

EXHIBIT 2

Applicant : Adama Makhteshim Ltd.
PCT Application Nos. : PCT/US2014/072566 & PCT/US2014/072569
Int'l Filing Date : December 29, 2014
For : 5-FLUORO-4-IMINO-3-(ALKYL/ SUBSTITUTED-
ALKYL)-1-(ARYLSULFONYL)-3,4-
DIHYDROPYRIMIDIN-2(1H)-ONE AND PROCESSES
FOR THEIR PREPARATION

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New York, New York 10112

**DECLARATION OF GAL SUEZ, PH.D. IN SUPPORT OF CORRECTION OF FORMULA II
TO ALKYLATING AGENT MOLAR RATIO**

I, Gal Suez, hereby declare that:

1. I am presently an Organic Lab Manager at Adama Makhteshim Ltd. A copy of my curriculum vitae is attached hereto as **Exhibit A**.
2. I have reviewed the specification of International PCT Application Nos. PCT/US2014/072566 and PCT/US2014/072569, published as International Application Publication Nos. WO 2015/103142 and WO 2015/103144, respectively, attached hereto as **Exhibits B** and **C**.
3. I have also reviewed the reactions disclosed in U.S. Patent Application Publication No. US 2011/0263627, published October 27, 2011 (also published as PCT International Patent Application Publication No. WO 2011/137002 on November 3, 2011), which issued as U.S. Patent No. 8,263,603 on September 11, 2012. US 2011/0263627 is attached hereto as **Exhibit D**.
4. I have been asked to provide my opinion on whether the correction of the molar ratio range of the compound of Formula II to the alkylating agent in PCT/US2014/072566 and PCT/US2014/072569 from "about 1:1 to about **3:1**" to "about 1:1 to about **1:3**" is obvious in the sense that it is immediately evident that no other molar

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ratio range would have been intended other than "about 1:1 to about **1:3**."

5. For reasons that I explain below, it is immediately evident to me, and I believe it would be immediately evident to a chemist reading PCT/US2014/072566 and PCT/US2014/072569, that the inventors, at the time of filing these applications, intended to write the molar ratio of the compound of Formula II to the alkylating agent as "about 1:1 to about **1:3**."
6. First, the molar ratio of the compound of Formula II to the alkylating agent required by original claim 9 ("claim 9") of both applications is outside the scope of the molar ratio range recited in original claim 8 ("claim 8"), from which claim 9 depends, in both applications.
7. PCT/US2014/072566 and PCT/US2014/072569 disclose preparing a compound of Formula III from a compound of Formula II, which includes contacting a compound of Formula II with an alkylating agent. See e.g., paragraph [0004] of PCT/US2014/072566 and PCT/US2014/072569. Paragraphs [0004] and [0023] of PCT/US2014/072566, paragraphs [0004] and [0026] of PCT/US2014/072569, and claim 8 of both applications recite in part, "wherein . . . a molar ratio of the compound of Formula II to alkylating agent is from about 1:1 to about **3:1**."
8. Paragraphs [0004] and [0023] of PCT/US2014/072566, paragraphs [0004] and [0026] of PCT/US2014/072569, and claim 9 of both applications, which depends from claim 8, recites in part, "wherein . . . a molar ratio of the compound of Formula II to alkylating agent is about **1:3**." "About **1:3**" recited in claim 9 is outside the scope of "about 1:1 to about **3:1**" recited in claim 8. The inventors would not have intended the inconsistency between

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claim 8 and claim 9. Claim 9 would properly depend on claim 8 in both applications if the molar ratio of the compound of Formula II to the alkylating agent was recited as "about 1:1 to about 3:1" in claim 8.

9. Second, the molar ratio of the compound of Formula II to the alkylating agent of "about 1:1 to about 1:3" is consistent with the molar ratio used in Example 2 of PCT/US2014/072566 and PCT/US2014/072569.
10. Example 2 in paragraph [0035] of PCT/US2014/072566 and paragraph [0036] of PCT/US2014/072569 illustrates preparing a compound of Formula III from a compound of Formula II, wherein the molar ratio of the compound of Formula II to methyl iodide (alkylating agent) is 20 mmol to 60 mmol, which is about 1:3. The inventors would have intended that the claims and embodiments in these applications encompass the molar ratio used in the Examples therein. The Examples would be encompassed by a recitation of the molar ratio of the compound of Formula II to alkylating agent of "about 1:1 to about 3:1" in both applications.
11. Third, in order for all of the compound of Formula II to undergo alkylation to form a compound of Formula III in the method recited in paragraph [0004] of PCT/US2014/072566 and PCT/US2014/072569, the molar amount of alkylating agent must be the same as or in excess of that of the compound of Formula II. This is achieved at a molar ratio range of the compound of Formula II to alkylating agent of "about 1:1 to about 1:3" but not at a molar ratio range of "about 1:1 to about 3:1."
12. Fourth, the molar ratio of the compound of Formula II to the alkylating agent of "about 1:1 to about 1:3" is consistent with the molar ratio of these components previously disclosed in the

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Examples of a prior version of a similar conversion in US 2011/0263627.

13. The reaction in Example 1 in paragraph [0055] of US 2011/0263627 taught a molar ratio of 4-amino-1-benzenesulfonyl-5-fluoro-1H-pyrimidine-2-one (starting pyrimidinone compound, i.e., Formula II) to iodomethane (alkylating agent) of 0.74 mmol to 1.5 mmol, which is about 1:2. The reactions in Examples 2 and 3 in paragraphs [0057]-[0061] of US 2011/0263627 taught a molar ratio of the starting pyrimidinone compound to the alkylating agent of about 1:6 and about 1:2, respectively. In other words, US 2011/0263627 taught examples wherein the molar amount of alkylating agent was in excess compared to that of the starting pyrimidinone compound.
14. The molar ratio of the compound of Formula II to alkylating agent was not intended by the inventors to be the novel feature of the method recited in PCT/US2014/072566 and PCT/US2014/072569 over the disclosure of US 2011/0263627.
15. I am a person skilled in this art and it is my opinion based on the foregoing that the molar ratio of the compound of Formula II to alkylating agent of "about 1:1 to about **3:1**" as recited in PCT claim 8 and the specifications of PCT/US2014/072566 and PCT/US2014/072569 is a transposition error and should correctly recite "about 1:1 to about **1:3**."
16. In my opinion, it is immediately evident that no molar ratio range of a compound of Formula II to alkylating agent other than "about 1:1 to about **1:3**" would have been intended by the inventors at the time of filing the subject applications.

Applicant: Adama Makhteshim Ltd.

PCT Application Nos.: PCT/US2014/072566 & PCT/US2014/072569

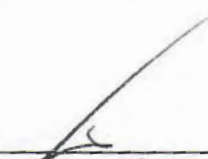
Int'l Filing Date: December 29, 2014

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to Alkylating Agent Molar Ratio

I hereby declare that all statements made herein of my own knowledge are true and that all statements made herein on information and belief are believed to be true.

Date:

12/5/2019



Gal Suez, Ph.D.

Curriculum Vitae Gal Suez

Contact information:

Year of birth: 1981

Telephone number: 054-5487567

Address: Beer-Sheva

Email address: galsuez@gmail.com

Open to relocate

Citizenship: Israel

Employment:

2018 Organic lab manager, Adama Makhteshim R&D

Matrix manager of team leaders in organic lab. Establish and monitor work plan, assist in process development and improvement of existing processes, building bill of materials (cost) based on raw materials.

Administrative manager of organic labs and responsible for enforcement of lab safety policies.

2012 - 2018 Team leader and project manager, Adama Makhteshim R&D

- Leading a team of researchers in organic chemistry department. Tutoring new researchers, develop and lead them to accomplish team's goals.

Setting priorities in research. Summarizing and presenting the team's work.

- Responsible for execution of R&D work plan by working on number of processes in parallel. Improve and assist in troubleshooting production processes. Leading the research of innovative AI by development of process from early stages through optimization up to scale-up.
- Collaborate with production, marketing, registration, procurement, IP departments. Lead collaboration with outsource companies in various synthetic projects.
- Experienced in developing processes of various chemistries including hydrogenations, oxidations, fluorinations and others.

Education:

2008 - 2012 PhD, Technion

- Major: Organic chemistry
- Studies under the supervision of Prof. Mark Gandelman
- Research Title: Catalysis with Metal-Free Molecules and by Non-Covalent Bonds

Applicant : Adama Makhteshim Ltd.
PCT Application Nos.: PCT/US2014/072566 & PCT/US2014/072569
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Exhibit A

2005 - 2008 MSc, Technion

- Major: Organic chemistry
- Studies under the supervision of Prof. Mark Gandelman
- Research Title: Development of New Organocatalysts Based on the Molecular Recognition of DNA Bases

2002 - 2005 BA, Technion

- Major: Chemistry

Military service:

2000 - 2001 Operations Sergeant in West Bank brigade

Publications:

- Suez, Gal; Grabarnick, Michael; Frenklah, Alexander; Steiner, Heinz; Process for preparing a hydroxylamine pyrazole compound, PCT Int. Appl., **2016**, WO 2016181386 A1
- Suez, Gal; Grabarnick, Michael; Frenklah, Alexander; Process for preparing 1-(4-chlorophenyl)-3-[(2-nitrophenyl)methoxy]-1H-pyrazole, PCT Int. Appl., **2016**, WO2016113741 A1.
- Suez, Gal; Bloch, Victoria; Nisnevich, Gennady; Gandelman, Mark; Design and development of bio-inspired guanine-based organic catalyst for asymmetric catalysis, *Eur. J. Org. Chem.* **2012**, 11, 2118-2122.



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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,

DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

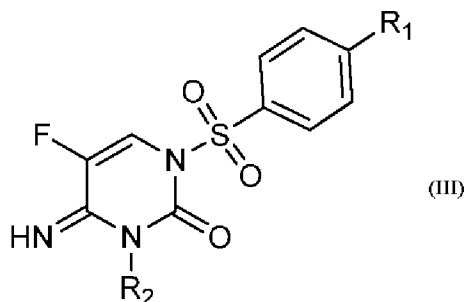
Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))

(54) Title: 5-FLUORO-4-IMINO-3-(ALKYL/SUBSTITUTED ALKYL)-1- (ARYLSULFONYL)-3,4-DIHYDROPYRIMIDIN-2(1H)-ONE AND PROCESSES FOR THEIR PREPARATION



(57) Abstract: Provided herein are 5-fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one and processes for their preparation which may include the use of an alkali carbonate and an alkylating agent (III):

Applicant : Adama Makhteshim Ltd.

PCT Application Nos.: PCT/US2014/072566 & PCT/US2014/072569

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Exhibit B

**5-FLUORO-4-IMINO-3-(ALKYL/SUBSTITUTED ALKYL)-1-(ARYLSULFONYL)-
3,4-DIHYDROPYRIMIDIN-2(1H)-ONE AND PROCESSES FOR THEIR
PREPARATION**

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial Nos. 61/922,582 and 61/922,572, each filed December 31, 2013, the disclosures of each are expressly incorporated by reference herein.

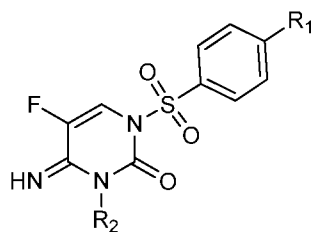
FIELD

[0002] Provided herein are 5-fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one and processes for their preparation.

BACKGROUND AND SUMMARY

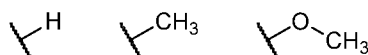
[0003] U.S. Patent Application Ser. No. 13/090,616, U.S. Pub. No. 2011/0263627, describes *inter alia* certain N3-substituted-N1-sulfonyl-5-fluoropyrimidinone compounds and their use as fungicides. The disclosure of the application is expressly incorporated by reference herein. This patent describes various routes to generate N3-substituted-N1-sulfonyl-5-fluoropyrimidinone compounds. It may be advantageous to provide more direct and efficient methods for the preparation, isolation, and purification of N3-substituted-N1-sulfonyl-5-fluoropyrimidinone fungicides and related compounds, *e.g.*, by the use of reagents and/or chemical intermediates and isolation and purification techniques which provide improved time and cost efficiency.

[0004] Provided herein are 5-fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one and processes for their preparation. In one embodiment, provided herein is a process for the preparation of compounds of Formula III:

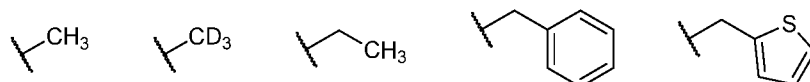


III

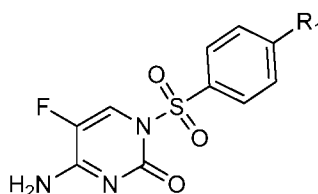
wherein R_1 is selected from:



and R_2 is selected from:



which comprises contacting compounds of Formula II with a base, such as an alkali carbonate, e.g., sodium-, potassium-, cesium-, and lithium carbonate (Na_2CO_3 , K_2CO_3 , Cs_2CO_3 , and Li_2CO_3 , respectively) or an alkali alkoxide, for example, potassium *tert*-butoxide (KO^tBu) and an alkylating agent, such as an alkyl halide of Formula $\text{R}_2\text{-X}$, wherein R_2 is as previously defined and X is a halogen, e.g., iodine, bromine, and chlorine, in a polar solvent, such as *N,N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide (DMA), *N*-methylpyrrolidone (NMP), acetonitrile (CH_3CN), and the like, at concentrations from about 0.1 molar (M) to about 3 M. In some embodiments, a molar ratio of compounds of Formula II to the base is from about 3:1 to about 1:1 and a molar ratio of compounds of Formula II to alkylating agent is from about 1:1 to about 3:1. In other embodiments, molar ratios of compounds of Formula II to the base and compounds of Formula II to the alkylating agent of about 2:1 and 1:3, respectively, are used. In some embodiments, the reactions are conducted at temperatures between $-78\text{ }^\circ\text{C}$ and $90\text{ }^\circ\text{C}$, and in other embodiments, the reactions are conducted between $22\text{ }^\circ\text{C}$ and $60\text{ }^\circ\text{C}$.

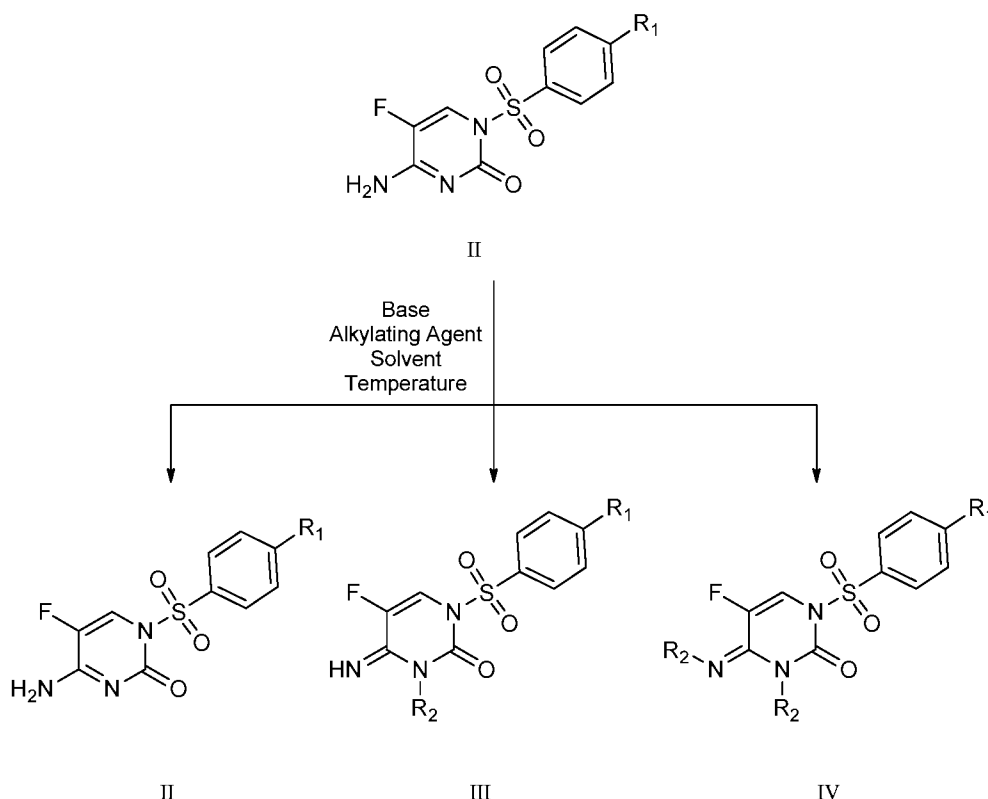


II

[0005] It will be understood by those skilled in the art that manipulation of the reaction parameters described above may result in the formation of product mixtures comprised of compounds of Formulas II, III, and IV, as shown in Scheme 1, wherein the ratios of compounds of Formulas II, III, and IV formed is from about 0:2:1 to about 1:2:0. In some embodiments, compositions comprising mixtures of compounds of Formulas II and III

are preferred, as isolation and purification can be achieved through precipitation and recrystallization, and the intermediate compounds of Formula II can be recovered and recycled. In contrast, compositions comprising mixtures of compounds of Formulas III and IV require chromatographic separation to give III along with the undesired dialkylated by-product of Formula IV.

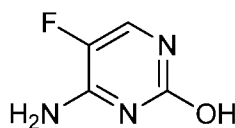
Scheme 1.



[0006] In another embodiment, the desired crude composition, i.e., mixtures of compounds of Formula II and compounds of Formula III, wherein R₁ is methoxy (OCH₃) and R₂ is methyl (CH₃), is obtained through contacting a compound of Formula II with Li₂CO₃ and methyl iodide (CH₃I) in DMF (1.0 M) in a molar ratio of about 1:0.6:3 at 45 °C. Upon completion, dilution of the crude composition with a polar, aprotic solvent, such as CH₃CN, wherein the ratio of CH₃CN:DMF is from about 2:1 to about 1:2, followed by an aqueous solution of sodium thiosulfate (Na₂S₂O₃) with a pH from about 8 to about 10.5, wherein the ratio of 2.5 wt.% aqueous Na₂S₂O₃:DMF is from about 1:2 to about 3:1, affords a precipitate which is isolable by filtration. In one embodiment, the ratio of CH₃CN:DMF is about 1:2 and the ratio of 2.5% aqueous Na₂S₂O₃:DMF is about 1:1, and the resultant solid is further purified by crystallization/precipitation from a warmed solution, about 30 °C – 40 °C, of the

solid in a solution of a polar, aprotic solvent, such as CH₃CN, by the addition of water (H₂O), wherein the ratio of H₂O:CH₃CN is from about 1:2 to about 3:1, to give the purified compound of Formula III, and in another embodiment the ratio of H₂O:CH₃CN to affect precipitation of pure III is about 2:1.

[0007] In another embodiment, compounds of Formula II may be prepared by contacting compounds of Formula I with bis-*N,O*-trimethylsilylacetamide (BSA) at an elevated temperature, such as 70 °C, for a period of about 1 hour (h), followed by cooling and contacting the solution containing the protected pyrimidinol with a substituted benzene sulfonyl chloride, generalized by R₁-PhSO₂Cl, wherein R₁ is as previously defined, at about 20 °C – 25 °C. In some embodiments, the molar ratio of the compound of Formula I to BSA and the sulfonyl chloride is about 1:3:1.1, respectively, and in another embodiment reducing the molar ratio of the reactants to about 1:1.1:1.1 affords improved yields.



I

[0008] The term "alkyl" refers to a branched, unbranched, or saturated cyclic carbon chain, including, but not limited to, methyl, ethyl, propyl, butyl, isopropyl, isobutyl, tertiary butyl, pentyl, hexyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like.

[0009] The term "alkenyl" refers to a branched, unbranched or cyclic carbon chain containing one or more double bonds including, but not limited to, ethenyl, propenyl, butenyl, isopropenyl, isobutenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, and the like.

[0010] The term "aryl" refers to any aromatic, mono- or bi-cyclic, containing heteroatoms.

[0011] The term "heterocycle" refers to any aromatic or non-aromatic ring, mono- or bi-cyclic, containing one or more heteroatoms.

[0012] The term "alkoxy" refers to an -OR substituent

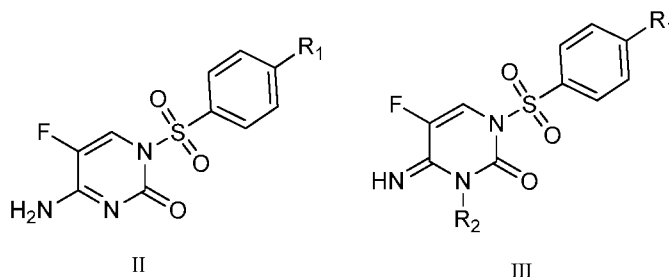
[0013] The term "halogen" or "halo" refers to one or more halogen atoms, defined as F, Cl, Br, and I.

[0014] The term "haloalkyl" refers to an alkyl, which is substituted with Cl, F, I, or Br or any combination thereof.

[0015] Throughout the disclosure, references to the compounds of Formulas I, II, III, and IV are read as also including optical isomers and salts. Exemplary salts may include: hydrochloride, hydrobromide, hydroiodide, and the like. Additionally, the compounds of Formulas I, II, III, and IV may include tautomeric forms.

[0016] Certain compounds disclosed in this document can exist as one or more isomers. It will be appreciated by those skilled in the art that one isomer may be more active than the others. The structures disclosed in the present disclosure are drawn in only one geometric form for clarity, but are intended to represent all geometric and tautomeric forms of the molecule.

[0017] In one exemplary embodiment, a method of making a compound of Formula III is provided. The method includes contacting a compound of Formula II with an alkali carbonate and an alkylating agent; and forming a compound of Formula III,



wherein R_1 is selected from the group consisting of: H , CH_3 , and O-CH_3 ; and

R_2 is selected from the group consisting of: CH_3 , CD_3 , CH_2CH_3 , $\text{CH}_2\text{CH}_2\text{C}_6\text{H}_5$, and $\text{CH}_2\text{CH}_2\text{C}_4\text{H}_4\text{S}$.

[0018] In a more particular embodiment, the contacting step is carried out between 22 °C and 60 °C.

[0019] In another more particular embodiment of any of the above embodiments, the contacting step further includes a solvent selected from the group consisting of DMF, DMSO, DMA, NMP, and CH_3CN .

[0020] In another more particular embodiment of any of the above embodiments, the alkali carbonate is selected from the group consisting of: Na_2CO_3 , K_2CO_3 , Cs_2CO_3 , and Li_2CO_3 .

[0021] In another more particular embodiment of any of the above embodiments, the alkylating agent is selected from the group consisting of: alkyl halides and benzyl halides. In

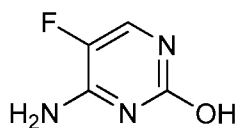
an even more particular embodiment, the alkyl halide and benzyl halide are selected from methyl iodide (CH_3I), ethyl iodide ($\text{C}_2\text{H}_5\text{I}$), and benzyl bromide (BnBr).

[0022] In another more particular embodiment of any of the above embodiments, the alkali carbonate base is Cs_2CO_3 , and the solvent is DMF.

[0023] In another more particular embodiment of any of the above embodiments, a molar ratio of Compound II to alkali carbonate base is from about 3:1 to about 1:1 and a molar ratio of Compound II to alkylating agent is from about 1:1 to about 3:1. In an even more particular embodiment, a molar ratio of Compound II to alkali carbonate base is about 2:1 a molar ratio of Compound II to alkylating agent is 1:3.

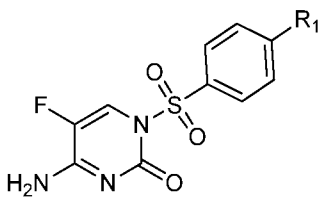
[0024] In another more particular embodiment of any of the above embodiments, the method further includes the step of diluting a completed reaction mixture with CH_3CN and 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$. In an even more particular embodiment, a ratio of DMF to CH_3CN is from about 1:1 to about 3:1 and a ratio of DMF to 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ is from about 1:2 to about 2:1. In a still more particular embodiment, a ratio of DMF to CH_3CN is about 2:1 and a ratio of DMF to 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ is about 1:1.

[0025] In another embodiment, a method of preparing a compound of Formula II is provided. The method includes contacting a compound of Formula I with bis-*N,O*-trimethylsilylacetamide (BSA):



I

and forming a compound of Formula II:



II

;

wherein a molar ratio of compound I to bis-*N,O*-trimethylsilylacetamide (BSA) is 1:1.1 and the contacting step is carried out at about 22 °C to about 70 °C.

[0026] In a more particular embodiment, the contacting step further includes contacting compound I with CH_3CN .

[0027] In another more particular embodiment of any of the above embodiments, the method comprises contacting a BSA treated reaction mixture with an arylsulfonyl chloride.

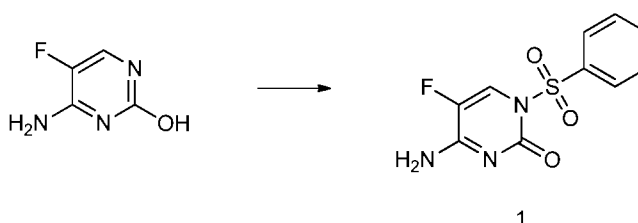
[0028] In another more particular embodiment of any of the above embodiments, a molar ratio of Compound I to arylsulfonyl chloride is from about 1:2 to about 2:1. In an even more particular embodiment, a molar ratio of Compound I to arylsulfonyl chloride is 1:1.1.

[0029] The embodiments described above are intended merely to be exemplary, and those skilled in the art will recognize, or will be able to ascertain using no more than routine experimentation, numerous equivalents of specific compounds, materials, and procedures. All such equivalents are considered to be within the scope of the invention and are encompassed by the appended claims.

DETAILED DESCRIPTION

[0030] 5-Fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one as shown in Examples 1 – 2.

[0031] **Example 1:** Preparation of 4-amino-5-fluoro-1-(phenylsulfonyl)pyrimidin-2(1H)-one (**1**):



[0032] To a dry 500 milliliter (mL) round bottom flask equipped with a mechanical stirrer, nitrogen inlet, addition funnel, thermometer, and reflux condenser were added 5-fluorocytocine (20.0 grams (g), 155 millimole (mmol)) and CH₃CN (100 mL). To the resulting mixture was added BSA (34.7 g, 170 mmol) in one portion and the reaction was warmed to 70 °C and stirred for 30 minutes (min). The resulting homogeneous solution was cooled to 5 °C with an ice bath and treated dropwise with benzenesulfonyl chloride. The reaction was stirred at 0 °C – 5 °C for 1 h and then overnight at room temperature. The resulting pale yellow suspension was poured into cold H₂O (1.5 liters (L)) and stirred vigorously for 1 h. The resulting solid was collected by vacuum filtration, washed with H₂O, and dried under vacuum overnight at 40 °C to give 4-amino-5-fluoro-1-

(phenylsulfonyl)pyrimidin-2(1*H*)-one (29.9 g, 72%) as a powdery white solid: ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 8.56 (s, 1H), 8.35 – 8.26 (m, 2H), 8.07 – 7.98 (m, 2H), 7.84 – 7.74 (m, 1H), 7.72 – 7.61 (m, 2H); ^{19}F NMR (376 MHz, $\text{DMSO-}d_6$) δ -163.46; ESIMS m/z 270 ($[\text{M}+\text{H}]^+$).

[0033] The following compounds **1** – **3** in Table 1a were made in accordance with the reaction depicted in Scheme 1 and the procedures described in Example 1. Characterization data for compounds **1** – **3** are shown in Table 1b.

Scheme 1.

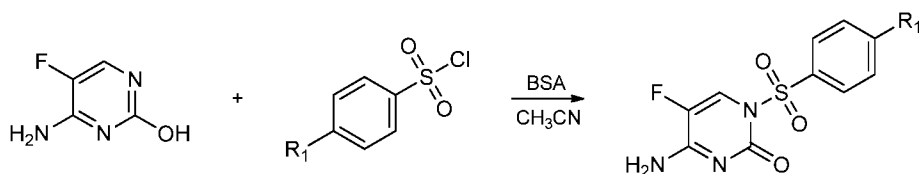


Table 1a.

Compound Number	R ₁	Appearance	Yield (%)
1	H	Powdery White Solid	72
2	CH ₃	Powdery White Solid	61
3	OCH ₃	Powdery White Solid	57

Table 1b.

Compound Number	Mass Spec.	^1H NMR (δ) ^a	^{13}C NMR or ^{19}F NMR (δ) ^{b,c}
1	ESIMS m/z 270 ($[\text{M}+\text{H}]^+$)	^1H NMR ($\text{DMSO-}d_6$) δ 8.56 (s, 1H), 8.35 – 8.26 (m, 2H), 8.07 – 7.98 (m, 2H), 7.84 – 7.74 (m, 1H), 7.72 – 7.61 (m, 2H)	^{19}F NMR ($\text{DMSO-}d_6$) δ -163.46

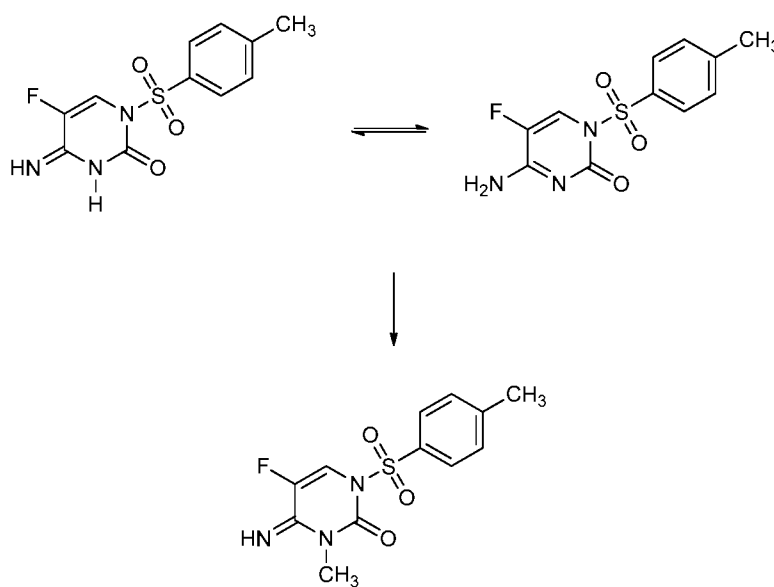
2	ESIMS m/z 284 ([M+H] ⁺)	¹ H NMR (DMSO- <i>d</i> ₆) δ 8.54 (s, 1H), 8.40 – 8.16 (m, 2H), 8.05 – 7.76 (m, 2H), 7.66 – 7.36 (m, 2H), 2.41 (s, 3H)	¹⁹ F NMR (DMSO- <i>d</i> ₆) δ -163.62
3	ESIMS m/z 300 ([M+H] ⁺)	¹ H NMR (CDCl ₃) δ 8.10 – 7.91 (m, 2H), 7.73 (d, <i>J</i> = 5.4 Hz, 2H), 7.11 – 6.94 (m, 2H), 3.90 (s, 3H), 3.32 (d, <i>J</i> = 0.6 Hz, 3H)	¹⁹ F NMR (CDCl ₃) δ -158.58

^a All ¹H NMR data measured at 400 MHz unless otherwise noted.

^b All ¹³C NMR data measured at 101 MHz unless otherwise noted.

^c All ¹⁹F NMR data measured at 376 MHz unless otherwise noted.

[0034] Example 2: Preparation of 5-fluoro-4-imino-3-methyl-1-tosyl-3,4-dihydropyrimidin-2(1*H*)-one (**5**):



5

[0035] To a mixture of 4-amino-5-fluoro-1-tosylpyrimidin-2(1*H*)-one (5.66 g, 20 mmol) and Li₂CO₃ (0.880 g, 12.0 mmol) in DMF (20 mL) was added CH₃I (8.52 g, 60.0 mmol), and the resulting mixture was warmed to 40 °C and stirred for 5 h. The reaction mixture was cooled to room temperature, diluted with CH₃CN (10 mL), and treated with 2.5% aqueous Na₂S₂O₃ (20 mL). The resulting mixture was stirred at room temperature for 10 min and the solids were collected by filtration. The filter cake was washed with aqueous

CH₃CN (10% CH₃CN in H₂O) and air dried for 2 h. The cake was dissolved in CH₃CN (15 mL) at 40 °C and the solution was treated with H₂O (30 mL). The resulting suspension was cooled to room temperature, stirred for 2.5 h, and filtered. The filter cake was again washed with 10% aqueous CH₃CN and then dried under vacuum at 50 °C to give the title compound (2.70 g, 45%) as a white solid: mp 156 – 158 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.54 (d, *J* = 2.3 Hz, 1H), 7.99 (dd, *J* = 6.0, 0.6 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.53 – 7.45 (m, 2H), 3.12 (d, *J* = 0.7 Hz, 3H), 2.42 (s, 3H); ¹⁹F NMR (376 MHz, DMSO-*d*₆) -157.86 (s); ESIMS *m/z* 298 ([M+H]⁺).

[0036] The following compounds **4** – **6** in Table 2a were made in accordance with the reaction depicted in Scheme 2 and the procedures described in Example 2. Characterization data for compounds **4** – **6** are shown in Table 2b.

Scheme 2.

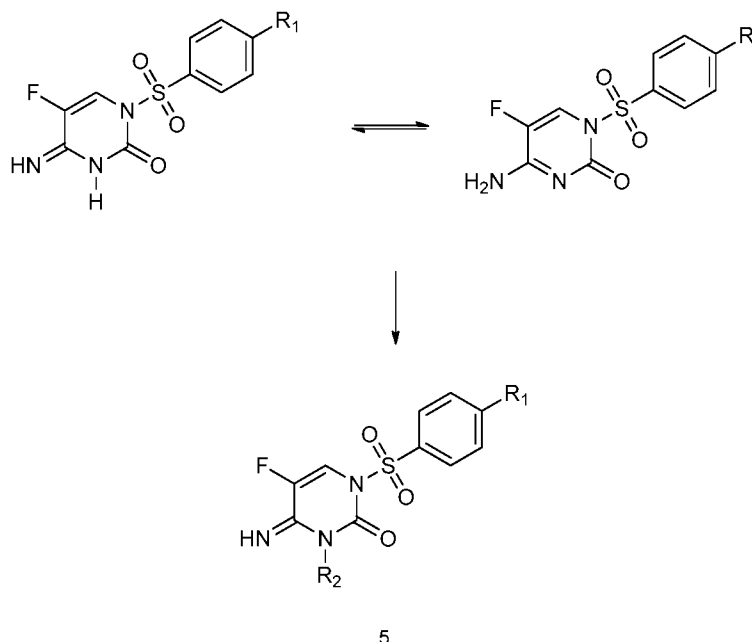


Table 2a.

Compound Number	R ₁	R ₂	Appearance	Yield (%)
4	H	CH ₃	White Solid	64
5	CH ₃	CH ₃	White Solid	45
6	OCH ₃	CH ₃	White Solid	62

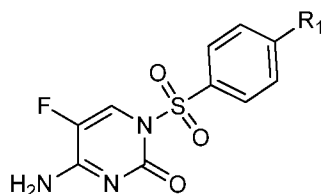
Table 2b.

Compound Number	Mass Spec.	^1H NMR (δ) ^a	^{13}C NMR or ^{19}F NMR (δ) ^{b,c}
4	ESIMS m/z 284 ([M+H] ⁺)	^1H NMR (CDCl ₃) δ 8.14 – 8.02 (m, 2H), 7.88 – 7.67 (m, 3H), 7.67 – 7.50 (m, 2H), 3.31 (d, J = 0.7 Hz, 3H)	^{19}F NMR (CDCl ₃) δ - 158.05
5	ESIMS m/z 298 ([M+H] ⁺)	^1H NMR (DMSO- d_6) δ 8.54 (d, J = 2.3 Hz, 1H), 7.99 (dd, J = 6.0, 0.6 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.53 – 7.45 (m, 2H), 3.12 (d, J = 0.7 Hz, 3H), 2.42 (s, 3H)	^{19}F NMR (DMSO- d_6) δ 157.86 (s)
6	ESIMS m/z 314 ([M+H] ⁺)	^1H NMR (CDCl ₃) δ 8.10 – 7.91 (m, 2H), 7.73 (d, J = 5.4 Hz, 2H), 7.11 – 6.94 (m, 2H), 3.90 (s, 3H), 3.32 (d, J = 0.6 Hz, 3H)	^{19}F NMR (CDCl ₃) δ - 158.58

^aAll ^1H NMR data measured at 400 MHz unless otherwise noted.^bAll ^{13}C NMR data measured at 101 MHz unless otherwise noted.^cAll ^{19}F NMR data measured at 376 MHz unless otherwise noted.

WHAT IS CLAIMED IS:

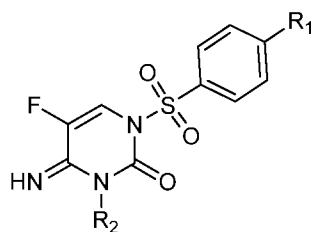
1. A method of making compounds of Formula III, including the steps of:
contacting a compound of Formula II with an alkali carbonate and an alkylating agent,



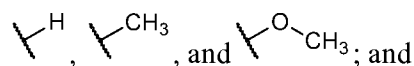
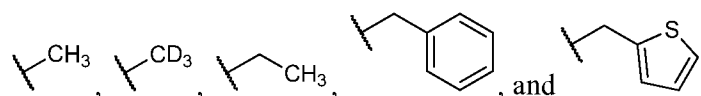
II

; and

forming a compound of Formula III:



III

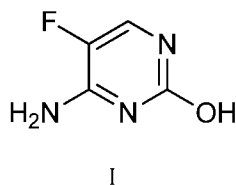
wherein R₁ is selected from the group consisting of:R₂ is selected from the group consisting of:

2. The method of Claim 1, wherein the contacting step is carried out between 22 °C and 60 °C.
3. The method of Claim 1, wherein the contacting step further includes a solvent selected from the group consisting of: DMF, DMSO, DMA, NMP, and CH₃CN.
4. The method of Claim 1, wherein the alkali carbonate is selected from the group

consisting of: Na_2CO_3 , K_2CO_3 , Cs_2CO_3 , and Li_2CO_3 .

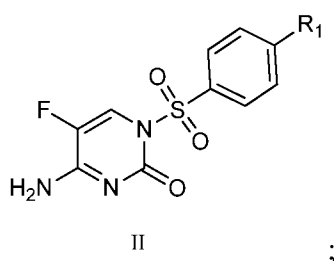
5. The method of Claim 1, wherein the alkylating agent is selected from the group consisting of: alkyl halides and benzyl halides.
6. The method of Claim 5, wherein the alkyl halides and benzyl halides are selected from the group consisting of: methyl iodide, ethyl iodide, and benzyl bromide.
7. The method of Claims 3, 4, 5, or 6, wherein the alkali carbonate is Cs_2CO_3 , and the solvent is DMF.
8. The method of Claims 2, 3, 4, 5, 6, or 7, wherein a molar ratio of the compound of Formula II to alkali carbonate is from about 3:1 to about 1:1 and a molar ratio of the compound of Formula II to alkylating agent is from about 1:1 to about 3:1.
9. The method of Claim 8, wherein a molar ratio of the compound of Formula II to alkali carbonate is about 2:1 and a molar ratio of the compound of Formula II to alkylating agent is about 1:3.
10. The method of Claim 9, further including the step of diluting a completed reaction mixture with CH_3CN and 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$.
11. The method of Claim 10, wherein a ratio of DMF to CH_3CN is from about 1:1 to about 3:1 and a ratio of DMF to 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ is from about 1:2 to about 2:1.
12. The method of Claim 11, wherein a ratio of DMF to CH_3CN is about 2:1 and a ratio of DMF to 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ is about 1:1.
13. A method of preparing a compound of Formula II, including the steps of:

contacting a compound of Formula I:



with bis-*N,O*-trimethylsilylacetamide; and

forming a compound of Formula II:



wherein a molar ratio of compound I to bis-*N,O*-trimethylsilylacetamide is 1:1.1 and the contacting step is carried out at about 22 °C to about 70 °C.

14. The method of Claim 13, wherein the contacting step further includes contacting compound I with CH₃CN.
15. The method of Claim 14, further comprising the step of contacting a bis-*N,O*-trimethylsilylacetamide treated reaction mixture with an arylsulfonyl chloride.
16. The method of Claim 15, wherein a molar ratio of the compound of Formula I to arylsulfonyl chloride is from about 1:2 to about 2:1.
17. The method of Claim 16, wherein a molar ratio of the compound of Formula I to arylsulfonyl chloride is about 1:1.1.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/72566

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07D 409/06 (2015.01)

CPC - C07D 239/47

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)

IPC(8) Classification - A61K 31/505 (2015.01)

CPC Classification - A01N 43/54; C07D 239/47, 409/12

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

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

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); ProQuest; Google; Google Scholar; SureChem; PubMed; PubChem; 5-fluoro-4-imino-3-(alkyl)-1-(arylsulfonyl)-3,4-Dihydropyrimidin-2(1H)-one; alkali carbonate; potassium carbonate; cesium carbonate; alkylating agent; alkyl halide; benzyl halide; dimethyl formamide; acetonitrile; bis-N,O-(trimethylsilyl)acetamide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0263627 A1 (BOEBEL, TA et al.) 27 October 2011; paragraphs [0055].	1-6, 7/3-6
X	US 2011/034493 A1 (BOEBEL, TA et al.) 10 February 2011; paragraphs [0004], [0090]	13-17



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

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

"T"

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

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

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

"&"

document member of the same patent family

Date of the actual completion of the international search

14 March 2015 (14.03.2015)

Date of mailing of the international search report

08 APR 2015

Name and mailing address of the ISA/

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer

Shane Thomas

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/72566

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 8-12
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.



(51) International Patent Classification:

C07D 409/06 (2006.01)

(21) International Application Number:

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29 December 2014 (29.12.2014)

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(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every

kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

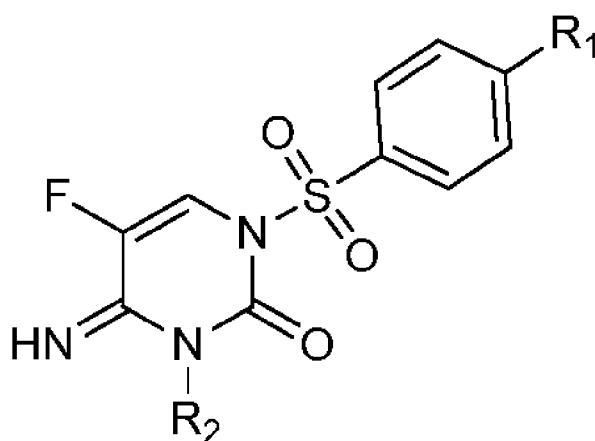
— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

— with international search report (Art. 21(3))

(54) Title: 5-FLUORO-4-IMINO-3-(ALKYL/SUBSTITUTED ALKYL)-1-(ARYLSULFONYL)-3,4-DIHYDROPYRIMIDIN-2(1H)-ONE AND PROCESSES FOR THEIR PREPARATION



III

(57) Abstract: Provided herein are 5-fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one and processes for their preparation which may include the use of an alkali alkoxide and an alkylating agent.

Applicant : Adama Makhteshim Ltd.
 PCT Application Nos.: PCT/US2014/072566 & PCT/US2014/072569
 Int'l Filing Date : December 29, 2014
 Exhibit C

**5-FLUORO-4-IMINO-3-(ALKYL/SUBSTITUTED ALKYL)-1-(ARYLSULFONYL)-
3,4-DIHYDROPYRIMIDIN-2(1H)-ONE AND PROCESSES FOR THEIR
PREPARATION**

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial Nos. 61/922,572 and 61/922,582, each filed December 31, 2013, the disclosures of which are expressly incorporated by reference herein.

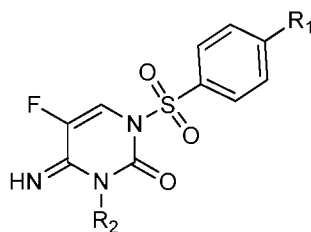
FIELD

[0002] Provided herein are 5-fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one and processes for their preparation.

BACKGROUND AND SUMMARY

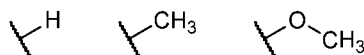
[0003] U.S. Patent Application Ser. No. 13/090,616, U.S. Pub. No. 2011/0263627, describes *inter alia* certain N3-substituted-N1-sulfonyl-5-fluoropyrimidinone compounds and their use as fungicides. The disclosure of the application is expressly incorporated by reference herein. This patent describes various routes to generate N3-substituted-N1-sulfonyl-5-fluoropyrimidinone compounds. It may be advantageous to provide more direct and efficient methods for the preparation, isolation, and purification of N3-substituted-N1-sulfonyl-5-fluoropyrimidinone fungicides and related compounds, *e.g.*, by the use of reagents and/or chemical intermediates and isolation and purification techniques which provide improved time and cost efficiency.

[0004] Provided herein are 5-fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one and processes for their preparation. In one embodiment, provided herein is a process for the preparation of compounds of Formula III:

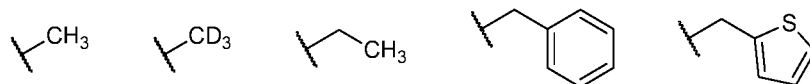


III

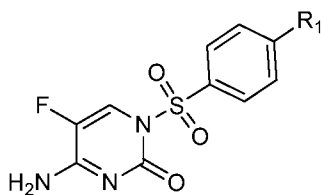
wherein R_1 is selected from:



and R_2 is selected from:



which comprises contacting compounds of Formula II with a base, such as an alkali carbonate, e.g., sodium-, potassium-, cesium-, and lithium carbonate (Na_2CO_3 , K_2CO_3 , Cs_2CO_3 , and Li_2CO_3 , respectively) or an alkali alkoxide, for example, potassium *tert*-butoxide (KO^tBu) and an alkylating agent, such as an alkyl halide of Formula $\text{R}_2\text{-X}$, wherein R_2 is as previously defined and X is a halogen, e.g., iodine, bromine, and chlorine, in a polar solvent, such as *N,N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO), dimethylacetamide (DMA), *N*-methylpyrrolidone (NMP), acetonitrile (CH_3CN), and the like, at concentrations from about 0.1 molar (M) to about 3 M. In some embodiments, a molar ratio of compounds of Formula II to the base is from about 3:1 to about 1:1 and a molar ratio of compounds of Formula II to alkylating agent is from about 1:1 to about 3:1. In other embodiments, molar ratios of compounds of Formula II to the base and compounds of Formula II to the alkylating agent of about 2:1 and about 1:3, respectively, are used. In some embodiments, the reactions are conducted at temperatures between -78°C and 90°C , and in other embodiments, the reactions are conducted between 22°C and 60°C .

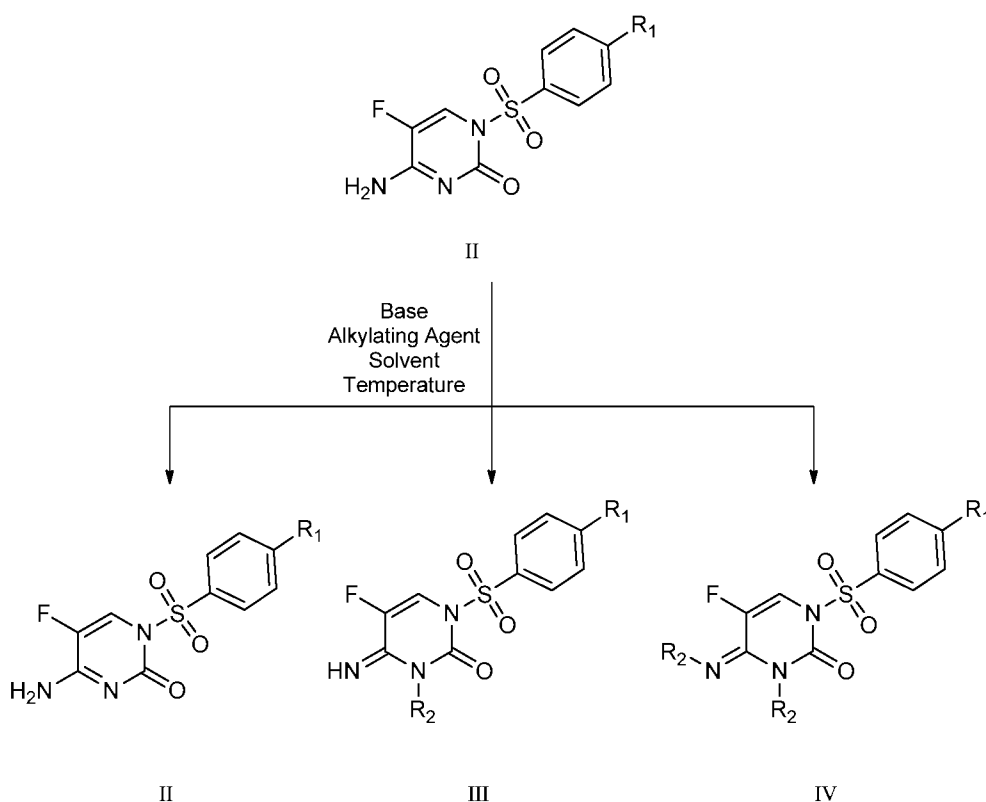


II

[0005] It will be understood by those skilled in the art that manipulation of the reaction parameters described above may result in the formation of product mixtures comprised of compounds of Formulas II, III, and IV, as shown in Scheme 1, wherein the ratios of compounds of Formulas II, III, and IV formed is from about 0:2:1 to about 1:2:0. In some embodiments, compositions comprising mixtures of compounds of Formulas II and III

are preferred, as isolation and purification can be achieved through precipitation and recrystallization, and the intermediate compounds of Formula II can be recovered and recycled. In contrast, compositions comprising mixtures of compounds of Formulas III and IV require chromatographic separation to give III along with the undesired dialkylated by-product of Formula IV.

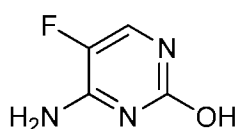
Scheme 1.



[0006] In another embodiment, the desired crude composition, i.e., mixtures of compounds of Formula II and compounds of Formula III, wherein R₁ is methoxy (OCH₃) and R₂ is methyl (CH₃), is obtained through contacting a compound of Formula II with Li₂CO₃ and methyl iodide (CH₃I) in DMF (1.0 M) in a molar ratio of about 1:0.6:3 at 45 °C. Upon completion, dilution of the crude composition with a polar, aprotic solvent, such as CH₃CN, wherein the ratio of CH₃CN:DMF is from about 2:1 to about 1:2, followed by an aqueous solution of sodium thiosulfate (Na₂S₂O₃) with a pH from about 8 to about 10.5, wherein the ratio of 2.5 wt.% aqueous Na₂S₂O₃:DMF is from about 1:2 to about 3:1, affords a precipitate which is isolable by filtration. In one embodiment, the ratio of CH₃CN:DMF is about 1:2 and the ratio of 2.5% aqueous Na₂S₂O₃:DMF is about 1:1, and the resultant solid is further

purified by crystallization/precipitation from a warmed solution, about 30 °C – 40 °C, of the solid in a solution of a polar, aprotic solvent, such as CH₃CN, by the addition of water (H₂O), wherein the ratio of H₂O:CH₃CN is from about 1:2 to about 3:1, to give the purified compound of Formula III, and in another embodiment the ratio of H₂O:CH₃CN to affect precipitation of pure III is about 2:1.

[0007] In another embodiment, compounds of Formula II may be prepared by contacting compounds of Formula I with bis-*N,O*-trimethylsilylacetamide (BSA) at an elevated temperature, such as 70 °C, for a period of about 1 hour (h), followed by cooling and contacting the solution containing the protected pyrimidinol with a substituted benzene sulfonyl chloride, generalized by R₁-PhSO₂Cl, wherein R₁ is as previously defined, at 20 – 25 °C. In some embodiments, the molar ratio of the compound of Formula I to BSA and the sulfonyl chloride is about 1:3:1.1, respectively, and in another embodiment reducing the molar ratio of the reactants to about 1:1.1:1.1 affords improved yields.



I

[0008] The term "alkyl" refers to a branched, unbranched, or saturated cyclic carbon chain, including, but not limited to, methyl, ethyl, propyl, butyl, isopropyl, isobutyl, tertiary butyl, pentyl, hexyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like.

[0009] The term "alkenyl" refers to a branched, unbranched or cyclic carbon chain containing one or more double bonds including, but not limited to, ethenyl, propenyl, butenyl, isopropenyl, isobutenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, and the like.

[0010] The term "aryl" refers to any aromatic, mono- or bi-cyclic, containing 0 heteroatoms.

[0011] The term "heterocycle" refers to any aromatic or non-aromatic ring, mono- or bi-cyclic, containing one or more heteroatoms.

[0012] The term "alkoxy" refers to an –OR substituent

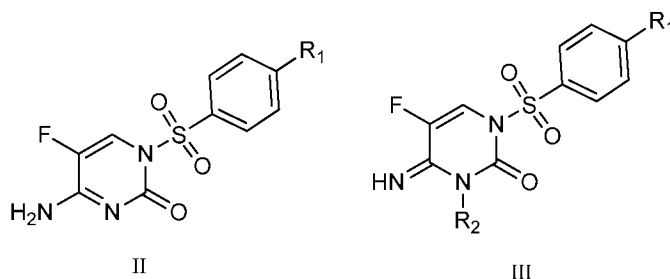
[0013] The term "halogen" or "halo" refers to one or more halogen atoms, defined as F, Cl, Br, and I.

[0014] The term "haloalkyl" refers to an alkyl, which is substituted with Cl, F, I, or Br or any combination thereof.

[0015] Throughout the disclosure, references to the compounds of Formulas I, II, III, and IV are read as also including optical isomers and salts. Exemplary salts may include: hydrochloride, hydrobromide, hydroiodide, and the like. Additionally, the compounds of Formulas I, II, III, and IV may include tautomeric forms.

[0016] Certain compounds disclosed in this document can exist as one or more isomers. It will be appreciated by those skilled in the art that one isomer may be more active than the others. The structures disclosed in the present disclosure are drawn in only one geometric form for clarity, but are intended to represent all geometric and tautomeric forms of the molecule.

[0017] In one exemplary embodiment, a method of making compounds of Formula III is provided. The method includes contacting a compound of Formula II with an alkali alkoxide and an alkylating agent, and forming a compound of Formula III:



[0018] wherein R_1 is selected from the group consisting of: $-H$, $-CH_3$, and $-O-CH_3$; and

[0019] R_2 is selected from the group consisting of: $-CH_3$, $-CD_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, and $-CH_2CH_2CH_2CH_3$.

[0020] In a more particular embodiment, the contacting step is carried out between 22 °C and 60 °C.

[0021] In a more particular embodiment of any of the above embodiments, the contacting step further includes a solvent selected from the group consisting of DMF, DMSO, DMA, NMP, and CH_3CN .

[0022] In a more particular embodiment of any of the above embodiments, the alkali alkoxide is selected from the group consisting of: KO^tBu , CH_3ONa , CH_3CH_2ONa , CH_3CH_2OLi , CH_3OLi , CH_3CH_2OK , and CH_3CH_2ONa .

[0023] In a more particular embodiment of any of the above embodiments, the

alkylating agent is selected from the group consisting of: alkyl halides and benzyl halides.

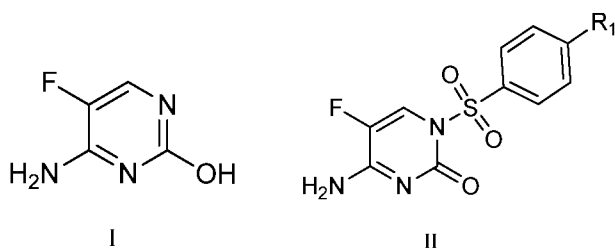
[0024] In a more particular embodiment of any of the above embodiments, the alkyl halide and benzyl halide are selected from methyl iodide (CH_3I), ethyl iodide ($\text{C}_2\text{H}_5\text{I}$), and benzyl bromide (BnBr).

[0025] In a more particular embodiment of any of the above embodiments, the alkali alkoxide is KO^tBu , and the solvent is DMF.

[0026] In a more particular embodiment of any of the above embodiments, a molar ratio of Compound II to alkali alkoxide is from about 3:1 to about 1:1 and a molar ratio of Compound II to alkylating agent is from about 1:1 to about 3:1. In an even more particular embodiment, a molar ratio of Compound II to alkali alkoxide base is about 2:1 a molar ratio of Compound II to alkylating agent is 1:3.

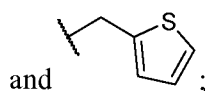
[0027] In a more particular embodiment of any of the above embodiments, the method includes diluting a completed reaction mixture with CH_3CN and 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$. In an even more particular embodiment, a ratio of DMF to CH_3CN is from about 1:1 to about 3:1 and a ratio of DMF to 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ is from about 1:2 to about 2:1. In another more particular embodiment, a ratio of DMF to CH_3CN is about 2:1 and a ratio of DMF to 2.5% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ is about 1:1.

[0028] In another embodiment, a method of preparing a compound of Formula II is provided. The method includes contacting a compound of Formula I with bis-*N,O*-trimethylsilylacetamide; and forming a compound of Formula II



wherein R_1 is selected from the group consisting of: H , CH_3 , and O-CH_3 ; and

R_2 is selected from the group consisting of: CH_3 , CD_3 , CH_2CH_3 , $\text{CH}_2\text{C}_6\text{H}_5$, and



wherein a molar ratio of compound I to bis-*N,O*-trimethylsilylacetamide (BSA) is 1:1.1 and the contacting step is carried out at about 22°C to about 70°C .

[0029] In a more particular embodiment, the contacting step further includes

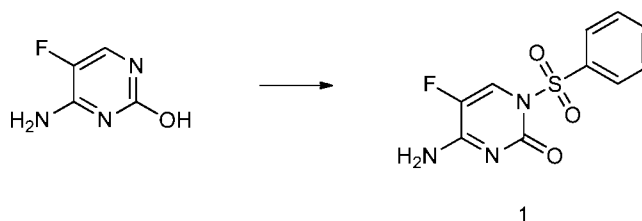
contacting compound I with CH₃CN. In another more particular embodiment, the method includes contacting a BSA treated reaction mixture with an arylsulfonyl chloride. In an even more particular embodiment, a molar ratio of Compound I to arylsulfonyl chloride is from about 1:2 to about 2:1. In another more particular embodiment, a molar ratio of Compound I to arylsulfonyl chloride is 1:1.1.

[0030] The embodiments described above are intended merely to be exemplary, and those skilled in the art will recognize, or will be able to ascertain using no more than routine experimentation, numerous equivalents of specific compounds, materials, and procedures. All such equivalents are considered to be within the scope of the invention and are encompassed by the appended claims.

DETAILED DESCRIPTION

[0031] 5-Fluoro-4-imino-3-(alkyl/substituted alkyl)-1-(arylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one as shown in Examples 1 – 2.

[0032] Example 1: Preparation of 4-amino-5-fluoro-1-(phenylsulfonyl)pyrimidin-2(1H)-one (**1**):



[0033] To a dry 500 milliliter (mL) round bottom flask equipped with a mechanical stirrer, nitrogen inlet, addition funnel, thermometer, and reflux condenser were added 5-fluorocytocine (20.0 grams (g), 155 millimole (mmol)) and CH₃CN (100 mL). To the resulting mixture was added BSA (34.7 g, 170 mmol) in one portion and the reaction was warmed to 70 °C and stirred for 30 minutes (min). The resulting homogeneous solution was cooled to 5 °C with an ice bath and treated dropwise with benzenesulfonyl chloride. The reaction was stirred at 0 °C – 5 °C for 1 h and then overnight at room temperature. The resulting pale yellow suspension was poured into cold H₂O (1.5 liters (L)) and stirred vigorously for 1 h. The resulting solid was collected by vacuum filtration, washed with H₂O, and dried under vacuum overnight at 40 °C to give 4-amino-5-fluoro-1-(phenylsulfonyl)pyrimidin-2(1H)-one (29.9 g, 72%) as a powdery white solid: ¹H NMR (400

MHz, DMSO-*d*₆) δ 8.56 (s, 1H), 8.35 – 8.26 (m, 2H), 8.07 – 7.98 (m, 2H), 7.84 – 7.74 (m, 1H), 7.72 – 7.61 (m, 2H); ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -163.46; ESIMS *m/z* 270 ([M+H]⁺).

[0034] The following compounds **1** – **3** in Table 1a were made in accordance with the reaction depicted in Scheme 1 and the procedures described in Example 1. Characterization data for compounds **1** – **3** are shown in Table 1b.

Scheme 1.

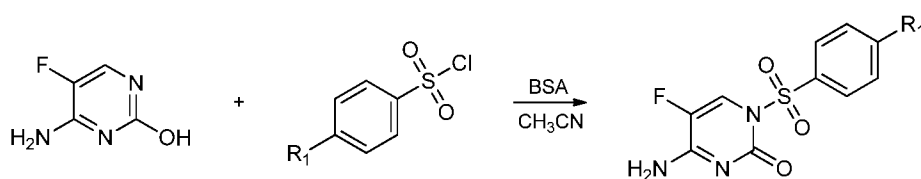


Table 1a.

Compound Number	R ₁	Appearance	Yield (%)
1	H	Powdery White Solid	72
2	CH ₃	Powdery White Solid	61
3	OCH ₃	Powdery White Solid	57

Table 1b.

Compound Number	Mass Spec.	¹ H NMR (δ) ^a	¹³ C NMR or ¹⁹ F NMR (δ) ^{b,c}
1	ESIMS <i>m/z</i> 270 ([M+H] ⁺)	¹ H NMR (DMSO- <i>d</i> ₆) δ 8.56 (s, 1H), 8.35 – 8.26 (m, 2H), 8.07 – 7.98 (m, 2H), 7.84 – 7.74 (m, 1H), 7.72 – 7.61 (m, 2H)	¹⁹ F NMR (DMSO- <i>d</i> ₆) δ -163.46

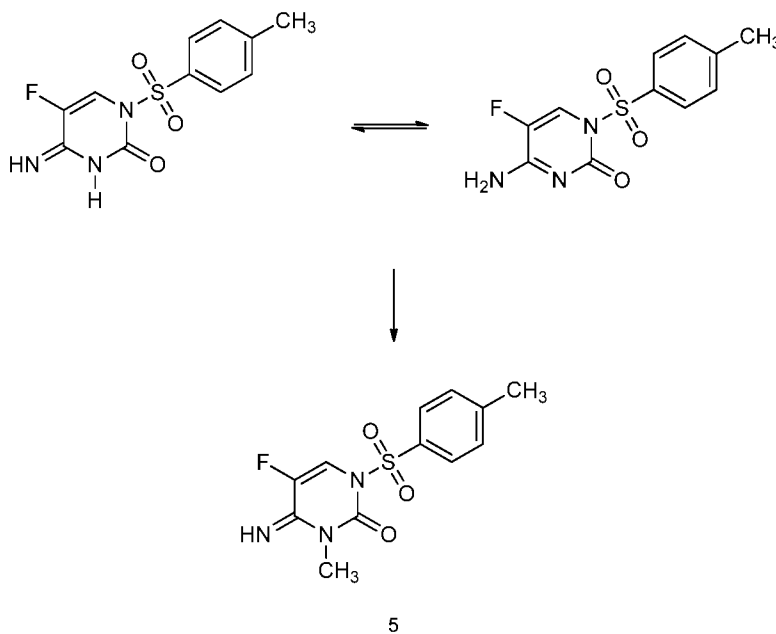
2	ESIMS m/z 284 ([M+H] ⁺)	¹ H NMR (DMSO- <i>d</i> ₆) δ 8.54 (s, 1H), 8.40 – 8.16 (m, 2H), 8.05 – 7.76 (m, 2H), 7.66 – 7.36 (m, 2H), 2.41 (s, 3H)	¹⁹ F NMR (DMSO- <i>d</i> ₆) δ -163.62
3	ESIMS m/z 300 ([M+H] ⁺)	¹ H NMR (CDCl ₃) δ 8.10 – 7.91 (m, 2H), 7.73 (d, <i>J</i> = 5.4 Hz, 2H), 7.11 – 6.94 (m, 2H), 3.90 (s, 3H), 3.32 (d, <i>J</i> = 0.6 Hz, 3H)	¹⁹ F NMR (CDCl ₃) δ -158.58

^a All ¹H NMR data measured at 400 MHz unless otherwise noted.

^b All ¹³C NMR data measured at 101 MHz unless otherwise noted.

^c All ¹⁹F NMR data measured at 376 MHz unless otherwise noted.

[0035] Example 2: Preparation of 5-fluoro-4-imino-3-methyl-1-tosyl-3,4-dihydropyrimidin-2(1*H*)-one (**5**):



[0036] To a mixture of 4-amino-5-fluoro-1-tosylpyrimidin-2(1*H*)-one (20 mmol, 5.66 g) and Li₂CO₃ (0.880 g, 12.0 mmol) in DMF (20 mL) was added CH₃I (8.52 g, 60 mmol), and the resulting mixture was warmed to 40 °C and stirred for 5 h. The reaction mixture was cooled to room temperature, diluted with CH₃CN (10 mL), and treated with 2.5% aqueous Na₂S₂O₃ (20 mL). The resulting mixture was stirred at room temperature for 10 min and the

solids were collected by filtration. The filter cake was washed with aqueous CH₃CN (10% CH₃CN in H₂O) and air dried for 2 h. The cake was dissolved in CH₃CN (15 mL) at 40 °C and the solution was treated with H₂O (30 mL). The resulting suspension was cooled to room temperature, stirred for 2.5 h, and filtered. The filter cake was again washed with 10% aqueous CH₃CN and then dried under vacuum at 50 °C to give the title compound (2.70 g, 45%) as a white solid: mp 156 – 158 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.54 (d, *J* = 2.3 Hz, 1H), 7.99 (dd, *J* = 6.0, 0.6 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.53 – 7.45 (m, 2H), 3.12 (d, *J* = 0.7 Hz, 3H), 2.42 (s, 3H); ¹⁹F NMR (376 MHz, DMSO-*d*₆) -157.86 (s); ESIMS *m/z* 298 ([M+H]⁺).

[0037] The following compounds 4 – 6 in Table 2a were made in accordance with the reaction depicted in Scheme 2 and the procedures described in Example 2. Characterization data for compounds 4 – 6 are shown in Table 2b.

Scheme 2.

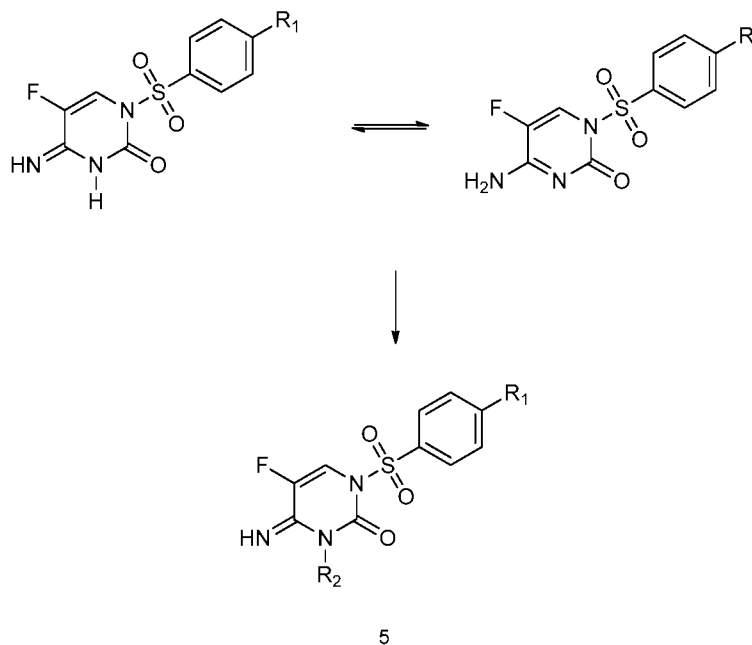


Table 2a.

Compound Number	R ₁	R ₂	Appearance	Yield (%)
4	H	CH ₃	White Solid	64
5	CH ₃	CH ₃	White Solid	45

6	OCH ₃	CH ₃	White Solid	62
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Table 2b.

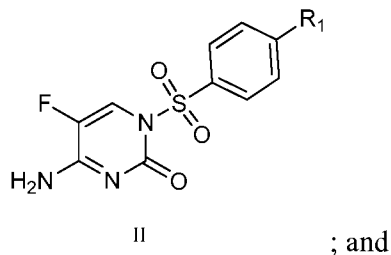
Compound Number	Mass Spec.	¹ H NMR (δ) ^a	¹³ C NMR or ¹⁹ F NMR (δ) ^{b,c}
4	ESIMS <i>m/z</i> 284 ([M+H] ⁺)	¹ H NMR (CDCl ₃) δ 8.14 – 8.02 (m, 2H), 7.88 – 7.67 (m, 3H), 7.67 – 7.50 (m, 2H), 3.31 (d, <i>J</i> = 0.7 Hz, 3H)	¹⁹ F NMR (CDCl ₃) δ - 158.05
5	ESIMS <i>m/z</i> 298 ([M+H] ⁺)	¹ H NMR (CDCl ₃) δ 8.54 (d, <i>J</i> = 2.3 Hz, 1H), 7.99 (dd, <i>J</i> = 6.0, 0.6 Hz, 1H), 7.95 – 7.89 (m, 2H), 7.53 – 7.45 (m, 2H), 3.12 (d, <i>J</i> = 0.7 Hz, 3H), 2.42 (s, 3H)	¹⁹ F NMR (CDCl ₃) δ 157.86 (s)
6	ESIMS <i>m/z</i> 314 ([M+H] ⁺)	¹ H NMR (CDCl ₃) δ 8.10 – 7.91 (m, 2H), 7.73 (d, <i>J</i> = 5.4 Hz, 2H), 7.11 – 6.94 (m, 2H), 3.90 (s, 3H), 3.32 (d, <i>J</i> = 0.6 Hz, 3H)	¹⁹ F NMR (CDCl ₃) δ - 158.58

^aAll ¹H NMR data measured at 400 MHz unless otherwise noted.^bAll ¹³C NMR data measured at 101 MHz unless otherwise noted.^cAll ¹⁹F NMR data measured at 376 MHz unless otherwise noted.

WHAT IS CLAIMED IS:

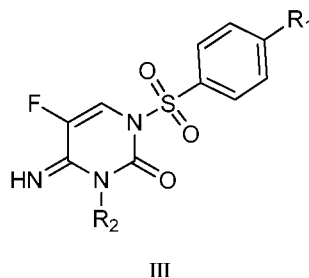
1. A method of making compounds of Formula III, including the steps of:

contacting a compound of Formula II with an alkali alkoxide and an alkylating agent,

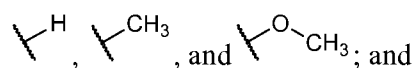


; and

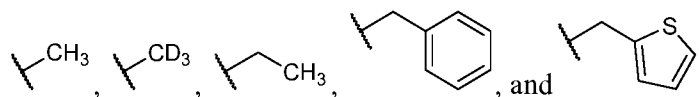
forming a compound of Formula III:



wherein R₁ is selected from the group consisting of:



R₂ is selected from the group consisting of:

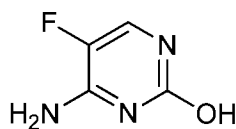


2. The method of Claim 1, wherein the contacting step is carried out between 22 °C and 60 °C.
3. The method of Claim 1, wherein the contacting step further includes a solvent selected from the group consisting of: DMF, DMSO, DMA, NMP, and CH₃CN.

4. The method of Claim 1, wherein the alkali alkoxide is selected from the group consisting of: KO^tBu, CH₃ONa, CH₃CH₂ONa, CH₃CH₂OLi, CH₃OLi, CH₃CH₂OK, and CH₃CH₂ONa.
5. The method of Claim 1, wherein the alkylating agent is selected from the group consisting of: alkyl halides and benzyl halides.
6. The method of Claim 5, wherein the alkyl halides and benzyl halides are selected from the group consisting of: methyl iodide, ethyl iodide, and benzyl bromide.
7. The method of Claims 3, 4, 5, or 6, wherein the alkali alkoxide is KO^tBu, and the solvent is DMF.
8. The method of Claims 2, 3, 4, 5, 6, or 7, wherein a molar ratio of the compound of Formula II to alkali alkoxide is from about 3:1 to about 1:1 and a molar ratio of the compound of Formula II to alkylating agent is from about 1:1 to about 3:1.
9. The method of Claim 8, wherein a molar ratio of the compound of Formula II to alkali alkoxide is about 2:1 and a molar ratio of the compound of Formula II to alkylating agent is about 1:3.
10. The method of Claim 9, further including the step of diluting a completed reaction mixture with CH₃CN and 2.5% aqueous Na₂S₂O₃.
11. The method of Claim 10, wherein a ratio of DMF to CH₃CN is from about 1:1 to about 3:1 and a ratio of DMF to 2.5% aqueous Na₂S₂O₃ is from about 1:2 to about 2:1.
12. 12. The method of Claim 11, wherein a ratio of DMF to CH₃CN is about 2:1 and a ratio of DMF to 2.5% aqueous Na₂S₂O₃ is about 1:1.

13. A method of preparing a compound of Formula II, including the steps of:

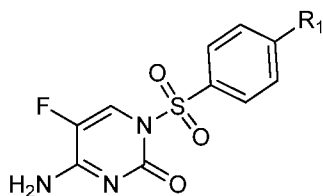
contacting a compound of Formula I:



I

with bis-*N,O*-trimethylsilylacetamide; and

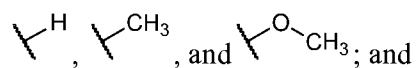
forming a compound of Formula II:



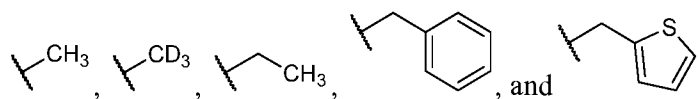
II

;

wherein R_1 is selected from the group consisting of:



R_2 is selected from the group consisting of:



wherein a molar ratio of compound I to bis-*N,O*-trimethylsilylacetamide is 1:1.1 and

the contacting step is carried out at about 22 °C to about 70 °C.

14. The method of Claim 13, wherein the contacting step further includes contacting compound I with CH_3CN .

15. The method of Claim 14, further comprising the step of contacting a bis-*N,O*-trimethylsilylacetamide treated reaction mixture with an arylsulfonyl chloride.
16. The method of Claim 15, wherein a molar ratio of the compound of Formula I to arylsulfonyl chloride is from about 1:2 to about 2:1.
17. The method of Claim 16, wherein a molar ratio of the compound of Formula I to arylsulfonyl chloride is about 1:1.1.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/72569

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07D 409/06 (2015.01)

CPC - C07D 239/47

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)

IPC(8) Classification - A61K 31/505 (2015.01)

CPC Classification - A01N 43/54; C07D 239/47, 409/12

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

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

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); ProQuest; Google; Google Scholar; SureChem; PubMed; PubChem; 5-fluoro-4-imino-3-(alkyl)-1-(arylsulfonyl)-3,4-Dihydropyrimidin-2(1H)-one; alkali alkoxide; potassium tert-butoxide; alkylating agent; alkyl halide; benzyl halide; dimethyl formamide; acetonitrile; bis-N,O-(trimethylsilyl)acetamide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011/0263627 A1 (BOEBEL, TA et al.) 27 October 2011; paragraphs [0055].	1-6, 7/3-6
Y	US 2011/0053891 A1 (BOEBEL, TA et al.) 03 March 2011; paragraphs [0090], [0115].	1-6, 7/3-6
X	US 2011/034493 A1 (BOEBEL, TA et al.) 10 February 2011; paragraphs [0004], [0090]	13-17

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

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

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

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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

"&" document member of the same patent family

Date of the actual completion of the international search

14 March 2015 (14.03.2015)

Date of mailing of the international search report

02 APR 2015

Name and mailing address of the ISA/

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer

Shane Thomas

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/72569

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 8-12
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.



US 20110263627A1

(19) **United States**(12) **Patent Application Publication**
Boebel et al.(10) **Pub. No.: US 2011/0263627 A1**(43) **Pub. Date: Oct. 27, 2011**(54) **N3-SUBSTITUTED-N1-SULFONYL-5-
FLUOROPYRIMIDINONE DERIVATIVES**(22) Filed: **Apr. 20, 2011****Related U.S. Application Data**(75) Inventors: **Timothy A. Boebel**, Indianapolis,
IN (US); **Beth Lorschach**,
Indianapolis, IN (US); **Timothy P.**
Martin, Noblesville, IN (US); **W.**
John Owen, Carmel, IN (US);
Michael T. Sullenberger,
Westfield, IN (US); **Jeffery D.**
Webster, New Palestine, IN (US);
Chenglin Yao, Westfield, IN (US)(60) Provisional application No. 61/327,855, filed on Apr.
26, 2010.**Publication Classification**(51) **Int. Cl.**
A01N 43/54 (2006.01)
A01P 3/00 (2006.01)
C07D 239/10 (2006.01)
(52) **U.S. Cl.** **514/274; 544/317**(73) Assignee: **DOW AGROSCIENCES LLC**,
Indianapolis, IN (US)(57) **ABSTRACT**This present disclosure is related to the field of N3-substi-
tuted-N1-sulfonyl-5-fluoropyrimidinones and their deriva-
tives and to the use of these compounds as fungicides.(21) Appl. No.: **13/090,616**Applicant : Adama Makhteshim Ltd.
PCT Application Nos.: PCT/US2014/072566 & PCT/US2014/072569
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Exhibit D

N3-SUBSTITUTED-N1-SULFONYL-5-FLUOROPYRIMIDINONE DERIVATIVES

CROSS-REFERENCE TO RELATED APPLICATIONS

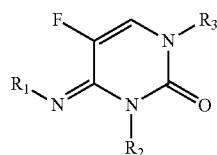
[0001] This application claims the benefit of U.S. Provisional Patent Application Ser. No. 61/327,855 filed Apr. 26, 2010, which is expressly incorporated by reference herein.

BACKGROUND AND SUMMARY OF THE INVENTION

[0002] Fungicides are compounds, of natural or synthetic origin, which act to protect and/or cure plants against damage caused by agriculturally relevant fungi. Generally, no single fungicide is useful in all situations. Consequently, research is ongoing to produce fungicides that may have better performance, are easier to use, and cost less.

[0003] The present disclosure relates to N3-substituted-M-sulfonyl-5-fluoropyrimidinone compounds and their use as fungicides. The compounds of the present disclosure may offer protection against ascomycetes, basidiomycetes, deuteromycetes and oomycetes.

[0004] One embodiment of the present disclosure may include compounds of Formula I:



wherein R₁ is:

[0005] H;

R₂ is:

[0006] C₁-C₆ alkyl optionally substituted with R₄;

[0007] benzyl optionally substituted with 1-3 R₅

R₃ is —S(O)₂R₆;

[0008] R₄ is independently halogen, C₁-C₆ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, C₁-C₄ alkylthio, C₁-C₄ haloalkylthio, amino, C₁-C₃ alkylamino, C₂-C₆ alkoxy-carbonyl, C₂-C₆ alkylcarbonyl, C₂-C₆ alkylaminocarbonyl, hydroxyl, or C₃-C₆ trialkylsilyl;

R₅ is independently halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkoxy, C₁-C₆ haloalkoxy, C₁-C₆ alkylthio, C₁-C₆ haloalkylthio, amino, C₁-C₆ alkylamino, C₂-C₆ dialkylamino, C₂-C₆ alkoxy-carbonyl, or C₂-C₆ alkylcarbonyl, nitro, hydroxyl, or cyano;

R₆ is C₁-C₆ alkyl, C₁-C₆ haloalkyl, amino, C₁-C₆ alkylamino, C₂-C₆ dialkylamino, a phenyl or benzyl wherein each of the phenyl or the benzyl may be optionally substituted with 1-3 R₅, or a 5- or 6-membered saturated or unsaturated ring containing 1-3 heteroatoms wherein each ring may be optionally substituted with 1-3 R₅.

[0009] Another embodiment of the present disclosure may include a fungicidal composition for the control or prevention of fungal attack comprising the compounds described above and a phytologically acceptable carrier material.

[0010] Yet another embodiment of the present disclosure may include a method for the control or prevention of fungal attack on a plant, the method including the steps of applying a fungicidally effective amount of one or more of the compounds described above to at least one of the fungus, the plant, an area adjacent to the plant, and the seed adapted to produce the plant.

[0011] The term “alkyl” refers to a branched, unbranched, or cyclic carbon chain, including methyl, ethyl, propyl, butyl, isopropyl, isobutyl, tertiary butyl, pentyl, hexyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like.

[0012] As used throughout this specification, the term “R” refers to the group consisting of C₂₋₈ alkyl unless stated otherwise.

[0013] The term “alkoxy” refers to an —OR substituent.

[0014] The term “alkoxycarbonyl” refers to a —C(O)—OR substituent.

[0015] The term “alkylcarbonyl” refers to a —C(O)—R substituent.

[0016] The term “alkylthio” refers to an —S—R substituent.

[0017] The term “haloalkylthio” refers to an alkylthio, which is substituted with Cl, F, I, or Br or any combination thereof.

[0018] The term “trialkylsilyl” refers to —SiR₃.

[0019] The term “cyano” refers to a —C≡N substituent.

[0020] The term “hydroxyl” refers to an —OH substituent.

[0021] The term “amino” refers to a —NH₂ substituent.

[0022] The term “alkylamino” refers to a —N(H)—R substituent.

[0023] The term “dialkylamino” refers to a —NR₂ substituent.

[0024] The term “haloalkoxy” refers to an —OR—X substituent, wherein X is Cl, F, Br, or I, or any combination thereof.

[0025] The term “haloalkyl” refers to an alkyl, which is substituted with Cl, F, I, or Br or any combination thereof.

[0026] The term “halogen” or “halo” refers to one or more halogen atoms, defined as F, Cl, Br, and I.

[0027] The term “nitro” refers to a —NO₂ substituent.

[0028] Throughout the disclosure, reference to the compounds of Formula I is read as also including optical isomers and salts of Formula I, and hydrates thereof. Specifically, when Formula I contains a branched chain alkyl group, it is understood that such compounds include optical isomers and racemates thereof. Exemplary salts include: hydrochloride, hydrobromide, hydroiodide, and the like.

[0029] It is also understood by those skilled in the art that additional substitution is allowable, unless otherwise noted, as long as the rules of chemical bonding and strain energy are satisfied and the product still exhibits fungicidal activity.

[0030] Another embodiment of the present disclosure is a use of a compound of Formula I, for protection of a plant against attack by a phytopathogenic organism or the treatment of a plant infested by a phytopathogenic organism, comprising the application of a compound of Formula I, or a composition comprising the compound to soil, a plant, a part of a plant, foliage, roots, and/or seeds.

[0031] Additionally, another embodiment of the present disclosure is a composition useful for protecting a plant against attack by a phytopathogenic organism and/or treat-

ment of a plant infested by a phytopathogenic organism comprising a compound of Formula I and a phytologically acceptable carrier material.

DETAILED DESCRIPTION OF THE PRESENT DISCLOSURE

[0032] The compounds of the present disclosure may be applied by any of a variety of known techniques, either as the compounds or as formulations comprising the compounds. For example, the compounds may be applied to the roots, seeds or foliage of plants for the control of various fungi, without damaging the commercial value of the plants. The materials may be applied in the form of any of the generally used formulation types, for example, as solutions, dusts, wettable powders, flowable concentrates, or emulsifiable concentrates.

[0033] Preferably, the compounds of the present disclosure are applied in the form of a formulation, comprising one or more of the compounds of Formula I with a phytologically acceptable carrier. Concentrated formulations may be dispersed in water, or other liquids, for application, or formulations may be dust-like or granular, which may then be applied without further treatment. The formulations can be prepared according to procedures that are conventional in the agricultural chemical art.

[0034] The present disclosure contemplates all vehicles by which one or more of the compounds may be formulated for delivery and use as a fungicide. Typically, formulations are applied as aqueous suspensions or emulsions. Such suspensions or emulsions may be produced from water-soluble, water suspendable, or emulsifiable formulations which are solids, usually known as wettable powders; or liquids, usually known as emulsifiable concentrates, aqueous suspensions, or suspension concentrates. As will be readily appreciated, any material to which these compounds may be added may be used, provided it yields the desired utility without significant interference with the activity of these compounds as antifungal agents.

[0035] Wettable powders, which may be compacted to form water dispersible granules, comprise an intimate mixture of one or more of the compounds of Formula I, an inert carrier and surfactants. The concentration of the compound in the wettable powder may be from about 1 percent to about 90 percent by weight based on the total weight of the wettable powder, more preferably about 25 weight percent to about 75 weight percent. In the preparation of wettable powder formulations, the compounds may be compounded with any finely divided solid, such as prophyllite, talc, chalk, gypsum, Fuller's earth, bentonite, attapulgite, starch, casein, gluten, montmorillonite clays, diatomaceous earths, purified silicates or the like. In such operations, the finely divided carrier and surfactants are typically blended with the compound(s) and milled.

[0036] Emulsifiable concentrates of the compounds of Formula I may comprise a convenient concentration, such as from about 1 weight percent to about 50 weight percent of the compound, in a suitable liquid, based on the total weight of the concentrate. The compounds may be dissolved in an inert carrier, which is either a water-miscible solvent or a mixture of water-immiscible organic solvents, and emulsifiers. The concentrates may be diluted with water and oil to form spray mixtures in the form of oil-in-water emulsions. Useful organic solvents include aromatics, especially the high-boiling naphthalenic and olefinic portions of petroleum such as

heavy aromatic naphtha. Other organic solvents may also be used, for example, terpenic solvents, including rosin derivatives, aliphatic ketones, such as cyclohexanone, and complex alcohols, such as 2-ethoxyethanol.

[0037] Emulsifiers which may be advantageously employed herein may be readily determined by those skilled in the art and include various nonionic, anionic, cationic and amphoteric emulsifiers, or a blend of two or more emulsifiers. Examples of nonionic emulsifiers useful in preparing the emulsifiable concentrates include the polyalkylene glycol ethers and condensation products of alkyl and aryl phenols, aliphatic alcohols, aliphatic amines or fatty acids with ethylene oxide, propylene oxides such as the ethoxylated alkyl phenols and carboxylic esters solubilized with the polyol or polyoxyalkylene. Cationic emulsifiers include quaternary ammonium compounds and fatty amine salts. Anionic emulsifiers include the oil-soluble salts (e.g., calcium) of alkylaryl sulphonic acids, oil-soluble salts or sulfated polyglycol ethers and appropriate salts of phosphated polyglycol ether.

[0038] Representative organic liquids which may be employed in preparing the emulsifiable concentrates of the compounds of the present invention are the aromatic liquids such as xylene, propyl benzene fractions; or mixed naphthalene fractions, mineral oils, substituted aromatic organic liquids such as dioctyl phthalate; kerosene; dialkyl amides of various fatty acids, particularly the dimethyl amides of fatty glycols and glycol derivatives such as the n-butyl ether, ethyl ether or methyl ether of diethylene glycol, the methyl ether of triethylene glycol, petroleum fractions or hydrocarbons such as mineral oil, aromatic solvents, paraffinic oils, and the like; vegetable oils such as soy bean oil, rape seed oil, olive oil, castor oil, sunflower seed oil, coconut oil, corn oil, cotton seed oil, linseed oil, palm oil, peanut oil, safflower oil, sesame oil, tung oil and the like; esters of the above vegetable oils; and the like. Mixtures of two or more organic liquids may also be employed in the preparation of the emulsifiable concentrate. Organic liquids include xylene, and propyl benzene fractions, with xylene being most preferred in some cases. Surface-active dispersing agents are typically employed in liquid formulations and in an amount of from 0.1 to 20 percent by weight based on the combined weight of the dispersing agent with one or more of the compounds. The formulations can also contain other compatible additives, for example, plant growth regulators and other biologically active compounds used in agriculture.

[0039] Aqueous suspensions comprise suspensions of one or more water-insoluble compounds of Formula I, dispersed in an aqueous vehicle at a concentration in the range from about 1 to about 50 weight percent, based on the total weight of the aqueous suspension. Suspensions are prepared by finely grinding one or more of the compounds, and vigorously mixing the ground material into a vehicle comprised of water and surfactants chosen from the same types discussed above. Other components, such as inorganic salts and synthetic or natural gums, may also be added to increase the density and viscosity of the aqueous vehicle.

[0040] The compounds of Formula I can also be applied as granular formulations, which are particularly useful for applications to the soil. Granular formulations generally contain from about 0.5 to about 10 weight percent, based on the total weight of the granular formulation of the compound(s), dispersed in an inert carrier which consists entirely or in large part of coarsely divided inert material such as attapulgite, bentonite, diatomite, clay or a similar inexpensive substance.

Such formulations are usually prepared by dissolving the compounds in a suitable solvent and applying it to a granular carrier which has been preformed to the appropriate particle size, in the range of from about 0.5 to about 3 mm. A suitable solvent is a solvent in which the compound is substantially or completely soluble. Such formulations may also be prepared by making a dough or paste of the carrier and the compound and solvent, and crushing and drying to obtain the desired granular particle.

[0041] Dusts containing the compounds of Formula I may be prepared by intimately mixing one or more of the compounds in powdered form with a suitable dusty agricultural carrier, such as, for example, kaolin clay, ground volcanic rock, and the like. Dusts can suitably contain from about 1 to about 10 weight percent of the compounds, based on the total weight of the dust.

[0042] The formulations may additionally contain adjuvant surfactants to enhance deposition, wetting and penetration of the compounds onto the target crop and organism. These adjuvant surfactants may optionally be employed as a component of the formulation or as a tank mix. The amount of adjuvant surfactant will typically vary from 0.01 to 1.0 percent by volume, based on a spray-volume of water, preferably 0.05 to 0.5 volume percent. Suitable adjuvant surfactants include, but are not limited to ethoxylated nonyl phenols, ethoxylated synthetic or natural alcohols, salts of the esters or sulphosuccinic acids, ethoxylated organosilicones, ethoxylated fatty amines, blends of surfactants with mineral or vegetable oils, crop oil concentrate (mineral oil (85%)+emulsifiers (15%)); nonylphenol ethoxylate; benzylcocoalkyldimethyl quaternary ammonium salt; blend of petroleum hydrocarbon, alkyl esters, organic acid, and anionic surfactant; C₉-C₁₁ alkylpolyglycoside; phosphated alcohol ethoxylate; natural primary alcohol(C₁₂-C₁₆) ethoxylate; di-sec-butylphenol EO—PO block copolymer; polysiloxane-methyl cap; nonylphenol ethoxylate+urea ammonium nitrate; emulsified methylated seed oil; tridecyl alcohol (synthetic) ethoxylate (8EO); tallow amine ethoxylate (15 EO); PEG(400) dioleate-99. The formulations may also include oil-in-water emulsions such as those disclosed in U.S. patent application Ser. No. 11/495,228, the disclosure of which is expressly incorporated by reference herein.

[0043] The formulations may optionally include combinations that contain other pesticidal compounds. Such additional pesticidal compounds may be fungicides, insecticides, herbicides, nematocides, miticides, arthropodicides, bactericides or combinations thereof that are compatible with the compounds of the present invention in the medium selected for application, and not antagonistic to the activity of the present compounds. Accordingly, in such embodiments, the other pesticidal compound is employed as a supplemental toxicant for the same or for a different pesticidal use. The compounds of Formula I and the pesticidal compound in the combination can generally be present in a weight ratio of from 1:100 to 100:1.

[0044] The compounds of the present disclosure may also be combined with other fungicides to form fungicidal mixtures and synergistic mixtures thereof. The fungicidal compounds of the present disclosure are often applied in conjunction with one or more other fungicides to control a wider variety of undesirable diseases. When used in conjunction with other fungicide(s), the presently claimed compounds may be formulated with the other fungicide(s), tank mixed with the other fungicide(s) or applied sequentially with the

other fungicide(s). Such other fungicides may include 2-(thiocyanatomethylthio)-benzothiazole, 2-phenylphenol, 8-hydroxyquinoline sulfate, ametoctradin, amisulbrom, antimycin, *Ampelomyces quisqualis*, azaconazole, azoxystrobin, *Bacillus subtilis*, benalaxyl, benomyl, benthiavalicarb-isopropyl, benzylaminobenzene-sulfonate (BABBS) salt, bicarbonates, biphenyl, bismethiazol, bitertanol, bixafen, blastidicin-S, borax, Bordeaux mixture, boscalid, bromuconazole, bupirimate, calcium polysulfide, captafol, captan, carbendazim, carboxin, carpropamid, carvone, chloroneb, chlorothalonil, chlozolate, *Coniothyrium minitans*, copper hydroxide, copper octanoate, copper oxychloride, copper sulfate, copper sulfate (tribasic), cuprous oxide, cyazofamid, cyflufenamid, cymoxanil, cyproconazole, cyprodinil, dazomet, debacarb, diammonium ethylenebis-(dithiocarbamate), dichlofluanid, dichlorophen, diclocymet, diclomezone, dichloran, diethofencarb, difenoconazole, difenzoquat ion, diflufenetorim, dimethomorph, dimoxystrobin, diniconazole, diniconazole-M, dinobuton, dinocap, diphenylamine, dithianon, dodemorph, dodemorph acetate, dodine, dodine free base, edifenphos, enestrobin, epoxiconazole, ethaboxam, ethoxyquin, etridiazole, famoxadone, fenamidone, fenarimol, fenbuconazole, fenfuram, fenhexamid, fenoxanil, fenpiclonil, fenpropidin, fenpropimorph, fentin, fentin acetate, fentin hydroxide, ferbam, ferimzone, fluaiznam, fludioxonil, flumorph, fluopicolide, fluopyram, fluoroimide, fluoxastrobin, fluquinconazole, flusilazole, flusulfamide, flutianil, flutolanil, flutriafol, folpet, formaldehyde, fosetyl, fosetyl-aluminium, fuberidazole, furalaxyl, furametpyr, guazatine, guazatine acetates, GY-81, hexachlorobenzene, hexaconazole, hymexazol, imazalil, imazalil sulfate, imibenconazole, iminoctadine, iminoctadine triacetate, iminoctadine tris(albesilate), ipconazole, iprobenfos, iprodione, iprovalicarb, isoprothiolane, isopyrazam, isotianil, kasugamycin, kasugamycin hydrochloride hydrate, kresoxim-methyl, mancopper, mancozeb, mandipropamid, maneb, mepanipyrim, mepronil, mercuric chloride, mercuric oxide, mercurous chloride, metalaxyl, mephenoxam, metalaxyl-M, metam, metam-ammonium, metam-potassium, metam-sodium, metconazole, methasulfocarb, methyl iodide, methyl isothiocyanate, metiram, metominostrobin, metrafenone, mildiomicin, myclobutanil, nabam, nitrothal-isopropyl, nuarimol, oethilnone, ofurace, oleic acid (fatty acids), orysastrobin, oxadixyl, oxine-copper, oxpoconazole fumarate, oxycarboxin, pefurazoate, penconazole, pencycuron, penflufen, pentachlorophenol, pentachlorophenyl laurate, penthiopyrad, phenylmercury acetate, phosphonic acid, phthalide, picoxystrobin, polyoxin B, polyoxins, polyoxorim, potassium bicarbonate, potassium hydroxyquinoline sulfate, probenazole, prochloraz, procymidone, propamocarb, propamocarb hydrochloride, propiconazole, propineb, proquinazid, prothioconazole, pyraclostrobin, pyrametostrobin, pyraoxystrobin, pyrazophos, pyribencarb, pyributicarb, pyrifenox, pyrimethanil, pyroquilon, quinoctamine, quinoxyfen, quintozone, *Reynoutria sachalinensis* extract, sedaxane, silthiofam, simeconazole, sodium 2-phenylphenoxide, sodium bicarbonate, sodium pentachlorophenoxide, spiroxamine, sulfur, SYP-Z071, SYP-Z048, tar oils, tebuconazole, tebufloquin, tecnazene, tetraconazole, thiabendazole, thifluzamide, thiophanate-methyl, thiram, tiadinil, tolclofos-methyl, tolylfluanid, triadimefon, triadimenol, triazoxide, tricyclazole, tridemorph, trifloxystrobin, triflumizole, triforine, triticonazole, validamycin, valifenalate, valiphenal, vinclozolin, zineb, ziram, zoxamide, *Candida*

oleophila, *Fusarium oxysporum*, *Gliocladium* spp., *Phlebiopsis gigantea*, *Streptomyces griseoviridis*, *Trichoderma* spp., (RS)—N-(3,5-dichlorophenyl)-2-(methoxymethyl)-succinimide, 1,2-dichloropropane, 1,3-dichloro-1,1,3,3-tetrafluoroacetone hydrate, 1-chloro-2,4-dinitronaphthalene, 1-chloro-2-nitropropane, 2-(2-heptadecyl-2-imidazolin-1-yl)ethanol, 2,3-dihydro-5-phenyl-1,4-dithiane 1,1,4,4-tetraoxide, 2-methoxyethylmercury acetate, 2-methoxyethylmercury chloride, 2-methoxyethylmercury silicate, 3-(4-chlorophenyl)-5-methylrhodanine, 4-(2-nitroprop-1-enyl)phenyl thiocyanate, propylfos, anilazine, azithiram, barium polysulfide, Bayer 32394, benodanil, benquinol, bentazone, benzamyl, benzamyl-isobutyl, benzamyl, binapacryl, bis(methylmercury) sulfate, bis(tributyltin) oxide, buthiobate, cadmium calcium copper zinc chromate sulfate, carbamorph, CECA, chlobenthiazole, chloranilformethan, chlorfenazole, chlorquinox, clomazone, copper bis(3-phenylsilylate), copper zinc chromate, cufraneb, cupric hydrazinium sulfate, cuprobam, cyclafuramid, cypendazole, cyproflumuron, decafenin, dichloro, dichlorozone, diclobutazone, dimethirimol, dinotol, dinosulfon, dinoterbon, dipyrithione, ditalimfos, dodicin, drazoxolon, EBP, ESBP, etaconazole, etem, ethirim, fenaminosulf, fenapanil, fenitropropan, flutrimazole, furcarbanil, furconazole, furconazole-cis, furmecyclox, furophosphate, glyodine, griseofulvin, halacrin, Hercules 3944, hexylthiofos, ICA0858, isopamphos, isovaldione, mebenil, mecarbinzid, metazoxolon, methfuroxam, methylmercury dicyandiamide, metsulfos, milneb, mucochloric anhydride, myclozolin, N-3,5-dichlorophenyl-succinimide, N-3-nitrophenylitaconimide, natamycin, N-ethylmercurio-4-toluenesulfonamide, nickel bis(dimethyldithiocarbamate), OCH, phenylmercury dimethyldithiocarbamate, phenylmercury nitrate, phosphidiphen, prothiocarb, prothiocarb hydrochloride, pyracarbolid, pyridinitril, pyroxychlor, pyroxyfur, quinacetol; quinacetol sulfate, quinazamid, quinconazole, rabenzazole, salicylanilide, SSF-109, sultropen, tecoram, thiadifluor, thicyofen, thiochlorfenphim, thiophanate, thioquinox, tioxyimid, triamphos, triarimol, triazbutil, trichlamide, urbacid, and zarilamid, and any combinations thereof.

[0045] Additionally, the compounds of the present invention may be combined with other pesticides, including insecticides, nematocides, miticides, arthropodicides, bactericides or combinations thereof that are compatible with the compounds of the present invention in the medium selected for application, and not antagonistic to the activity of the present compounds to form pesticidal mixtures and synergistic mixtures thereof. The fungicidal compounds of the present disclosure may be applied in conjunction with one or more other pesticides to control a wider variety of undesirable pests. When used in conjunction with other pesticides, the presently claimed compounds may be formulated with the other pesticide(s), tank mixed with the other pesticide(s) or applied sequentially with the other pesticide(s). Typical insecticides include, but are not limited to: 1,2-dichloropropane, abamectin, acephate, acetamiprid, acetion, acetoprole, acrinathrin, acrylonitrile, alanycarb, aldicarb, aldoxycarb, aldrin, allethrin, allosamidin, allyxycarb, alpha-cypermethrin, alpha-ecdysone, alpha-endosulfan, amidithion, aminocarb, amiton, amiton oxalate, amitraz, anabasine, athidathion, azadirachtin, azamethiphos, azinphos-ethyl, azinphos-methyl, azothoate, barium hexafluorosilicate, barthrin, bendiocarb, benfuracarb, bensultap, beta-cyfluthrin, beta-cypermethrin, bifenthrin, bioallethrin, bioethanomethrin, biopermethrin,

bistrifluoron, borax, boric acid, bromfeninfos, bromocyclen, bromo-DDT, bromophos, bromophos-ethyl, bufencarb, buprofezin, butacarb, butathiofos, butocarboxim, butonate, butoxycarboxim, cadusafos, calcium arsenate, calcium polysulfide, camphechlor, carbanolate, carbaryl, carbofuran, carbon disulfide, carbon tetrachloride, carbophenothion, carbosulfan, cartap, cartap hydrochloride, chlorantranilprole, chlorbicyclen, chlordane, chlordecone, chlordimeform, chlordimeform hydrochloride, chlorethoxyfos, chlorfenapyr, chlorfeninfos, chlorfluazuron, chlormephos, chloroform, chloropicrin, chlorphoxim, chlorprazophos, chlorpyrifos, chlorpyrifos-methyl, chlorthiophos, chromafenozide, cinerin I, cinerin II, cinerins, cismethrin, cloethocarb, closantel, clothianidin, copper acetoarsenite, copper arsenate, copper naphthenate, copper oleate, coumaphos, coumthioate, crotamiton, crotoxyphos, crufomate, cryolite, cyanofenphos, cyanophos, cyanthoate, cyantranilprole, cyclothrin, cycloprothrin, cyfluthrin, cyhalothrin, cypermethrin, cyphenothrin, cyromazine, cythioate, DDT, decarbofuran, deltamethrin, demephion, demephion-O, demephion-S, demeton, demeton-methyl, demeton-O, demeton-O-methyl, demeton-S, demeton-S-methyl, demeton-S-methylsulphon, diafenthion, dialifos, diatomaceous earth, diazinon, dicapthion, dichlorfenthion, dichlorvos, dicresyl, dicrotophos, dicyclanil, dieldrin, diflubenzuron, dilor, dimethluthrin, dimethox, dimetan, dimethoate, dimethrin, dimethylvinphos, dimetilan, dinex, dinex-diclexine, dinoprop, dinosam, dinotefuran, diofenolan, dioxabenzofos, dioxacarb, dioxathion, disulfoton, dithicrofos, d-limonene, DNOC, DNOC-ammonium, DNOC-potassium, DNOC-sodium, doramectin, ecdysterone, emamectin, emamectin benzoate, EMPC, emperthrin, endosulfan, endothion, endrin, EPN, epofenonane, epinomectin, esdepalléthrine, esfenvalerate, etaphos, ethiofen-carb, ethion, ethiprole, ethoate-methyl, ethoprophos, ethyl formate, ethyl-DDD, ethylene dibromide, ethylene dichloride, ethylene oxide, etofenprox, etrimfos, EXD, famphur, fenamiphos, fenazaflo, fenchlorphos, fenethacarb, fenfluthrin, fenitrothion, fenobucarb, fenoxacrim, fenoxycarb, fenpirithrin, fenpropathrin, fensulfathion, fenthion, fenthion-ethyl, fenvalerate, fipronil, flonicamid, flubendiamide, flucifuron, flucycloxuron, flucythrinate, flufenenerim, flufenoxuron, flufenprox, fluvalinate, fonofos, formetanate, formetanate hydrochloride, formothion, formparanate, formparanate hydrochloride, fosmethilan, fospirate, fothietan, furathio-carb, furethrin, gamma-cyhalothrin, gamma-HCH, halfenprox, halofenozide, HCH, HEOD, heptachlor, heptenophos, heterophos, hexaflumuron, HHDN, hydramethylnon, hydrogen cyanide, hydroprene, hyquincarb, imidacloprid, imiprothrin, indoxacarb, iodomethane, IPSP, isazofos, isobenzan, isocarboxphos, isodrin, isofenphos, isofenphos-methyl, isoprocarb, isoprothiolane, isothioate, isoxathion, ivermectin, jasmolin I, jasmolin II, jodfenphos, juvenile hormone I, juvenile hormone II, juvenile hormone III, kelevan, kinoprene, lambda-cyhalothrin, lead arsenate, lepimectin, leptophos, lindane, lirimfos, lufenuron, lythidathion, malathion, malonoben, mazidox, mecarbam, mecarphon, menazon, mephosfolan, mercurous chloride, mesulfenfos, metaflumizone, methacrifos, methamidophos, methidathion, methiocarb, methocrotophos, methomyl, methoprene, methoxychlor, methoxyfenozide, methyl bromide, methyl isothiocyanate, methylchloroform, methylene chloride, metofluthrin, metolcarb, metoxadiazole, mevinphos, mexacarbate, milbemectin, milbemycin oxime, mipafox, mirex, molosultap, monocrotophos, monomehypo, monosultap,

morphothion, moxidectin, naftalofos, naled, naphthalene, nicotine, nifluridide, nitenpyram, nithiazine, nitrilacarb, nov-aluron, noviflumuron, omethoate, oxamyl, oxydemeton-methyl, oxydeprofos, oxydisulfoton, para-dichlorobenzene, parathion, parathion-methyl, penfluron, pentachlorophenol, permethrin, phenkapton, phenothrin, phenthoate, phorate, phosalone, phosfolan, phosmet, phosnichlor, phosphamidon, phosphine, phoxim, phoxim-methyl, pirimetaphos, pirimicarb, pirimiphos-ethyl, pirimiphos-methyl, potassium arsenite, potassium thiocyanate, pp'-DDT, prallethrin, precocene I, precocene II, precocene III, primidophos, profenofos, profuralin, promacyl, promecarb, propaphos, propetamphos, propoxur, prothidathion, prothiofos, prothoate, prototrifenbutate, pyraclofos, pyrafluprole, pyrazophos, pyresmethrin, pyrethrin I, pyrethrin II, pyrethrins, pyridaben, pyridalyl, pyridaphenthion, pyrifluquinazon, pyrimidifen, pyrimitate, pyriprole, pyriproxyfen, quassia, quinalphos, quinalphos-methyl, quinothion, rafoxanide, resmethrin, rotenone, ryania, sabadilla, schradan, selamectin, silafluofen, silica gel, sodium arsenite, sodium fluoride, sodium hexafluorosilicate, sodium thiocyanate, sophamide, spinetoram, spinosad, spiromesifen, spirotetramat, sulcofuron, sulcofuron-sodium, sulfluramid, sulfotep, sulfoxaflo, sulfuryl fluoride, sulprofos, tau-fluvalinate, tazimcarb, TDE, tebufenozide, tebufenpyrad, tebufirimfos, teflubenzuron, tefluthrin, temephos, TEPP, terallethrin, terbufos, tetrachloroethane, tetrachlorvinphos, tetramethrin, tetramethylfluthrin, theta-cypermethrin, thiacloprid, thiamethoxam, thicofos, thiocarboxime, thiocyclam, thiocyclam oxalate, thiodicarb, thiofanox, thiometon, thiosultap, thiosultap-disodium, thiosultap-monosodium, thuringiensin, tolfenpyrad, tralomethrin, transfluthrin, transpermethrin, triarathene, triazamate, triazophos, trichlorfon, trichlorometaphos-3, trichloronat, trifenofos, triflururon, trimethacarb, triprene, vamidothion, vaniliprole, XMC, xylylcarb, zeta-cypermethrin, zolaprofos, and any combinations thereof.

[0046] Additionally, the compounds of the present invention may be combined with herbicides that are compatible with the compounds of the present invention in the medium selected for application, and not antagonistic to the activity of the present compounds to form pesticidal mixtures and synergistic mixtures thereof. The fungicidal compounds of the present disclosure may be applied in conjunction with one or more herbicides to control a wide variety of undesirable plants. When used in conjunction with herbicides, the presently claimed compounds may be formulated with the herbicide(s), tank mixed with the herbicide(s) or applied sequentially with the herbicide(s). Typical herbicides include, but are not limited to: 4-CPA; 4-CPB; 4-CPP; 2,4-D; 3,4-DA; 2,4-DB; 3,4-DB; 2,4-DEB; 2,4-DEP; 3,4-DP; 2,3,6-TBA; 2,4,5-T; 2,4,5-TB; acetochlor, acifluorfen, acetonifin, acrolein, alachlor, alldochlor, alloxymid, allyl alcohol, alorac, ametrifone, ametryn, amibuzin, amicarbazone, amidosulfuron, aminocyclopyrachlor, aminopyralid, amiprofos-methyl, amitrole, ammonium sulfamate, anilofos, anisuron, asulam, atraton, atrazine, azafenidin, azimsulfuron, aziprot-ryne, barban, BCPC, beflubutamid, benazolin, bencarbazone, benfluralin, benfuresate, bensulfuron, bensulide, bentazone, benzadox, benzfendazole, benzipram, benzobicyclon, benzofenap, benzooflur, benzoilprop, benzthiazuron, bicyclopyrone, bifentox, bilanafos, bispyribac, borax, bromacil, bromobonil, bromobutide, bromofenoxim, bromoxynil, brompyrazon, butachlor, butafenacil, butamifos, butenachlor, buthiazole, buthiuron, butralin, butoxydim, buturon, buty-

late, cacodylic acid, cafenstrole, calcium chlorate, calcium cyanamide, cambendichlor, carbasulam, carbetamide, carboxazole chlorprocarb, carfentrazone, CDEA, CEPC, chlo-methoxyfen, chloramben, chloranocryl, chlorazifop, chlora-zine, chlorbromuron, chlorbufam, chloreturon, chlorfenac, chlorfenprop, chlorflurazole, chlorflurenol, chloridazon, chlorimuron, chlornitrofen, chloropon, chlorotoluron, chloroxuron, chloroxynil, chlorpropham, chlorsulfuron, chlorthal, chlorthiamid, cinidon-ethyl, cinmethylin, cinosul-furon, cisanilide, clethodim, clidinate, clodinafop, clofop, clomazone, clomeprop, cloprop, cloproxydim, clopyralid, cloransulam, CMA, copper sulfate, CPMF, CPPC, credazine, cresol, cumyluron, cyanatryl, cyanazine, cycloate, cyclosul-famuron, cycloxydim, cycluron, cyhalofop, cyperquat, cyprazine, cyprazole, cypromid, daimuron, dalapon, dazomet, delachlor, desmedipham, desmetryn, di-allate, dicamba, dichlobenil, dichloralurea, dichlormate, dichlor-prop, dichlorprop-P, diclofop, diclosulam, diethamquat, diethatyl, difenopenten, difenoxuron, difenzoquat, diflufeni-can, diflufenzopyr, dimefuron, dimepiperate, dimethachlor, dimethametryn, dimethenamid, dimethenamid-P, dimexano, dimidazon, dinitramine, dinofenate, dinoprop, dinosam, dinoseb, dinoterb, diphenamid, dipropetryn, diquat, disul, dithiopyr, diuron, DMPA, DNOC, DSMA, EBEP, eglazine, endothal, epronaz, EPTC, erbon, esprocarb, ethalfluralin, ethametsulfuron, ethidimuron, ethiolate, ethofumesate, ethoxyfen, ethoxysulfuron, etinofen, etipromid, etobenza-nid, EXD, fenasulam, fenoprop, fenoxaprop, fenoxaprop-P, fenoxasulfone, fenteracol, fenthiafop, fentrazamide, fenu-ron, ferrous sulfate, flamprop, flamprop-M, flazasulfuron, florasulam, fluazifop, fluazifop-P, fluzolate, flucarbazone, flucetosulfuron, fluchloralin, flufenacet, flufenican, flufen-pyr, flumetsulam, flumezin, flumiclorac, flumioxazin, flumi-propyn, fluometuron, fluorodifen, fluoroglycofen, fluoromi-dine, fluoronitrofen, fluothiuuron, flupoxam, flupropacil, flupropanate, flupyrsulfuron, fluridone, fluorochloridone, fluoroxypry, flurtamone, fluthiacet, fomesafen, foramsulfu-ron, fosamine, furyloxyfen, glufosinate, glufosinate-P, gly-phosate, halosafen, halosulfuron, haloxydine, haloxyfop, haloxyfop-P, hexachloroacetone, hexaflurate, hexazinone, imazamethabenz, imazamox, imazapic, imazapyr, imaza-quin, imazethapyr, imazosulfuron, indanofan, indaziflam, iodobonil, iodomethane, iodosulfuron, ioxynil, ipazine, ipfencarbazone, iprymidam, isocarbamid, isocil, isome-thiozin, isonoruron, isopolinate, isopropalin, isoproturon, isouron, isoxaben, isoxachlortole, isoxaflutole, isoxapyrifop, karbutilate, ketospiradox, lactofen, lenacil, linuron, MAA, MAMA, MCPA, MCPA-thioethyl, MCPB, mecoprop, meco-prop-P, medinoterb, mefenacet, mefluidide, mesoprazine, mesosulfuron, mesotrione, metam, metamifop, metamitron, metazachlor, metazosulfuron, metflurazon, methabenzthia-zuron, methalpropalin, methazole, methiobencarb, methio-zolin, methiuron, methometon, methoprotetryne, methyl bro-mide, methyl isothiocyanate, methylidymron, metobenzuron, metobromuron, metolachlor, metosulam, metoxuron, metribuzin, metsulfuron, molinate, monalide, monisouron, monochloroacetic acid, monolinuron, monuron, morfam-quat, MSMA, naproanilide, napropamide, naptalam, nebu-ron, nicosulfuron, nipyraclufen, nitralin, nitrofen, nitrofluor-fen, norflurazon, noruron, OCH, orbenicarb, ortho-dichlorobenzene, orthosulfamuron, oryzalin, oxadiargyl, oxadiazon, oxapyrazon, oxasulfuron, oxaziclomefone, oxy-fluorfen, parafluoron, paraquat, pebulate, pelargonic acid, pendimethalin, penoxsulam, pentachlorophenol, pen-

tanochlor, pentoxazone, perfluidone, pethoxamid, phenisopham, phenmedipham, phenmedipham-ethyl, phenobenzuron, phenylmercury acetate, picloram, picolinafen, pinoxaden, piperophos, potassium arsenite, potassium azide, potassium cyanate, pretilachlor, primisulfuron, procyzine, prodiamine, profluzol, profluralin, profoxydim, proglinazone, prometon, prometryn, propachlor, propanil, propaquizafop, propazine, propham, propisochlor, propoxycarbazine, propyrisulfuron, propyzamide, prosulfalin, prosulfocarb, prosulfuron, proxan, prynachlor, pydanon, pyraclostrobin, pyraflufen, pyrasulfotole, pyrazolynate, pyrazosulfuron, pyrazoxyfen, pyribenzoxim, pyributicarb, pyriclor, pyridafol, pyridate, pyrifthalid, pyriminobac, pyrimisulfan, pyriothiobac, pyroxasulfone, pyroxulam, quinclorac, quinmerac, quincloramine, quinonamid, quizalofop, quizalofop-P, rhodethanil, rimsulfuron, saflufenacil, S-metolachlor, sebuthylazine, sebumeton, sethoxydim, siduron, simazine, simeton, simetryn, SMA, sodium arsenite, sodium azide, sodium chlorate, sulcotrione, sulfallate, sulfentrazone, sulfometuron, sulfosulfuron, sulfuric acid, sulglycapin, swep, TCA, tebutam, tebuthiuron, tefuryltrione, tembotrione, tepaloxymid, terbacil, terbucarb, terbuchlor, terbutometon, terbuthylazine, terbutryn, tetrafluoron, thenylchlor, thiazafuoron, thiazopyr, thidiazimin, thidiazuron, thiencarbazine-methyl, thifensulfuron, thiobencarb, tiocarbazil, tioclorim, topramezone, tralkoxydim, tri-allate, triasulfuron, triaziflam, tribenuron, tricamba, triclopyr, tridiphane, trietazine, trifloxysulfuron, trifluralin, triflurosulfuron, trifop, trifoposime, trihydroxytriazine, trimeturon, tripropindan, tritac tritosulfuron, vernolate, and xylachlor.

[0047] Another embodiment of the present disclosure is a method for the control or prevention of fungal attack. This method comprises applying to the soil, plant, roots, foliage, seed or locus of the fungus, or to a locus in which the infestation is to be prevented (for example applying to cereal or grape plants), a fungicidally effective amount of one or more of the compounds of Formula I. The compounds are suitable for treatment of various plants at fungicidal levels, while exhibiting low phytotoxicity. The compounds may be useful both in a protectant and/or an eradicant fashion.

[0048] The compounds have been found to have significant fungicidal effect particularly for agricultural use. Many of the compounds are particularly effective for use with agricultural crops and horticultural plants.

[0049] It will be understood by those in the art that the efficacy of the compound for the foregoing fungi establishes the general utility of the compounds as fungicides.

[0050] The compounds have broad ranges of activity against fungicidal pathogens. Exemplary pathogens may include, but are not limited to, wheat leaf blotch (*Septoria tritici*, also known as *Mycosphaerella graminicola*), apple scab (*Venturia inaequalis*), and *Cercospora* leaf spots of sugar beets (*Cercospora beticola*), peanuts (*Cercospora arachidicola* and *Cercosporidium personatum*) and other crops, and black sigatoka of bananas (*Mycosphaerella fijiensis*). The exact amount of the active material to be applied is dependent not only on the specific active material being applied, but also on the particular action desired, the fungal species to be controlled, and the stage of growth thereof, as well as the part of the plant or other product to be contacted with the compound. Thus, all the compounds, and formulations containing the same, may not be equally effective at similar concentrations or against the same fungal species.

[0051] The compounds are effective in use with plants in a disease-inhibiting and phytologically acceptable amount. The term "disease-inhibiting and phytologically acceptable amount" refers to an amount of a compound that kills or inhibits the plant disease for which control is desired, but is not significantly toxic to the plant. This amount will generally be from about 0.1 to about 1000 ppm (parts per million), with 1 to 500 ppm being preferred. The exact concentration of compound required varies with the fungal disease to be controlled, the type of formulation employed, the method of application, the particular plant species, climate conditions, and the like. A suitable application rate is typically in the range from about 0.10 to about 4 pounds/acre (about 0.01 to 0.45 grams per square meter, g/m²).

[0052] Any range or desired value given herein may be extended or altered without losing the effects sought, as is apparent to the skilled person for an understanding of the teachings herein.

[0053] The compounds of Formula I may be made using well-known chemical procedures. Intermediates not specifically mentioned in this disclosure are either commercially available, may be made by routes disclosed in the chemical literature, or may be readily synthesized from commercial starting materials utilizing standard procedures.

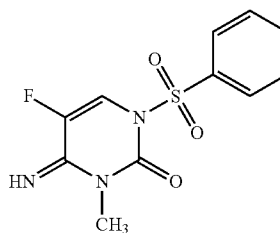
[0054] The following examples are presented to illustrate the various aspects of the compounds of the present disclosure and should not be construed as limitations to the claims.

EXAMPLES

Example 1

Preparation of 1-Benzenesulfonyl-5-fluoro-4-imino-3-methyl-3,4-dihydro-1H-pyrimidin-2-one (Compound 1)

[0055]



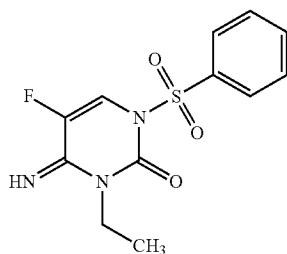
4-Amino-1-benzenesulfonyl-5-fluoro-1H-pyrimidine-2-one (200 mg, 0.74 mmol) was stirred at room temperature in dimethyl formamide (3 mL) together with anhydrous potassium carbonate (210 mg, 1.5 mmol). Iodomethane (210 mg, 1.5 mmol) was added and the mixture was heated at 60° C. for 3 hours. After cooling to room temperature, the mixture was partitioned between ethyl acetate (EtOAc) and water. The organic phase was dried over magnesium sulfate, filtered, and evaporated. The crude product was purified by chromatography on silica gel (gradient, 20 to 80% EtOAc in petroleum ether) to isolate 1-benzenesulfonyl-5-fluoro-4-imino-3-methyl-3,4-dihydro-1H-pyrimidin-2-one (106 mg, 50%) as a white solid: mp 144° C.; ¹H NMR (600 MHz, DMSO-d₆) δ 8.52 (s, 1H), 8.03-8.00 (m, 2H), 7.97 (d, J=5.9 Hz, 1H), 7.80-7.76 (m, 1H), 7.67-7.63 (m, 2H), 3.09 (s, 3H); ESIMS m/z 284 ([M+H]⁺).

[0056] Compounds 2-4 in Table 1 were prepared via this route.

Example 2

Preparation of 1-benzenesulfonyl-5-fluoro-4-imino-3-ethyl-3,4-dihydro-1H-pyrimidin-2-one (Compound 6)

[0057]



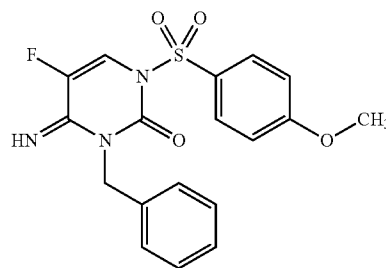
[0058] To a 25 mL sealed tube were added 4-amino-1-benzenesulfonyl-5-fluoro-1H-pyrimidine-2-one (1.0 g, 3.71 mmol), anhydrous potassium carbonate (K_2CO_3 ; 2.05 g, 14.9 mmol), and N,N-dimethylformamide (DMF; 10 mL), followed by iodoethane (EtI; 3.45 g, 22.3 mmol). The reaction vessel was sealed, and the reaction mixture was warmed to 60° C. and stirred for 1 hour. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (EtOAc; 250 mL), and washed with water (H_2O ; 3×100 mL). The organic phase was dried over magnesium sulfate ($MgSO_4$), filtered, and the solvent evaporated under reduced pressure. Purification by flash chromatography (SiO_2 , EtOAc/Hexanes gradient) afforded benzenesulfonyl-5-fluoro-4-imino-3-ethyl-3,4-dihydro-1H-pyrimidin-2-one as a pale yellow solid (200 mg; 18%); mp 163-166° C.; ^1H NMR (400 MHz, DMSO- d_6) δ 8.82 (m, 1H), 8.29 (d, J=6.8 Hz, 1H), 8.02 (dd, J=8.4, 1.1 Hz, 2H), 7.79 (ddd, J=6.9, 2.3, 1.1 Hz, 1H), 7.66 (dd, J=10.7, 4.9 Hz, 2H), 3.31 (q, J=7.2 Hz, 2H), 1.09 (t, J=7.2 Hz, 3H); ESIMS m/z 298 ($[M+H]^+$).

[0059] Compounds 7-9 were prepared as described in Example 2.

Example 3

Preparation of 3-benzyl-5-fluoro-4-imino-1-(4-methoxyphenylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one (Compound 5)

[0060]



[0061] In a 20 mL microwave vial, 5-fluoro-4-imino-1-(4-methoxyphenylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one (111 mg, 0.37 mmol) was stirred at room temperature in dimethyl formamide (3 mL) together with anhydrous potassium carbonate (210 mg, 0.55 mmol). Benzylbromide (89 μ L, 0.75 mmol) was added. The reaction was capped and placed on a Biotage Initiator microwave reactor for 20 min at 130° C., with external IR-sensor temperature monitoring from the side of the vessel. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (EtOAc; 250 mL), and washed with water (H_2O ; 3×100 mL). The organic phase was dried over magnesium sulfate ($MgSO_4$), filtered, and the solvent evaporated under reduced pressure. Purification by flash chromatography (SiO_2 , EtOAc/Hexanes gradient) afforded 3-benzyl-5-fluoro-4-imino-1-(4-methoxyphenylsulfonyl)-3,4-dihydropyrimidin-2(1H)-one as a pale yellow oil (15 mg; 11%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09-8.02 (m, 3H), 7.38-7.27 (m, 6H), 7.00-6.96 (m, 2H), 4.65 (d, J=5.7 Hz, 2H), 3.87 (s, 3H). ESIMS m/z 391 ($[M+H]^+$).

TABLE I

Compounds and Related Characterization Data				
Compound No.	Structure	Appearance	mp (° C.)	ESIMS + ^1H NMR ¹
1		white solid	144	284 δ 8.52 (s, 1H), 8.03-8.00 (m, 2H), 7.97 (d, J=5.9 Hz, 1H), 7.80-7.76 (m, 1H), 7.67-7.63 (m, 2H), 3.09 (s, 3H).

TABLE I-continued

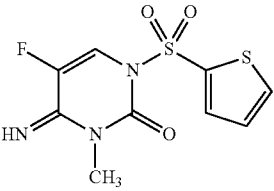
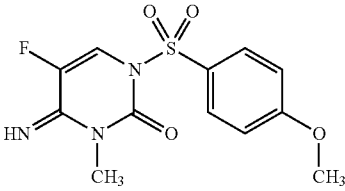
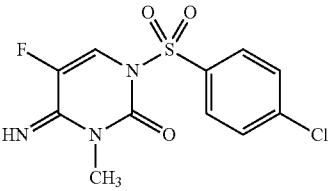
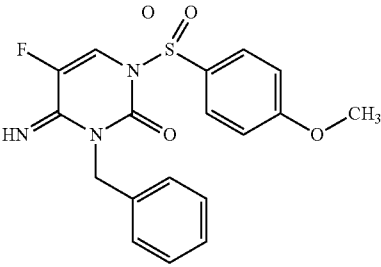
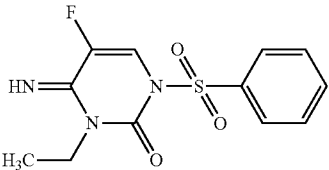
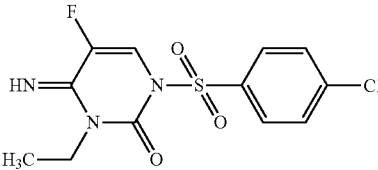
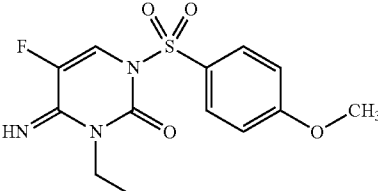
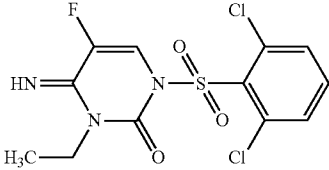
Compounds and Related Characterization Data					
Compound No.	Structure	Appearance	mp (° C.)	ESIMS +	¹ H NMR ¹
2		pale yellow solid	136-139	290	δ 8.00 (d, J = 1.32 Hz, 1H), 7.81 (m, 2H), 7.69 (d, J = 5.27 Hz, 1H), 7.18 (m, 1H), 3.37 (s, 3H).
3		pale yellow solid	158-162	314	δ 8.01 (d, J = 9.22 Hz, 2H), 7.74 (d, J = 5.27 Hz, 1H), 7.04 (d, J = 9.23 Hz, 2H), 3.90 (s, 3H), 3.31 (s, 3H).
4		white solid	147-150	318, 321	δ 8.02 (d, J = 8.9 Hz, 2H), 7.71 (d, J = 5.27 Hz, 1H), 7.57 (d, J = 8.90 Hz, 2H), 3.32 (s, 3H).
5		Yellow Oil	—	391	¹ H NMR (400 MHz, CDCl ₃) δ 8.09-8.02 (m, 3H), 7.38-7.27 (m, 6H), 7.00-6.96 (m, 2H), 4.65 (d, J = 5.7 Hz, 2H), 3.87 (s, 3H).
6		Pale Yellow solid	163-166	298	δ 8.82 (m, 1H), 8.29 (d, J = 6.8 Hz, 1H), 8.02 (dd, J = 8.4, 1.1 Hz, 2H), 7.79 (ddd, J = 6.9, 2.3, 1.1 Hz, 1H), 7.66 (dd, J = 10.7, 4.9 Hz, 2H), 3.31 (q, J = 7.2 Hz, 2H), 1.09 (t, J = 7.2 Hz, 3H).

TABLE I-continued

Compounds and Related Characterization Data				
Compound No.	Structure	Appearance	mp (° C.)	ESIMS + ¹ H NMR ¹
7		Pale Yellow Solid	165-168	332 ¹ H NMR (400 MHz, DMSO-d ₆ + D ₂ O (95:5)) δ 8.26 (d, J = 6.7 Hz, 1H), 8.04 (d, J = 8.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 2H), 3.33 (q, J = 7.3 Hz, 2H), 1.09 (t, J = 7.2 Hz, 3H).
8		Pale Yellow Solid	107-111	328 δ 8.75 (dd, J = 7.2, 3.4 Hz, 1H), 8.26 (d, J = 6.8 Hz, 1H), 7.96 (d, J = 8.9 Hz, 2H), 7.17 (d, J = 9.0 Hz, 2H), 3.87 (s, 3H), 3.32 (q, J = 7.2 Hz, 2H), 1.09 (t, J = 7.2 Hz, 3H).
9		Pale Yellow Solid	182-185	366 ¹ H NMR (400 MHz, DMSO-d ₆ + D ₂ O (95:5)) δ 8.29 (d, J = 6.5 Hz, 1H), 7.71 (m, 3H), 3.35 (q, J = 7.2 Hz, 2H), 1.11 (t, J = 1.2 Hz, 3H).

¹ All spectra were recorded in DMSO-d₆ at 300, 400 or 600 MHz unless otherwise stated.

Example 4

Evaluation of Fungicidal Activity: Leaf Blotch of Wheat (*Mycosphaerella graminicola*; anamorph: *Septoria tritici*; Bayer code SEPTTR)

[0062] Wheat plants (variety Yuma) were grown from seed in a greenhouse in 50% mineral soil/50% soil-less Metro mix until the first leaf was fully emerged, with 7-10 seedlings per pot. These plants were inoculated with an aqueous spore suspension of *Septoria tritici* either prior to or after fungicide treatments. After inoculation the plants were kept in 100% relative humidity (one day in a dark dew chamber followed by two days in a lighted dew chamber) to permit spores to germinate and infect the leaf. The plants were then transferred to a greenhouse for disease to develop.

[0063] The following table presents the activity of typical compounds of the present disclosure when evaluated in these experiments. The effectiveness of the test compounds in controlling disease was determined by assessing the severity of disease on treated plants, and then converting the severity to percent control based on the level of disease on untreated, inoculated plants.

[0064] In each case of Table II the rating scale is as follows:

% Disease Control	Rating
76-100	A
51-75	B
26-50	C
0-25	D
Not Tested	E

TABLE II

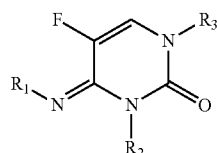
One-Day Protectant (1 DP) and Three-Day Curative (3 DC) Activity of Compounds on SEPTTR at 100 ppm		
Cmpd	SEPTTR 100 PPM 1 DP	SEPTTR 100 PPM 3 DC
1	A	A
2	A	A
3	A	A
4	A	A
5	D	D

TABLE II-continued

One-Day Protectant (1 DP) and Three-Day Curative (3 DC) Activity of Compounds on SEPTTR at 100 ppm		
Cmpd	SEPTTR 100 PPM 1 DP	SEPTTR 100 PPM 3 DC
6	D	D
7	B	A
8	D	B
9	D	A

What is claimed is:

1.



wherein R₁ is:

H;

R₂ is:

H;

C₁-C₆ alkyl optionally substituted with R₄;

benzyl optionally substituted with 1-3 R₅

R₃ is —S(O)₂R₆;

R₄ is independently halogen, C₁-C₆ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkoxy, C₁-C₄ alkylthio, C₁-C₄

haloalkylthio, amino, C₁-C₃ alkylamino, C₂-C₆ alkoxy-carbonyl, C₂-C₆ alkylcarbonyl, C₂-C₆ alkylaminocarbonyl, hydroxyl, or C₃-C₆ trialkylsilyl;

R₅ is independently halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkoxy, C₁-C₆ haloalkoxy, C₁-C₆ alkylthio, C₁-C₆ haloalkylthio, amino, C₁-C₆ alkylamino, C₂-C₆ dialkylamino, C₂-C₆ alkoxy-carbonyl, or C₂-C₆ alkylcarbonyl, nitro, hydroxyl, or cyano;

R₆ is C₁-C₆ alkyl, C₁-C₆ haloalkyl, amino, C₁-C₆ alkylamino, C₂-C₆ dialkylamino, a phenyl or benzyl wherein each of the phenyl or the benzyl may be optionally substituted with 1-3 R₅, or a 5- or 6-membered saturated or unsaturated ring containing 1-3 heteroatoms wherein each ring may be optionally substituted with 1-3 R₅.

2. A composition for the control of a fungal pathogen including the compound of claim 1 and a phylogenetically acceptable carrier material.

3. The composition of claim 2 wherein the fungal pathogen is Apple Scab (*Venturia inaequalis*), Leaf Blotch of Wheat (*Septoria tritici*), Leaf spot of sugarbeets (*Cercospora beticola*), Leaf Spot of peanut (*Cercospora arachidicola*), and Black Sigatoka (*Mycosphaerella fijiensis*).

4. A method for the control and prevention of fungal attack on a plant, the method including the steps of:

applying a fungicidally effective amount of at least one of the compounds of claim 1 to at least one of the plant, an area adjacent to the plant, soil adapted to support growth of the plant, a root of the plant, foliage of the plant, and a seed adapted to produce the plant.

* * * * *