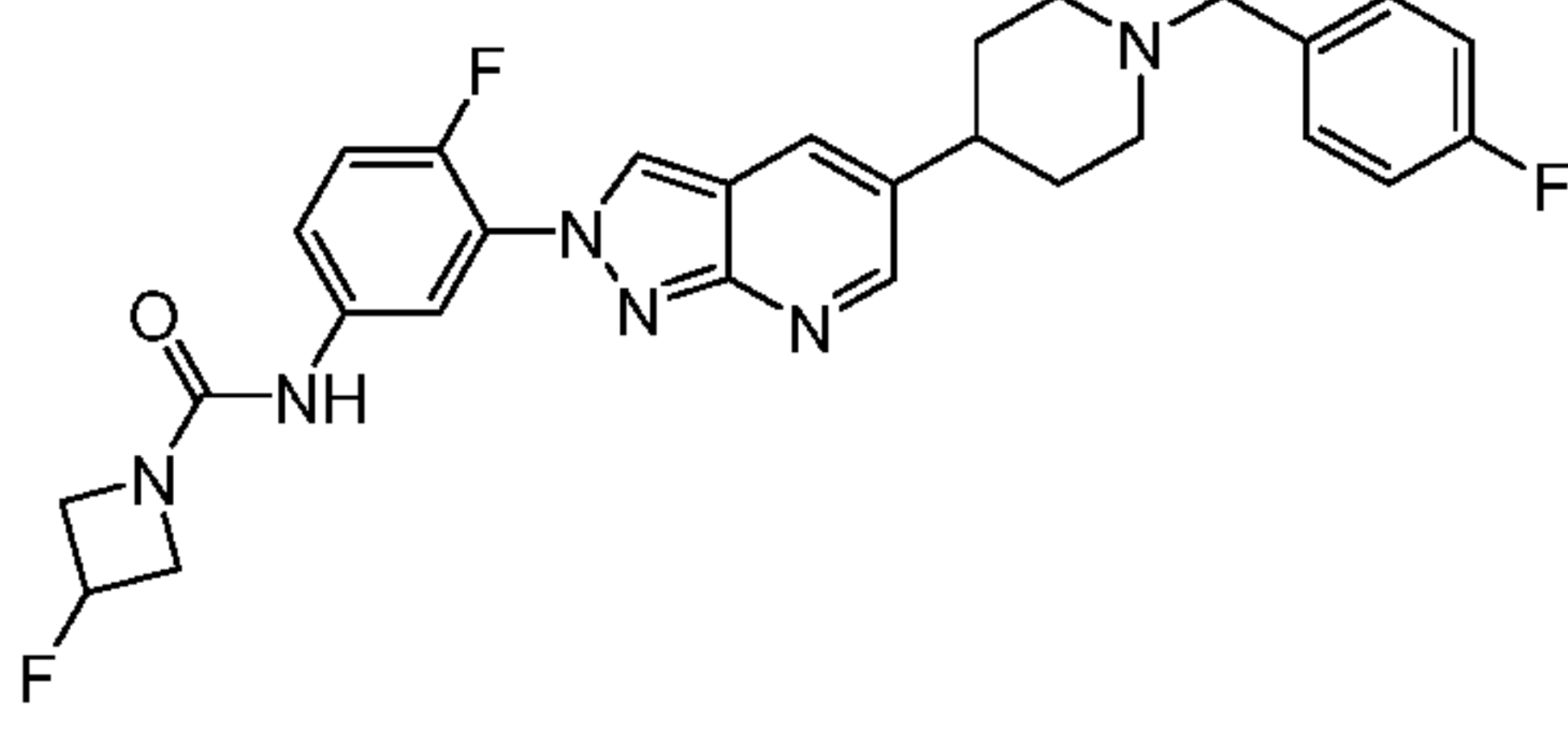
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
275		¹ H NMR (400 MHz, DMSO) δ 8.52 - 8.66 (m, 2 H), 8.32 (d, <i>J</i> = 2.81 Hz, 1 H), 8.23 (dd, <i>J</i> = 6.97, 2.57 Hz, 1 H), 7.68 (dt, <i>J</i> = 9.08, 3.35 Hz, 1 H), 7.42 (dd, <i>J</i> = 11.19, 9.23 Hz, 1 H), 7.03 (d, <i>J</i> = 2.69 Hz, 1 H), 5.24 - 5.50 (m, 1 H), 4.09 - 4.26 (m, 2 H), 3.99 (dd, <i>J</i> = 8.01, 5.44 Hz, 2 H), 3.50 - 3.84 (m, 4 H), 3.38 - 3.47 (m, 1 H), 1.97 - 2.29 (m, 2 H). Method 1: RT = 2.86 min.; M+H = 467.3
276		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.99 (s, 1 H), 8.90 (d, <i>J</i> = 2.51 Hz, 1 H), 8.70 (d, <i>J</i> = 2.51 Hz, 1 H), 8.47 (d, <i>J</i> = 2.51 Hz, 1 H), 8.24 (dd, <i>J</i> = 7.03, 2.76 Hz, 1 H), 7.64 - 7.76 (m, 1 H), 7.48 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 5.26 - 5.53 (m, 1 H), 4.23 - 4.40 (m, 2 H), 3.94 - 4.12 (m, 2 H). Method 1: RT = 2.76 min.; M+H = 364.0
277		¹ H NMR (400 MHz, DMSO-d ₆) δ ppm 9.00 (d, <i>J</i> = 2.20 Hz, 1 H), 8.94 (d, <i>J</i> = 1.96 Hz, 1 H), 8.53 - 8.63 (m, 2 H), 8.51 (d, <i>J</i> = 2.20 Hz, 1 H), 7.85 - 7.95 (m, 1 H), 7.81 (br d, <i>J</i> = 7.34 Hz, 1 H), 7.55 - 7.67 (m, 1 H), 7.37 (dd, <i>J</i> = 7.46, 4.77 Hz, 1 H), 4.69 (s, 2 H), 2.55 (s, 3 H), 2.45 (s, 3 H). Method 1: RT = 2.50 min.; M+H = 459.0
278		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.54 (s, 1 H), 9.00 (d, <i>J</i> = 2.32 Hz, 1 H), 8.93 (d, <i>J</i> = 2.20 Hz, 1 H), 8.60 (td, <i>J</i> = 6.91, 3.30 Hz, 2 H), 8.51 (d, <i>J</i> = 2.20 Hz, 1 H), 7.89 - 7.97 (m, 1 H), 7.84 (d, <i>J</i> = 7.46 Hz, 1 H), 7.60 (dd, <i>J</i> = 11.07, 9.23 Hz, 1 H), 7.40 (dd, <i>J</i> = 7.58, 4.77 Hz, 1 H), 2.45 (s, 3 H), 2.41 (s, 3 H). Method 1: RT = 2.61 min.; M+H = 446.1
279		¹ H NMR (400 MHz, Methanol-d ₄) δ 8.51 (d, <i>J</i> = 2.6 Hz, 1 H), 8.38 (dd, <i>J</i> = 6.9, 2.7 Hz, 1 H), 8.28 (d, <i>J</i> = 2.8 Hz, 1 H), 7.85 (ddd, <i>J</i> = 9.1, 4.2, 2.7 Hz, 1 H), 7.41 (dd, <i>J</i> = 11.1, 9.1 Hz, 1 H), 7.10 (d, <i>J</i> = 2.8 Hz, 1 H), 4.23 (t, <i>J</i> = 8.2 Hz, 2 H), 4.08 (dd, <i>J</i> = 8.0, 5.4 Hz, 2 H), 3.64 (qt, <i>J</i> = 8.8, 5.4 Hz, 1 H), 2.55 (s, 3 H), 2.46 (s, 3 H).

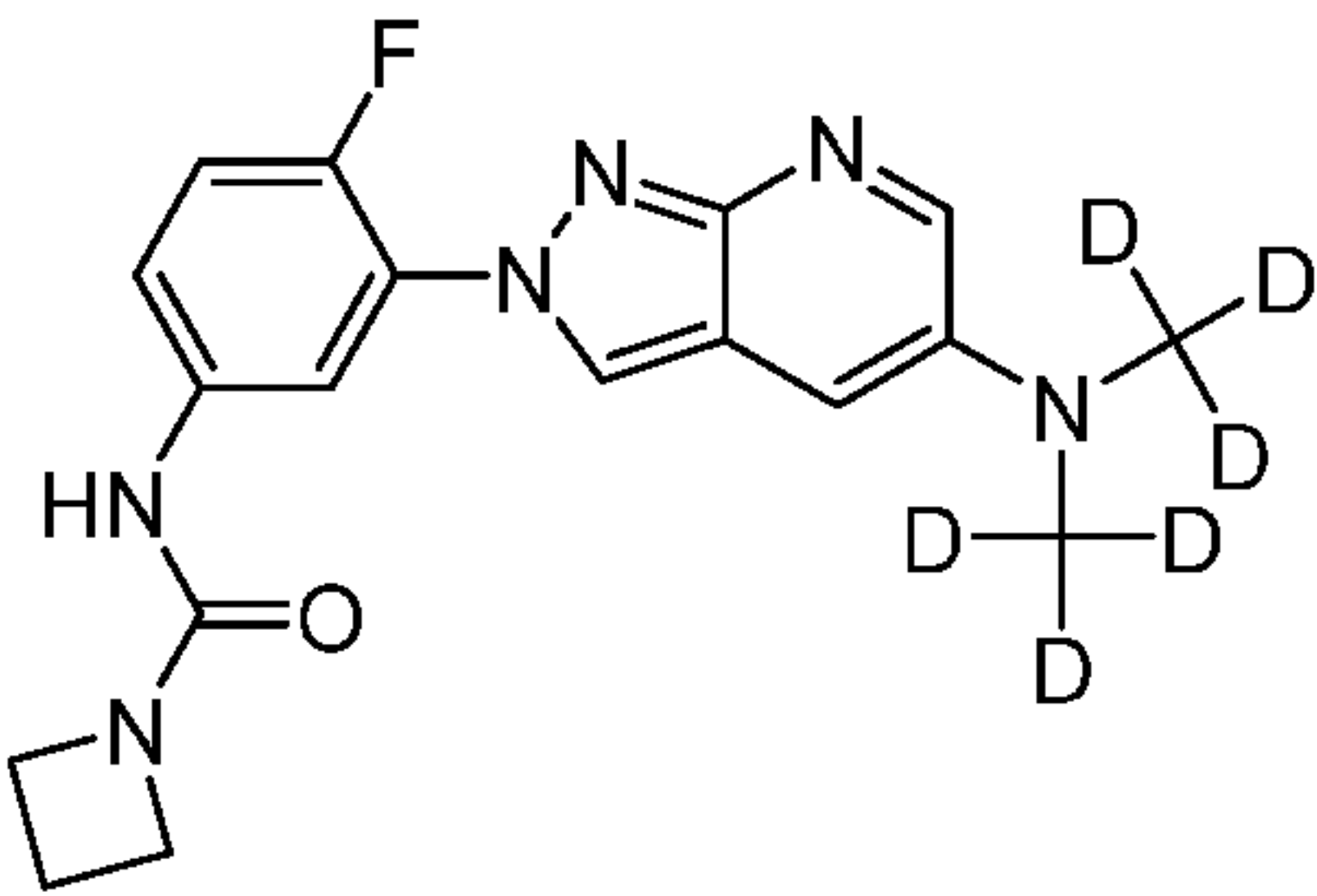
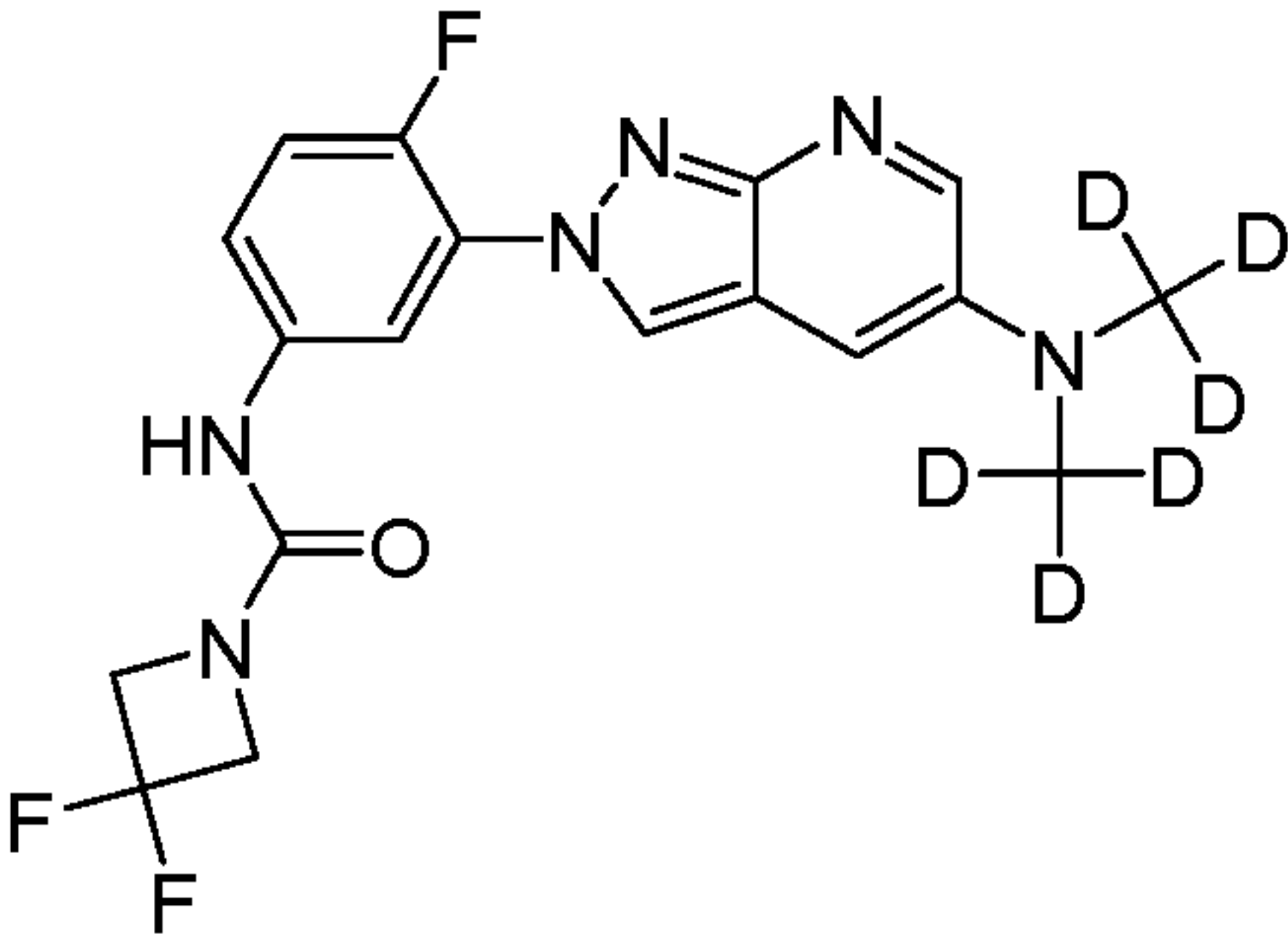
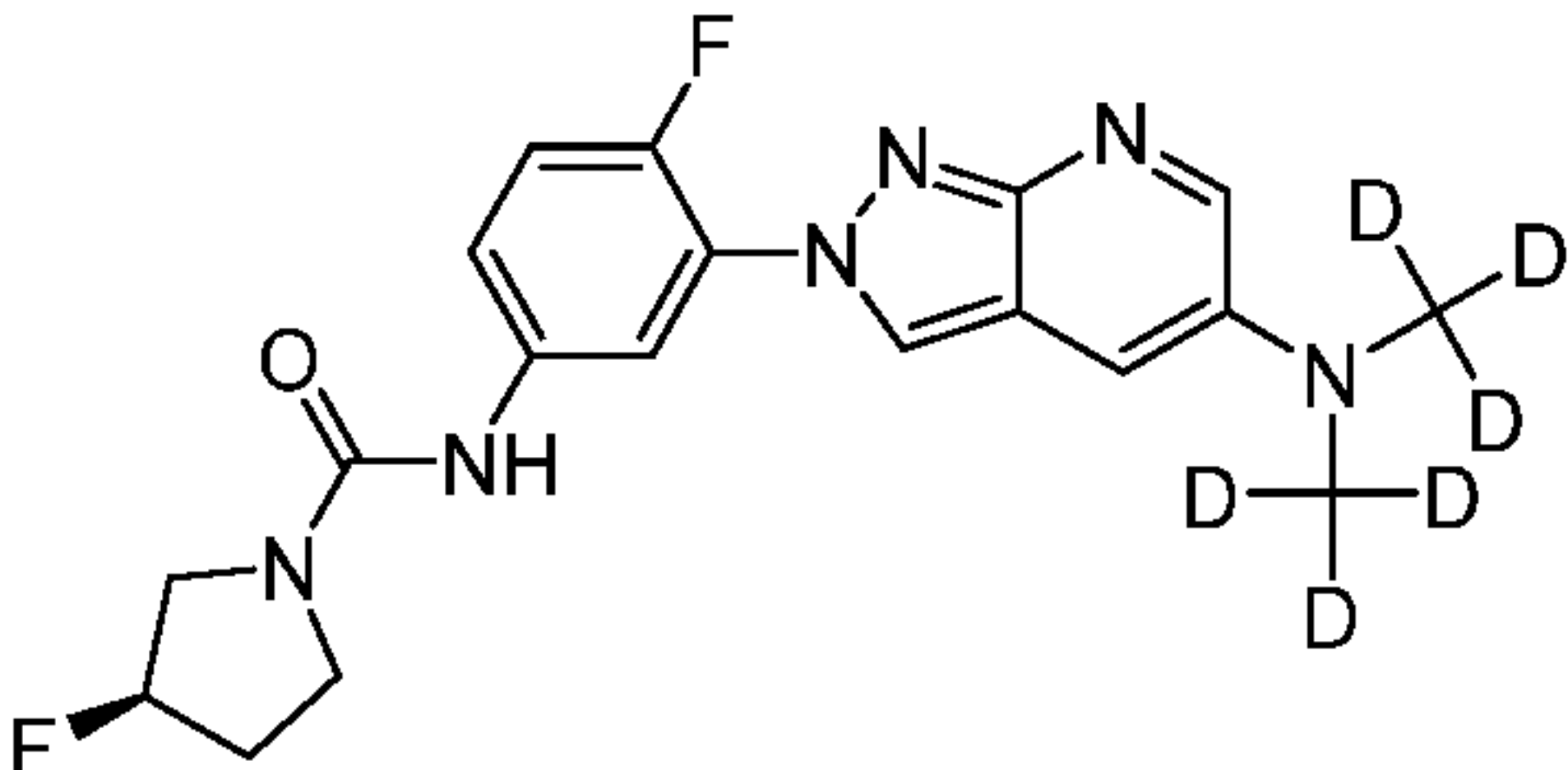
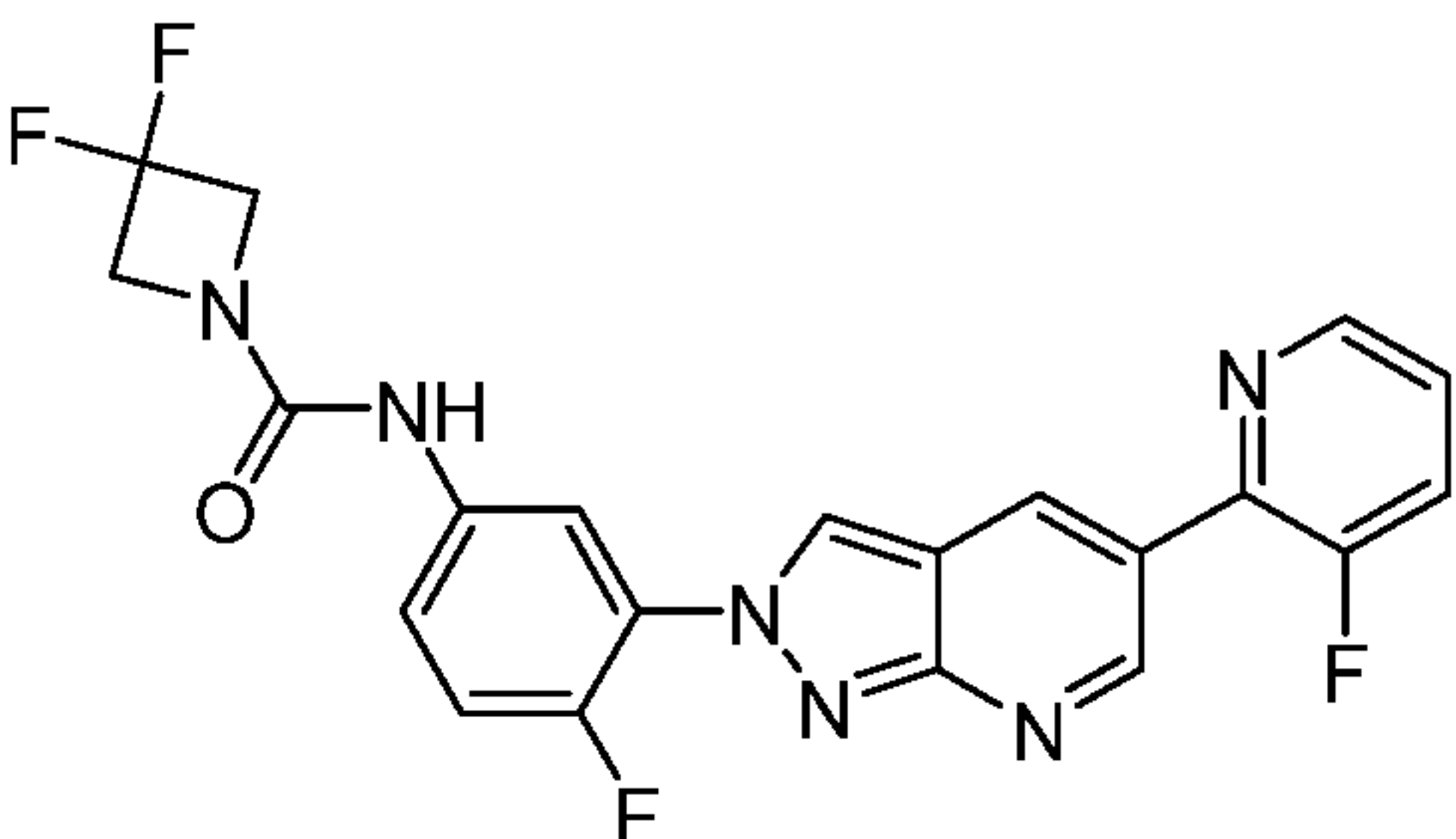
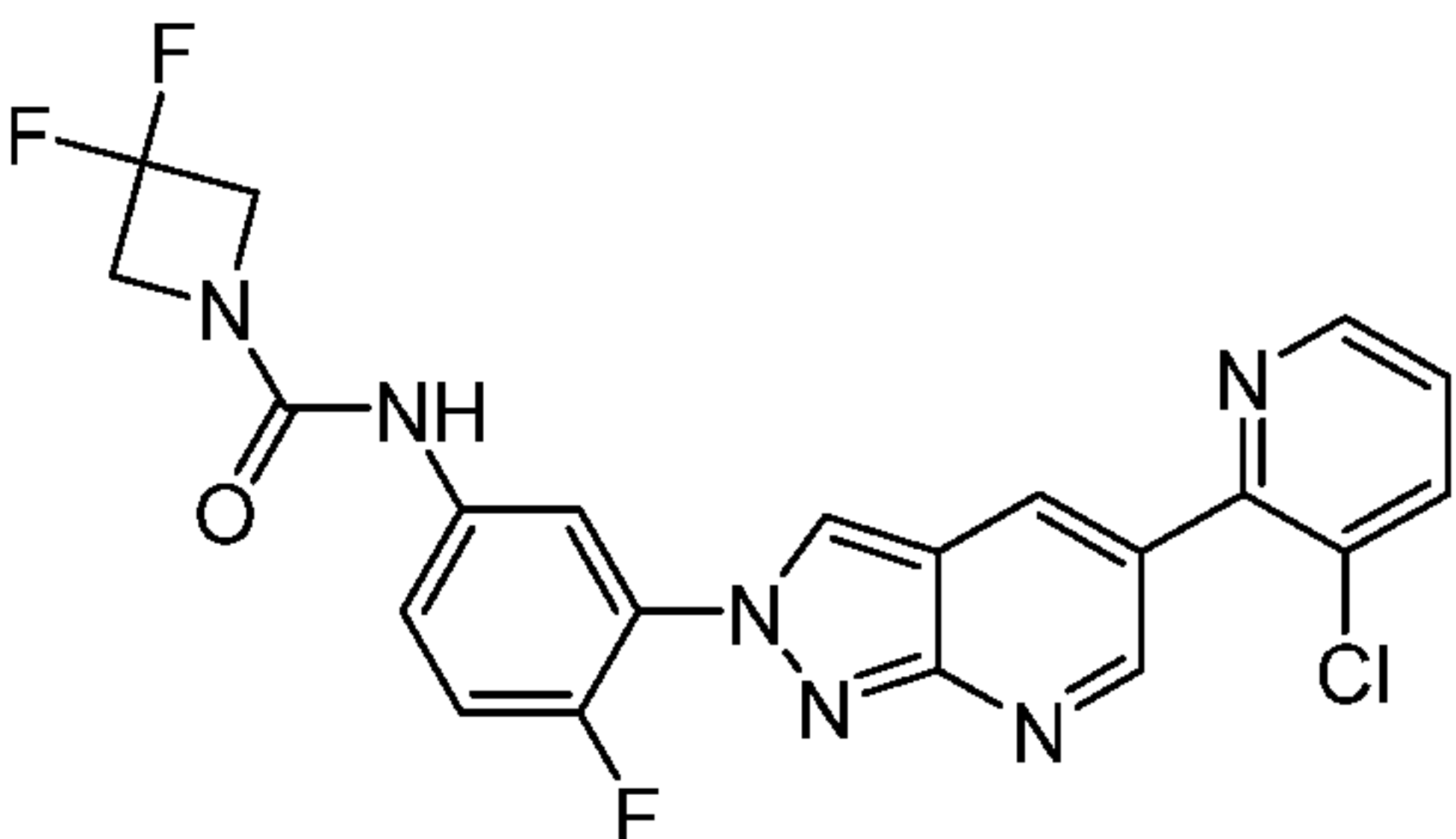
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
280		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.18 (s, 1 H), 8.99 (s, 1 H), 8.44 (d, J=1.76 Hz, 1 H), 8.36 (d, J=2.76 Hz, 1 H), 8.31 (d, J=5.77 Hz, 1 H), 7.67 (dd, J=5.52, 2.01 Hz, 1 H), 7.14 (d, J=2.76 Hz, 1 H), 4.42 (t, J=12.17 Hz, 4 H), 4.04 (t, J=7.53 Hz, 4 H), 2.16 - 2.29 (m, 2 H). Method 1: RT = 2.76 min.; M+H = 386.0
281		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.70 (s, 1 H), 9.47 (d, J=2.20 Hz, 1 H), 9.38 (s, 1 H), 8.95 (d, J=2.20 Hz, 1 H), 8.71 - 8.77 (m, 1 H), 8.49 (d, J=1.71 Hz, 1 H), 8.42 (d, J=5.62 Hz, 1 H), 8.12 (d, J=8.07 Hz, 1 H), 7.96 (td, J=7.76, 1.83 Hz, 1 H), 7.72 (dd, J=5.62, 1.96 Hz, 1 H), 7.39 - 7.47 (m, 1 H), 4.49 (t, J=12.72 Hz, 4 H). Method 1: RT = 2.81 min.; M+H = 408.0
282		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.16 (s, 1 H), 8.91 (s, 1 H), 8.42 (d, J=1.76 Hz, 1 H), 8.26 - 8.32 (m, 2 H), 7.66 (dd, J=5.77, 2.01 Hz, 1 H), 6.91 (d, J=2.76 Hz, 1 H), 4.00 - 4.08 (m, 8 H), 2.17 - 2.28 (m, 2 H), 0.68 (s, 4 H). Method 1: RT = 2.93 min.; M+H = 376.0
283		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.47 (d, J=2.26 Hz, 1 H), 9.08 (br s, 1 H), 8.90 - 9.00 (m, 2 H), 8.70 - 8.79 (m, 1 H), 8.13 (d, J=8.03 Hz, 1 H), 8.03 (d, J=2.51 Hz, 1 H), 7.96 (td, J=7.72, 1.88 Hz, 1 H), 7.72 - 7.78 (m, 1 H), 7.66 (d, J=9.03 Hz, 1 H), 7.42 (ddd, J=7.53, 4.77, 1.00 Hz, 1 H), 5.28 - 5.53 (m, 1 H), 4.25 - 4.42 (m, 2 H), 3.95 - 4.11 (m, 2 H). Method 1: RT = 2.69 min.; M+H = 423.0
284		¹ H NMR (400 MHz, DMSO) δ 8.80 (s, 1 H), 8.55 (s, 1 H), 8.35 (d, J = 2.81 Hz, 1 H), 7.96 (d, J = 2.45 Hz, 1 H), 7.71 (dd, J = 8.99, 2.51 Hz, 1 H), 7.58 (d, J = 9.05 Hz, 1 H), 7.16 (d, J = 2.81 Hz, 1 H), 4.40 (br t, J = 12.23 Hz, 4 H), 3.96 (br t, J = 7.52 Hz, 4 H), 2.08 - 2.32 (m, 2 H). Method 1: RT = 2.81 min.; M+H = 419.2
285		¹ H NMR (400 MHz, DMSO) δ 9.46 (d, J = 1.96 Hz, 1 H), 8.93 (s, 2 H), 8.82 (s, 1 H), 8.73 (br d, J = 4.04 Hz, 1 H), 8.12 (br d, J = 8.07 Hz, 1 H), 8.04 (d, J = 2.20 Hz, 1 H), 7.94 (br t, J = 7.15 Hz, 1 H), 7.75 (dd, J = 8.86, 2.26 Hz, 1 H), 7.62 (d, J = 8.93 Hz, 1 H), 7.41 (dd, J = 6.97, 5.01 Hz, 1 H), 3.97 (br t, J = 7.46 Hz, 4 H), 2.19 (quin, J = 7.55 Hz, 2 H). Method 1: RT = 2.69 min.; M+H = 405.2

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
286		¹ H NMR (400 MHz, DMSO) δ 8.79 (s, 1 H), 8.45 (s, 1 H), 8.27 (d, <i>J</i> = 2.57 Hz, 1 H), 7.96 (d, <i>J</i> = 2.32 Hz, 1 H), 7.71 (dd, <i>J</i> = 8.86, 2.38 Hz, 1 H), 7.57 (d, <i>J</i> = 8.80 Hz, 1 H), 6.93 (d, <i>J</i> = 2.69 Hz, 1 H), 4.01 (s, 4 H), 3.96 (br t, <i>J</i> = 7.58 Hz, 4 H), 2.19 (quin, <i>J</i> = 7.61 Hz, 2 H), 0.68 (s, 4 H). Method 1: RT = 2.98 min.; M+H = 409.3
287		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.70 (s, 1 H), 8.68 (s, 1 H), 8.29 (s, 1 H), 8.25 (d, <i>J</i> = 2.81 Hz, 1 H), 7.52 - 7.66 (m, 2 H), 7.37 - 7.45 (m, 1 H), 6.90 (d, <i>J</i> = 2.69 Hz, 1 H), 3.97 - 4.05 (m, 8 H), 2.18 - 2.23 (m, 2 H), 0.69 (s, 4 H). Method 1: RT = 2.82 min.; M+H = 375.1
288		¹ H NMR (400 MHz, Methanol-d ₄) δ 9.03 (d, <i>J</i> = 2.2 Hz, 1H), 8.73 (d, <i>J</i> = 4.9 Hz, 1H), 8.19 (dd, <i>J</i> = 6.8, 2.7 Hz, 1H), 7.63 (ddd, <i>J</i> = 9.1, 4.2, 2.7 Hz, 1H), 7.37 (dd, <i>J</i> = 10.9, 9.1 Hz, 1H), 7.32 (dd, <i>J</i> = 5.0, 0.9 Hz, 1H), 4.92 (ddt, <i>J</i> = 2.7, 1.4, 0.7 Hz, 1H), 4.23 (d, <i>J</i> = 10.3 Hz, 1H), 4.17 - 4.07 (m, 2H), 3.74 (td, <i>J</i> = 11.6, 2.5 Hz, 1H), 3.37 - 3.32 (m, 2H), 2.33 (p, <i>J</i> = 7.6 Hz, 2H), 2.15 - 1.98 (m, 2H), 1.92 - 1.57 (m, 4H). Method 2: RT = 0.89 min.; M+H = 396.0
289		¹ H NMR (400 MHz, Methanol-d ₄) δ 9.05 (d, <i>J</i> = 2.2 Hz, 1H), 8.73 (d, <i>J</i> = 4.8 Hz, 1H), 8.18 (dd, <i>J</i> = 6.8, 2.7 Hz, 1H), 7.63 (ddd, <i>J</i> = 9.1, 4.1, 2.7 Hz, 1H), 7.37 (dd, <i>J</i> = 10.9, 9.1 Hz, 1H), 7.32 (dd, <i>J</i> = 4.8, 0.9 Hz, 1H), 5.20 - 5.12 (m, 1H), 4.17 - 4.04 (m, 4H), 3.99 (ddd, <i>J</i> = 11.8, 10.6, 3.0 Hz, 1H), 3.89 - 3.75 (m, 2H), 3.59 (dd, <i>J</i> = 11.5, 9.9 Hz, 1H), 3.40 - 3.32 (m, 2H), 2.33 (p, <i>J</i> = 7.7 Hz, 2H). Method 2: RT = 0.74 min.; M+H = 398.0
290		¹ H NMR (400 MHz, DMSO) δ 8.69 (s, 1 H), 8.62 (d, <i>J</i> = 2.64 Hz, 1 H), 8.36 (d, <i>J</i> = 2.76 Hz, 1 H), 8.22 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.65 - 7.72 (m, 1 H), 7.42 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 7.15 (d, <i>J</i> = 2.89 Hz, 1 H), 4.41 (t, <i>J</i> = 12.23 Hz, 4 H), 3.98 (t, <i>J</i> = 7.53 Hz, 4 H), 2.20 (quin, <i>J</i> = 7.56 Hz, 2 H). Method 1: RT = 2.73 min.; LCMS: M+H = 403.2

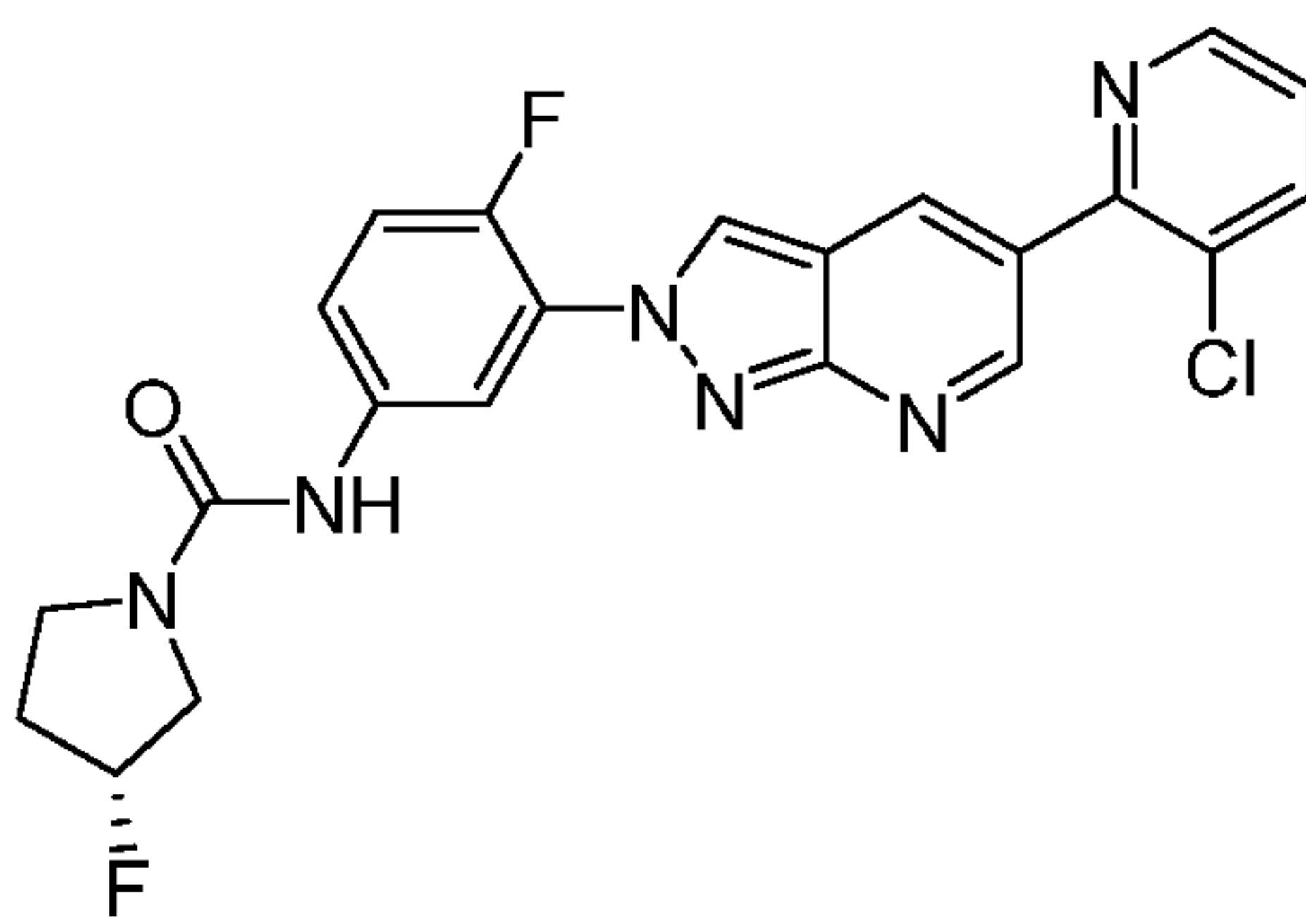
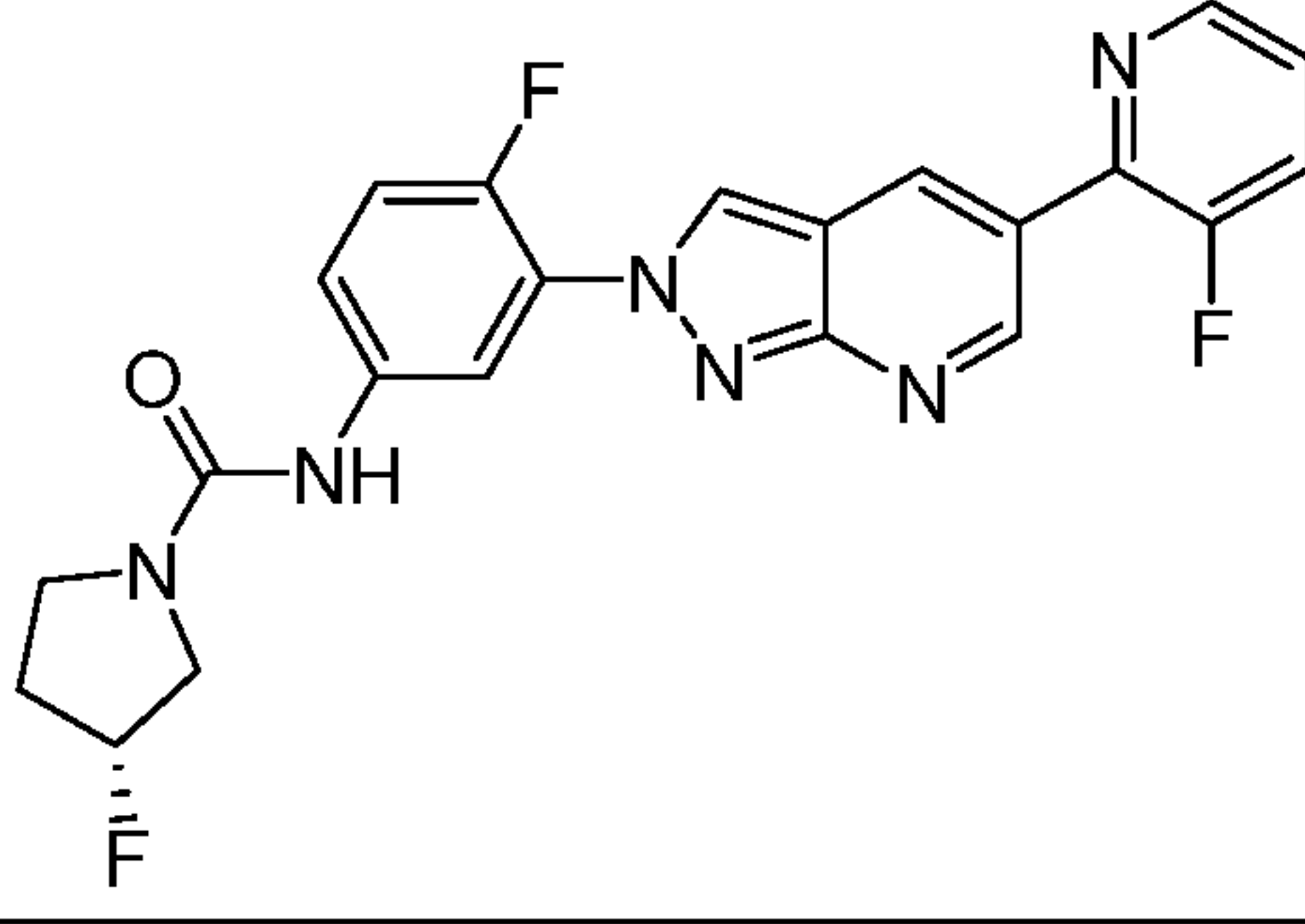
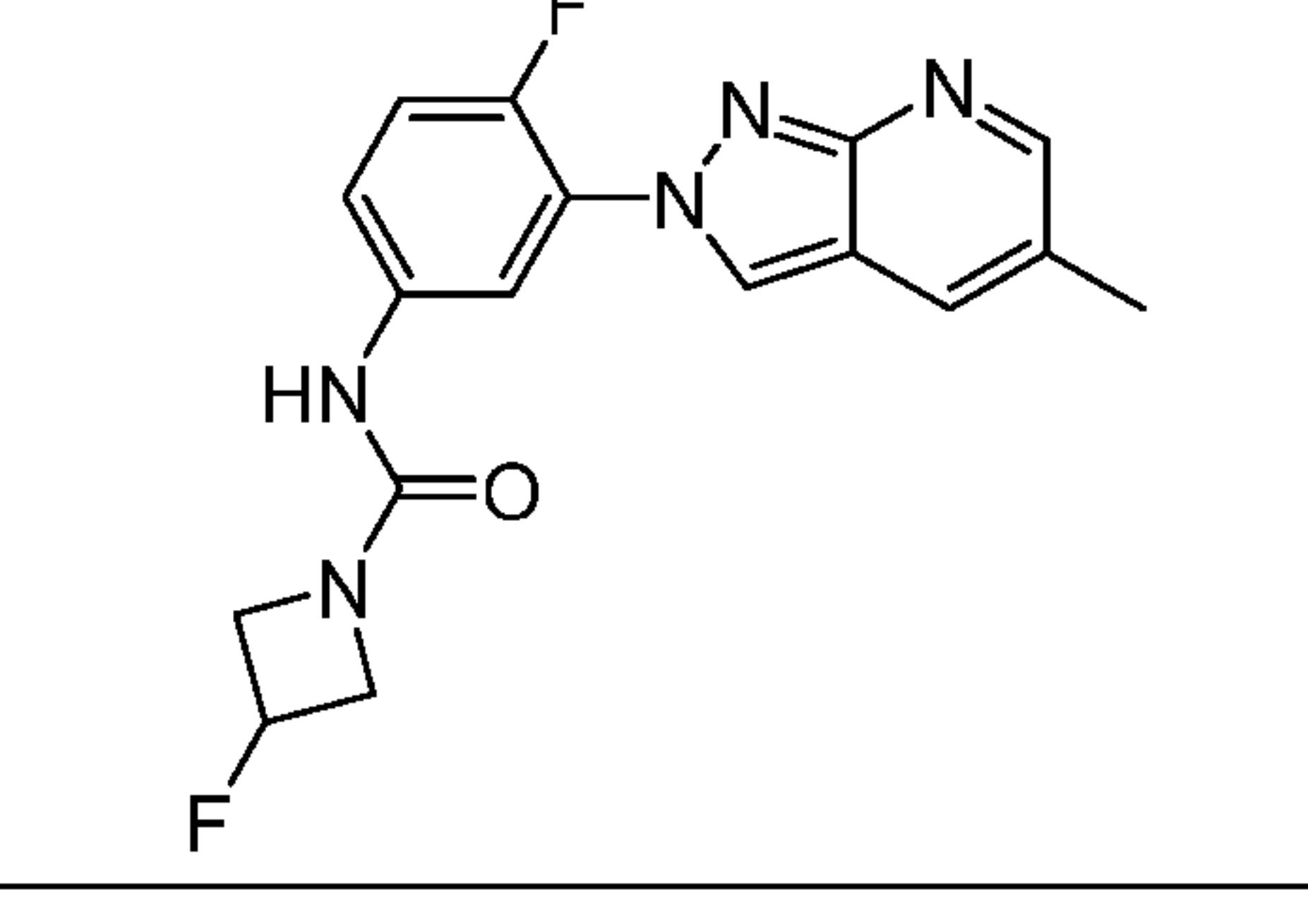
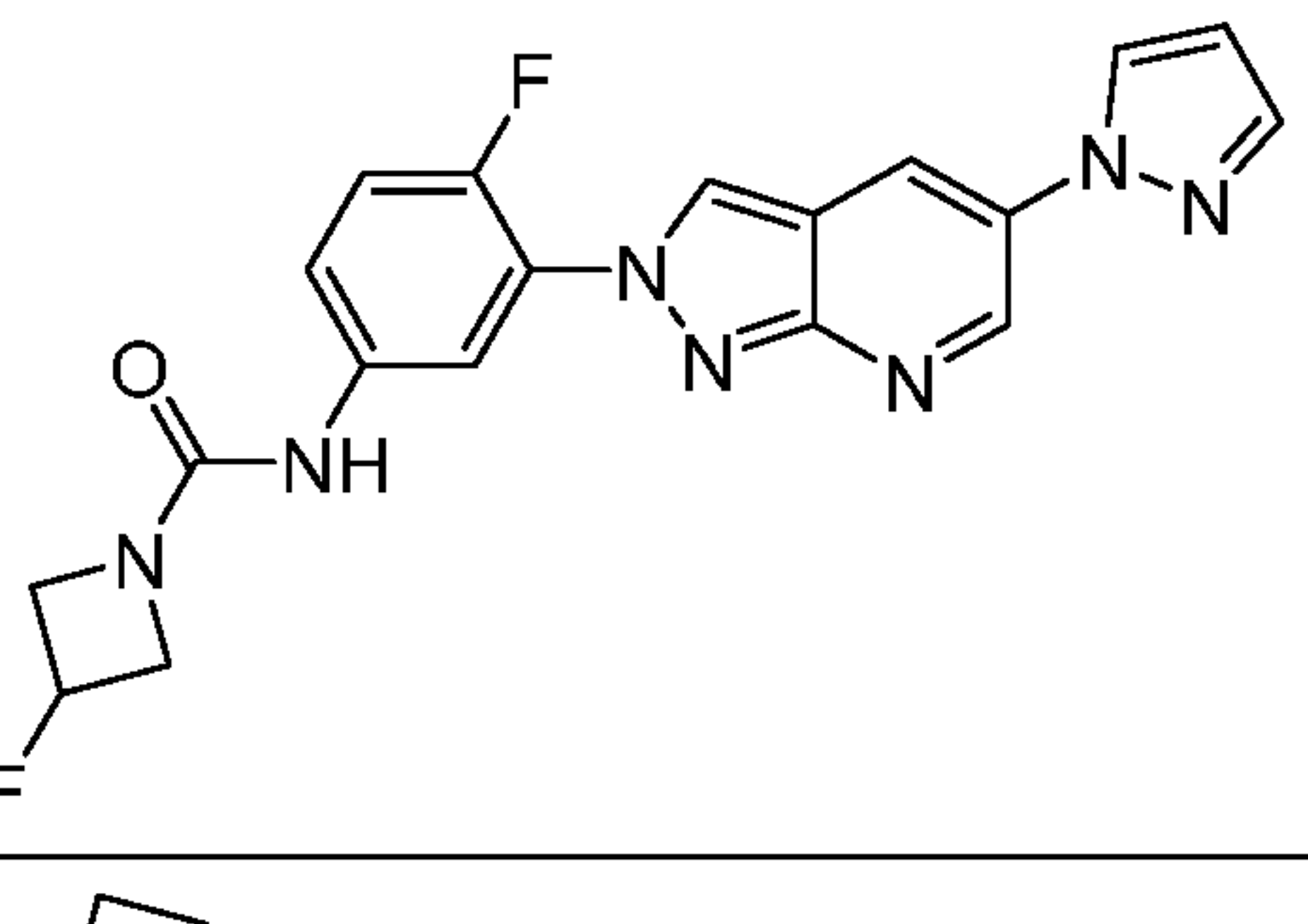
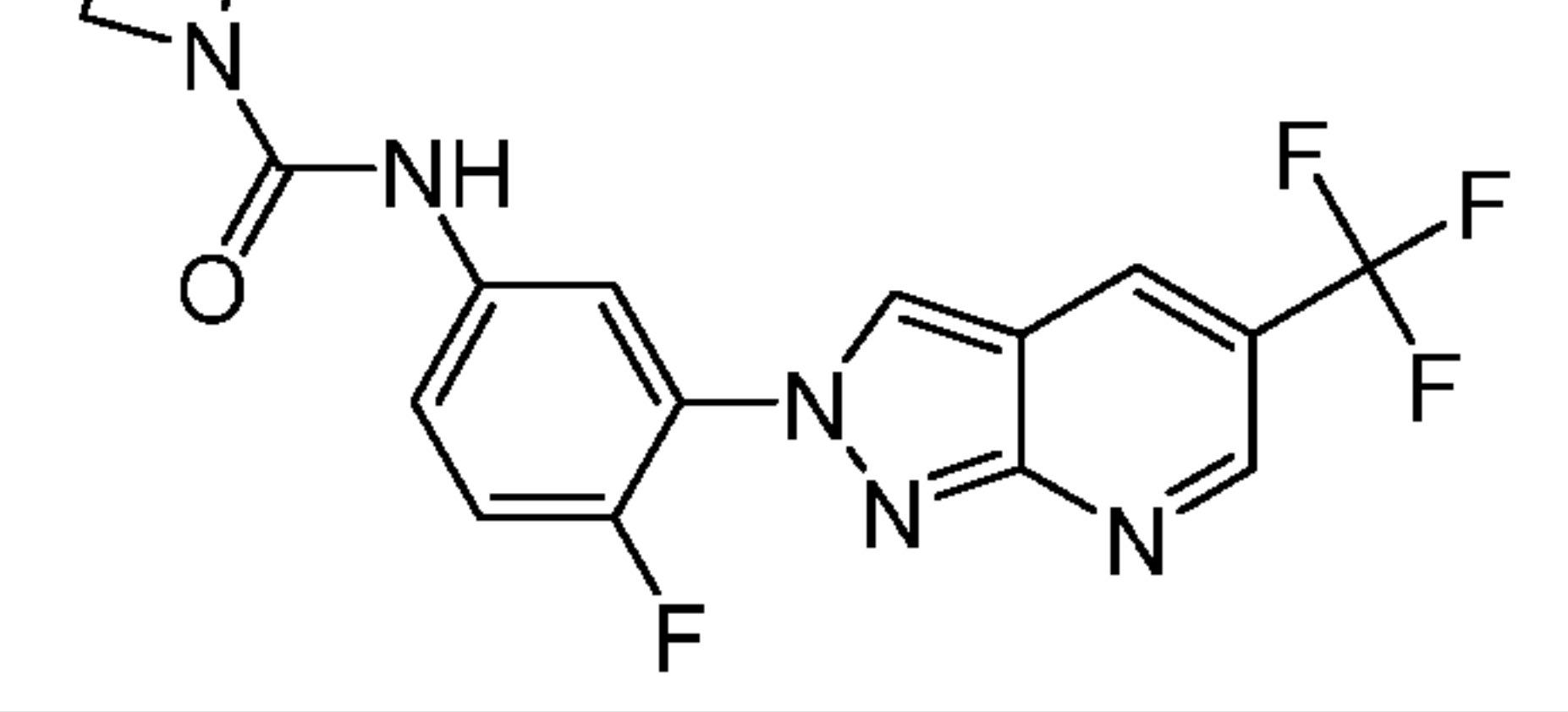
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
291		¹ H NMR (400 MHz, DMSO) δ 8.95 (s, 1 H), 8.56 (d, <i>J</i> = 2.63 Hz, 1 H), 8.30 (d, <i>J</i> = 2.89 Hz, 1 H), 8.19 (dd, <i>J</i> = 7.09, 2.70 Hz, 1 H), 7.60 - 7.69 (m, 1 H), 7.42 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.00 (d, <i>J</i> = 2.76 Hz, 1 H), 5.28 - 5.63 (m, 2 H), 4.20 - 4.37 (m, 4 H), 3.93 - 4.09 (m, 4 H). Method 1: RT = 2.63 min.; M+H = 403.2
292		¹ H NMR (400 MHz, DMSO) δ 8.70 (s, 1 H), 8.56 (d, <i>J</i> = 2.76 Hz, 1 H), 8.31 (d, <i>J</i> = 2.76 Hz, 1 H), 8.21 (dd, <i>J</i> = 7.03, 2.64 Hz, 1 H), 7.59 - 7.72 (m, 1 H), 7.41 (dd, <i>J</i> = 11.36, 9.10 Hz, 1 H), 7.01 (d, <i>J</i> = 2.76 Hz, 1 H), 5.39 - 5.66 (m, 1 H), 4.20 - 4.36 (m, 2 H), 3.89 - 4.09 (m, 6 H), 2.12 - 2.28 (m, 2 H). Method 1: RT = 2.63 min.; M+H = 385.3
293		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.05 (s, 1 H), 8.83 (d, <i>J</i> = 2.26 Hz, 1 H), 8.66 (s, 1 H), 8.44 (br s, 1 H), 8.24 (dd, <i>J</i> = 7.03, 2.51 Hz, 1 H), 8.05 (s, 1 H), 7.64 - 7.73 (m, 1 H), 7.47 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 5.28 - 5.52 (m, 1 H), 4.25 - 4.41 (m, 2 H), 3.96 - 4.11 (m, 2 H), 3.29 (br d, <i>J</i> = 9.03 Hz, 2 H), 2.91 (br d, <i>J</i> = 8.28 Hz, 3 H), 1.96 (br d, <i>J</i> = 12.55 Hz, 2 H), 1.82 (br d, <i>J</i> = 11.04 Hz, 2 H). Method 2: RT = 0.51 min.; M+H = 413.2
294		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.48 (d, <i>J</i> = 2.26 Hz, 1 H), 9.42 (d, <i>J</i> = 1.25 Hz, 1 H), 9.01 - 9.13 (m, 3 H), 8.76 - 8.83 (m, 1 H), 8.68 (d, <i>J</i> = 2.51 Hz, 1 H), 8.29 (dd, <i>J</i> = 7.03, 2.51 Hz, 1 H), 7.67 - 7.78 (m, 1 H), 7.50 (dd, <i>J</i> = 11.17, 9.16 Hz, 1 H), 5.26 - 5.57 (m, 1 H), 4.21 - 4.46 (m, 2 H), 3.92 - 4.15 (m, 2 H). Method 1: RT = 2.53 min.; M+H = 408.1
295		¹ H NMR (400 MHz, METHANOL-d ₄) δ 9.14 (d, <i>J</i> = 2.26 Hz, 1 H), 8.77 (d, <i>J</i> = 2.26 Hz, 1 H), 8.57 (d, <i>J</i> = 2.26 Hz, 1 H), 8.17 (dd, <i>J</i> = 6.78, 2.76 Hz, 1 H), 7.85 (d, <i>J</i> = 1.00 Hz, 1 H), 7.64 - 7.71 (m, 2 H), 7.38 (dd, <i>J</i> = 11.04, 9.03 Hz, 1 H), 5.27 - 5.51 (m, 1 H), 4.35 - 4.47 (m, 2 H), 4.09 - 4.23 (m, 2 H). Method 1: RT = 1.95 min.; M+H = 396.1

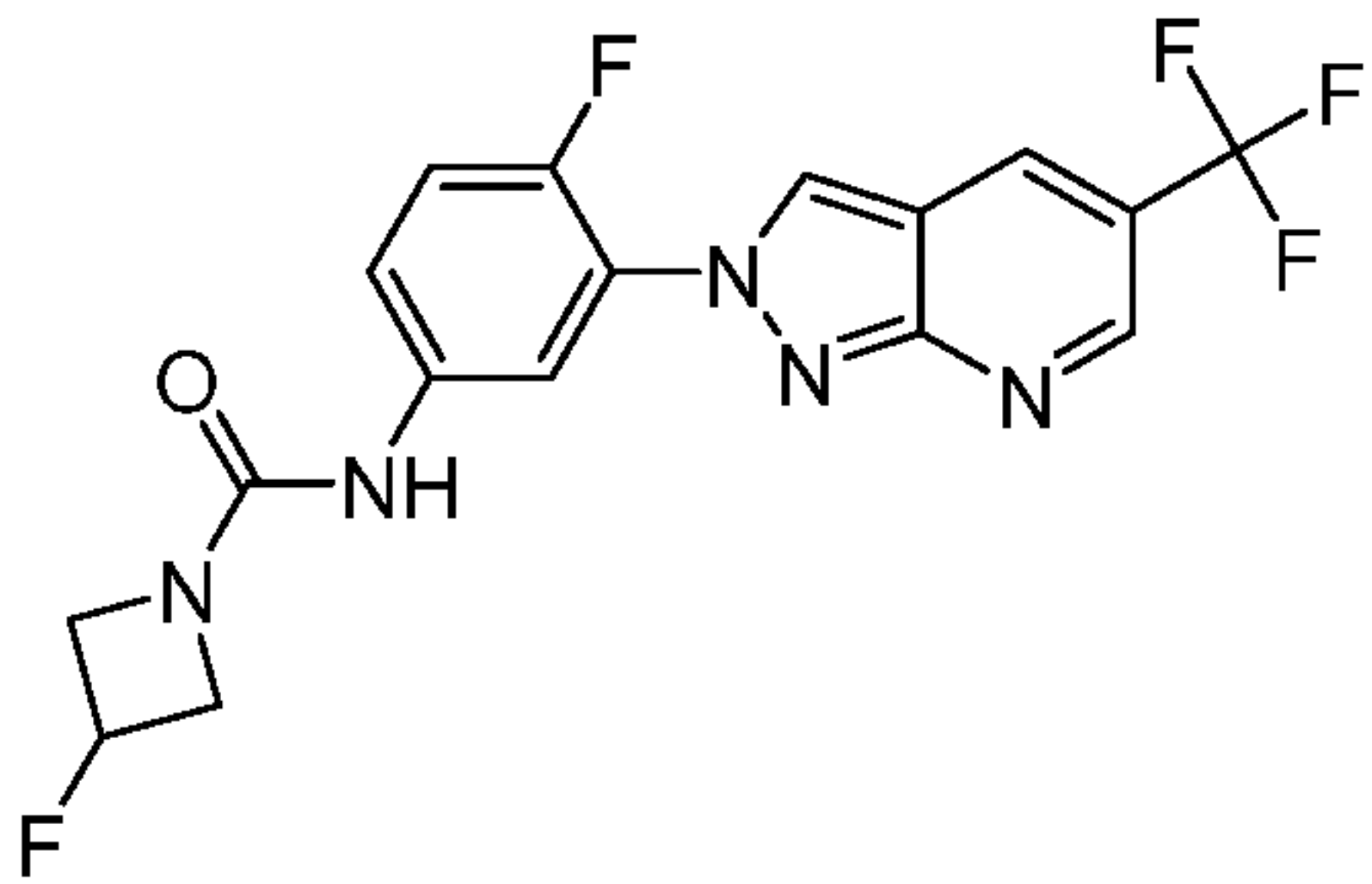
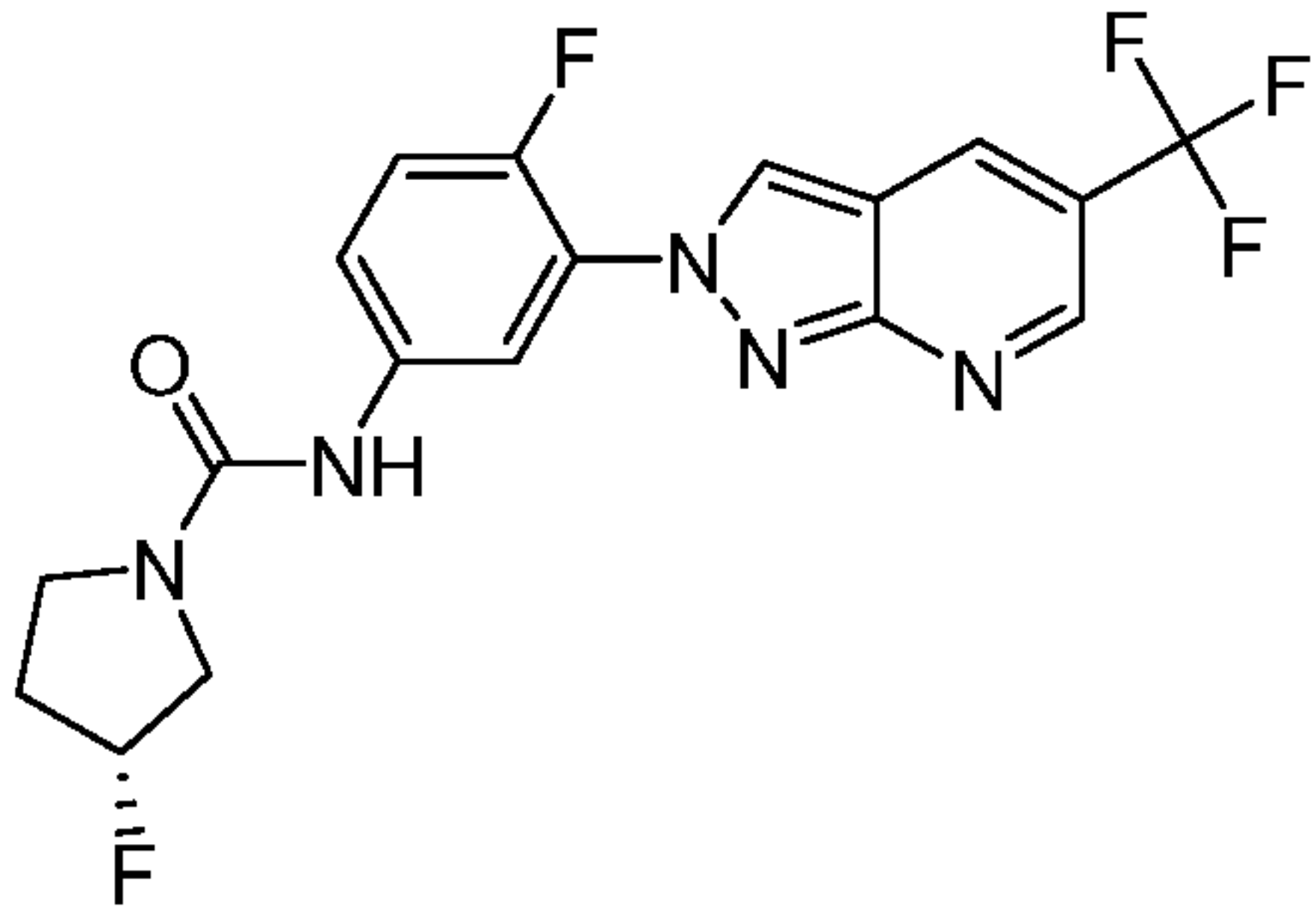
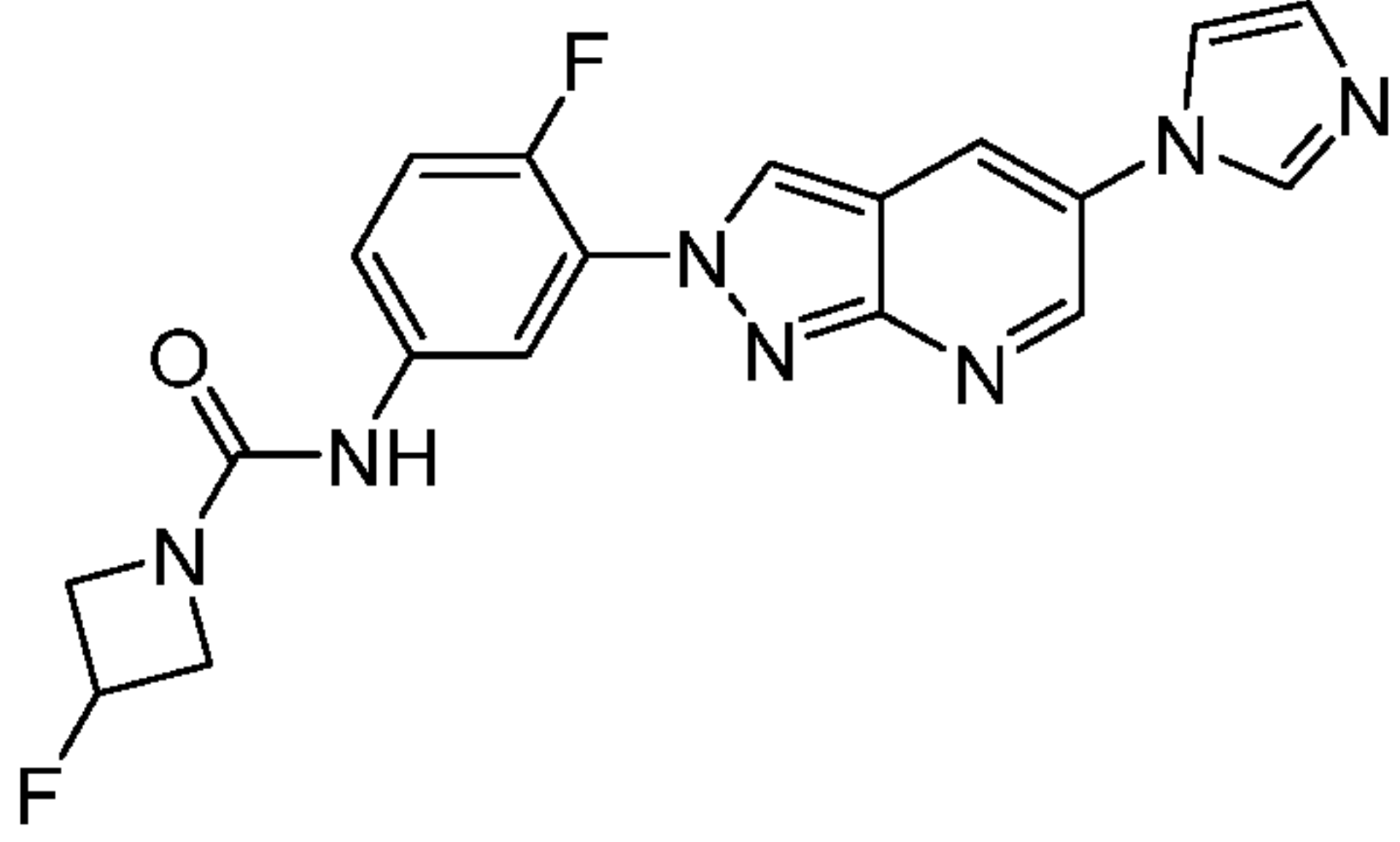
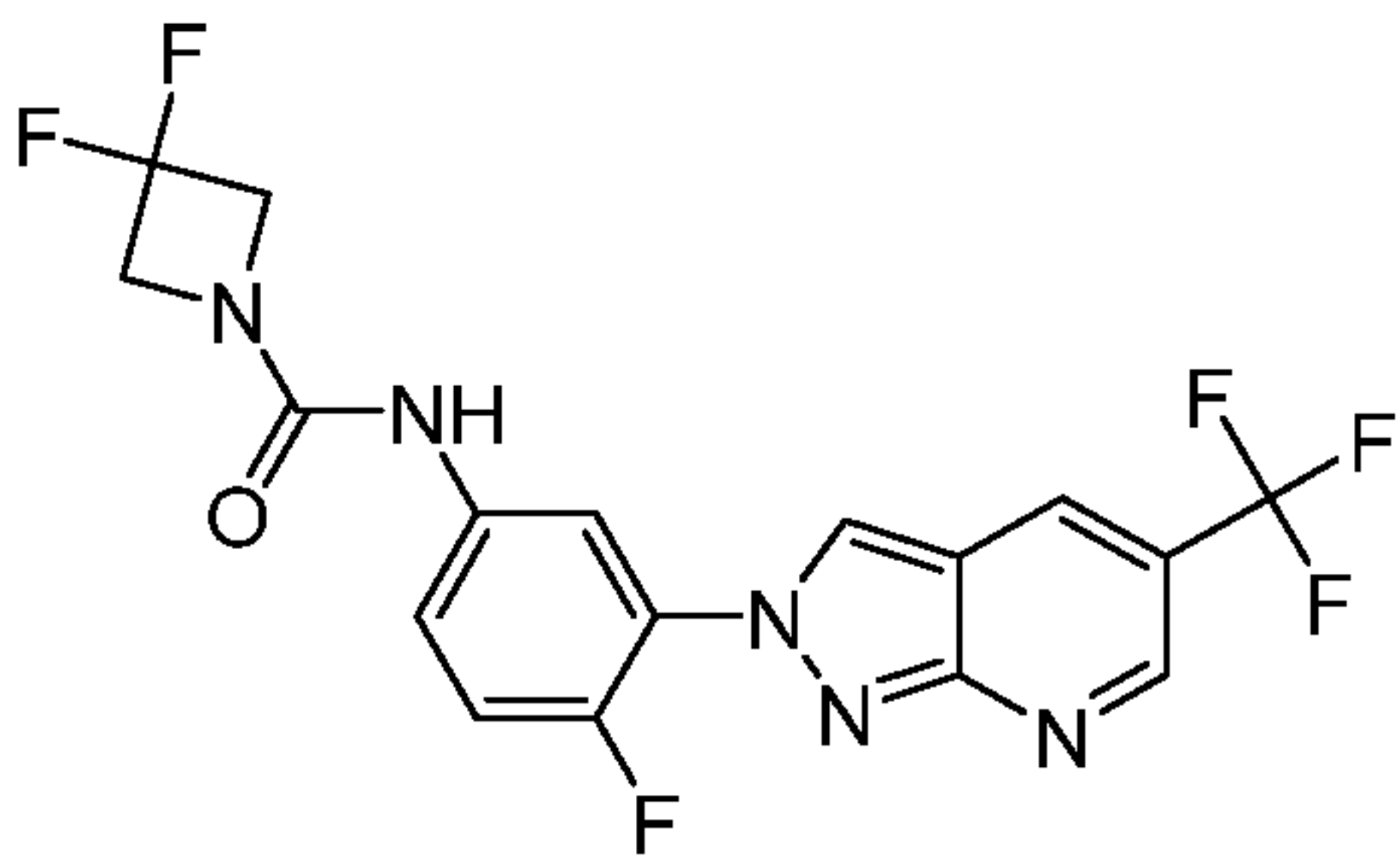
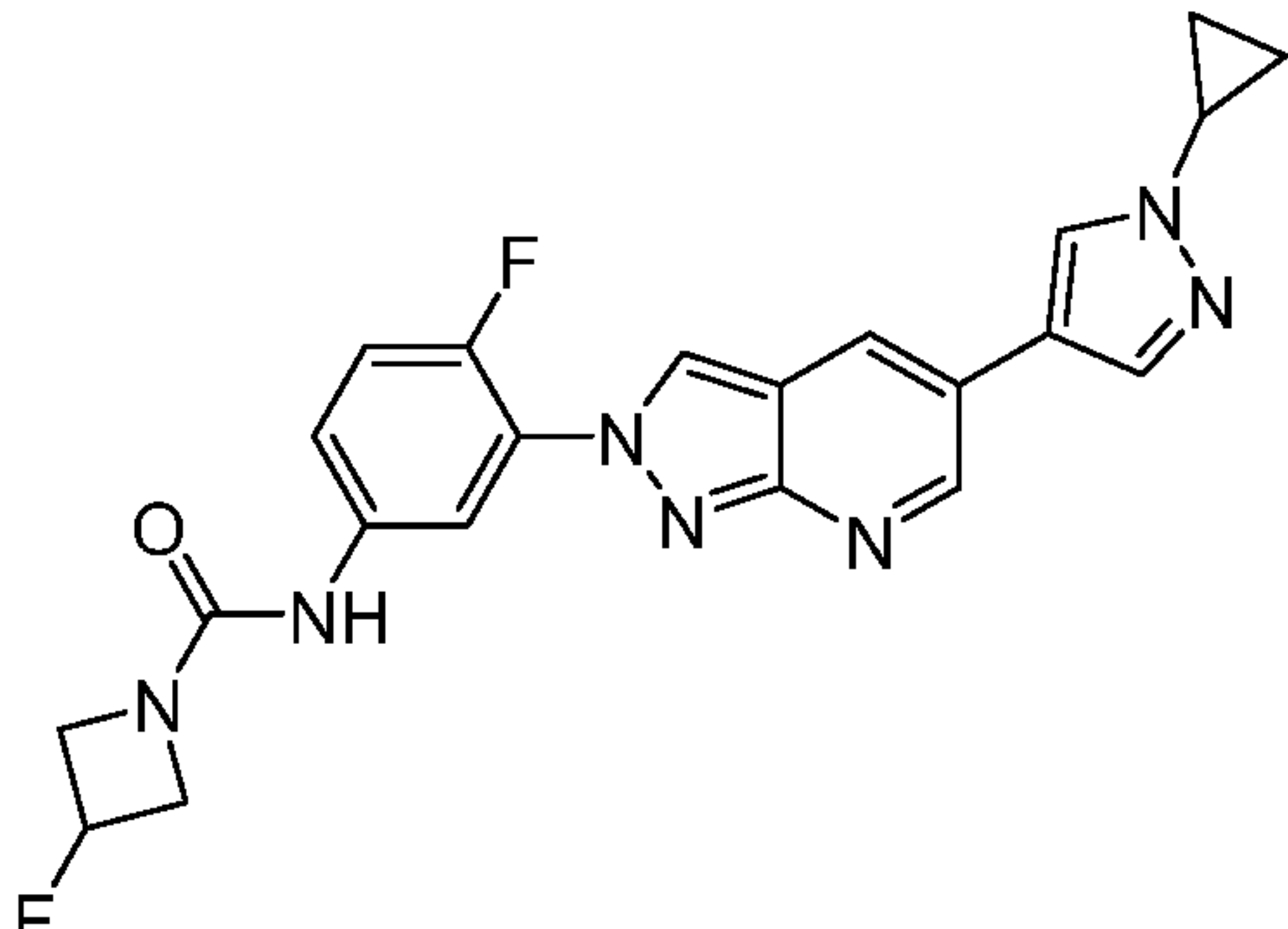
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
296		¹ H NMR (400 MHz, METHANOL-d ₄) δ 8.69 (d, J=2.45 Hz, 1 H), 8.65 (d, J=2.20 Hz, 1 H), 8.11 - 8.18 (m, 2 H), 7.61 - 7.69 (m, 1 H), 7.27 - 7.43 (m, 6 H), 5.26 - 5.49 (m, 1 H), 4.33 - 4.46 (m, 2 H), 4.08 - 4.21 (m, 2 H), 3.63 (s, 2 H), 3.11 (br d, J=11.74 Hz, 2 H), 2.72 - 2.85 (m, 1 H), 2.20 - 2.31 (m, 2 H), 1.82 - 2.01 (m, 4 H). Method 1: RT = 2.16 min.; M+H = 503.2
297		¹ H NMR (400 MHz, DMSO-d ₆) δ 13.13 (br s, 1 H), 9.08 (d, J=2.26 Hz, 1 H), 9.02 (s, 1 H), 8.84 (d, J=2.51 Hz, 1 H), 8.47 (s, 1 H), 8.40 (d, J=2.26 Hz, 1 H), 8.26 (dd, J=7.03, 2.76 Hz, 2 H), 7.69 (ddd, J=9.16, 4.14, 2.76 Hz, 1 H), 7.48 (dd, J=11.17, 9.16 Hz, 1 H), 5.30 - 5.51 (m, 1 H), 4.26 - 4.40 (m, 2 H), 3.97 - 4.10 (m, 2 H). Method 2: RT = 0.69 min.; M+H = 396.1
298		¹ H NMR (400 MHz, DMSO), δ 8.94 (s, 1 H), 8.62 (d, J = 2.57 Hz, 1 H), 8.36 (d, J = 2.81 Hz, 1 H), 8.20 (dd, J = 7.03, 2.63 Hz, 1 H), 7.57 - 7.71 (m, 1 H), 7.44 (dd, J = 11.19, 9.11 Hz, 1 H), 7.14 (d, J = 2.81 Hz, 1 H), 5.26 - 5.53 (m, 1 H), 4.22 - 4.51 (m, 6 H), 3.91 - 4.11 (m, 2 H). Method 1: RT = 2.74 min.; M+H = 421.2
299		¹ H NMR (400 MHz, DMSO) δ 9.19 (s, 1 H) 8.62 (d, J = 2.76 Hz, 1 H), 8.35 (d, J = 2.89 Hz, 1 H), 8.19 (dd, J = 7.03, 2.64 Hz, 1 H), 7.61 - 7.67 (m, 1 H), 7.45 (dd, J = 11.36, 9.10 Hz, 1 H), 7.13 (d, J = 2.76 Hz, 1 H), 4.35 - 4.45 (m, 8 H) Method 1: RT = 2.90 min.; M+H = 439.2
300		¹ H NMR (400 MHz, DMSO) δ 8.57 - 8.65 (m, 2 H) 8.35 (d, J=2.76 Hz, 1 H) 8.22 (dd, J=7.09, 2.70 Hz, 1 H) 7.64 - 7.72 (m, 1 H) 7.42 (dd, J=11.29, 9.16 Hz, 1 H) 7.14 (d, J=2.76 Hz, 1 H) 5.27 - 5.47 (m, 1 H) 4.40 (t, J=12.23 Hz, 4 H) 3.39 - 3.76 (m, 4 H) 1.98 - 2.25 (m, 2 H). Method 1: RT = 2.73 min.; M+H = 435.3

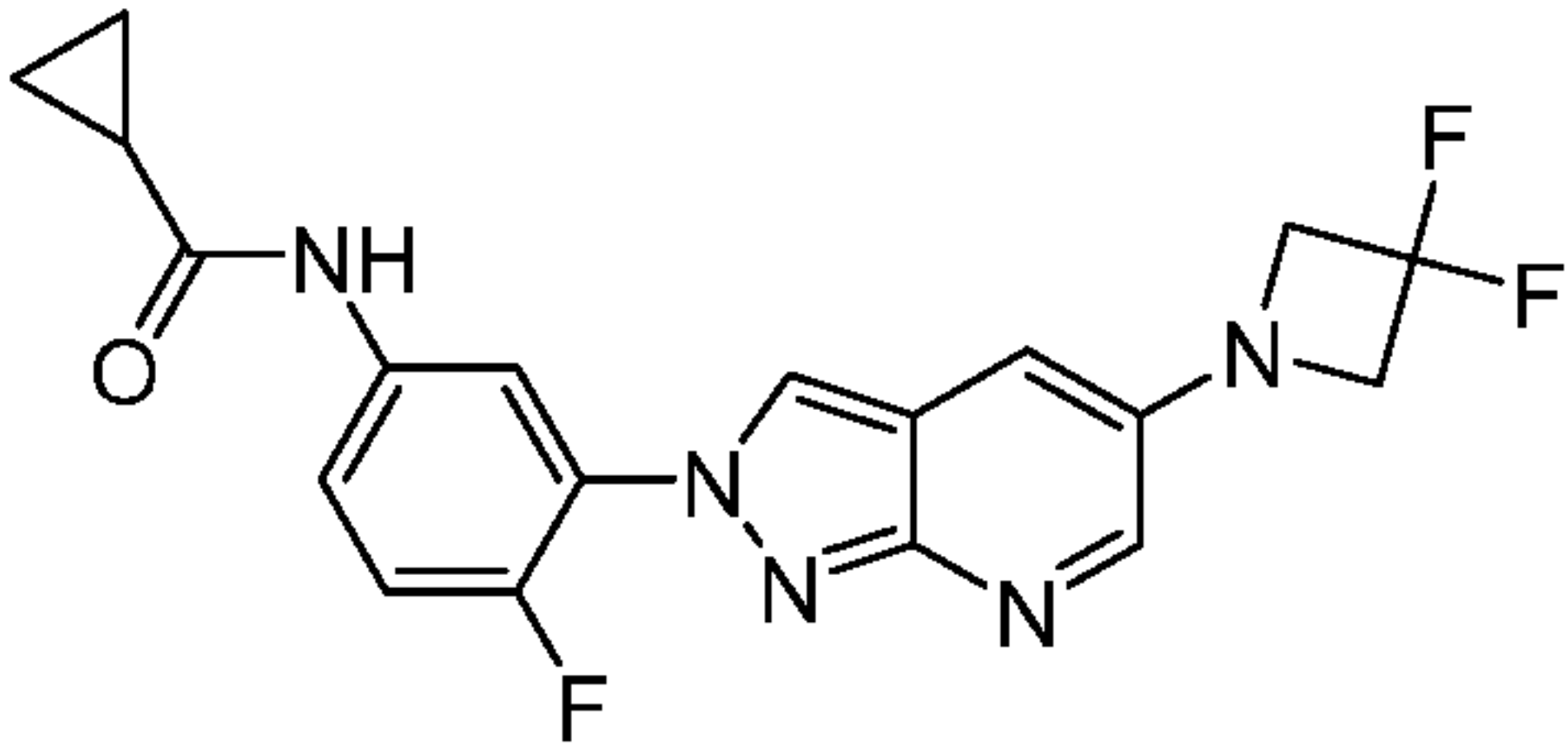
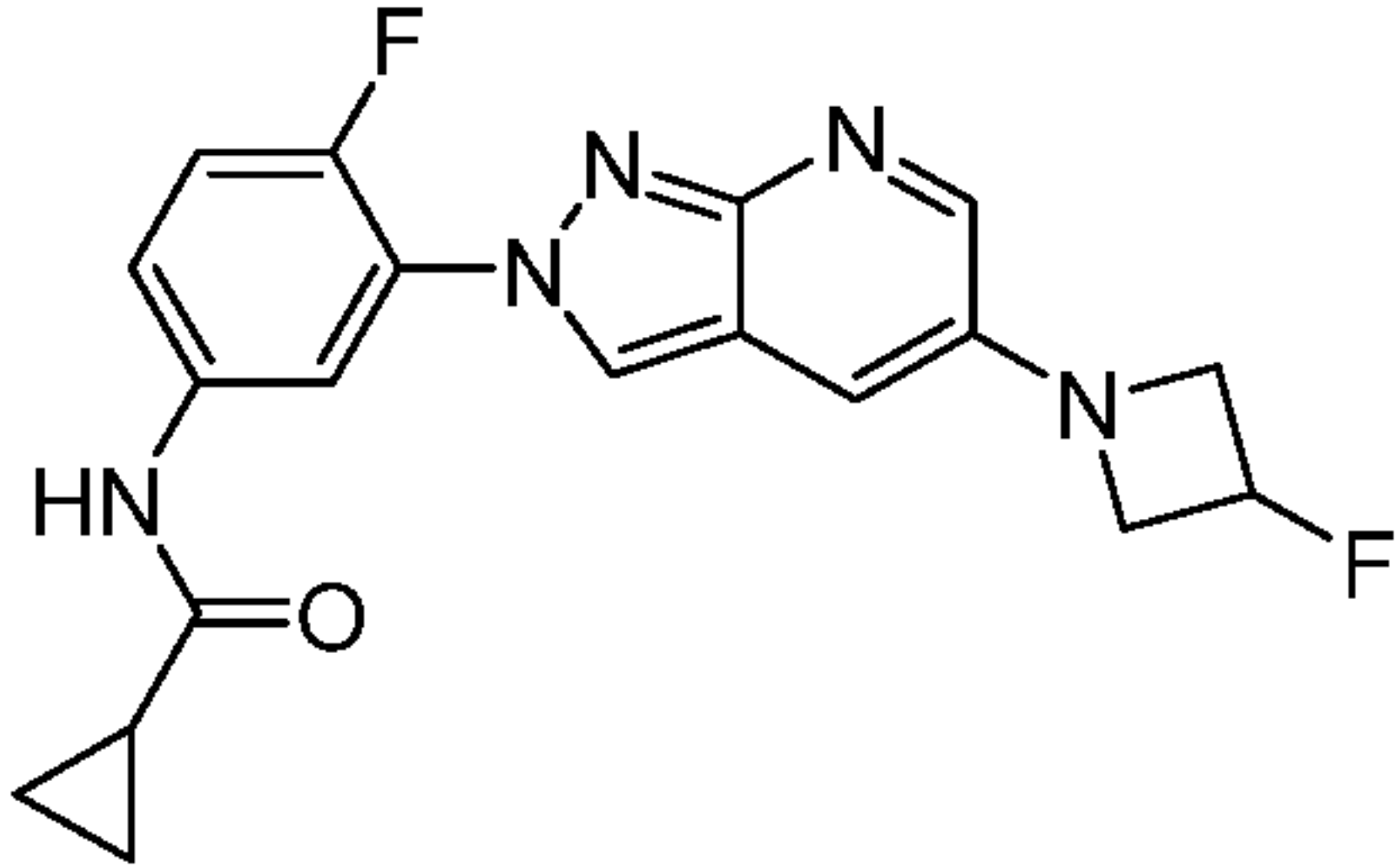
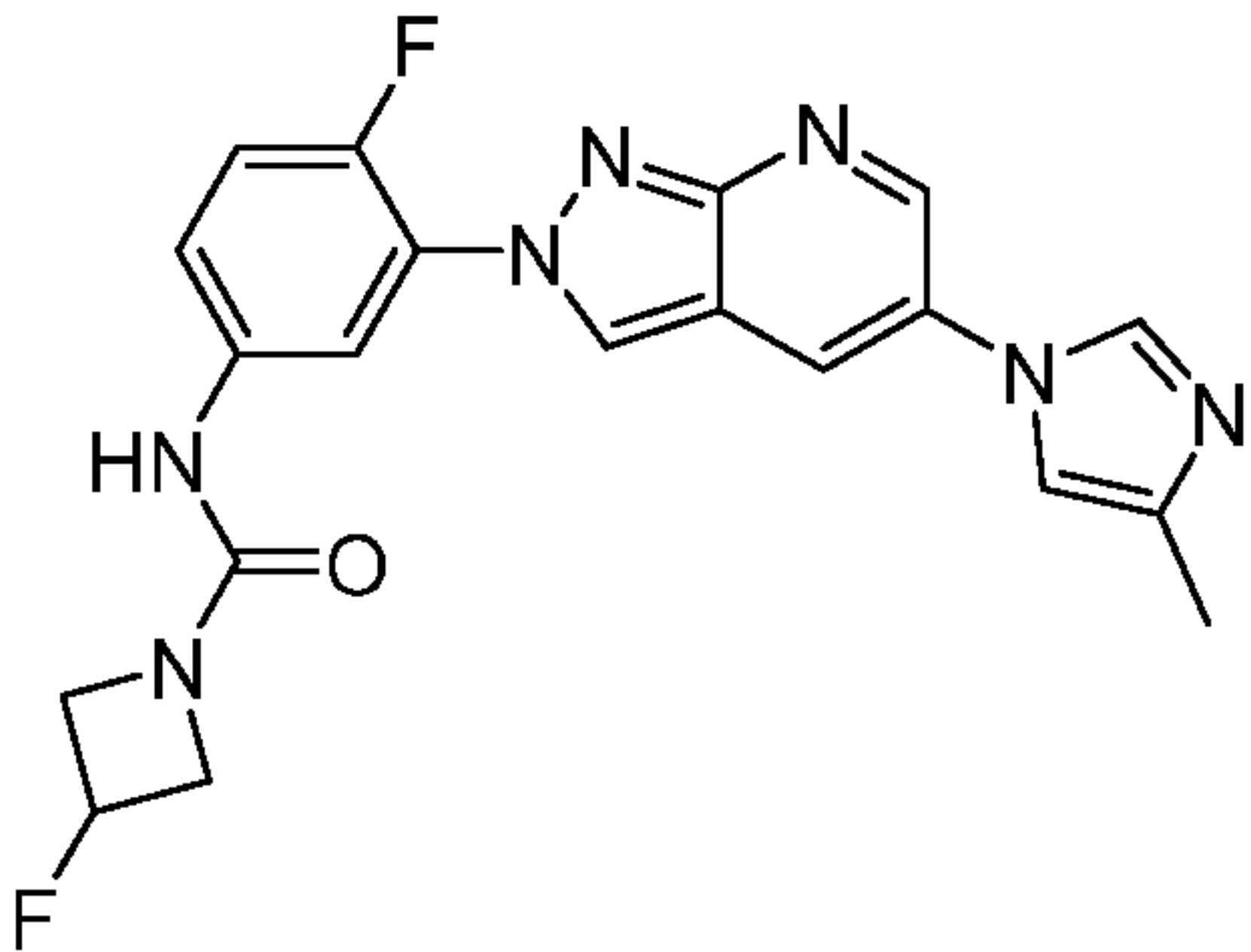
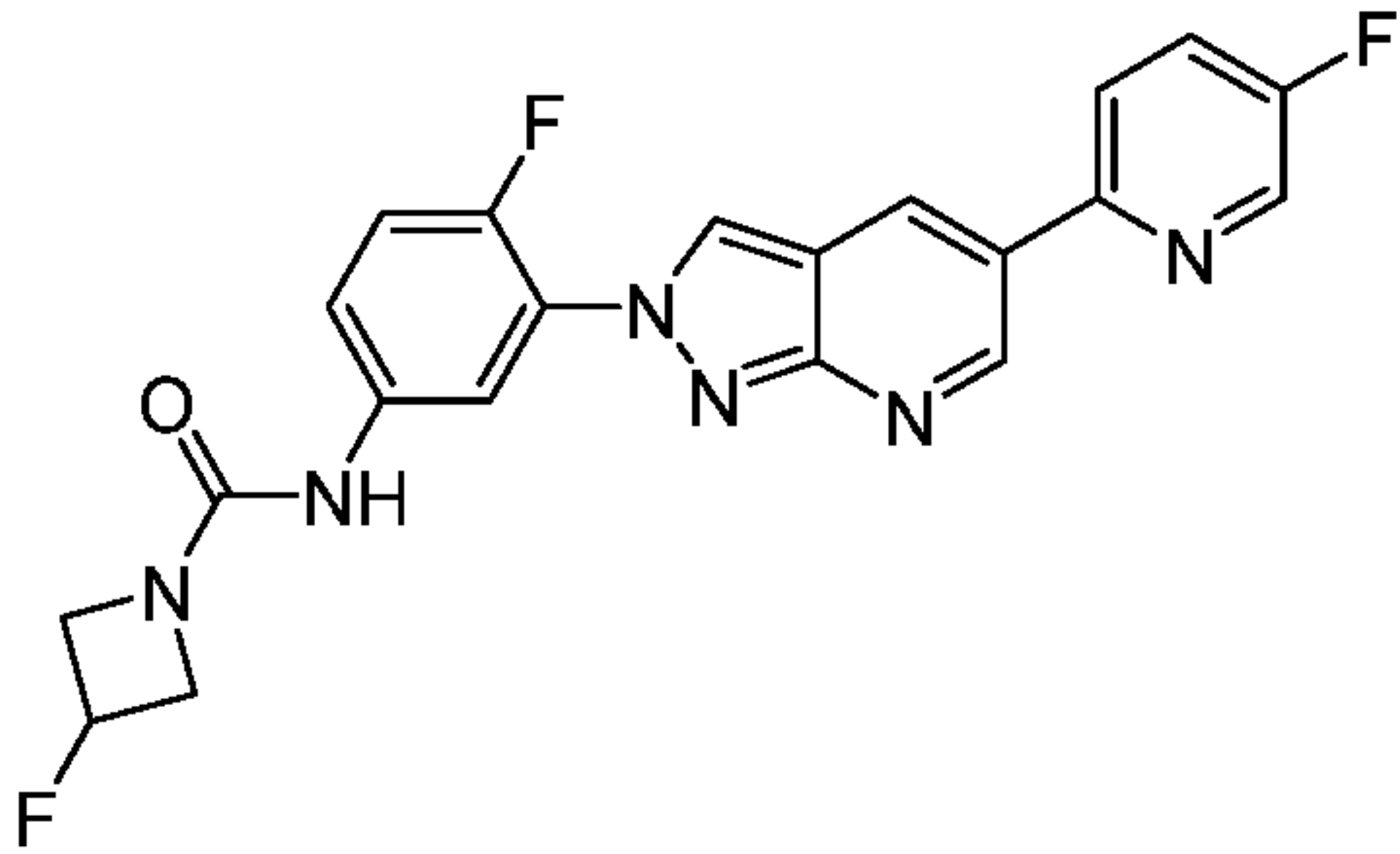
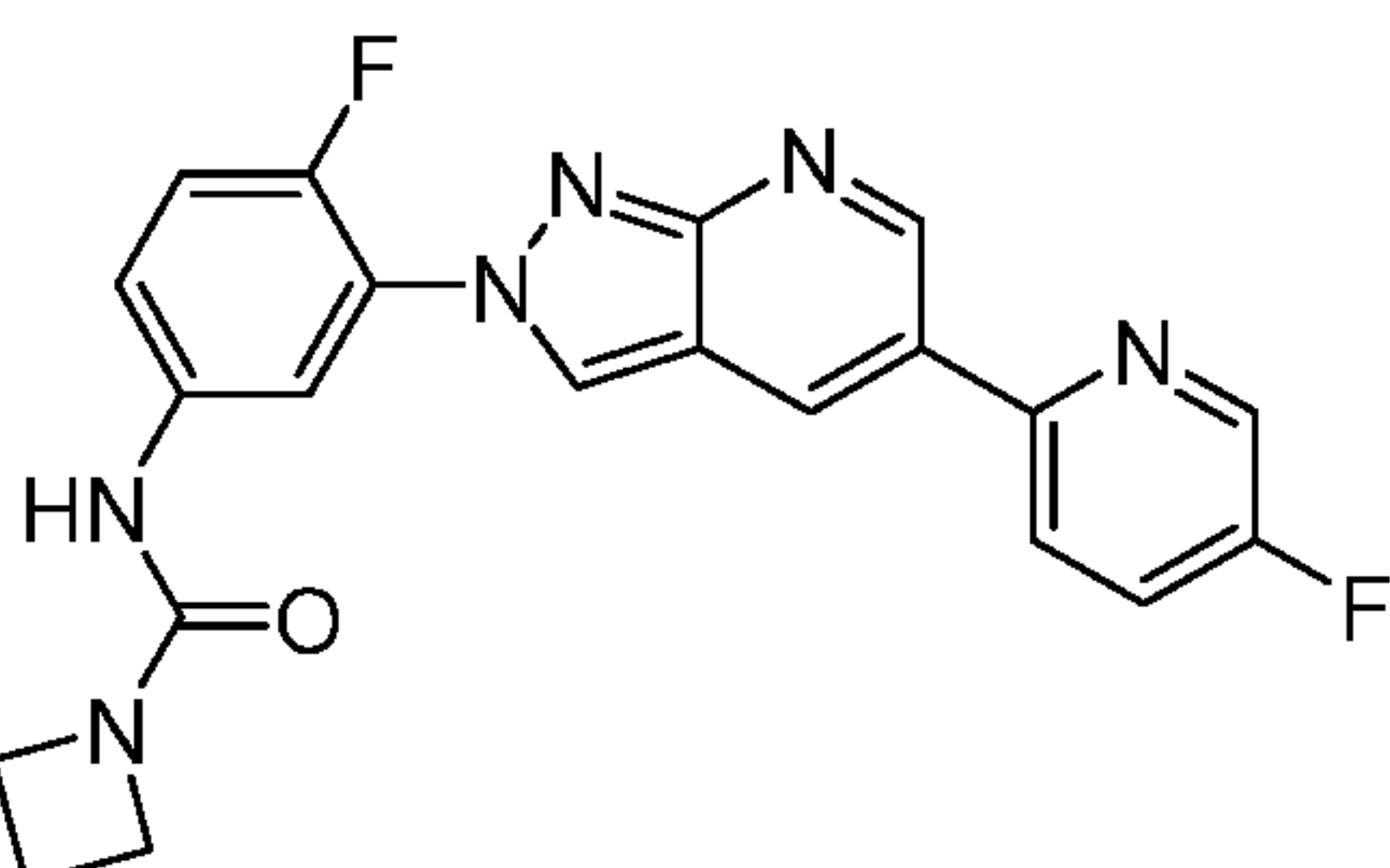
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
301		¹ H NMR (400 MHz, METHANOL-d ₄) δ 9.11 (d, J=1.96 Hz, 1 H), 8.76 (d, J=2.20 Hz, 1 H), 8.54 (d, J=1.96 Hz, 1 H), 8.16 (dd, J=6.72, 2.57 Hz, 1 H), 7.76 (s, 1 H), 7.63 - 7.70 (m, 2 H), 7.37 (dd, J=11.00, 9.29 Hz, 1 H), 5.27 - 5.50 (m, 1 H), 4.33 - 4.48 (m, 2 H), 4.09 - 4.22 (m, 2 H), 3.84 (s, 3 H). Method 1: RT = 1.97 min.; M+H = 410.2
302		¹ H NMR (400 MHz, DMSO), δ 8.55 - 8.62 (m, 2 H), 8.31 (d, J = 2.76 Hz, 1 H), 8.22 (dd, J = 7.03, 2.76 Hz, 1 H), 7.68 (dt, J = 8.97, 3.42 Hz, 1 H), 7.42 (dd, J = 11.29, 9.16 Hz, 1 H), 7.01 (d, J = 2.76 Hz, 1 H), 5.28 - 5.64 (m, 2 H), 4.20 - 4.33 (m, 2 H), 3.93 - 4.07 (m, 2 H), 3.60 - 3.76 (m, 4 H), 2.10 - 2.22 (m, 2 H). Method 2: RT = 0.83 min.; M+H = 417.1
303		¹ H NMR (400 MHz, DMSO) δ 9.22 (s, 1 H), 8.58 (d, J = 2.64 Hz, 1 H), 8.31 (d, J = 2.76 Hz, 1 H), 8.20 (dd, J = 6.96, 2.70 Hz, 1 H), 7.61 - 7.68 (m, 1 H), 7.46 (dd, J = 11.29, 9.16 Hz, 1 H), 7.01 (d, J = 2.89 Hz, 1 H), 5.42 - 5.64 (m, 1 H), 4.41 (t, J = 12.67 Hz, 4 H), 4.21 - 4.33 (m, 2 H), 3.93 - 4.06 (m, 2 H). Method 1: RT = 2.74 min.; M+H = 421.3
304		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.02 (d, J=2.26 Hz, 1 H), 8.98 (s, 1 H), 8.84 (d, J=2.76 Hz, 1 H), 8.36 (d, J=2.26 Hz, 1 H), 8.31 (s, 1 H), 8.25 (dd, J=7.03, 2.76 Hz, 1 H), 8.02 (s, 1 H), 7.65 - 7.73 (m, 1 H), 7.48 (dd, J=11.17, 9.16 Hz, 1 H), 5.29 - 5.52 (m, 1 H), 4.26 - 4.39 (m, 2 H), 3.97 - 4.10 (m, 2 H), 3.91 (s, 3 H). Method 2: RT = 0.75 min.; M+H = 410.2
305		¹ H NMR (400 MHz, METHANOL-d ₄) δ 8.69 (d, J=2.51 Hz, 1 H), 8.65 (d, J=2.26 Hz, 1 H), 8.12 - 8.17 (m, 2 H), 7.62 - 7.68 (m, 1 H), 7.32 - 7.45 (m, 3 H), 7.06 - 7.13 (m, 2 H), 5.27 - 5.48 (m, 1 H), 4.33 - 4.46 (m, 2 H), 4.07 - 4.23 (m, 2 H), 3.61 (s, 2 H), 3.08 (br d, J=11.80 Hz, 2 H), 2.70 - 2.86 (m, 1 H), 2.24 (td, J=11.86, 2.38 Hz, 2 H), 1.93 - 2.01 (m, 2 H), 1.81 - 1.93 (m, 2 H). Method 2: RT = 0.64 min.; M+H = 521.2

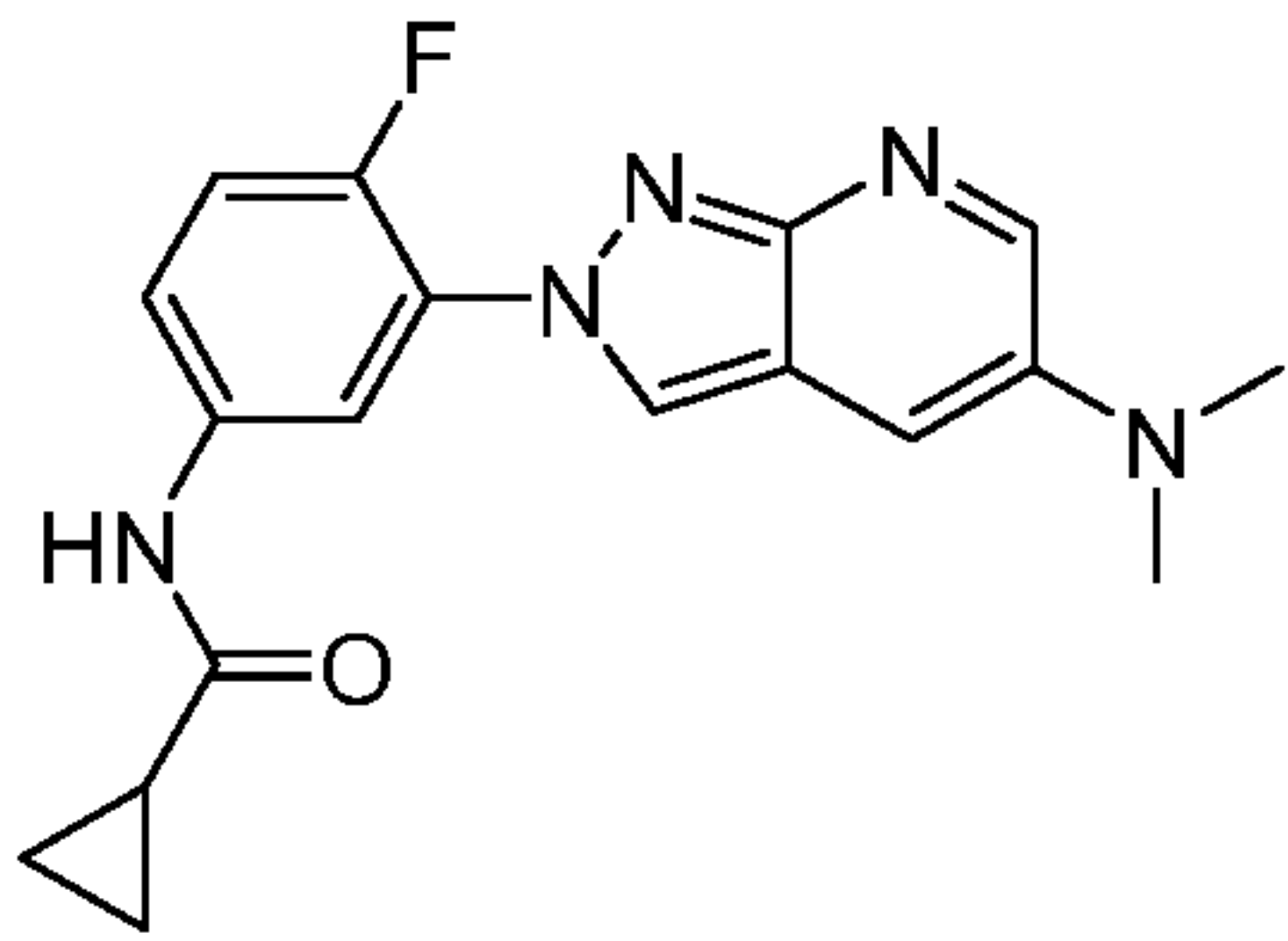
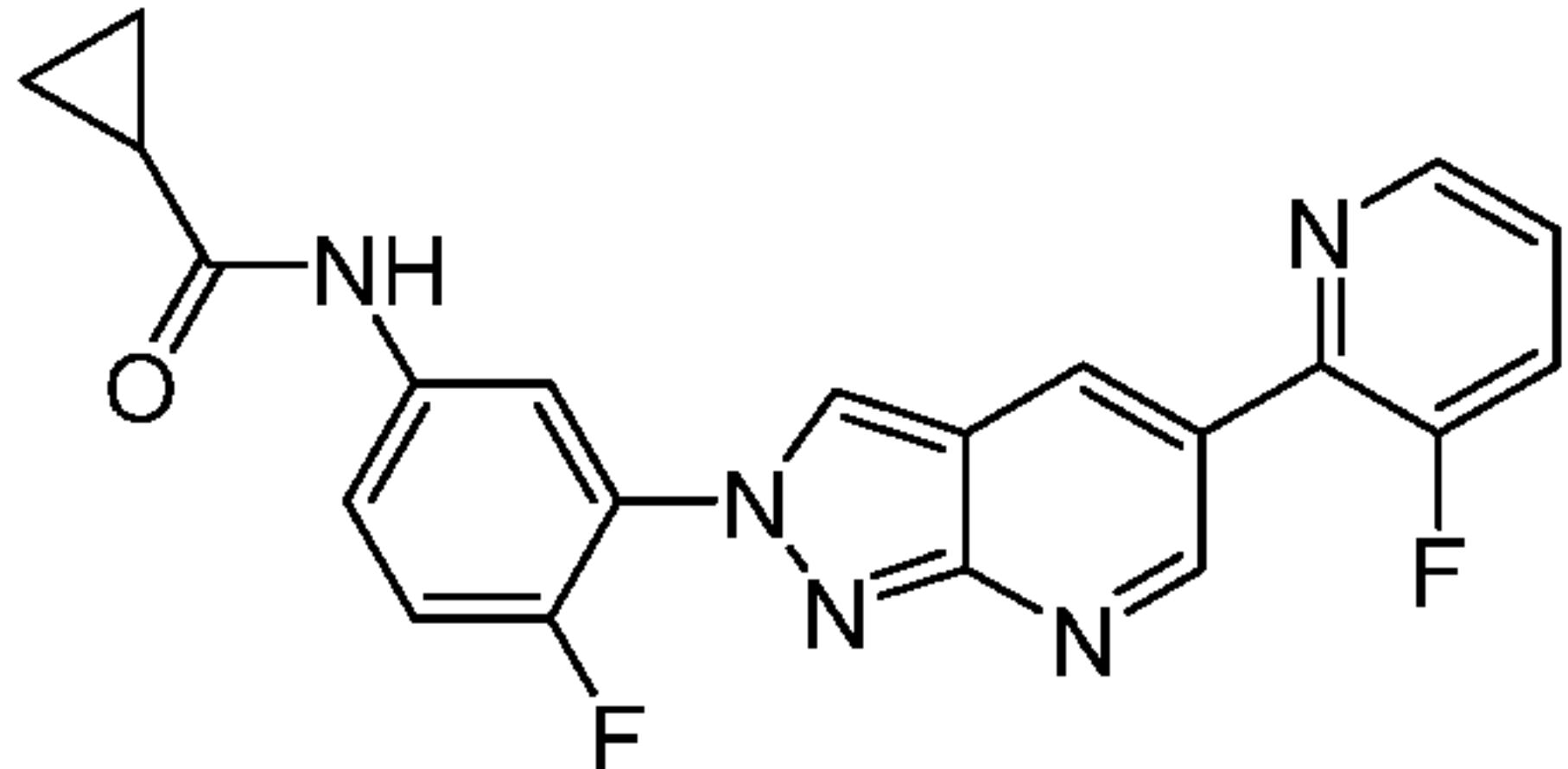
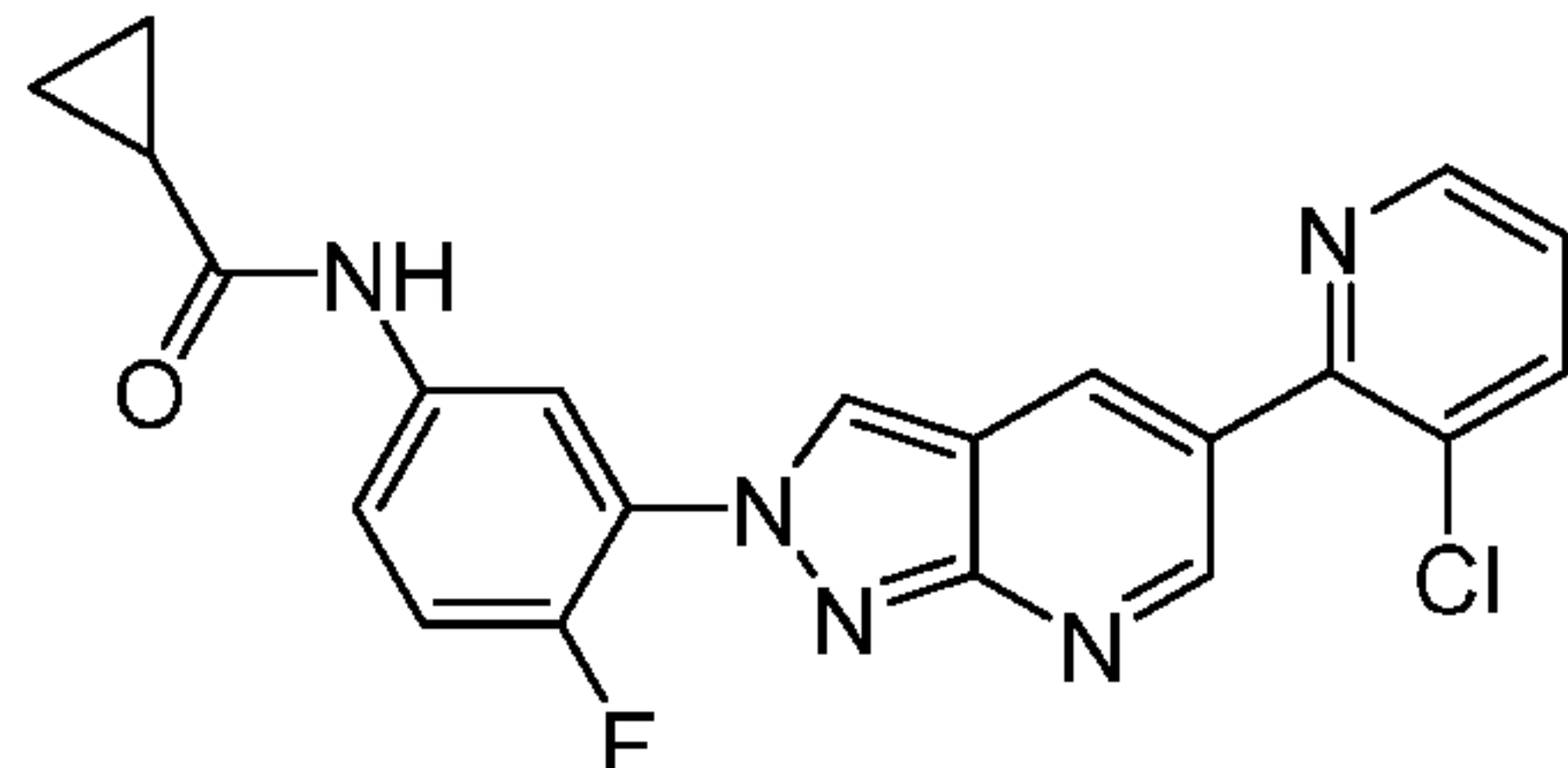
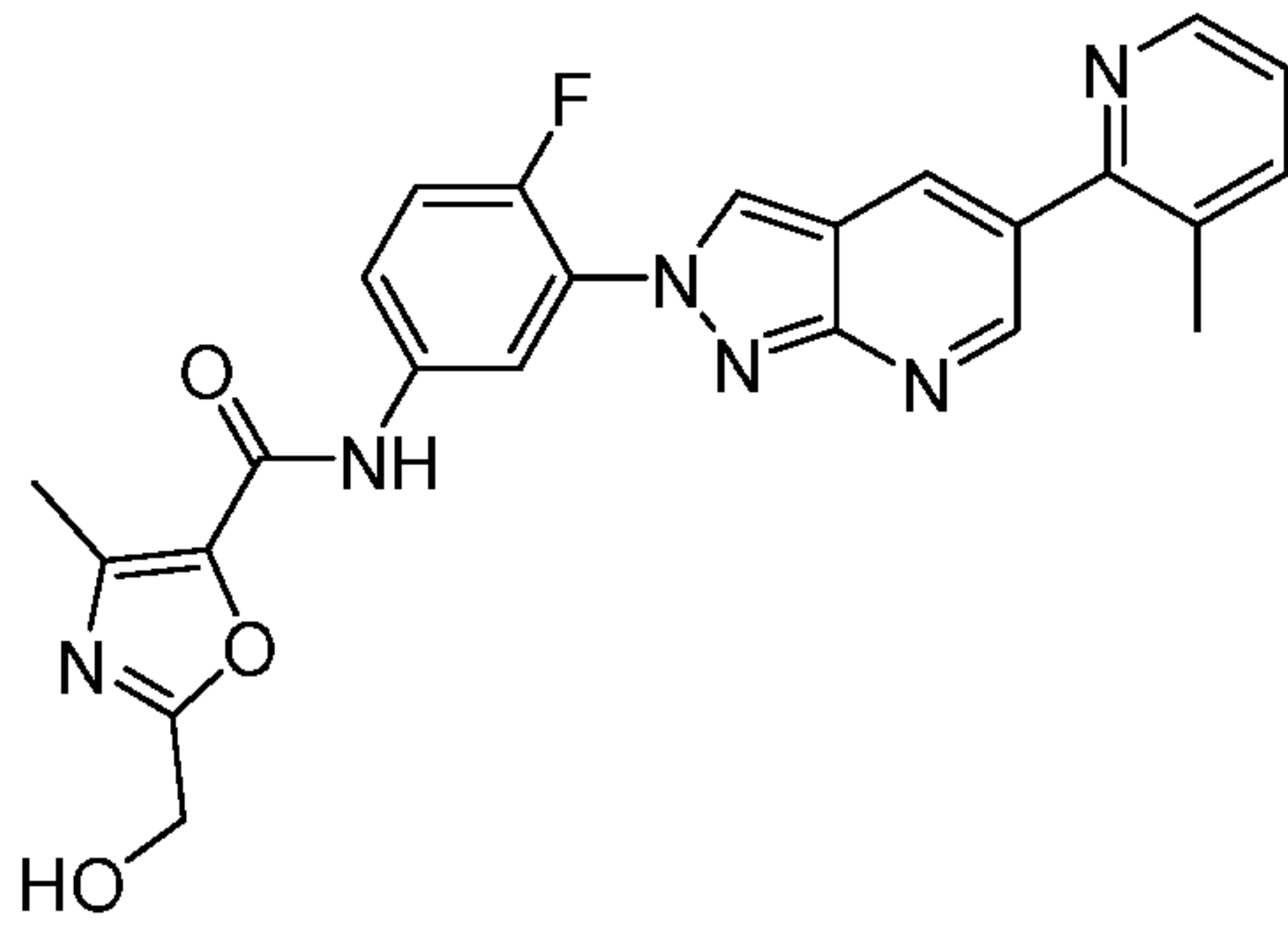
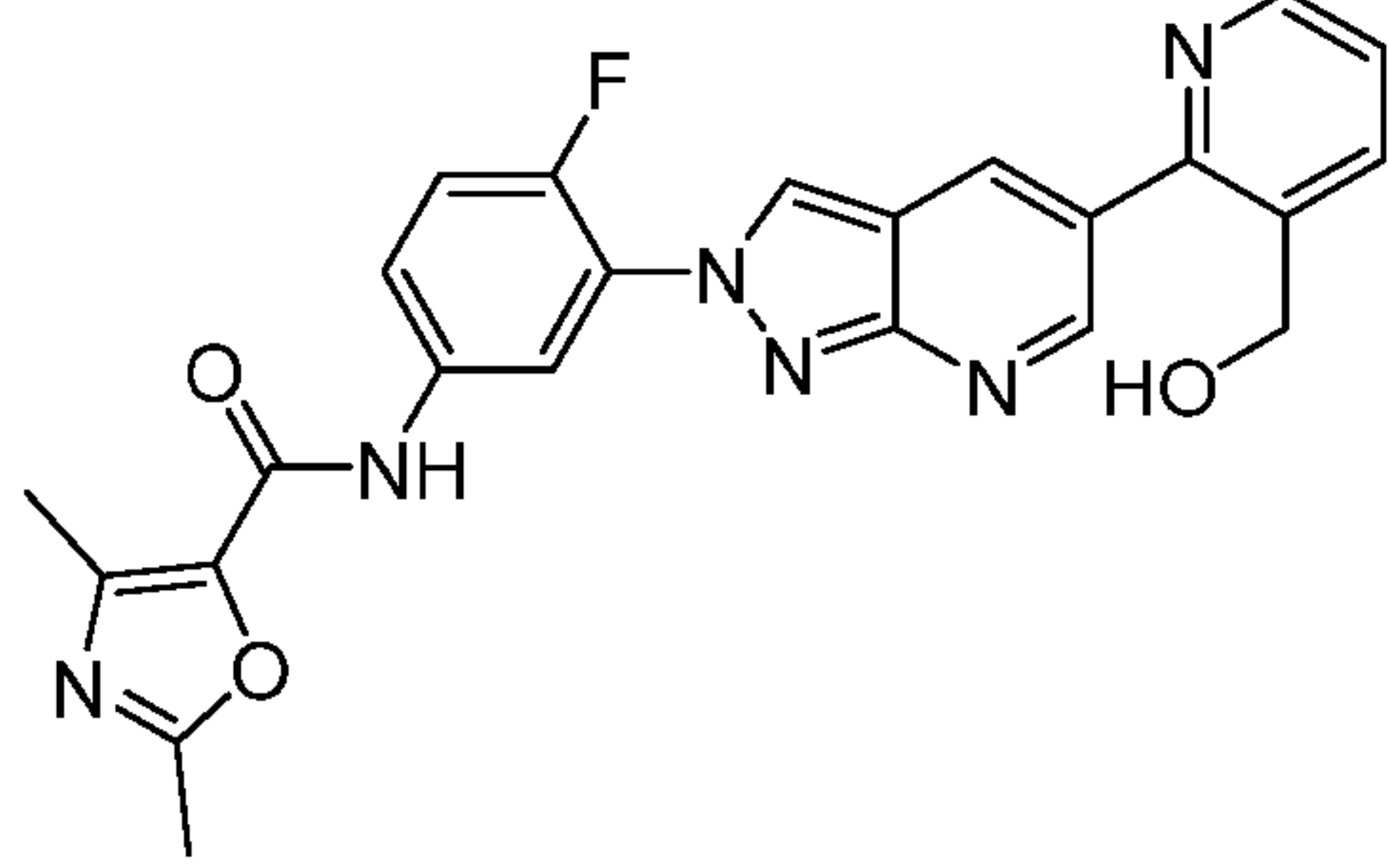
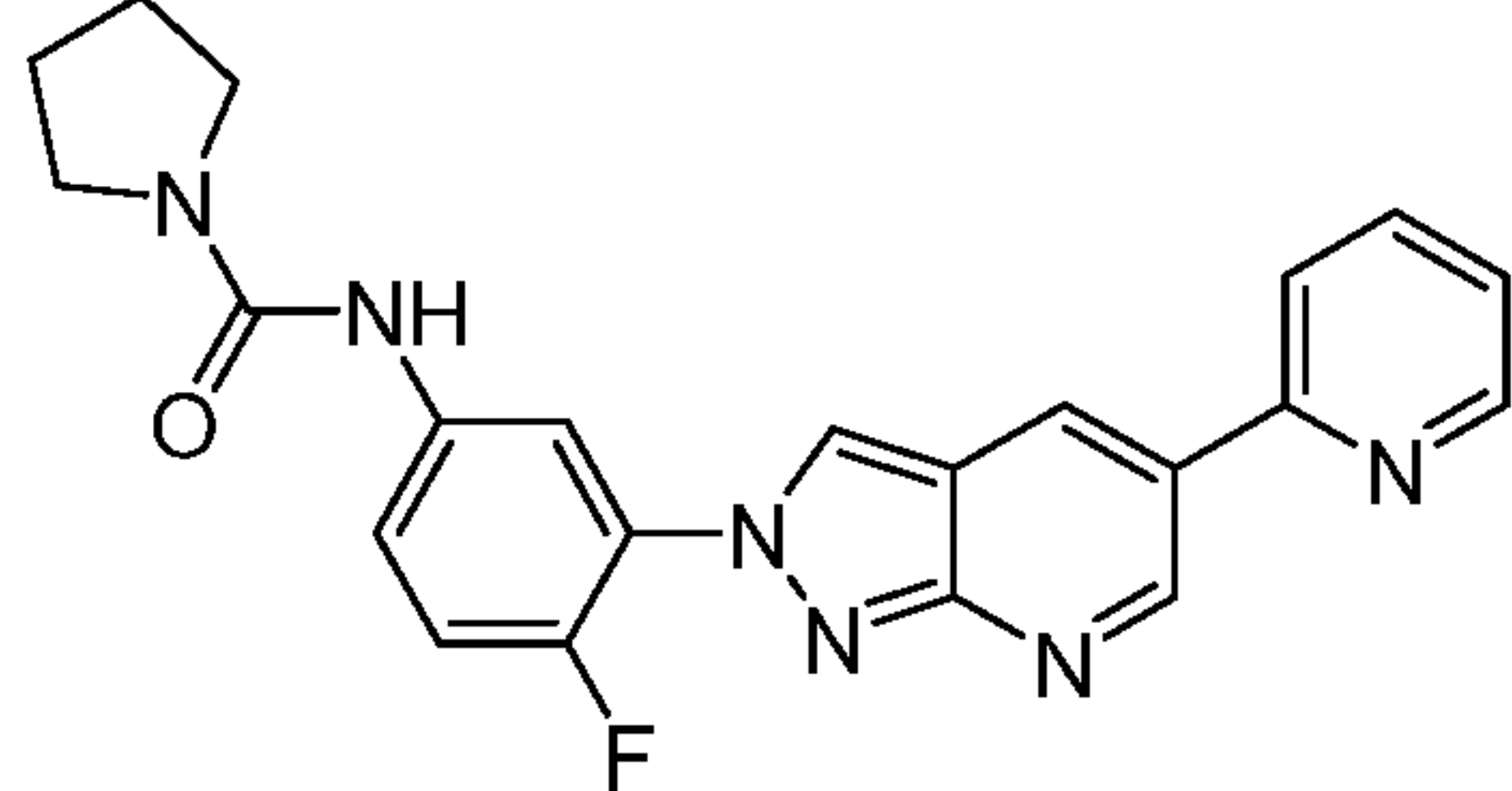
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
306		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.67 - 8.74 (m, 2 H), 8.54 (d, J=2.69 Hz, 1 H), 8.22 (dd, J=7.21, 2.81 Hz, 1 H), 7.59 - 7.77 (m, 1 H), 7.41 (dd, J=11.37, 9.17 Hz, 1 H), 7.14 (d, J=2.93 Hz, 1 H), 3.98 (t, J=7.58 Hz, 4 H), 2.20 (t, J=7.58 Hz, 2 H). Method 1: RT = 2.62 min.; M+H = 361.2
307		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.23 (s, 1 H), 8.69 (d, J=2.93 Hz, 1 H), 8.56 (d, J=2.93 Hz, 1 H), 8.21 (dd, J=6.85, 2.69 Hz, 1 H), 7.60 - 7.72 (m, 1 H), 7.46 (dd, J=11.37, 9.17 Hz, 1 H), 7.14 (d, J=2.93 Hz, 1 H), 4.41 (t, J=12.72 Hz, 4 H). Method 1: RT = 2.73 min.; M+H = 397.2
308		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.69 (d, J=2.93 Hz, 1 H), 8.62 (s, 1 H), 8.55 (d, J=2.69 Hz, 1 H), 8.24 (dd, J=7.21, 2.81 Hz, 1 H), 7.64 - 7.74 (m, 1 H), 7.43 (dd, J=11.25, 9.05 Hz, 1 H), 7.14 (d, J=2.93 Hz, 1 H), 5.27 - 5.50 (m, 1 H), 3.51 - 3.77 (m, 4 H), 2.04 - 2.25 (m, 2 H). Method 2: RT = 0.79 min.; M+H = 393.2
309		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.27 (s, 2 H), 9.06 (d, J=2.01 Hz, 1 H), 8.82 (s, 1 H), 8.63 (br d, J=4.27 Hz, 1 H), 8.28 (dd, J=6.78, 2.51 Hz, 1 H), 7.93 (dd, J=11.42, 8.41 Hz, 1 H), 7.67 - 7.76 (m, 1 H), 7.47 - 7.59 (m, 2 H), 4.42 (t, J=12.67 Hz, 4 H). Method 1: RT = 2.85 min.; M+H = 443.1
310		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.28 (s, 1 H), 9.02 (dd, J=16.81, 2.01 Hz, 2 H), 8.64 - 8.75 (m, 2 H), 8.28 (dd, J=6.78, 2.51 Hz, 1 H), 8.14 (d, J=8.28 Hz, 1 H), 7.67 - 7.77 (m, 1 H), 7.45 - 7.57 (m, 2 H), 4.43 (t, J=12.67 Hz, 4 H). Method 1: RT = 2.86 min.; M+H = 459.1

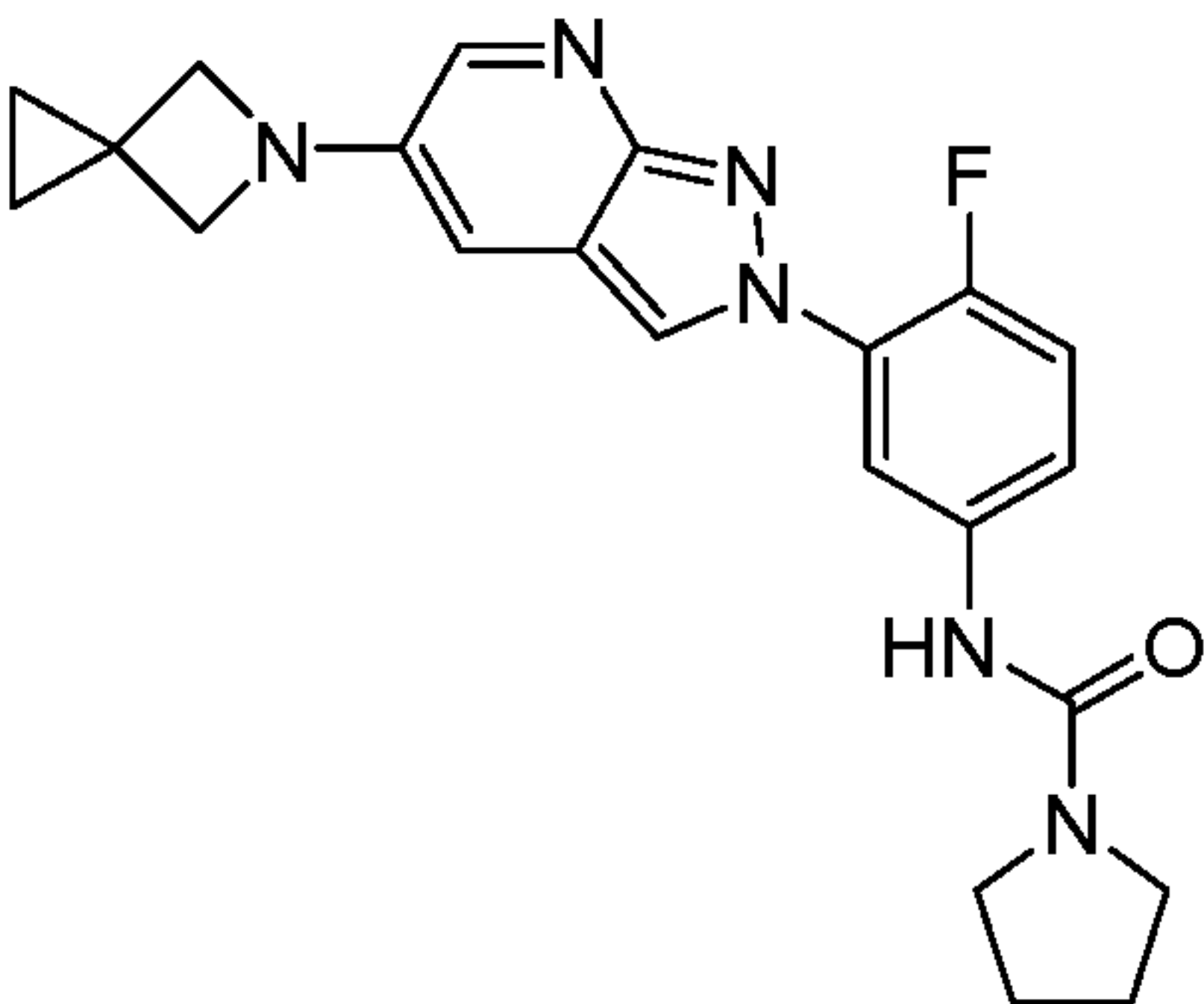
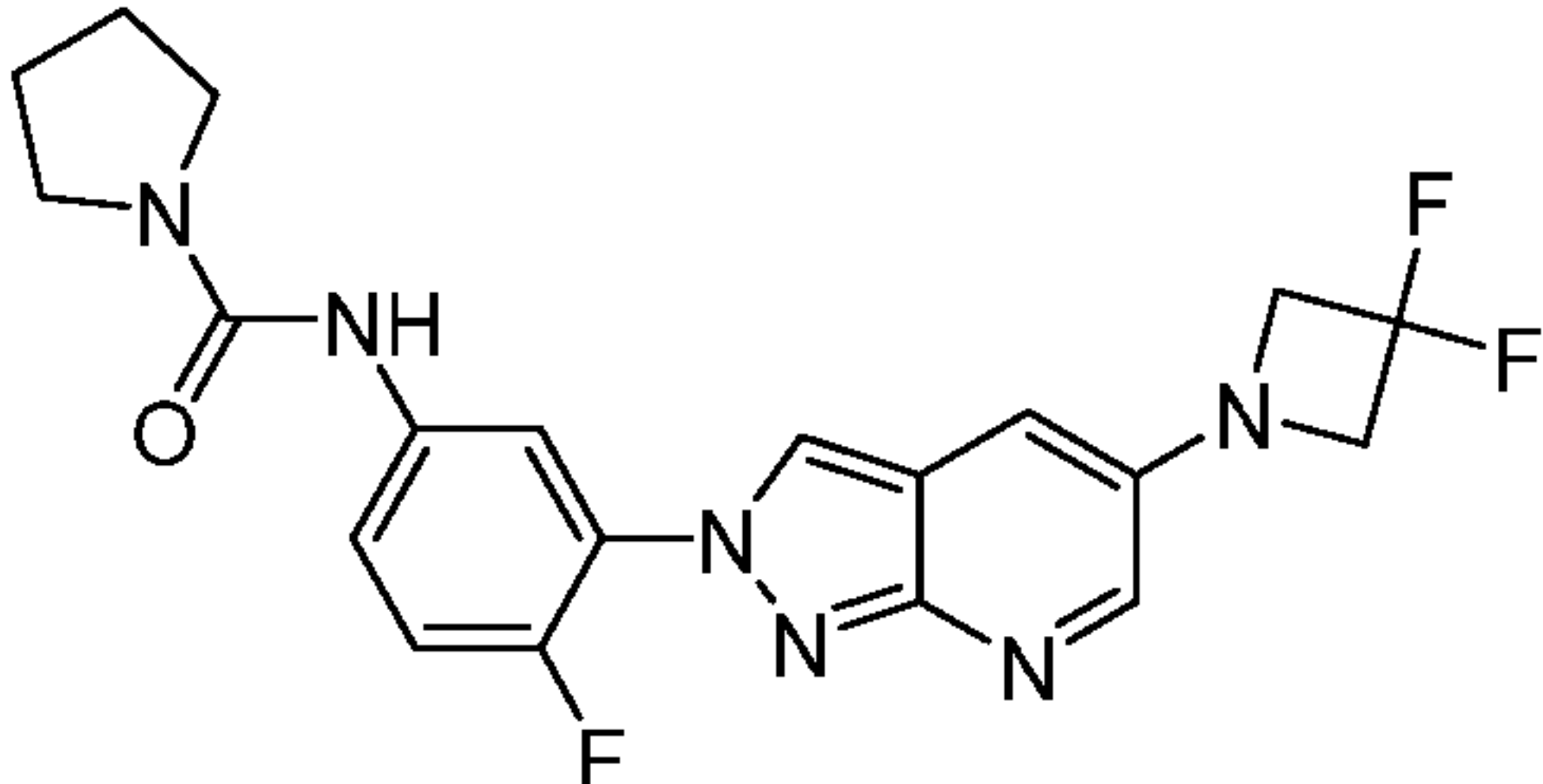
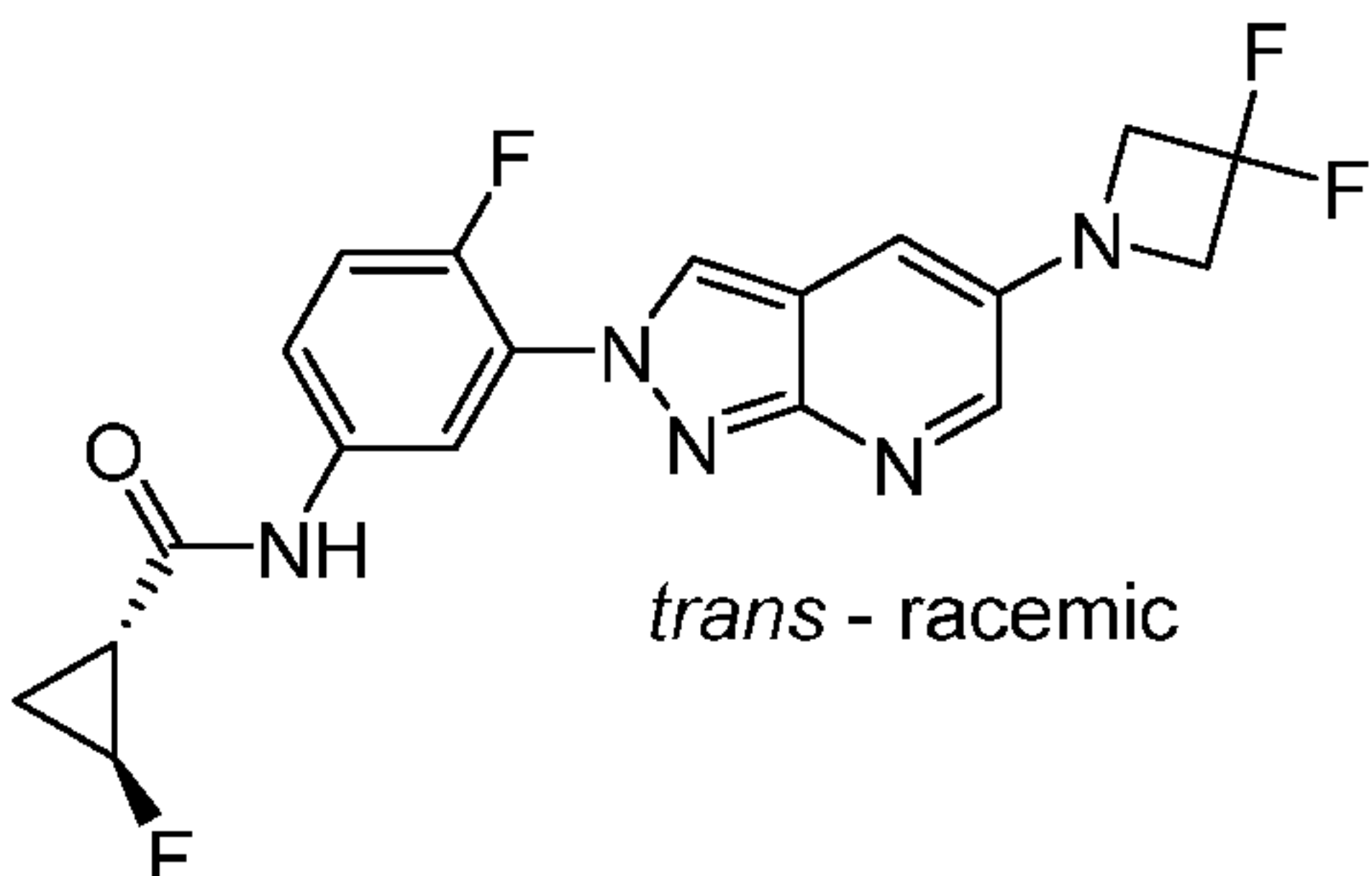
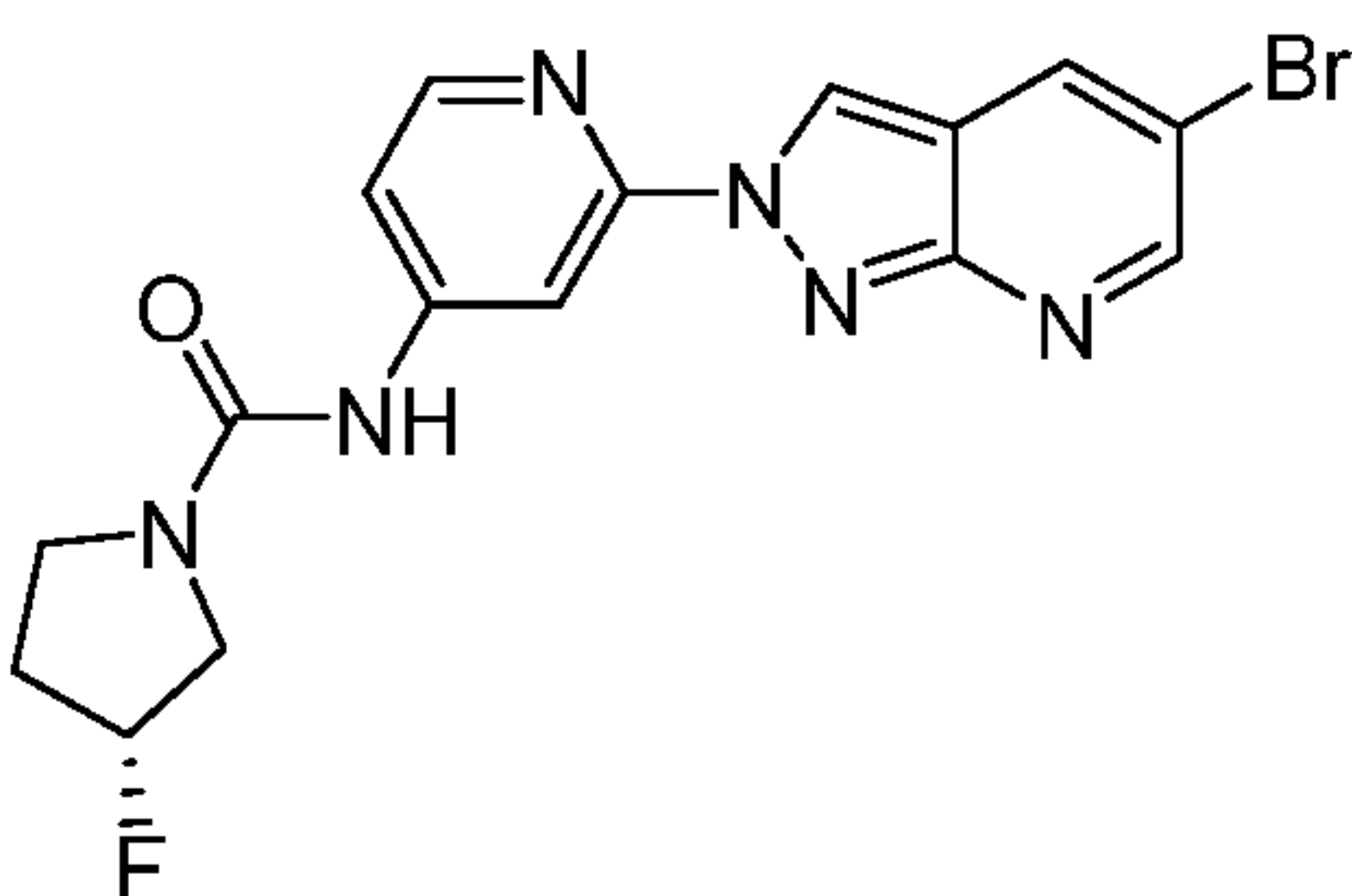
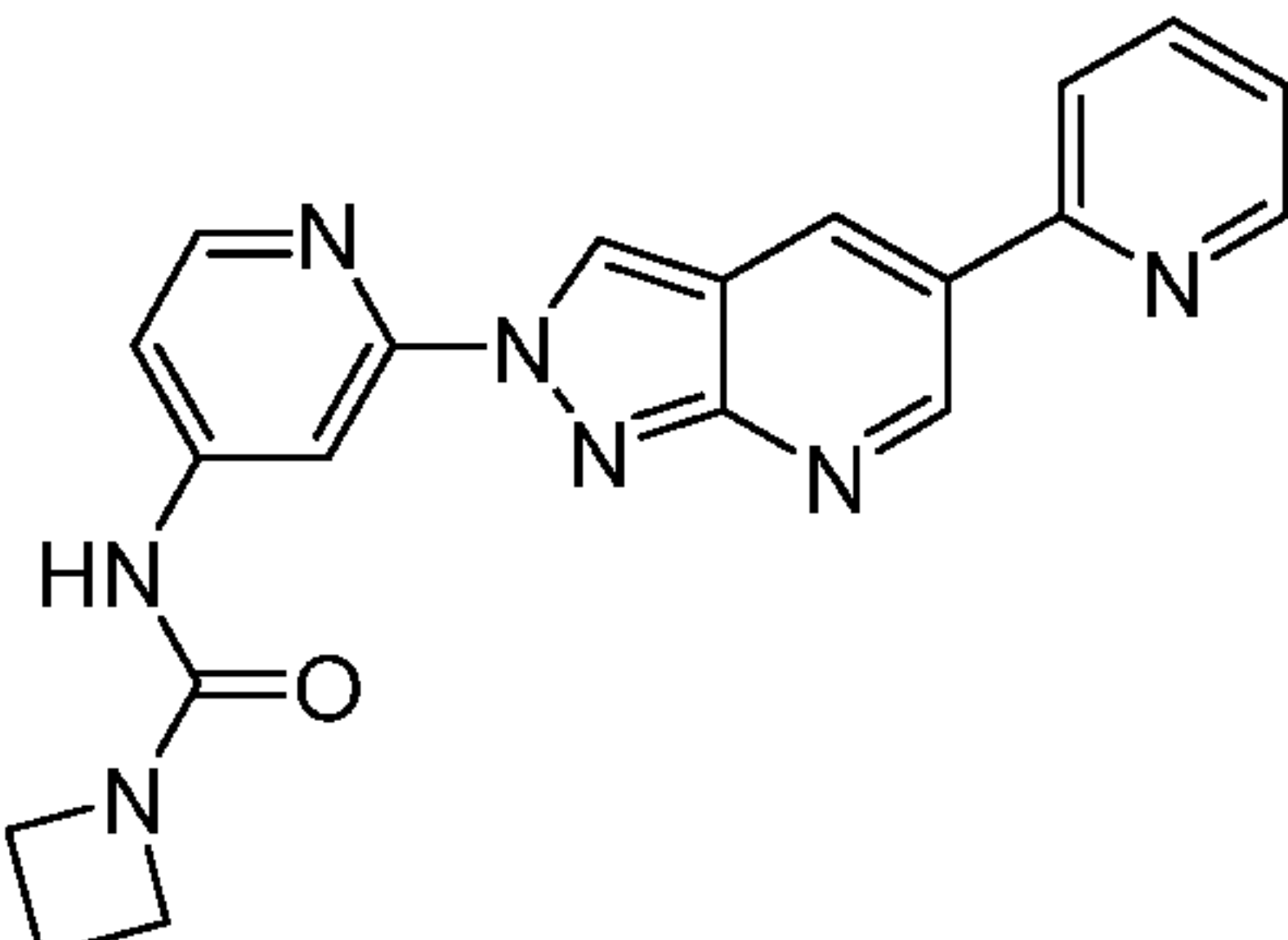
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
311		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.98 (s, 1 H), 8.90 (d, J=2.26 Hz, 1 H), 8.72 (d, J=3.01 Hz, 1 H), 8.31 (d, J=8.28 Hz, 1 H), 8.25 (dd, J=7.03, 2.51 Hz, 1 H), 7.66 - 7.73 (m, 1 H), 7.43 - 7.51 (m, 1 H), 7.20 (dd, J=8.41, 4.14 Hz, 1 H), 5.29 - 5.51 (m, 1 H), 4.24 - 4.39 (m, 2 H), 3.96 - 4.10 (m, 2 H). Method 1: RT = 2.41 min.; M+H = 330.1
312		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.93 - 9.06 (m, 3 H), 8.54 - 8.68 (m, 3 H), 8.29 (dd, J=6.90, 2.38 Hz, 1 H), 7.67 - 7.76 (m, 1 H), 7.49 (t, J=10.16 Hz, 1 H), 5.27 - 5.55 (m, 1 H), 4.25 - 4.42 (m, 2 H), 3.94 - 4.14 (m, 2 H), 2.68 (s, 3 H). Method 1: RT = 2.48 min.; M+H = 422.1
313		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.27 (s, 1 H), 9.04 (d, J=2.26 Hz, 1 H), 8.82 (d, J=1.51 Hz, 1 H), 8.75 (s, 1 H), 8.63 (br d, J=4.52 Hz, 1 H), 8.30 (dd, J=6.90, 2.64 Hz, 1 H), 7.93 (dd, J=10.92, 8.91 Hz, 1 H), 7.73 (dt, J=9.03, 3.39 Hz, 1 H), 7.55 (dt, J=8.34, 4.24 Hz, 1 H), 7.48 (dd, J=11.29, 9.03 Hz, 1 H), 3.91 - 4.07 (m, 4 H), 2.21 (quin, J=7.53 Hz, 2 H). Method 2: RT = 0.85 min.; M+H = 407.1
314		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.94 (s, 1 H), 8.69 (d, J=3.01 Hz, 1 H), 8.54 (d, J=2.76 Hz, 1 H), 8.21 (dd, J=7.03, 2.76 Hz, 1 H), 7.61 - 7.71 (m, 1 H), 7.43 (dd, J=11.42, 9.16 Hz, 1 H), 7.14 (d, J=3.01 Hz, 1 H), 5.28 - 5.53 (m, 1 H), 4.22 - 4.43 (m, 2 H), 3.92 - 4.11 (m, 2 H). Method 1: RT = 2.63 min.; M+H = 379.3
315		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.02 (d, J=2.51 Hz, 1 H), 9.00 (d, J=2.26 Hz, 1 H), 8.76 (s, 1 H), 8.72 (dd, J=4.64, 1.38 Hz, 1 H), 8.68 (d, J=2.26 Hz, 1 H), 8.29 (dd, J=6.90, 2.64 Hz, 1 H), 8.14 (dd, J=8.16, 1.38 Hz, 1 H), 7.68 - 7.82 (m, 1 H), 7.40 - 7.55 (m, 2 H), 3.99 (t, J=7.53 Hz, 4 H), 2.21 (quin, J=7.59 Hz, 2 H). Method 1: RT = 2.73 min.; M+H = 423.1

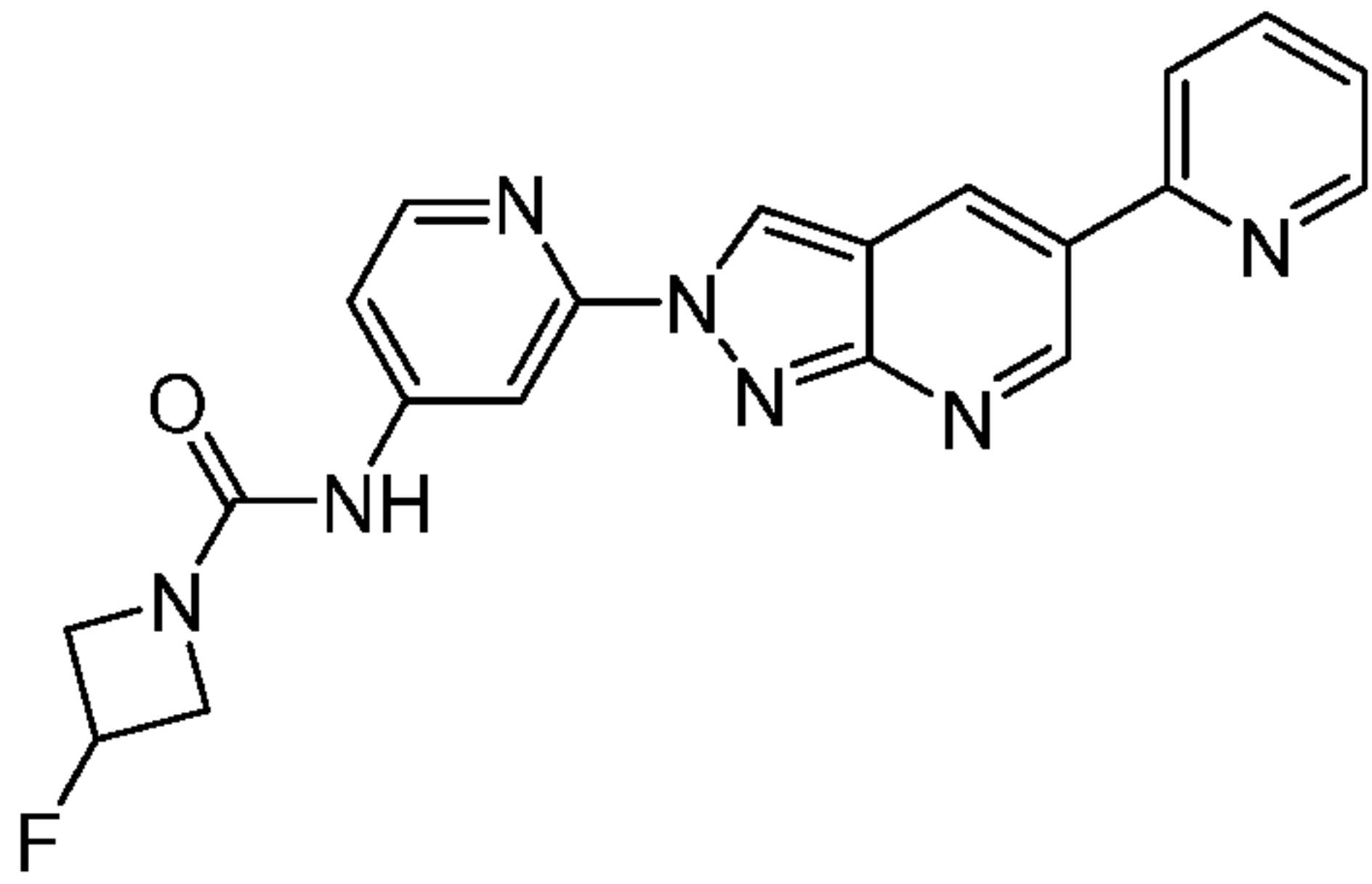
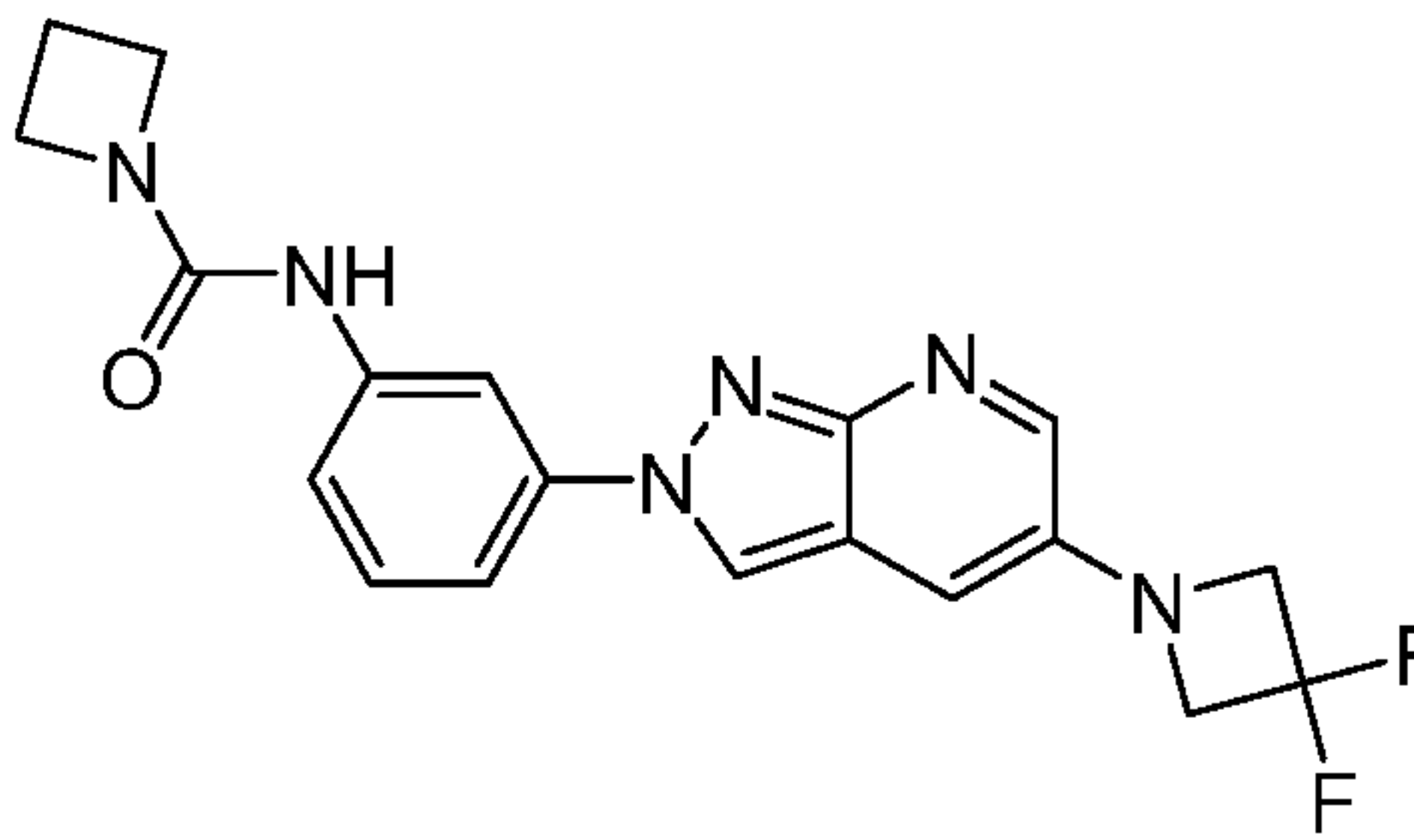
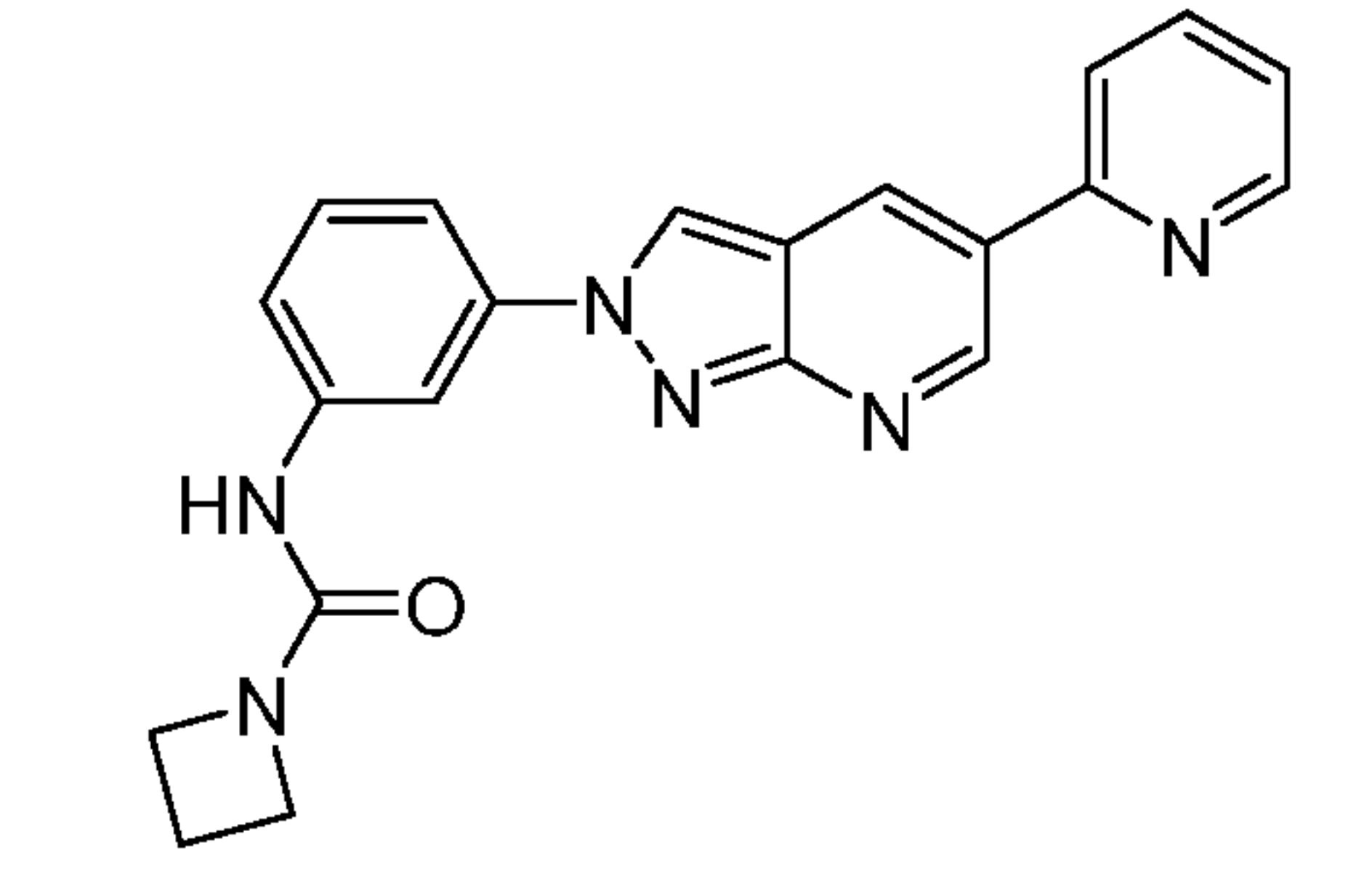
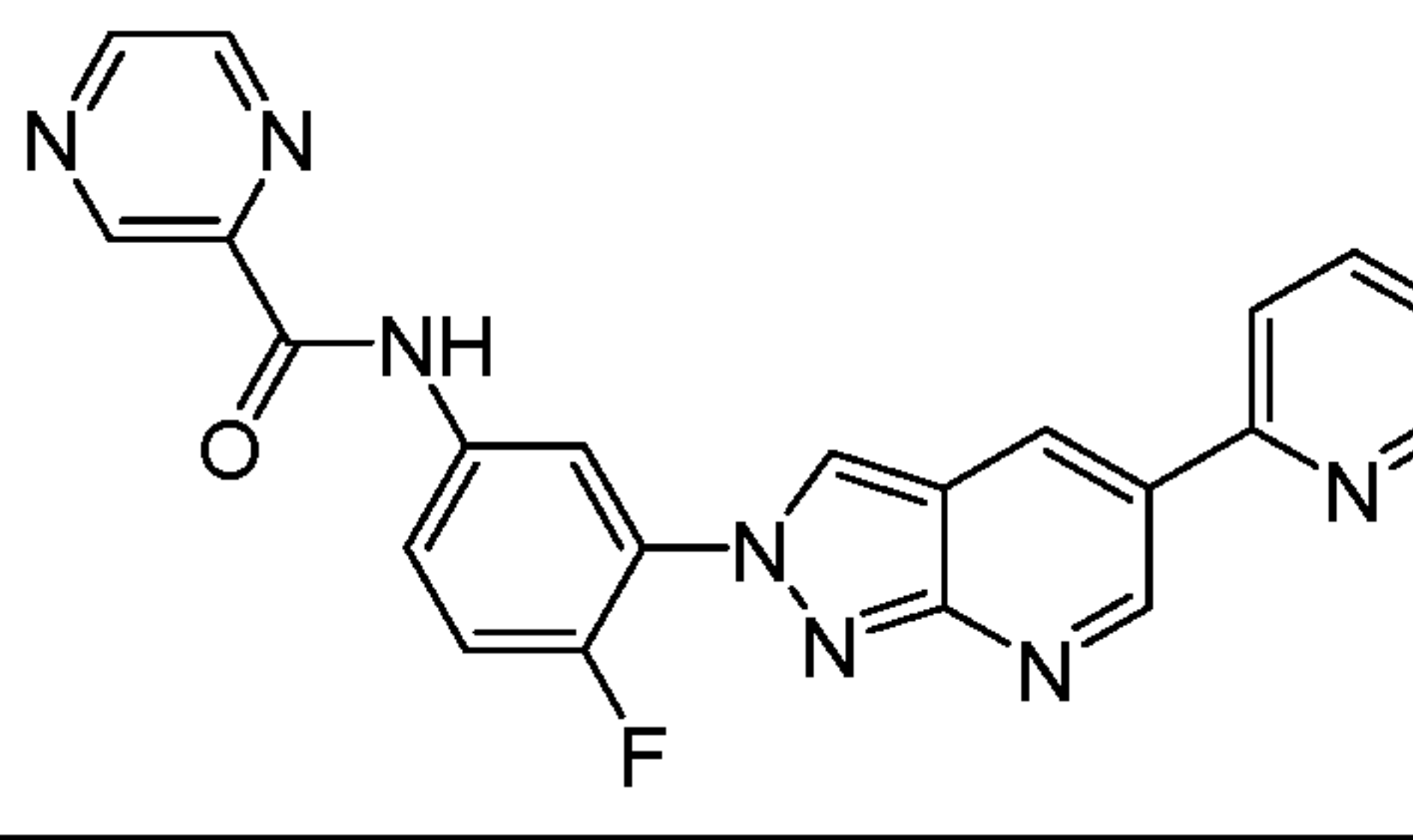
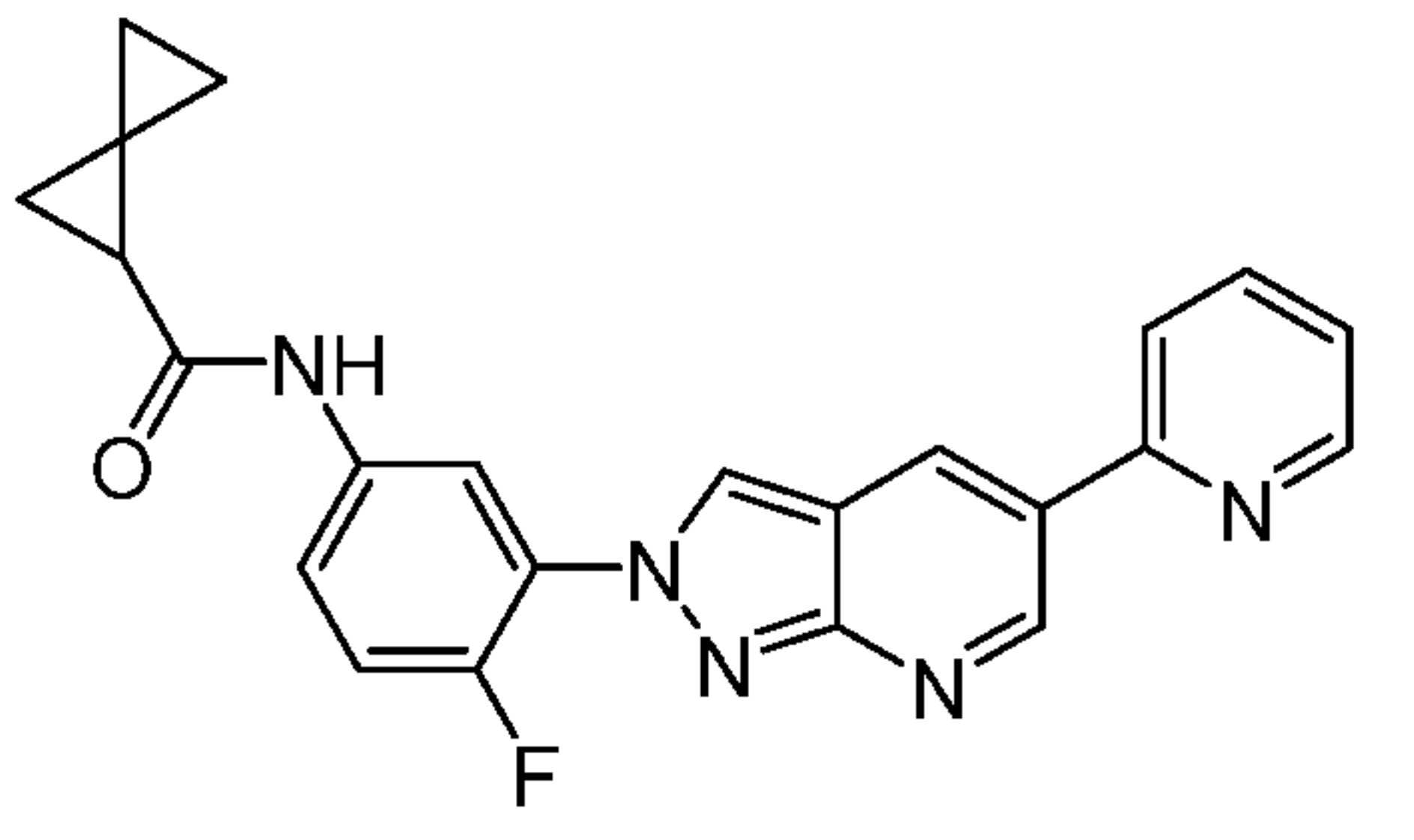
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
316		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.04 (d, J=2.45 Hz, 1 H), 9.00 (d, J=2.20 Hz, 1 H), 8.72 (dd, J=4.65, 1.47 Hz, 1 H), 8.65 - 8.70 (m, 2 H), 8.32 (dd, J=6.85, 2.69 Hz, 1 H), 8.14 (dd, J=8.19, 1.35 Hz, 1 H), 7.71 - 7.80 (m, 1 H), 7.45 - 7.56 (m, 2 H), 5.26 - 5.52 (m, 1 H), 3.40 - 3.81 (m, 4 H), 2.01 - 2.28 (m, 2 H). Method 2: RT = 0.89 min.; M+H = 455.2
317		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.27 (dd, J=2.20, 1.22 Hz, 1 H), 9.05 (d, J=2.45 Hz, 1 H), 8.80 - 8.86 (m, 1 H), 8.67 (s, 1 H), 8.63 (dt, J=4.65, 1.71 Hz, 1 H), 8.31 (dd, J=7.09, 2.69 Hz, 1 H), 7.93 (ddd, J=11.68, 8.38, 1.22 Hz, 1 H), 7.71 - 7.79 (m, 1 H), 7.55 (dt, J=8.38, 4.25 Hz, 1 H), 7.49 (dd, J=11.25, 9.05 Hz, 1 H), 5.26 - 5.54 (m, 1 H), 3.42 - 3.80 (m, 4 H), 2.01 - 2.27 (m, 2 H). Method 2: RT = 0.87 min.; M+H = 439.1
318		¹ H NMR (400 MHz, METHANOL-d ₄) δ 8.65 (d, J=2.45 Hz, 1 H), 8.60 (d, J=2.20 Hz, 1 H), 8.14 (dd, J=6.72, 2.81 Hz, 1 H), 8.09 (dd, J=2.08, 1.10 Hz, 1 H), 7.62 - 7.70 (m, 1 H), 7.36 (dd, J=11.00, 9.05 Hz, 1 H), 5.26 - 5.51 (m, 1 H), 4.33 - 4.48 (m, 2 H), 4.06 - 4.23 (m, 2 H), 2.50 (d, J=0.98 Hz, 3 H). Method 1: RT = 2.62 min.; M+H = 344.1
319		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.29 - 9.35 (m, 1 H), 8.94 - 9.07 (m, 2 H), 8.64 (d, J=2.51 Hz, 1 H), 8.62 (d, J=2.76 Hz, 1 H), 8.27 (dd, J=7.03, 2.76 Hz, 1 H), 7.85 (d, J=1.76 Hz, 1 H), 7.67 - 7.75 (m, 1 H), 7.67 - 7.75 (m, 1 H), 7.50 (dd, J=11.17, 9.16 Hz, 1 H), 6.61 - 6.68 (m, 1 H), 5.27 - 5.61 (m, 1 H), 4.23 - 4.43 (m, 2 H), 3.95 - 4.14 (m, 2 H). Method 1: RT = 2.59 min.; M+H = 396.1
320		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.14 (d, J=2.26 Hz, 1 H), 9.01 (d, J=2.51 Hz, 1 H), 8.86 - 8.91 (m, 1 H), 8.78 (s, 1 H), 8.30 (dd, J=6.90, 2.64 Hz, 1 H), 7.70 - 7.78 (m, 1 H), 7.49 (dd, J=11.17, 9.16 Hz, 1 H), 3.98 (t, J=7.53 Hz, 4 H), 2.15 - 2.27 (m, 2 H). Method 1: RT = 2.82 min.; M+H = 380.1

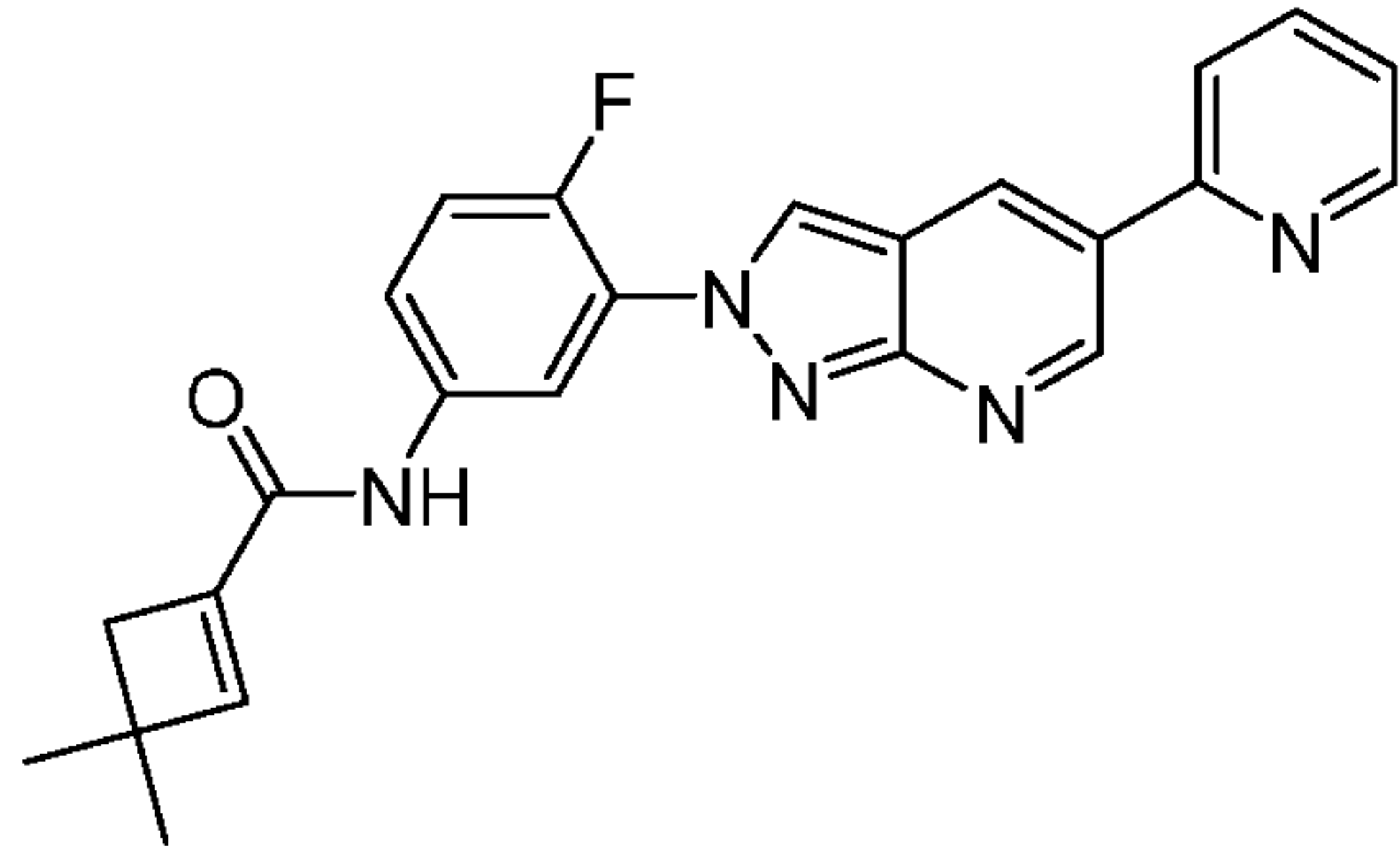
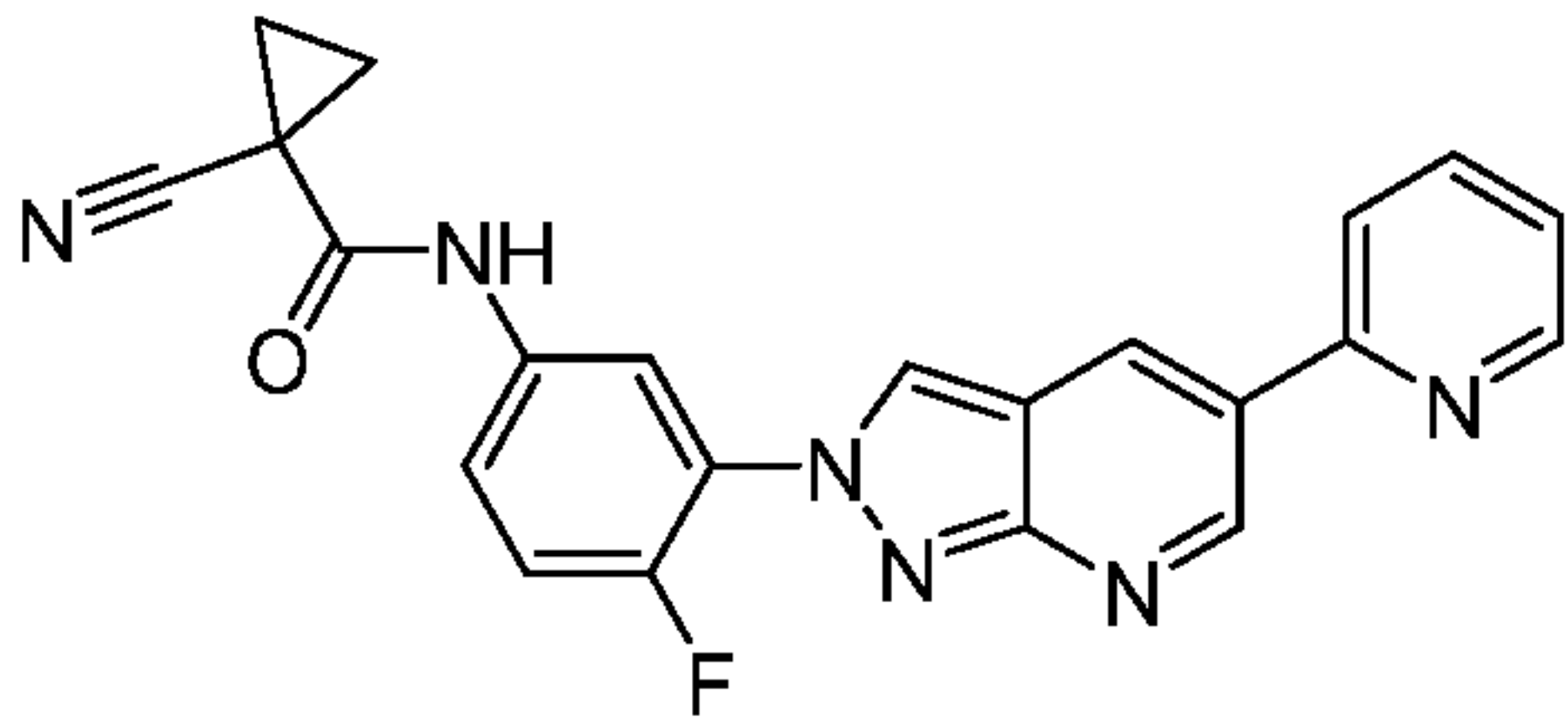
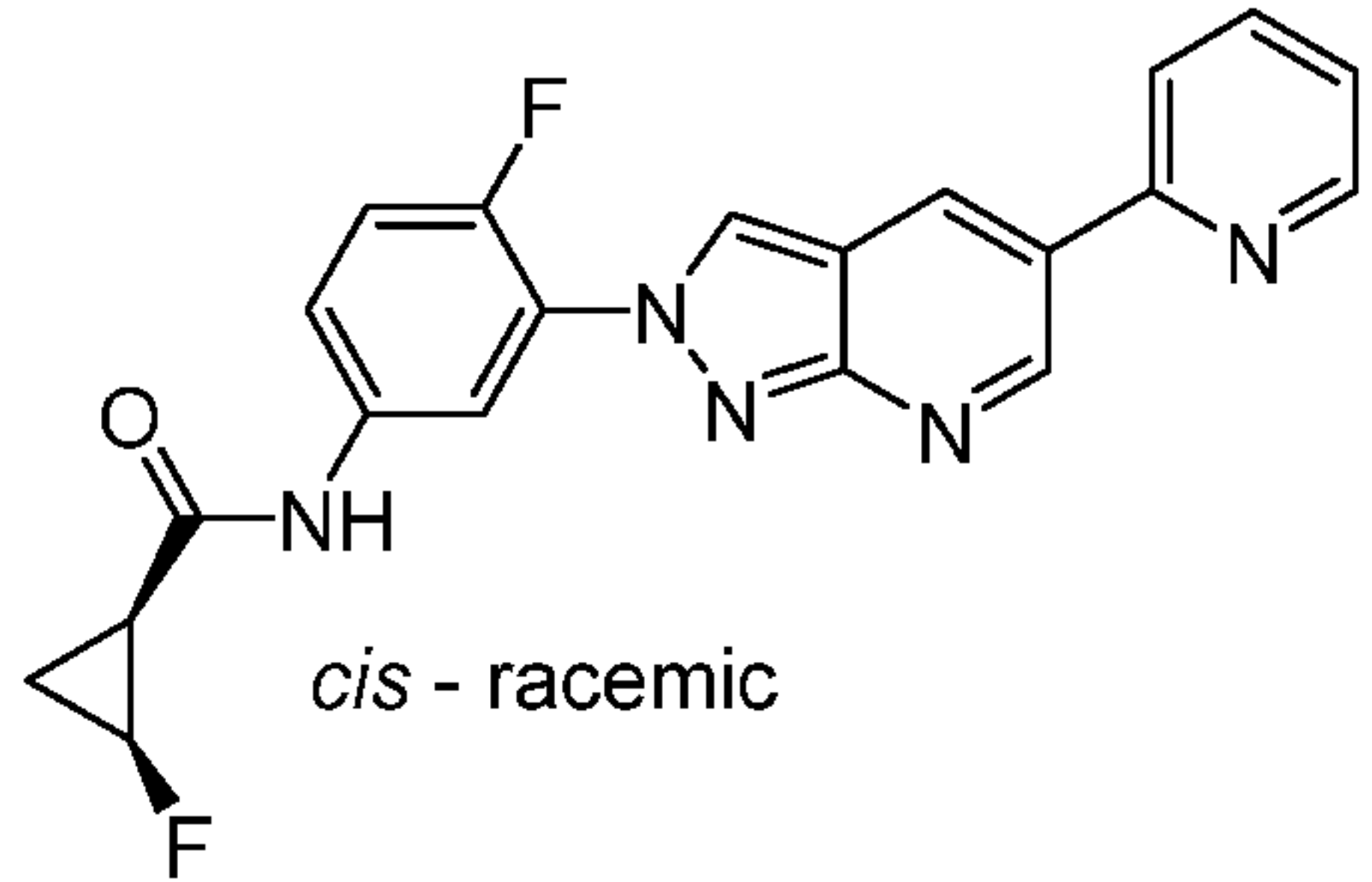
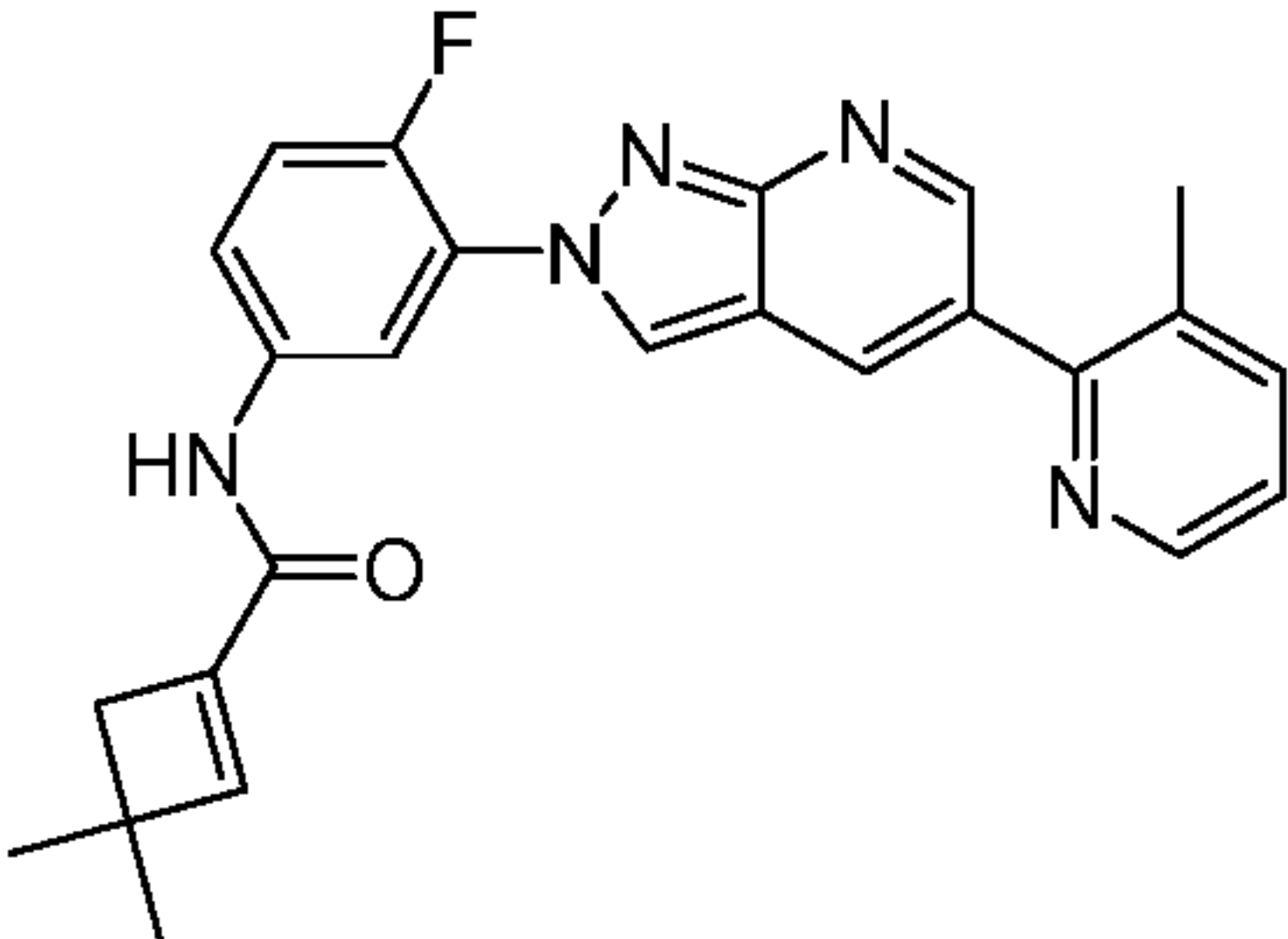
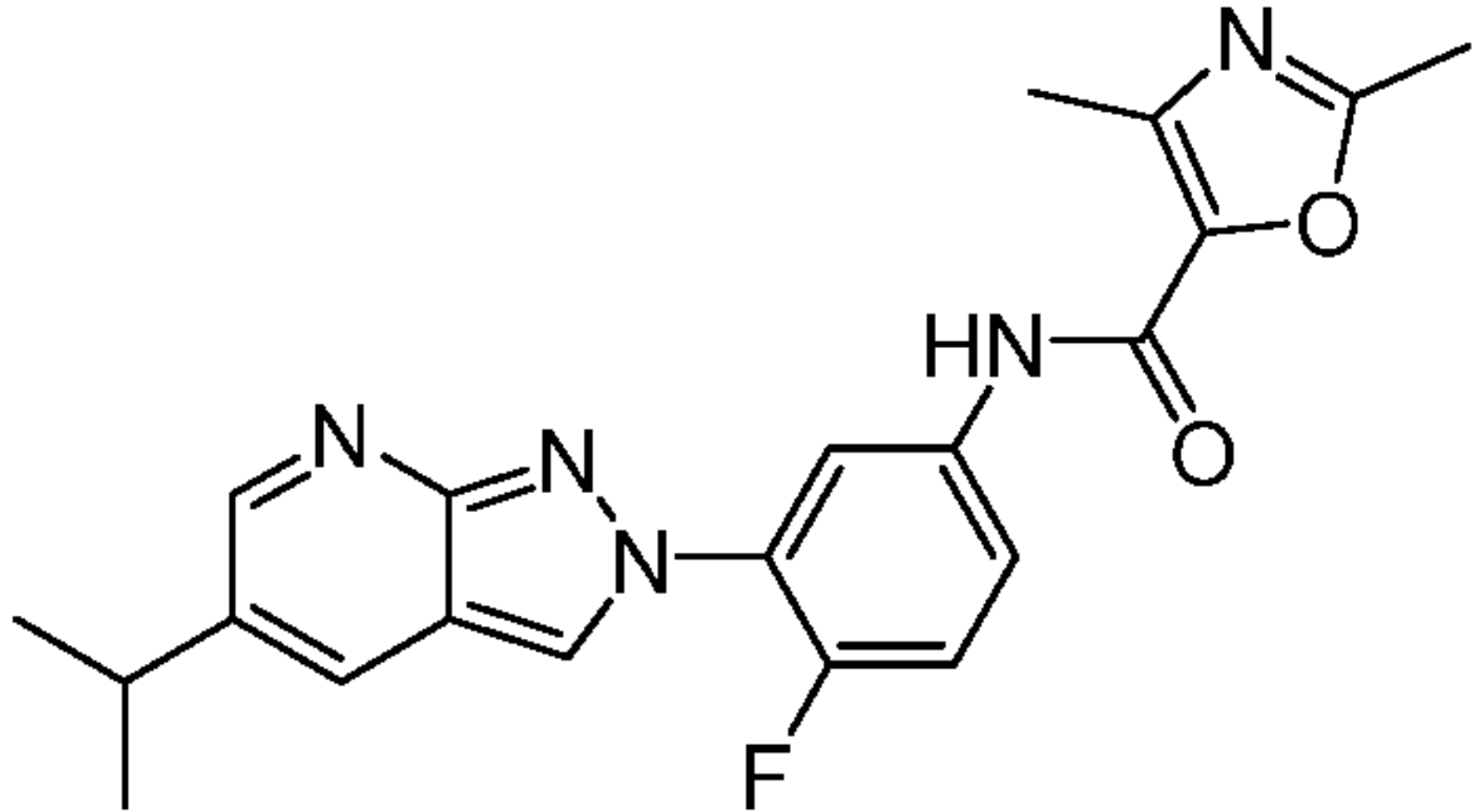
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
321		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.14 (d, J=2.45 Hz, 1 H), 8.94 - 9.07 (m, 2 H), 8.88 (d, J=1.22 Hz, 1 H), 8.28 (dd, J=6.85, 2.69 Hz, 1 H), 7.67 - 7.80 (m, 1 H), 7.51 (dd, J=11.13, 9.17 Hz, 1 H), 5.27 - 5.56 (m, 1 H), 4.23 - 4.44 (m, 2 H), 3.93 - 4.13 (m, 2 H). Method 1: RT = 2.83 min.; M+H = 398.0
322		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.14 (d, J=2.20 Hz, 1 H), 9.01 (d, J=2.20 Hz, 1 H), 8.88 (d, J=1.22 Hz, 1 H), 8.67 (s, 1 H), 8.32 (dd, J=7.09, 2.69 Hz, 1 H), 7.73 - 7.81 (m, 1 H), 7.50 (dd, J=11.13, 9.17 Hz, 1 H), 5.28 - 5.51 (m, 1 H), 3.41 - 3.78 (m, 4 H), 1.98 - 2.30 (m, 2 H). Method 1: RT = 2.83 min.; M+H = 412.1
323		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.06 (d, J=2.51 Hz, 1 H), 9.00 (d, J=2.26 Hz, 2 H), 8.51 (d, J=2.51 Hz, 1 H), 8.27 (dd, J=7.03, 2.76 Hz, 1 H), 7.86 (br s, 1 H), 7.64 - 7.77 (m, 1 H), 7.50 (dd, J=11.04, 9.29 Hz, 1 H), 7.19 (br s, 1 H), 5.26 - 5.57 (m, 1 H), 4.26 - 4.44 (m, 2 H), 3.94 - 4.14 (m, 2 H). Method 1: RT = 1.83 min.; M+H = 396.1
324		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.27 (br s, 1 H), 9.15 (d, J=2.26 Hz, 1 H), 9.01 (d, J=2.26 Hz, 1 H), 8.89 (dd, J=2.26, 1.00 Hz, 1 H), 8.28 (dd, J=6.90, 2.63 Hz, 1 H), 7.69 - 7.76 (m, 1 H), 7.54 (dd, J=11.17, 9.16 Hz, 1 H), 4.42 (t, J=12.67 Hz, 4 H). Method 2: RT = 0.98 min.; M+H = 416.0
325		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.04 (d, J=2.45 Hz, 1 H), 8.97 (s, 1 H), 8.84 (d, J=2.44 Hz, 1 H), 8.42 (s, 1 H), 8.37 (d, J=2.20 Hz, 1 H), 8.24 (dd, J=7.09, 2.69 Hz, 1 H), 8.02 (s, 1 H), 7.63 - 7.73 (m, 1 H), 7.47 (dd, J=11.13, 9.17 Hz, 1 H), 5.28 - 5.53 (m, 1 H), 4.24 - 4.41 (m, 2 H), 3.95 - 4.11 (m, 2 H), 3.78 (tt, J=7.34, 3.79 Hz, 1 H), 0.96 - 1.17 (m, 4 H). Method 1: RT = 2.73 min.; M+H = 436.1

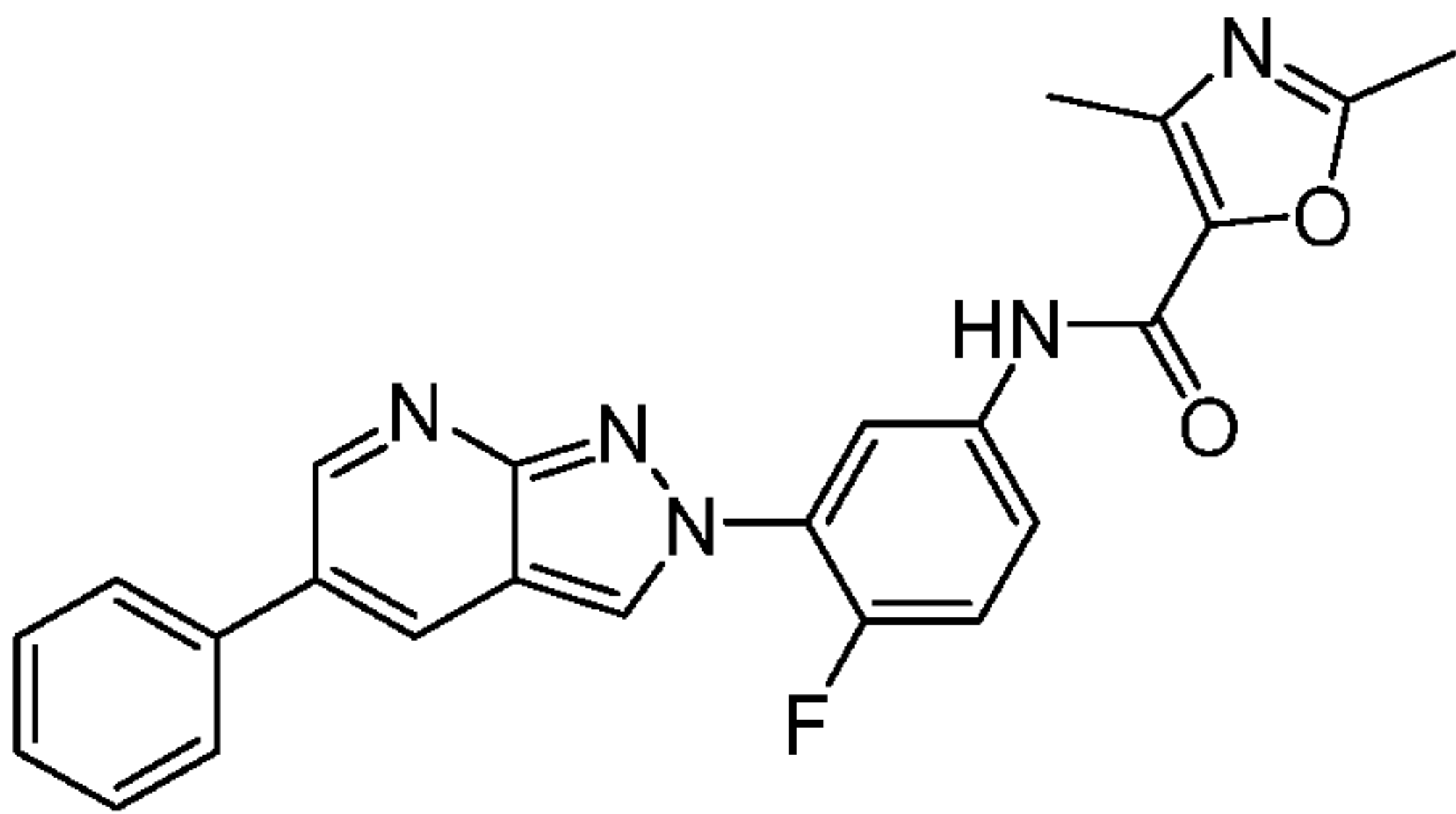
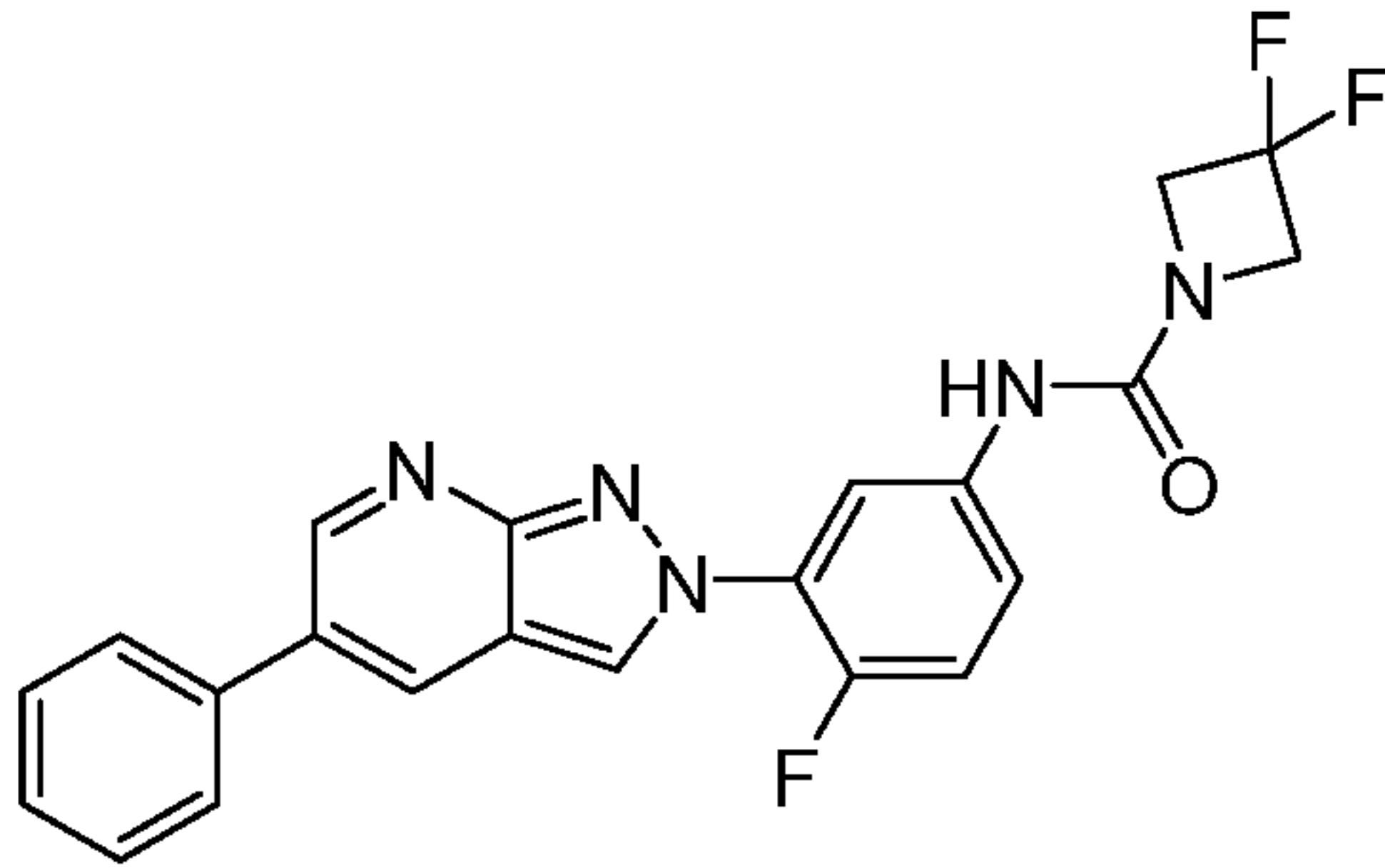
Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
326		¹ H NMR (400 MHz, DMSO) δ 10.54 (s, 1 H), 8.63 (d, <i>J</i> = 2.38 Hz, 1 H), 8.29 - 8.41 (m, 2 H), 7.66 (br d, <i>J</i> = 9.29 Hz, 1 H), 7.40 - 7.55 (m, 1 H), 7.14 (d, <i>J</i> = 2.64 Hz, 1 H), 4.40 (t, <i>J</i> = 12.17 Hz, 4 H), 1.72 - 1.85 (m, 1 H), 0.83 (br d, <i>J</i> = 6.02 Hz, 4 H). Method 2: RT = 0.93 min.; M+H = 388.2
327		¹ H NMR (400 MHz, DMSO) δ 10.53 (s, 1 H), 8.58 (d, <i>J</i> = 2.51 Hz, 1 H), 8.26 - 8.39 (m, 2 H), 7.60 - 7.71 (m, 1 H), 7.40 - 7.55 (m, 1 H), 7.00 (d, <i>J</i> = 2.76 Hz, 1 H), 5.39 - 5.67 (m, 1 H), 4.19 - 4.35 (m, 2 H), 3.92 - 4.09 (m, 2 H), 1.74 - 1.82 (m, 1 H), 0.83 (br d, <i>J</i> = 5.90 Hz, 4 H). Method 1: RT = 2.79 min.; M+H = 370.2
328		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.02 (d, <i>J</i> = 2.69 Hz, 1 H), 8.97 (d, <i>J</i> = 2.44 Hz, 1 H), 8.44 (d, <i>J</i> = 2.69 Hz, 1 H), 8.26 (dd, <i>J</i> = 7.09, 2.69 Hz, 1 H), 8.20 (d, <i>J</i> = 1.47 Hz, 1 H), 7.67 - 7.74 (m, 1 H), 7.44 - 7.56 (m, 2 H), 5.29 - 5.52 (m, 1 H), 4.26 - 4.39 (m, 2 H), 3.96 - 4.11 (m, 2 H), 2.21 (s, 3 H). Method 1: RT = 1.87 min.; M+H = 410.1
329		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.43 (d, <i>J</i> = 2.20 Hz, 1 H), 8.97 - 9.05 (m, 2 H), 8.91 (d, <i>J</i> = 2.45 Hz, 1 H), 8.74 (d, <i>J</i> = 3.18 Hz, 1 H), 8.28 (dd, <i>J</i> = 7.09, 2.69 Hz, 1 H), 8.21 (dd, <i>J</i> = 8.93, 4.28 Hz, 1 H), 7.92 (td, <i>J</i> = 8.80, 2.93 Hz, 1 H), 7.68 - 7.75 (m, 1 H), 7.50 (dd, <i>J</i> = 11.25, 9.05 Hz, 1 H), 5.29 - 5.53 (m, 1 H), 4.25 - 4.41 (m, 2 H), 3.95 - 4.12 (m, 2 H). Method 2: RT = 0.88 min.; M+H = 425.0
330		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.43 (d, <i>J</i> = 2.20 Hz, 1 H), 9.00 (d, <i>J</i> = 2.45 Hz, 1 H), 8.90 (d, <i>J</i> = 2.20 Hz, 1 H), 8.70 - 8.81 (m, 2 H), 8.29 (dd, <i>J</i> = 7.09, 2.69 Hz, 1 H), 8.21 (dd, <i>J</i> = 8.80, 4.16 Hz, 1 H), 7.91 (td, <i>J</i> = 8.68, 2.93 Hz, 1 H), 7.68 - 7.77 (m, 1 H), 7.47 (dd, <i>J</i> = 11.13, 9.17 Hz, 1 H), 3.99 (t, <i>J</i> = 7.58 Hz, 4 H), 2.21 (quin, <i>J</i> = 7.52 Hz, 2 H). Method 1: RT = 2.82 min.; M+H = 407.0

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
331		¹ H NMR (400 MHz, DMSO) δ 10.53 (s, 1 H), 8.70 (d, <i>J</i> = 2.93 Hz, 1 H), 8.56 (d, <i>J</i> = 2.69 Hz, 1 H), 8.35 (dd, <i>J</i> = 7.15, 2.63 Hz, 1 H), 7.63 - 7.71 (m, 1 H), 7.48 (dd, <i>J</i> = 11.31, 9.11 Hz, 1 H), 7.15 (d, <i>J</i> = 2.93 Hz, 1 H), 2.95 (s, 6 H), 1.79 (quin, <i>J</i> = 6.24 Hz, 1 H) 0.79 - 0.87 (m, 4 H). Method 2: RT = 0.85 min.; M+H = 340.2
332		¹ H NMR (400 MHz, DMSO) δ 10.50 (s, 1 H), 9.18 (d, <i>J</i> = 0.88 Hz, 1 H), 8.97 (d, <i>J</i> = 2.51 Hz, 1 H), 8.69 - 8.81 (m, 1 H), 8.54 (dd, <i>J</i> = 4.52, 1.88 Hz, 1 H), 8.33 (dd, <i>J</i> = 7.09, 2.57 Hz, 1 H), 7.84 (dd, <i>J</i> = 10.98, 8.85 Hz, 1 H), 7.57 - 7.69 (m, 1 H), 7.38 - 7.53 (m, 2 H), 1.61 - 1.75 (m, 1 H), 0.67 - 0.85 (m, 4 H). Method 1: RT = 2.85 min.; M+H = 392.2
333		¹ H NMR (400 MHz, DMSO) δ 10.57 (s, 1 H), 9.03 (d, <i>J</i> = 2.26 Hz, 1 H), 8.99 (d, <i>J</i> = 2.38 Hz, 1 H), 8.65 - 8.73 (m, 2 H), 8.41 (br d, <i>J</i> = 7.28 Hz, 1 H), 8.13 (d, <i>J</i> = 8.16 Hz, 1 H), 7.71 (br s, 1 H), 7.48 - 7.58 (m, 2 H), 1.73 - 1.83 (m, 1 H), 0.80 - 0.88 (m, 4 H). Method 1: RT = 2.87 min.; M+H = 408.2
334		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.63 (s, 1 H), 9.00 (d, <i>J</i> = 2.20 Hz, 1 H), 8.94 (d, <i>J</i> = 2.20 Hz, 1 H), 8.62 (dd, <i>J</i> = 7.09, 2.45 Hz, 1 H), 8.57 (d, <i>J</i> = 3.67 Hz, 1 H), 8.51 (d, <i>J</i> = 2.20 Hz, 1 H), 7.91 - 8.01 (m, 1 H), 7.81 (d, <i>J</i> = 7.34 Hz, 1 H), 7.60 (dd, <i>J</i> = 11.00, 9.05 Hz, 1 H), 7.37 (dd, <i>J</i> = 7.70, 4.77 Hz, 1 H), 5.83 (t, <i>J</i> = 5.99 Hz, 1 H), 4.60 (d, <i>J</i> = 6.11 Hz, 2 H), 2.45 (s, 6 H). Method 1: RT = 2.57 min.; M+H = 459.0
335		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.55 (s, 1 H), 9.03 (d, <i>J</i> = 2.20 Hz, 1 H), 8.98 (d, <i>J</i> = 2.20 Hz, 1 H), 8.65 (dd, <i>J</i> = 4.65, 1.71 Hz, 1 H), 8.61 (dd, <i>J</i> = 7.09, 2.45 Hz, 1 H), 8.57 (d, <i>J</i> = 2.20 Hz, 1 H), 8.00 - 8.07 (m, 1 H), 7.94 (dt, <i>J</i> = 9.05, 3.42 Hz, 1 H), 7.60 (dd, <i>J</i> = 11.00, 9.29 Hz, 1 H), 7.48 (dd, <i>J</i> = 7.70, 4.77 Hz, 1 H), 5.55 (br s, 1 H), 4.60 (s, 2 H), 2.52 (br s, 3 H), 2.41 (s, 3 H). Method 1: RT = 2.49 min.; M+H = 458.9
336		¹ H NMR (400 MHz, DMSO) δ 9.46 (d, <i>J</i> = 2.32 Hz, 1 H), 8.99 (d, <i>J</i> = 2.32 Hz, 1 H), 8.93 (d, <i>J</i> = 2.32 Hz, 1 H), 8.73 (d, <i>J</i> = 4.04 Hz, 1 H), 8.51 (s, 1 H), 8.30 (dd, <i>J</i> = 6.97, 2.57 Hz, 1 H), 8.11 (d, <i>J</i> = 7.95 Hz, 1 H), 7.95 (td, <i>J</i> = 7.76, 1.71 Hz, 1 H), 7.74 (dt, <i>J</i> = 8.99, 3.45 Hz, 1 H), 7.37 - 7.50 (m, 2 H), 3.42 - 3.48 (m, 4 H), 1.86 (br s, 4 H)

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
		Method 1: RT = 2.67 min.; M+H = 403.3
337		¹ H NMR (400 MHz, DMSO) δ 8.52 (d, <i>J</i> = 2.64 Hz, 1 H), 8.46 (s, 1 H), 8.28 (d, <i>J</i> = 2.76 Hz, 1 H), 8.23 (dd, <i>J</i> = 7.09, 2.57 Hz, 1 H), 7.67 (dt, <i>J</i> = 8.60, 3.54 Hz, 1 H), 7.40 (dd, <i>J</i> = 11.29, 9.16 Hz, 1 H), 6.92 (d, <i>J</i> = 2.76 Hz, 1 H), 4.02 (s, 4 H), 3.46 - 3.49 (m, 4 H), 1.86 (br t, <i>J</i> = 6.34 Hz, 4 H), 0.68 (s, 4 H), M+H = 407.3
338		¹ H NMR (400 MHz, DMSO) δ 8.62 (d, <i>J</i> = 2.69 Hz, 1 H), 8.47 (s, 1 H), 8.36 (d, <i>J</i> = 2.81 Hz, 1 H), 8.23 (dd, <i>J</i> = 7.09, 2.69 Hz, 1 H), 7.65 - 7.73 (m, 1 H), 7.41 (dd, <i>J</i> = 11.25, 9.17 Hz, 1 H), 7.14 (d, <i>J</i> = 2.81 Hz, 1 H), 4.40 (t, <i>J</i> = 12.23 Hz, 4 H), 3.38 - 3.41 (m, 4 H), 1.86 (br t, <i>J</i> = 6.48 Hz, 4 H) Method 1: RT = 2.86 min.; M+H = 417.0
339	 <i>trans</i> - racemic	¹ H NMR (400 MHz, DMSO-d ₆) δ 10.69 (s, 1 H), 8.64 (d, <i>J</i> = 2.64 Hz, 1 H), 8.37 (d, <i>J</i> = 2.89 Hz, 1 H), 8.32 (dd, <i>J</i> = 7.03, 2.63 Hz, 1 H), 7.59 - 7.69 (m, 1 H), 7.51 (dd, <i>J</i> = 11.11, 9.10 Hz, 1 H), 7.14 (d, <i>J</i> = 2.76 Hz, 1 H), 4.79 - 5.06 (m, 1 H), 4.41 (t, <i>J</i> = 12.23 Hz, 4 H), 2.23 - 2.33 (m, 1 H), 1.49 - 1.64 (m, 1 H), 1.27 (dq, <i>J</i> = 13.11, 6.46 Hz, 1 H). Method 2: RT = 0.97 min.; M+H = 406.2
340		¹ H NMR (400 MHz, METHANOL-d ₄) δ 9.12 (s, 1 H), 8.59 (d, <i>J</i> = 2.20 Hz, 1 H), 8.41 - 8.47 (m, 1 H), 8.33 (d, <i>J</i> = 1.96 Hz, 1 H), 8.24 (d, <i>J</i> = 5.62 Hz, 1 H), 7.64 (dd, <i>J</i> = 5.75, 2.08 Hz, 1 H), 5.13 - 5.36 (m, 1 H), 3.48 - 3.79 (m, 4 H), 1.99 - 2.28 (m, 2 H). Method 2: RT = 0.90 min.; M+H = 405.1, 407.1
341		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.46 (d, <i>J</i> = 2.20 Hz, 1 H), 9.37 (s, 1 H), 9.26 (s, 1 H), 8.95 (d, <i>J</i> = 2.45 Hz, 1 H), 8.74 (d, <i>J</i> = 3.91 Hz, 1 H), 8.52 (d, <i>J</i> = 1.71 Hz, 1 H), 8.37 (d, <i>J</i> = 5.62 Hz, 1 H), 8.12 (d, <i>J</i> = 8.07 Hz, 1 H), 7.96 (td, <i>J</i> = 7.70, 1.71 Hz, 1 H), 7.74 (dd, <i>J</i> = 5.62, 1.96 Hz, 1 H), 7.42 (dd, <i>J</i> = 7.09, 5.14 Hz, 1 H), 4.05 (t, <i>J</i> = 7.58 Hz, 4 H), 2.23 (quin, <i>J</i> = 7.58 Hz, 2 H). Method 1: RT = 2.67 min.; M+H = 372.0

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
342		¹ H NMR (400 MHz, DMSO-d ₆), δ 9.43 - 9.50 (m, 2 H), 9.38 (s, 1 H), 8.95 (d, J=2.26 Hz, 1 H), 8.74 (d, J=4.02 Hz, 1 H), 8.50 (d, J=1.76 Hz, 1 H), 8.39 (d, J=5.77 Hz, 1 H), 8.13 (d, J=8.03 Hz, 1 H), 7.97 (td, J=7.78, 1.76 Hz, 1 H), 7.73 (dd, J=5.65, 1.88 Hz, 1 H), 7.43 (dd, J=6.78, 4.77 Hz, 1 H), 5.31 - 5.54 (m, 1 H), 4.32 - 4.48 (m, 2 H), 4.01 - 4.17 (m, 2 H). Method 1: RT = 2.67 min.; M+H = 390.0
343		¹ H NMR (400 MHz, DMSO-d ₆) δ 8.80 (s, 1 H), 8.68 (s, 1 H), 8.30 - 8.35 (m, 2 H), 7.63 (br d, J=8.41 Hz, 1 H), 7.59 (br d, J=8.03 Hz, 1 H), 7.39 - 7.47 (m, 1 H), 7.13 (d, J=2.76 Hz, 1 H), 4.41 (t, J=12.23 Hz, 4 H), 3.99 (t, J=7.53 Hz, 4 H), 2.21 (quin, J=7.56 Hz, 2 H). Method 2: RT = 0.84 min.; M+H = 385.2
344		¹ H NMR (400 MHz, DMSO-d ₆) δ 9.44 (d, J=2.20 Hz, 1 H), 9.18 (s, 1 H), 8.91 (d, J=2.32 Hz, 1 H), 8.70 - 8.78 (m, 2 H), 8.36 - 8.42 (m, 1 H), 8.14 (d, J=8.07 Hz, 1 H), 7.95 (td, J=7.73, 1.77 Hz, 1 H), 7.65 - 7.71 (m, 2 H), 7.44 - 7.51 (m, 1 H), 7.42 (dd, J=7.15, 5.20 Hz, 1 H), 4.01 (t, J=7.58 Hz, 4 H), 2.22 (quin, J=7.58 Hz, 2 H), 1.47 - 1.61 (m, 1 H), 1.19 - 1.34 (m, 1 H), 1.00 - 1.08 (m, 1 H), 0.85 (t, J=7.40 Hz, 1 H). Method 2: RT = 0.74 min.; M+H = 371.0
345		¹ H NMR (400 MHz, DMSO-d ₆) δ 11.31 (s, 1H), 9.60 (d, J = 2.3 Hz, 1H), 9.45 (d, J = 1.5 Hz, 1H), 9.18 (d, J = 2.5 Hz, 1H), 9.08 (t, J = 2.1 Hz, 2H), 8.97 (dd, J = 2.5, 1.5 Hz, 1H), 8.92 - 8.79 (m, 2H), 8.31 - 8.15 (m, 2H), 8.08 (td, J = 7.7, 1.9 Hz, 1H), 7.76 (dd, J = 11.1, 9.1 Hz, 1H), 7.54 (ddd, J = 7.5, 4.8, 1.0 Hz, 1H). Method 1: RT = 2.71 min.; M+H = 412.10
346		¹ H NMR (400 MHz, DMSO-d ₆) δ 10.52 (s, 1H), 9.59 (d, J = 2.3 Hz, 1H), 9.13 (d, J = 2.5 Hz, 1H), 9.05 (d, J = 2.3 Hz, 1H), 8.85 (ddd, J = 4.8, 1.9, 0.9 Hz, 1H), 8.55 (dd, J = 7.0, 2.7 Hz, 1H), 8.24 (dt, J = 8.1, 1.1 Hz, 1H), 8.07 (td, J = 7.7, 1.8 Hz, 1H), 7.81 (ddd, J = 9.1, 4.2, 2.7 Hz, 1H), 7.65 (dd, J = 11.1, 9.1 Hz, 1H), 7.53 (ddd, J = 7.5, 4.8, 1.0 Hz, 1H), 2.26 (dd, J = 7.4, 4.3 Hz, 1H), 1.59 - 1.44 (m, 2H), 1.12 - 0.84 (m, 4H). Method 1: RT = 2.85 min.; M+H = 400.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
347		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.12 (s, 1H), 9.48 (d, <i>J</i> = 2.3 Hz, 1H), 9.04 (d, <i>J</i> = 2.5 Hz, 1H), 8.95 (d, <i>J</i> = 2.3 Hz, 1H), 8.74 (ddd, <i>J</i> = 4.8, 1.8, 0.9 Hz, 1H), 8.48 (dd, <i>J</i> = 7.1, 2.7 Hz, 1H), 8.13 (dt, <i>J</i> = 8.0, 1.1 Hz, 1H), 8.02 - 7.87 (m, 2H), 7.57 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.43 (ddd, <i>J</i> = 7.5, 4.8, 1.0 Hz, 1H), 6.93 (s, 1H), 2.47 (s, 2H), 1.24 (s, 6H). Method 1: RT = 3.08 min.; M+H = 414.1
348		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.38 (s, 1H), 9.48 (d, <i>J</i> = 2.3 Hz, 1H), 9.04 (d, <i>J</i> = 2.5 Hz, 1H), 8.95 (d, <i>J</i> = 2.3 Hz, 1H), 8.74 (ddd, <i>J</i> = 4.8, 1.9, 1.0 Hz, 1H), 8.41 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 8.13 (dt, <i>J</i> = 8.0, 1.1 Hz, 1H), 7.96 (td, <i>J</i> = 7.7, 1.9 Hz, 1H), 7.80 (ddd, <i>J</i> = 9.1, 4.2, 2.7 Hz, 1H), 7.59 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.43 (ddd, <i>J</i> = 7.5, 4.8, 1.0 Hz, 1H), 1.73 (d, <i>J</i> = 1.0 Hz, 4H). Method 2: RT = 0.83 min.; M+H = 399.1
349	 <i>cis</i> - racemic	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 10.65 (s, 1H), 9.48 (d, <i>J</i> = 2.3 Hz, 1H), 9.04 (d, <i>J</i> = 2.5 Hz, 1H), 8.95 (d, <i>J</i> = 2.3 Hz, 1H), 8.74 (ddd, <i>J</i> = 4.8, 1.8, 1.0 Hz, 1H), 8.43 (dd, <i>J</i> = 7.0, 2.7 Hz, 1H), 8.13 (dt, <i>J</i> = 8.0, 1.1 Hz, 1H), 7.96 (td, <i>J</i> = 7.7, 1.8 Hz, 1H), 7.74 (ddd, <i>J</i> = 9.1, 4.2, 2.7 Hz, 1H), 7.57 (dd, <i>J</i> = 11.2, 9.1 Hz, 1H), 7.42 (ddd, <i>J</i> = 7.5, 4.8, 1.1 Hz, 1H), 4.98 (dtd, <i>J</i> = 66.2, 6.2, 3.7 Hz, 1H), 2.04 (dtd, <i>J</i> = 9.2, 7.0, 3.6 Hz, 1H), 1.67 (dtd, <i>J</i> = 23.2, 6.7, 3.6 Hz, 1H), 1.19 (dtd, <i>J</i> = 12.5, 9.2, 6.4 Hz, 1H). Method 2: RT = 0.80 min.; M+H = 392.1
350		¹ H NMR (400 MHz, Methanol- <i>d</i> ₄) δ 8.78 (d, <i>J</i> = 2.4 Hz, 1H), 8.76 (d, <i>J</i> = 2.3 Hz, 1H), 8.44 - 8.39 (m, 1H), 8.38 (d, <i>J</i> = 2.2 Hz, 1H), 8.32 (dd, <i>J</i> = 6.8, 2.7 Hz, 1H), 7.88 (s, 1H), 7.81 - 7.72 (m, 2H), 7.39 - 7.26 (m, 2H), 6.83 (s, 1H), 2.43 (s, 2H), 2.35 (s, 3H), 1.19 (s, 6H). Method 2: RT = 0.90 min.; M+H = 428.1
351		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ ppm 10.52 (br s, 1 H), 8.83 (d, <i>J</i> =2.64 Hz, 1 H), 8.70 (d, <i>J</i> =2.26 Hz, 1 H), 8.56 (dd, <i>J</i> =7.03, 2.64 Hz, 1 H), 8.07 (d, <i>J</i> =1.76 Hz, 1 H), 7.86 - 7.94 (m, 1 H), 7.56 (dd, <i>J</i> =11.11, 9.10 Hz, 1 H), 3.04 - 3.15 (m, 1 H), 2.50 - 2.51 (m, 3 H), 2.40 (s, 3 H), 1.31 (d, <i>J</i> =6.90 Hz, 6 H); M+H = 394.1

Cpd No.	Structure	¹ H NMR and HPLC retention time and/or MS
352		¹ H NMR (400 MHz, CD ₃ OD) 9.00-8.99 (d, J=2.4, 1H), 8.84-8.83 (d, J=2.4, 1H), 8.50-8.49 (d, J=2.0, 1H), 8.47-8.45 (dd, J=2.4, 6.8, 1H), 7.90-7.86 (m, 1H), 7.74-7.71 (m, 2H), 7.53-7.50 (m, 2H), 7.47-7.42 (m, 2H), 2.54 (s, 3H), 2.45 (s, 3H).; M+H = 428.1
353		¹ H NMR (400 MHz, DMSO-d ₆) 9.25 (s, 1H), 9.06-9.05 (d, J=2.8, 1H), 8.96-8.95 (d, J=2.0, 1H), 8.52-8.51 (d, J=2.4, 1H), 8.27-8.25 (m, 1H), 7.80-7.78 (d, J=7.2, 2H), 7.72-7.67 (m, 1H), 7.56-7.48 (m, 3H), 7.44-7.41 (m, 1H), 4.44-4.38 (t, J=16.4, 4H).

BIOLOGICAL ASSAYS

The assays described herein illustrate and do not limit the scope of the invention.

Abbreviations

Abbreviations as used herein below have the corresponding meaning:

CPRG	Chlorophenol Red-β-D-galactopyranoside
ATP	adenosine triphosphate
BSA	bovine serum albumin
DMSO	dimethyl sulfoxide
FBS	fetal bovine serum
PBS	phosphate buffered saline
RPMI 1640	Roswell Park Memorial Institute (RPMI) 1640 medium

5 *in vitro* Assay for growth inhibition of *Leishmania donovani* axenic amastigote

Leishmania donovani axenic amastigote parasites are grown at 37 °C, 5% CO₂ in media made of RPMI 1640, 4mM L-glutamine, 20% heat inactivated FBS, 100 units/ml of penicillin and 100 µg/ml of streptomycin, 23 µM folic acid, 100 µM adenosine, 22 mM D-glucose, 25 mM MES. The pH of media is adjusted to 5.5 at 37 °C using HCl. 20 µL of media is first dispensed into 384 well plates and 100 nL of the compounds of invention in DMSO are added to the plate wells. At the same time control compounds and DMSO are added to plates to serve as the positive and negative controls, respectively. 40 µL of parasite culture (9600 parasites) are then added to the plate wells. The plates are then placed into incubators. After two days incubation, 20 µL of Cell TiterGlo® (Promega) is added to the plate wells. The luminescence signal of each well is measured using the Envision reader (Perkin Elmer).

Assay for inhibition of parasitemia of *Leishmania donovani* in mouse macrophages

The assay measures the increase in the parasite number in the assayed plate well using a DNA intercalating dye, SYBR Green I® dye (INVITROGEN) to stain *Leishmania* cell nuclei. *L. donovani* HU3 strain is propagated by infecting BALB/c mice through tail vein injection with

5 10^7 *Leishmania* parasites. Infected mice are allowed to develop infection during 9-11 weeks post-infection. During this time, the parasites accumulate in the infected mouse spleens to large numbers, and the infected mice serve as the source of parasites for the *in vitro* measurement of compound efficacies. To assay a compound for anti-leishmanial activity, peritoneal

10 macrophages isolated from non-infected BALB/c mice are seeded into 384-well plates at density 2×10^4 macrophages per well in 25 mL of medium (RPMI1640, 10% fetal serum albumin, 10 mM HEPES, 1 mM sodium pyruvate, 1% Pen/Strep). Subsequently, the seeded plates are placed into an incubator set to maintain 37 °C temperature and atmosphere with 5% CO₂.

The next day, *Leishmania* parasites are isolated from the spleens of mice infected for 9-11 weeks and 4×10^5 isolated parasites in 10 mL of the above media are added to each plate well.

15 Plates are then returned into incubators and infection is allowed to proceed for 24 hours. After the infection of macrophages is completed, 5 mL of compounds of the invention in the above medium, which also contains 5% DMSO, are added to plate wells containing infected macrophages. At the same time control compounds (miltefosine and amphotericin B) and DMSO are added to plates to serve as the positive and negative controls, respectively. After

20 the compound addition, the plates are returned into incubator and cells infected with parasites are cultured for 5 days. At the end of cultivation, 40 mL of 8% paraformaldehyde is added to plate wells and incubated for 15 min at room temperature. Following the incubation, the paraformaldehyde from plate wells is aspirated, and 40 mL of PBS containing 0.2% Triton X-100 is added to wells. After 15 min incubation, the solution is aspirated from wells again, and

25 replaced with Sybr® Green Dye solution in PBS (1:125,000 dilution). Infected cells are imaged with Evotec Opera high-content microscope, and the number of parasites in well is determined by counting parasite nuclei visualized by staining with Sybr® Green dye.

Assay for growth inhibition of kinetoplastid parasite *Trypanosoma cruzi*

Compounds of the invention can be assayed for inhibitor activity against *Trypanosoma*

30 *cruzi* amastigotes cultured in 3T3 fibroblast cells. The assay is done using the mammalian stage (amastigotes) of *T. cruzi* that replicates in the intracellular space of host cells. The host cells are initially infected with the culture-derived trypomastigotes that rapidly invade and then divide as amastigotes. The protocol uses the Tulahuen strain of *T. cruzi* that has been engineered to express the *E. coli* beta-galactosidase gene (Lac-Z) (Antimicrob. Agents Chemother. 40:2592, 1996). This allows for a colorimetric readout by using the substrate CPRG and an

35 absorbance plate reader.

3T3 fibroblast cells are re-suspended in RPMI-1640 medium without phenol red medium supplemented with 10% FBS (heat inactivated), 100 µg/ml penicillin, and 100 µg /ml

streptomycin. Forty μL of suspension (1,000 cells) is dispensed into 384-well plates and incubated overnight at 37 °C temperature and in atmosphere containing 5% CO_2 . The following day, 100 nL of compounds of the invention in DMSO are added to plate wells containing 3T3 cells. At the same time control compounds (benznidazole and nifurtimox) and DMSO are added to plates to serve as the positive and negative controls, respectively. After that, 10 μL of media containing 10,000 *T. cruzi* trypomastigotes are added to each plate well and plates are placed back into incubators. After 6 day incubation, 10 μL of reagent solution (0.6 mM CPRG, 0.6% NP-40 in PBS) is added to plates and incubated at room temperature for 2 hours. Absorbance is then measured on SpectraMax GEMINI fluorimeter to determine relative number of *T. cruzi* cells present in each plate well.

Assay for growth inhibition against *Trypanosoma brucei brucei*

The proliferation is quantified by the addition of Cell TiterGlo® (Promega®) a luminescent cell viability assay that measures the number of viable cells in culture based on the quantification of cellular ATP amount, which is an indicator of metabolically active cells.

Trypanosoma brucei brucei (Lister 427) strain was grown in Hirumi 9 (HMI-9) media supplemented with 10% v/v fetal bovine serum (FBS) and 10% v/v serum plus. For measurement of cell proliferation inhibition, test compounds were three fold serially diluted in duplicates to 384-well white plates, resulting in 10 dilutions for each compound. A volume of 40 μL of *T. b. brucei* culture (10,000 parasites/mL) was added to each well, and the assay plates were incubated at 37°C for 2 days in a CO_2 incubator. Growth inhibition was monitored by measuring ATP levels, which, is used as a surrogate marker for growth. Relative luminescence units were measured using TECAN® M1000 after 30min of adding 40 μL of Cell TiterGlo®. IC_{50} values were determined by analyzing the data using HELIOS software. IC_{50} is defined as the lowest concentration of the compound that inhibited 50% growth of the *T. b. brucei* wild type strain compared to untreated controls.

Table 3 shows the inhibitory efficacy of the compounds (EC_{50}) against *L. donovani* axenic amastigotes *in vitro* (column 2); *L. donovani* in mouse peritoneal macrophages (column 3); *T. cruzi* (column 4); and *T. brucei brucei* (column 5). Compounds of the invention have an EC_{50} ranging from >10 μM to <0.01 μM . In particular embodiments, compounds of the invention have an EC_{50} <1 μM , <500 nM, <100 nM or < 50 nM.

Table 3

Cpd. No.	<i>L. donovani</i> amastigotes EC_{50} (μM)	<i>L. donovani</i> in Mouse Macrophages EC_{50} (μM)	Buckner infectious <i>T. cruzi</i> EC_{50} (μM)	<i>T. Brucei</i> (HAT) EC_{50} (μM)
1	0.0071	n.d.	0.0052	<0.023
2	0.003	0.0044	0.0010	<0.023
3	0.0018	0.0020	0.0016	<0.023
4	0.0013	n.d.	0.0010	<0.023
5	0.0036	n.d.	0.0053	<0.023
6	0.012	n.d.	0.0099	<0.023

Cpd. No.	<i>L. donovani</i> amastigotes EC ₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC ₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (μM)	<i>T. Brucei</i> (HAT) EC ₅₀ (μM)
7	0.0077	0.004	0.0016	<0.023
8	0.0077	0.0033	0.0045	<0.023
9	0.0087	0.011	0.0098	0.035
10	0.016	0.0078	0.0048	<0.023
11	0.0028	n.d.	0.0010	>50
12	0.041	n.d.	n.d.	<0.023
13	0.071	n.d.	n.d.	<0.023
14	0.012	0.0097	0.0020	<0.023
15	0.013	0.017	0.005	<0.023
16	0.089	n.d.	0.012	n.d.
17	0.064	n.d.	0.016	n.d.
18	0.29	n.d.	0.16	n.d.
19	0.011	0.081	0.011	<0.023
20	0.010	0.037	0.0042	<0.023
21	0.0077	0.0065	0.0017	<0.023
22	0.028	21	0.0072	<0.023
23	0.14	0.11	0.078	<0.023
24	0.88	1.0	0.44	0.61
25	0.021	0.047	0.017	<0.023
26	0.0096	n.d.	0.012	<0.023
27	0.033	0.015	0.038	<0.023
28	0.0013	0.0020	0.0010	<0.023
29	0.0082	0.0097	0.011	<0.023
30	0.59	n.d.	n.d.	n.d.
31	0.0062	n.d.	0.0083	<0.023
32	0.012	0.013	0.005	<0.023
33	0.29	0.56	0.72	0.28
34	0.20	0.27	0.16	0.15
35	0.58	0.52	0.38	0.85
36	0.21	0.25	n.d.	n.d.
37	0.023	n.d.	0.026	<0.023
38	0.031	0.033	0.062	0.024
39	0.0024	0.0038	0.0020	<0.023
40	n.d.	n.d.	n.d.	<0.023
41	0.02	n.d.	n.d.	n.d.
42	0.0030	0.006	0.0018	<0.023
43	0.0047	n.d.	0.0052	n.d.
44	0.029	0.032	0.022	n.d.
45	0.04	n.d.	0.028	<0.023
46	0.0084	0.0035	0.0017	<0.023
47	0.023	0.027	0.0028	n.d.
48	0.35	0.33	0.29	0.050
49	25	12	12	3.4
50	0.078	0.10	0.079	<0.023
51	0.015	n.d.	0.019	<0.023
52	0.019	0.011	0.013	<0.023
53	0.0013	0.0020	0.0010	<0.023
54	0.028	n.d.	0.0041	n.d.
55	0.057	0.035	0.0063	n.d.
56	0.24	0.55	n.d.	n.d.
57	0.71	n.d.	0.36	n.d.
58	n.d.	n.d.	n.d.	<0.023
59	0.068	0.021	0.0047	<0.023
60	2.0	2.4	0.44	1.3

Cpd. No.	<i>L. donovani</i> amastigotes EC ₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC ₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (μM)	<i>T. Brucei</i> (HAT) EC ₅₀ (μM)
61	0.24	n.d.	0.052	n.d.
62	0.039	n.d.	0.0051	<0.023
63	0.089	0.09	0.014	n.d.
64	0.0022	0.0039	0.0010	<0.023
65	1.0	1.2	0.96	1.4
66	0.74	0.87	0.15	0.12
67	0.21	0.31	0.042	>50
68	2.2	2.8	0.16	0.51
69	0.17	0.15	0.068	0.04
70	0.14	0.10	0.022	0.038
71	4.8	2.8	1.4	3.0
72	2.1	1.4	0.18	0.42
73	0.10	0.22	0.057	0.037
74	0.76	0.82	0.057	0.11
75	0.20	0.17	0.12	0.17
76	1.1	0.93	0.41	0.48
77	17	n.d.	6.5	8.5
78	0.80	0.87	0.45	0.53
79	3.0	2.4	0.14	0.35
80	0.41	0.41	0.092	0.17
81	3.16	3.6	0.42	0.36
82	0.47	0.31	0.059	0.054
83	0.014	0.0070	0.0073	<0.023
84	2.4	6.9	3.7	2.03
85	1.2	0.75	0.15	0.18
86	0.13	0.12	0.014	<0.023
87	0.062	0.071	0.016	<0.023
88	5.3	3.2	1.8	1.5
89	0.47	0.27	0.032	0.033
90	0.28	0.31	0.14	0.077
91	0.0087	0.0086	0.0041	<0.023
92	n.d.	n.d.	n.d.	<0.023
93	0.034	0.032	0.0070	<0.023
94	0.012	0.0081	0.0018	<0.023
95	0.42	0.35	0.17	0.085
96	0.023	0.021	0.018	<0.023
97	0.012	0.44	0.0088	<0.023
98	0.025	0.023	0.015	<0.023
99	0.0013	0.0020	0.0010	>50
100	0.0092	n.d.	0.0042	<0.023
101	0.30	0.31	0.13	0.15
102	0.11	n.d.	0.046	n.d.
103	0.68	0.40	0.15	0.31
104	3.1	2.1	1.2	4.2
105	0.72	0.89	0.43	0.38
106	0.13	0.085	0.061	>50
107	0.22	0.13	0.077	0.088
108	0.0033	0.004	0.0038	<0.023
109	0.074	n.d.	0.015	n.d.
110	0.64	n.d.	0.15	n.d.
111	8.7	n.d.	2.9	10
112	0.016	n.d.	0.0028	<0.023
113	0.037	n.d.	0.00522	n.d.
114	0.31	n.d.	0.045	0.054

Cpd. No.	<i>L. donovani</i> amastigotes EC ₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC ₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (μM)	<i>T. Brucei</i> (HAT) EC ₅₀ (μM)
115	0.15	n.d.	0.014	<0.023
116	3.1	n.d.	0.88	1.5
117	9.3	n.d.	5.5	13
118	0.69	n.d.	1.1	1.4
119	1.6	n.d.	4.5	13
120	5.2	n.d.	4.3	1.8
121	0.21	n.d.	n.d.	0.12
122	0.015	n.d.	0.0042	n.d.
123	0.0094	0.0089	0.0044	<0.023
124	0.018	n.d.	0.016	n.d.
125	0.044	0.031	0.034	<0.023
126	0.024	0.014	0.014	<0.023
127	0.025	0.017	0.0068	<0.023
128	0.38	0.19	0.14	0.18
129	0.029	0.031	0.015	<0.023
130	0.19	0.16	0.036	0.040
131	0.007	0.0051	0.0052	<0.023
132	0.011	0.007	0.013	<0.023
133	0.012	0.0080	0.0059	<0.023
134	0.023	0.0054	0.02	<0.023
135	0.0046	0.0086	0.0066	<0.023
136	0.030	0.019	0.17	<0.023
137	0.0088	0.0060	0.0051	<0.023
138	0.011	0.0057	0.047	<0.023
139	0.74	0.32	3.0	<0.023
140	0.10	0.041	0.023	<0.023
141	0.08	0.012	0.022	<0.023
142	7.8	9.2	11	4.3
143	0.15	0.11	n.d.	<0.023
144	0.023	0.023	0.017	<0.023
145	0.0054	0.0047	0.018	<0.023
146	0.026	0.012	0.085	<0.023
147	0.0061	0.026	0.0048	<0.023
148	0.0081	0.012	0.014	<0.023
149	0.011	0.0079	0.0054	<0.023
150	0.014	0.025	0.021	<0.023
151	0.06	0.013	0.012	<0.023
152	0.0037	0.0053	0.0017	<0.023
153	0.21	27	0.15	0.50
154	0.053	0.078	0.023	0.037
155	0.053	0.022	0.018	<0.023
156	0.0093	n.d.	0.0051	<0.023
157	0.025	0.018	0.013	<0.023
158	0.016	0.016	0.015	<0.023
159	0.013	0.017	0.037	<0.023
160	0.0043	0.0098	0.0051	<0.023
161	0.0077	0.0073	0.0098	<0.023
162	0.007	0.0045	0.0018	<0.023
163	0.0058	0.0041	0.0027	<0.023
164	0.006	0.01	0.0017	<0.023
165	0.010	0.010	0.04	<0.023
166	0.0025	0.0037	0.0017	<0.023
167	0.0029	0.0082	0.0022	<0.023
168	0.0032	0.0082	0.027	<0.023

Cpd. No.	<i>L. donovani</i> amastigotes EC ₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC ₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (μM)	<i>T. Brucei</i> (HAT) EC ₅₀ (μM)
169	0.010	0.030	0.014	<0.023
170	0.008	0.011	0.0046	<0.023
171	0.0095	0.016	0.047	<0.023
172	0.0067	0.011	0.033	<0.023
173	0.41	0.50	0.14	0.12
174	2	2.7	0.72	1.0
175	0.024	0.0081	0.0049	<0.023
176	0.071	0.069	0.0095	n.d.
177	0.027	n.d.	0.055	<0.023
178	0.16	n.d.	1.6	0.036
179	0.41	n.d.	0.043	<0.023
180	0.55	n.d.	3.9	0.038
181	0.025	n.d.	0.82	<0.023
182	0.0076	n.d.	0.0067	<0.023
183	0.012	n.d.	0.055	<0.023
184	0.0073	n.d.	n.d.	<0.023
185	0.2	n.d.	n.d.	<0.023
186	0.46	n.d.	n.d.	0.24
187	0.0013	n.d.	n.d.	<0.023
188	0.0024	n.d.	n.d.	<0.023
189	0.003	n.d.	n.d.	<0.023
190	n.d.	n.d.	n.d.	>50
191	n.d.	n.d.	n.d.	<0.023
192	n.d.	n.d.	n.d.	<0.023
193	n.d.	n.d.	n.d.	<0.023
194	n.d.	n.d.	n.d.	<0.023
195	0.010	0.0064	0.004	<0.023
196	0.076	27	0.012	<0.023
197	0.199	0.013	0.037	0.005
198	0.546	0.049	0.023	0.005
199	0.502	0.021	0.024	0.005
200	0.974	0.007	0.015	0.005
201	0.192	0.004	0.02	0.005
202	0.463	0.01	0.025	0.005
203	0.49	0.009	0.02	0.005
204	0.074	0.004	0.002	0.005
205	0.197	0.011	0.015	0.005
206	0.002	0.013	0.001	0.005
207	1.827	2.062	1.271	1.821
208	0.921	1.918	0.358	0.375
209	25.0	0.381	5.09	6.538
210	0.494	n.d.	0.079	n.d.
211	0.496	0.302	0.072	0.035
212	11.31	8.86	1.753	2.027
213	1.561	n.d.	0.363	n.d.
214	4.6	0.658	1.415	1.056
215	4.7	2.975	0.738	0.947
216	3.7	4.67	0.435	0.620
217	14.46	n.d.	4.35	n.d.
218	0.004	0.212	0.038	0.003
219	0.034	n.d.	0.015	0.017
220	0.015	n.d.	0.006	0.042
221	0.003	n.d.	0.001	0.009
222	0.08	n.d.	0.045	0.073

Cpd. No.	<i>L. donovani</i> amastigotes EC ₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC ₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (μM)	<i>T. Brucei</i> (HAT) EC ₅₀ (μM)
223	0.082	n.d.	0.037	0.064
224	0.111	n.d.	0.046	0.067
225	0.037	n.d.	0.05	0.238
226	0.134	n.d.	0.129	0.343
227	0.03	n.d.	0.011	0.059
228	0.031	n.d.	0.01	0.030
229	25.0	n.d.	15.55	12.500
230	0.037	0.022	0.047	0.005
231	0.034	0.113	0.126	0.006
232	0.012	0.01	0.012	0.005
233	0.013	0.01	0.005	0.004
234	0.027	0.003	0.009	0.005
235	0.011	0.01	0.011	0.005
236	0.264	29.67	20.0	1.463
237	0.016	0.009	0.021	0.005
238	0.025	0.032	0.033	0.005
239	1.761	0.009	0.01	0.005
240	0.579	0.027	0.021	0.005
241	1.191	0.006	0.003	0.005
242	1.972	0.106	0.007	0.013
243	2.105	0.065	0.082	0.005
244	0.55	0.021	0.014	0.005
245	0.311	1.491	0.951	0.062
246	0.535	0.379	2.845	0.396
247	0.04	0.023	0.014	0.005
248	0.117	0.008	0.011	0.005
249	0.864	0.125	0.11	0.005
250	0.043	0.01	0.001	0.005
251	0.024	n.d.	0.367	0.005
252	0.183	n.d.	0.022	0.005
253	0.003	n.d.	0.004	0.005
254	0.091	0.673	0.05	0.259
255	0.042	0.028	0.015	0.005
256	0.011	0.038	0.005	0.027
257	0.014	0.007	0.002	0.004
258	0.023	0.039	0.012	0.028
259	0.012	0.016	0.003	0.004
260	0.221	0.224	0.049	0.043
261	0.004	n.d.	0.002	n.d.
262	0.033	n.d.	0.004	n.d.
263	0.012	0.068	0.045	0.010
264	0.357	13.68	0.48	0.384
265	0.003	0.004	0.002	0.001
266	0.008	0.029	0.065	0.005
267	1.713	13.83	9.4	0.081
268	0.084	0.273	0.082	0.116
269	0.019	0.032	0.009	0.020
270	0.233	2.174	1.703	0.079
271	0.12	0.003	0.144	0.388
272	0.131	0.085	0.114	0.351
273	0.027	0.006	0.017	0.045
274	0.002	0.003	0.001	0.001
275	0.003	0.003	0.001	0.001
276	0.029	0.1	0.021	0.033

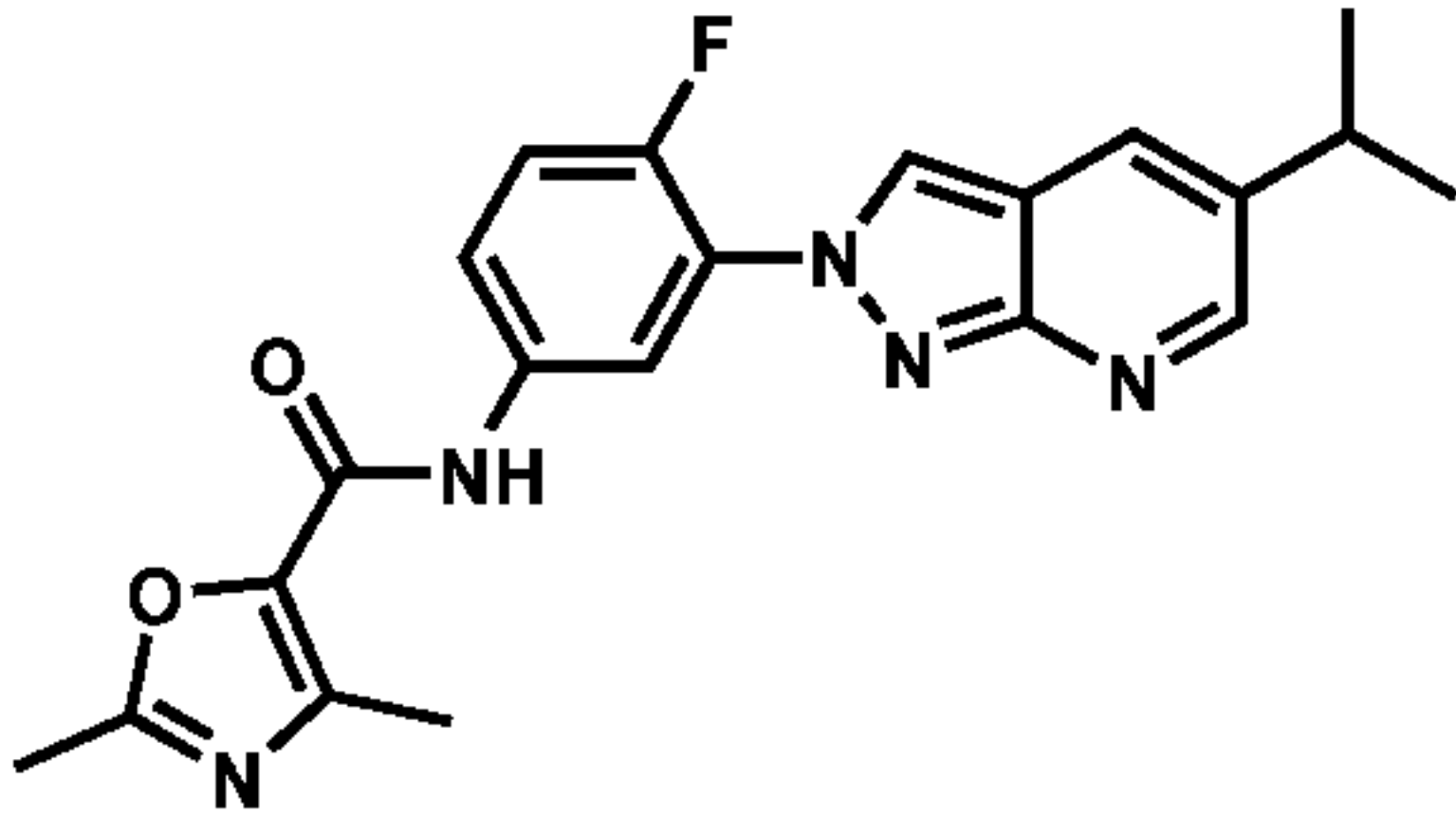
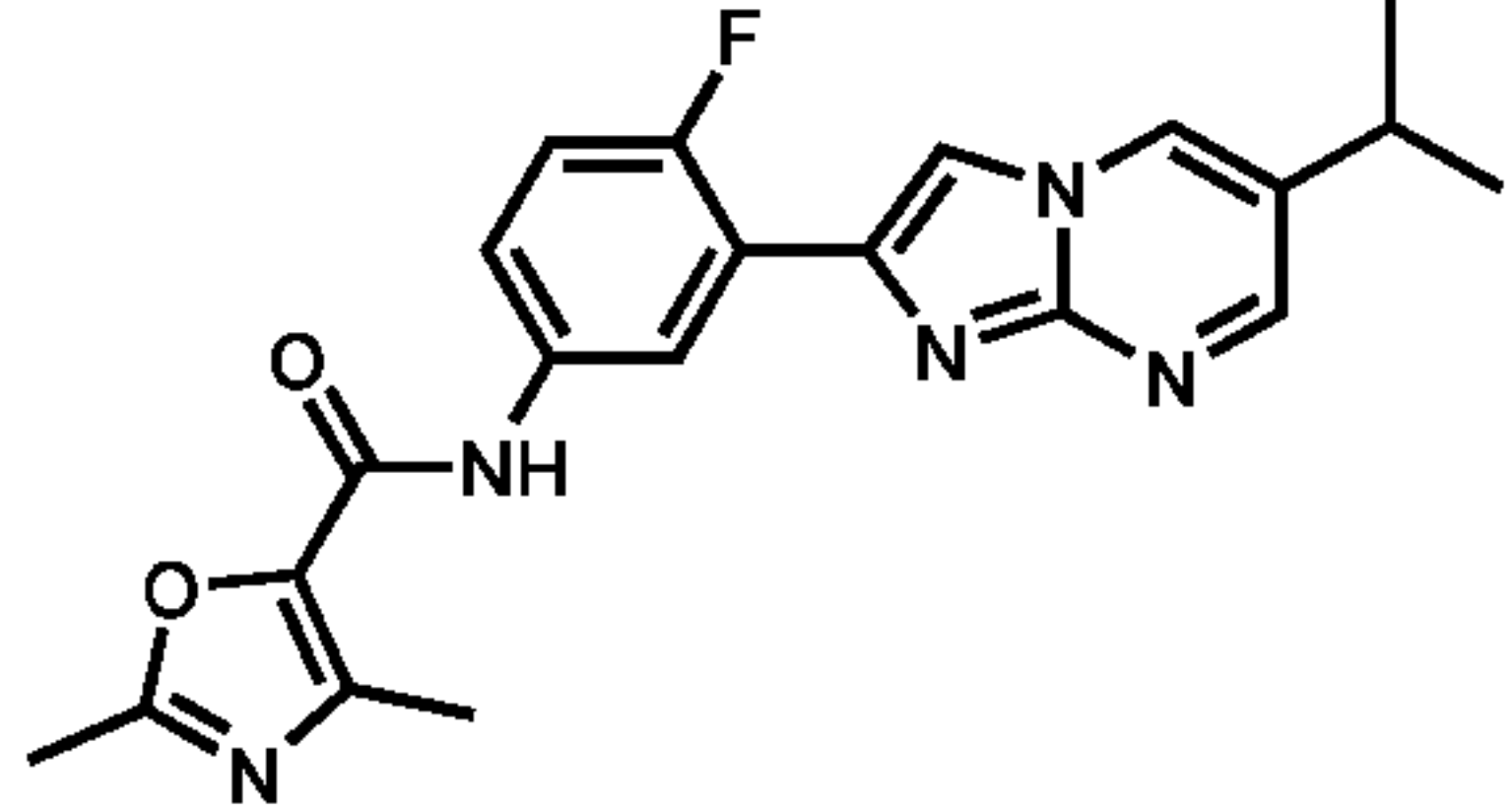
Cpd. No.	<i>L. donovani</i> amastigotes EC₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC₅₀ (μM)	<i>T. Brucei</i> (HAT) EC₅₀ (μM)
277	0.04	0.138	0.144	0.082
278	0.007	n.d.	n.d.	0.013
279	0.01	n.d.	0.003	n.d.
280	0.033	0.028	0.048	0.040
281	0.009	0.026	0.015	0.014
282	0.034	0.07	0.04	0.027
283	0.007	0.019	0.005	0.008
284	0.027	0.056	0.015	0.015
285	0.004	0.009	0.003	0.004
286	0.025	0.047	0.014	0.030
287	0.021	0.03	0.021	0.010
288	0.176	n.d.	n.d.	0.260
289	0.199	n.d.	n.d.	0.208
290	0.007	0.004	0.004	0.004
291	0.01	0.005	0.005	0.005
292	0.005	0.008	0.003	0.005
293	6.82	17.61	1.207	0.167
294	0.004	0.004	0.005	0.005
295	0.292	1.973	4.29	0.038
296	0.216	0.002	0.005	0.005
297	0.105	0.472	0.73	0.005
298	0.014	0.004	0.004	0.004
299	0.029	0.007	0.014	0.005
300	0.022	0.006	0.004	0.003
301	0.073	0.097	0.472	0.008
302	0.118	0.015	0.002	0.005
303	0.49	0.015	0.01	0.005
304	0.004	0.003	0.03	0.005
305	0.11	0.003	0.001	0.005
306	0.09	0.004	0.002	0.005
307	0.281	0.012	0.016	0.005
308	0.568	0.002	0.004	0.005
309	0.001	0.002	0.001	0.005
310	0.002	0.002	0.001	0.005
311	0.058	0.033	0.031	0.027
312	0.003	0.002	0.004	0.033
313	0.001	0.002	0.001	0.005
314	0.242	0.006	0.005	n.d.
315	0.002	0.002	0.001	0.005
316	0.002	0.002	0.001	0.005
317	0.002	0.002	0.001	0.005
318	0.027	0.032	0.013	0.015
319	0.001	n.d.	0.001	0.005
320	0.008	n.d.	0.002	0.005
321	0.018	n.d.	0.011	0.005
322	0.012	n.d.	0.003	0.005
323	0.012	0.113	0.062	0.015
324	0.015	0.045	0.016	0.037
325	0.008	0.05	0.036	0.011
326	0.189	0.761	0.119	0.236
327	0.351	1.205	0.149	0.232
328	0.023	0.16	0.083	0.017
329	0.001	0.002	0.001	0.002
330	0.001	0.002	0.001	0.001

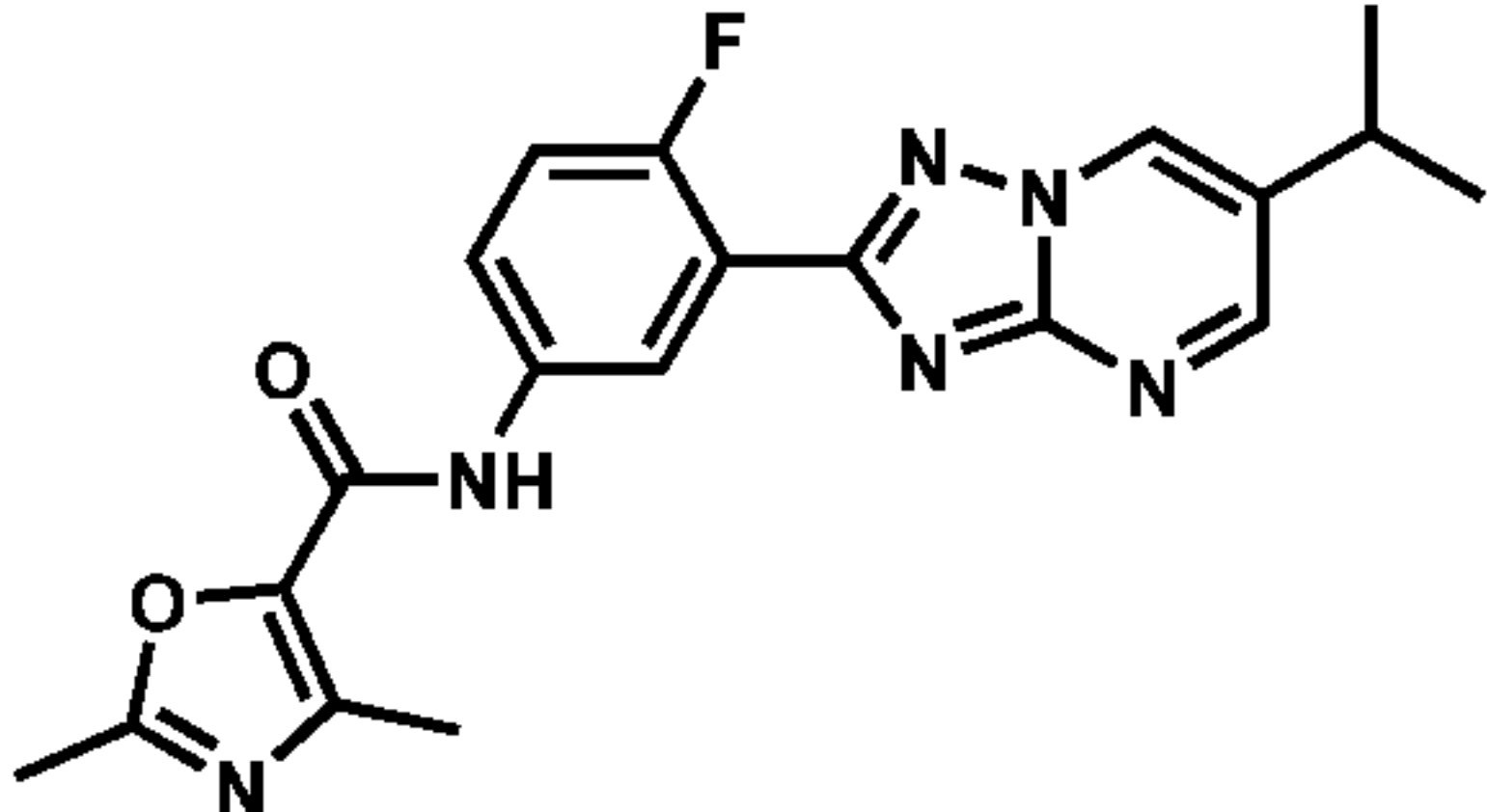
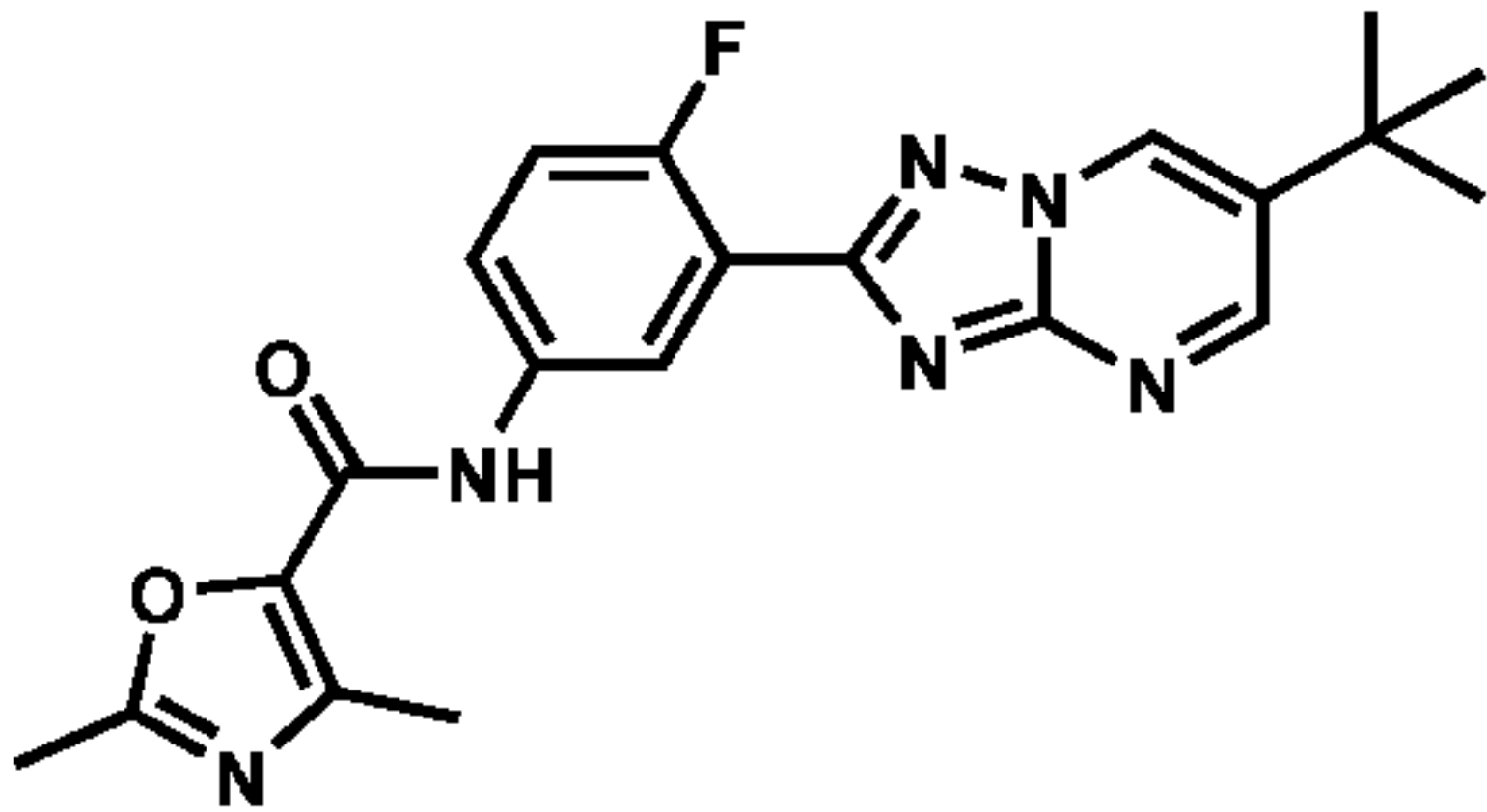
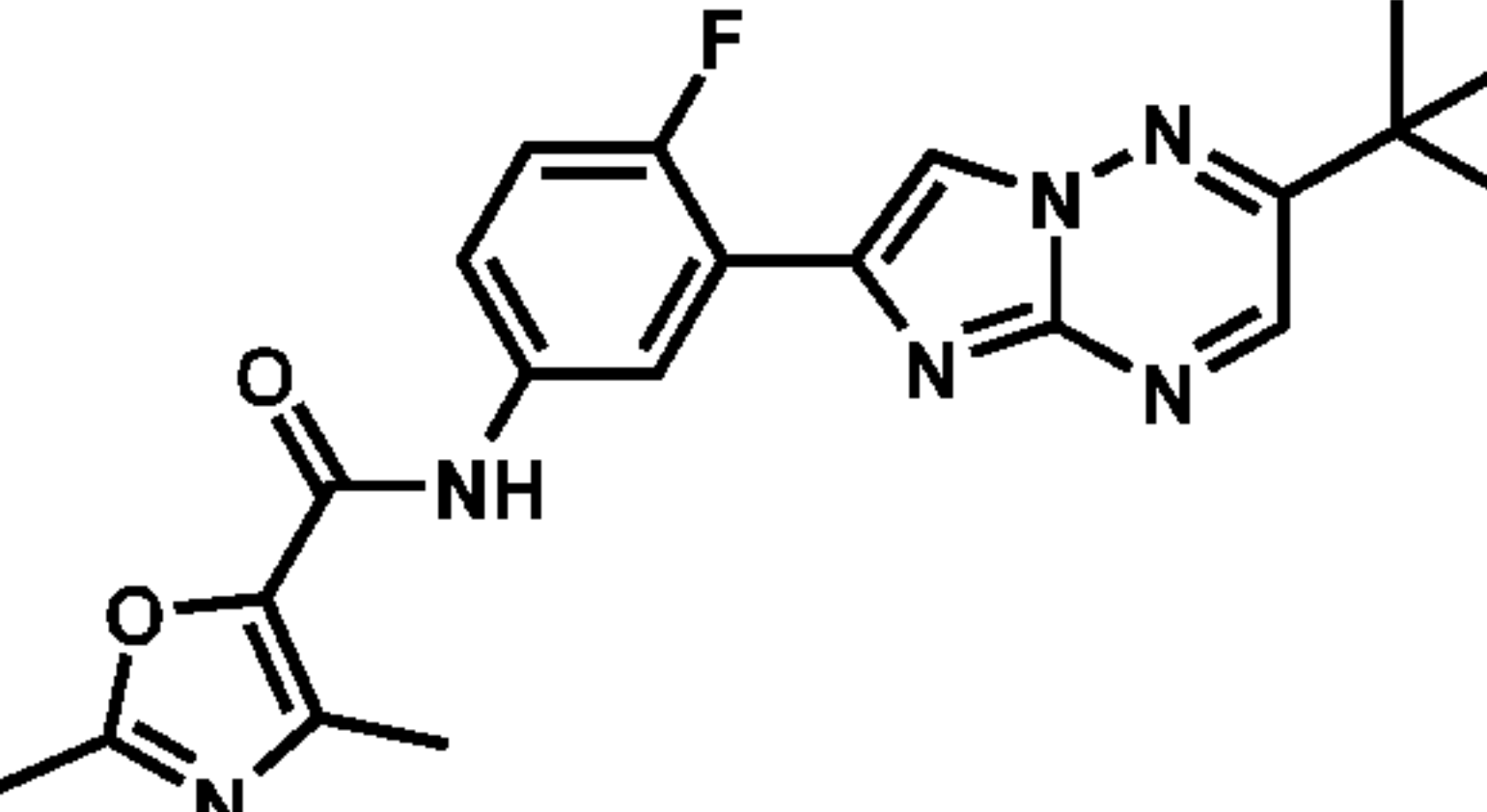
Cpd. No.	<i>L. donovani</i> amastigotes EC ₅₀ (μM)	<i>L. donovani</i> in Mouse Macrophages EC ₅₀ (μM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (μM)	<i>T. Brucei</i> (HAT) EC ₅₀ (μM)
331	0.217	0.91	0.138	0.206
332	0.028	0.075	0.015	0.038
333	0.043	n.d.	0.016	n.d.
334	0.236	1.866	1.459	0.269
335	0.013	0.111	0.47	0.036
336	0.002	0.004	0.001	0.001
337	n.d.	0.013	0.004	0.007
338	0.005	0.002	0.003	0.003
339	1.586	0.31	0.112	0.163
340	0.225	0.087	0.061	0.035
341	0.006	0.033	0.01	0.009
342	0.007	0.024	0.017	0.010
343	0.01	0.032	0.014	0.009
344	0.002	0.005	0.003	0.001
345	0.011	0.033	0.004	0.005
346	0.239	0.155	0.034	0.041
347	0.007	0.015	0.002	0.007
348	0.347	0.963	0.142	0.112
349	0.096	0.102	0.085	0.043
350	0.016	0.058	0.016	0.028
351	0.049	0.024	0.015	0.031
352	0.017	0.031	n.d.	0.039
353	0.005	0.004	n.d.	0.013

Table 4 compares the activity of a compound of Formula (I) with compounds having a different core. EC₅₀ values are obtained from assays described above unless otherwise indicated.

5

Table 4

	<i>L. donovani</i> amastigotes EC ₅₀ (nM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (nM)
	18 nM	15 nM
	180 nM	48 nM

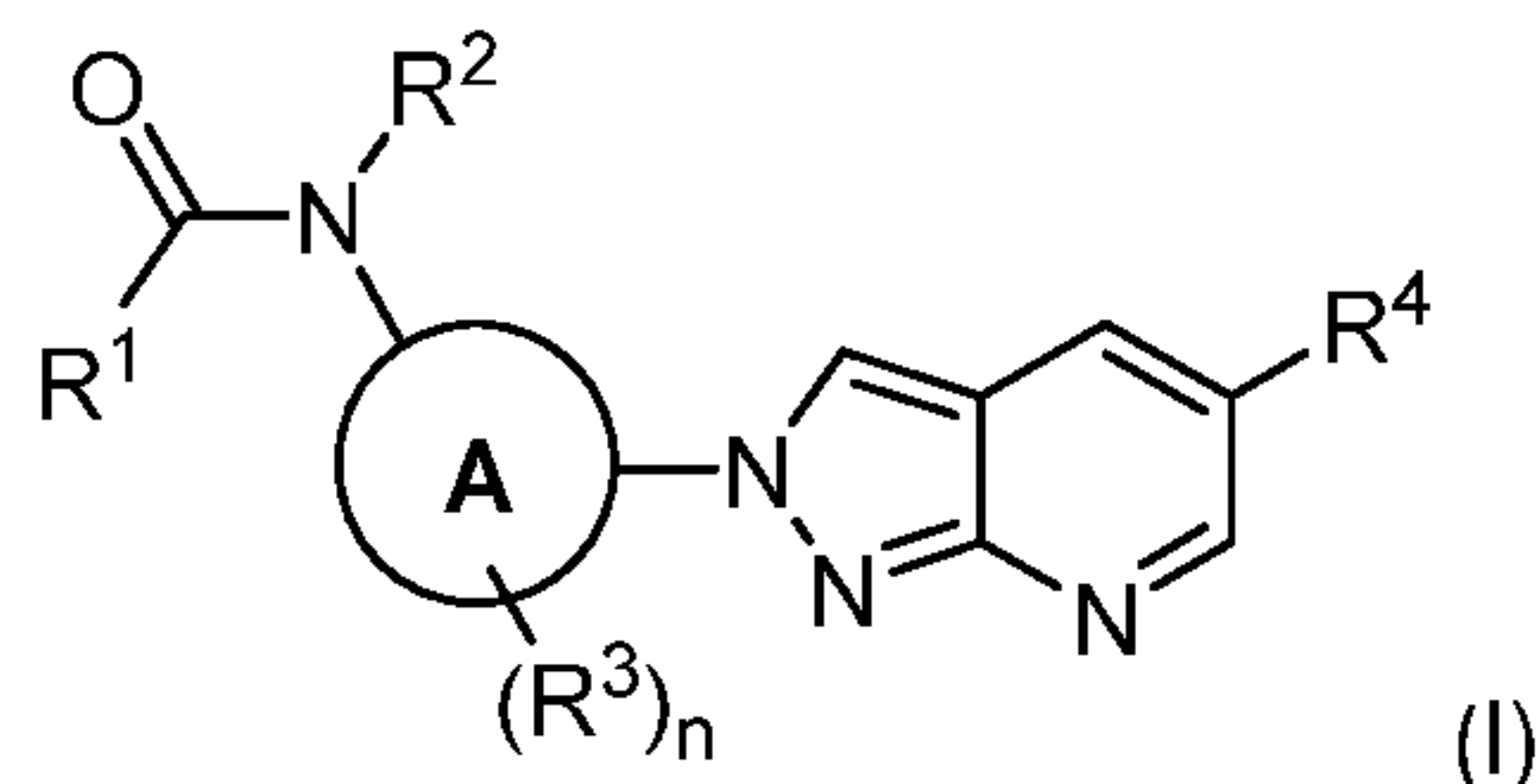
	<i>L. donovani</i> amastigotes EC ₅₀ (nM)	Buckner infectious <i>T. cruzi</i> EC ₅₀ (nM)
	210 nM	45 nM
	80 nM	22 nM
	367 nM	57 nM

It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. All publications, patents, and patent applications cited
5 herein are hereby incorporated by reference for all purposes.

CLAIMS

WE CLAIM:

- 5 1. A compound of Formula (I):



or a pharmaceutically acceptable salt, or stereoisomer thereof; wherein

Ring A is phenyl or pyridinyl;

R¹ is selected from:

- 10 (a) C₁₋₆alkyl that is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen and C₃₋₆cycloalkyl; and said C₃₋₆cycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl;
- (b) C₁₋₄alkoxy that is unsubstituted or substituted by C₁₋₄haloalkyl;
- (c) -NR^{5a}R^{5b} wherein R^{5a} and R^{5b} are independently hydrogen, C₁₋₄alkyl or C₁₋₄haloalkyl; or R^{5a} and R^{5b} together with the nitrogen atom to which both are attached form a 4- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O and S as ring atoms;
- 15 wherein the 4 to 7-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, C₁₋₄alkyl, and C₁₋₄alkoxy; or two substituents on the same or different ring atoms of the 4- to 7-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused Ring B attached to the 4- to 7-membered heterocycloalkyl;
- 20 wherein Ring B is C₃₋₆cycloalkyl or a 3- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms;
- 25 (d) monocyclic C₃₋₆cycloalkyl, C₃₋₆cycloalkenyl or spiropentyl; each of which is unsubstituted or substituted by 1 to 3 substituents independently selected from halogen, cyano, C₁₋₄alkyl, and C₁₋₄haloalkyl, and C₁₋₄alkoxy;
- (e) phenyl or a 5-6 membered heteroaryl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms; each of which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, C₁₋₄alkyl, C₁₋₄haloalkyl, di-C₁₋₄alkylamino-C₁₋₄alkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, and C₃₋₆cycloalkyl;
- 30 R² and R⁷ are independently hydrogen or C₁₋₄alkyl;
- R³ is hydrogen or halogen, and n is 0 or 1; and
- R⁴ is selected from

(a) hydrogen;

(b) halogen;

(c) C₁₋₆haloalkyl or C₁₋₆alkyl that is unsubstituted or substituted by C₃₋₆cycloalkyl; and said C₃₋₆cycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C₁₋₄alkyl;

(d) -NR^{6a}R^{6b} wherein R^{6a} is hydrogen or C₁₋₄alkyl; R^{6b} is hydrogen, C₁₋₄alkoxycarbonyl, C₁₋₄ haloalkyl, C₃₋₆ cycloalkyl, or C₁₋₄alkyl that is unsubstituted or substituted by C₁₋₄alkoxy; or R^{6a} and R^{6b} together with the nitrogen atom to which both are attached form a 4- to 7-membered heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms;

wherein the 4- to 7-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkoxy, oxo, 1,1-dioxo, -C(O)-OR⁷ or a 4-6 membered heterocycloalkyl comprising 1-2 heteroatoms independently selected from N, O and S; or two substituents on the same or different ring atoms of the 4- to 7-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused Ring C attached to the 4- to 7-membered heterocycloalkyl;

wherein Ring C is selected from C₃₋₆cycloalkyl, and 3- to 7-membered heterocycloalkyl comprising 1 to 3 heteroatoms independently selected from N, O or S as ring atoms; and is independently unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, and oxo;

(e) C₃₋₆cycloalkyl;

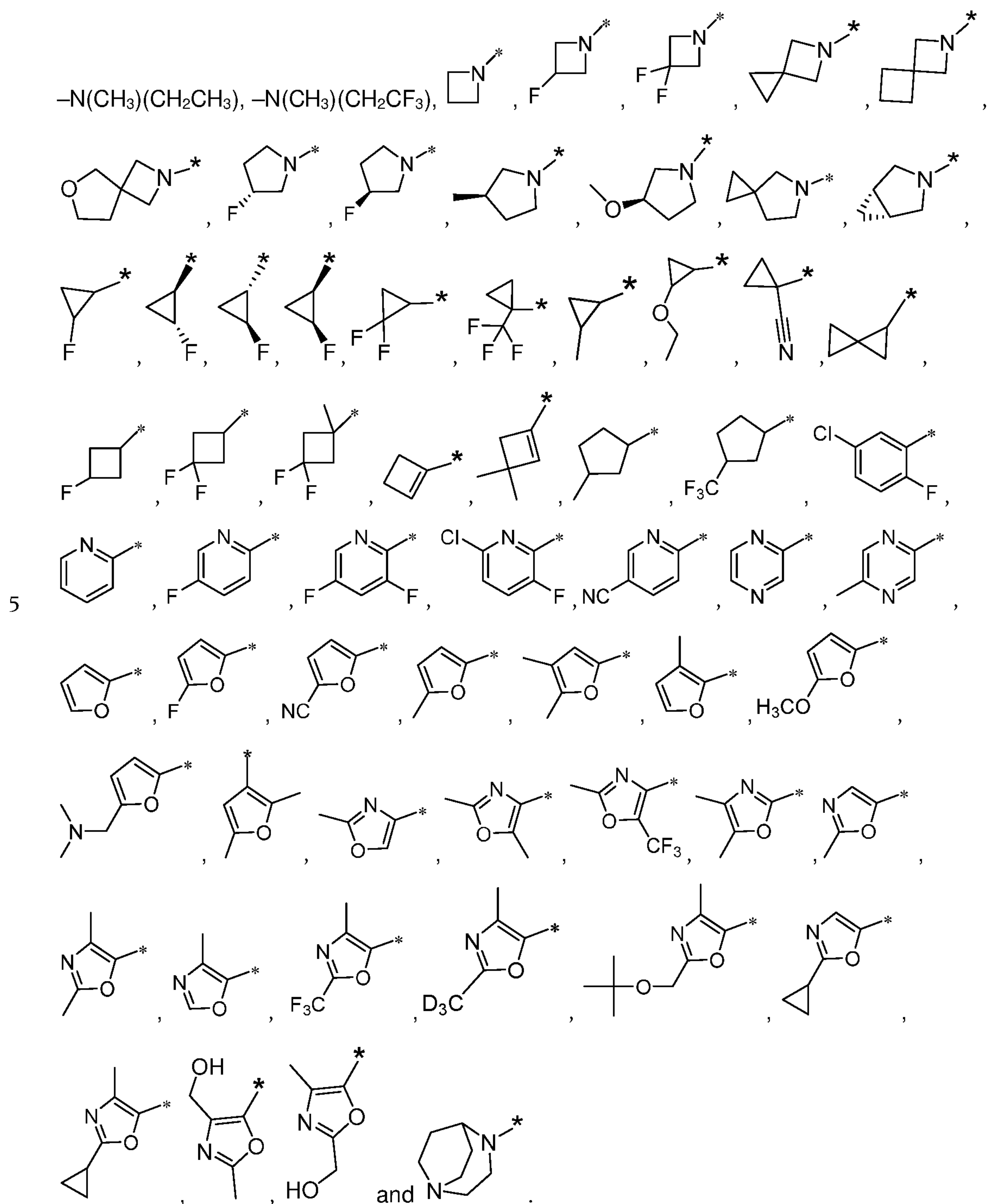
(f) 4- to 6-membered heterocycloalkyl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms; and is unsubstituted or substituted by -C(O)OR⁸, -C(O)R⁸ wherein R⁸ is C₁₋₄ alkyl, and arylC₁₋₄ alkyl that is unsubstituted or substituted by 1 to 2 halo substituents; and

(g) 5- to 6-membered heteroaryl comprising 1 to 2 heteroatoms independently selected from N, O and S as ring atoms; which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, C₁₋₄alkyl, C₁₋₄ hydroxyalkyl, and C₃₋₆cycloalkyl.

2. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein Ring A is phenyl.

3. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, wherein Ring A is pyridinyl.

4. The compound according to any of claims 1-3 or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from -(CH₂)₁₋₃CF₃, -(CH₂)-CH(CH₃)-CF₃, -(CH₂)-C(CH₃)₃, -O(CH₂)₂CF₃, -(CH₂)₀₋₂-cyclopropyl, -(CH₂)₀₋₂-cyclobutyl, -NHCH₃, -N(CH₃)₂, -N(CD₃)₂,

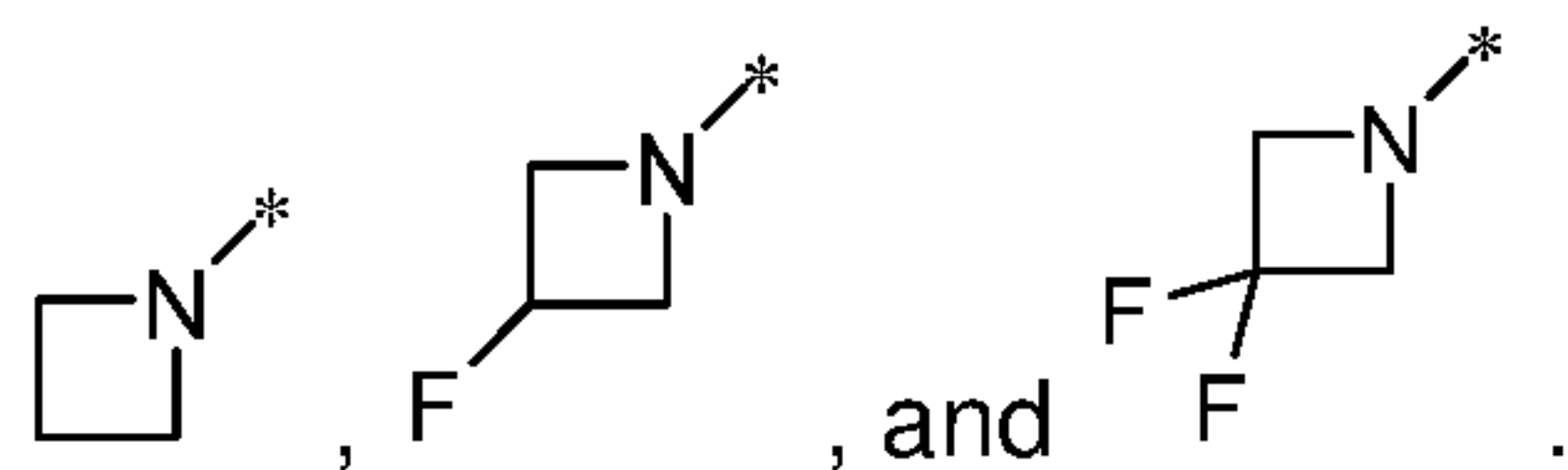


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5. The compound according to any one of claims 1-3 or a pharmaceutically acceptable salt thereof, wherein R^1 is azetidyl, which is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen and C_{1-4} alkyl; or two substituents on the same ring atom of the azetidyl, together with the ring atom to which both are attached, form a spiro cyclopropyl or

15 spiro tetrahydrofuranyl attached to the azetidyl ring.

6. The compound according to any one of claims 1-3 or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from

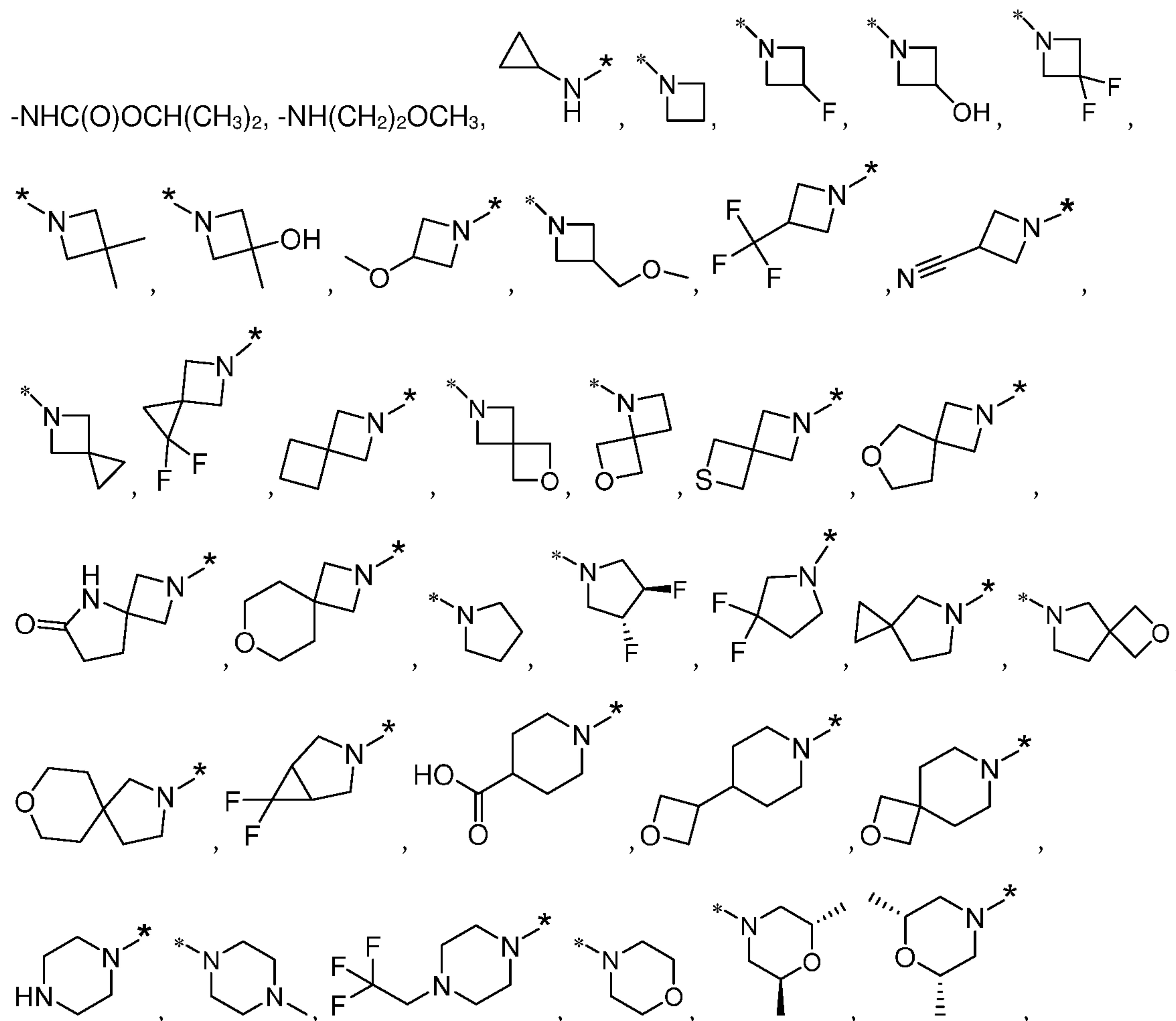


7. The compound according to any one of claims 1-6 or a pharmaceutically acceptable salt thereof, wherein R³ is halo and n is 1.

8. The compound according to claim 7 or a pharmaceutically acceptable salt thereof, wherein R³ is fluoro.

9. The compound according to any one of claims 1-8 or a pharmaceutically acceptable salt thereof, wherein R⁴ is selected from hydrogen, chloro, bromo, methyl, *iso*-propyl,

10 $-(CH_2)_{1-2}CH(CH_3)_2$, $-(CH_2)_{0-1}C(CH_3)_3$, $-C(CH_3)_2CH_2CH_3$, $-CH(CH_3)(CH_2)_{1-2}CH_3$, $-CH_2$ -cyclobutyl, $-(CH_2)_{0-1}CF_3$, $-NH-(CH_2)_{0-1}CH_3$, $-N-(CD_3)_2$, $-N(CH_3)_2$, $-NH-CH-(CH_3)_2$, $-NH-(CH_2)-CH-(CH_3)_2$,



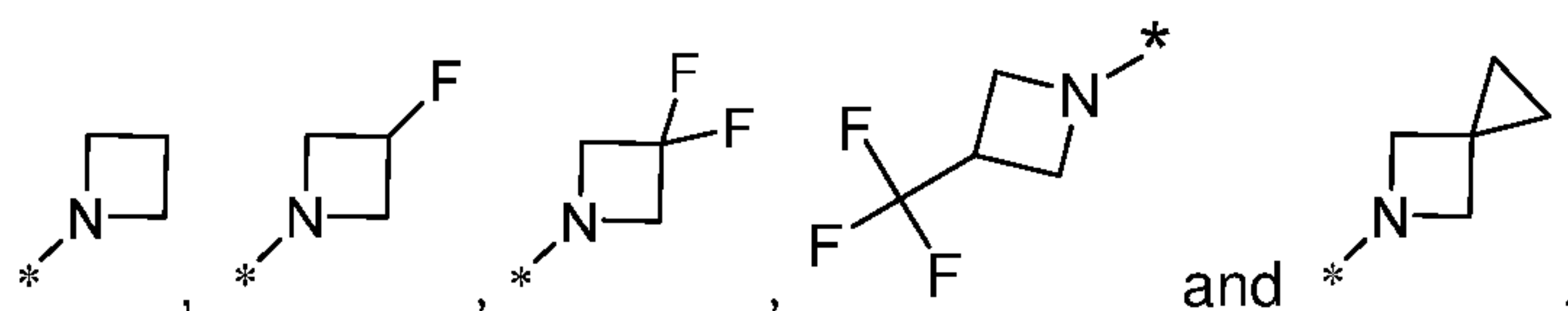


10 R^{6a} is hydrogen or C₁₋₄alkyl;

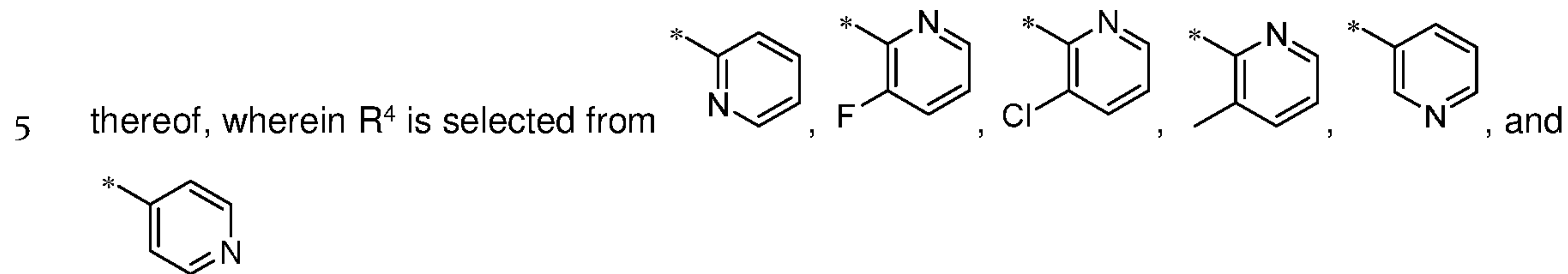
15 wherein the 4- to 6-membered heterocycloalkyl is unsubstituted or substituted by 1 to 2 substituents independently selected from halogen, cyano, hydroxyl, C₁₋₄alkyl, C₁₋₄haloalkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkoxy, and oxo; or two substituents on the same or different ring atoms of the 4- to 6-membered heterocycloalkyl, together with the atoms to which they are attached, form a spiro, bridged or fused, Ring C attached to the 4- to 6-membered heterocycloalkyl;

20

11. The compound according to any one of claims 1-8 or a pharmaceutically acceptable salt thereof, wherein R⁴ is selected from



12. The compound according to any one of claims 1-8 or a pharmaceutically acceptable salt



13. A compound or a pharmaceutically acceptable salt thereof, selected from Compounds 1 to 353 disclosed in Table 1.

14. A pharmaceutical composition comprising a compound according to any one of claims 1-13 or a pharmaceutically acceptable salt thereof, and at least one excipient.

15. A combination comprising a compound according to any one of claims 1-13 or a pharmaceutically acceptable salt thereof, and one or more therapeutically active agent.

16. Use of a compound according to any one of claims 1-13 in the manufacture of a medicament for the treatment of a disorder or disease selected from leishmaniasis, Chagas diseases and human African trypanosomiasis.

17. The method of claim 16, wherein said disease is leishmaniasis selected from visceral leishmaniasis and cutaneous leishmaniasis.

18. The method of claim 17, wherein said second agent selected from stibogluconate, meglumine antimoniate, amphotericin, miltefosine, and paromomycin.

19. The method of claim 16, wherein said disease is Chagas disease; and said second agent is selected from benznidazole, nifurtimox and amphotericin.

20. The method of claim 16, wherein said disease is human African trypanosomiasis; and said second agent is pentamidine, suramin, melarsoprol, eflornithine, and nifurtimox.

