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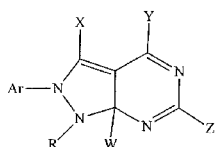
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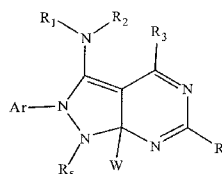
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(54) Title: PYRAZOLOPYRIMIDINE-BASED INSECTICIDAL COMPOSITIONS AND RELATED METHODS



(I)



(II)

(57) Abstract: An pesticidal composition comprises a pyrazolopyrimidine compound of general formula (I) or any agriculturally acceptable salt thereof, wherein Ar, W, X, Y, Z and R are as described herein. An pesticidal composition includes a pyrazolopyrimidine compound of general formula (II) or any agriculturally acceptable salt thereof, wherein A, W, R₁, R₂, R₃, R₄ and R₅ are as described herein. Methods of preparing such pesticidal compositions and methods of controlling insects include using such pesticidal compositions.

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PYRAZOLOPYRIMIDINE-BASED PESTICIDAL COMPOSITIONS AND RELATED METHODS

PRIORITY CLAIM

5 This application claims the benefit of U.S. Provisional Patent Application Serial No. 61/798,550 filed March 15, 2013, the entire disclosure of which is hereby expressly incorporated by reference.

TECHNICAL FIELD

10 Various aspects and embodiments relate generally to pesticidal compositions and to methods of preparing and using such pesticidal compositions. Particular aspects and embodiments generally relate to pyrazolopyrimidine-based pesticidal compositions and the methods of producing and using the pyrazolopyrimidine-based pesticidal compositions.

BACKGROUND

15 Controlling insect populations is essential to modern agriculture, food storage, and hygiene. There are more than ten thousand species of insects that cause losses in agriculture. The world-wide agricultural losses amount to billions of U.S. dollars each year. Accordingly, there exists a continuous need for new pesticides and for methods of producing and using such
20 pesticides.

DISCLOSURE

 Embodiments of the present disclosure include pyrazolopyrimidine compounds, and the pesticidal compositions comprising such pyrazolopyrimidine compounds.

25 Embodiments of the present disclosure further include methods of producing pyrazolopyrimidine-based pesticidal compositions.

 Further embodiments of the present disclosure include methods of controlling insects that include applying an pesticidal composition comprising a pyrazolopyrimidine -based compound near a population of insects.

30

MODE(S) FOR CARRYING OUT THE INVENTION

 As used herein, the term "alkyl" means and includes a saturated, straight, or branched hydrocarbon. Examples may include, but are not limited to, methyl, ethyl, propyl, isopropyl, 1-

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butyl, isobutyl, t-butyl, 2-methylbutyl, pentyl, isopentyl, hexyl, isohexyl, heptyl, octyl, nonyl, decyl, 3-methylpentyl, 2,2-dimethylbutyl, or 2,3-dimethylbutyl.

As used herein the term “cycloalkyl” means a monocyclic or polycyclic, saturated substituent consisting of carbon and hydrogen, such as, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclodecyl, norbornyl, bicycle[2.2.2]octyl, and decahydronaphthyl.

As used herein, the term “alkenyl” means and includes a straight or branched hydrocarbon containing at least one carbon-carbon double bond. Examples may include, but are not limited to, ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, or decenyl.

As used herein the term “cycloalkenyl” means a cyclic hydrocarbon containing at least one carbon-carbon double bond, such as, for example, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, and cyclodecenyl.

As used herein, the term “alkynyl” means and includes a straight, branched, or hydrocarbon containing at least one carbon-carbon triple bond. Examples may include, but are not limited to, ethynyl, propargyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, or decynyl.

As used herein the term “cycloalkynyl” means a cyclic hydrocarbon containing at least one carbon-carbon triple bond.

As used herein, the term “aryl” means and includes an aromatic ring compound with or without any substitution, such as, for example, phenyl and naphthyl.

As used herein, the term “alkoxy” means and includes an alkyl group containing at least one carbon-oxygen single bond. Non-limiting examples may include methoxyl, ethoxy, propoxy, or butoxy.

As used herein, the term “alkylthio” means and includes an alkyl group containing at least one carbon-sulfur single bond.

As used herein, the term “haloalkylthio” means and includes an alkyl group containing at least one carbon-sulfur single bond and halogen atom.

As used herein, the terms “halo” and “halogen” mean and include fluorine, chlorine, bromine, or iodine.

As used herein, the terms “haloalkyl” and “haloalkoxy,” respectively, mean and include, an alkyl group and an alkoxy group substituted with at least one halogen atom or halothio group.

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As used herein, the term “heteroatom” means and includes sulfur (S), oxygen (O) or nitrogen (N) atom.

As used herein, the term “heteroaryl” means and includes an aromatic moiety containing at least one sulfur (S), oxygen (O), or nitrogen (N) atom in the aromatic ring. Non-limiting
5 examples may include furyl, pyridyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, benzofuranyl, benzothiophenyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, isoindolyl, benzimidazolyl, purinyl, carbozoyl, oxazolyl, thiazolyl, isothiazolyl, 1,2,4-thiadiazolyl, isooxazolyl, pyrrolyl, pyrazolyl, quinazolinyl, pyridazinyl, pyrazinyl, cinnolyl, phthalazinyl, quinoxalinyl, xanthinyl, hypoxanthinyl, pteridinyl,
10 5-azacytidinyl, 5-azauracilyl, triazolopyridinyl, imidazolopyridinyl, pyrrolopyrimidinyl, or pyrazolopyrimidinyl.

As used herein, the term “heteroalkyl” means and includes an alkyl moiety as defined herein containing at least one sulfur (S), oxygen (O), or nitrogen (N) atom.

As used herein, the term “cyano” means and includes a functional group containing a
15 carbon–nitrogen triple bond.

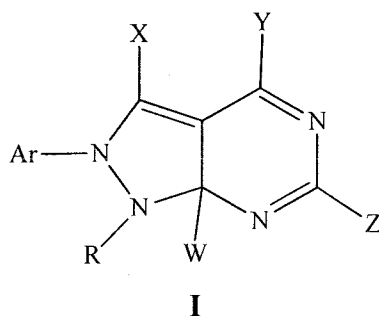
As used herein, the term “nitro” means and includes a functional group containing a nitrogen atom joined to two oxygen atoms.

As used herein the term, “pesticidally effective amount” means and includes an amount of active material that causes an adverse effect to the at least one pest, wherein the adverse effect
20 may include deviations from natural development, killing, regulation, or the like.

As used herein, the term “control” or grammatical variations thereof means and includes regulating the number of living insects or regulating the number of viable eggs of the pests.

The pyrazolopyrimidine-based pesticidal composition may comprise a pyrazolopyrimidine compound of general formula I or any agriculturally acceptable salt thereof:

25



wherein,

Ar may be any aryl group including, but are not limited to, phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, pyrazolo, imidazolo, thiophenyl, or any other heteroaromatic rings. Ar may be substituted or unsubstituted. Ar may be substituted at any open position with
5 hydrogen, halogen, alkyl, alkenyl, alkynyl, or combinations thereof. Ar may include one or more heteroatoms such as N, O, Si, or SO_n ($n = 0, 1, 2$) at any position. Additionally, Ar may be substituted with alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, sulfoxide, unsubstituted amines, substituted amines, unsubstituted aryloxy, substituted aryloxy group, esters, acetates, amides, or combinations thereof;

10 X may be nitrogen (N), oxygen (O) or sulfur (S),

where X is nitrogen, it may be substituted with alkyl, cycloalkyl, alkenyl, alkynyl, or combinations thereof, wherein the alkyl, alkenyl or alkynyl may include one or more heteroatoms such as N, O, Si, or SO_n ($n = 0, 1, 2$) at any position. Furthermore, N may be substituted directly with N, O or SO_n ($n = 1, 2$) with each individually substituted with hydrogen
15 and/or an alkyl moiety including one or more heteroatoms such as N, O, Si, or SO_n ($n = 0, 1, 2$) at any position. N may also be substituted with $\text{C}(\text{O})\text{R}'$, $\text{C}(\text{O})\text{OR}'$, $\text{C}(\text{O})\text{NR}'$, where R' may be a substituted alkyl moiety which may include one or more heteroatoms such as N, O, Si, or SO_n ($n = 0, 1, 2$) at any position; an aryl or heteroaryl moiety where substituents may be any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano,
20 nitro, sulfone, and aryloxy that may be substituted or unsubstituted,

when X is oxygen, it may be substituted with hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, amino, $\text{C}(\text{O})\text{R}'$, or $\text{C}(\text{O})\text{NR}'$ where R' may be substituted alkyl moiety which may include one or more heteroatoms such as N, O, Si, or SO_n ($n = 0, 1, 2$) at any position. Additionally, R' may be aryl, heteroalkyl or heteroaryl where substituents may be any
25 combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy that may be substituted or unsubstituted,

where X is sulfur, it may be SO_n ($n = 0, 1, 2$). It may connect to hydrogen ($n=0$), alkyl or cycloalkyl group that may include one or more heteroatoms such as N, O, Si, or SO_n ($n = 0, 1, 2$) at any position. It may connect to aryl or heteroaryl group that may be substituted with any
30 combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro and sulfone group. It may connect to an amino moiety having at least one substituted alkyl, heteroalkyl, aryl, or heteroaryl group where the substituents may be any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, and sulfone;

Y and Z may independently be hydrogen, halogen, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano amine, unsubstituted amine, or substituted amine;

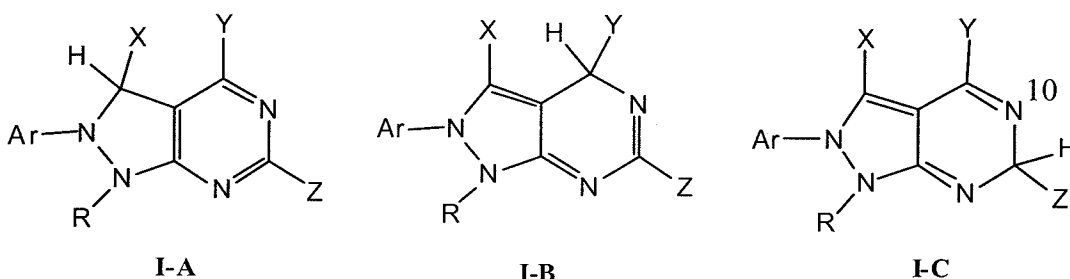
R may be selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, S(=O)_n(C₁-C₈ alkyl) (n = 0, 1, 2), C(=O)NR_xR_y, (C₁-C₈ alkyl)NR_xR_y, C(=O)O(C₁-C₈ alkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl), (C₁-C₈ alkyl)O(C₁-C₈ alkyl), (C₁-C₈ alkyl)OC(=O)(C₁-C₈ alkyl), (C₁-C₈ alkyl)OC(=O)(C₂-C₈ alkenyl), (C₁-C₈ alkyl)OC(=O)(C₂-C₈ alkynyl), (C₁-C₈ alkyl)OC(=O)(C₁-C₈ cycloalkyl), (C₁-C₈ alkyl)OC(=O)(C₃-C₈ cycloalkenyl), (C₁-C₈ alkyl)OC(=O)(C₇-C₈ cycloalkynyl), (C₁-C₈ alkyl)S(C₁-C₈ alkyl), C(=O)(C₁-C₈ alkyl)C(=O)O(C₁-C₈ alkyl), wherein each alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl and cycloalkynyl may optionally be substituted with one or more substituents independently selected from the group consisting of hydrogen, halogen, cyano, nitro, oxo, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₃-C₈ cycloalkyl, C₃-C₈ halocycloalkyl, C₃-C₈ cycloalkoxy, C₃-C₈ halocycloalkoxy, C₁-C₈ alkoxy, C₁-C₈ haloalkoxy, C₂-C₈ alkenyl, C₂-C₈ alkynyl, S(=O)_n(C₁-C₈ alkyl) (n = 0, 1, 2), S(=O)_n(C₁-C₈ haloalkyl) (n = 0, 1, 2), OSO₂(C₁-C₈ alkyl), OSO₂(C₁-C₈ haloalkyl), C(=O)NR_xR_y, (C₁-C₈ alkyl)NR_xR_y, C(=O)(C₁-C₈ alkyl), C(=O)O(C₁-C₈ alkyl), C(=O)(C₁-C₈ haloalkyl), C(=O)O(C₁-C₈ haloalkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl), (C₁-C₈ alkyl)O(C₁-C₈ alkyl), (C₁-C₈ alkyl)S(C₁-C₈ alkyl), C(=O)(C₁-C₈ alkyl)C(=O)O(C₁-C₈ alkyl), phenyl, and phenoxy, and wherein R_x and R_y each is independently selected from the group consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy; and

W may be selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, and benzyl, wherein each alkyl, alkenyl, and benzyl may optionally be substituted with one or more substituents independently selected from the group consisting of hydrogen, halogen, cyano, nitro, oxo, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₃-C₈ cycloalkyl, C₃-C₈ halocycloalkyl, C₃-C₈ cycloalkoxy, C₃-C₈ halocycloalkoxy, C₁-C₈ alkoxy, C₁-C₈ haloalkoxy, C₂-C₈ alkenyl, C₂-C₈ alkynyl, S(=O)_n(C₁-C₈ alkyl), S(=O)_n(C₁-C₈ haloalkyl) (wherein n= 0, 1, or 2), OSO₂(C₁-C₈ alkyl), OSO₂(C₁-C₈ haloalkyl), C(=O)NR_xR_y, (C₁-C₈ alkyl)NR_xR_y, C(=O)(C₁-C₈ alkyl), C(=O)O(C₁-C₈ alkyl), C(=O)(C₁-C₈ haloalkyl), C(=O)O(C₁-C₈ haloalkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl), (C₁-C₈ alkyl)O(C₁-C₈ alkyl), (C₁-C₈ alkyl)S(C₁-C₈ alkyl), C(=O)(C₁-C₈ alkyl)C(=O)O(C₁-C₈ alkyl), phenyl, and phenoxy, wherein R_x and R_y each is independently selected from the group

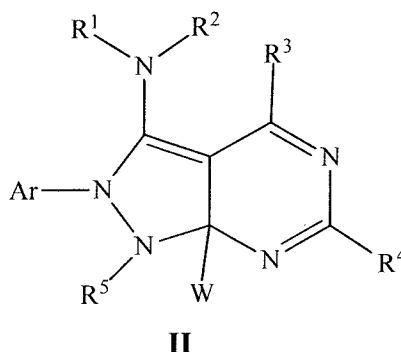
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consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy.

The pyrazolopyrimidine compound of the general formula **I** may exist in various isomeric forms. Non-limiting examples of such isomeric forms may include, but are not limited to, compounds **I-A**, **I-B** and **I-C** as shown below. The pyrazolopyrimidine compound of the present disclosure may include at least one of these isomeric forms.



In one embodiment, the pyrazolopyrimidine compound may have general formula **II** or any agriculturally acceptable salt thereof:



wherein,

Ar may be a substituted phenyl, pyridyl, pyrimidinyl, pyridazinyl, triazinyl, pyrazolo, imidazolo, triazole, thiophenyl, furyl, wherein the substituent group may include at least one of hydrogen, alkyl, alkoxy, halogen, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, nitro, sulfone, aryloxy, and any combination thereof;

W may be selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, benzyl, wherein each alkyl, alkenyl, and benzyl may optionally be substituted with one or more substituents independently selected from the group consisting of hydrogen, halogen, cyano, nitro, oxo, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₃-C₈ cycloalkyl, C₃-C₈ halocycloalkyl,

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C₃-C₈ cycloalkoxy, C₃-C₈ halocycloalkoxy, C₁-C₈ alkoxy, C₁-C₈ haloalkoxy, C₂-C₈ alkenyl, C₂-C₈ alkynyl, S(=O)_n(C₁-C₈ alkyl), S(=O)_n(C₁-C₈ haloalkyl) (wherein n= 0, 1, or 2), OSO₂(C₁-C₈ alkyl), OSO₂(C₁-C₈ haloalkyl), C(=O)NR_xR_y, (C₁-C₈ alkyl)NR_xR_y, C(=O)(C₁-C₈ alkyl), C(=O)O(C₁-C₈ alkyl), C(=O)(C₁-C₈ haloalkyl), C(=O)O(C₁-C₈ haloalkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl), (C₁-C₈ alkyl)O(C₁-C₈ alkyl), (C₁-C₈ alkyl)S(C₁-C₈ alkyl), C(=O)(C₁-C₈ alkyl)C(=O)O(C₁-C₈ alkyl), phenyl, and phenoxy;

R¹, R² and R⁵ may be independently selected from:

- (a) hydrogen, hydroxy, or thiol;
- 10 (b) (C₁-C₈) alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S (C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;
- (c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
- 15 S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;
- (d) (C₃-C₈)alkynyl, C(=O)(C₃-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₃-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₃-C₈)alkynyl, S(O)(C₃-C₈)alkynyl, or S(O)₂(C₃-C₈)alkynyl;
- (e) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
- 20 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;
- (f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, S-heterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;
- (g) N(R⁸)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂,
- 25 S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; or
- (h) C₃-C₈ cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b), (c), (d) and (h) may independently be substituted with one or more substituents selected from:

- (a1) F, Cl, Br, I, CN, NO₂, OH, or OSi((C₁-C₈)alkyl)₃;
- 30 (b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;

(c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, or S(O)₂(C₂-C₈)alkynyl;

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;

(g1) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; or

(h1) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e) and (f) may independently be substituted with one or more substituents selected from:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, or OSi((C₁-C₈)alkyl)₃;

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;

(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, or S(O)₂(C₂-C₈)alkynyl;

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;

(g2) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; or

(h2) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in **(b1)**, **(b2)**, **(c1)**, **(c2)**, **(d1)**, **(d2)**, **(h1)**, and **(h2)** may independently be substituted with one or more substituents selected from:

5 **(a3)** F, Cl, Br, I, CN, NO₂, OH, or OSi((C₁-C₈)alkyl)₃;

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;

10 **(c3)** C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, or S(O)₂(C₂-C₈)alkynyl;

15 **(e3)** phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;

20 **(g3)** N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; or

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in **(e1)**, **(e2)**, **(f1)**, and **(f2)** may independently be substituted with one or more substituents selected from:

25 **(a4)** F, Cl, Br, I, CN, NO₂, OH, SF₅, or OSi((C₁-C₈)alkyl)₃;

(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;

30 **(c4)** (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, or S(O)₂(C₂-C₈)alkynyl;

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
5 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;

(g4) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
10 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, or S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; or

(h4) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b3), (b4), (c3), (c4), (d3), (d4), (h3), and (h4) may independently be substituted with one or more substituents selected from:

15 (a5) F, Cl, Br, I, CN, NO₂, OH, or OSi((C₁-C₈)alkyl)₃;

(b5) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;

(c5) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;

(d5) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, or S(O)₂(C₂-C₈)alkynyl;

25 (e5) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;

(f5) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;

30 (g5) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; or

(h5) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e3), (e4), (f3), and (f4) may independently be substituted with one or more substituents selected from:

(a6) F, Cl, Br, I, CN, NO₂, OH, SF₅, or OSi((C₁-C₈)alkyl)₃;

(b6) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl,
5 OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl;

(c6) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl,
OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, or S(O)₂(C₂-C₈)alkenyl;

10 (d6) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl,
O(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, or S(O)₂(C₂-C₈)alkynyl;

(e6) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, or S(O)₂phenyl;

15 (f6) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl,
OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl,
Sheterocyclyl, S(O)heterocyclyl, or S(O)₂heterocyclyl;

(g6) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; or

20 (h6) (C₃-C₈)cycloalkyl,
wherein R⁸ may be selected from:

(a) H, CN, OH,

(b) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, C(=O)NH(C₁-C₈)alkyl,
C(=S)NH(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,
25 C₈)alkyl,

(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, C(=O)NH(C₂-C₈)alkenyl,
C(=S)NH(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d) (C₃-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, C(=O)NH(C₂-C₈)alkynyl,
30 C₈)alkynyl, C(=S)NH(C₂-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(O)(C₃-C₈)alkynyl, S(O)₂(C₃-C₈)alkynyl,

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, C(=O)NHphenyl, C(=S)NHphenyl, C(=S)phenyl, C(=S)Ophenyl, S(O)phenyl, S(O)₂phenyl,

(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, C(=O)NH-heterocyclyl, C(=S)NH-heterocyclyl, C(=S)heterocyclyl, C(=S)Oheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h) (C₃-C₈)cycloalkyl,

5 wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl in (b), (c), (d) and (h) of R⁸ may independently be substituted with one or more substituents selected from:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl

(c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g1) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h1) (C₃-C₈)cycloalkyl,

25 wherein each of the phenyl and heterocyclyl in (e) and (f) of R⁸ may independently be substituted with one or more substituents selected from:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g2) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, and S(O)₂N(R⁹)₂, and

(h2) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b1), (b2), (c1), (c2), (d1), (d2), (h1), and (h2) of R⁸ may independently be substituted with one or more substituents selected from:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g3) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) of R⁸ may independently be substituted with one or more substituents selected from:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl,
5 OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl,
OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

10 (d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl,
OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl,
S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

15 (f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl,
OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl,
Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g4) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

20 (h4) (C₃-C₈)cycloalkyl,

wherein R⁹ may be selected from:

(a) H, CN, OH, OSi((C₁-C₈)alkyl)₃,

(b) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl,
OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-
25 C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₃-C₈)alkenyl,
OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl,
30 OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-
C₈)alkynyl, S(O)(C₃-C₈)alkynyl, S(O)₂(C₃-C₈)alkynyl,

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, C(=S)phenyl,
C(=S)Ophenyl, S(O)phenyl, S(O)₂phenyl

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(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, C(=S)heterocyclyl, C(=S)Oheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(g) (C₃-C₈)cycloalkyl,

5 wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b), (c), (d) and (g) of R⁹ may independently be substituted with one or more substituents selected from:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-
10 C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,
15

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and
20

(h1) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e) and (f) of R⁹ may independently be substituted with one or more substituents selected from:

25 (a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,
30

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(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
5 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h2) (C₃-C₈)cycloalkyl,

10 wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b1), (b2), (c1), (c2), (d1), (d2), (h1), and (h2) of R⁹ may independently be substituted with one or more substituents selected from:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl,
15 OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

20 (d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

25 (f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) of R⁹ may
30 independently be substituted with one or more substituents selected from:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

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(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h4) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b3), (b4), (c3), (c4), (d3), (d4), (h3), and (h4) of R⁹ may independently be substituted with one or more substituents selected from:

(a5) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b5) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c5) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d5) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e5) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f5) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

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(h5) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e3), (e4), (f3), and (f4) of R⁹ may independently be substituted with one or more substituents selected from:

(a6) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

5 (b6) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c6) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, 10 S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d6) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e6) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, 15 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

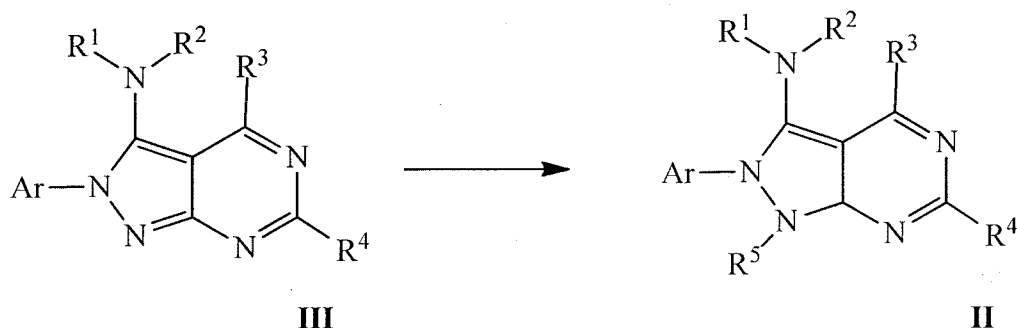
(f6) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h6) (C₃-C₈)cycloalkyl.

20 R³ and R⁴ may independently be hydrogen, halogen, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano amine, unsubstituted amine, or substituted amine.

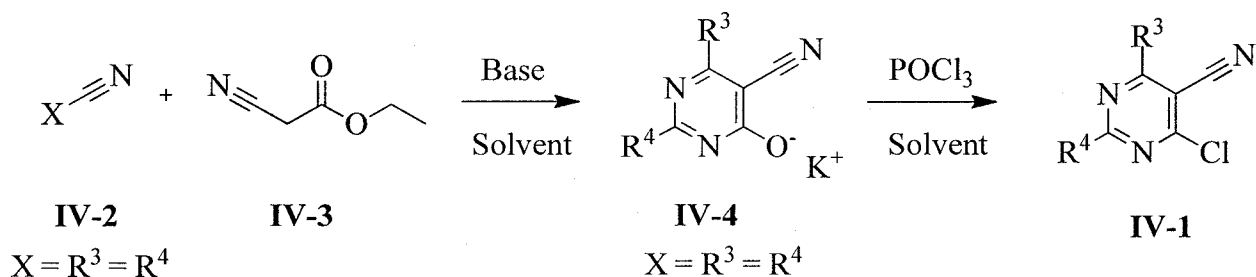
The pyrazolopyrimidine compound of the general formula II may be produced by reducing the corresponding pyrazolopyrimidine compound of general formula III, as shown in

25 Scheme 1.

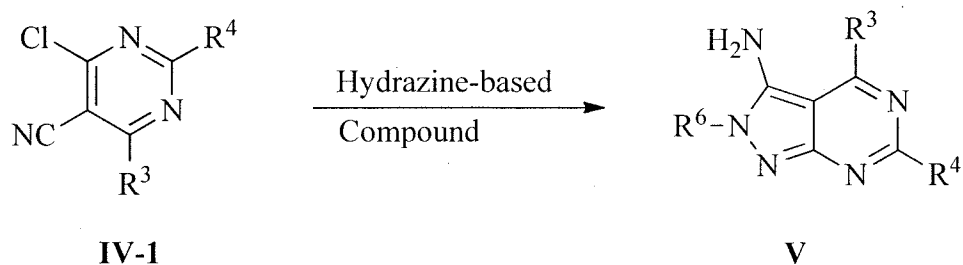
Scheme 1

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The pyrazolopyrimidine compound **III** may be produced from 4-chloro-2,6-substituted pyrimidine-5-carbonitrile of formula **IV-1**. In one embodiment, the compound 4-chloro-2,6-substituted pyrimidine-5-carbonitrile of formula **IV-1** may be produced as shown in **Scheme 2**, wherein each substituent groups R^3 and R^4 is a C_1 - C_8 alkyl group substituted with at least two or more halogen atoms. First, two equivalents of the cyanoalkyl compound **IV-2** is reacted with ethyl 2-cyanoacetate (**IV-3**) in a solvent, such as tetrahydrofuran (THF), and a non-nucleophilic base, such as potassium *tert*-butoxide (KO*t*Bu), at a temperature of approximately 25° C to provide the 4-hydroxy-2,6-substituted pyrimidine-5-carbonitrile salt of formula **IV-4**. See Parker, M. H. et al. *Synth. Commun.* **2004**, 34, 903–907. Then, the hydroxyl substituent group at the 4-position of the pyrimidine compound **IV-4** is converted to a chloride substituent group by reacting with phosphorus oxychloride (POCl₃) in a solvent, such as acetonitrile (MeCN), at a temperature between about 60 °C and about 70 °C to provide the 4-chloro-2,6-substituted pyrimidine-5-carbonitrile of formula **IV-1**.

Scheme 2

The pyrazolopyrimidine compound **V** may be synthesized by reacting 4-chloro-2,6-substituted pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine-based compound as shown in **Scheme 3**.

Scheme 3

- 20 -

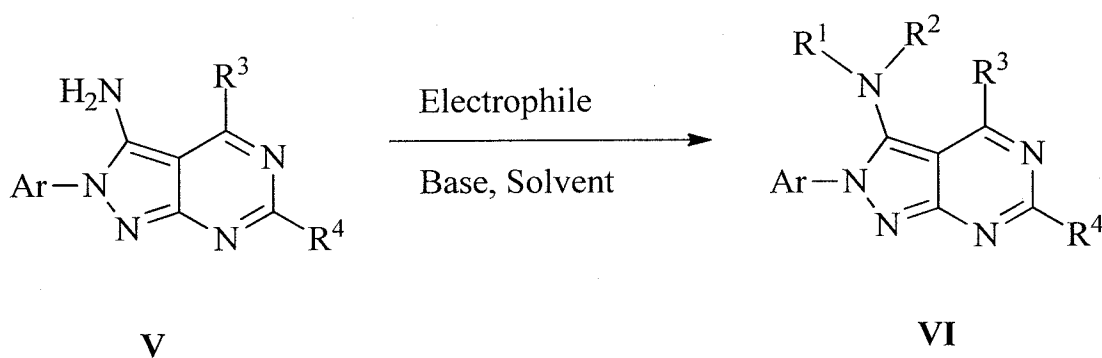
In one embodiment of the synthetic **Scheme 3**, compound 4-chloro-2,6-substituted pyrimidine-5-carbonitrile **IV-1** may react with a hydrazine-based compound in the presence of a base, such as triethylamine (TEA), and a polar aprotic solvent, such as 1,4-dioxane or *N,N*-dimethylformamide (DMF), at a temperature from approximately 25° C to about 90° C.

5 In one embodiment of the synthetic **Scheme 3**, compound 4-chloro-2,6-substituted pyrimidine-5-carbonitrile **IV-1** may react with a *tert*-butoxycarbonyl (Boc)-protected hydrazine in the presence of a polar, aprotic solvent, such as 1,4-dioxane. Then, the resulting Boc-protected compound may react with triethylsilane and an acid, such as trifluoroacetic acid (TFA), in a non-reactive solvent, such as dichloromethane (CH₂Cl₂), at a temperature from
10 approximately 25° C to about 50 °C.

In one embodiment of the synthetic **Scheme 3**, compound 4-chloro-2,6-substituted pyrimidine-5-carbonitrile **IV-1** may react with a hydrazine-based compound in the presence of a polar protic solvent, such as ethanol (EtOH), with or without a base, such as TEA, at an ambient temperature i.e. room temperature (RT, about 22 °C).

15 The amine group of the pyrazolopyrimidine compound **V** may be substituted with at least one electrophile to provide the pyrazolopyrimidine compound of general formula **VI**, as shown in **Scheme 4**.

Scheme 4



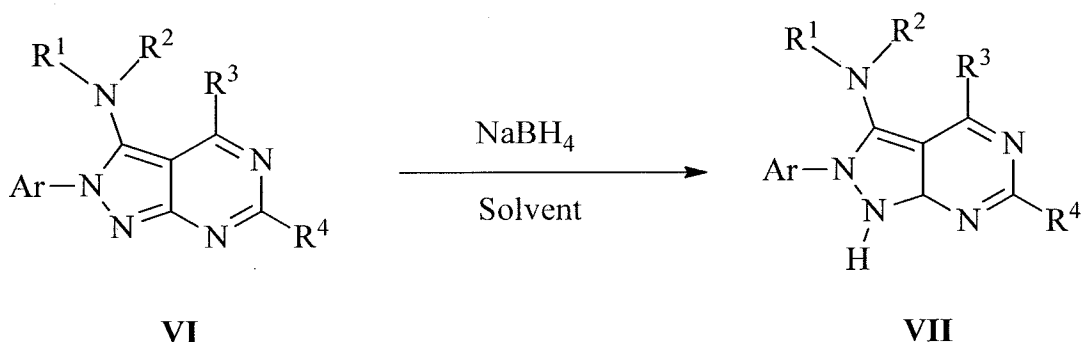
The pyrazolopyrimidine compound **V** may be reacted with at least one electrophile in the presence of a base in a polar aprotic solvent at a temperature from approximately 25° C to 60° C
25 to provide the pyrazolopyrimidine compound **VI**. Non-limiting examples of electrophiles may include: alkyl halides, anhydrides, acid chlorides, isocyanates, isothiocyanate, or sulfonyl chlorides. Examples of suitable bases may include, but are not limited to, TEA, diisopropylethylamine (DIPEA), pyridine, *N,N'*-dimethylpyridin-4-amine (DMAP), potassium

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carbonate (K_2CO_3), or potassium phosphate tribasic (K_3PO_4). Non-limiting examples of the polar aprotic solvents may include, but are not limited to, MeCN, THF, or CH_2Cl_2 .

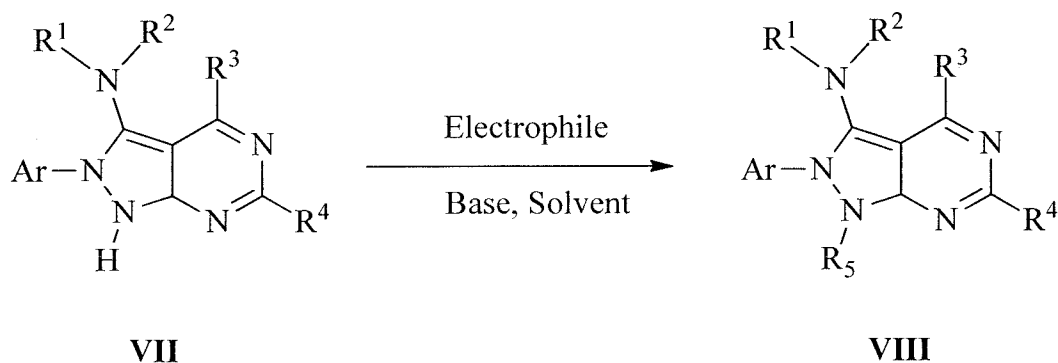
In one embodiment, the pyrazolopyrimidine compound **VI** may then be reduced by a hydride reducing agent, such as sodium borohydride ($NaBH_4$), in a polar protic solvent at a temperature from approximately $25^\circ C$ to about $60^\circ C$ to provide the pyrazolopyrimidine compound **VII**, as shown in **Scheme 5**. Non-limited examples of suitable polar protic solvents may include water, methanol (MeOH) or EtOH. In one embodiment, both R^3 and R^4 groups may be electron withdrawing groups, such as trifluoromethyl and trichloromethyl group.

10

Scheme 5

15

The internal nitrogen atom of the pyrazolopyrimidine compound **VII** may be substituted with an electrophile (*i.e.*, R^5 in Scheme 6) in the presence of a base in a polar aprotic solvent at a temperature from approximately $25^\circ C$ to about $60^\circ C$ to produce the pyrazolopyrimidine compound **VIII**, as shown in **Scheme 6**.

Scheme 6

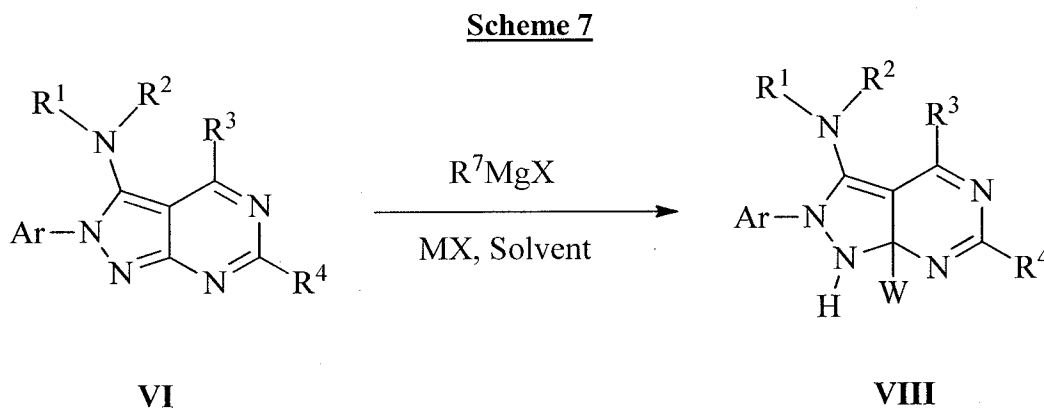
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Non-limiting examples of electrophiles suitable for **Scheme 6** may include alkyl halides, anhydrides, acid chlorides, isocyanates, isothiocyanates, or sulfonyl chlorides. Examples of

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suitable bases may include, but are not limited to, TEA, DIPEA, pyridine, DMAP, K_2CO_3 , or K_3PO_4 . Non-limited examples of suitable polar protic solvents may include MeCN, THF, or CH_2Cl_2 . In one embodiment, the R^1 and R^2 groups on the substituted amine of the pyrazolopyrimidine compound **VIII** may include an electron withdrawing group, such, for example, as carbamates, amides, ureas or sulfonamides. In one embodiment, both R^3 and R^4 groups may be electron withdrawing groups, such as trifluoromethyl. In one embodiment, the R^5 group on the nitrogen atom of the pyrazolopyrimidine compound **VIII** may be prepared using the same electrophiles as in R^1 and R^2 groups.

In one embodiment, the pyrazolopyrimidine compound **VI** may be converted to the pyrazolopyrimidine compound **VIII** by Grignard reaction as shown in **Scheme 7**.

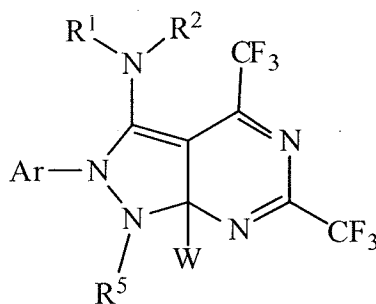


Pyrazolopyrimidine compound **VI** may react with an alkyl metal such methyl magnesium halide in the presence of metal halide, such as lithium chloride (LiCl), in a polar aprotic solvent, such as THF or ether, at a temperature from approximately $-78^\circ C$ to about $25^\circ C$ to provide pyrazolopyrimidine compound **VIII**. In one embodiment, both R^3 and R^4 groups may be electron withdrawing groups, such as trifluoromethyl. In one embodiment, W may be derived from a small alkyl magnesium halide such, for example, as methyl magnesium chloride (MeMgCl), *iso*-propyl magnesium chloride (*i*PrMgCl) and benzyl magnesium chloride ($PhCH_2MgCl$).

In one embodiment, the pyrazolopyrimidine compound may have general formula **IX** or any agriculturally acceptable salt thereof, wherein Ar, R^1 , R^2 , R^5 and W may be as previously disclosed.

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5



IX

In one embodiment, the pyrazolopyrimidine compound may have the general formula IX, wherein Ar represents 2,6-dichloro-4-(trifluoromethyl)phenyl group.

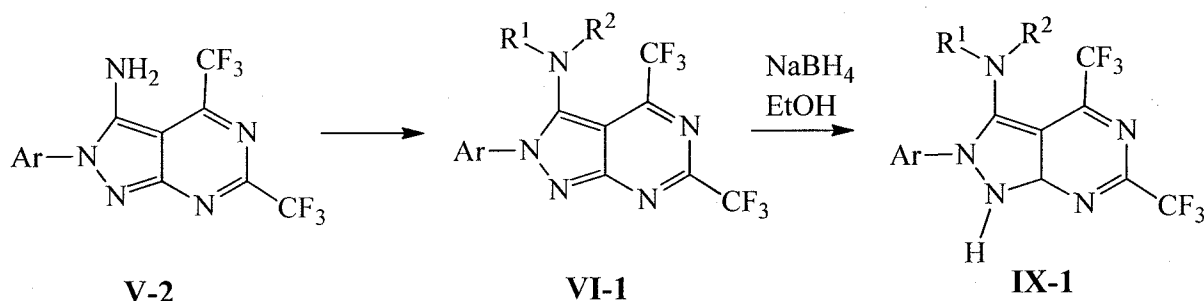
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In one embodiment, the pyrazolopyrimidine compound may have the general formula IX, wherein R¹, R², R⁵ and W may independently be hydrogen, alkyl, acyl, or alkylthioalkyl, or R¹ may be hydrogen and R² may be alkyl, acyl, or alkylthioalkyl.

In one embodiment, the pyrazolopyrimidine compound may have the general formula IX, wherein Ar, R¹, R² and R⁵ may be as previously disclosed, and W is hydrogen.

15

One embodiment of a method of producing the pyrazolopyrimidine compound IX is shown in Scheme 8, as follows:

Scheme 8

20

Briefly, the method of Scheme 8 includes alkylating the amine substituent group of the pyrazolopyrimidine compound V-2 to produce N',N'-bis-alkylated pyrazolopyrimidine compound VI-1, and then reducing Compound VI-1 to provide the pyrazolopyrimidine compound IX-1. In one embodiment, the reduction of the pyrazolopyrimidine compound VI-1 may be achieved using ethanolic NaBH₄.

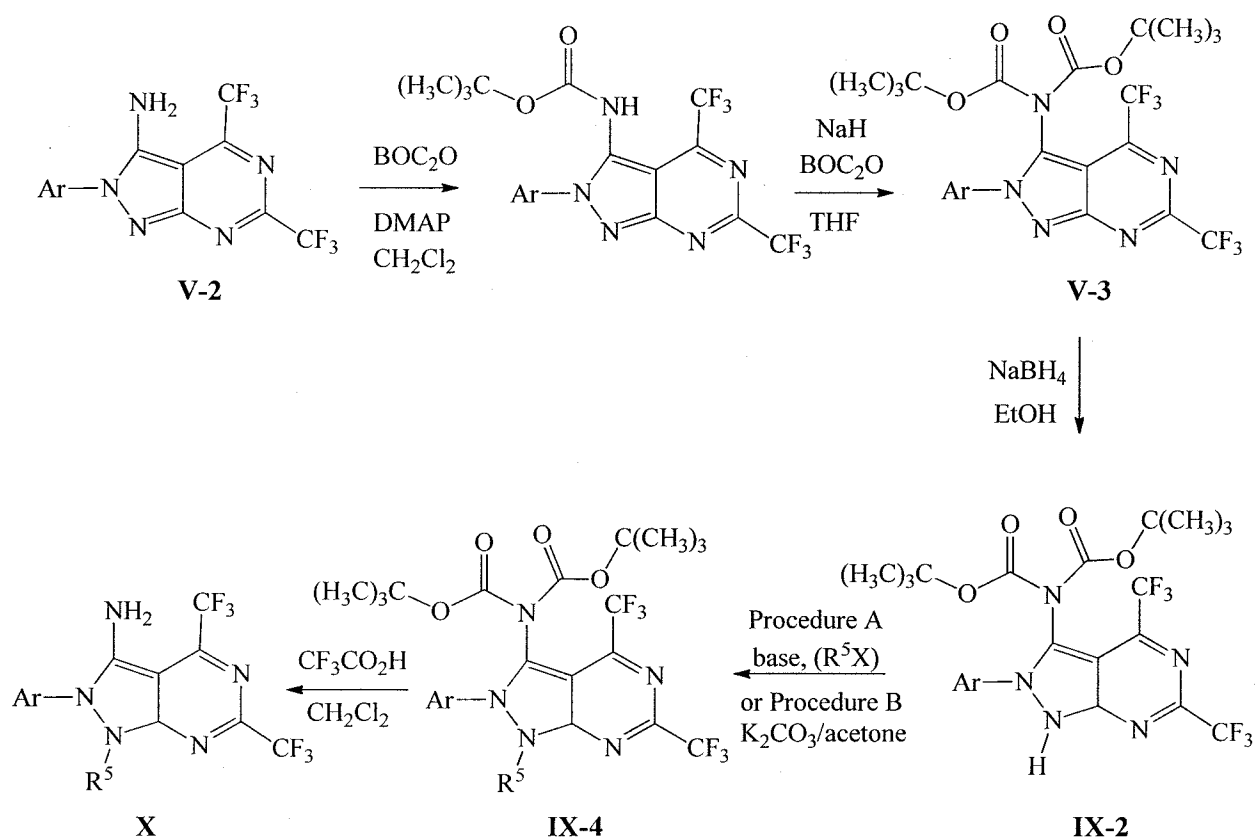
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In one embodiment, the pyrazolopyrimidine compound may have general formula X or any agriculturally acceptable salt thereof. One embodiment of a method of producing the pyrazolopyrimidine compound X is shown in Scheme 9. The method of Scheme 9 includes protecting the amine substitution group of the pyrazolopyrimidine compound V-2 with tert-butyloxycarbonyl (BOC) group to provide the bis-BOC protected compound V-3, and reducing

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Compound **V-3** using NaBH_4 in EtOH to produce the pyrazolopyrimidine compound **IX-2**. The substitution of the nitrogen at the 1-position of the bis-BOC protected compound **IX-2** may be achieved using Procedure A or B, depending on the substituent group. Procedure A may be used when alkyl or benzyl halide is used the alkylating agent. Procedure B may be used when substituted bromomethyl esters, chloroformates, sulfonyl chlorides, or acyl chlorides is employed as the alkylating agent. An external base, such as TEA, DMAP or DIPEA, may be used to affect the substitution of the amine group in an appropriate solvent (*e.g.*, THF, acetone or CH_2Cl_2).

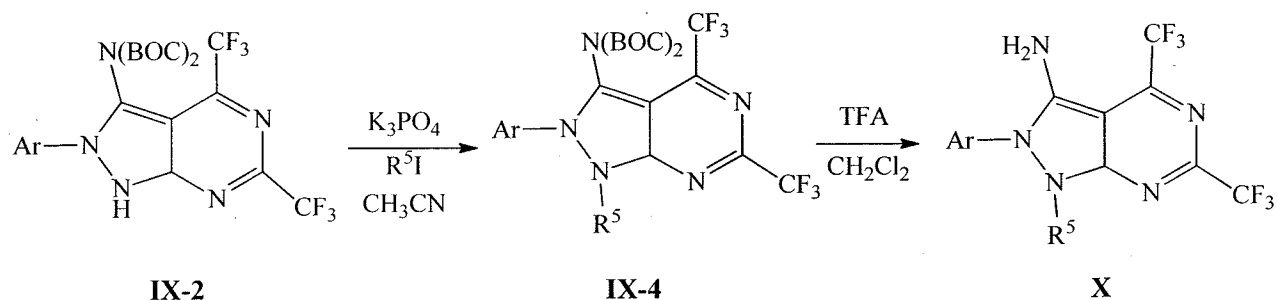
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Scheme 9

Procedure A may be performed as shown in **Scheme 10**, as follows:

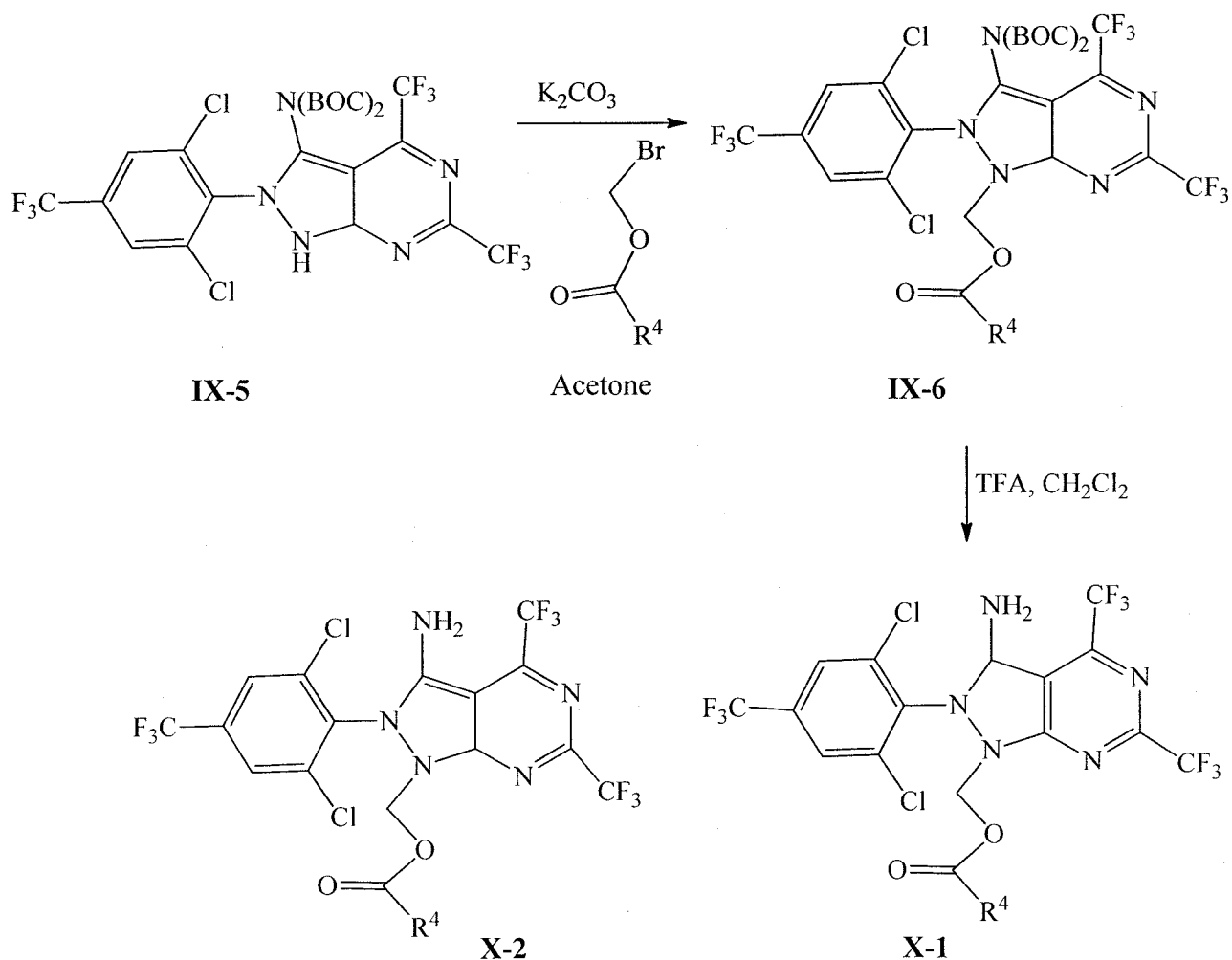
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Scheme 10

The method of **Scheme 10** includes alkylating the internal nitrogen at the 1-position of the bis-BOC protected compound **IX-2** with alkyl halide to provide compound **IX-4**, and then removing the bis-BOC protecting groups on the amine substituent group of compound **IX-4** to provide the pyrazolopyrimidine compound **X**.

Procedure B may be performed as shown in **Scheme 11**, as follows:

Scheme 11

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The method of **Scheme 11** includes substituting the internal nitrogen at the 1-position of the pyrazolopyrimidine compound **IX-5** with bromomethyl ester to provide compound **IX-6**, and then removing the bis-BOC protecting groups on the amine substituent group at the 3-position of compound **IX-6** to provide the pyrazolopyrimidine compound **X-1**. In some
5 embodiments, the BOC-deprotection of Compound **IX-6** may provide compound **X-2** in addition to the pyrazolopyrimidine compound **X-1** in resonance form **I-A**, **I-B** or **I-C**.

The pyrazolopyrimidine compound of the general formula **I** may be used to control a wide variety of pests. As a non-limiting example, in one or more embodiments, the pyrazolopyrimidine compound **I** may be used to control one or more members of at least one of
10 Phylum Arthropoda, Phylum Nematoda, Subphylum Chelicerata, Subphylum Myriapoda, Subphylum Hexapoda, Class Insecta, Class Arachnida, and Class Symphyla. In at least some embodiments, the method of the present disclosure may be used to control one or more members of at least one of Class Insecta and Class Arachnida.

As a non-limiting example, in one or more embodiments, the method of the present
15 disclosure may be used to control one or more members of at least one of Phylum Arthropoda, Phylum Nematoda, Subphylum Chelicerata, Subphylum Myriapoda, Subphylum Hexapoda, Class Insecta, Class Arachnida, and Class Symphyla. In at least some embodiments, the method of the present disclosure may be used to control one or more members of at least one of Class Insecta and Class Arachnida.

20 In additional embodiments, the method of the present disclosure may be used to control members of the Order *Coleoptera* (beetles) including, but not limited to, *Acanthoscelides spp.* (weevils), *Acanthoscelides obtectus* (common bean weevil), *Agrilus planipennis* (emerald ash borer), *Agriotes spp.* (wireworms), *Anoplophora glabripennis* (Asian longhorned beetle), *Anthonomus spp.* (weevils), *Anthonomus grandis* (boll weevil), *Aphidius spp.*, *Apion spp.*
25 (weevils), *Apogonia spp.* (grubs), *Ataenius spretulus* (Black Turfgrass Ataenius), *Atomaria linearis* (pygmy mangold beetle), *Aulacophore spp.*, *Bothynoderes punctiventris* (beet root weevil), *Bruchus spp.* (weevils), *Bruchus pisorum* (pea weevil), *Cacoesia spp.*, *Callosobruchus maculatus* (southern cow pea weevil), *Carpophilus hemipteras* (dried fruit beetle), *Cassida vittata*, *Cerosterna spp.*, *Cerotoma spp.* (chrysomelids), *Cerotoma trifurcata* (bean leaf beetle),
30 *Ceutorhynchus spp.* (weevils), *Ceutorhynchus assimilis* (cabbage seedpod weevil), *Ceutorhynchus napi* (cabbage curculio), *Chaetocnema spp.* (chrysomelids), *Colaspis spp.* (soil beetles), *Conoderus scalaris*, *Conoderus stigmatus*, *Conotrachelus nenuphar* (plum curculio), *Cotinus nitidis* (Green June beetle), *Crioceris asparagi* (asparagus beetle), *Cryptolestes*

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ferrugineus (rusty grain beetle), *Cryptolestes pusillus* (flat grain beetle), *Cryptolestes turcicus* (Turkish grain beetle), *Ctenicera* spp. (wireworms), *Curculio* spp. (weevils), *Cyclocephala* spp. (grubs), *Cylindropturus adspersus* (sunflower stem weevil), *Deporaus marginatus* (mango leaf-cutting weevil), *Dermestes lardarius* (larder beetle), *Dermestes maculatus* (hide beetle),

5 *Diabrotica* spp. (chrysomelids), *Epilachna varivestis* (Mexican bean beetle), *Faustinus cubae*, *Hylobius pales* (pales weevil), *Hypera* spp. (weevils), *Hypera postica* (alfalfa weevil), *Hyperdoes* spp. (Hyperodes weevil), *Hypothenemus hampei* (coffee berry beetle), *Ips* spp. (engravers), *Lasioderma serricorne* (cigarette beetle), *Leptinotarsa decemlineata* (Colorado potato beetle), *Liogenys fuscus*, *Liogenys suturalis*, *Lissorhoptrus oryzophilus* (rice water

10 weevil), *Lyctus* spp. (wood beetles/powder post beetles), *Maecolaspis jolivetii*, *Megascelis* spp., *Melanotus communis*, *Meligethes* spp., *Meligethes aeneus* (blossom beetle), *Melolontha melolontha* (common European cockchafer), *Oberea brevis*, *Oberea linearis*, *Oryctes rhinoceros* (date palm beetle), *Oryzaephilus mercator* (merchant grain beetle), *Oryzaephilus surinamensis* (sawtoothed grain beetle), *Otiorhynchus* spp. (weevils), *Oulema melanopus* (cereal

15 leaf beetle), *Oulema oryzae*, *Pantomorus* spp. (weevils), *Phyllophaga* spp. (May/June beetle), *Phyllophaga cuyabana* (chrysomelids), *Phynchites* spp., *Popillia japonica* (Japanese beetle), *Prostephanus truncatus* (larger grain borer), *Rhizopertha dominica* (lesser grain borer), *Rhizotrogus* spp. (European chafer), *Rhynchophorus* spp. (weevils), *Scolytus* spp. (wood beetles), *Shenophorus* spp. (Billbug), *Sitona lineatus* (pea leaf weevil), *Sitophilus* spp. (grain

20 weevils), *Sitophilus granaries* (granary weevil), *Sitophilus oryzae* (rice weevil), *Stegobium paniceum* (drugstore beetle), *Tribolium* spp. (flour beetles), *Tribolium castaneum* (red flour beetle), *Tribolium confusum* (confused flour beetle), *Trogoderma variabile* (warehouse beetle), and *Zabrus tenebrioides*.

In additional embodiments, the method of the present disclosure may be used to control

25 members of the Order *Dermaptera* (earwigs).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Dictyoptera* (cockroaches) including, but is not limited to, *Blattella germanica* (German cockroach), *Blatta orientalis* (oriental cockroach), *Parcoblatta pennsylvanica*, *Periplaneta americana* (American cockroach), *Periplaneta australoasicae*

30 (Australian cockroach), *Periplaneta brunnea* (brown cockroach), *Periplaneta fuliginosa* (smokybrown cockroach), *Pycnoselus suninamensis* (Surinam cockroach), and *Supella longipalpa* (brownbanded cockroach).

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In additional embodiments, the method of the present disclosure may be used to control members of the Order *Diptera* (true flies) including, but is not limited to, *Aedes spp.* (mosquitoes), *Agromyza frontella* (alfalfa blotch leafminer), *Agromyza spp.* (leaf miner flies), *Anastrepha spp.* (fruit flies), *Anastrepha suspensa* (Caribbean fruit fly), *Anopheles spp.* (mosquitoes), *Batrocera spp.* (fruit flies), *Bactrocera cucurbitae* (melon fly), *Bactrocera dorsalis* (oriental fruit fly), *Ceratitis spp.* (fruit flies), *Ceratitis capitata* (Mediterranean fruit fly), *Chrysops spp.* (deer flies), *Cochliomyia spp.* (screwworms), *Contarinia spp.* (Gall midges), *Culex spp.* (mosquitoes), *Dasineura spp.* (gall midges), *Dasineura brassicae* (cabbage gall midge), *Delia spp.*, *Delia platura* (seedcorn maggot), *Drosophila spp.* (vinegar flies), *Fannia spp.* (filth flies), *Fannia canicularis* (little house fly), *Fannia scalaris* (latrine fly), *Gasterophilus intestinalis* (horse bot fly), *Gracillia perseae*, *Haematobia irritans* (horn fly), *Hylemyia spp.* (root maggots), *Hypoderma lineatum* (common cattle grub), *Liriomyza spp.* (leafminer flies), *Liriomyza brassica* (serpentine leafminer), *Melophagus ovinus* (sheep ked), *Musca spp.* (muscid flies), *Musca autumnalis* (face fly), *Musca domestica* (house fly), *Oestrus ovis* (sheep bot fly), *Oscinella frit* (frit fly), *Pegomyia betae* (beet leafminer), *Phorbia spp.*, *Psila rosae* (carrot rust fly), *Rhagoletis cerasi* (cherry fruit fly), *Rhagoletis pomonella* (apple maggot), *Sitodiplosis mosellana* (orange wheat blossom midge), *Stomoxys calcitrans* (stable fly), *Tabanus spp.* (horse flies), and *Tipula spp.* (crane flies).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Hemiptera* (true bugs) including, but is not limited to, *Acrosternum hilare* (green stink bug), *Blissus leucopterus* (chinch bug), *Calocoris norvegicus* (potato mirid), *Cimex hemipterus* (tropical bed bug), *Cimex lectularius* (bed bug), *Dagbertus fasciatus*, *Dichelops furcatus*, *Dysdercus suturellus* (cotton stainer), *Edessa meditabunda*, *Eurygaster maura* (cereal bug), *Euschistus heros*, *Euschistus servus* (brown stink bug), *Helopeltis antonii*, *Helopeltis theivora* (tea blight plantbug), *Lagynotomus spp.* (stink bugs), *Leptocorisa oratorius*, *Leptocorisa varicornis*, *Lygus spp.* (plant bugs), *Lygus hesperus* (western tarnished plant bug), *Maconellicoccus hirsutus*, *Neurocolpus longirostris*, *Nezara viridula* (southern green stink bug), *Phytocoris spp.* (plant bugs), *Phytocoris californicus*, *Phytocoris relativus*, *Piezodorus guildingi*, *Poecilocapsus lineatus* (fourlined plant bug), *Psallus vaccinicola*, *Pseudacysta perseae*, *Scaptocoris castanea*, and *Triatoma spp.* (bloodsucking conenose bugs/kissing bugs).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Homoptera* (aphids, scales, whiteflies, leafhoppers) including, but is not limited to, *Acrythosiphon pisum* (pea aphid), *Adelges spp.* (adelgids), *Aleurodes proletella*

(cabbage whitefly), *Aleurodicus disperses*, *Aleurothrixus floccosus* (woolly whitefly), *Aluacaspis* spp., *Amrasca bigutella bigutella*, *Aphrophora* spp. (leafhoppers), *Aonidiella aurantii* (California red scale), *Aphis* spp. (aphids), *Aphis gossypii* (cotton aphid), *Aphis pomi* (apple aphid), *Aulacorthum solani* (foxglove aphid), *Bemisia* spp. (whiteflies), *Bemisia argentifolii*, *Bemisia tabaci* (sweetpotato whitefly), *Brachycolus noxius* (Russian aphid), *Brachycorynella asparagi* (asparagus aphid), *Brevennia rehi*, *Brevicoryne brassicae* (cabbage aphid), *Ceroplastes* spp. (scales), *Ceroplastes rubens* (red wax scale), *Chionaspis* spp. (scales), *Chrysomphalus* spp. (scales), *Coccus* spp. (scales), *Dysaphis plantaginea* (rosy apple aphid), *Empoasca* spp. (leafhoppers), *Eriosoma lanigerum* (woolly apple aphid), *Icerya purchasi* (cottony cushion scale), *Idioscopus nitidulus* (mango leafhopper), *Laodelphax striatellus* (smaller brown planthopper), *Lepidosaphes* spp., *Macrosiphum* spp., *Macrosiphum euphorbiae* (potato aphid), *Macrosiphum granarium* (English grain aphid), *Macrosiphum rosae* (rose aphid), *Macrosteles quadrilineatus* (aster leafhopper), *Mahanarva frimbiolata*, *Metopolophium dirhodum* (rose grain aphid), *Mictis longicornis*, *Myzus* spp., *Myzus persicae* (green peach aphid), *Nephotettix* spp. (leafhoppers), *Nephotettix cinctipes* (green leafhopper), *Nilaparvata lugens* (brown planthopper), *Parlatoria pergandii* (chaff scale), *Parlatoria ziziphi* (ebony scale), *Peregrinus maidis* (corn delphacid), *Philaenus* spp. (spittlebugs), *Phylloxera vitifoliae* (grape phylloxera), *Physokermes piceae* (spruce bud scale), *Planococcus* spp. (mealybugs), *Pseudococcus* spp. (mealybugs), *Pseudococcus brevipes* (pine apple mealybug), *Quadraspidotus perniciosus* (San Jose scale), *Rhapalosiphum* spp. (aphids), *Rhapalosiphum maida* (corn leaf aphid), *Rhapalosiphum padi* (oat bird-cherry aphid), *Saissetia* spp. (scales), *Saissetia oleae* (black scale), *Schizaphis graminum* (greenbug), *Sitobion avenae* (English grain aphid), *Sogatella furcifera* (white-backed planthopper), *Therioaphis* spp. (aphids), *Toumeyella* spp. (scales), *Toxoptera* spp. (aphids), *Trialeurodes* spp. (whiteflies), *Trialeurodes vaporariorum* (greenhouse whitefly), *Trialeurodes abutiloneus* (bandedwing whitefly), *Unaspis* spp. (scales), *Unaspis yanonensis* (arrowhead scale), and *Zulia entreriana*. In at least some embodiments, the method of the present disclosure may be used to control *Myzus persicae*.

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Hymenoptera* (ants, wasps, and bees) including, but not limited to, *Acromyrmex* spp., *Athalia rosae*, *Atta* spp. (leafcutting ants), *Camponotus* spp. (carpenter ants), *Diprion* spp. (sawflies), *Formica* spp. (ants), *Iridomyrmex humilis* (Argentine ant), *Monomorium* spp., *Monomorium minimum* (little black ant), *Monomorium pharaonis* (Pharaoh ant), *Neodiprion* spp. (sawflies), *Pogonomyrmex* spp. (harvester ants), *Polistes* spp. (paper

wasps), *Solenopsis* spp. (fire ants), *Tapinoma sessile* (odorous house ant), *Tetranorium* spp. (pavement ants), *Vespula* spp. (yellow jackets), and *Xylocopa* spp. (carpenter bees).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Isoptera* (termites) including, but not limited to, *Coptotermes* spp.,
 5 *Coptotermes curvignathus*, *Coptotermes frenchii*, *Coptotermes formosanus* (Formosan subterranean termite), *Cornitermes* spp. (nasute termites), *Cryptotermes* spp. (drywood termites), *Heterotermes* spp. (desert subterranean termites), *Heterotermes aureus*, *Kaloterme*
spp. (drywood termites), *Incistitermes* spp. (drywood termites), *Macrotermes* spp. (fungus growing termites), *Marginitermes* spp. (drywood termites), *Microcerotermes* spp. (harvester
 10 termites), *Microtermes obesi*, *Procornitermes* spp., *Reticulitermes* spp. (subterranean termites), *Reticulitermes banyulensis*, *Reticulitermes grassei*, *Reticulitermes flavipes* (eastern subterranean termite), *Reticulitermes hageni*, *Reticulitermes hesperus* (western subterranean termite), *Reticulitermes santonensis*, *Reticulitermes speratus*, *Reticulitermes tibialis*, *Reticulitermes virginicus*, *Schedorhinotermes* spp., and *Zootermopsis* spp. (rotten-wood termites).

15 In additional embodiments, the method of the present disclosure may be used to control members of the Order *Lepidoptera* (moths and butterflies) including, but not limited to, *Achoea janata*, *Adoxophyes* spp., *Adoxophyes orana*, *Agrotis* spp. (cutworms), *Agrotis ipsilon* (black cutworm), *Alabama argillacea* (cotton leafworm), *Amorbia cuneana*, *Amyelosis transitella* (navel orangeworm), *Anacamptodes defectaria*, *Anarsia lineatella* (peach twig borer), *Anomis*
 20 *sabulifera* (jute looper), *Anticarsia gemmatilis* (velvetbean caterpillar), *Archips argyrospila* (fruittree leafroller), *Archips rosana* (rose leaf roller), *Argyrotaenia* spp. (tortricid moths), *Argyrotaenia citrana* (orange tortrix), *Autographa gamma*, *Bonagota cranaodes*, *Borbo cinnara* (rice leaf folder), *Bucculatrix thurberiella* (cotton leafperforator), *Caloptilia* spp. (leaf miners), *Capua reticulana*, *Carposina niponensis* (peach fruit moth), *Chilo* spp., *Chlumetia transversa*
 25 (mango shoot borer), *Choristoneura rosaceana* (obliquebanded leafroller), *Chrysodeixis* spp., *Cnaphalocerus medinalis* (grass leafroller), *Colias* spp., *Conpomorpha cramerella*, *Cossus cossus* (carpenter moth), *Crambus* spp. (Sod webworms), *Cydia funebrana* (plum fruit moth), *Cydia molesta* (oriental fruit moth), *Cydia nignicana* (pea moth), *Cydia pomonella* (codling moth), *Darna diducta*, *Diaphania* spp. (stem borers), *Diatraea* spp. (stalk borers), *Diatraea*
 30 *saccharalis* (sugarcane borer), *Diatraea graniosella* (southwester corn borer), *Earias* spp. (bollworms), *Earias insulata* (Egyptian bollworm), *Earias vitella* (rough northern bollworm), *Ecdytopopha aurantianum*, *Elasmopalpus lignosellus* (lesser cornstalk borer), *Epiphysias postruttana* (light brown apple moth), *Ephestia* spp. (flour moths), *Ephestia cautella* (almond

moth), *Ephestia elutella* (tobacco moth), *Ephestia kuehniella* (Mediterranean flour moth), *Epimeces* spp., *Epinotia aporema*, *Erionota thrax* (banana skipper), *Eupoecilia ambiguella* (grape berry moth), *Euxoa auxiliaris* (army cutworm), *Feltia* spp. (cutworms), *Gortyna* spp. (stemborers), *Grapholita molesta* (oriental fruit moth), *Hedylepta indicata* (bean leaf webber),

5 *Helicoverpa* spp. (noctuid moths), *Helicoverpa armigera* (cotton bollworm), *Helicoverpa zea* (bollworm/corn earworm), *Heliothis* spp. (noctuid moths), *Heliothis virescens* (tobacco budworm), *Hellula undalis* (cabbage webworm), *Indarbela* spp. (root borers), *Keiferia lycopersicella* (tomato pinworm), *Leucinodes orbonalis* (eggplant fruit borer), *Leucoptera malifoliella*, *Lithocolletis* spp., *Lobesia botrana* (grape fruit moth), *Loxagrotis* spp. (noctuid

10 moths), *Loxagrotis albicosta* (western bean cutworm), *Lymantria dispar* (gypsy moth), *Lyonetia clerkella* (apple leaf miner), *Mahasena corbetti* (oil palm bagworm), *Malacosoma* spp. (tent caterpillars), *Mamestra brassicae* (cabbage armyworm), *Maruca testulalis* (bean pod borer), *Metisa plana* (bagworm), *Mythimna unipuncta* (true armyworm), *Neoleucinodes elegantalis* (small tomato borer), *Nymphula depunctalis* (rice caseworm), *Operophtera brumata* (winter

15 moth), *Ostrinia nubilalis* (European corn borer), *Oxydia vesulia*, *Pandemis cerasana* (common currant tortrix), *Pandemis heparana* (brown apple tortrix), *Papilio demodocus*, *Pectinophora gossypiella* (pink bollworm), *Peridroma* spp. (cutworms), *Peridroma saucia* (variegated cutworm), *Perileucoptera coffeella* (white coffee leafminer), *Phthorimaea operculella* (potato tuber moth), *Phyllocnistis citrella*, *Phyllonorycter* spp. (leafminers), *Pieris rapae* (imported

20 cabbageworm), *Plathypena scabra*, *Plodia interpunctella* (Indian meal moth), *Plutella xylostella* (diamondback moth), *Polychrosis viteana* (grape berry moth), *Prays endocarpa*, *Prays oleae* (olive moth), *Pseudaletia* spp. (noctuid moths), *Pseudaletia unipunctata* (armyworm), *Pseudoplusia includens* (soybean looper), *Rachiplusia nu*, *Scirpophaga incertulas*, *Sesamia* spp. (stemborers), *Sesamia inferens* (pink rice stem borer), *Sesamia nonagrioides*, *Setora nitens*,

25 *Sitotroga cerealella* (Angoumois grain moth), *Sparganothis pilleriana*, *Spodoptera* spp. (armyworms), *Spodoptera exigua* (beet armyworm), *Spodoptera fugiperda* (fall armyworm), *Spodoptera oridania* (southern armyworm), *Synanthedon* spp. (root borers), *Thecla basilides*, *Thermisia gemmatilis*, *Tineola bisselliella* (webbing clothes moth), *Trichoplusia ni* (cabbage looper), *Tuta absoluta*, *Yponomeuta* spp., *Zeuzera coffeae* (red branch borer), and *Zeuzera*

30 *pyrina* (leopard moth). In at least some embodiments, the method of the present disclosure may be used to control *Spodoptera exigua*.

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Mallophaga* (chewing lice) including, but not limited to, *Bovicola ovis*

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(sheep biting louse), *Menacanthus stramineus* (chicken body louse), and *Menopon gallinea* (common hen house).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Orthoptera* (grasshoppers, locusts, and crickets) including, but not limited to, *Anabrus simplex* (Mormon cricket), *Gryllotalpidae* (mole crickets), *Locusta migratoria*,
 5 *Melanoplus spp.* (grasshoppers), *Microcentrum retinerve* (angularwinged katydid), *Pterophylla spp.* (kaydids), *chistocerca gregaria*, *Scudderia furcata* (forktailed bush katydid), and *Valanga nigricorni*.

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Phthiraptera* (sucking lice) including, but not limited to, *Haematopinus spp.* (cattle and hog lice), *Linognathus ovillus* (sheep louse), *Pediculus humanus capitis* (human
 10 body louse), *Pediculus humanus humanus* (human body lice), and *Pthirus pubis* (crab louse).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Siphonaptera* (fleas) including, but not limited to, *Ctenocephalides canis*
 15 (dog flea), *Ctenocephalides felis* (cat flea), and *Pulex irritans* (human flea).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Thysanoptera* (thrips) including, but not limited to, *Frankliniella fusca* (tobacco thrips), *Frankliniella occidentalis* (western flower thrips), *Frankliniella shultzei*,
Frankliniella williamsi (corn thrips), *Heliothrips haemorrhaidalis* (greenhouse thrips),
 20 *Rhipiphorothrips cruentatus*, *Scirtothrips spp.*, *Scirtothrips citri* (citrus thrips), *Scirtothrips dorsalis* (yellow tea thrips), *Taeniothrips rhopalantennalis*, and *Thrips spp.*

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Thysanura* (bristletails) including, but not limited to, *Lepisma spp.* (silverfish) and *Thermobia spp.* (firebrats).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Acari* (mites and ticks) including, but not limited to, *Acarapsis woodi* (tracheal mite of honeybees), *Acarus spp.* (food mites), *Acarus siro* (grain mite), *Aceria mangiferae* (mango bud mite), *Aculops spp.*, *Aculops lycopersici* (tomato russet mite), *Aculops pelekasi*, *Aculus pelekassi*, *Aculus schlechtendali* (apple rust mite), *Amblyomma americanum*
 25 (lone star tick), *Boophilus spp.* (ticks), *Brevipalpus obovatus* (privet mite), *Brevipalpus phoenicis* (red and black flat mite), *Demodex spp.* (mange mites), *Dermacentor spp.* (hard ticks), *Dermacentor variabilis* (american dog tick), *Dermatophagoides pteronyssinus* (house dust mite), *Eotetranychus spp.*, *Eotetranychus carpini* (yellow spider mite), *Epitimerus spp.*,

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Eriophyes spp., *Ixodes* spp. (ticks), *Metatetranychus* spp., *Notoedres cati*, *Oligonychus* spp., *Oligonychus coffee*, *Oligonychus ilicus* (southern red mite), *Panonychus* spp., *Panonychus citri* (citrus red mite), *Panonychus ulmi* (European red mite), *Phyllocoptruta oleivora* (citrus rust mite), *Polyphagotarsonemus latus* (broad mite), *Rhipicephalus sanguineus* (brown dog tick),
 5 *Rhizoglyphus* spp. (bulb mites), *Sarcoptes scabiei* (itch mite), *Tegolophus perseae*, *Tetranychus* spp., *Tetranychus urticae* (twospotted spider mite), and *Varroa destructor* (honey bee mite).

In additional embodiments, the method of the present disclosure may be used to control members of the Order *Nematoda* (nematodes) including, but not limited to, *Aphelenchoides* spp.
 10 (bud and leaf& pine wood nematodes), *Belonolaimus* spp. (sting nematodes), *Criconemella* spp. (ring nematodes), *Dirofilaria immitis* (dog heartworm), *Ditylenchus* spp. (stem and bulb nematodes), *Heterodera* spp. (cyst nematodes), *Heterodera zeae* (corn cyst nematode), *Hirschmanniella* spp. (root nematodes), *Hoplolaimus* spp. (lance nematodes), *Meloidogyne* spp. (root knot nematodes), *Meloidogyne incognita* (root knot nematode), *Onchocerca volvulus*
 15 (hook-tail worm), *Pratylenchus* spp. (lesion nematodes), *Radopholus* spp. (burrowing nematodes), and *Rotylenchus reniformis* (kidney-shaped nematode).

In at least some embodiments, the method of the present disclosure may be used to control at least one insect in one or more of the Orders *Lepidoptera*, *Coleoptera*, *Homoptera*, *Hemiptera*, *Thysanoptera*, *Isoptera*, *Orthoptera*, *Diptera*, *Hymenoptera*, and *Siphonaptera*, and
 20 at least one mite in the Order *Acari*.

Example A: Bioassays on Beet Armyworm (“BAW”) and Corn Earworm (“CEW”) and Cabbage Looper (“CL”)

BAW has few effective parasites, diseases, or predators to lower its population. BAW
 25 infests many weeds, trees, grasses, legumes, and field crops. In various places, it is of economic concern upon asparagus, cotton, corn, soybeans, tobacco, alfalfa, sugar beets, peppers, tomatoes, potatoes, onions, peas, sunflowers, and citrus, among other plants. CEW is known to attack corn and tomatoes, but it also attacks artichoke, asparagus, cabbage, cantaloupe, collards, cowpeas, cucumbers, eggplant, lettuce, lima beans, melon, okra, peas, peppers, potatoes, pumpkin, snap
 30 beans, spinach, squash, sweet potatoes, and watermelon, among other plants. CEW is also known to be resistant to certain insecticides. CL feeds on a wide variety of cultivated plants and weeds. It feeds readily on crucifers, and has been reported damaging broccoli, cabbage, cauliflower, Chinese cabbage, collards, kale, mustard, radish, rutabaga, turnip, and watercress.

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Other vegetable crops injured include beet, cantaloupe, celery, cucumber, lima bean, lettuce, parsnip, pea, pepper, potato, snap bean, spinach, squash, sweet potato, tomato, and watermelon. CL is also known to be resistant to certain insecticides. Consequently, because of the above factors control of these pests is important. Furthermore, molecules that control these pests are useful in controlling other pests.

Certain molecules disclosed in this document were tested against BAW, CEW and CL using procedures described in the following examples. In the reporting of the results, the **“Mortality Rating for Beet Armyworm (BAW), Corn Earworm (CEW), and Cabbage Looper (CL) Insects”** was used (See Table Section).

BIOASSAYS ON BAW (*Spodoptera exigua*)

Bioassays on BAW were conducted using a 128-well diet tray assay. One to five second instar BAW larvae were placed in each well (3 mL) of the diet tray that had been previously filled with 1 mL of artificial diet to which 50 µg/cm² of the test compound (dissolved in 50 µL of 90:10 acetone-water mixture) had been applied (to each of eight wells) and then allowed to dry. Trays were covered with a clear self-adhesive cover, and held at 25° C, 14:10 light-dark for five to seven days. Percent mortality was recorded for the larvae in each well; activity in the eight wells was then averaged. The results are indicated in the tables entitled **“Table 1”** (See Table Section).

BIOASSAYS ON CEW (*Helicoverpa zea*)

Bioassays on CEW were conducted using a 128-well diet tray assay. One to five second instar CEW larvae were placed in each well (3 mL) of the diet tray that had been previously filled with 1 mL of artificial diet to which 50 µg/cm² of the test compound (dissolved in 50 µL of 90:10 acetone-water mixture) had been applied (to each of eight wells) and then allowed to dry. Trays were covered with a clear self-adhesive cover, and held at 25° C, 14:10 light-dark for five to seven days. Percent mortality was recorded for the larvae in each well; activity in the eight wells was then averaged. The results are indicated in the table entitled **“Table 1”** (See Table Section).

Bioassays on CL (*Trichoplusia ni*)

Bioassays on CL were conducted using a 128-well diet tray assay. One to five second instar CL larvae were placed in each well (3 mL) of the diet tray that had been previously filled

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with 1 mL of artificial diet to which 50 µg /cm² of the test compound (dissolved in 50 µL of 90:10 acetone–water mixture) had been applied (to each of eight wells) and then allowed to dry. Trays were covered with a clear self-adhesive cover, and held at 25° C, 14:10 light-dark for five to seven days. Percent mortality was recorded for the larvae in each well; activity in the eight
5 wells was then averaged. The results are indicated in the table entitled “**Table 1**” (See Table Section).

Example B: Bioassays on Green Peach Aphid (“GPA”) (*Myzus persicae*).

GPA is the most significant aphid pest of peach trees, causing decreased growth,
10 shriveling of the leaves, and the death of various tissues. It is also hazardous because it acts as a vector for the transport of plant viruses, such as potato virus Y and potato leafroll virus to members of the nightshade/potato family *Solanaceae*, and various mosaic viruses to many other food crops. GPA attacks such plants as broccoli, burdock, cabbage, carrot, cauliflower, daikon, eggplant, green beans, lettuce, macadamia, papaya, peppers, sweet potatoes, tomatoes,
15 watercress, and zucchini, among other plants. GPA also attacks many ornamental crops such as carnation, chrysanthemum, flowering white cabbage, poinsettia, and roses. GPA has developed resistance to many pesticides.

Certain molecules disclosed in this document were tested against GPA using procedures described in the following example. In the reporting of the results, the “**Mortality Rating for**
20 **Green Peach Aphid (GPA) Insects**” was used (See Table Section).

Cabbage seedlings grown in 3-inch pots, with 2-3 small (3-5 cm) true leaves, were used as test substrate. The seedlings were infested with 20-50 GPA (wingless adult and nymph stages) one day prior to chemical application. Four pots with individual seedlings were used for each treatment. Test compounds (2 mg) were dissolved in 2 mL of acetone/MeOH (1:1) solvent,
25 forming stock solutions of 1000 ppm test compound. The stock solutions were diluted 5X with 0.025% Tween 20 in H₂O to obtain the solution at 200 ppm test compound. A hand-held aspirator-type sprayer was used for spraying a solution to both sides of cabbage leaves until runoff. Reference plants (solvent check) were sprayed with the diluent only containing 20% by volume of acetone/MeOH (1:1) solvent. Treated plants were held in a holding room for three
30 days at approximately 25° C and ambient relative humidity (RH) prior to grading. Evaluation was conducted by counting the number of live aphids per plant under a microscope. Percent Control was measured by using Abbott’s correction formula (W.S. Abbott, “A Method of

Computing the Effectiveness of an Insecticide” J. Econ. Entomol. 18 (1925), pp.265-267) as follows.

$$\text{Corrected \% Control} = 100 * (X - Y) / X$$

where

5 X = No. of live aphids on solvent check plants and

 Y = No. of live aphids on treated plants

The results are indicated in the tables entitled “**Table 1**” (See Table Section).

Example C: BIOASSAYS ON Yellow Fever Mosquito “YFM” (*Aedes aegypti*).

10 YFM prefers to feed on humans during the daytime and is most frequently found in or near human habitations. YFM is a vector for transmitting several diseases. It is a mosquito that can spread the dengue fever and yellow fever viruses. Yellow fever is the second most dangerous mosquito-borne disease after malaria. Yellow fever is an acute viral hemorrhagic disease and up to 50% of severely affected persons without treatment will die from yellow fever.

15 There are an estimated 200,000 cases of yellow fever, causing 30,000 deaths, worldwide each year. Dengue fever is a nasty, viral disease; it is sometimes called "breakbone fever" or "break-heart fever" because of the intense pain it can produce. Dengue fever kills about 20,000 people annually. Consequently, because of the above factors control of this pest is important. Furthermore, molecules that control this pest (YFM), which is known as a sucking pest, are

20 useful in controlling other pests that cause human and animal suffering.

Certain molecules disclosed in this document were tested against YFM using procedures described in the following paragraph. In the reporting of the results, the “**TABLE 4: Mortality Rating for Yellow Fever Mosquitos (YFM)**” was used (See Table Section).

25 Master plates containing 400 µg of a molecule dissolved in 100 µL of dimethyl sulfoxide (DMSO) (equivalent to a 4000 ppm solution) are used. A master plate of assembled molecules contains 15 µL per well. To this plate, 135 µL of a 90:10 water:acetone mixture is added to each well. A robot (Biomek® NXP Laboratory Automation Workstation) is programmed to dispense 15 µL aspirations from the master plate into an empty 96-well shallow plate (“daughter” plate). There are 6 reps (“daughter” plates) created per master. The created daughter plates are then

30 immediately infested with YFM larvae.

The day before plates are to be treated, mosquito eggs are placed in Millipore water containing liver powder to begin hatching (4 g. into 400 ml). After the daughter plates are created using the robot, they are infested with 220 µL of the liver powder/larval mosquito

mixture. (about 1 day-old larvae). After plates are infested with mosquito larvae, a non-evaporative lid is used to cover the plate to reduce drying. Plates are held at RT for 3 days prior to grading. After 3 days, each well is observed and scored based on mortality.

The results are indicated in **Table 1** (See Table Section).

5 **TABLE 1** shows the pesticidal activities of the pyrazolopyrimidine compounds against several insects: beet armyworm (BAW), corn earworm (CEW), cabbage looper (CL), green peach aphid (GPA), and yellow fever mosquitos (YFM). The mortality efficiency of the pyrazolopyrimidine compounds against BAW, CEW, CL and GPA insects is determined after
10 five days of treatment. The mortality efficiency against YFM is determined after three days of treatment. The mortality efficiency is rated as shown in **TABLES 2–4**.

TABLE 1 shows the mortality study results of the pyrazolopyrimidine compounds **1–96** against several insects: beet armyworm (BAW), corn earworm (CEW), cabbage looper (CL), green peach aphid (GPA), and yellow fever mosquitos (YFM).

15

TABLE 1

Compound No.	BAW Results	CEW Results	CL Results	GPA Results	YFM Results
1	A	A	C	D	A
2	A	A	C	D	B
3	A	A	C	C	C
4	A	A	C	C	C
5	A	A	C	C	C
6	A	A	C	C	C
7	A	A	C	C	C
8	A	A	C	C	C
9	A	D	C	C	C
10	A	A	C	C	C
11	C	C	C	C	D
12	D	D	C	C	C
13	A	B	C	D	C
14	A	A	C	D	D
15	A	A	C	D	D
16	D	B	C	C	C
17	A	A	C	C	D
18	A	A	C	B	D

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Compound No.	BAW Results	CEW Results	CL Results	GPA Results	YFM Results
19	A	A	C	C	D
20	A	A	C	B	A
21	A	D	C	D	D
22	A	A	C	C	C
23	A	A	C	B	D
24	D	D	C	C	C
25	D	D	C	C	C
26	A	D	C	B	D
27	A	A	C	B	B
28	A	A	C	C	C
29	A	D	C	C	C
30	D	D	C	C	D
31	D	D	C	C	C
32	A	B	C	D	D
33	A	A	C	C	C
34	B	D	C	C	C
35	A	A	C	B	B
36	D	A	C	C	D
37	A	C	A	C	B
38	A	C	D	C	C
39	C	C	C	C	C
40	A	A	C	C	C
41	A	A	C	D	D
42	C	C	C	C	D
43	A	A	C	B	A
44	A	A	C	C	C
45	D	A	C	C	D
46	A	A	C	C	C
47	B	D	C	C	D
48	A	A	C	B	D
49	A	A	C	C	C
50	D	D	C	D	C
51	C	C	C	B	C
52	A	A	C	C	C
53	A	A	C	B	D

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Compound No.	BAW Results	CEW Results	CL Results	GPA Results	YFM Results
54	D	D	C	C	C
55	A	D	C	C	C
56	A	A	C	C	C
57	C	C	C	C	D
58	C	C	C	C	D
59	C	C	C	C	C
60	A	A	C	B	D
61	D	D	C	C	C
62	D	D	C	C	C
63	A	A	C	B	A
64	A	A	C	D	A
65	A	D	C	C	C
66	A	A	C	C	C
67	A	A	C	B	D
68	A	A	C	B	A
69	D	D	C	C	D
70	A	A	C	C	D
71	A	A	C	C	C
72	C	C	C	C	C
73	A	A	C	C	D
74	C	C	C	C	D
75	A	A	C	C	C
76	A	A	C	C	C
77	A	D	C	C	C
78	D	D	C	C	C
79	D	D	C	C	C
80	C	C	C	C	D
81	C	C	C	C	D
82	A	A	C	C	C
83	A	D	C	C	D
84	A	D	C	D	C
85	D	D	C	C	D
86	A	B	C	C	C
87	D	D	C	C	D
88	A	A	C	C	C

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Compound No.	BAW Results	CEW Results	CL Results	GPA Results	YFM Results
89	D	D	C	C	C
90	D	A	C	C	C
91	D	D	C	C	C
92	D	D	C	C	D
93	D	D	C	C	C
94	C	C	C	C	C
95	C	C	C	C	C
96	A	A	C	C	C

TABLE 2: Mortality Rating for Beet Armyworm (BAW), Corn Earworm (CEW), and Cabbage Looper (CL) Insects

% Control (or Mortality)	Rating
50–100	A
More than 0 – Less than 50	B
Not Tested	C
No activity noticed in this bioassay	D

5

TABLE 3: Mortality Rating for Green Peach Aphid (GPA) Insects

% Control (or Mortality)	Rating
80–100	A
More than 0 – Less than 80	B
Not Tested	C
No activity noticed in this bioassay	D

TABLE 4: Mortality Rating for Yellow Fever Mosquitos (YFM)

% Control (or Mortality)	Rating
≥ 80	A
More than 0 – Less than 80	B
Not Tested	C
No activity noticed in this bioassay	D

Embodiments of the present disclosure further include methods of controlling pests that comprises applying an pesticidal composition comprising a pyrazolopyrimidine compound of the general formula I near a population of pests.

5 In some embodiments, the pesticidal composition may comprise a pyrazolopyrimidine compound of the general formula I in a phytologically-acceptable inert carrier (*e.g.*, solid carrier or liquid carrier), and may be applied near a population of pests.

The control of insects may be achieved by applying an pesticidally effective amount of the pyrazolopyrimidine-based composition in form of sprays, topical treatment, gels, seed coatings, microcapsulations, systemic uptake, baits, eartags, boluses, foggers, fumigants
10 aerosols, dusts, or the like.

In some embodiments, the pyrazolopyrimidine-based pesticidal compositions may be in the form of solid. Non-limiting examples of the solid forms may include power, dust or granular formulations.

15 In some embodiments, the pyrazolopyrimidine-based pesticidal compositions may be in the form of liquid formulation. Examples of the liquid forms may include, but not limited to, dispersion, suspension, emulsion or solution in appropriate liquid carrier.

In some embodiments, the pyrazolopyrimidine-based pesticidal compositions may be in the form of liquid dispersion, wherein the pyrazolopyrimidine compound may be dispersed in water or other agriculturally suitable liquid carrier.

20 In some embodiments, the pyrazolopyrimidine-based pesticidal compositions may be in the form of solution in an appropriate organic solvent. In one embodiment, the spray oils, which are widely used in agricultural chemistry, may be used as the organic solvent for the pyrazolopyrimidine-based pesticidal compositions.

25 When desired, the pyrazolopyrimidine-based pesticidal compositions may be used in conjunction with at least one of other insecticides, fungicides and herbicides to obtain control of a wider variety of pests, diseases and weeds. When used in conjunction with other insecticides or fungicides or herbicides, the pyrazolopyrimidine-based pesticidal compositions may be formulated with the other insecticides or fungicides or herbicide, or applied sequentially with the other insecticides or fungicides or herbicides.

30 The following examples serve to explain embodiments of the present disclosure in more detail. These examples are not to be construed as being exhaustive or exclusive as to the scope of the disclosure.

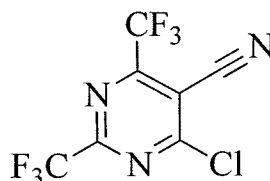
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EXAMPLES

Example 1

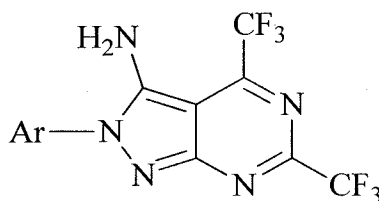
Preparation of 4-chloro-2,6-bis(trifluoromethyl)pyrimidine-5-carbonitrile
[Compound IV-1]

5



IV-1

10 To a solution of 5-cyano-4-oxo-2,6-bis(trifluoromethyl)-4*H*-pyrimidin-3-ide potassium salt (prepared as in Parker, M. H. et al. *Synth. Commun.* **2004**, 34, 903–907; 23 g, 78 mmol) in MeCN (250 mL) was added POCl₃ (10.89 mL, 117 mmol), which formed an off-white suspension. The mixture was heated at 65° C for two hours (h) and then was cooled to RT. The mixture was filtered over a Büchner funnel, and the white solid material was washed with
15 MeCN (4 x 25 mL). The filtrate was concentrated under vacuum at 35° C to give golden oil which was diluted with CH₂Cl₂ (300 mL) and washed with warm distilled water (35° C) and brine. The organic layer was dried over magnesium sulfate (MgSO₄), filtered and concentrated under vacuum to give golden oil residue. The oil was Kugelrohr distilled at a temperature of 95° C and a pressure of about five mbar to provide Compound **IV-1** as light yellow oil (18.36 g,
20 81%): ¹³C NMR (101 MHz, CDCl₃) δ 167.48, 160.80, 160.41, 160.03, 159.64, 158.77, 157.87, 157.45, 157.06, 122.58, 121.89, 119.87, 119.14, 117.10, 116.38, 114.33, 113.63, 109.69, 108.85; ¹⁹F NMR (376 MHz, CDCl₃) δ -67.25 (s), -70.54 (s); EIMS: *m/z* 275 ([M]⁺).

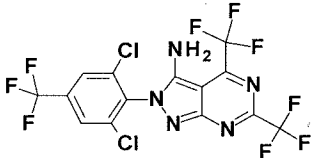
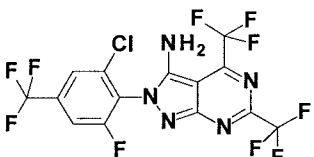
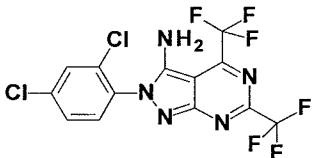
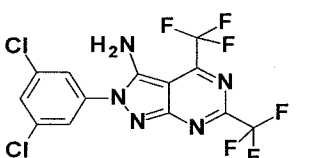
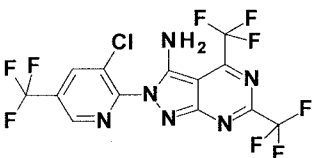
Example 2**Preparation of 4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amines****[Compound V-1]****V-1**

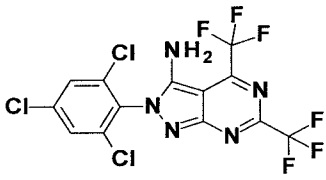
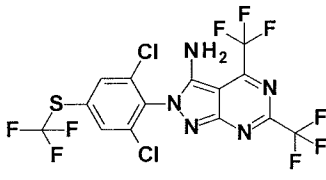
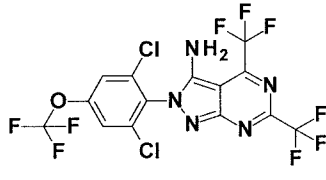
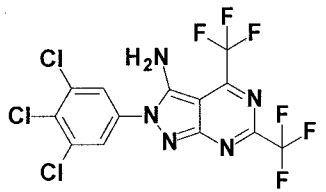
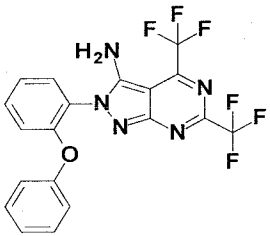
To a solution of 4-chloro-2,6-bis(trifluoromethyl)pyrimidine-5-carbonitrile **IV-1** (1 equivalent) in 1,4-dioxane (3 mL) was added an appropriate solution of hydrazine (1 equivalent) dissolved in 1,4-dioxane (2–5 mL). When hydrazine hydrochlorides were used, they were pre-treated with TEA (1 equivalent). The mixture was stirred at RT from 30 minutes (min) to 24 h. The resulting suspension was then treated with TEA (2 equivalents) and heated at 95° C from two h to 24 h. After cooling, the mixture was purified by column chromatography to give 4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amines as Compounds **V-2** to **V-11**.

The hydrazines may include: (2,6-dichloro-4-(trifluoromethyl)phenyl)hydrazine, (2-chloro-6-fluoro-4-(trifluoromethyl)phenyl)hydrazine, (2,4-dichlorophenyl)hydrazine, (3,5-dichlorophenyl)hydrazine hydrochloride, 3-chloro-2-hydrazinyl-5-(trifluoromethyl)pyridine, (2,4,6-trichlorophenyl)hydrazine, (2,6-dichloro-4-((trifluoromethyl)thio)phenyl)hydrazine (as prepared in WO 2005/090313 by Critcher, D. J. et al.), (2,6-dichloro-4-(trifluoromethoxy)phenyl)hydrazine (as prepared in WO 2005/090313 by Critcher, D. J. et al.), (3,4,5-trichlorophenyl)hydrazine hydrochloride, or (2-phenoxyphenyl) hydrazine hydrochloride.

Compounds **V-2** to **V-11** in **TABLE 5** were made in accordance with the procedure disclosed in Example 2.

TABLE 5

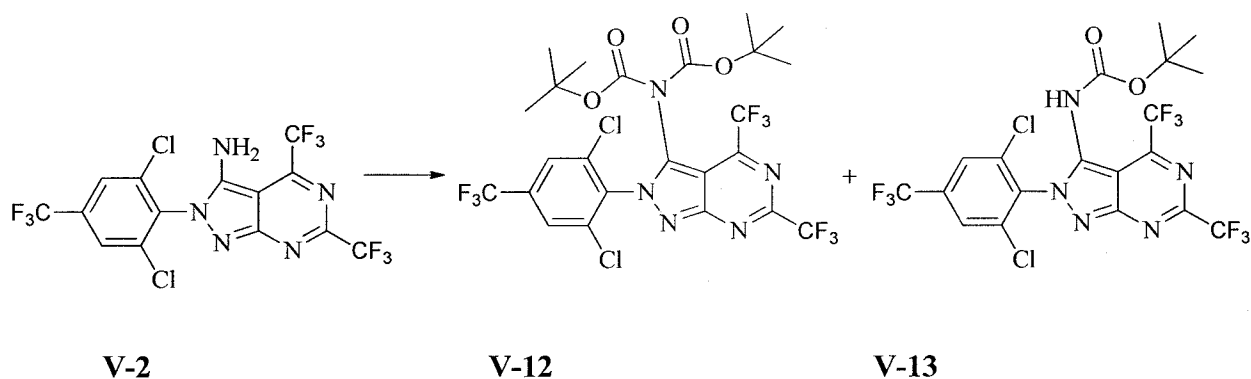
No.	Structure	Appearance	Melting Point (° C)	Mass Spectrum	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆)
V-2		Yellow Solid	262–264	484.01 ([M+H] ⁺)	8.33 (s, 2H), 7.70 (s, 2H)
V-3		Yellow Solid	233–235	466.2 ([M-H] ⁻)	8.23–8.17 (m, 2H), 7.72 (s, 2H)
V-4		Yellow Solid	264–266	417.98 ([M+H] ⁺)	8.03 (d, <i>J</i> = 2.1 Hz, 1H), 7.7–7.69 (m, 2H), 7.41 (s, 2H)
V-5		Yellow Solid Foam		416.04 ([M+H] ⁺)	7.88 (t, <i>J</i> = 1.9 Hz, 1H), 7.80 (d, <i>J</i> = 1.8 Hz, 2H), 7.38 (s, 2H)
V-6		Yellow Solid	232–233	449.10 ([M-H] ⁻)	9.16–9.10 (m, 1H), 8.98–8.92 (m, 1H), 7.65 (s, 2H)

No.	Structure	Appearance	Melting Point (° C)	Mass Spectrum	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆)
V-7		Yellow Solid	270–272	449.21 ([M-H] ⁻)	8.08 (s, 2H), 7.65 (s, 2H)
V-8		Yellow Solid	227–228	515.19 ([M-H] ⁻)	8.24 (s, 2H), 7.76 (s, 2H)
V-9		Yellow Solid	232–234	499.19 ([M-H] ⁻)	8.04 (d, <i>J</i> = 0.8 Hz, 2H), 7.71 (s, 2H)
V-10		Yellow Foam Solid		451.01 ([M+H] ⁺)	8.06 (s, 2H), 7.45 (s, 2H)
V-11		Yellow Solid	193–195	441 ([M+H] ⁺)	7.67–7.57 (m, 2H), 7.42–7.30 (m, 3H), 7.25 (s, 2H), 7.16–7.03 (m, 4H)

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Example 3

Preparation of bis-*tert*-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-yl)carbamate [Compound V-12]
and
tert-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-yl)carbamate
[Compound V-13]

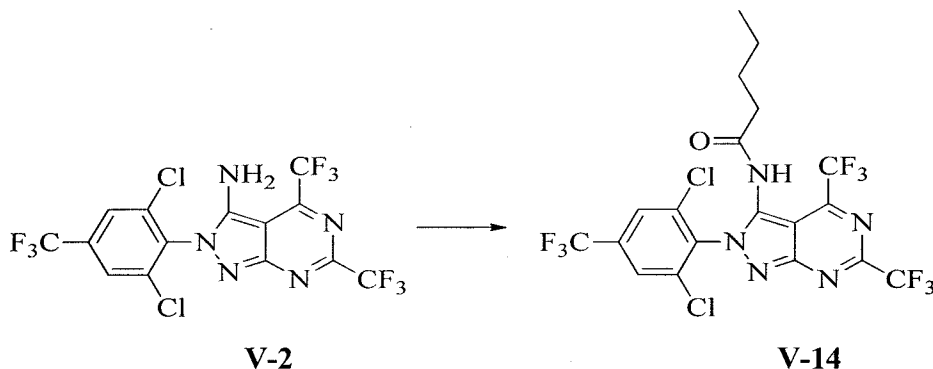


To a stirred solution of Compound V-2 (100 mg, 0.207 mmol) in CH₂Cl₂ (2.1 mL) was added di-*tert*-butyl carbonate (54 mg, 0.248 mmol) followed by DMAP (25 mg, 0.207 mmol). The reaction mixture was stirred at RT for 3 h. Then, hydrochloric acid (HCl, 1 N, 4 mL) was added and the mixture was stirred for an additional 15 min. The solution was extracted with ethyl acetate (EtOAc) and washed with water and brine. The organic phase was dried with MgSO₄, filtered and concentrated under vacuum. The residue was purified via radial chromatography (6:1 hexane–EtOAc). The first isolated fraction (*R_f* = 0.41) afforded Compound V-12 as a yellow solid (97 mg; 69%): ¹H NMR (400 MHz, CDCl₃) δ 7.82 (s, 2H), 1.43 (s, 18H). ESIMS: *m/z* 684 ([M+H]⁺). The second isolated fraction (*R_f* = 0.30) afforded Compound V-13 as a yellow solid (32 mg; 27%): ¹H NMR (400 MHz, CDCl₃) δ 7.85 (s, 2H), 6.51 (s, 1H), 1.36 (s, 9H); ESIMS: *m/z* 584 ([M+H]⁺).

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Example 4

Preparation of *N*-(2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)pentanamide
[Compound V-14]

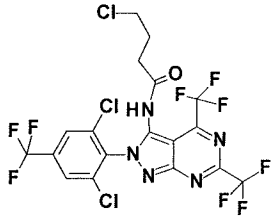
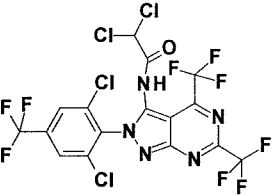
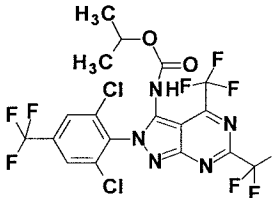
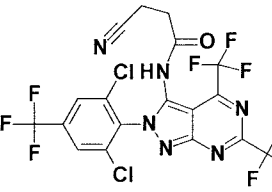
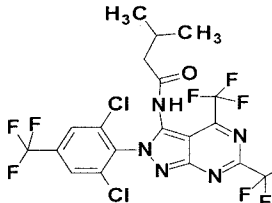


To a solution of Compound V-2 (100 mg, 0.21 mmol) and TEA (60 mg, 0.59 mmol) in anhydrous CH₂Cl₂ (2.5 mL) was added DMAP (61 mg, 0.49 mmol) and pentanoyl chloride (30.4 mg, 0.25 mmol). The reaction mixture was stirred for two h under nitrogen (N₂) at RT. The mixture was diluted with distilled water (10 mL) and extracted with EtOAc (2 x 15 mL). The combined organic phase was concentrated under vacuum to give a residue, which was purified by preparative thin layer chromatography to afford Compound V-14 as a yellow solid (60 mg, 51.1%): mp 169.4° C –171.8° C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 11.00 (s, 1H), 8.44 (s, 2H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.43–1.38 (m, 2H), 1.11–1.03 (m, 2H), 0.79 (t, *J* = 7.2 Hz, 3H); ESIMS: *m/z* 566 ([M-H]).

Electrophiles for the above reaction were: 4-chlorobutyryl chloride, dichloroacetyl chloride, isopropyl chloroformate, 3-cyanopropanoyl chloride, or 3-methylbutanoyl chloride.

Compounds V-15 to V-19 in TABLE 6 were made in accordance with the procedure disclosed in Example 4.

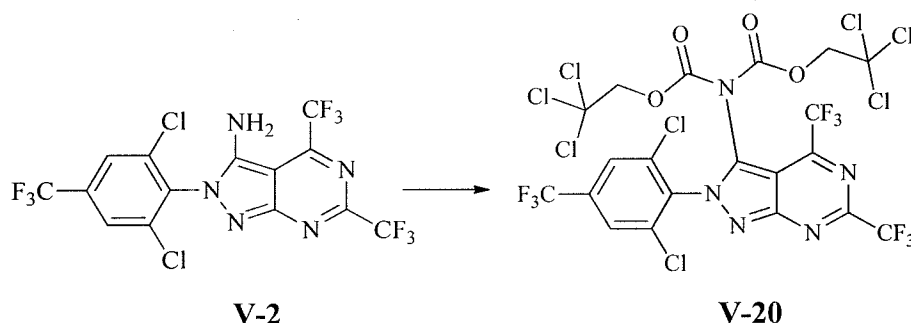
TABLE 6

No.	Structure	Appearance	Melting Point (° C)	ESI-Mass Spectrum (m/z)	¹ H NMR (300 MHz)
V-15		Yellow Solid	97.6–99.2	588 [(M+H)] ⁺	(DMSO- <i>d</i> ₆): δ 11.16 (s, 1H), 8.44 (s, 2H), 3.54 (t, <i>J</i> = 6.4 Hz, 2H), 2.57–2.45 (m, 2H), 1.96–1.84 (m, 2H)
V-16		White Solid	165.5–168.9	595 [(M+H)] ⁺	(CDCl ₃): δ 8.26 (s, 1H), 7.85 (s, 2H), 5.90 (s, 1H).
V-17		Yellow Solid	156.1–158.7	570 [(M+H)] ⁺	(CDCl ₃): δ 7.86 (s, 2H), 6.54 (s, 1H), 4.89 (p, <i>J</i> = 6.3 Hz, 1H), 1.18 (d, <i>J</i> = 6.3 Hz, 6H).
V-18		Yellow Solid	256.1–257.9	565 [(M+H)] ⁺	(DMSO- <i>d</i> ₆): δ 11.26 (s, 1H), 8.37 (s, 2H), 2.74–2.57 (m, 4H).
V-19		White Solid	214.3–217.2	568 [(M+H)] ⁺	(CDCl ₃): δ 7.83 (s, 2H), 7.25 (br, 1H), 2.25–2.13 (m, 2H), 2.08–1.88 (m, 1H), 0.80 (d, <i>J</i> = 6.6 Hz, 6H)

Example 5

Preparation of bis-2,2,2-trichloroethyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate

[Compound V-20]



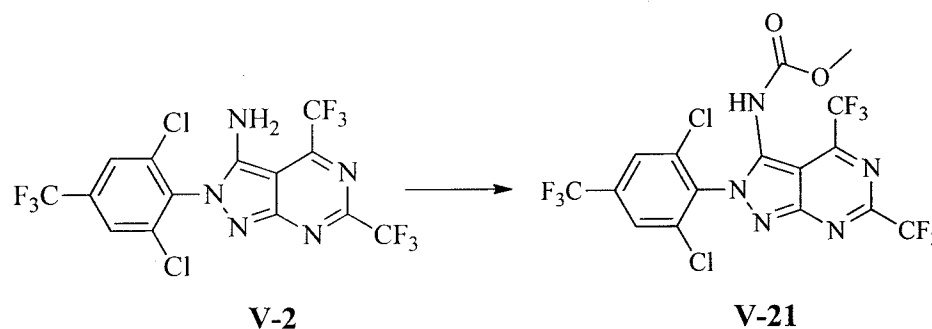
To a 0° C solution of Compound V-2 (107 mg, 0.221 mmol) and *N*-ethyl-*N*-isopropylpropan-2-amine (96 μL, 0.553 mmol) in THF (2.2 mL), 2,2,2-trichloroethyl carbonochloridate (38 μL, 0.276 mmol) was added dropwisely. The mixture was stirred at RT for three h. Then, one equivalent of *N*-ethyl-*N*-isopropylpropan-2-amine and one equivalent of chloroformate were added, and the mixture was heated at 50° C for three h. The mixture was diluted with EtOAc (10 mL). The organic layer was washed with water and brine, dried over MgSO₄ and evaporated. The residue was triturated with hexane-EtOAc solution (6:1), filtered and dried to afford Compound V-20 as a tan solid (103 mg, 56%): ¹H NMR (400 MHz, CDCl₃) δ 7.83 (s, 2H), 4.98 (d, *J* = 11.8 Hz, 2H), 4.71 (d, *J* = 11.8 Hz, 2H); ¹⁹F NMR (376 MHz, CDCl₃) δ -63.32, -66.71, -70.03; ESIMS: *m/z* 835 ([*M*+*H*]⁺).

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Example 6

Preparation of methyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-
2H-pyrazolo[3,4-d]pyrimidin-3-yl)carbamate
[Compound V-21]

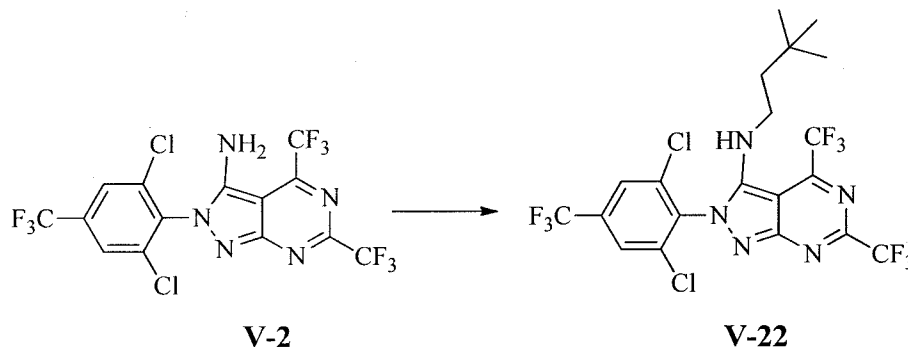
5



To a stirred solution of Compound V-2 (110 mg, 0.227 mmol) in CH₂Cl₂ (2.3 mL) was
10 added methyl chloroformate (18 μL, 0.227 mmol) followed by DMAP (28 mg, 0.227 mmol).
The reaction mixture was stirred at RT overnight. The mixture was diluted with CH₂Cl₂ (20
mL) and washed with 1 N HCl, saturated aqueous sodium bicarbonate (NaHCO₃) solution,
water and brine. The solution was dried over MgSO₄, filtered and concentrated under vacuum.
The residue was purified via radial chromatography (4:1 hexane–EtOAc; R_f = 0.25) to afford
15 Compound V-21 as a tan solid (57 mg, 46%): ¹H NMR (400 MHz, CDCl₃) δ 7.86 (s, 2H), 7.25
(br, 1H), 3.69 (s, 3H); ¹⁹F NMR (376 MHz, CDCl₃) δ -63.30, -67.17, -70.14; ESIMS: *m/z* 542
([M+H]⁺).

Example 7

Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-*N*-(3,3-dimethylbutyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amine
[Compound V-22]

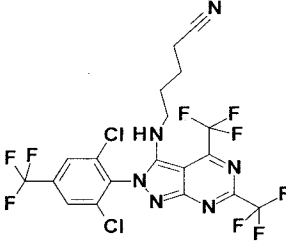
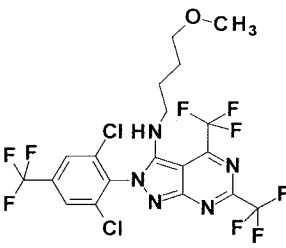
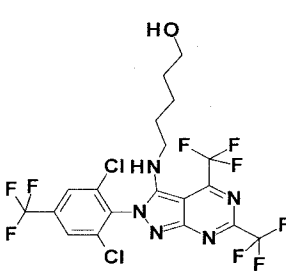
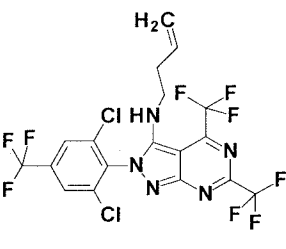


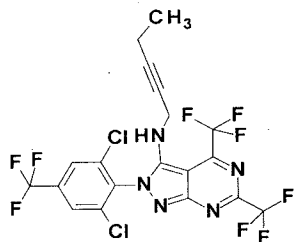
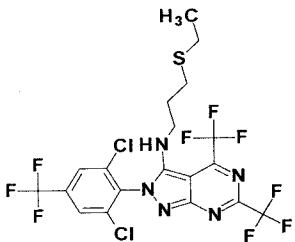
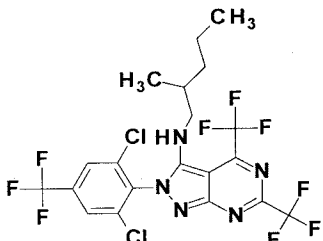
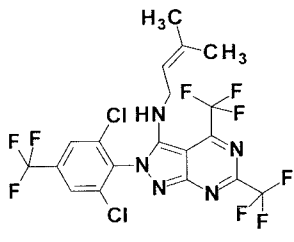
To a mixture of Compound **V-2** (100 mg, 0.21 mmol, 1 equivalent), 1-bromo-3,3-dimethylbutane (69.3 mg, 0.42 mmol, 2 equivalents) in MeCN (3.0 mL) was added potassium iodide (KI, 34.9 mg, 0.21 mmol, 1 equivalent) and K₃PO₄ (89.2 mg, 0.42 mmol, 2 equivalents). The dark mixture was heated at 60° C for five h. The cooled mixture was diluted with EtOAc and washed with water (10 mL). The organic phase was concentrated under vacuum to give a residue, which was purified by preparative thin layer chromatography to afford Compound **V-22** as a yellow solid (23 mg, 19.6%): ¹H NMR (300 MHz, CDCl₃) δ 7.84 (s, 2H), 5.20 (br, 1H), 2.92.84 (m, 2H), 1.46–1.41 (m, 2H), 0.77 (s, 9H); ESIMS: *m/z* 568 [(M+H)]⁺.

Electrophiles used in the above reaction may include: 5-bromopentanenitrile, 1-bromo-4-methoxybutane, 5-bromopentan-1-ol, 4-bromobut-1-ene, 1-bromopent-2-yne, 1-bromo-3-(ethylsulfanyl)propane, 1-bromo-2-methylpentane, 4-bromo-2-methyl-2-butene, 2-(bromomethyl)thiazole, or 2-[(2-bromoethyl)sulfanyl]propane.

Compounds **V-23** to **V-32** in **TABLE 7** were made in accordance with the procedure disclosed in Example 7.

TABLE 7

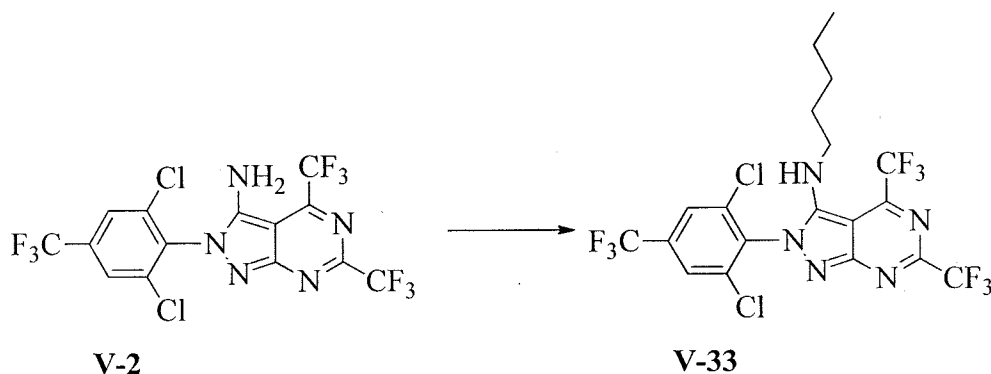
No.	Structure	Appearance	Melting Point (° C)	Mass Spectrum	¹ H NMR (300 MHz, CDCl ₃)
V-23		Yellow Solid	118.3–120.4	565 ([M+H] ⁺)	7.85 (s, 2H), 5.08 (br, 1H), 2.96 (q, <i>J</i> = 6.4 Hz, 2H), 2.35 (t, <i>J</i> = 6.6 Hz, 2H), 1.81–1.51 (m, 4H)
V-24		Yellow Oil		570 ([M+H] ⁺)	7.82 (s, 2H), 5.29 (br, 1H), 3.59 (t, <i>J</i> = 6.2 Hz, 2H), 2.88 (q, <i>J</i> = 6.6 Hz, 2H), 1.76–1.18 (m, 7H)
V-25		Yellow Oil		570 ([M+H] ⁺)	7.82 (s, 2H), 5.55 (br, 1H), 3.43–3.17 (m, 2H), 3.28 (s, 3H), 2.94 (q, <i>J</i> = 5.8 Hz, 2H), 1.82–1.33 (m, 4H)
V-26		Yellow Solid	131.4–133.7	536 ([M+H] ⁺)	7.82 (s, 2H), 5.73–5.57 (m, 1H), 5.43 (br, 1H), 5.29–5.17 (m, 2H), 2.92 (q, <i>J</i> = 6.0 Hz, 2H), 2.32 (q, <i>J</i> = 6.4 Hz, 2H)

No.	Structure	Appearance	Melting Point (° C)	Mass Spectrum	¹ H NMR (300 MHz, CDCl ₃)
V-27		Yellow Oil		548 [$(M+H)^+$]	7.83 (s, 2H), 5.37 (br s, 1H), 3.77–3.69 (m, 2H), 2.09 (q, $J = 7.5$ Hz, 2H), 1.05 (t, $J = 7.5$ Hz, 3H)
V-28		Yellow Solid	106.9– 108.7	586 [$(M+H)^+$]	7.83 (s, 2H), 5.39 (s, 1H), 3.05 (q, $J = 6.7$ Hz, 2H), 2.53–2.42 (m, 4H), 1.84–1.75 (m, 2H), 1.21 (t, $J = 7.4$ Hz, 3H)
V-29		Yellow Oil		568 [$(M+H)^+$]	7.83 (s, 2H), 5.38 (s, 1H), 2.85–2.60 (m, 2H), 1.65–1.50 (m, 2H), 1.26–1.07 (m, 3H), 0.94–0.77 (s, 6H)
V-30		Yellow Oil		552 [$(M+H)^+$]	7.81 (s, 2H), 5.29–5.10 (m, 2H), 3.45 (t, $J = 5.9$ Hz, 2H), 1.71 (s, 3H), 1.51 (s, 3H)

No.	Structure	Appearance	Melting Point (° C)	Mass Spectrum	¹ H NMR (300 MHz, CDCl ₃)
V-31		Yellow Solid	144.1–145.7	581 [(M+H)] ⁺	7.80 (s, 2H), 7.70 (d, <i>J</i> = 3.2 Hz, 1H), 7.34 (d, <i>J</i> = 3.3 Hz, 1H), 6.42 (s, 1H), 4.46 (d, <i>J</i> = 5.6 Hz, 2H)
V-32		Yellow Oil		586 [(M+H)] ⁺	7.83 (s, 2H), 6.07 (s, 1H), 3.03 (q, <i>J</i> = 5.7 Hz, 2H), 2.89–2.76 (m, 1H), 2.72 (t, <i>J</i> = 6.2 Hz, 2H), 1.26 (d, <i>J</i> = 6.7 Hz, 6H)

Example 8

Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-N-pentyl-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-amine [Compound V-33]



To a solution of Compound V-2 (0.1 g, 0.21 mmol, 1 equivalent) and 1-iodopentane (83.2 mg, 0.42 mmol) in MeCN (3.0 mL) was added K₃PO₄ (89.2 mg, 0.42 mmol). The dark mixture was heated to 60° C for 8 h. The cooled mixture was diluted with EtOAc (50 mL) and washed with water (10 mL). The organic phase was dried over sodium sulfate (Na₂SO₄), filtered and concentrated under vacuum to give a yellow/orange solid residue which was purified by

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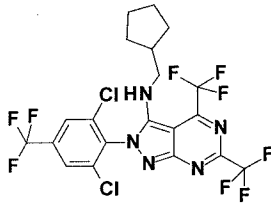
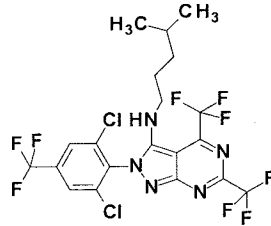
Preparative thin layer chromatography to afford Compound **V-33** as a yellow solid (70 mg, 61.1%): mp 98° C–101° C; ¹H NMR (300 MHz, CDCl₃) 7.82 (s, 2H), 5.26 (br, 1H), 2.91–2.81 (m, 2H), 1.56–1.49 (m, 2H), 1.25–1.18 (m, 4H), 0.86 (t, *J* = 6.9 Hz, 3H); ESIMS: *m/z* 554 ([M+H]⁺).

- 5 Electrophiles used (1–9 equivalents) may include the following: (iodomethyl)cyclopentane, 1-iodo-4-methylpentane, or 2-(3-iodopropyl)-2-methyl-1,3-dioxolane.

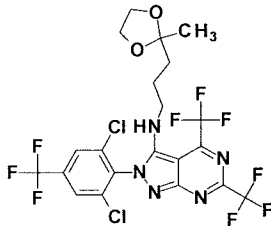
Compounds **V-34** to **V-36** in **TABLE 8** were made in accordance with the procedure disclosed in Example 8.

10

TABLE 8

No.	Structure	Appearance	Melting Point (° C)	ESI-Mass Spectrum (<i>m/z</i>)	¹ H NMR (300 MHz, CDCl ₃)
V-34		Yellow Solid	112.4–114.6	566 ([M+H] ⁺)	7.82 (s, 2H), 5.35 (br, 1H), 2.76 (t, <i>J</i> = 6.2 Hz, 2H), 2.11–1.97 (m, 1H), 1.83–1.68 (m, 2H), 1.62–1.49 (m, 3H), 1.15–0.96 (m, 2H), 0.94–0.86 (m, 1H)
V-35		Yellow Solid	92.4–94.0	568 [M+H] ⁺	7.82 (s, 2H), 5.26 (br, 1H), 2.91–2.76 (m, 2H), 1.61–1.36 (m, 3H), 1.16–0.95 (m, 2H), 0.85 (d, <i>J</i> = 6.6 Hz, 6H)

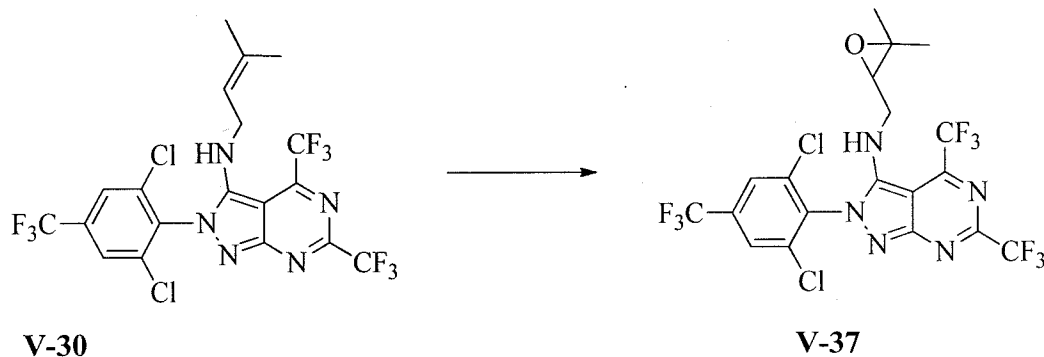
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No.	Structure	Appearance	Melting Point (° C)	ESI-Mass Spectrum (m/z)	¹ H NMR (300 MHz, CDCl ₃)
V-36		Yellow Solid	102.6–103.9	612 [(M+H)] ⁺	7.82 (s, 2H), 5.51 (s, 1H), 4.00–3.82 (m, 4H), 2.97–2.89 (m, 2H), 1.64–1.54 (m, 4H), 1.25 (s, 3H)

Example 9

Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-N-((3,3-dimethyloxiran-2-yl)methyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-amine

[Compound V-37]



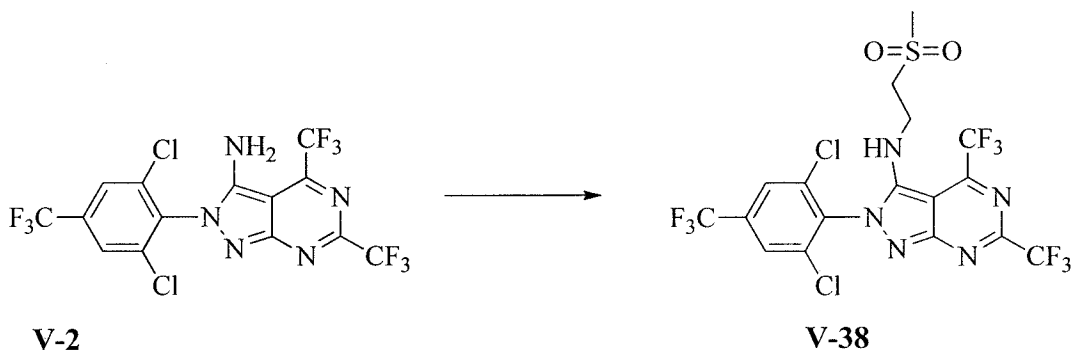
10 To a stirred solution of Compound V-30 (65 mg, 0.12 mmol) in CH₂Cl₂ (3.0 mL) was added NaHCO₃ (20.2 mg, 0.24 mmol) and *meta*-chloroperoxybenzoic acid (*m*-CPBA, 31 mg, 0.18 mmol). The mixture was stirred at RT for one h, and then treated with saturated sodium sulfite aqueous solution (Na₂SO₃, 10 mL) and extracted with CH₂Cl₂ (2 x 10 mL). The organic phase was dried over Na₂SO₄, filtered and concentrated under vacuum. The resulting residue

15 was purified by preparative thin layer chromatography to afford Compound V-37 as a yellow solid (30 mg, 45%): ¹H NMR (300 MHz, CDCl₃) δ 7.84 (s, 2H), 5.54 (s, 1H), 3.22–3.10 (m, 1H), 3.00–2.88 (m, 2H), 1.32 (s, 3H), 1.20 (s, 3H); ESIMS: *m/z* 568 [(M+H)]⁺.

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Example 10

Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-N-(2-(methylsulfonyl)ethyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-amine
[Compound V-38]



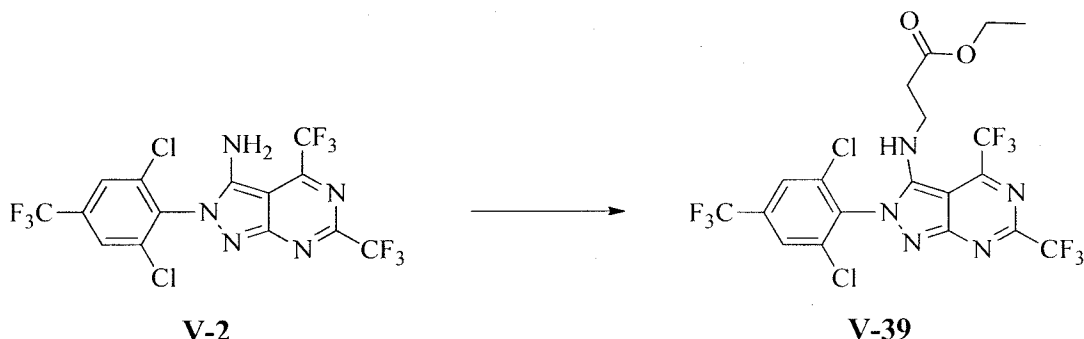
Procedure was adapted from Yeom, C-E, et. al. *Tetrahedron*, **2006**, 63, 904. A solution of Compound V-2 (100 mg, 0.21 mmol), methyl vinyl sulfone (20 μ L, 0.22 mmol) and 1,8-diazabicycloundec-7-ene (DBU, 3 drops) in DMF (3 mL) was heated to 100 $^{\circ}$ C for 1 h. The cooled mixture was diluted with water and extracted with EtOAc (2 x 10 mL). The combined organic phase was washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated to give a residue that was purified by preparative thin layer chromatography to afford Compound V-38 as a yellow solid (55 mg, 44%): ^1H NMR (300 MHz, CDCl_3) δ 7.87 (s, 2H), 5.96 (s, 1H), 3.55 (q, J = 5.9 Hz, 2H), 3.17 (dd, J = 6.8, 4.6 Hz, 2H), 2.98 (s, 3H); ESIMS: m/z 590 $[(\text{M}+\text{H})]^+$.

10

15

Example 11

Preparation of ethyl 3-((2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-yl)amino)propanoate
[Compound V-39]

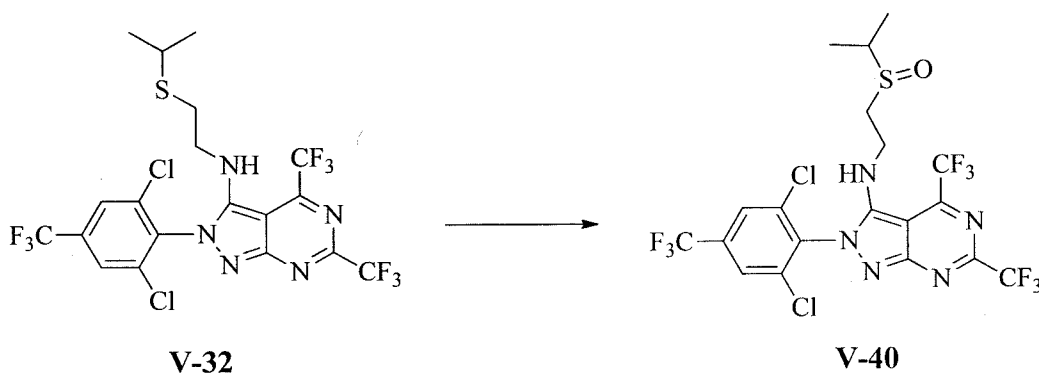


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Procedure was adapted from Yeom, C-E, et. al. *Tetrahedron*, **2006**, *63*, 904. A solution of Compound **V-2** (100 mg, 0.21 mmol), ethyl acrylate (22 mg, 0.22 mmol) and DBU (3 drops) in DMF (3 mL) was heated to 100 °C for 1 h. The cooled mixture was diluted with water and extracted with EtOAc (2 x 10 mL). The combined organic phase was washed with brine (10 mL), dried over Na₂SO₄ and concentrated under vacuum to give a residue that was purified by preparative thin layer chromatography to afford Compound **V-39** as a yellow solid (55 mg, 44%): ¹H NMR(300 MHz, CDCl₃) δ 7.84 (s, 2H), 6.03 (s, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.18 (q, *J* = 5.9 Hz, 2H), 2.48 (t, *J* = 5.8 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); ESIMS: *m/z* 584 [(M+H)]⁺.

Example 12

Preparation of Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-*N*-(2-(isopropylsulfinyl)ethyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amine [Compound **V-40**]

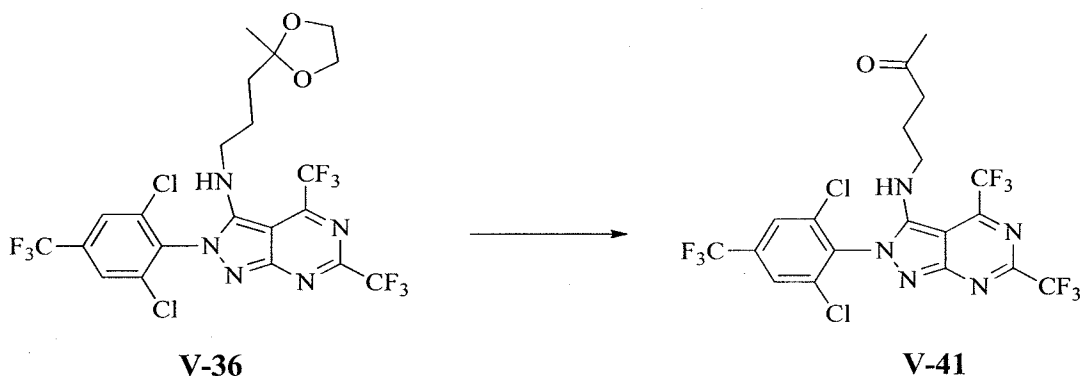


Procedure adapted from Alder, C. M. *et al.*, WO 2010/106016, a solution of Compound **V-32** (120 mg, 0.206 mmol) in MeOH/water (2:1, 10.0 mL) was treated with oxone (potassium peroxymonosulfate, 192 mg, 0.312 mmol) and stirred at 0 °C for six h under nitrogen atmosphere. The mixture was extracted with EtOAc (2 x 10 mL), and the combined organic phase was dried over Na₂SO₄, filtered and concentrated to give a residue, which was purified by column chromatography to afford Compound **V-40** as a yellow solid (50 mg, 41%): mp 139° C –140° C; ¹H NMR (300 MHz, CDCl₃) δ 7.85 (s, 2H), 6.52 (s, 1H), 3.63–3.51 (m, 2H), 2.92–2.68 (m, 3H), 1.28 (dd, *J* = 17.8, 6.7 Hz, 6H); ESIMS: *m/z* 602 [(M+H)]⁺.

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Example 13

Preparation of 5-((2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-yl)amino)pentan-2-one
[Compound V-41]



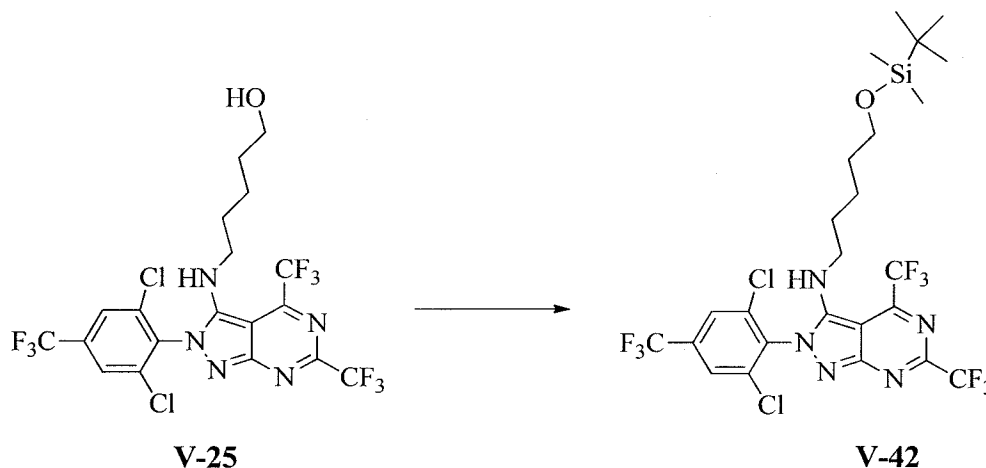
Procedure adapted from Sterzycki, R. *Synthesis*, **1979**, 724, a solution of Compound V-36 (100 mg, 0.16 mmol) dissolved in acetone/water (1:1, 3 mL) was treated with concentrated HCl (2–3 drops). The mixture was stirred at RT for 1 h and then extracted with EtOAc (2 x 10 mL), dried over Na₂SO₄, filtered, and concentrated under vacuum to give a residue which was purified by column chromatography to afford Compound V-41 as a yellow solid (40 mg, 43%): ¹H NMR (CDCl₃) δ 1.765–1.808 (m, 2H), 2.110 (s, 3H), 2.467 (t, 2H, *J* = 6.6 Hz), 2.898–2.961 (m, 2H), 5.576 (br, 1H), 7.812 (s, 2H). ESIMS *m/z* 568 [(M+H)]⁺.

15

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Example 14

Preparation of *N*-(5-(*tert*-butyldimethylsilyloxy)pentyl)-2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amine
[Compound V-42]



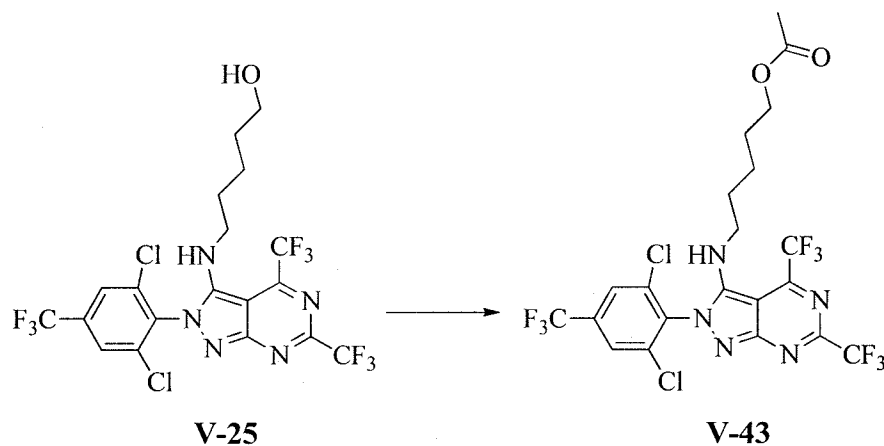
A solution of Compound V-25 (100 mg, 0.18 mmol) in CH₂Cl₂ (5 mL) was treated with imidazole (12 mg, 0.18 mmol) and *tert*-butylchlorodimethylsilane (33 mg, 0.22 mmol). The mixture was stirred at RT for six h and concentrated under vacuum to give a residue, which was purified by column chromatography to afford Compound V-42 as a yellow solid (60 mg, 49%): mp 98.6° C-99.9° C; ¹H NMR (300 MHz, CDCl₃) δ 7.82 (s, 2H), 5.26 (br, 1H), 3.57 (t, *J* = 6.6 Hz, 2H), 2.90–2.84 (m, 2H), 1.60–1.55 (m, 2H), 1.46–1.39 (m, 2H), 1.35–1.26 (m, 2H), 0.87 (s, 9H), 0.02 (s, 6H); ESIMS *m/z* 684 ([M+H]⁺).

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Example 15

Preparation of 5-(2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis (trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-ylamino)pentyl acetate
[Compound V-43]

5



A solution of Compound **V-25** (100 mg, 0.18 mmol) in CH_2Cl_2 (5 mL) was treated with TEA (36 mg, 0.35 mmol) and acetyl chloride (21 mg, 0.26 mmol). The mixture was stirred at 0° C for 30 min, and concentrated under vacuum to give a residue that was purified by column chromatography to afford Compound **V-43** as a yellow oil (90 mg, 82%): ^1H NMR (300 MHz, CDCl_3) δ 7.84 (s, 2H), 5.21 (br, 1H), 4.03 (t, $J = 6.6$ Hz, 2H), 2.89–2.87 (m, 2H), 2.04 (s, 3H), 1.61–1.55 (m, 4H), 1.34–1.29 (m, 2H); ESIMS m/z 612 ($[\text{M}+\text{H}]^+$).

15

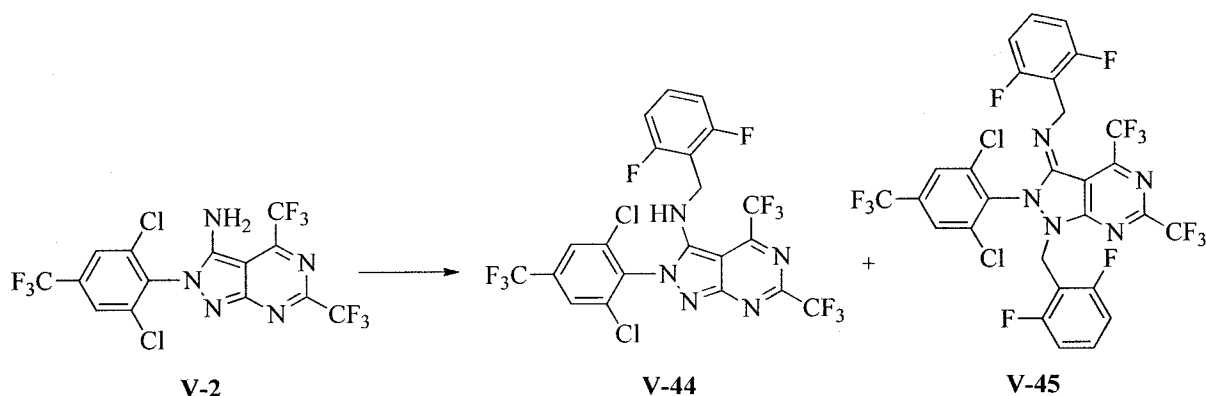
- 62 -

Example 16

Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-*N*-(2,6-difluorobenzyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amine [Compound V-44]

and

5 (E)-*N*-(2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-1-(2,6-difluorobenzyl)-4,6-bis(trifluoromethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-3(2*H*)-ylidene)-1-(2,6-difluorophenyl)methanamine [Compound V-45]



10 To a stirred solution of Compound **V-2** (200 mg, 0.413 mmol) in MeCN (4.1 mL) was added 2,6-difluorobenzyl bromide (103 mg, 0.496 mmol) followed by K_3PO_4 (88 mg, 0.413 mmol). The mixture was heated at 70° C for 5 h. The mixture was diluted with EtOAc (20 mL), and the organic solution was washed with water and brine. The solution was dried over $MgSO_4$, filtered and concentrated. The residue was purified via radial chromatography (6:1–1:1 hexane–

15 EtOAc). The first fraction ($R_f = 0.36$) afforded the bis-alkylated compound **V-45** as a yellow solid (78 mg, 26%): 1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 2H), 7.21–7.11 (m, 2H), 6.80 (t, $J = 7.8$ Hz, 2H), 6.72 (t, $J = 8.1$ Hz, 2H), 5.19 (s, 2H), 4.15 (s, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.29, -66.51, -70.59, -115.53; ESIMS: m/z 736 ($[M+H]^+$). The second fraction isolated at $R_f =$

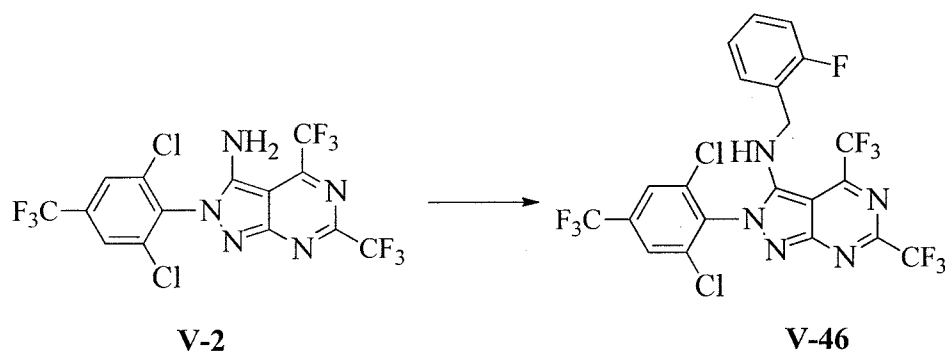
20 0.25 afforded the mono-alkylated compound **V-44**, as a yellow solid (137 mg, 54%): 1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.32 (ddd, $J = 15.0, 8.4, 6.6$ Hz, 1H), 6.89 (t, $J = 8.0$ Hz, 2H), 5.31 (s, 1H), 4.22 (d, $J = 6.2$ Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.25, -66.45, -70.58, -115.55; ESIMS m/z 610 ($[M+H]^+$).

Electrophiles used in the above reaction may include: 2-fluorobenzyl bromide, 4-trifluoromethylbenzyl bromide and 1-(bromomethyl)-4-(trifluoromethoxy)benzene.

25 The following compounds **V-46** to **V-50** were made in accordance with the procedures disclosed in Example 16.

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Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-*N*-(2-fluorobenzyl)-4,6-bis(trifluoromethyl)-2*H*-pyrazolo[3,4-*d*]pyrimidin-3-amine [Compound V-46]

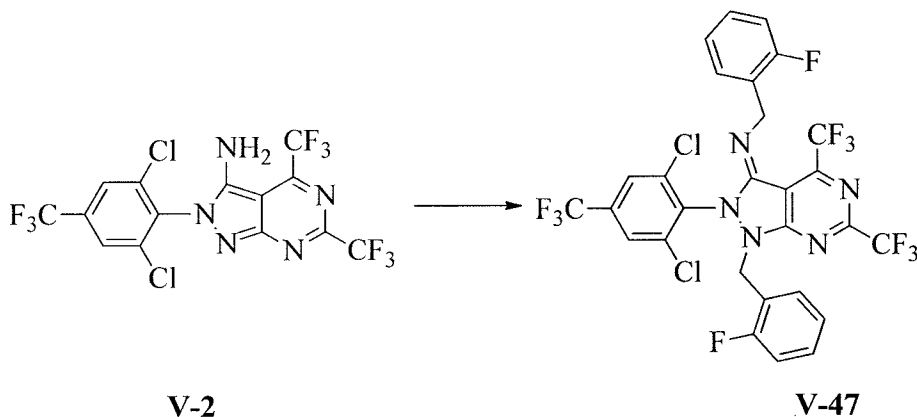


Compound **V-46** was obtained when 2-fluorobenzyl bromide was used as the electrophile, and was isolated as a yellow solid (60 mg, 33%): ^1H NMR (400 MHz, CDCl_3) δ 7.70 (s, 2H), 7.36–7.25 (m, 1H), 7.20–7.07 (m, 2H), 7.04–6.94 (m, 1H), 5.55 (br, 1H), 4.25 (d, J = 6.2 Hz, 2H); ^{19}F NMR (376 MHz, CDCl_3): δ -63.26, -66.26, -70.63, -118.63; ESIMS m/z 592 ($[\text{M}+\text{H}]^+$).

10

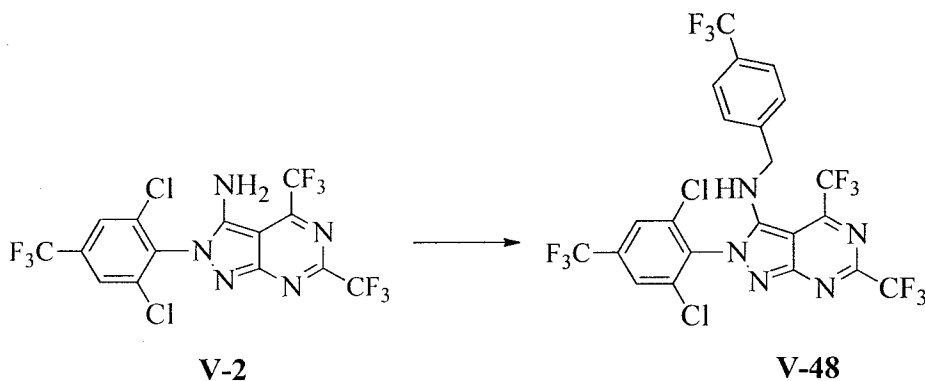
- 64 -

Preparation of (E)-N-(2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-1-(2-fluorobenzyl)-4,6-bis(trifluoromethyl)-1H-pyrazolo[3,4-d]pyrimidin-3(2H)-ylidene)-1-(2-fluorophenyl)methanamine [Compound V-47]



Compound **V-47** was obtained when 2-fluorobenzyl bromide was used as the electrophile, and was isolated as a yellow solid (49 mg, 23%): ^1H NMR (400 MHz, CDCl_3) δ 7.57 (t, $J = 7.0$ Hz, 1H), 7.35 (s, 2H), 7.20–7.02 (m, 4H), 6.95–6.74 (m, 3H), 5.18 (s, 2H), 4.32 (s, 2H); ^{19}F NMR (376 MHz, CDCl_3) δ -63.55, -67.54, -70.58, -117.14, -120.08; ESIMS: m/z 700 ($[\text{M}+\text{H}]^+$).

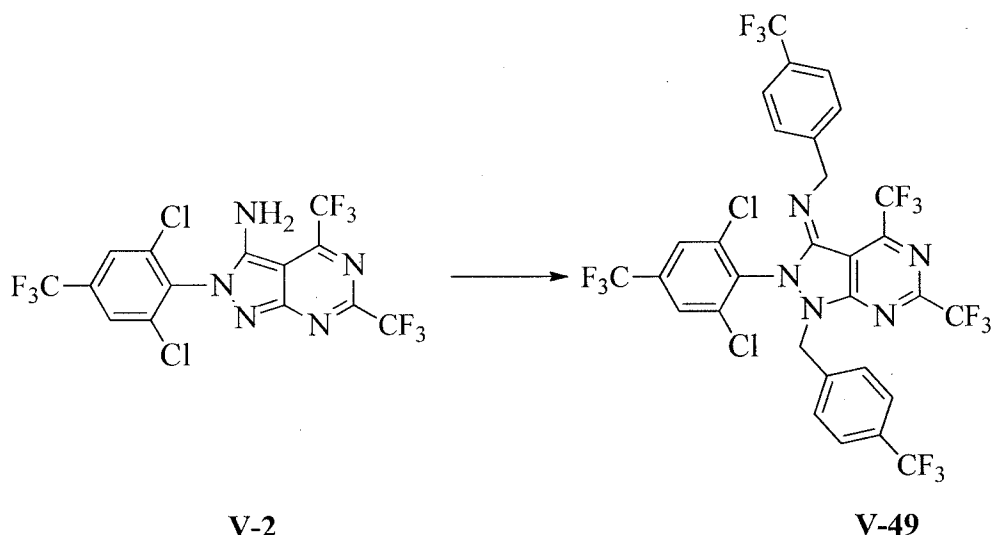
Preparation of 2-(2,6-Dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-N-(4-(trifluoromethyl)-benzyl)-2H-pyrazolo[3,4-d]pyrimidin-3-amine [Compound V-48]



Compound **V-48** was obtained when 4-trifluoromethylbenzyl bromide was used as the electrophile, and was isolated as a yellow solid (103 mg, 39%): ^1H NMR (400 MHz, CDCl_3) δ 7.63 (s, 2H), 7.54 (d, $J = 8.1$ Hz, 2H), 7.17 (d, $J = 8.0$ Hz, 2H), 5.62 (br, 1H), 4.31 (d, $J = 6.4$ Hz, 2H); ^{19}F NMR (376 MHz, CDCl_3) δ -62.88, -63.35, -66.09, -70.62; ESIMS: m/z 642 ($[\text{M}+\text{H}]^+$).

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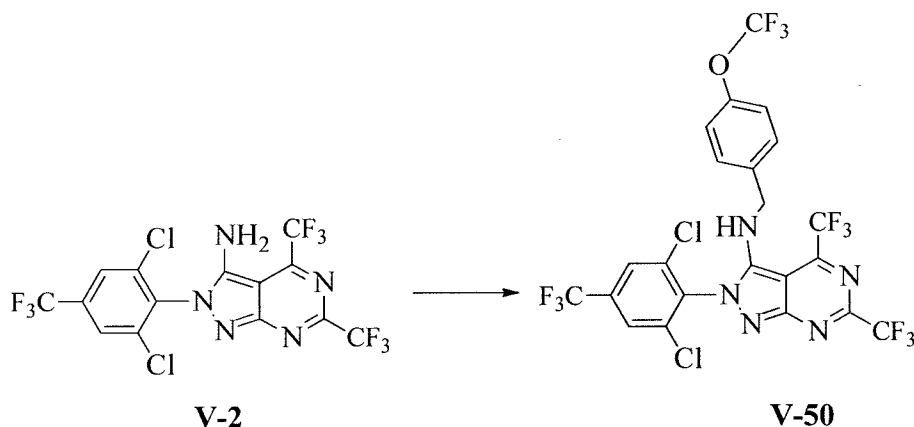
Preparation of (*E*)-*N*-(2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-1-(4-(trifluoromethyl)benzyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-3(2*H*)-ylidene)-1-(4-(trifluoromethyl)phenyl)methanamine [Compound V-49]



Compound **V-49** was obtained when 4-trifluoromethylbenzyl bromide was used as the electrophile, and was isolated as a yellow solid (61 mg, 18%): ^1H NMR (400 MHz, CDCl_3) δ 7.44 (d, $J = 8.0$ Hz, 2H), 7.38 (d, $J = 8.0$ Hz, 2H), 7.31 (s, 2H), 7.27–7.19 (m, 4H), 5.19 (s, 2H), 4.32 (s, 2H); ^{19}F NMR (376 MHz, CDCl_3) δ -62.53, -63.16, -63.77, -67.53, -70.52; ESIMS m/z 800 ($[\text{M}+\text{H}]^+$).

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Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-N-(4-(trifluoromethoxy)benzyl)-4,6-bis(trifluoromethyl)-2H-pyrazolo[3,4-d]pyrimidin-3-amine [Compound V-50]



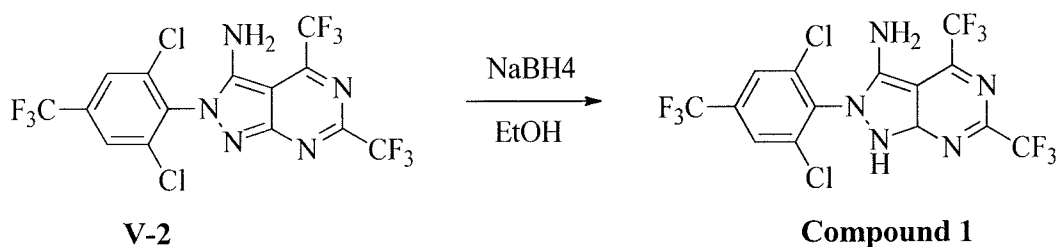
Compound **V-50** was obtained when 1-(bromomethyl)-4-(trifluoromethoxy) benzene was used as the electrophile, and was isolated as a yellow solid (72 mg, 35%): ^1H NMR (400 MHz, CDCl_3) δ 7.67 (s, 2H), 7.16–7.11 (m, 2H), 7.09–7.05 (m, 2H), 5.63 (br, 1H), 4.22 (d, J = 6.2 Hz, 2H); ^{19}F NMR (376 MHz, CDCl_3) δ -58.03, -63.35, -66.13, -70.65; ESIMS m/z 658 ($[\text{M}+\text{H}]^+$).

Example 17

Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1H-pyrazolo[3,4-d]pyrimidin-3-amine

[Compound 1]

The pyrazolo[3,4-d]pyrimidin-3-amine compound **V-2** was reduced to provide **Compound 1** as shown below:



To a solution of Compound **V-2** (110 mg, 0.227 mmol) in EtOH (2.5 mL, 42.8 mmol) was added NaBH_4 (18.91 mg, 0.500 mmol), causing the mixture to turn a deep red color and then a very pale tan color. The reaction mixture was allowed to stir at RT for 1 h, followed by the addition of 4-5 drops of glacial acetic acid (AcOH) that caused gas evolution and the mixture

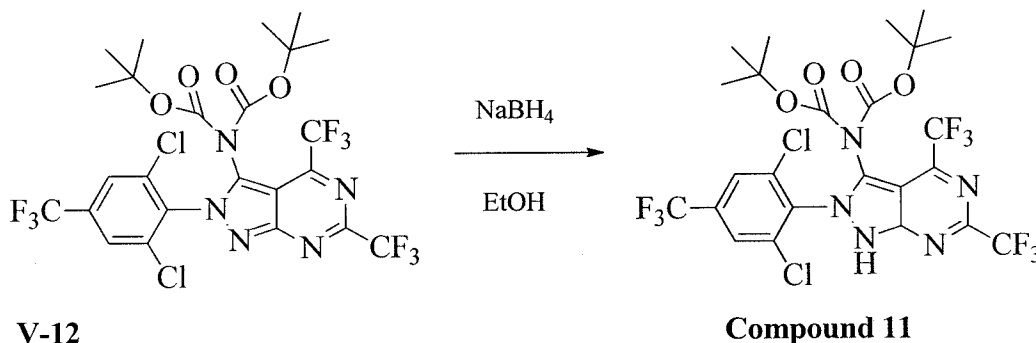
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to turn a pale clear yellow. After the solvent was removed under vacuum, the residue was diluted in EtOAc (50 mL) and washed with distilled water (3 x 20 mL), then brine (1 x 25mL), aqueous NaHCO₃ solution (2 x 10mL) and finally aqueous ammonium chloride (NH₄Cl, 1 x 15mL). The organic phase was dried over Na₂SO₄, filtered and concentrated under vacuum to give a light tan solid residue that was purified by column chromatography (Hexane–EtOAc; gradient 40 g column) to afford **Compound 1** as a white solid (0.094 g, 86%): mp 257° C–259° C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.19 (d, *J* = 3.4 Hz, 1H), 8.15 (d, *J* = 1.8 Hz, 2H), 5.89–5.74 (m, 2H), 5.59–5.38 (m, 1H); ESIMS *m/z* 486.6 ([M+1]⁺).

Compounds 2–10 in **TABLE 9** were prepared from compounds **V-2** to **V-11** in accordance with the procedure disclosed in Example 17.

Example 18

Preparation of bis-*tert*-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate
[**Compound 11**]

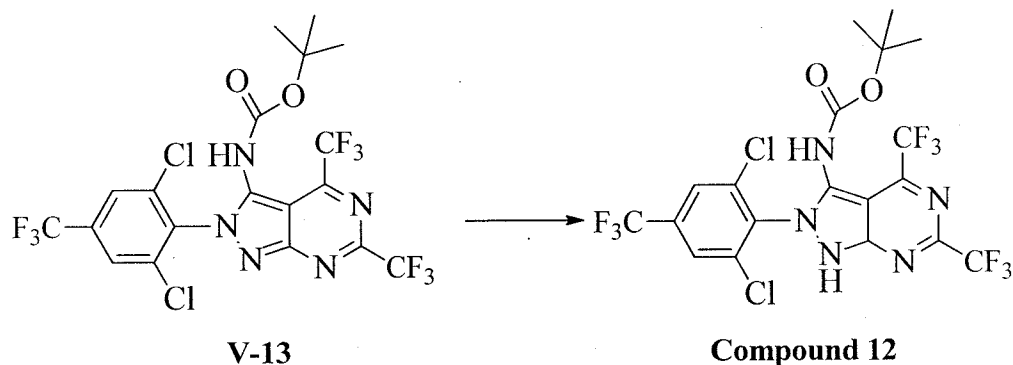


To a solution containing **Compound V-12** (44 mg, 0.064 mmol) dissolved in EtOH (1.1 mL, 0.06 M) was added NaBH₄ (5 mg, 0.129 mmol), and the reaction stirred at RT for 3 h. AcOH was added (10 equivalents), and the mixture was stirred for an additional 10 min, followed by dilution with water (5 mL) and mixture was extracted with EtOAc (3 x 5 mL). The organic layer was washed with water (5 mL) and brine (5 mL), dried over MgSO₄, filtered and concentrate under vacuum. The residue was purified by silica chromatography using a 3:1 hexane/EtOAc mixture as the eluent to afford **Compound 11** as a white solid (42 mg, 94%): ¹H NMR (400 MHz, CDCl₃) δ 7.72 (s, 2H), 5.63–5.35 (m, 2H), 1.60–1.40 (m, 18H); ESIMS *m/z* 686 ([M+H]⁺).

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Example 19

Preparation of *tert*-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate
[Compound 12]



To a solution containing Compound **V-13** (239 mg, 0.409 mmol) dissolved in EtOH (1.1 mL, 0.06 M) was added NaBH₄ (31 mg, 0.818 mmol), and the reaction was stirred at RT for overnight. Then, glacial AcOH (10 equivalents) was added, and the mixture was stirred for 10 min. The reaction mixture was diluted with water (5 mL), and the solution was extracted with EtOAc (3 x 5 mL). The organic layer was washed with water (5 mL) and brine (5 mL), dried over MgSO₄, filtered and concentrated under vacuum to afford **Compound 12** as a white solid (220 mg, 92%): ¹H NMR (400 MHz, CDCl₃) δ 7.77 (s, 2H), 6.08 (s, 1H), 5.87–5.74 (m, 2H), 1.45 (s, 9H); ESIMS *m/z* 586 ([M+H]⁺).

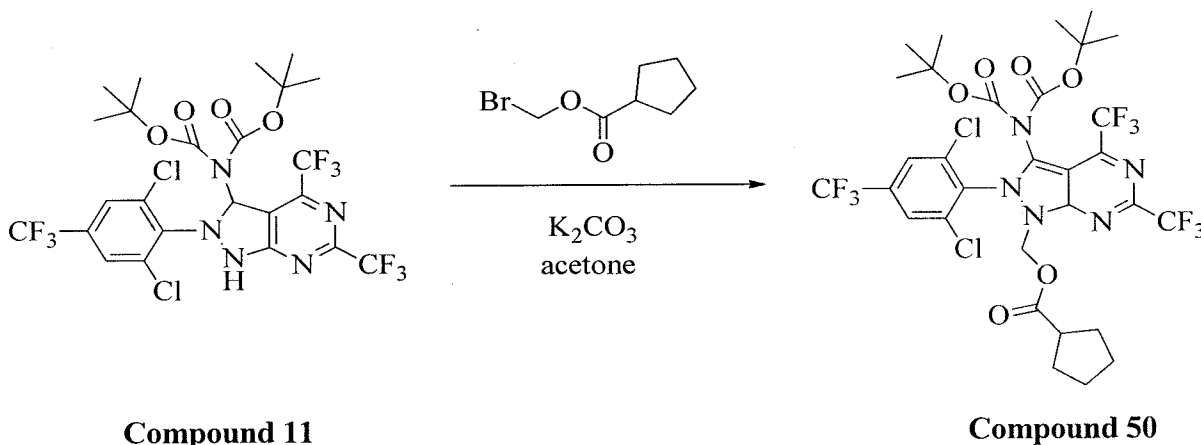
Compounds 13–49 in **TABLE 9** were prepared from Compounds **V-14** to **V-50** in accordance with the procedure disclosed in Example 19.

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Example 20

Preparation of (3-((bis-*tert*-butoxycarbonyl)amino)-2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-
d]pyrimidin-1-yl)methyl cyclopentanecarboxylate

[Compound 50]



To a stirred solution of **Compound 11** (27 mg, 0.039 mmol) dissolved in acetone (1 mL, 0.04 M) was added bromomethyl cyclopentanecarboxylate (12 mg, 0.059 mmol, 1.5 equivalents) followed by K_2CO_3 (16 mg, 0.118 mmol, 3 equivalents). The reaction mixture was stirred at RT overnight. Then, the mixture was diluted with water (5 mL) and extracted with EtOAc (3 x 5 mL). The organic solution was washed with brine (5 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified via radial chromatography using a 6:1 hexane/EtOAc mixture as the eluent to afford **Compound 50** (19 mg, 59%): 1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 2H), 5.95–5.85 (m, 2H), 5.61 (q, $J = 6.6$ Hz, 1H), 2.81–2.69 (m, 1H), 1.92–1.24 (m, 26H); ESIMS m/z 812 ($[M+H]^+$).

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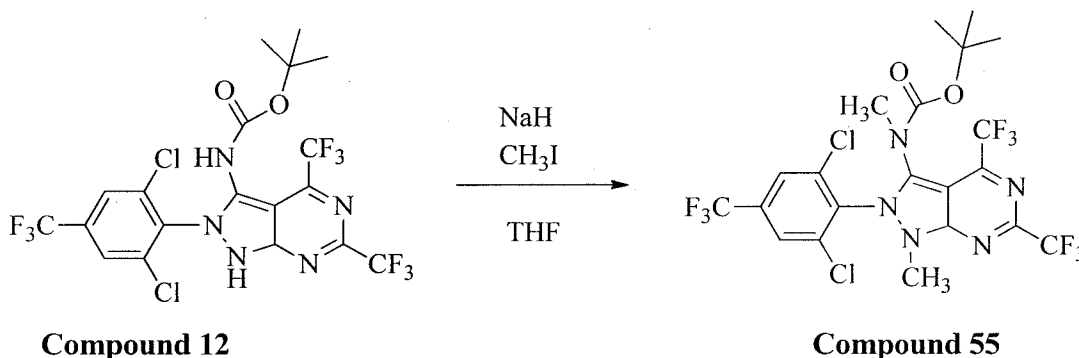
The electrophiles used may include: bromomethylisobutyrate, bromomethylacetate, bromomethyl 2-ethoxyacetate.

20 **Compounds 51–54** in TABLE 9 were made in accordance with the procedure disclosed in Example 20.

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Example 21

Preparation of *tert*-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-1-methyl-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)(methyl)carbamate
[Compound 55]



To a stirred solution of **Compound 12** (87 mg, 0.148 mmol) in THF (1.5 mL, 0.1M) cooled to 0° C was added sodium hydride (NaH, 60% dispersion in mineral oil, 13 mg, 0.326 mmol, 2.2 eq.), and the reaction mixture was stirred at 0° C for 20 min. Methyl iodide (CH₃I, 46 μL, 0.742 mmol, 5 eq.) was then added. The reaction was allowed to warm to RT, and stirred overnight. Water was added (5 mL), and the mixture was extracted with EtOAc (3 x 5 mL). The solution was washed with water (5 mL) and brine (5 mL). The organic phase was dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified via silica chromatography using a 5:1 hexane/EtOAc mixture as the eluent (*R_f* = 0.25) to afford **Compound 55** as a purple oil (44 mg, 48%): ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J* = 16.7 Hz, 2H), 5.31 (s, 1H), 3.37 (s, 3H), 2.78 (s, 3H), 1.49 (s, 9H); ESIMS: *m/z* 614 ([*M*+*H*]⁺).

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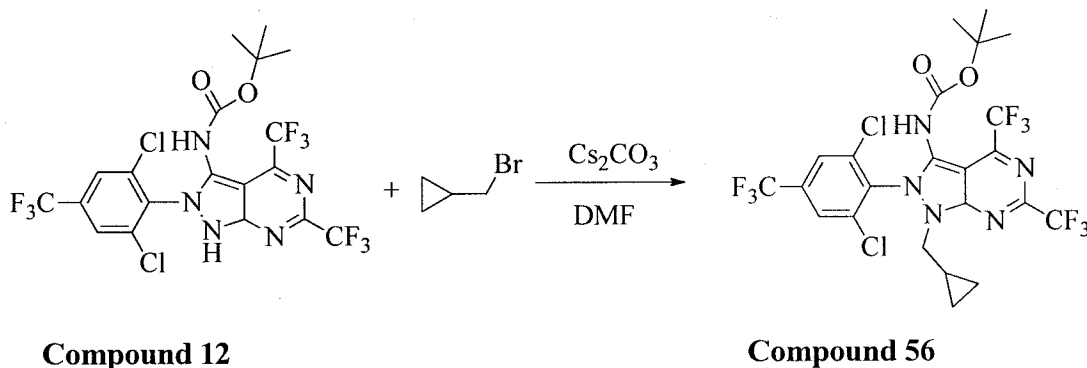
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Example 22

Preparation of *tert*-butyl (1-(cyclopropylmethyl)-2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate

[Compound 56]



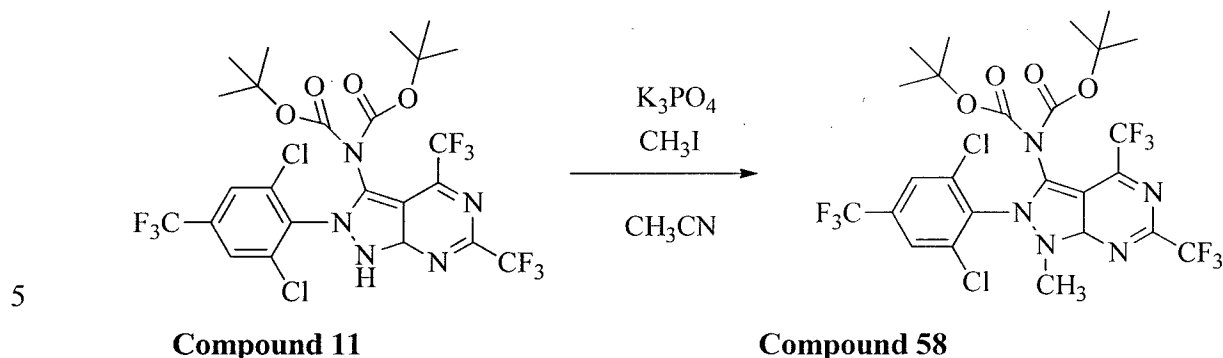
To a stirred solution of **Compound 12** (51 mg, 0.087 mmol) dissolved in DMF (0.9 mL, 0.1 M) was added (bromomethyl)cyclopropane (10 μ L, 0.104 mmol, 1.2 eq.) followed by cesium carbonate (Cs_2CO_3 , 85 mg, 0.261 mmol, 3 eq.). The reaction was stirred at RT overnight, diluted with a saturated sodium chloride (NaCl) solution (10 mL) and extracted with EtOAc (4 x 10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL). The organic phase was dried over MgSO_4 , filtered and concentrated under vacuum. The residue was purified by silica chromatography using a 6:1 hexane/EtOAc mixture as the eluent ($R_f = 0.25$) to afford **Compound 56** as a white solid (27 mg, 49%): ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 7.1$ Hz, 2H), 6.02 (s, 1H), 5.81 (br, 1H), 3.86–3.71 (m, 2H), 1.43 (s, 9H), 0.93–0.77 (m, 1H), 0.52–0.38 (m, 4H); ESIMS m/z 640 ($[\text{M}+\text{H}]^+$).

The electrophiles used may include: 2-(bromomethyl)-1,1-difluorocyclopropane. **Compound 57** in TABLE 9 was made in accordance with the procedure disclosed in Example 22.

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Example 23

Preparation of bis-*tert*-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-1-methyl-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate
[Compound 58]



To a solution containing **Compound 11** (56 mg, 0.082 mmol) dissolved in MeCN (0.8 mL, 0.1 M) was added potassium phosphate (17.3 mg, 0.082 mmol, 1 equivalent) followed by CH_3I (26 μL , 0.408 mmol, 5 equivalents). The reaction was heated at 70° C for 5 h. The mixture was cooled to RT and was diluted with EtOAc (20 mL). The organic solution was washed with water (10 mL) and brine (10 mL). The organic phase was dried over MgSO_4 , filtered and concentrated under vacuum to afford **Compound 58** as a yellow solid (55 mg, 96%): mp 54° C-56° C; ^1H NMR (400 MHz, CDCl_3) δ 7.71 (s, 2H), 5.58 (q, J = 6.6 Hz, 1H), 3.49 (s, 3H), 1.60–1.09 (m, 18H); ESIMS: m/z 700 ($[\text{M}+\text{H}]^+$).

The electrophiles used may include: ethyl iodide, isopropyl iodide, 1-(bromomethyl)-2-fluorobenzene, 1-(bromomethyl)-4-(trifluoromethoxy)benzene, 5-bromopentane nitrile, 1-bromopent-2-yne, 3-(iodomethyl)heptane.

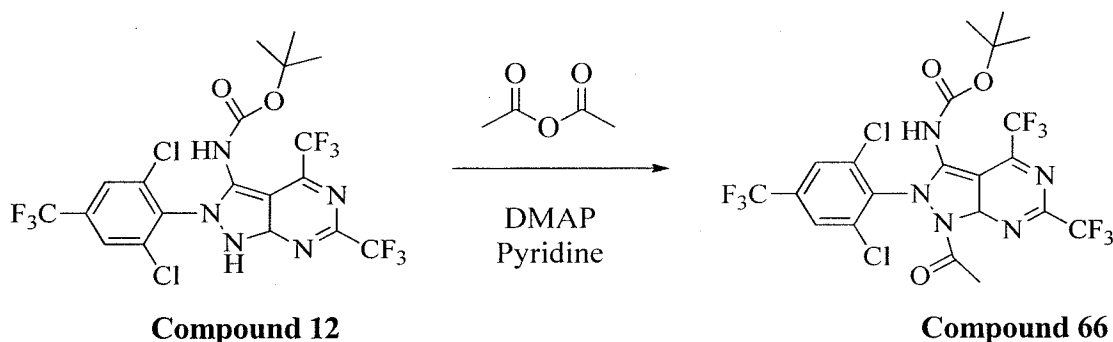
Compounds 59–65 in **TABLE 9** were made in accordance with the procedure disclosed in Example 23.

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Example 24

Preparation of *tert*-butyl (1-acetyl-2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate
[Compound 66]

5



To a stirred solution containing **Compound 12** (85 mg, 0.145 mmol) dissolved in THF
 10 (1.5 mL, 0.1 M) was added acetic anhydride (27 μ L, 0.290 mmol, 2 eq.), DMAP (1 mg, 0.008
 mmol, 0.05 eq.) and pyridine (2.5 μ L, 0.029 mmol, 0.2 eq.). The reaction was allowed to stir at
 RT overnight. The solution was diluted with EtOAc (20 mL) and washed with water (10 mL)
 and brine (10 mL). The organic phase was dried over MgSO_4 , filtered and concentrated under
 vacuum. The residue was purified by silica chromatography using a 5:1 hexane mixture as the
 15 eluent to afford **Compound 66** as a white solid in a 4:1 mixture of isomers (87 mg, 95%): ^1H
 NMR (400 MHz, CDCl_3) δ 7.78–7.65 (m, 2H, a mixture of isomers 1 and 2), 6.43 (br, 1H,
 isomer 1), 6.21 (br, 1H, isomer 2), 5.84 (br, 1H, isomer 2), 5.50 (br, 1H, isomer 1), 2.51 (s, 3H,
 isomer 1), 2.32 (s, 3H, isomer 2), 1.42 (s, 9H, isomer 1), 1.32 (s, 9H, isomer 2); ^{19}F NMR (376
 MHz, CDCl_3) δ -63.27, -63.31, -72.93, -73.04, -79.15; ESIMS m/z 628 ($[\text{M}+\text{H}]^+$).

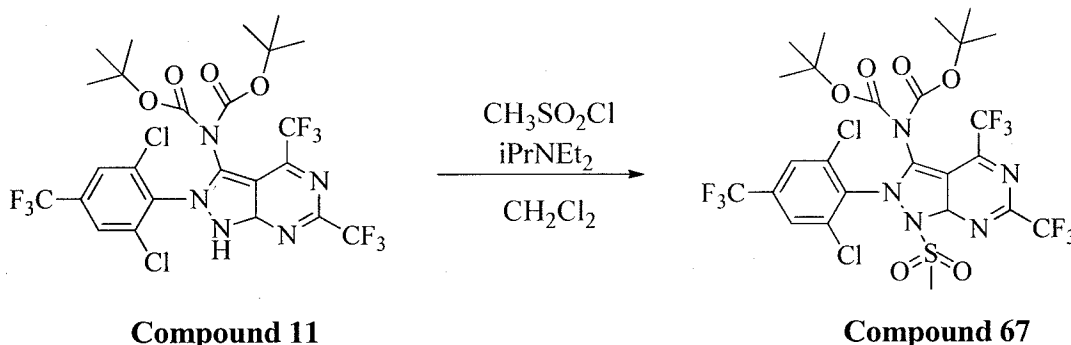
20

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Example 25

Preparation of bis-*tert*-butyl (2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-1-(methylsulfonyl)-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl)carbamate

[Compound 67]



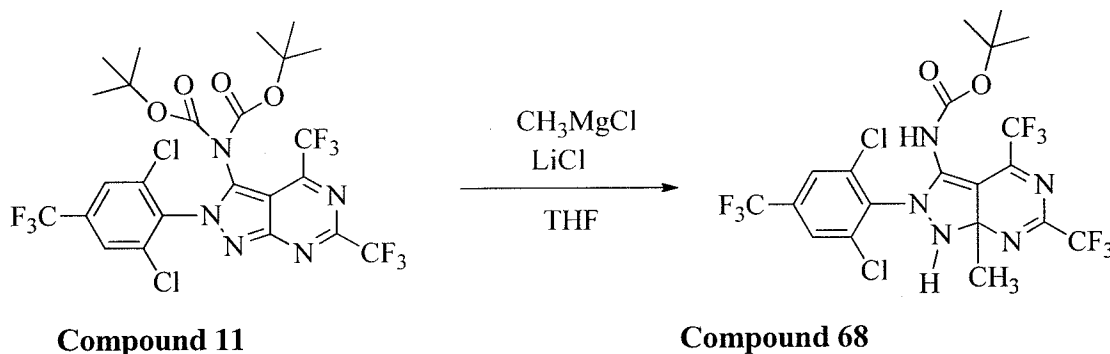
To a stirred solution of **Compound 11** (100 mg, 0.146 mmol) dissolved in CH₂Cl₂ (1.5 mL, 0.1 M) was added methanesulfonyl chloride (14 μL, 0.175 mmol, 1.2 eq) followed by *N*-ethyl-*N*-isopropylpropan-2-amine (53 μL, 0.306 mmol, 2.1 eq), and the reaction was stirred at RT overnight. Additional methanesulfonyl chloride (15 μL) and *N*-ethyl-*N*-isopropyl propan-2-amine (30 μL) were added to the reaction and heated at 50° C for 5 h. The cooled reaction mixture was diluted with EtOAc (20 mL) and washed with water (10 mL), 0.1 N HCl (10 mL) and brine (10 mL). The solution was dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified by silica chromatography using a 6:1 hexane/EtOAc mixture as the eluent (*R_f* = 0.20) to afford **Compound 67** as a clear oil (23 mg, 21%): ¹H NMR (300 MHz, CDCl₃) δ 7.72 (d, *J* = 6.4 Hz, 2H), 6.14 (q, *J* = 7.1 Hz, 1H), 3.31 (s, 3H), 1.42 (s, 18H); ESIMS *m/z* 764 ([*M*+*H*]⁺).

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Example 26

Preparation of *tert*-butyl *N*-[2-[2,6-dichloro-4-(trifluoromethyl)phenyl]-7a-methyl-4,6-bis(trifluoromethyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-yl]carbamate
[Compound 68]



To a stirred solution of **Compound 11** (103 mg, 0.151 mmol) and LiCl (7 mg, 0.166 mmol, 1.1 eq) dissolved in THF (1.5 mL, 0.1 M) was added CH₃MgCl (3.0 M in THF, 56 μL, 0.166 mmol, 1.1 eq), and the reaction was stirred at RT for 3 h. The reaction was quenched by the addition of saturated NH₄Cl solution (5 mL) and then extracted with EtOAc (3 x 5 mL). The organic phase was dried over MgSO₄, filtered and concentrated under vacuum. The residue was purified by silica chromatography using a 4:1 hexane/EtOAc mixture as the eluent (*R_f* = 0.17) to afford **Compound 68** as a white solid (54 mg, 60%): ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, *J* = 9.4 Hz, 2H), 6.04 (s, 1H), 5.77 (s, 1H), 1.87 (s, 3H), 1.30 (s, 9H); ¹⁹F NMR (376 MHz, CDCl₃) δ -63.25, -72.76, -80.55; ESIMS *m/z* 600 ([*M*+H]⁺).

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The Grignard reagents used may include: isopropylmagnesium chloride, ethylmagnesium chloride, *n*-propylmagnesium chloride, benzylmagnesium chloride.

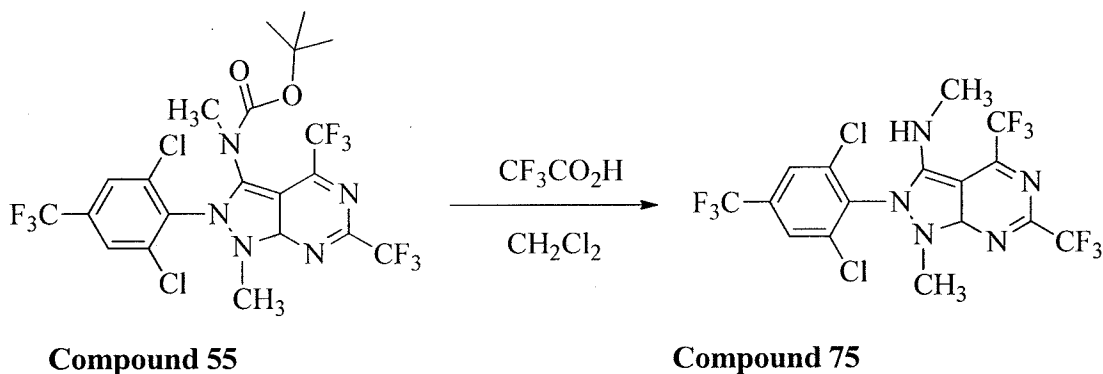
Compounds 69–74 in **TABLE 9** were made in accordance with the procedure disclosed in Example 26.

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Example 27

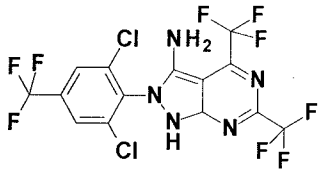
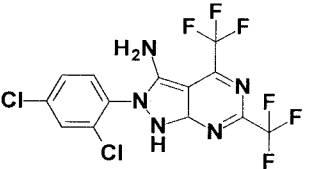
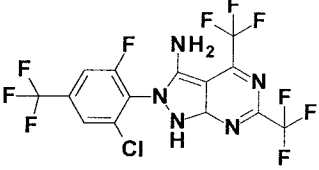
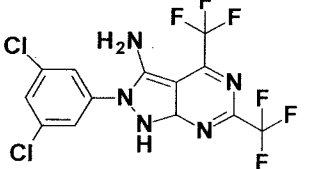
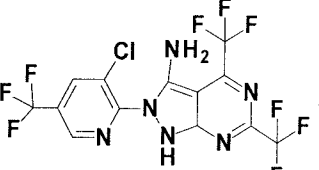
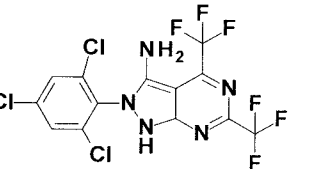
Preparation of 2-(2,6-dichloro-4-(trifluoromethyl)phenyl)-*N*,1-dimethyl-4,6-bis(trifluoromethyl)-2,7a-dihydro-1*H*-pyrazolo[3,4-*d*]pyrimidin-3-amine
[Compound 75]

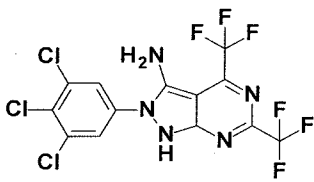
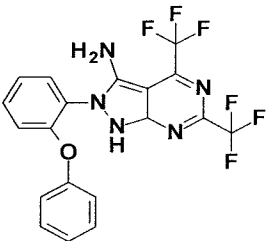
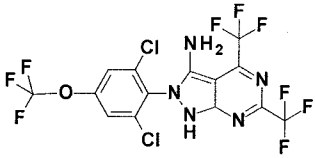
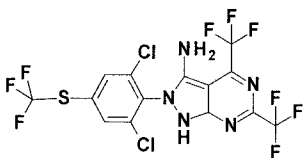
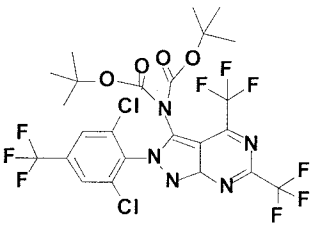


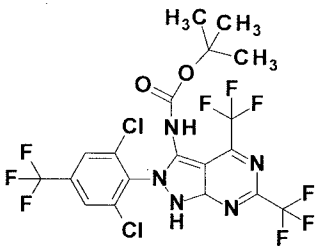
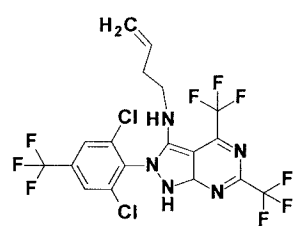
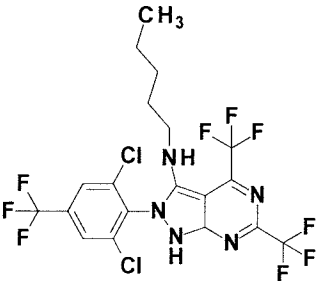
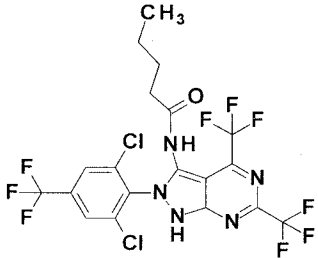
To a stirred solution of **Compound 55** (35 mg, 0.057 mmol) dissolved in CH₂Cl₂ (1 mL, 0.06 M) was added TFA (0.13 mL, 1.709 mmol), and the reaction was stirred at RT for 2 h.
10 Saturated NaHCO₃ was added carefully (10 mL), and the mixture was stirred for an additional 15 min. The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated under vacuum to afford **Compound 75** as a yellow solid (24 mg, 82%): ¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 2H), 5.30 (s, 1H), 5.02 (q, *J* = 5.4 Hz, 1H), 3.38 (s, 3H), 2.85 (d, *J* = 5.4 Hz, 3H); ESIMS *m/z* 514 ([M+H]⁺).
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Compounds 76–96 in TABLE 9 were made in accordance with the procedure disclosed in Example 27.

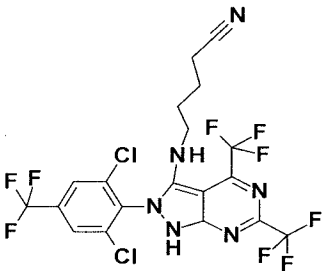
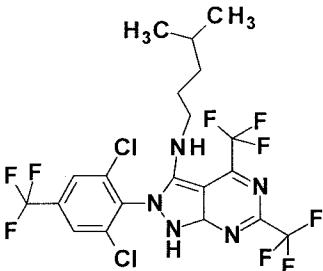
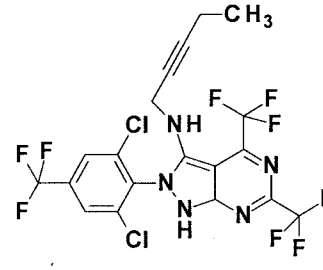
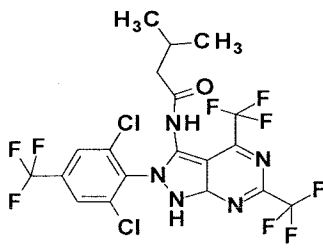
TABLE 9

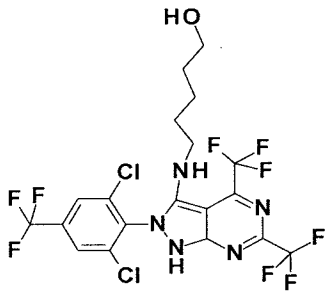
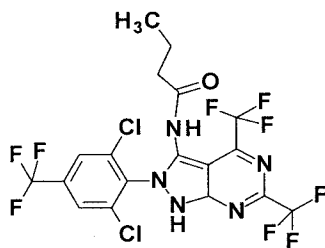
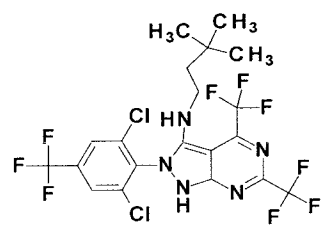
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
1		White Solid	250–254	484.53 ([M-H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.19 (d, <i>J</i> = 3.4 Hz, 1H), 8.15 (d, <i>J</i> = 1.8 Hz, 2H), 5.89–5.74 (m, 2H), 5.59–5.38 (m, 1H)
2		White Solid	258–260	417.1 ([M-H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.17 (s, 1H), 7.86 (d, <i>J</i> = 2.2 Hz, 1H), 7.63–7.46 (m, 2H), 5.61 (s, 2H), 5.45 (s, 1H)
3		White Solid	241–243	467.3 ([M-H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.27 (s, 1H), 8.09–8.01 (m, 2H), 5.88 (s, 2H), 5.49–5.41 (m, 1H)
4		Yellow Solid	---	417.1 ([M-H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.35 (s, 1H), 7.68–7.63 (m, 2H), 7.60–7.55 (m, 1H), 5.94 (s, 2H), 5.58–5.51 (m, 1H)
5		Pale Yellow Solid	---	451.4 ([M-H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.35 (s, 1H), 8.91 (s, 1H), 8.74 (d, <i>J</i> = 2.1 Hz, 1H), 6.10 (s, 2H), 5.58–5.46 (m, 1H)
6		White Solid	279–281	451.1 ([M-H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.19 (s, 1H), 7.95–7.87 (m, 2H), 5.74 (s, 2H), 5.47–5.38 (m, 1H)

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
7		Yellow Solid	---	451.1 ([M-H])	(400 MHz, DMSO- <i>d</i> ₆): δ 9.37 (s, 1H), 7.87 (s, 2H), 5.98 (s, 2H), 5.59–5.48 (s, 1H)
8		Pale Yellow Solid	245–248	442.7 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.08 (s, 1H), 7.48–7.42 (m, 2H), 7.37–7.31 (m, 2H), 7.29–7.23 (m, 1H), 7.12 (t, <i>J</i> = 7.4 Hz, 1H), 7.05 (d, <i>J</i> = 7.8 Hz, 2H), 7.00 (d, <i>J</i> = 8.1 Hz, 1H), 5.54–5.38 (m, 3H)
9		Pale Yellow Solid	261–263	502.5 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.21 (s, 1H), 7.88 (s, 2H), 5.79 (s, 2H), 5.48–5.39 (m, 1H)
10		Pale Yellow Solid	278–285	517.1 ([M-H])	(400 MHz, DMSO- <i>d</i> ₆): δ 9.23 (s, 1H), 8.12–8.05 (m, 2H), 5.82 (s, 2H), 5.48–5.41 (m, 1H)
11		White Solid	---	686 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.72 (s, 2H), 5.63–5.35 (m, 2H), 1.60–1.40 (m, 18H)

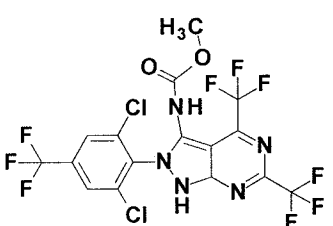
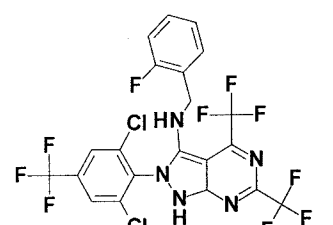
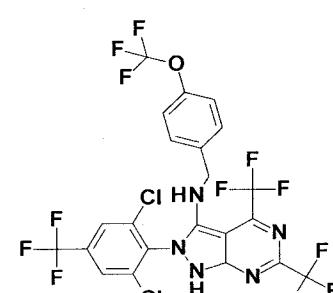
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
12		White Solid	173– 176	586 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.77 (s, 2H), 6.08 (s, 1H), 5.87–5.74 (m, 2H), 1.45 (s, 9H)
13		White Solid	203– 206	540 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.98 (s, 0.5H, isomer 1), 7.74 (s, 2H), 5.93 (s, 0.5H, isomer 2), 5.70–5.56 (m, 1H), 5.47–5.41 (m, 0.5H, isomer 1), 5.30–5.24 (m, 0.5H, isomer 2), 5.08–4.97 (m, 2H), 3.65–3.48 (m, 0.5H, isomer 1), 3.38–3.29 (m, 0.5H, isomer 2), 3.12–2.90 (m, 2H), 2.2–2.16 (m, 2H)
14		White Solid	194– 197	556 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 8.01 (s, 0.38H, isomer 1), 7.75 (s, 2H), 5.94 (s, 0.62H, isomer 2), 5.49–5.21 (m, 1H), 3.46–3.18 (m, 1H), 3.05–2.86 (m, 2H), 1.49–1.39 (m, 2H), 1.28–1.16 (m, 4H), 0.85 (t, <i>J</i> = 7.0 Hz, 3H)
15		White Solid	143– 148	570 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.74 (s, 2H), 7.15 (s, 1H), 6.12 (s, 1H), 5.79 (s, 1H), 2.25 (t, <i>J</i> = 7.5 Hz, 2H), 1.61–1.49 (m, 2H), 1.34–1.18 (m, 2H), 0.86 (t, <i>J</i> = 7.3 Hz, 3H)

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
16		Tan Solid	---	597 ([M+H] ⁺)	(300 MHz, CDCl ₃): δ 8.02 (s, 1H), 7.77 (d, <i>J</i> = 3.9 Hz, 2H), 6.08 (s, 1H), 5.96 (s, 1H), 5.76– 5.68 (m, 1H)
17		Tan Solid	179– 181	572 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.40 (s, 1H), 8.20 (s, 2H), 5.79–5.69 (m, 1H), 5.52–5.41 (m, 1H), 3.23 (t, <i>J</i> = 5.8 Hz, 2H), 3.18 (s, 3H), 3.06– 2.82 (m, 2H), 1.48–1.31 (m, 4H)
18		Tan Solid	187– 191	554 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.39 (s, 1H), 8.19 (s, 2H), 5.91 (t, <i>J</i> = 6.0 Hz, 1H), 5.44–5.38 (m, 1H), 5.07 (t, <i>J</i> = 5.8 Hz, 1H), 3.66– 3.49 (m, 2H), 1.63 (s, 3H), 1.53 (s, 3H)
19		Tan Solid	101– 105	572 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 6.23 (s, 1H), 5.90 (bs, 1H), 5.82 (bs, 1H), 4.96 (hept, <i>J</i> = 6.2 Hz, 1H), 1.24 (dd, <i>J</i> = 6.1, 3.6 Hz, 6H)
20		Tan Solid	196– 200	568 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.37 (s, 1H), 8.21 (s, 2H), 5.78 (t, <i>J</i> = 6.2 Hz, 1H), 5.50–5.39 (m, 1H), 2.96–2.81 (m, 1H), 2.79–2.62 (m, 1H), 2.00–1.83 (m, 1H), 1.71–0.97 (m, 8H)

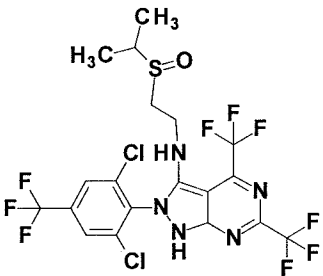
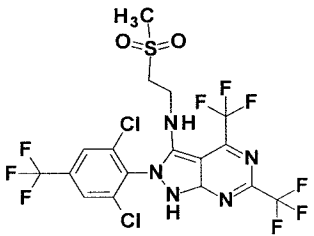
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
21		Tan Solid	223– 227	567 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.42 (s, 1H), 8.20 (s, 2H), 5.78 (t, <i>J</i> = 6.1 Hz, 1H), 5.56–5.47 (m, 1H), 3.09–2.85 (m, 2H), 2.46 (t, <i>J</i> = 6.4 Hz, 2H), 1.58–1.36 (m, 4H)
22		Tan Solid	195– 198	570 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.75 (s, 2H), 5.86 (s, 1H), 5.45 (q, <i>J</i> = 6.0 Hz, 1H), 5.32–5.31 (m, 1H), 3.07–2.82 (m, 2H), 1.52–1.37 (m, 3H), 1.13–1.00 (m, 2H), 0.83 (d, <i>J</i> = 6.6 Hz, 6H)
23		Tan Solid	178– 182	552 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.67 (s, 2H), 5.76 (s, 1H), 5.55 (q, <i>J</i> = 6.2 Hz, 1H), 5.40–5.32 (m, 1H), 3.73–3.51 (m, 2H), 2.12–1.99 (m, 2H), 1.06–0.95 (m, 3H)
24		Tan Solid	127– 130	570 ([M+H] ⁺)	(300 MHz, CD ₃ OD): δ 8.01 (d, <i>J</i> = 8.8 Hz, 2H), 5.75 (q, <i>J</i> = 6.1 Hz, 1H), 2.24–1.85 (m, 3H), 0.99–0.78 (m, 6H)

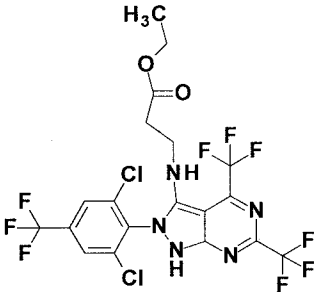
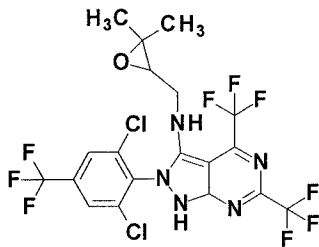
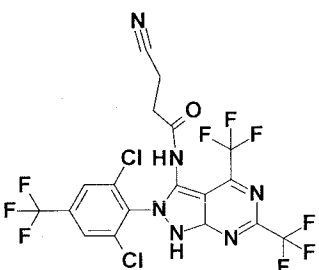
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
25		Tan Oil	---	572 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 8.81 (bs, 1H), 7.74 (s, 2H), 6.08 (bs, 1H), 5.48–5.28 (m, 2H), 3 .60 (t, <i>J</i> = 6.3 Hz, 2H), 3.07–2.84 (m, 2H), 1.60–1.15 (m, 6H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.20, -72.91, -77.04, -80.26
26		Tan Solid	238– 241	556 ([M+H] ⁺) (- Cl)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (d, <i>J</i> = 8.7 Hz, 2H), 5.89 (s, 1H), 5.59–5.57 (m, 2H), 3.51–3.36 (m, 1H), 3.14–2.97 (m, 1H), 2.59–2.31 (m, 2H), 2.17–1.89 (m, 2H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.18, -72.98, -80.20
27		Tan Solid	---	570 ([M+H] ⁺)	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆): δ 9.33 (s, 1H), 8.19 (s, 2H), 5.67 (t, <i>J</i> = 6.2 Hz, 1H), 5.45 (bs, 1H), 2.95–2.81 (m, 2H), 1.39–1.25 (m, 2H), 0.80 (s, 9H) ¹⁹ F NMR (376 MHz, DMSO- <i>d</i> ₆): δ -61.44, -71.33, -79.05

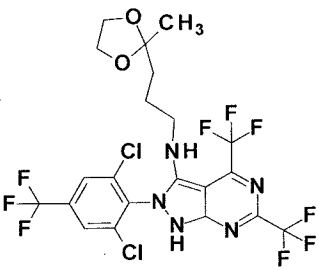
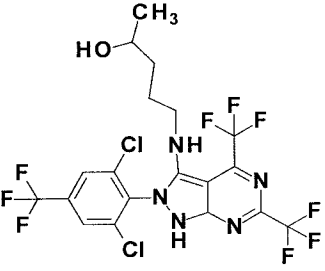
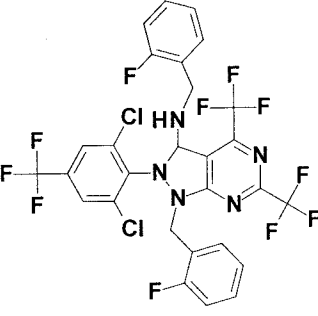
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
28		Yellow Solid	---	570 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.74 (s, 2H), 6.12 (bs, 1H), 5.53–5.23 (m, 2H), 2.93–2.64 (m, 2H), 1.52–1.41 (m, 1H), 1.22–1.15 (m, 2H), 1.05–0.79 (m, 8H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.23, -72.91, -77.05
29		Yellow Solid	---	686 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.72 (s, 2H), 6.02 (bs, 1H), 5.46–5.23 (m, 2H), 3.53 (t, <i>J</i> = 6.2 Hz, 2H), 3.02–2.87 (m, 2H), 1.49–1.39 (m, 3H), 1.31–1.20 (m, 3H), 0.85 (s, 9H), -0.00 (s, 6H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.21, -72.93, -77.07
30		White Solid	---	664 ([M+H] ⁺) ([C(O)-OCH ₂ -CCl ₃])	¹ H NMR (400 MHz, CDCl ₃): δ 7.74 (s, 2H), 6.19 (bs, 1H), 5.82–5.70 (m, 1H), 4.92–4.59 (m, 4H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.30, -72.95, -79.95

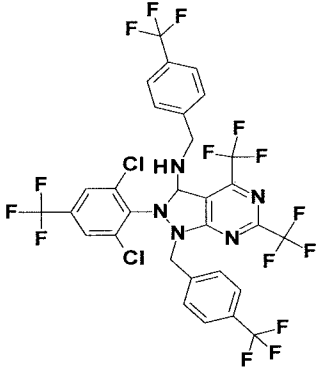
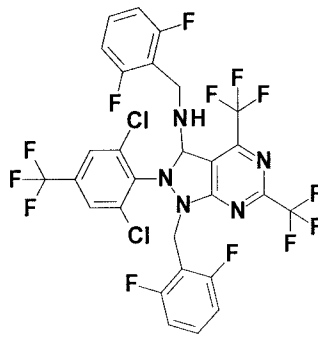
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
31		Tan Solid	---	544 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.74 (s, 2H), 6.53 (s, 1H), 6.21 (bs, 1H), 5.79 (bs, 1H), 3.73 (s, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.30, -73.04, -80.13
32		Off White Solid	---	594 ([M+H] ⁺)	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆): δ 9.41 (d, <i>J</i> = 3.7 Hz, 1H), 8.13 (d, <i>J</i> = 7.1 Hz, 2H), 7.36–7.24 (m, 2H), 7.18–7.06 (m, 2H), 6.43 (t, <i>J</i> = 6.5 Hz, 1H), 5.41 (bs, 1H), 4.29 (dd, <i>J</i> = 15.9, 6.7 Hz, 1H), 4.16 (dd, <i>J</i> = 15.9, 6.7 Hz, 1H) ¹⁹ F NMR (376 MHz, DMSO- <i>d</i> ₆): δ -61.42, -71.31, -79.13, - 119.67
33		White Solid	---	660 ([M+H] ⁺)	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆): δ 9.40 (s, 1H), 8.12 (d, <i>J</i> = 11.0 Hz, 2H), 7.38–7.22 (m, 4H), 6.48 (t, <i>J</i> = 6.5 Hz, 1H), 5.40 (bs, 1H), 4.29–4.11 (m, 2H) ¹⁹ F NMR (376 MHz, DMSO- <i>d</i> ₆): δ -56.85, -61.47, -71.27, - 79.05

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
37		White Solid	---	583 ([M+H] ⁺)	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆): δ 9.48 (d, <i>J</i> = 4.0 Hz, 1H), 8.19 (d, <i>J</i> = 4.4 Hz, 2H), 7.69 (d, <i>J</i> = 3.3 Hz, 1H), 7.66 (d, <i>J</i> = 3.2 Hz, 1H), 6.79 (t, <i>J</i> = 6.7 Hz, 1H), 5.64 (bs, 1H), 4.49 (d, <i>J</i> = 6.9 Hz, 2H) ¹⁹ F NMR (376 MHz, DMSO- <i>d</i> ₆): δ -61.40, -71.31, -78.97
38		Tan Solid	---	588 ([M+H] ⁺)	(400 MHz, DMSO- <i>d</i> ₆): δ 9.43 (s, 1H), 8.22 (s, 2H), 7.36 (bs, 1H), 5.56–5.44 (m, 1H), 3.12–3.00 (m, 2H), 2.94–2.73 (m, 2H), 1.70–1.58 (m, 1H), 1.13 (d, <i>J</i> = 6.7 Hz, 6H)
39		Tan Solid	---	588 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone- <i>d</i> ₆): δ 8.23 (bs, 1H), 7.90 (d, <i>J</i> = 4.1 Hz, 2H), 5.62–5.52 (m, 1H), 5.09–5.93 (m, 1H), 3.24–2.96 (m, 2H), 2.48–2.27 (m, 4H), 1.68–1.55 (m, 2H), 1.03 (t, <i>J</i> = 7.4 Hz, 3H) ¹⁹ F NMR (376 MHz, Acetone- <i>d</i> ₆): δ 113.98, 104.17, 96.72

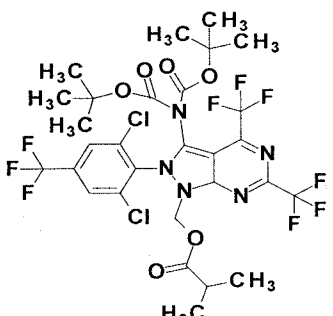
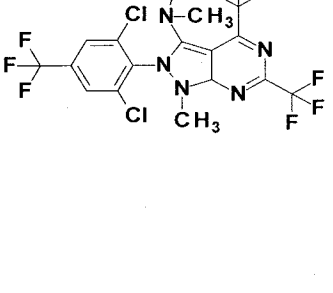
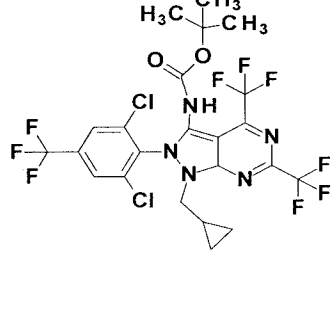
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
40		Tan Solid	---	604 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone- <i>d</i> ₆): δ 8.30 (s, 1H, Isomer A, N-H), 8.25 (s, 1H, Isomer B, N-H), 7.90 (s, 2H, Ar-H), 5.88–5.81 (m, 1H, Isomer A, N-H), 5.79–5.67 (m, 1H, Isomer B, N-H), 5.46–5.25 (m, 1H), 3.66–3.35 (m, 3H), 2.7–2.55 (m, 2H), 1.06–0.99 (m, 6H) ¹⁹ F NMR (376 MHz, Acetone): δ 113.96 (Isomer A), 113.96 (Isomer B), 104.18 (Isomer A), 104.17 (Isomer B), 96.91 (Isomer A), 96.80 (Isomer B)
41		Tan Solid	---	592 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone- <i>d</i> ₆): δ 8.47 (bs, 1H), 8.06 (s, 2H), 5.83–5.69 (m, 1H), 5.39–3.51 (m, 1H), 3.77–3.53 (m, 2H), 3.42–3.25 (m, 2H), 2.99 (s, 3H) ¹⁹ F NMR (376 MHz, Acetone- <i>d</i> ₆): δ 113.95, 104.15, 96.75

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
42		Tan Solid	---	586 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone- <i>d</i> ₆): δ 8.25 (bs, 1H), 7.90 (s, 2H), 5.64–5.53 (m, 1H), 5.05 (bs, 1H), 3.91 (q, <i>J</i> = 7.1 Hz, 2H), 3.37–3.15 (m, 2H), 2.41–2.30 (m, 2H), 1.04 (t, <i>J</i> = 7.1 Hz, 3H) ¹⁹ F NMR (376 MHz, Acetone): δ 113.96, 104.16, 96.74
43		Tan Solid	---	570 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone- <i>d</i> ₆): δ 8.25 (bs, 1H), 7.90 (s, 2H), 5.73–5.66 (m, 1H), 5.64–5.56 (m, 1H), 3.36–3.24 (m, 1H), 3.08–2.93 (m, 2H), 2.70 (s, 3H), 2.67 (s, 3H) ¹⁹ F NMR (376 MHz, Acetone- <i>d</i> ₆): δ 113.97, 104.11, 96.95, 96.74
44		Tan Solid	---	567 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone- <i>d</i> ₆): δ 9.90 (bs, 1H), 8.49 (bs, 1H), 8.09 (s, 2H), 5.97 (bs, 1H), 2.73 (s, 4H) ¹⁹ F NMR (376 MHz, Acetone- <i>d</i> ₆): δ 113.93, 104.07, 96.87

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
45		Tan Solid	---	614 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone-d ₆): δ 8.37 (bs, 1H), 8.04 (s, 2H), 5.69–5.61 (m, 1H), 5.24–5.13 (m, 1H), 3.92–3.78 (m, 4H), 3.22–3.03 (m, 2H), 1.68–1.50 (m, 4H), 1.18 (s, 3H) ¹⁹ F NMR (376 MHz, Acetone-d ₆): δ 113.99, 104.18, 96.72
46		Brown Solid	---	572 ([M+H] ⁺)	¹ H NMR (400 MHz, Acetone-d ₆): δ 8.35 (bs, 1H), 8.03 (s, 2H), 5.75–5.56 (m, 2H), 5.28–5.17 (m, 1H), 3.71–3.59 (m, 2H), 3.24–3.03 (m, 3H), 1.64–1.49 (m, 2H), 1.08–1.04 (m, 3H) ¹⁹ F NMR (376 MHz, Acetone-d ₆): δ 113.99, 104.18, 96.72
47		Off White Solid	---	702 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.50 (s, 1H), 7.30–7.19 (m, 3H), 7.16–7.01 (m, 3H), 6.99–6.90 (m, 2H), 6.76 (t, <i>J</i> = 9.2 Hz, 1H), 5.54 (q, <i>J</i> = 6.6 Hz, 1H), 5.14 (d, <i>J</i> = 16.2 Hz, 1H), 4.92 (d, <i>J</i> = 16.1 Hz, 1H), 4.70–4.60 (m, 1H), 4.42–4.27 (m, 2H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.62, -73.65, -77.12, -118.50, -118.78

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
48		Tan Solid	---	ESIMS <i>m/z</i> 802 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃) δ 7.51–6.96 (m, 10H), 6.20–6.12 (m, 1H), 5.60–5.50 (m, 2H), 5.37 (d, <i>J</i> = 16.0 Hz, 1H), 4.96 (d, <i>J</i> = 16.2 Hz, 1H), 4.69 (d, <i>J</i> = 16.1 Hz, 1H), 4.47 (d, <i>J</i> = 16.6 Hz, 1H), 4.31 (d, <i>J</i> = 16.5 Hz, 1H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 62.92, -63.10, -63.97, -70.29, - 73.68, -76.85, -79.78
49		Yellow Solid	---	738 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.56 (s, 2H; Isomer A), 7.44 (s, 2H; isomer B), 7.34–7.21 (m, 1H; Isomer A), 7.19–7.07 (m, 1H; Isomer B), 6.93–6.78 (m, 2H; Isomer A), 6.76–6.57 (m, 2H; Isomer B), 6.12 (q, <i>J</i> = 6.3, 5.2 Hz, 1H; Isomer A), 5.66 (q, <i>J</i> = 6.1 Hz, 1H; Isomer B), 5.24 (d, <i>J</i> = 15.6 Hz, 1H; Isomer A), 4.91 (d, <i>J</i> = 15.6 Hz, 1H; Isomer A), 4.39 (s, 2H; Isomer B) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.56, -70.60, -73.68, -77.51, - 79.94, -111.86, -115.19

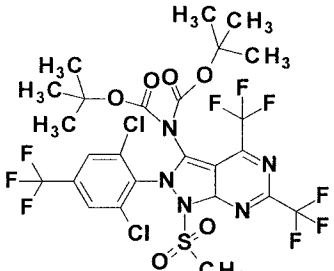
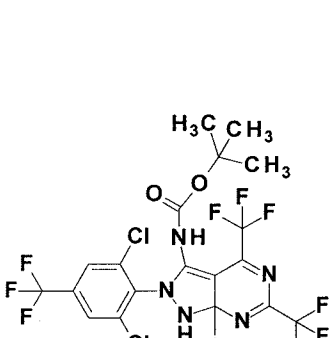
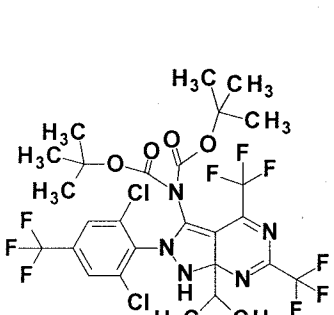
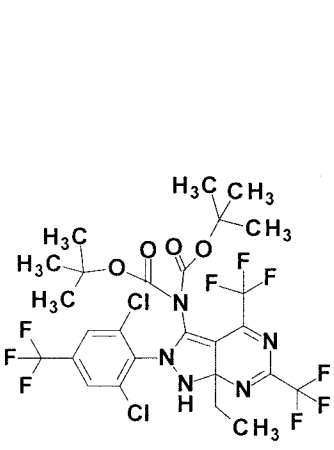
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
50		Clear Oil	---	812 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.70 (s, 2H), 5.95–5.85 (m, 2H), 5.61 (q, <i>J</i> = 6.6 Hz, 1H), 2.81–2.69 (m, 1H), 1.92–1.24 (m, 26H)
51		Greenish Yellow Solid	---	686 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (d, <i>J</i> = 3.1 Hz, 2H), 6.06 (bs, 1H), 5.93–5.79 (m, 3H), 2.53 (p, <i>J</i> = 7.0 Hz, 1H), 1.44 (s, 9H), 1.13 (d, <i>J</i> = 7.0 Hz, 6H)
52		Off-White Foam	---	658 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.75 (s, 2H), 5.94–5.84 (m, 2H), 5.73–5.49 (m, 1H), 4.84 (bs, 1H), 2.06 (s, 3H), 1.57–1.40 (m, 9H) ¹³ C NMR (101MHz, CDCl ₃): δ 169.65, 146.53, 138.40, 126.04, 125.75, 123.12, 120.62, 118.82, 115.64, 84.41, 79.23, 67.75, 60.52, 36.43, 27.82, 20.70, 14.17
53		Clear Oil	---	702 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 6.07–5.81 (m, 4H), 4.06 (s, 2H), 3.55 (q, <i>J</i> = 7.0 Hz, 2H), 1.44 (s, 9H), 1.21 (t, <i>J</i> = 7.0 Hz, 3H)

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
54		Clear Oil	---	786 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.70 (s, 2H), 5.98–5.83 (m, 2H), 5.61 (q, <i>J</i> = 6.6 Hz, 1H), 2.64– 2.49 (m, 1H), 1.62–1.24 (m, 18H), 1.21–1.10 (m, 6H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.29, -67.15, -75.95
55		Purple Oil	---	614 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.75 (d, <i>J</i> = 16.7 Hz, 2H), 5.31 (s, 1H), 3.37 (s, 3H), 2.78 (s, 3H), 1.49 (s, 9H)
56		White Solid	---	640 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (d, <i>J</i> = 7.1 Hz, 2H), 6.02 (s, 1H), 5.81 (bs, 1H), 3.86–3.71 (m, 2H), 1.43 (s, 9H), 0.93–0.77 (m, 1H), 0.5–0.38 (m, 4H)

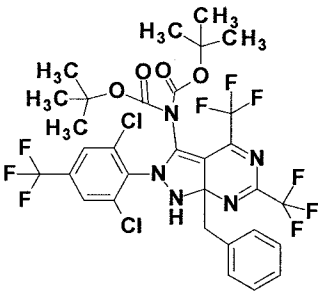
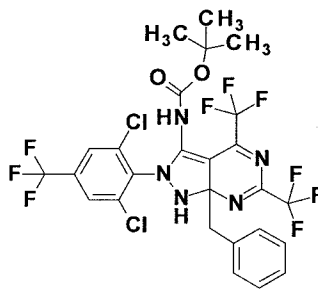
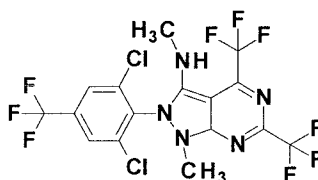
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
57		White Solid	---	676 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.77 (s, 2H), 6.02 (bs, 1H), 5.82 (bs, 1H), 4.23–4.15 (m, 1H), 3.99–3.81 (m, 1H), 2.14–2.05 (m, 1H), 1.43 (s, 9H), 0.99–0.84 (m, 2H)
58		Yellow Solid	54-56	700 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.71 (s, 2H), 5.58 (q, <i>J</i> = 6.6 Hz, 1H), 3.49 (s, 3H), 1.60–1.09 (m, 18H)
59		Yellow Oil	---	714 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.71 (s, 2H), 5.57 (q, <i>J</i> = 6.7 Hz, 1H), 4.02–3.90 (m, 2H), 1.57–1.21 (m, 21H)
60		White Solid	---	728 ([M+H] ⁺)	(300 MHz, CDCl ₃): δ 7.71 (s, 2H), 5.52 (q, <i>J</i> = 6.7 Hz, 1H), 4.43 (dq, <i>J</i> = 14.6, 7.7, 7.2 Hz, 1H), 1.83–1.08 (m, 25H)

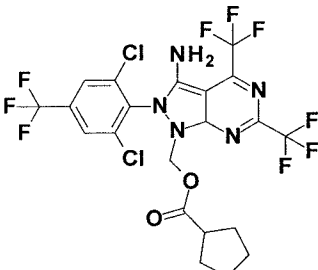
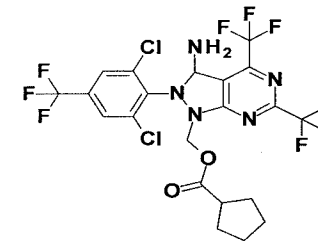
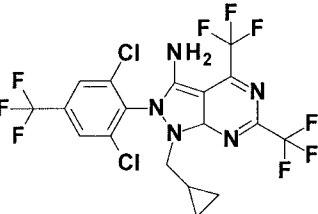
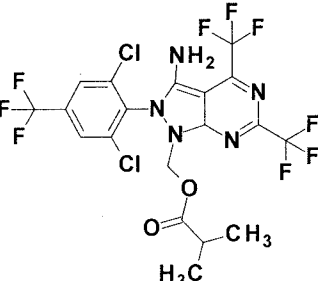
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
61		Clear Oil	---	794 ([M+H] ⁺)	(300 MHz, CDCl ₃): δ 7.62 (d, <i>J</i> = 7.0 Hz, 2H), 7.31–6.96 (m, 4H), 5.65 (q, <i>J</i> = 6.3 Hz, 1H), 5.21 (dd, <i>J</i> = 12.6, 12.4 Hz, 2H), 1.70–1.05 (m, 18H)
62		Clear Oil	---	860 ([M+H] ⁺)	
63		Clear Oil	---	767 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.72 (s, 2H), 5.58 (q, <i>J</i> = 6.6 Hz, 1H), 4.01–3.81 (m, 2H), 2.37 (t, <i>J</i> = 7.2 Hz, 2H), 2.03–1.91 (m, 2H), 1.78–1.67 (m, 2H), 1.59–1.21 (m, 18H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.28, -66.77, -76.53
64		Clear Oil	---	752 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.70 (s, 2H), 5.58 (q, <i>J</i> = 6.6 Hz, 1H), 4.63 (s, 2H), 2.14 (qt, <i>J</i> = 7.5, 1.9 Hz, 2H), 1.64–1.21 (m, 18H), 1.07 (t, <i>J</i> = 7.5 Hz, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.29, -67.05, -76.20

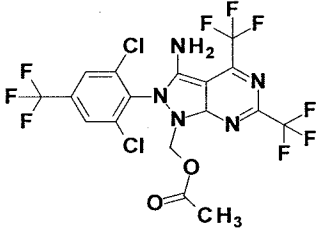
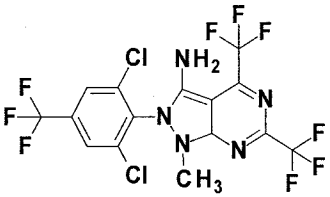
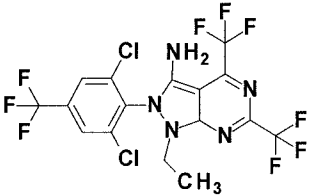
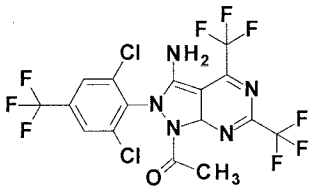
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
65		Yellow Oil	---	798 ([M+H] ⁺)	¹ H NMR (300 MHz, CDCl ₃): δ 7.70 (s, 2H), 5.56 (q, <i>J</i> = 6.6 Hz, 1H), 3.96–3.82 (m, 1H), 3.77–3.60 (m, 1H), 3.32–3.23 (m, 1H), 2.18–2.03 (m, 1H), 1.62–1.01 (m, 25H), 0.97–0.74 (m, 6H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.23, -63.26, -72.86, -72.94, -76.15, -79.42, mixture of isomers)
66		White Solid	---	628 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.78–7.65 (m, 2H, mixture isomer 1 & 2), 6.43 (bs, 1H, isomer 1), 6.21 (bs, 1H, isomer 2), 5.84 (bs, 1H, isomer 2), 5.50 (bs, 1H, isomer 1), 2.51 (s, 3H, isomer 1), 2.32 (s, 3H, isomer 2), 1.42 (s, 9H, isomer 1), 1.32 (s, 9H, isomer 2) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.27, -63.31, -72.93, -73.04, -79.15

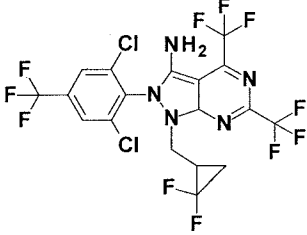
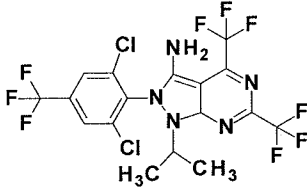
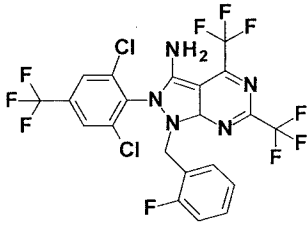
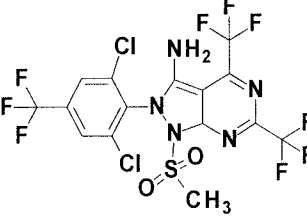
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
67		Clear Oil	---	764 ([M+H] ⁺)	(300 MHz, CDCl ₃): δ 7.72 (d, <i>J</i> = 6.4 Hz, 2H), 6.14 (q, <i>J</i> = 7.1 Hz, 1H), 3.31 (s, 3H), 1.42 (s, 18H)
68		White Solid	---	600 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.73 (d, <i>J</i> = 9.4 Hz, 2H), 6.04 (s, 1H), 5.77 (s, 1H), 1.87 (s, 3H), 1.30 (s, 9H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.25, -72.76, -80.55
69		Tan Solid	---	728 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.85 (s, 2H, isomer A), 7.83 (s, 2H, isomer B), 5.54–5.50 (m, 1H, isomer A,B), 2.56 (p, <i>J</i> = 7.0 Hz, 1H, isomer A), 2.46 (p, <i>J</i> = 7.0 Hz, 1H, isomer B), 1.45–1.35 (m, 24H, isomer A,B)
70		White Solid	---	714 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.82 (s, 1H, Isomer A & B), 7.69 (s, 2H, Isomer A & B), 2.13–1.93 (m, 2H, Isomer A & B), 1.46 (s, 9H, Isomer A), 1.36 (s, 9H, Isomer B), 1.02 (t, <i>J</i> = 7.3 Hz, 3H, Isomer A), 0.84 (t, <i>J</i> = 7.3 Hz, 3H, Isomer B) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.26 (Isomer A), -63.28 (Isomer B), -72.61 (Isomer A), -

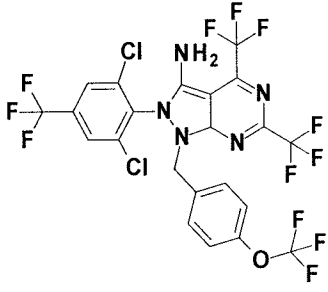
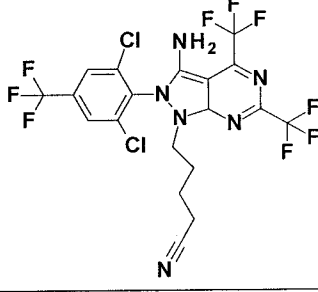
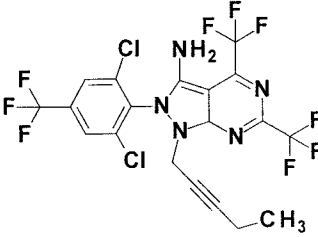
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
					72.70 (Isomer B), -77.60 (Isomer A), -79.63 (Isomer B)
71		Yellow Oil	---	728 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 8.38 (s, 1H), 7.68 (s, 2H), 2.25– 1.80 (m, 2H), 1.47 (s, 9H, isomer A, t-Bu), 1.45 (s, 9H, isomer B, t-Bu), 1.31–1.24 (m, 2H), 1.37 (s, 9H, isomer A, t-Bu), 1.35 (s, 9H, isomer B, t-Bu), 0.99–0.87 (m, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.28 (Isomer A), -63.33 (Isomer B), -72.71 (Isomer A), - 72.81 (Isomer B), -77.81 (Isomer A), -79.77 (Isomer B)
72		White Solid	---	628 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.71 (s, 2H), 6.10 (s, 1H), 2.20– 2.08 (m, 2H), 1.84–1.65 (m, 2H), 1.31 (s, 9H), 1.02–0.92 (m, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.24, -70.89, -83.40

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
73		White Solid	---	776 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.75–7.67 (m, 2H, mixture of isomers, Ar-H), 7.29–7.11 (m, 5H), 6.95 (s, 1H), 3.62 (d, <i>J</i> = 12.5 Hz, 1H), 3.08 (d, <i>J</i> = 12.5 Hz, 1H), 1.52, 1.48, 1.39, 1.38 (s, 18H, mixture of isomers, t-Bu) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.23, -72.54, -72.60, -76.13, - 77.22.
74		White Solid	---	676 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (s, 2H, Isomer A, Ar-H), 7.71 (s, 2H, Isomer B, Ar-H), 7.23–7.06 (m, 6H), 6.00 (bs, 1H), 3.34–3.26 (m, 2H), 1.56 (s, 9H, Isomer A, t-Bu), 1.31 (s, 9H, Isomer B, t-Bu) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.22, -71.08, -72.84, -77.09, - 78.99, -81.66
75		Yellow Solid	---	514 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.73 (s, 2H), 5.30 (s, 1H), 5.02 (q, <i>J</i> = 5.4 Hz, 1H), 3.38 (s, 3H), 2.85 (d, <i>J</i> = 5.4 Hz, 3H)

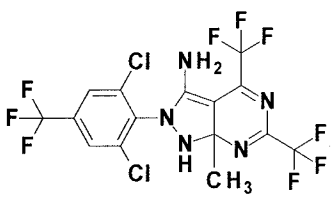
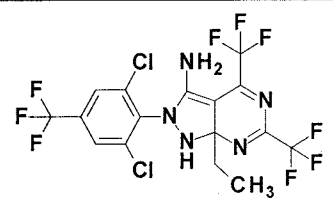
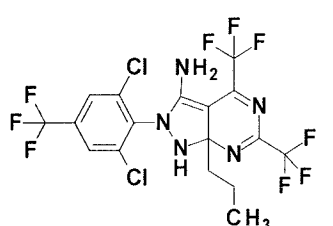
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
76		Yellow Oil	---	612 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.57 (d, <i>J</i> = 12.6 Hz, 1H), 5.52 (q, <i>J</i> = 6.2 Hz, 1H), 5.43 (d, <i>J</i> = 12.6 Hz, 1H), 3.72 (s, 2H), 2.81– 2.74 (m, 1H), 1.94–1.54 (m, 8H)
77		Tan Solid	---	612 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.85 (s, 2H), 5.46 (q, <i>J</i> = 6.3 Hz, 1H), 3.83 (s, 2H), 2.72 (p, <i>J</i> = 7.9 Hz, 1H), 1.93– 1.46 (m, 8H)
78		Yellow Oil	---	540 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.43 (q, <i>J</i> = 6.4 Hz, 1H), 3.89–3.61 (m, 4H), 1.36–1.17 (m, 1H), 0.61–0.34 (m, 4H)
79		Brownish Yellow Solid	---	586 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.85 (s, 2H), 5.46 (q, <i>J</i> = 6.1 Hz, 1H), 3.81 (s, 2H), 2.54 (hept, <i>J</i> = 7.0 Hz, 1H), 1.13 (d, <i>J</i> = 7.0 Hz, 6H)

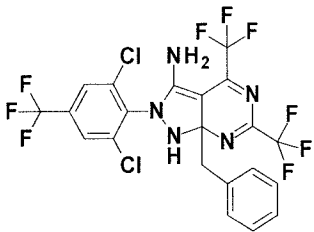
No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
80		Yellow Oil	---	558 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.86 (s, 2H), 5.46 (q, <i>J</i> = 6.2 Hz, 1H), 3.82 (s, 2H), 2.06 (s, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.26, -67.09, -76.24
81		White Solid	---	500 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.43 (q, <i>J</i> = 6.3 Hz, 1H), 3.77 (s, 2H), 3.44 (s, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.26, -67.43, -76.80
82		Yellow Solid	47-51	514 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.42 (q, <i>J</i> = 6.2 Hz, 1H), 3.92 (hept, <i>J</i> = 7.6 Hz, 2H), 3.76 (s, 2H), 1.33 (t, <i>J</i> = 6.9 Hz, 3H)
83		White Solid	---	528 ([M+H] ⁺)	(400 MHz, Methanol-d ₄): δ 8.05 (d, <i>J</i> = 7.1 Hz, 2H), 5.76 (q, <i>J</i> = 6.1 Hz, 1H), 5.51 (s, 2H), 2.05 (s, 3H)

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
84		Yellow Solid	---	576 ([M+H] ⁺)	(400 MHz, CDCl ₃): δ 7.77 (s, 2H), 5.49–5.37 (m, 1H), 4.28–4.06 (m, 1H), 4.03–3.76 (m, 1H), 3.77 (s, 2H), 2.23–1.99 (m, 1H), 1.61–1.37 (m, 2H)
85		White Solid	140– 143	528 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.39 – 5.26 (m, 1H), 4.44 – 4.27 (m, 1H), 3.66 (s, 2H), 1.65 – 1.39 (m, 6H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.23, -66.11, -77.18
86		Off White Solid	---	594 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃) δ 7.69 (d, <i>J</i> = 8.7 Hz, 2H), 7.23–7.16 (m, 1H), 7.15–7.08 (m, 1H), 7.06–6.96 (m, 2H), 5.51 (q, <i>J</i> = 6.4 Hz, 1H), 5.26–5.11 (m, 2H), 3.77 (s, 2H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.32, -67.02, -76.74, -118.94
87		Yellow Solid	---	564 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.78 (s, 2H), 5.90 (q, <i>J</i> = 6.8 Hz, 1H), 3.82 (s, 2H), 3.38 (s, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.30, -65.24, -78.75

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
88		Yellow Solid	---	660 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.71 (d, <i>J</i> = 7.1 Hz, 2H), 7.26 (d, <i>J</i> = 8.7 Hz, 2H), 7.12 (d, <i>J</i> = 8.1 Hz, 2H), 5.49 (q, <i>J</i> = 6.3 Hz, 1H), 5.21–4.99 (m, 2H), 3.77 (s, 2H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 57.96, -63.33, -66.45, -76.81
89		Tan Solid	---	567 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.77 (s, 2H), 5.42 (q, <i>J</i> = 6.3 Hz, 1H), 3.92–3.76 (m, 4H), 2.36 (t, <i>J</i> = 7.2 Hz, 2H), 2.00–1.82 (m, 2H), 1.77–1.61 (m, 2H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.25, -66.68, -76.98
90		Yellow Solid	---	552 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.45 (q, <i>J</i> = 6.3 Hz, 1H), 4.58 (s, 2H), 3.78 (s, 2H), 2.14 (q, <i>J</i> = 7.5 Hz, 2H), 1.07 (t, <i>J</i> = 7.5 Hz, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.27, -66.96, -76.70

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
91		tan solid	---	598 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.76 (s, 2H), 5.40 (q, <i>J</i> = 6.4 Hz, 1H), 3.92–3.80 (m, 1H), 3.76–3.58 (m, 1H), 3.72 (s, 2H), 2.10–1.87 (s, 1H), 1.41–1.07 (m, 8H), 1.04–0.76 (m, 6H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.22, -65.41, -77.03
92		Tan Solid	---	528 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 8.50 (s, 1H, isomer A), 7.778–7.76 (m, 2H, isomer A,B,C), 5.43 (s, 1H, isomer B), 4.83 (s, 1H, isomer C), 4.37 (s, 2H, isomer A), 3.81 (s, 2H, isomer B), 3.67 (s, 2H, isomer C), 2.50 (p, <i>J</i> = 6.7 Hz, 1H, isomer A), 2.40 (p, <i>J</i> = 6.7 Hz, 1H, isomer B), 2.26 (p, <i>J</i> = 6.7 Hz, 1H, isomer C), 1.15–1.09 (m, 3H, isomer A), 1.07 (d, <i>J</i> = 6.1 Hz, 3H, isomer B), 1.03–0.97 (m, 9H, isomer A,B,C), 0.92 (d, <i>J</i> = 6.8 Hz, 3H, isomer C) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.21, -63.23, -71.01, -72.75, -72.94, -73.09, -75.37, -78.90

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
93		Tan Solid	---	500 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 8.76 (s, 0.5H, NH, isomer A), 7.75 (s, 2H, Ar-H), 5.55 (s, 0.5H, NH, isomer B), 3.85 (s, 1H, NH ₂ , isomer A), 3.71 (s, 1H, NH ₂ , isomer B), 1.83 (s, 1.5H, - CH ₃ , isomer A), 1.71 (s, 1.5H, - CH ₃ , isomer B) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.25 (Isomer A), -63.32 (Isomer B), -72.83 (Isomer A), - 73.12 (Isomer B), -80.26 (Isomer A), -82.97 (Isomer B)
94		Yellow Solid	---	514 ([M+H] ⁺)	¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.21 (Isomer A), -63.25 (Isomer B), -72.73 (Isomer A), - 72.76 (Isomer B), -79.11 (Isomer A), -81.79 (Isomer B)
95		Yellow Solid	---	528 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.77 (s, 2H, Isomer A, Ar-H), 7.75 (s, 2H, Isomer B, Ar-H), 5.32 (s, 1H), 3.77 (s, 2H, Isomer A, NH ₂), 3.63 (s, 2H, Isomer B, NH ₂), 2.22–1.67 (m, 2H), 1.49– 1.05 (m, 2H), 1.03–0.85 (m, 3H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ - 63.21 (Isomer A), -63.24 (Isomer B), -72.73 (Isomer A), - 72.82 (Isomer B), -79.32 (Isomer A), -81.98 (Isomer B)

No.	Structure	Appearance	MP (°C)	ESI-MS Mass (<i>m/z</i>)	¹ H NMR
96		Yellow Solid	---	576 ([M+H] ⁺)	¹ H NMR (400 MHz, CDCl ₃): δ 7.79–7.74 (m, 2H, mixture of isomers, Ar-H), 7.29–7.05 (m, 5H, mixture of isomers, Ph-H), 5.37 (s, 1H, isomer A), 3.91 (s, 2H, isomer A, NH ₂), 3.77 (s, 2H, isomer B, NH ₂), 3.44 (d, <i>J</i> = 14.1 Hz, 1H, isomer A, Bn-H), 3.34 (d, <i>J</i> = 13.0 Hz, 1H, isomer B, Bn-H), 3.22 (d, <i>J</i> = 13.0 Hz, 1H, isomer B, Bn-H), 3.10 (d, <i>J</i> = 14.1 Hz, 1H, isomer A, Bn-H) ¹⁹ F NMR (376 MHz, CDCl ₃): δ -63.20 (isomer A), -63.22 (isomer B), -72.88 (isomer A), -72.95 (isomer B), -77.82 (isomer A), -79.91 (isomer B)

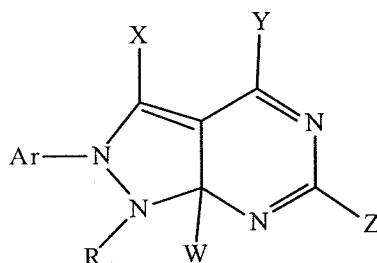
While the present disclosure may be susceptible to various modifications and alternative forms, specific embodiments have been described by way of example in detail herein. However, it should be understood that the present disclosure is not intended to be limited to the particular forms disclosed. Rather, the present disclosure is to cover all modifications, equivalents, and alternatives falling within the scope of the present disclosure as defined by the following appended claims and their legal equivalents.

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CLAIMS

What is claimed is:

1. A pyrazolopyrimidine compound of formula **I** or a salt thereof:

**I**

wherein,

Ar is an aryl group,

X is nitrogen, oxygen or sulfur,

Y and Z are independently hydrogen, halogen, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano amine, or amine,

W is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, and benzyl, and

R is selected from the group consisting of:

- (a) hydrogen,
- (b) C₁-C₈ alkyl, C₃-C₈ cycloalkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl,
- (c) S(=O)_n(C₁-C₈ alkyl) (n = 0, 1, 2),
- (d) C(=O)NR_xR_y,
- (e) (C₁-C₈ alkyl)NR_xR_y,
- (f) C(=O)O(C₁-C₈ alkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl),
- (g) (C₁-C₈ alkyl)O(C₁-C₈ alkyl),
- (h) (C₁-C₈ alkyl)OC(=O)(C₁-C₈ alkyl), (C₁-C₈ alkyl)OC(=O)(C₂-C₈ alkenyl), (C₁-C₈ alkyl)OC(=O)(C₂-C₈ alkynyl), (C₁-C₈ alkyl)OC(=O)(C₃-C₈ cycloalkyl), (C₁-C₈ alkyl)OC(=O)(C₃-C₈ cycloalkenyl), (C₁-C₈ alkyl)OC(=O)(C₇-C₈ cycloalkynyl),

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(i) $(C_1-C_8 \text{ alkyl})S(C_1-C_8 \text{ alkyl}), C(=O)(C_1-C_8 \text{ alkyl})C(=O)O(C_1-C_8 \text{ alkyl}),$

wherein each of the alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl and cycloalkynyl in (b), (c), (f), (g), (h) is independently substituted with one or more substituents selected from the group consisting of hydrogen, halogen, cyano, nitro, oxo, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, C_3-C_8 halocycloalkyl, C_3-C_8 cycloalkoxy, C_3-C_8 halocycloalkoxy, C_1-C_8 alkoxy, C_1-C_8 haloalkoxy, C_2-C_8 alkenyl, C_2-C_8 alkynyl, $S(=O)_n(C_1-C_8 \text{ alkyl})$ ($n = 0, 1, 2$), $S(=O)_n(C_1-C_8 \text{ haloalkyl})$ ($n = 0, 1, 2$), $OSO_2(C_1-C_8 \text{ alkyl})$, $OSO_2(C_1-C_8 \text{ haloalkyl})$, $C(=O)NR_xR_y$, $(C_1-C_8 \text{ alkyl})NR_xR_y$, $C(=O)(C_1-C_8 \text{ alkyl})$, $C(=O)O(C_1-C_8 \text{ alkyl})$, $C(=O)(C_1-C_8 \text{ haloalkyl})$, $C(=O)O(C_1-C_8 \text{ haloalkyl})$, $C(=O)(C_3-C_8 \text{ cycloalkyl})$, $C(=O)O(C_3-C_8 \text{ cycloalkyl})$, $C(=O)(C_2-C_8 \text{ alkenyl})$, $C(=O)O(C_2-C_8 \text{ alkenyl})$, $(C_1-C_8 \text{ alkyl})O(C_1-C_8 \text{ alkyl})$, $(C_1-C_8 \text{ alkyl})S(C_1-C_8 \text{ alkyl})$, $C(=O)(C_1-C_8 \text{ alkyl})C(=O)O(C_1-C_8 \text{ alkyl})$, phenyl, and phenoxy, and

wherein each R_x and R_y in (d) and (e) is independently selected from the group consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy; and

2. The compound of claim 1, wherein the aryl or heteroaryl group is selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, pyrazolo, imidazolo, and thiophenyl, and wherein the aryl or heteroaryl group is substituted at any open position with at least one of hydrogen, halogen, alkyl, alkenyl, alkynyl, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, sulfoxide, amines, aryloxy, esters, acetates, amides, and combinations thereof.

3. The compound of claim 1, wherein each of the alkyl, alkenyl, alkynyl, and benzyl of W is substituted with one or more substituents independently selected from the group consisting of hydrogen, halogen, cyano, nitro, oxo, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₃-C₈ cycloalkyl, C₃-C₈ halocycloalkyl, C₃-C₈ cycloalkoxy, C₃-C₈ halocycloalkoxy, C₁-C₈ alkoxy, C₁-C₈ haloalkoxy, C₂-C₈ alkenyl, C₂-C₈ alkynyl, S(=O)_n(C₁-C₈ alkyl) (n = 0, 1, 2), S(=O)_n(C₁-C₈ haloalkyl) (n = 0, 1, 2), OSO₂(C₁-C₈ alkyl), OSO₂(C₁-C₈ haloalkyl), C(=O)NR_xR_y, (C₁-C₈ alkyl)NR_xR_y, C(=O)(C₁-C₈ alkyl), C(=O)O(C₁-C₈ alkyl), C(=O)(C₁-C₈ haloalkyl), C(=O)O(C₁-C₈ haloalkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl), (C₁-C₈ alkyl)O(C₁-C₈ alkyl), (C₁-C₈ alkyl)S(C₁-C₈ alkyl), C(=O)(C₁-C₈ alkyl)C(=O)O(C₁-C₈ alkyl), phenyl, and phenoxy, wherein R_x and R_y each is independently selected from the group consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy.

4. The compound of claim 1, wherein X is nitrogen and substituted with at least one of alkyl, cycloalkyl, alkenyl, alkynyl, heteroatom, C(O)R', C(O)OR', C(O)NR', where R' is selected from the group consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy.

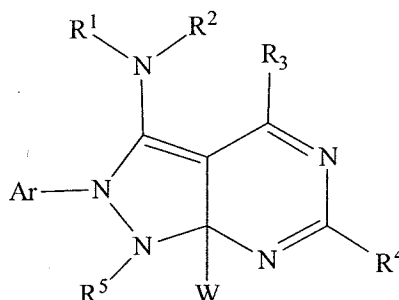
5. The compound of claim 1, wherein X is oxygen and substituted with at least one of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, amino, C(O)R', or C(O)NR' where R' is selected from the group consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy.

6. The compound of claim 1, wherein X is SO_n where n is 0, 1 or 2, and wherein sulfur is substituted with at least one of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, amino, C(O)R', and C(O)NR' where R' is selected from the group consisting of alkyl moiety including one or more heteroatoms, aryl and heteroaryl substituted with any combination of halo, alkoxy, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano, nitro, sulfone, and aryloxy.

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7. The compound of claim 1 having formula **II** or a salt thereof:

5

II

wherein,

Ar is selected from the group consisting of substituted phenyl, pyridyl, pyrimidinyl, pyridazinyl, triazinyl, pyrazolo, imidazolo, triazole, thiophenyl, and furyl, wherein the substituent group includes at least one of hydrogen, alkyl, alkoxy, halogen, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, halothio, nitro, sulfone, aryloxy, and any combination thereof;

W is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, and benzyl;

R¹, R² and R⁵ are independently selected from the group consisting of:

(a) hydrogen, hydroxy, thiol;

(b) (C₁-C₈) alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S-(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₃-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, S-heterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl

(g) N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; and

(h) C₃-C₈ cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl in (b), (c), (d) and (h) is independently substituted with one or more substituents selected from the group consisting of:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃;

5 (b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl; C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

10 (d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

15 (f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g1) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

20 (h1) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e) and (f) is independently substituted with one or more substituents selected from the group consisting of:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃;

25 (b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

30 (d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

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(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g2) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h2) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b1), (b2), (c1), (c2), (d1), (d2), (h1), and (h2) is independently substituted with one or more substituents selected from the group consisting of:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃;

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g3) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) is independently substituted with one or more substituents selected from the group consisting of:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃;

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(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, 5 OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

10 (e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

15 (g4) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, or S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h4) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b3), (b4), (c3), (c4), (d3), (d4), (h3), and (h4) is independently substituted with one or more substituents selected from the 20 group consisting of:

(a5) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃;

(b5) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

25 (c5) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d5) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

30 (e5) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f5) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g5) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
5 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h5) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e3), (e4), (f3), and (f4) is independently substituted with one or more substituents selected from the group consisting of:

(a6) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃;

10 (b6) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c6) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
15 S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d6) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e6) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
20 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f6) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g6) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
25 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂;

(h6) (C₃-C₈)cycloalkyl,

wherein R⁸ is selected from the group consisting of:

(a) H, CN, OH,

(b) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, C(=O)NH(C₁-C₈)alkyl,
30 C(=S)NH(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

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(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, C(=O)NH(C₂-C₈)alkenyl, C(=S)NH(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, C(=O)NH(C₂-C₈)alkynyl, C(=S)NH(C₂-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(O)(C₃-C₈)alkynyl, S(O)₂(C₃-C₈)alkynyl,

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, C(=O)NHphenyl, C(=S)NHphenyl, C(=S)phenyl, C(=S)Ophenyl, S(O)phenyl, S(O)₂phenyl,

(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, C(=O)NH-heterocyclyl, C(=S)NH-heterocyclyl, C(=S)heterocyclyl, C(=S)Oheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h) (C₃-C₈)cycloalkyl,

wherein R⁹ is selected from the group consisting of:

(a) H, CN, OH, OSi((C₁-C₈)alkyl)₃,

(b) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₃-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(O)(C₃-C₈)alkynyl, S(O)₂(C₃-C₈)alkynyl,

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, C(=S)phenyl, C(=S)Ophenyl, S(O)phenyl, S(O)₂phenyl,

(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, C(=S)heterocyclyl, C(=S)Oheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(g) (C₃-C₈)cycloalkyl; and

R³ and R⁴ are independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano amine, and amine.

8. The compound of claim 7, wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl in **(b)**, **(c)**, **(d)** and **(h)** of R⁸ is independently substituted with one or more substituents selected from the group consisting of:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

5 **(b1)** C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl

(c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g1) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h1) (C₃-C₈)cycloalkyl, and

wherein each of the phenyl and heterocyclyl in **(e)** and **(f)** of R⁸ is independently substituted with one or more substituents selected from the group consisting of:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

25 **(b2)** (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

30 **(d2)** (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g2) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, and S(O)₂N(R⁹)₂, and

(h2) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b1), (b2), (c1), (c2), (d1), (d2), (h1), and (h2) of R⁸ is independently be substituted with one or more substituents selected from the group consisting of:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g3) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) of R⁸ is independently substituted with one or more substituents selected from the group consisting of:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

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(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g4) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h4) (C₃-C₈)cycloalkyl.

9. The compound of claim 7, wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b), (c), (d) and (g) of R⁹ is independently be substituted with one or more substituents selected from the group consisting of:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h1) (C₃-C₈)cycloalkyl,

5 wherein each of the phenyl and heterocyclyl in (e) and (f) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h2) (C₃-C₈)cycloalkyl,

25 wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b1), (b2), (c1), (c2), (d1), (d2), (h1), and (h2) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

30 (c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
5 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl,
OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl,
Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h3) (C₃-C₈)cycloalkyl,

10 wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl,
OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl S(C₁-
15 C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl,
OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl,
20 OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl,
S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl,
25 OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl,
Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h4) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b3), (b4), (c3), (c4), (d3),
(d4), (h3), and (h4) of R⁹ is independently substituted with one or more substituents selected
30 from the group consisting of:

(a5) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b5) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c5) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d5) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e5) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f5) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h5) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e3), (e4), (f3), and (f4) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a6) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b6) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c6) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d6) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e6) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f6) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h6) (C₃-C₈)cycloalkyl.

10. The compound of claim 7, wherein R^3 and R^4 each is trifluoromethyl group.

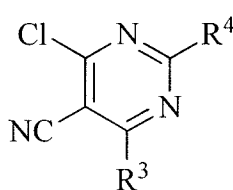
11. The compound of claim 1, wherein Ar is 2,6-dichloro-4-(trifluoromethyl)phenyl
5 group.

12. The compound of claim 1 selected from the group consisting of **Compounds 1–96** as specified in **TABLE 9**.

10 13. A method of producing a pyrazolopyrimidine compound, the method comprising:

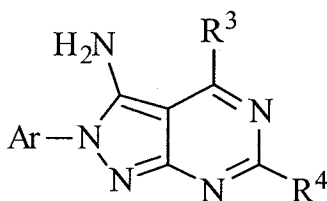
reacting a 2- R^4 -4-chloro-6- R^3 -pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine
compound to produce a pyrazolopyrimidine compound **V**;

15 reacting the pyrazolopyrimidine compound **V** with at least one first electrophile in a presence of
base to provide a pyrazolopyrimidine compound **VI**,



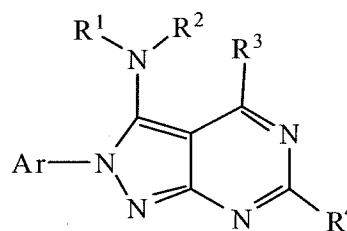
IV-1

wherein



A

V



VI

selected from the group consisting of substituted phenyl, pyridyl, pyrimidinyl, pyridazinyl,
triazinyl, pyrazolo, imidazolo, triazole, thiophenyl, and furyl, wherein the substituent group
includes at least one of hydrogen, alkyl, alkoxy, halogen, haloalkyl, haloalkoxy, alkylthio,
25 haloalkylthio, halothio, nitro, sulfone, aryloxy, and any combination thereof;

R^1 and R^2 are independently selected from the group consisting of:

(a) hydrogen, hydroxy, thiol;

(b) (C_1-C_8) alkyl, $C(=O)(C_1-C_8)alkyl$, $C(=O)O(C_1-C_8)alkyl$, $O(C_1-C_8)alkyl$,
 $OC(=O)(C_1-C_8)alkyl$, $OC(=O)O(C_1-C_8)alkyl$, $C(=S)(C_1-C_8)alkyl$, $C(=S)O(C_1-C_8)alkyl$, $S-(C_1-$
30 $C_8)alkyl$, $S(O)(C_1-C_8)alkyl$, $S(O)_2(C_1-C_8)alkyl$;

(c) $(C_2-C_8)alkenyl$, $C(=O)(C_2-C_8)alkenyl$, $C(=O)O(C_2-C_8)alkenyl$, $O(C_2-C_8)alkenyl$,
 $OC(=O)(C_2-C_8)alkenyl$, $OC(=O)O(C_2-C_8)alkenyl$, $C(=S)(C_2-C_8)alkenyl$, $C(=S)O(C_2-C_8)alkenyl$,
 $S(C_2-C_8)alkenyl$, $S(O)(C_2-C_8)alkenyl$, $S(O)_2(C_2-C_8)alkenyl$;

(d) (C₃-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
5 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, S-heterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl

(g) N(R⁸)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂,
10 S(O)N(R⁹)₂, or S(O)₂N(R⁹)₂; and

(h) C₃-C₈ cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl in (b), (c), (d) and (h) is independently substituted with one or more substituents selected from the group consisting of:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃;

(b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl,
15 OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, or S(O)₂(C₁-C₈)alkyl; C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl,
20 OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl,
25 OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g1) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h1) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e) and (f) is independently substituted with one or more substituents selected from the group consisting of:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃;

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, 5 OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

10 **(e2)** phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

15 **(g2)** N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h2) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in **(b1)**, **(b2)**, **(c1)**, **(c2)**, **(d1)**, **(d2)**, **(h1)**, and **(h2)** is independently substituted with one or more substituents selected from the 20 group consisting of:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃;

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

25 **(c3)** C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

30 **(e3)** phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g3) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
5 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) is independently substituted with one or more substituents selected from the group consisting of:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃;

10 (b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
15 S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
20 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g4) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
25 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, or S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h4) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b3), (b4), (c3), (c4), (d3), (d4), (h3), and (h4) is independently substituted with one or more substituents selected from the group consisting of:

30 (a5) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃;

(b5) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c5) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d5) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e5) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f5) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g5) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂; and

(h5) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e3), (e4), (f3), and (f4) is independently substituted with one or more substituents selected from the group consisting of:

(a6) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃;

(b6) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl;

(c6) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl;

(d6) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl;

(e6) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl;

(f6) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl;

(g6) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂;

(h6) (C₃-C₈)cycloalkyl,

wherein R⁸ is selected from the group consisting of:

(a) H, CN, OH,

(b) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, C(=O)NH(C₁-C₈)alkyl,
5 C(=S)NH(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, C(=O)NH(C₂-C₈)alkenyl, C(=S)NH(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

10 (d) (C₃-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, C(=O)NH(C₂-C₈)alkynyl, C(=S)NH(C₂-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(O)(C₃-C₈)alkynyl, S(O)₂(C₃-C₈)alkynyl,

(e) phenyl, C(=O)phenyl, C(=O)Ophenyl, C(=O)NHphenyl, C(=S)NHphenyl, C(=S)phenyl, C(=S)Ophenyl, S(O)phenyl, S(O)₂phenyl,

15 (f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, C(=O)NH-heterocyclyl, C(=S)NH-heterocyclyl, C(=S)heterocyclyl, C(=S)Oheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h) (C₃-C₈)cycloalkyl,

wherein R⁹ is selected from the group consisting of:

20 (a) H, CN, OH, OSi((C₁-C₈)alkyl)₃,

(b) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₃-C₈)alkenyl,
25 OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(O)(C₃-C₈)alkynyl, S(O)₂(C₃-C₈)alkynyl,

30 (e) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, C(=S)phenyl, C(=S)Ophenyl, S(O)phenyl, S(O)₂phenyl,

(f) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, C(=S)heterocyclyl, C(=S)Oheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(g) (C₃-C₈)cycloalkyl; and

5 R³ and R⁴ are independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio, halothio, cyano amine, and amine.

14. The method of claim 13, wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl in (b), (c), (d) and (h) of R⁸ is independently substituted with one or more
10 substituents selected from the group consisting of:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b1) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl

15 (c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,
20

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,
25

(g1) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h1) (C₃-C₈)cycloalkyl, and

wherein each of the phenyl and heterocyclyl in (e) and (f) of R⁸ is independently
30 substituted with one or more substituents selected from the group consisting of:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g2) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂, C(=S)N(R⁹)₂, ON(R⁹)₂, OC(=O)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, and S(O)₂N(R⁹)₂, and

(h2) (C₃-C₈)cycloalkyl,

wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in **(b1)**, **(b2)**, **(c1)**, **(c2)**, **(d1)**, **(d2)**, **(h1)**, and **(h2)** of R⁸ is independently be substituted with one or more substituents selected from the group consisting of:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g3) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
 5 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h3) (C₃-C₈)cycloalkyl,

wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) of R⁸ is independently substituted with one or more substituents selected from the group consisting of:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

10 (b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl,
 15 S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
 20 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl,

(g4) N(R⁹)₂, NHC(=O)N(R⁹)₂, NHC(=S)N(R⁹)₂, C(=O)N(R⁹)₂, C(=O)ON(R⁹)₂,
 25 ON(R⁹)₂, OC(=O)N(R⁹)₂, C(=S)N(R⁹)₂, SN(R⁹)₂, S(O)N(R⁹)₂, S(O)₂N(R⁹)₂, and

(h4) (C₃-C₈)cycloalkyl.

15. The method of claim 13, wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in **(b)**, **(c)**, **(d)** and **(g)** of R⁹ is independently be substituted with one or more substituents selected from the group consisting of:

(a1) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

5 **(b1)** C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c1) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d1) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₃-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e1) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f1) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h1) (C₃-C₈)cycloalkyl,

20 wherein each of the phenyl and heterocyclyl in **(e)** and **(f)** of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a2) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b2) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c2) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d2) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e2) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f2) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h2) (C₃-C₈)cycloalkyl,

5 wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b1), (b2), (c1), (c2), (d1), (d2), (h1), and (h2) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a3) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b3) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl,
10 OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c3) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d3) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e3) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f3) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h3) (C₃-C₈)cycloalkyl,

25 wherein each of the phenyl and heterocyclyl in (e1), (e2), (f1), and (f2) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a4) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

(b4) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c4) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

30

(d4) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e4) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl,
5 OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f4) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h4) (C₃-C₈)cycloalkyl,

10 wherein each of the alkyl, alkenyl, alkynyl, and cycloalkyl, in (b3), (b4), (c3), (c4), (d3), (d4), (h3), and (h4) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a5) F, Cl, Br, I, CN, NO₂, OH, OSi((C₁-C₈)alkyl)₃,

(b5) C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl,
15 OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c5) C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

20 (d5) C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)(C₂-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

(e5) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

25 (f5) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h5) (C₃-C₈)cycloalkyl,

30 wherein each of the phenyl and heterocyclyl in (e3), (e4), (f3), and (f4) of R⁹ is independently substituted with one or more substituents selected from the group consisting of:

(a6) F, Cl, Br, I, CN, NO₂, OH, SF₅, OSi((C₁-C₈)alkyl)₃,

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(b6) (C₁-C₈)alkyl, C(=O)(C₁-C₈)alkyl, C(=O)O(C₁-C₈)alkyl, O(C₁-C₈)alkyl, OC(=O)(C₁-C₈)alkyl, OC(=O)O(C₁-C₈)alkyl, C(=S)(C₁-C₈)alkyl, C(=S)O(C₁-C₈)alkyl, S(C₁-C₈)alkyl, S(O)(C₁-C₈)alkyl, S(O)₂(C₁-C₈)alkyl,

(c6) (C₂-C₈)alkenyl, C(=O)(C₂-C₈)alkenyl, C(=O)O(C₂-C₈)alkenyl, O(C₂-C₈)alkenyl, OC(=O)(C₂-C₈)alkenyl, OC(=O)O(C₂-C₈)alkenyl, C(=S)(C₂-C₈)alkenyl, C(=S)O(C₂-C₈)alkenyl, S(C₂-C₈)alkenyl, S(O)(C₂-C₈)alkenyl, S(O)₂(C₂-C₈)alkenyl,

(d6) (C₂-C₈)alkynyl, C(=O)(C₂-C₈)alkynyl, C(=O)O(C₃-C₈)alkynyl, O(C₂-C₈)alkynyl, OC(=O)(C₂-C₈)alkynyl, OC(=O)O(C₃-C₈)alkynyl, C(=S)O(C₃-C₈)alkynyl, S(C₂-C₈)alkynyl, S(O)(C₂-C₈)alkynyl, S(O)₂(C₂-C₈)alkynyl,

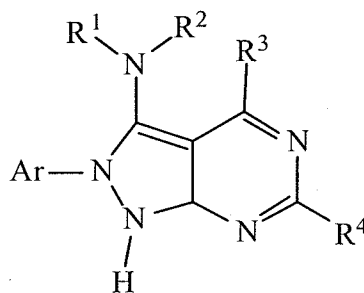
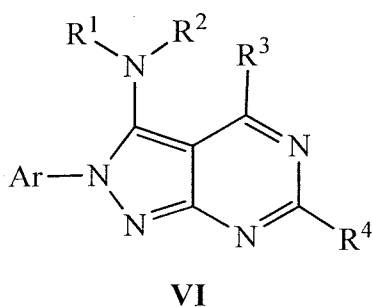
(e6) phenyl, C(=O)phenyl, C(=O)Ophenyl, Ophenyl, OC(=O)phenyl, OC(=O)Ophenyl, C(=S)Ophenyl, C(=S)phenyl, Sphenyl, S(O)phenyl, S(O)₂phenyl,

(f6) heterocyclyl, C(=O)heterocyclyl, C(=O)Oheterocyclyl, Oheterocyclyl, OC(=O)heterocyclyl, OC(=O)Oheterocyclyl, C(=S)Oheterocyclyl, C(=S)heterocyclyl, Sheterocyclyl, S(O)heterocyclyl, S(O)₂heterocyclyl, and

(h6) (C₃-C₈)cycloalkyl.

16. The method of claim 13, wherein the first electrophile is a member selected from the group consisting of alkyl halides, anhydrides, acid chlorides, isocyanates, isothiocyanate, and sulfonyl chlorides.

17. The method of claim 13, further comprising reducing the pyrazolopyrimidine compound **VI** to produce a pyrazolopyrimidine compound **VII**.

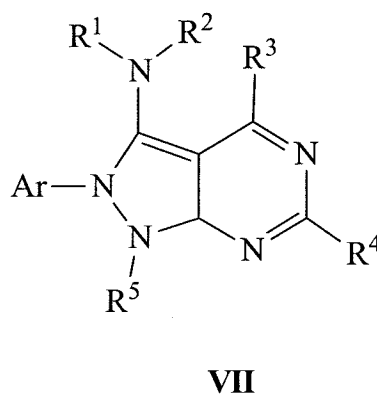
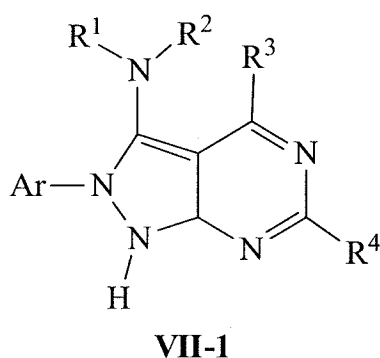


18. The method of claim 17, wherein reducing the pyrazolopyrimidine compound **VI** comprises reducing the pyrazolopyrimidine compound **VI** with a hydride reducing agent to produce a pyrazolopyrimidine compound **VII-1**.

19. The method of claim 18, wherein the hydride reducing agent includes sodium borohydride.

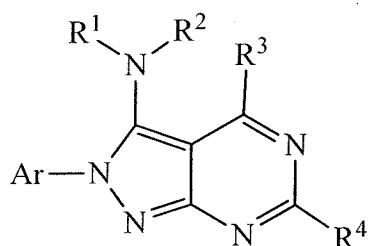
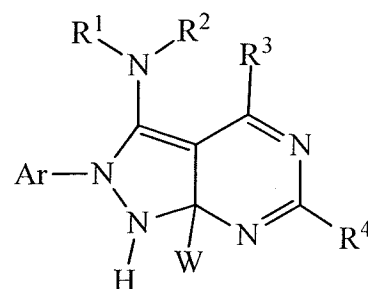
20. The method of claim 18, wherein R_3 and R_4 is independently selected from the group consisting of trifluoromethyl and trichloromethyl groups.

21. The method of claim 13, further comprising reacting the pyrazolopyrimidine compound **VII-1** with a second electrophile in a presence of base to provide a pyrazolopyrimidine compound **VII**, wherein R^5 is selected from the group consisting of members described for R^1 and R^2 in claim 13.



22. The method of claim 21, wherein the second electrophile is a member selected from the group consisting of alkyl halides, anhydrides, acid chlorides, isocyanates, isothiocyanate, and sulfonyl chlorides.

23. The method of claim 13, further comprising reacting the pyrazolopyrimidine compound **VI** with a Grignard reagent to provide a pyrazolopyrimidine compound **VIII**,

**VI****VIII**

wherein W is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, and benzyl.

24. The method of claim 23, wherein each of the alkyl, alkenyl, and benzyl of W is substituted with one or more substituents independently selected from the group consisting of hydrogen, halogen, cyano, nitro, oxo, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C₃-C₈ cycloalkyl, C₃-C₈ halocycloalkyl, C₃-C₈ cycloalkoxy, C₃-C₈ halocycloalkoxy, C₁-C₈ alkoxy, C₁-C₈ haloalkoxy, C₂-C₈ alkenyl, C₂-C₈ alkynyl, S(=O)_n(C₁-C₈ alkyl), S(=O)_n(C₁-C₈ haloalkyl), OSO₂(C₁-C₈ alkyl), OSO₂(C₁-C₈ haloalkyl), C(=O)NR_xR_y, (C₁-C₈ alkyl)NR_xR_y, C(=O)(C₁-C₈ alkyl), C(=O)O(C₁-C₈ alkyl), C(=O)(C₁-C₈ haloalkyl), C(=O)O(C₁-C₈ haloalkyl), C(=O)(C₃-C₈ cycloalkyl), C(=O)O(C₃-C₈ cycloalkyl), C(=O)(C₂-C₈ alkenyl), C(=O)O(C₂-C₈ alkenyl), (C₁-C₈ alkyl)O(C₁-C₈ alkyl), (C₁-C₈ alkyl)S(C₁-C₈ alkyl), C(=O)(C₁-C₈ alkyl)C(=O)O(C₁-C₈ alkyl), phenyl, and phenoxy.

25. The method of claim 13, wherein reacting a 2-R⁴-4-chloro-6-R³-pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine compound comprises: reacting the 2-R⁴-4-chloro-6-R³-pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine compound in a presence of a base in a polar aprotic solvent to produce a pyrazolopyrimidine compound **V**.

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26. The method of claim 13, wherein reacting a 2-R⁴-4-choloro-6-R³-pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine compound comprises:

reacting the 2-R⁴-4-choloro-6-R³-pyrimidine-5-carbonitrile compound **IV-1** with a *tert*-butoxycarbonyl (Boc)-protected hydrazine in a polar aprotic solvent to produce a Boc-protected compound; and

reacting the Boc-protected compound with triethylsilane and an acid in a non-reactive solvent to produce a pyrazolopyrimidine compound **V**.

27. The method of claim 13, wherein reacting a 2-R⁴-4-choloro-6-R³-pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine compound comprises: reacting the 2-R⁴-4-choloro-6-R³-pyrimidine-5-carbonitrile compound **IV-1** with a hydrazine in a presence of a polar protic solvent with or without a base at an ambient temperature to produce a pyrazolopyrimidine compound **V**.

28. An pesticidal composition, comprising a pyrazolopyrimidine compound of claim 1.

29. An pesticidal composition, comprising a pyrazolopyrimidine compound of claim 7.

30. An pesticidal composition, comprising a pyrazolopyrimidine compound of claim 12.

31. A method of controlling insect, comprising applying an pesticidal composition near a population of insects, wherein the pesticidal composition comprises a pyrazolopyrimidine compound of claim 1.

32. A method of controlling insect, comprising applying an pesticidal composition near a population of insects, wherein the pesticidal composition comprises a pyrazolopyrimidine compound of claim 7.

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33. A method of controlling insect, comprising applying an pesticidal composition near a population of insects, wherein the pesticidal composition comprises a pyrazolopyrimidine compound of claim 12.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/014707**A. CLASSIFICATION OF SUBJECT MATTER****C07D 487/04(2006.01)i, A01N 43/50(2006.01)i, A01P 7/04(2006.01)i**

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D 487/04; A01N 43/90; A01N 9/22; A01C 1/06; A01N 43/50; A01P 7/04

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal), PubMed, NCBI, Esp@snet, PAJ, USPTO, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 04163846 A (ALBERT PERCIVAL, et al.) 7 August 1979 See the whole document.	1-33
A	US 2008-0312078 A1 (JOCHEN DIETZ, et al.) 18 December 2008 See the whole document.	1-33
A	H. H. ABDEL-RAZIK, et al., Enaminonitrile in Heterocyclic synthesis: Synthesis and Reactions of Some Pyrimidine Derivatives. Chemical Papers. 2004, 58(3), pp.209-213 See the whole document.	1-33
A	RUTH BRENK, et al., Virtual Screening for Submicromolar Leads of tRNA-guanine Transglycosylase Based on a New Unexpected Binding Mode Detected by Crystal Structure Analysis. Journal of Medicinal Chemistry. 27 March 2003, 46(7), pp.1133-1143 See the whole document.	1-33
A	A. M. EL-REEDY, et al., Azolopyrimidines and Pyrimidoquinazolines From 4-Chloropyrimidines. Journal of Heterocyclic Chemistry. March/April 1989, 26(2), pp.313-316 See the whole document.	1-33



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2014/014707

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