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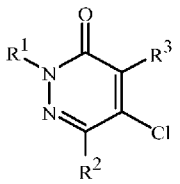
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(54) Title: INTERMEDIATES FOR PREPARING HERBICIDAL PYRIDAZINONES

(57) Abstract: Disclosed is a compound of Formula I, including *N*-oxides, and salts thereof, wherein R^1, R^2 and R^3 are defined as set forth in the disclosure. Also disclosed is a process for preparing a compound of Formula I. A compound of Formula I can also be used as a synthetic intermediate to prepare pyridazinone-based herbicides.



I

WO 2020/069056 A1

TITLE

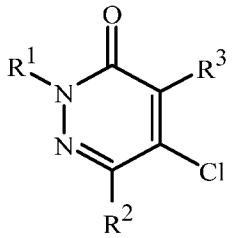
INTERMEDIATES FOR PREPARING HERBICIDAL PYRIDAZINONES

BACKGROUND OF THE INVENTION

The present disclosure provides pyridazinones and a process for preparing pyridazinones. The pyridazinones disclosed herein can be used as synthetic intermediates to prepare pyridazinone-based herbicides. WO 2015/168010 and WO 2017/074988 disclose herbicidal pyridazinones and synthetic intermediates used to prepare herbicidal pyridazinones. There exists a need for improved methods of preparing herbicidal pyridazinones.

SUMMARY OF THE INVENTION

In one aspect, the present disclosure provides a compound of Formula **I** and *N*-oxides or salts thereof,



I

wherein

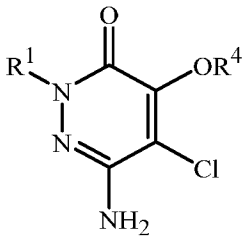
R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

R^2 is Cl or NH_2;

R^3 is Cl or OR^4; and

R^4 is C_1–C_4 alkyl, SO_2CF_3 or SO_2(4-Me-Ph).

In another aspect, the present disclosure provides a process for preparing a compound of Formula **I-A**,



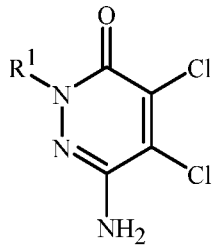
I-A

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl

comprising reacting a compound of Formula **II**



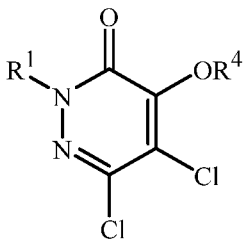
II

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl

with an alkoxylating agent.

In another aspect, the present disclosure provides a process for preparing a compound of Formula **I-B**



I-B

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl

comprising reacting a compound of Formula **I-A**, as set forth above, with an alkyl nitrite in the presence of CuCl or $CuCl_2$.

DETAILED DESCRIPTION OF THE INVENTION

As used herein, the terms “comprises,” “comprising,” “includes,” “including,” “has,” “having,” “contains”, “containing,” “characterized by” or any other variation thereof, are intended to cover a non-exclusive inclusion, subject to any limitation explicitly indicated. For example, a process or method that comprises a list of elements is not necessarily limited to

only those elements but may include other elements not expressly listed or inherent to such composition process or method.

The transitional phrase "consisting of" excludes any element, step, or ingredient not specified. If in the claim, this phrase excludes materials other than those expressly recited except for impurities ordinarily associated therewith. When the phrase "consisting of" appears in a clause of the body of a claim, rather than immediately following the preamble, it limits only the element set forth in that clause; other elements are not excluded from the claim as a whole.

The transitional phrase "consisting essentially of" is used to define a process or method that includes materials, steps, features, components, or elements, in addition to those literally disclosed, provided that these additional materials, steps, features, components, or elements do not materially affect the basic and novel characteristic(s) of the disclosure. The term "consisting essentially of" occupies a middle ground between "comprising" and "consisting of".

Where applicants have defined the disclosure or a portion thereof with an open-ended term such as "comprising," it should be readily understood that (unless otherwise stated) the description should be interpreted to also describe such a disclosure using the terms "consisting essentially of" or "consisting of."

Further, unless expressly stated to the contrary, "or" refers to an inclusive or and not to an exclusive or. For example, a condition A or B is satisfied by any one of the following: A is true (or present) and B is false (or not present), A is false (or not present) and B is true (or present), and both A and B are true (or present).

Also, the indefinite articles "a" and "an" preceding an element or component of the disclosure are intended to be nonrestrictive regarding the number of instances (i.e. occurrences) of the element or component. Therefore "a" or "an" should be read to include one or at least one, and the singular word form of the element or component also includes the plural unless the number is obviously meant to be singular.

As used herein, the term "C_1–C_6 alkyl" includes straight-chain or branched alkyl groups having one to six carbon atoms, e.g., methyl, ethyl, *n*-propyl, *i*-propyl, or the different butyl, pentyl, or hexyl isomers. Likewise, the term "C_1–C_4 alkyl" includes straight-chain or branched alkyl having one to four carbon atoms, e.g., methyl, ethyl, *n*-propyl, *i*-propyl, or the different butyl isomers, and the term "C_1–C_3 alkyl" includes methyl, ethyl, *n*-propyl, and *i*-propyl. As used herein, the term "C_3–C_6 cycloalkyl" includes cyclopropyl, cyclobutyl,

cyclopentyl and cyclohexyl. As used herein, the term "halogen" includes fluorine, chlorine, bromine and iodine.

The term "reacting" and the like refer to adding, contacting, or mixing two or more reagents under appropriate conditions to produce the indicated and/or the desired product. It should be appreciated that the reaction which produces the indicated and/or the desired product may not necessarily result directly from the combination of two reagents which were initially added, i.e. there may be one or more intermediates which are produced in the mixture which ultimately leads to the formation of the indicated and/or the desired product. Reacting can take place in the presence or absence of solvent, at a temperature above room temperature or below room temperature, under an inert atmosphere, etc.

Pressure is defined as the pressure measured relative to the ambient atmospheric pressure. The term "psig" means pounds per square inch gague.

The term "alkoxylating agent" as used herein refers to a chemical reagent used to add a C_1–C_4 alkoxy group to a compound. As used herein, the term "C_1–C_4 alkoxy" includes methoxy, ethoxy, *n*-propyloxy, isopropyloxy and the different butoxy isomers. Exemplary non-limiting alkoxylating agents include sodium methoxide and sodium ethoxide. Likewise, the term "methoxylating agent" as used herein refers to a chemical reagent used to add a methoxy group, i.e. OCH_3, to a starting compound. The term "alkyl nitrite" as used herein refers to a compound having the formula R-ONO, wherein R is a C_1–C_6 alkyl. Exemplary non-limiting alkyl nitrites include *tert*-butyl nitrite, amyl nitrite and *n*-butyl nitrite. When R^4 is "SO_2(4-Me-Ph)" this is alternatively defined as "SO_2(*p*-tolyl)."

Compounds of Formula **I** typically exist in more than one solid form. Thus, compounds of Formula **I** include all crystalline and non-crystalline forms of the compounds within the genus represented by Formula **I**. Non-crystalline forms include embodiments which are solids such as waxes and gums as well as embodiments which are liquids such as solutions and melts. Crystalline forms include embodiments which represent essentially a single crystal type and embodiments which represent a mixture of polymorphs (i.e. different crystalline types). The term "polymorph" refers to a particular crystalline form of a chemical compound that can crystallize in different crystalline forms, these forms having different arrangements and/or conformations of the molecules in the crystal lattice. Although polymorphs can have the same chemical composition, they can also differ in composition due the presence or absence of co-crystallized water or other molecules, which can be weakly or strongly bound in the lattice. Polymorphs can differ in such chemical, physical and biological properties as crystal shape,

density, hardness, color, chemical stability, melting point, hygroscopicity, suspensibility, dissolution rate and biological availability.

One skilled in the art will appreciate that a polymorph of a compound of Formula **I** can exhibit beneficial effects (e.g., suitability for improved solubility) relative to another polymorph or a mixture of polymorphs of the same compound of Formula **I**. Preparation and isolation of a particular polymorph of a compound of Formula **I** can be achieved by methods known to those skilled in the art including, for example, crystallization using selected solvents and temperatures. For a comprehensive discussion of polymorphism see R. Hilfiker, Ed., *Polymorphism in the Pharmaceutical Industry*, Wiley-VCH, Weinheim, 2006.

Synthetic methods for the preparation of *N*-oxides of heterocycles and tertiary amines are well known by one skilled in the art. Exemplary procedures for preparing *N*-oxides include the oxidation of heterocycles and tertiary amines with peroxy acids such as peracetic and *m*-chloroperbenzoic acid (MCPBA), hydrogen peroxide, alkyl hydroperoxides such as *t*-butyl hydroperoxide, sodium perborate, and dioxiranes such as dimethyldioxirane. Methods for the preparation of *N*-oxides have been extensively described and reviewed in the literature, see for example: T. L. Gilchrist in *Comprehensive Organic Synthesis*, vol. 7, pp 748–750, S. V. Ley, Ed., Pergamon Press; M. Tisler and B. Stanovnik in *Comprehensive Heterocyclic Chemistry*, vol. 3, pp 18–20, A. J. Boulton and A. McKillop, Eds., Pergamon Press; M. R. Grimmett and B. R. T. Keene in *Advances in Heterocyclic Chemistry*, vol. 43, pp 149–161, A. R. Katritzky, Ed., Academic Press; M. Tisler and B. Stanovnik in *Advances in Heterocyclic Chemistry*, vol. 9, pp 285–291, A. R. Katritzky and A. J. Boulton, Eds., Academic Press; and G. W. H. Cheeseman and E. S. G. Werstiuk in *Advances in Heterocyclic Chemistry*, vol. 22, pp 390–392, A. R. Katritzky and A. J. Boulton, Eds., Academic Press. That said, one skilled in the art will appreciate that not all nitrogen-containing heterocycles can form *N*-oxides since the nitrogen requires an available lone pair of electrons for oxidation to the oxide; one skilled in the art will recognize those nitrogen-containing heterocycles which can form *N*-oxides.

One skilled in the art recognizes that under some process conditions, chemical compounds can be isolated in nonsalt or salt forms. Thus, a wide variety of salts of the compounds disclosed here can be isolated using the present process or processes depending on the base utilized in the method to prepare the compounds. Suitable salts include acid-addition salts with inorganic or organic acids such as hydrobromic, hydrochloric, nitric,

phosphoric, sulfuric, acetic, butyric, fumaric, lactic, maleic, malonic, oxalic, propionic, salicylic, tartaric, 4-toluenesulfonic or valeric acids.

Embodiments of the present disclosure include:

Embodiment A1. A compound of Formula **I** and *N*-oxides or salts thereof as described in the Summary of the Invention.

Embodiment A2. The compound of Embodiment A1 wherein R^1 is C_1–C_4 alkyl.

Embodiment A3. The compound of Embodiment A1 wherein R^1 is C_3–C_6 cycloalkyl.

Embodiment A4. The compound of any one of Embodiments A1 to A2 wherein R^1 is methyl or ethyl.

Embodiment A5. The compound of Embodiment A4 wherein R^1 is methyl.

Embodiment A6. The compound of any one of Embodiments A1 to A5 wherein R^2 is Cl.

Embodiment A7. The compound of any one of Embodiments A1 to A5 wherein R^2 is NH_2.

Embodiment A8. The compound of any one of Embodiments A1 to A7 wherein R^3 is Cl.

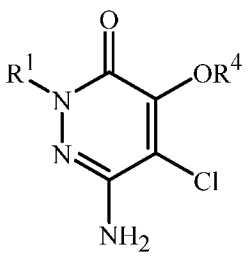
Embodiment A9. The compound of any one of Embodiments A1 to A7 wherein R^3 is OR^4.

Embodiment A10. The compound of Embodiment A9 wherein R^4 is C_1–C_4 alkyl.

Embodiment A11. The compound of Embodiment A10 wherein R^4 is methyl, ethyl, *n*-propyl or *i*-propyl.

Embodiment A12. The compound of Embodiment A9 wherein R^4 is SO_2CF_3 or SO_2(4-Me-Ph).

Embodiment A13. A compound of Formula **I** in the Summary of the Invention that is a compound of Formula **I-A**



I-A

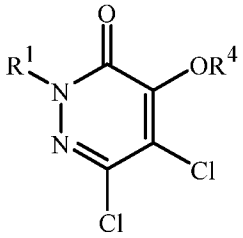
wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

R^3 is OR^4; and

R^4 is C_1–C_4 alkyl.

Embodiment A14. A compound of Formula **I** in the Summary of the Inveniton that is a compound Formula **I-B**



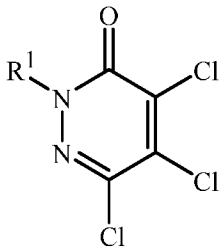
I-B

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl.

Embodiment A15. A compound of Formula **I** in the Summary of the Invention that is a compound Formula **I-C**



I-C

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl.

Embodiment A16. A compound of any one of Embodiments A1, A2, A4 or A6 through A15 wherein R^1 is methyl.

Embodiment A17. A compound of any one of Embodiments A1 through A5 or A-6 through A16 wherein R^2 is other than Cl (i.e. is other than a compound of Formula **I-B** or **I-C**).

Embodiment A18. A compound of Embodiment A1 that is other than 4,5,6-trichloro-2-methyl-3(2*H*)-pyridazinone (CAS No. 37648-42-3) and 6-amino-4,5-dichloro-2-methyl-3(2*H*)-pyridazinone (CAS No. 25717-64-0).

Embodiment B1. A process for preparing a compound of Formula **I-A** as described in the Summary of the Invention.

Embodiment B2. The process of Embodiment B1 wherein R^1 is C_3–C_6 cycloalkyl.

Embodiment B3. The process of Embodiment B1 wherein R^1 is C_1–C_4 alkyl.

Embodiment B4. The process of Embodiment B1 or B3 wherein R^1 is methyl.

Embodiment B5. The process of any one of Embodiments B1 to B4 wherein the reacting is performed in a suitable solvent.

Embodiment B6. The process of Embodiment B5 wherein the suitable solvent is methanol or dioxane.

Embodiment B7. The process of any one of Embodiments B1 to B6 wherein the reacting is performed at a temperature at or below 0 °C.

Embodiment B8. The process of any one of Embodiments B1 to B6 wherein the reacting is performed at a temperature above 0 °C.

Embodiment B9. The process of any one of Embodiments B1 to B8 wherein the alkoxylating agent is sodium methoxide or potassium methoxide.

Embodiment B10. The process of any one of Embodiments B1 and B3 to B9 wherein R^1 is methyl.

Embodiment B11. The process of any one of Embodiments B1 to B10 wherein the compound of Formula **I-A** is isolated.

Embodiment C1. A process for preparing a compound of Formula **I-B** as described in the Summary of the Invention.

Embodiment C2. The process of Embodiment C1 wherein R^1 is C_3–C_6 cycloalkyl.

Embodiment C3. The process of Embodiment C1 wherein R^1 is C_1–C_4 alkyl.

Embodiment C4. The process of any one of Embodiments C1 or C3 wherein R^1 is methyl.

Embodiment C5. The process of any one of Embodiments C1 to C4 wherein R^4 is methyl or ethyl.

Embodiment C6. The process of any one of Embodiments C1 to C5 wherein the reacting is performed in a suitable solvent.

Embodiment C7. The process of Embodiment C6 wherein the suitable solvent is acetonitrile.

Embodiment C8. The process of any one of Embodiments C1 to C7 wherein the reacting is performed at a temperature at or below 0 °C.

Embodiment C9. The process of any one of Embodiments C1 to C7 wherein the reacting is performed at a temperature above 0 °C.

Embodiment C10. The process of any one of Embodiments C1 through C9 wherein the alkyl nitrite is *tert*-butyl nitrite.

Embodiment C11. The process of any one of Embodiments C1 to C6 or C9 to C10 wherein the reacting is performed at a temperature between 0 °C and 180 °C.

Embodiment C12. The process of Embodiment C11 wherein the reacting is performed at a temperature between 0 °C and 80 °C.

Embodiment C13. The process of any one of Embodiments C1, C3 or C5 through C12 wherein R^1 is methyl.

Embodiment C14. The process of any one of Embodiments C1 to C13 wherein the compound of Formula **I-B** is isolated.

Embodiment D1. A process for preparing a compound of Formula **I-C** as described in the Summary of the Invention.

Embodiment D2. The process of Embodiment D1 wherein R^1 is C_3–C_6 cycloalkyl.

Embodiment D3. The process of Embodiment D1 wherein R^1 is C_1–C_4 alkyl.

Embodiment D4. The process of Embodiment D1 or D3 wherein R^1 is methyl.

Embodiment D5. The process of any one of Embodiments D1 to D4 wherein the reacting is performed neat or in a suitable solvent.

Embodiment D6. The process of Embodiment D5 wherein the suitable solvent is acetonitrile.

Embodiment D7. The process of Embodiment D5 wherein the reacting is performed neat.

Embodiment D8. The process of any one of Embodiments D1 to D7 wherein the reacting is performed at a temperature between 80 °C and 150 °C.

Embodiment D9. The process of any one of Embodiment D8 wherein the reacting is performed at a temperature between 100 °C and 140 °C.

Embodiment D10. The process of Embodiment D8 wherein the reacting is performed at a temperature between 120 °C and 140 °C.

Embodiment D11. The process of Embodiment D8 wherein the reacting is performed at a temperature between 100 °C and 120 °C.

Embodiment D12. The process of Embodiment D8 wherein the reacting is performed at a temperature of 120 °C.

Embodiment D13. The process of Embodiment D8 wherein the pressure at 100 °C is up to 117 psig (807 kPa).

Embodiment D14. The process of Embodiment D8 wherein the pressure at 120 °C is up to 150 psig (1034 kPa).

Embodiment D15. The process of Embodiment D8 wherein the pressure at 140 °C is up to 223 psig (1538 kPa).

Embodiment D16. The process of any one of Embodiments D1 to D9 wherein the reacting is in the presence of *N*,*N*-dimethylformamide.

Embodiment D17. The process of Embodiment D10 wherein the reacting is in the presence of *N*,*N*-dimethylformamide between 10 mol% and 100 mol%.

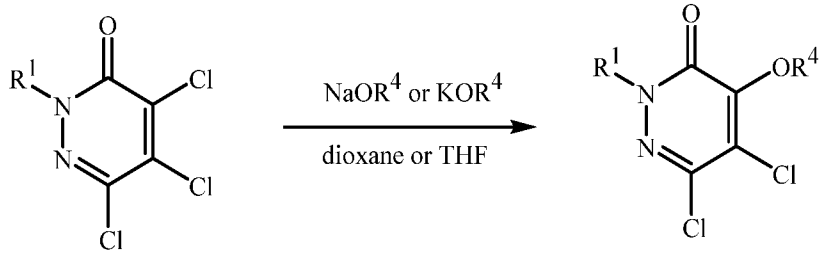
Embodiment D18. The process of Embodiment D11 wherein the reacting is in the presence of *N*,*N*-dimethylformamide between 20 mol% and 30 mol%.

Embodiment D19. The process of any one of Embodiments D1 to D12 wherein the compound of Formula **I-C** is isolated.

Embodiments A1 through A18, B1 through B11, C1 through C14 and D1 through D19 and any other Embodiment or Embodiments described herein can be combined in any manner.

A compound of Formula **I-B** can be prepared by the reaction of a trichloropyridazinone compound of Formula **I-C** with either sodium or potassium alkoxide in a solvent such as 1,4-dioxane or tetrahydrofuran at temperatures ranging from 0 °C up to the reflux temperature of the solvent as depicted in Scheme 1. The preparation of a compound of Formula **I-C** is described in *J. Het. Chem.* **1972**, vol. 9, p. 471.

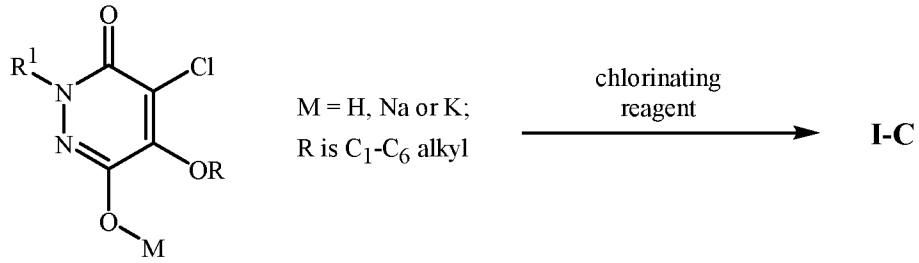
Scheme 1



I-C **I-B**

As shown in Scheme 2, a compound of Formula **I-C** can alternatively be prepared by the chlorination of a compound of Formula **3** (wherein M is H, Na or K) using one or more chlorinating reagents, such as $POCl_3$, PCl_3, PCl_5 and combinations thereof. Typically, the reaction is conducted neat in the chlorinating reagent, or in the combination of chlorinating reagents, at 80 °C to 150 °C, preferably around 100 °C.

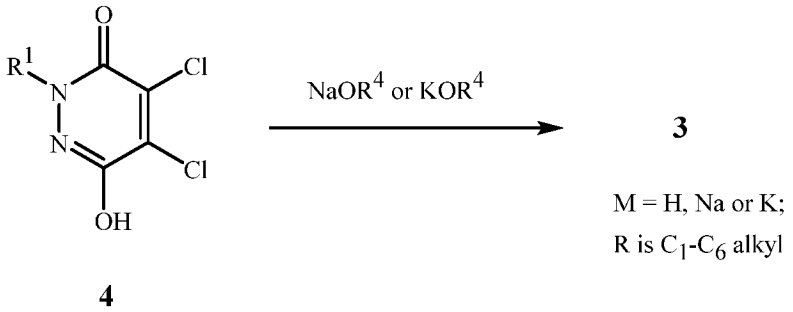
Scheme 2



3

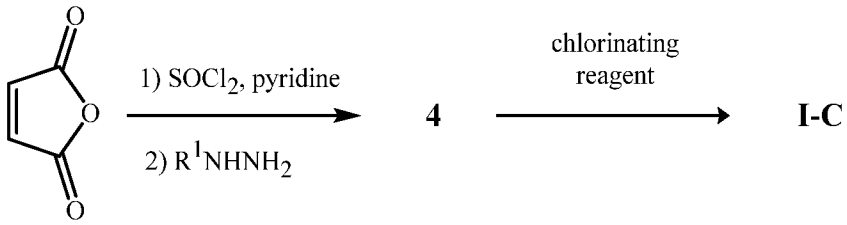
As shown in Scheme 3, a compound of Formula **3** can be prepared by treatment of a compound of Formula **4** with sodium or potassium alkoxide in an organic solvent, such as methanol, ethanol, isopropanol or tetrahydrofuran. Typically, in alcoholic solvents the reaction is conducted at 60 °C to 150 °C, preferably 70 °C to 80 °C. Typically, in non-alcoholic solvents, such as tetrahydrofuran, the reaction is conducted at 0 °C to 20 °C, preferably 0 °C to 5 °C. The method of Scheme 3 is illustrated in present Synthesis Example 3.

Scheme 3



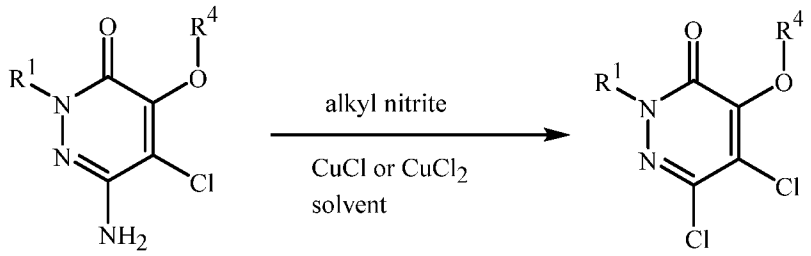
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A compound of Formula **I-C** can also be prepared from maleic anhydride in two steps as described in WO 8704321 A2 and JP47024029B and as shown in Scheme 4. Alternative conditions for the second reaction of Scheme 4 include using one or more chlorinating reagents, such as $POCl_3$, PCl_3, PCl_5 and combinations thereof in the presence of *N*,*N*-dimethylformamide in a sealed reactor. Typically, the reaction is conducted neat at 80 °C to 150 °C, preferably 100 °C to 120 °C. The amount of *N*,*N*-dimethylformamide can be from 10 mol% to 100 mol%, preferably 20 mol% to 30 mol%. The reaction can be conducted neat or in an organic solvent, such as acetonitrile. The second reaction of Scheme 4 is illustrated in present Synthesis Example 4. Scheme 4



A compound of Formula **I-B** can be prepared using the procedures depicted in Scheme 5. An amino-pyridazinone compound of Formula **I-A** can be treated with an alkyl nitrite, such as tert-butyl nitrite or isoamyl nitrite, and either CuCl or $CuCl_2$ in a solvent such as acetonitrile at temperatures ranging from 0 °C to the refluxing temperature of the solvent. An analogous procedure can be found on page 82 in WO2010/009183. Alternative conditions for the reaction in Scheme 5 include reacting a compound of Formula **I-A** with sodium nitrite and concentrated hydrochloric acid, optionally in a solvent such as acetonitrile. An analogous procedure can be found on page 223 in WO2012/091156.

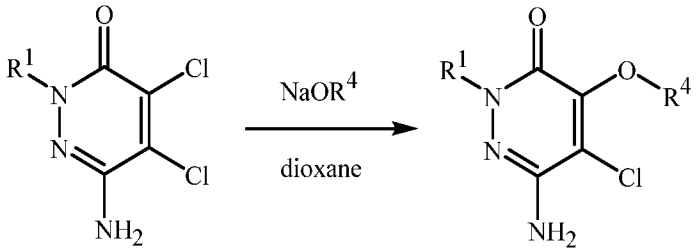
Scheme 5



I-A **I-B**

The preparation of a compound of Formula **I-A** can be achieved by the treatment of a compound of Formula **5** with sodium alkoxide in dioxane as depicted in Scheme 6. In Scheme 5, sodium alkoxide (1.0-1.5 molar equivalents), either as a solid or as a 25% alcoholic solution, can be added to a solution of Compound **5** in dioxane, and the resulting mixture can be stirred at a temperature of preferably 10 °C up to the reflux temperature of the solvent. The preparation of a compound of Formula **5** is described in *J. Het. Chem.* **1996**, vol. 33, p. 1915. See also *J. Het. Chem.* **1996**, vol. 33, p. 1579.

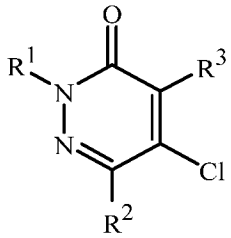
Scheme 6



5 **I-A**

Without further elaboration, it is believed that one skilled in the art using the preceding description can utilize the present disclosure to its fullest extent. The following non-limiting Examples are illustrative of the disclosure. Steps in the following Examples illustrate a procedure for each step in an overall synthetic transformation, and the starting material for each step may not have necessarily been prepared by a particular preparative run whose procedure is described in other Examples or Steps.

The compounds and processes described for preparing a compound of Formula **I**, **I-A**, **I-B** and **I-C** herein are useful for preparing herbicidal pyridazinones. Notably where a compound of Formula **I**



I

wherein

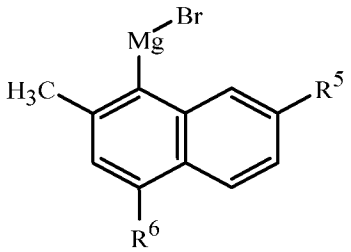
R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

R^2 is Cl;

R^3 is Cl or OR^4; and

R^4 is C_1–C_4 alkyl, SO_2CF_3 or SO_2(4-Me-Ph);

can be reacted with a compound of Formula **III**



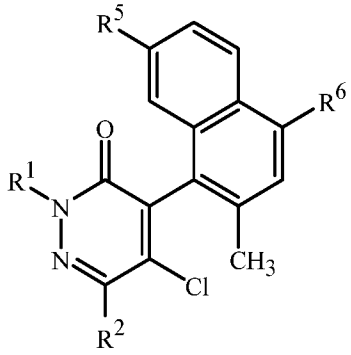
III

wherein

R^5 is H, F, Cl or CH_3; and

R^6 is H or Cl;

under suitable conditions to provide a compound of Formula **IV**



IV

wherein

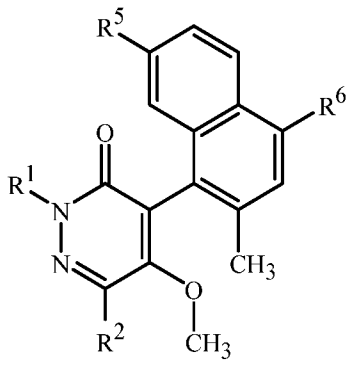
R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

R^2 is Cl;

R^5 is H, F, Cl or CH_3; and

R^6 is H or Cl.

A compound of Formula **IV** can further be reacted with a methoxylating agent to prepare a compound of Formala **V**



V

wherein

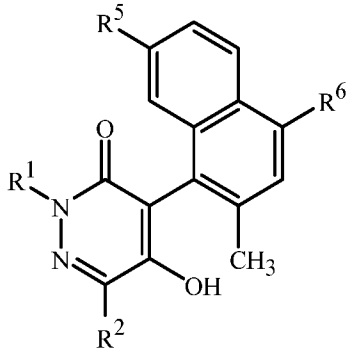
R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

R^2 is Cl;

R^5 is H, F, Cl or CH_3;

R^6 is H or Cl; and

A compound of Formula **V** can be reacted with a demethylating agent (such as morpholine) to prepare a compound of Formula **VI**



VI

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

R^2 is Cl;

R^5 is H, F, Cl or CH_3; and

R^6 is H or Cl.

Preferrably in the compounds of Formulae **I**, **IV**, **V** and **VI**; R^1 is methyl. Preferrably in the compounds of Formulae **IV**, **V** and **VI**; R^5 is H. Preferrably in the compounds of Formulae **IV**, **V** and **VI**; R^5 is CH_3. Preferrably in the compound of Formulae **IV**, **V** and **VI**; R^6 is H. Compounds of Formula **VI** are known from WO 2015/168010 to posess herbicidal activity.

Without further elaboration, it is believed that one skilled in the art using the preceding description can utilize the present disclosure to its fullest extent. The following non-limiting Examples are illustrative of the disclosure. Steps in the following Examples illustrate a procedure for each step in an overall synthetic transformation, and the starting material for each step may not have necessarily been prepared by a particular preparative run whose procedure is described in other Examples or Steps. Percentages are by weight except for chromatographic solvent mixtures or where otherwise indicated. Parts and percentages for chromatographic solvent mixtures are by volume unless otherwise indicated. ^{1}H NMR spectra are reported in ppm downfield from tetramethylsilane in $CDCl_3$ unless otherwise indicated; "s" means singlet and "br s" means broad singlet.

SYNTHESIS EXAMPLE 1

Preparation of 6-amino-5-chloro-4-methoxy-2-methyl-3(2*H*)-pyridazinone

A solution of sodium methoxide in methanol (4.8 mL of a 4.4 M solution, 21.0 mmol) was added to a suspension of 6-amino-4,5-dichloro-2-methyl-3(2*H*)-pyridazinone (3.70 g, 19.1 mmol) and dioxane (95 mL, anhydrous) with ice-water bath cooling. The resulting suspension was stirred at ambient temperature for 3 h and was then poured into a saturated aqueous ammonium chloride solution (150 mL) and the resulting mixture was extracted with methylene chloride (150 mL). The aqueous layer was extracted two more times with methylene chloride and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated to give 3.45 g of the title compound as a yellow semi-solid. ^{1}H NMR (500 MHz) δ 4.34 (br s, 2H), 4.29 (s, 3H), 3.60 (s, 3H).

SYNTHESIS EXAMPLE 2

Preparation of 5,6-dichloro-4-methoxy-2-methyl-3(2*H*)-pyridazinone

To a solution of 6-amino-5-chloro-4-methoxy-2-methyl-3(2*H*)-pyridazinone (i.e. the product obtained in Synthesis Example 1, 529 mg, 2.8 mmol), copper(II) chloride (618 mg,

4.6 mmol) and acetonitrile (8 mL, anhydrous) was added *tert*-butyl nitrite (0.48 mL, 90% by weight, 3.6 mmol) with ice-water bath cooling. The resulting mixture was stirred at ambient temperature for 1 h and was then partitioned between ethyl acetate and a saturated aqueous ammonium chloride solution. The organic layer was washed with a saturated aqueous ammonium chloride solution, dried over anhydrous magnesium sulfate, filtered and concentrated to give 0.51 g of the title compound as a yellow semi-solid.

^{1}H NMR (500 MHz) δ 4.33 (s, 3H), 3.74 (s, 3H).

SYNTHESIS EXAMPLE 3

Preparation of 2-methyl-4,5,6-trichloro-3(2*H*)-pyridazinone

A mixture of 4,5-dichloro-1,2-dihydro-1-methyl-3,6-pyridazinedione (10 g, 51 mmol), phosphorous oxychloride (8.4 g, 55 mmol) and *N*,*N*-dimethylformamide (0.37 g, 5.1 mmol) was sealed in a pressure reactor, heated to 120 °C. The reaction was agitated for 6 h. During the reaction, the reaction pressure increased by 150 psig (1034 kPa). The reaction was cooled to room temperature. Water (100 mL) was added to the resultant mixture, agitated for 1 h, filtered, washed with water (20 mL) and dried under vacuum. To the filtered solid was added hexanes (30 mL) at 5 °C, filtered and dried to give 8.7 g of the title compound as a beige solid.

^{1}H NMR (500 MHz) δ 3.86 (s).

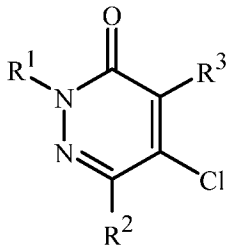
SYNTHESIS EXAMPLE 4

Preparation of 5,6-dichloro-4-methoxy-2-methyl-3(2*H*)-pyridazinone

To a solution of 2-methyl-4,5,6-trichloro-3(2*H*)-pyridazinone (i.e. the product obtained in Synthesis Example 3, 12 g, 56 mmol) in tetrahydrofuran (96 mL) at 1 °C was slowly added sodium methoxide (25% in methanol, 12.7 g, 59 mmol) over 30 min. The resulting mixture was warmed to room temperature over 30 min. Water (100 mL) was added. The organic layer was separated and concentrated to give 21 g of a beige solid. The solid was recrystallized from methanol/water (60 mL/60 mL) to yield 8.25 g of the title compound as a beige solid.

^{1}H NMR (500 MHz) δ 4.33 (s, 3H), 3.74 (s, 3H). Representative examples of synthetic intermediates useful in the preparation of herbicidal pyridazinones are shown in Table 1.

TABLE 1



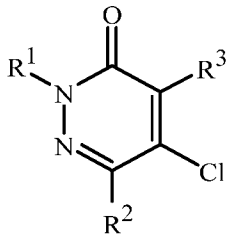
R^1	R^2	R^3
CH_3	NH_2	OCH_3
CH_3	Cl	OCH_3
CH_3	Cl	Cl

All patents and publications cited herein are fully incorporated by reference in their entirety.

CLAIMS

What is claimed is:

1. A compound of Formula **I** and *N*-oxides and/or salts thereof



I

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl;

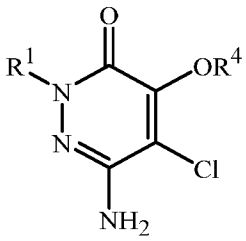
R^2 is Cl or NH_2;

R^3 is Cl or OR^4; and

R^4 is C_1–C_4 alkyl, SO_2CF_3 or SO_2(4-Me-Ph)

provided the compound of Formula **I** is other than 4,5,6-trichloro-2-methyl-3(2*H*)-pyridazinone and 6-amino-4,5-dichloro-2-methyl-3(2*H*)-pyridazinone.

2. The compound of Claim 1 that is a compound of Formula **I-A**



I-A

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl.

3. The compound of Claim 2 wherein

R^1 is C_1–C_4 alkyl; and

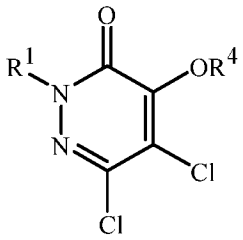
R^4 is methyl, ethyl, *n*-propyl or *i*-propyl.

4. The compound of Claim 3 wherein

R^1 is methyl; and

R^4 is methyl.

5. The compound of Claim 1 that is a compound of Formula **I-B**



I-B

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl.

6. The compound of Claim 5 wherein

R^1 is C_1–C_4 alkyl; and

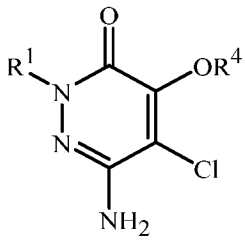
R^4 is methyl, ethyl, *n*-propyl or *i*-propyl.

7. The compound of Claim 6 wherein

R^1 is methyl; and

R^4 is methyl.

8. A process for preparing a compound of Formula **I-A**



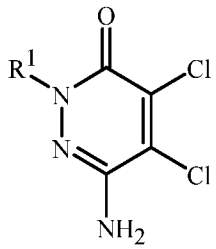
I-A

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl

comprising reacting a compound of Formula **II**



II

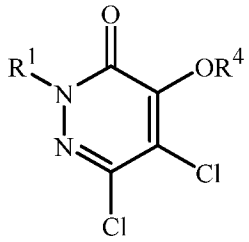
wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl

with an alkoxylating agent.

9. The process of Claim 8 wherein R^1 is methyl.

10. A process for preparing a compound of Formula **I-B**



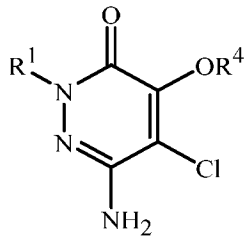
I-B

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl

comprising reacting a compound of Formula **I-A**



I-A

wherein

R^1 is C_1–C_4 alkyl or C_3–C_6 cycloalkyl; and

R^4 is C_1–C_4 alkyl

with an alkyl nitrite in the presence of CuCl or $CuCl_2$.

11. The process of Claim 10 wherein R^1 is methyl.

12. The process of Claim 10 wherein R^4 is methyl.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/053052

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D237/14 C07D237/16 C07D237/22
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

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)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 519 092 A (SYNGENTA LTD [GB]) 15 April 2015 (2015-04-15) pages 10,11 -----	1-7
X	PARK ET AL: "Synthesis of novel acyclonucleosides containing pyridazine", JOURNAL OF HETEROCYCLIC CHEMISTRY, vol. 37, no. 1, 1 January 2000 (2000-01-01), pages 5-10, XP055641424, compounds 5b,c -----	1
X	US 3 661 904 A (IIZUKI MASAO ET AL) 9 May 1972 (1972-05-09) claims 1-3 -----	1
	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
14 November 2019	20/02/2020

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Grassi, Damian

2

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 978 665 A (TANIKAWA KEIZO [JP] ET AL) 18 December 1990 (1990-12-18) EXAMPLE 11: 2-ethyl-4,5,6-trichloro-3(2H)pyridazinone	1
X	DATABASE PubChem compound [Online] 20 May 2016 (2016-05-20), XP002795585, retrieved from NCBI Database accession no. 119054678 compound 119054678	1
X	DATABASE PubChem compound [Online] 20 May 2016 (2016-05-20), XP002795586, retrieved from NCBI Database accession no. 119054682 compound 119054682	1
X	DATABASE PubChem compound [Online] 20 May 2016 (2016-05-20), XP002795587, retrieved from NCBI Database accession no. 119054681 compound 119054681	1
X	DATABASE PubChem compound [Online] 20 May 2016 (2016-05-20), XP002795588, retrieved from NCBI Database accession no. 119054680 compound 119054680	1
X	DATABASE PubChem compound [Online] 20 May 2016 (2016-05-20), XP002795589, retrieved from NCBI Database accession no. 119054679 compound 119054679	1
X	US 9 693 556 B2 (SYNGENTA LTD [GB]) 4 July 2017 (2017-07-04) column 16, lines 5-53	1-7
X	US 9 049 864 B2 (SYNGENTA LTD [GB]) 9 June 2015 (2015-06-09) formula (2); columns 1,10	1-7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/053052

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.:
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:

see additional sheet

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 an 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.:

1-7

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-7

   Compounds according to claim 1 (the group is still not unitary).

   ---

2. claims: 8-12

   Process according to claim 8 or 10 (the group is still not unitary).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2019/053052

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2519092 A	15-04-2015	NONE	
US 3661904 A	09-05-1972	NONE	
US 4978665 A	18-12-1990	AT 83773 T	15-01-1993
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		EP 2836488 A1	18-02-2015
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		PT 2836488 E	03-06-2016
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		US 2015031540 A1	29-01-2015
		UY 34737 A	29-11-2013
		WO 2013160126 A1	31-10-2013