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Señora Jefe de la
DIVISION DE NUEVAS CREACIONES
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
E. S. D.

Referencia : Expediente No. 01.002.407
Solicitante : DOW AGROSCIENCES LLC
Asunto : Solicitud de patente para:
"4-AMINOPICOLINATOS Y SU USO COMO HERBICIDAS"
Fecha de solicitud : 15 de enero de 2001

TRAMITE 002 EVENTO 001 ACTUACION 829

1. Yo, Emilio FERRERO, obrando como apoderado de la solicitante en el asunto de la referencia, atentamente, presento con este escrito la copia certificada de la solicitud de patente estadounidense No. 60/176,720^V del 14 de enero de 2000.

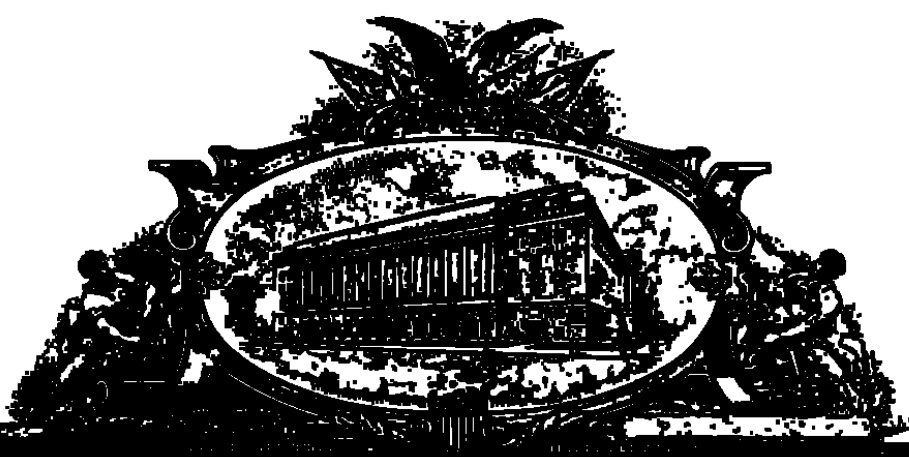
2. Ruego a la Señora Jefe se sirva aceptar este escrito con sus anexos, y se continúe con el trámite de la solicitud.

Bogotá, - 2 ABR. 2001
Señora Jefe,


EMILIO FERRERO
T.P.A. No. 31.929

COLO 10975-801-006-9
ASN- ID-74

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United States Patent and Trademark Office

November 22, 2000

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE UNDER 35 USC 111.

APPLICATION NUMBER: 60/176,720 ✓
FILING DATE: January 14, 2000



By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS

L. Edelen
L. EDELEN
Certifying Officer

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U.S. PATENT AND TRADEMARK OFFICE
PROVISIONAL APPLICATION COVER SHEET

This is a request for filing a **PROVISIONAL APPLICATION** under 37 CFR 1.53(b)(2).

Docket Number		80,888 PROV1	Type a plus sign (+) inside this box	+
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TITLE OF THE INVENTION (280 characters max)				
4-AMINOPICOLINATES AND THEIR USE AS HERBICIDES				
CORRESPONDENCE ADDRESS				
Dow AgroSciences LLC 9330 Zionsville Road Indianapolis				
State: Indiana		Zip Code: 46268	Country: USA	
ENCLOSED APPLICATION PARTS (check all that apply)				
☒ Specification		Number of Pages: 55	☐ Small Entity Statement	
☐ Drawing(s)		Number of Sheets: None	☐ Other (specify)	
METHOD OF PAYMENT (check one)				
A check or money order is enclosed to cover the Provisional Filing fees			PROVISIONAL FILING FEE	
☒ The Commissioner is hereby authorized to charge filing fees and credit Deposit Account Number: 04-1629			AMOUNT \$150.00	

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

Craig E. Mijan

Date

January 14, 2000

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☐ Additional inventors are being named on separately numbered sheets attached hereto

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4-AMINOPICOLINATES AND THEIR USE AS HERBICIDES

Background of the Invention

5 This invention relates to certain novel 4-aminopicolinates and their derivatives and to the use of these compounds as herbicides.

10 A number of picolinic acids and their pesticidal properties have been described in the art. For example, U.S. Patent 3,285,925 discloses 4-amino-3,5,6-trichloropicolinic acid derivatives and their use as plant growth control agents and herbicides. U.S. Patent 3,325,272 discloses 4-amino-3,5-dichloropicolinic acid derivatives and their use for the control of plant growth. U.S. Patent 3,317,549 discloses 3,6-dichloro-picolinic acid derivatives and their use as plant growth control agents. U.S. Patent 3,334,108 discloses chlorinated dithiopicolinic acid derivatives and their use as parasitocides. U.S. Patent 3,234,229 discloses 4-amino-polychloro-2-trichloromethylpyridines and their use as herbicides. In 20 *Applied and Environmental Microbiology*, Vol. 59, No. 7, July 1993, pp. 2251-2256, 4-amino-3,6-dichloropicolinic acid is identified as a product of the anaerobic degradation of 4-amino-3,5,6-trichloropicolinic acid, the commercially available herbicide picloram.

25 While picloram is recommended for the control of woody plants and broadleaf weeds in certain applications, its properties are not ideal. It would be highly desirable to discover related compounds that are more potent, more selective or of broader spectrum in their herbicidal 30 activity and/or that have improved toxicological or environmental properties.

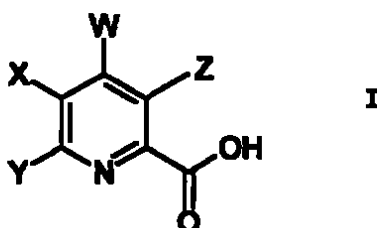
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Summary of the Invention

It has now been found that certain 4-amino-
picolinic acids and their derivatives having selected
substituents in the 3-, 5-, and 6-positions are potent
5 herbicides with a broad spectrum of weed control and
excellent crop selectivity. The compounds further possess
excellent toxicological or environmental profiles.

The invention includes compounds of Formula I:



10

wherein

X represents H, halogen, C₁-C₆ alkoxy, C₁-C₆
alkylthio, aryloxy, cyano or trifluoromethyl;

Y represents halogen, C₁-C₆ alkoxy, C₁-C₆
15 alkylthio, aryloxy, cyano or trifluoromethyl;

Z represents halogen, C₁-C₆ alkoxy, C₁-C₆
alkylthio, aryloxy, cyano or trifluoromethyl;

W represents -NR₁R₂, -N=CR₃R₄ or -NHN=CR₃R₄

where

20 R₁ and R₂ independently represent H, C₁-C₆ alkyl,
C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl, heteroaryl, hydroxy, C₁-
C₆ alkoxy, amino, C₁-C₆ acyl, C₁-C₆ carboalkoxy, C₁-C₆
alkylcarbonyl, C₁-C₆ alkylsulfonyl, C₁-C₆ trialkylsilyl or
C₁-C₆ dialkyl phosphonyl or R₁ and R₂ taken together with N

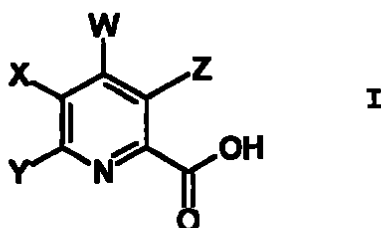
represent a 5- or 6-membered saturated or unsaturated ring which may contain additional O or N heteroatoms; and

5 R_3 and R_4 independently represent H, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, aryl or heteroaryl or R_3 and R_4 taken together with -C represent a 5- or 6-membered saturated ring; and

agriculturally acceptable derivatives of the carboxylic acid, with the proviso that when X represents H or Cl, then Y and Z are not both Cl.

10 Compounds of Formula I wherein X represents H or F, wherein Y represents F, Cl, or Br, wherein Z represents Cl and wherein R_1 and R_2 represent H or C_1-C_6 alkyl are independently preferred.

15 The invention includes herbicidal compositions comprising a herbicidally effective amount of a 4-aminopicolinate of Formula I:



wherein

20 X represents H, halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

Y represents halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

25 Z represents halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

W represents $-NR_1R_2$, $-N-CR_3R_4$ or $-NHN-CR_3R_4$

where

5 R_1 and R_2 independently represent H, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, aryl, heteroaryl, hydroxy, C_1-C_6 alkoxy, amino, C_1-C_6 acyl, C_1-C_6 carboalkoxy, C_1-C_6 alkylcarbamyl, C_1-C_6 alkylsulfonyl, C_1-C_6 trialkylsilyl or C_1-C_6 dialkyl phosphonyl or R_1 and R_2 taken together with N represent a 5- or 6-membered saturated or unsaturated ring which may contain additional O or N heteroatoms; and

10 R_3 and R_4 independently represent H, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl, aryl or heteroaryl or R_3 and R_4 taken together with $-C$ represent a 5- or 6-membered saturated ring; and

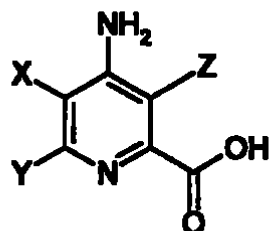
15 agriculturally acceptable derivatives of the carboxylic acid, with the proviso that when X represents Cl, then Y and Z are not both Cl

in admixture with an agriculturally acceptable adjuvant or carrier. The invention also includes a method of use of the compounds and compositions of the present invention to
20 kill or control undesirable vegetation by application of an herbicidal amount of the compound to the vegetation or to the locus of the vegetation as well as to the soil prior to emergence of the vegetation. The use of the compounds to kill or control woody plants and broadleaf weeds in grass
25 crops is a preferred utility and post-emergent application of the compounds to the undesirable vegetation is a preferred method of application.

Detailed Description of the Invention

30 The herbicidal compounds of the present invention are derivatives of 4-aminopicolinic acids:

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These compounds are characterized by possessing halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl substituents in the 3-position with chlorine being preferred; by possessing hydrogen, halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl substituents in the 5-position with hydrogen being preferred; and by possessing halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl substituents in the 6-position with fluorine, chlorine or bromine being preferred.

The amino group at the 4-position can be unsubstituted or substituted with one or more C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl, heteroaryl, hydroxy, C₁-C₆ alkoxy or amino substituents. The amino group can be further derivatized as an amide, a carbamate, a urea, a sulfonamide, a silylamine, a phosphoramidate, an imine or a hydrazone. Such derivatives are capable of breaking down into the amine. An unsubstituted amino group or one substituted with one or more alkyl substituents is preferred.

The carboxylic acids of Formula I are believed to be the compounds that actually kill or control undesirable vegetation and are typically preferred. Analogs of these compounds in which the acid group of the picolinic acid is derivatized to form a related substituent that can be transformed within plants or the environment to a acid group possess essentially the same herbicidal effect and are within the scope of the invention. Therefore, an "agriculturally acceptable derivative", when used to describe the carboxylic acid functionality at the 2-

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position, is defined as any salt, ester, amide or any other acid derivative well known in the art which (a) does not substantially affect the herbicidal activity of the active ingredient, i.e., the 4-aminopicolinic acid, and (b) is or
5 can be hydrolyzed in plants or soil to the picolinic acid of Formula I that, depending upon the pH, is in the dissociated or the undissociated form.

Suitable salts include those derived from alkali or alkaline earth metals and those derived from ammonia and
10 amines. Preferred cations include sodium, potassium, magnesium, and aminium cations of the formula:



wherein R_5 , R_6 , and R_7 each, independently represents hydrogen or C_1 - C_{12} alkyl, C_3 - C_{12} alkenyl or C_3 - C_{12} alkynyl,
15 each of which is optionally substituted by one or more hydroxy, C_1 - C_4 alkoxy, C_1 - C_4 alkylthio or phenyl groups, provided that R_5 , R_6 , and R_7 are sterically compatible. Additionally, any two of R_5 , R_6 , and R_7 together may represent an aliphatic difunctional moiety containing 1 to
20 12 carbon atoms and up to two oxygen or sulfur atoms. Salts of the compounds of Formula I can be prepared by treatment of compounds of Formula I with a metal hydroxide, such as sodium hydroxide, or an amine, such as ammonia, trimethylamine, diethanolamine, 2-methylthiopropylamine,
25 bisallylamine, 2-butoxyethylamine, morpholine, cyclo-dodecylamine, or benzylamine. Amine salts are often preferred forms of the compounds of Formula I because they are water-soluble and lend themselves to the preparation of desirable aqueous based herbicidal compositions.

30 Suitable esters include those derived from C_1 - C_{12} alkyl, C_3 - C_{12} alkenyl or C_3 - C_{12} alkynyl alcohols, such as methanol, iso-propanol, butanol, 2-ethylhexanol, butoxyethanol, methoxypropanol, allyl alcohol, propargyl alcohol or cyclohexanol. Esters can be prepared by
35 reacting the corresponding acid chloride of a picolinic

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acid of Formula I with an appropriate alcohol or by
reacting the corresponding picolinic acid of Formula I with
an appropriate alcohol in the presence of an acid catalyst.
Suitable amides include those derived from ammonia or from
5 C₁-C₁₂ alkyl, C₃-C₁₂ alkenyl or C₃-C₁₂ alkynyl mono- or di-
substituted amines, such as but not limited to trimethyl-
amine, diethanolamine, 2-methylthiopropylamine, bisallyl-
amine, 2-butoxyethylamine, morpholine, cyclododecylamine,
or benzylamine. Amides can be prepared by reacting the
10 corresponding picolinic acid chloride of Formula I with
ammonia or an appropriate amine.

The terms "alkyl", "alkenyl" and "alkynyl", as
well as derivative terms such as "alkoxy", "acyl",
"alkylthio" and "alkylsulfonyl", as used herein, include
15 within their scope straight chain, branched chain and
cyclic moieties. Unless specifically stated otherwise,
each may be unsubstituted or substituted with one or more
substituents selected from but not limited to halogen,
hydroxy, alkoxy, alkylthio, C₁-C₆ acyl, formyl, cyano,
20 aryloxy or aryl, provided that the substituents are
sterically compatible and the rules of chemical bonding and
strain energy are satisfied. The terms "alkenyl" and
"alkynyl" are intended to include one or more unsaturated
bonds.

The term "aryl" refers to a phenyl or naphthyl
group. The term "heteroaryl" refers to a 5- or 6-membered
aromatic ring containing one or more heteroatoms, viz., N,
O or S; these heteroaromatic rings may be fused to other
aromatic systems. The aryl or heteroaryl substituents may
25 be unsubstituted or substituted with one or more
substituents selected from halogen, hydroxy, nitro, cyano,
aryloxy, formyl, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl,
C₁-C₆ alkoxy, halogenated C₁-C₆ alkyl, halogenated C₁-C₆
alkoxy, C₁-C₆ acyl, C₁-C₆ alkylthio, C₁-C₆ alkylsulfinyl, C₁-C₆
35 alkylsulfonyl, aryl, C₁-C₆ OC(O)alkyl, C₁-C₆ NHC(O)alkyl,
C(O)OH, C₁-C₆ C(O)Oalkyl, C(O)NH₂, C₁-C₆ C(O)NHalkyl, or C₁-C₆

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C(O)N(alkyl)₂, provided that the substituents are sterically compatible and the rules of chemical bonding and strain energy are satisfied.

Unless specifically limited otherwise, the term
5 halogen includes fluorine, chlorine, bromine, and iodine.

The compounds of Formula I can be made using well-known chemical procedures. The required starting materials are commercially available or readily synthesized utilizing standard procedures.

10 4-N- amide, carbamate, urea, sulfonamide, silylamine and phosphoramidate amino derivatives can be prepared by the reaction of the free amino compound with, for example, a suitable acid halide, chloroformate, carbamyl chloride, sulfonyl chloride, silyl chloride or
15 chlorophosphate. The imine or hydrazone can be prepared by reaction of the free amine or hydrazine with a suitable aldehyde or ketone.

6-Bromo analogs can be prepared by the reduction of several key intermediates, e.g., the corresponding 6-
20 bromo-4-azido, 6-bromo-4-nitro, and 6-bromo-4-nitro pyridine N-oxide analogs. These intermediates, in turn, can be prepared either by nucleophilic displacement of 6-bromo-4-halo analogs with NaN₃ or by electrophilic nitration of the corresponding 6-bromopyridine-N-oxides.
25 Alternatively, such analogs can be prepared by direct amination of the corresponding 4,6-dibromo analogs.

6-Fluoro analogs can be prepared by direct amination of the corresponding 4,6-difluoro analog.

3- and 5-Alkoxy and aryloxy analogs can be
30 prepared by reduction of the corresponding 4-azido derivatives, which in turn can be prepared by nucleophilic displacement of the corresponding 4-bromopyridines with

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NaN₃. The required 3- and 5-alkoxy-4-bromopyridines can be prepared according to literature procedures.

6-Alkoxy, alkylthio and aryloxy analogs can be prepared by nucleophilic displacement with alkoxide or
5 thioalkoxide on the appropriate 6-halopyridine.

3- and 5-Alkylthio analogs can be prepared by lithiation of the appropriate chloropyridines at low temperature and sequential treatment with alkyl disulfides and carbon dioxide. Reaction of the resulting picolinic
10 acids with ammonium hydroxide gave the desired products.

6-Cyano analogs can be prepared by amination of the appropriate 4-halo-6-cyanopicolinate. 4-Halo-6-cyanopicolinate can be prepared by action of TMSCN on the appropriate pyridine N-oxide, which can be prepared by
15 hydrogen peroxide mediated oxidation of the corresponding pyridine.

3- and 5-Cyano analogs can be prepared by action of KCN on the appropriate fluoropyridine at high temperature.

20 6-Trifluoromethyl analogs can be prepared by amination of readily available methyl trifluoromethylpicolinate (oxidative halogenation of the 4-position followed by displacement with ammonia or an amine equivalent) followed by chlorination of the 3- and 5-
25 positions.

3- and 5-Trifluoromethyl analogs can be prepared by standard manipulations known to those skilled in the art starting from the known compounds 2-fluoro-3-chloro-5-trifluoromethylpyridine and 2,5-dichloro-3-
30 trifluoromethylpyridine.

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Substituted 4-amino analogs can be prepared by reacting the corresponding 4-halopyridine-2-carboxylate with the substituted amine.

5 The compounds of Formula I, obtained by any of these processes, can be recovered by conventional means. Typically, the reaction mixture is acidified with an aqueous acid, such as hydrochloric acid, and extracted with an organic solvent, such as ethyl acetate or dichloro-
10 methane. The organic solvent and other volatiles can be removed by distillation or evaporation to obtain the desired compound of Formula I, which can be purified by standard procedures, such as by recrystallization or chromatography.

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15 The compounds of Formula I have been found to be useful pre-emergence and post-emergence herbicides. They can be employed at non-selective (higher) rates of application to control a broad spectrum of the vegetation in an area or at lower rates of application for the selective control of undesirable vegetation. Areas of
20 application include pasture and rangelands, roadsides and rights of ways, and crops such as corn, rice and cereals. It is usually preferred to employ the compounds post-emergence. It is further usually preferred to use the compounds to control a wide spectrum of broadleaf weeds,
25 including Dock species (*Rumex* spp), Canada thistle (*Cirsium arvense*), pigweed species (*Amaranthus* spp.), Senna species (*Cassia* spp.), spurge species (*Euphorbia* spp), ragweed species (*Ambrosia* spp.), Sida species (*Sida* spp.), field bindweed (*Convolvulus arvensis*), and knapweed
30 species (*Centaurea* spp.), among others. Use of the compounds to control undesirable vegetation in grassy areas is especially indicated. While each of the 4-aminopicolinate compounds encompassed by Formula I is within the scope of the invention, the degree of herbicidal
35 activity, the crop selectivity, and the spectrum of weed control obtained varies depending upon the substituents

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present. An appropriate compound for any specific herb-
icidal utility can be identified by using the information
presented herein and routine testing.

5 The term herbicide is used herein to mean an
active ingredient that kills, controls or otherwise
adversely modifies the growth of plants. An herbicidally
effective or vegetation controlling amount is an amount of
active ingredient which causes an adversely modifying
effect and includes deviations from natural development,
10 killing, regulation, desiccation, retardation, and the
like. The terms plants and vegetation include germinant
seeds, emerging seedlings and established vegetation.

Herbicidal activity is exhibited by the compounds
of the present invention when they are applied directly to
15 the plant or to the locus of the plant at any stage of
growth or before planting or emergence. The effect
observed depends upon the plant species to be controlled,
the stage of growth of the plant, the application
parameters of dilution and spray drop size, the particle
20 size of solid components, the environmental conditions at
the time of use, the specific compound employed, the
specific adjuvants and carriers employed, the soil type,
and the like, as well as the amount of chemical applied.
These and other factors can be adjusted as is known in the
25 art to promote non-selective or selective herbicidal
action. Generally, it is preferred to apply the compounds
of Formula I postemergence to relatively immature
undesirable vegetation to achieve the maximum control of
weeds.

30 Application rates of about 1 to about 500 g/Ha
are generally employed in postemergence operations; for
preemergence applications, rates of about 10 to about 1000
g/Ha are generally employed. The higher rates designated
generally give non-selective control of a broad variety of
35 undesirable vegetation. The lower rates typically give

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selective control and can be employed in the locus of crops.

5 The herbicidal compounds of the present invention are often best applied in conjunction with one or more other herbicides to obtain control of a wider variety of undesirable vegetation. When used in conjunction with other herbicides, the presently claimed compounds can be formulated with the other herbicide or herbicides, tank mixed with the other herbicide or herbicides, or applied sequentially with the other herbicide or herbicides. Some of the herbicides that can be employed in conjunction with the compounds of the present invention include sulfonamides such as metosulam, flumetsulam, cloransulam-methyl, diclosulam, and N-2,6-dichlorophenyl-5-ethoxy-7-fluoro- [1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonamide, sulfonylureas such as chlorimuron, nicosulfuron and metsulfuron, imidazolinones such as imazaquin, imazapic, imazethapyr and imazamox, phenoxyalkanoic acids such as 2,4-D and MCPA, pyridinyloxyacetic acids such as triclopyr and fluroxypyr, carboxylic acids such as clopyralid and dicamba, dinitroanilines such as trifluralin and pendimethalin, chloroacetanilides such as alachlor, acetochlor and metolachlor and other common herbicides including acifluorfen, bentazon, clomazone, fumiclorac, fluometuron, fomesafen, lactofen, linuron, isoproturon, and metribuzin. They can, further, be used in conjunction with glyphosate and glufosinate on glyphosate-tolerant or glufosinate-tolerant crops. It is generally preferred to use the compounds of the invention in combination with herbicides that are selective for the crop being treated and which complement the spectrum of weeds controlled by these compounds at the application rate employed. It is further generally preferred to apply the compounds of the invention and other complementary herbicides at the same time, either as a combination formulation or as a tank mix.

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The compounds of the present invention can generally be employed in combination with known herbicide safeners, such as cloquintocet, furilazole, dichlormid, benoxacor, mefenpyr-ethyl, fenclorazole-ethyl, flurazole, and fluxofenim, to enhance their selectivity. They can additionally be employed to control undesirable vegetation in many crops that have been made tolerant to or resistant to them or to other herbicides by genetic manipulation or by mutation and selection. For example, corn, wheat, rice, soybean, sugarbeet, cotton, canola, and other crops that have been made tolerant or resistant to compounds that are acetolactate synthase inhibitors in sensitive plants can be treated. Many glyphosate and glufosinate tolerant crops can be treated as well, alone or in combination with these herbicides. Some crops (e.g. cotton) have been made tolerant to auxinic herbicides such as 2,4-dichlorophenoxyacetic acid. These herbicides may be used to treat such resistant crops or other auxin tolerant crops.

While it is possible to utilize the 4-aminopicolinate compounds of Formula I directly as herbicides, it is preferable to use them in mixtures containing a herbicidally effective amount of the compound along with at least one agriculturally acceptable adjuvant or carrier. Suitable adjuvants or carriers should not be phytotoxic to valuable crops, particularly at the concentrations employed in applying the compositions for selective weed control in the presence of crops, and should not react chemically with the compounds of Formula I or other composition ingredients. Such mixtures can be designed for application directly to weeds or their locus or can be concentrates or formulations that are normally diluted with additional carriers and adjuvants before application. They can be solids, such as, for example, dusts, granules, water dispersible granules, or wettable powders, or liquids, such as, for example, emulsifiable concentrates, solutions, emulsions or suspensions.

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Suitable agricultural adjuvants and carriers that are useful in preparing the herbicidal mixtures of the invention are well known to those skilled in the art.

Liquid carriers that can be employed include
5 water, toluene, xylene, petroleum naphtha, crop oil, acetone, methyl ethyl ketone, cyclohexanone, trichloroethylene, perchloroethylene, ethyl acetate, amyl acetate, butyl acetate, propylene glycol monomethyl ether and diethylene glycol monomethyl ether, methanol, ethanol,
10 isopropanol, amyl alcohol, ethylene glycol, propylene glycol, glycerine, and the like. Water is generally the carrier of choice for the dilution of concentrates.

Suitable solid carriers include talc, pyrophyllite clay, silica, attapulgus clay, kieselguhr, chalk,
15 diatomaceous earth, lime, calcium carbonate, bentonite clay, Fuller's earth, cotton seed hulls, wheat flour, soybean flour, pumice, wood flour, walnut shell flour, lignin, and the like.

It is usually desirable to incorporate one or
20 more surface-active agents into the compositions of the present invention. Such surface-active agents are advantageously employed in both solid and liquid compositions, especially those designed to be diluted with carrier before application. The surface-active agents can
25 be anionic, cationic or nonionic in character and can be employed as emulsifying agents, wetting agents, suspending agents, or for other purposes. Typical surface-active agents include salts of alkyl sulfates, such as diethanolammonium lauryl sulfate; alkylarylsulfonate salts, such as
30 calcium dodecylbenzenesulfonate; alkylphenol-alkylene oxide addition products, such as nonylphenol-C₁₂ ethoxylate; alcohol-alkylene oxide addition products, such as tridecyl alcohol-C₁₂ ethoxylate; soaps, such as sodium stearate; alkyl-naphthalenesulfonate salts, such as sodium dibutyl-
35 naphthalenesulfonate; dialkyl esters of sulfosuccinate

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salts, such as sodium di(2-ethylhexyl) sulfosuccinate; sorbitol esters, such as sorbitol oleate; quaternary amines, such as lauryl trimethylammonium chloride; polyethylene glycol esters of fatty acids, such as polyethylene glycol stearate; block copolymers of ethylene oxide and propylene oxide; and salts of mono and dialkyl phosphate esters.

Other adjuvants commonly used in agricultural compositions include compatibilizing agents, antifoam agents, sequestering agents, neutralizing agents and buffers, corrosion inhibitors, dyes, odorants, spreading agents, penetration aids, sticking agents, dispersing agents, thickening agents, freezing point depressants, antimicrobial agents, and the like. The compositions may also contain other compatible components, for example, other herbicides, plant growth regulants, fungicides, insecticides, and the like and can be formulated with liquid fertilizers or solid, particulate fertilizer carriers such as ammonium nitrate, urea and the like.

The concentration of the active ingredients in the herbicidal compositions of this invention is generally from about 0.001 to about 98 percent by weight. Concentrations from about 0.01 to about 90 percent by weight are often employed. In compositions designed to be employed as concentrates, the active ingredient is generally present in a concentration from about 5 to about 98 weight percent, preferably about 10 to about 90 weight percent. Such compositions are typically diluted with an inert carrier, such as water, before application. The diluted compositions usually applied to weeds or the locus of weeds generally contain about 0.0001 to about 1 weight percent active ingredient and preferably contain about 0.001 to about 0.05 weight percent.

The present compositions can be applied to weeds or their locus by the use of conventional ground or aerial

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dusters, sprayers, and granule applicators, by addition to irrigation water, and by other conventional means known to those skilled in the art.

The following Examples are presented to
5 illustrate the various aspects of this invention and should not be construed as limitations to the claims.

Examples

1. Preparation of 4-amino-3,6-dichloropyridine-2-carboxylic acid (Compound 1)

10 In a 3-liter (L) beaker was added 2000 grams (g) of hot water, 115.1 g of 50 percent by weight NaOH, and 200 g of wet 4-amino-3,5,6-trichloropyridine-2-carboxylic acid (79.4 percent). The solution was stirred for 30 minutes (min), filtered through a paper filter, and transferred to
15 a 5-L feed/recirculation tank. This solution weighed 2315 g and contained 6.8 percent 4-amino-3,5,6-trichloropyridine-2-carboxylic acid. This feed was recirculated at a rate of about 9.46 L/min and a temperature of 30 °C through an undivided electrochemical
20 cell having a Hastelloy C anode and an expanded silver mesh screen cathode. After normal anodization at +0.7 volt (v), the polarity of the cell was reversed and the electrolysis was started. The cathode working potential was controlled at -1.1 to -1.4 v relative to an Ag/AgCl (3.0 M Cl⁻)
25 reference electrode. While recirculating the feed, a solution of 50 percent NaOH is slowly pumped into the recirculation tank to maintain the NaOH concentration at a 1.5 to 2.0 percent excess. After about 15 hours (h), the electrolysis was terminated and the cell effluent was
30 filtered through a paper filter. The solution was neutralized with concentrated HCl and concentrated to about 750 g of crude concentrate. The concentrate was warmed to 85 °C with stirring and the pH was adjusted to less than 1 with concentrated HCl over 30 min. The resulting slurry
35 was cooled to ambient temperature and filtered. The filter

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cake was washed with 3x200 milliliter (mL) portions of water and dried under vacuum at 80 °C. The dried product, 118.1 g assayed at 90.6 percent desired product; gas chromatography (GC) indicated about 4 percent 4-amino-3,5,6-trichloropyridine-2-carboxylic acid remaining as an impurity. A purified sample of 4-amino-3,6-dichloropyridine-2-carboxylic acid had a melting point (mp) of 185-187 °C (dec.); ¹H NMR (DMSO-d₆): δ 13.9 (br, 1H), 7.0 (br m, 2H), 6.8 (s, 1H); ¹³C NMR (DMSO-d₆): δ 165.4 (1C), 153.4 (1C), 149.5 (1C), 147.7 (1C), 111.0 (1C), 108.1 (1C).

2. Preparation of 2-ethylhexyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 2)

To a solution of 2-ethylhexanol (10 mL) and sulfuric acid (1 mL) was added 4-amino-3,6-dichloropyridine-2-carboxylic acid (0.0097 mol, 2.0 g). After heating the reaction to reflux overnight, the reaction mixture was cooled, poured into water (75 mL), and extracted with ethyl acetate (75 mL). The organic phase was washed with sodium bicarbonate (75 mL), dried (Na₂SO₄), and concentrated. The resulting solid was recrystallized out of dichloromethane and hexane and filtered to give 2-ethylhexyl 4-amino-3,6-dichloropyridine-2-carboxylate (0.0074 mol, 2.36 g) as a crystalline solid (mp 55 °C). ¹H NMR (CDCl₃): δ 0.9 (7 H, m), 1.3 (7 H, m), 1.7 (1 H, m), 4.3 (2 H, d), 5.1 (2 H, bs), 6.7 (1 H, s).

The following esters of 4-amino-3,5,6-trichloropyridine-2-carboxylic acid were prepared according to the procedure of Example 2:

methyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 3); mp 134-135 °C.

ethyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 4); mp 98-99 °C.

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n-propyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 5); mp 94-95 °C.

i-propyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 6); mp 114-115 °C.

5 *n*-butyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 7); mp 78-79 °C.

n-pentyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 8); mp 71-73 °C.

10 *n*-hexyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 9); mp 65-66 °C.

phenyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 10);

3. Preparation of *N*-ethyl 4-amino-3,6-dichloropyridine-2-carboxamide (Compound 11)

15 A solution of ethylamine 2.0 M in methanol (34 mL) and methyl 4-amino-3,6-dichloropyridine-2-carboxylate (0.00678 mol, 1.5 g) was stirred and heated to reflux for 60 h. The reaction mixture was cooled, concentrated, and dissolved in ethyl acetate. The resulting solution was
20 washed with water (50 mL) and brine (50 mL), dried (Na₂SO₄), and concentrated. The resulting solid was dissolved in methanol and purified by reverse phase HPLC to give ethyl 4-amino-3,6-dichloropyridine-2-carboxamide (0.0035 mol, 0.820 g); mp 136-137 °C.

25 4. Preparation of methyl *N*-acetyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 12) and *N,N*-diacetyl 4-amino-3,6-dichloropyridine-2-carboxylate (Compound 13)

30 A solution of acetic anhydride (75 mL) and methyl 4-amino-3,6-dichloropyridine-2-carboxylate (0.00904 mol, 2.0 g) was stirred and heated to reflux overnight. The

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solution was cooled, concentrated, taken up in ethyl acetate (100 mL), and washed with water (100 mL). The organic phase was washed with saturated sodium bicarbonate (100 mL), dried (Na_2SO_4), and concentrated. The solution was purified by chromatography on silica gel. The front running spot was isolated and gave a yellow oil identified as the diacylated 4-amide (0.0023 mol, 0.700 g). ^1H NMR 2.2 (6 H, s), 3.9 (3 H, s), 7.3 (1 H, s). The second spot gave a yellow solid identified as the monoacylated 4-amide (0.0035 mol, 0.920 g); mp 102-103 °C.

5. Preparation of 4-amino-6-bromo-3-chloropyridine-2-carboxylic acid (Compound 14)

15 A. Methyl 6-bromo-3-chloro-pyridine-2-carboxylate, N-oxide

To a solution of methyl 6-bromo-3-chloro-pyridine-2-carboxylate (0.13 mol, 32.1 g) in trifluoroacetic acid (75 mL) and trifluoroacetic anhydride (40 mL) was cautiously added 50% hydrogen peroxide (0.17 mol, 13 g). The reaction exothermed to reflux. After stirring for 30 min, the solution was poured into a mixture of ice and 10 percent sodium bisulfite (150 mL). The resulting solid was collected and dried in vacuo to give a white solid (0.08 mol, 21.4 g). ^1H NMR (CDCl_3): δ 4.1 (3H, s), 7.3 (1H, d), 7.7 (1H, d).

B. Methyl 6-bromo-3-chloro-4-nitropyridine-2-carboxylate, N-oxide

To a solution of fuming nitric acid (10 mL) and fuming sulfuric acid (10 mL) was added methyl 6-bromo-3-chloro-pyridine-2-carboxylate, N-oxide and the reaction was heated to 70° C in an oil bath for 4 h. The mixture was poured over ice water (100 mL) and extracted with ethyl acetate (3 x 75 mL) and the combined extracts were backwashed with brine, dried (Na_2SO_4) and concentrated. The

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dark oil was chromatographed over silica in 4:1 EtOAc/hexane to give methyl 6-bromo-3-chloro-4-nitropyridine-2-carboxylate, N-oxide (0.007 mol, 2.2 g). ¹H NMR (CDCl₃): δ 4.1 (3H, s), 8.4 (1H, s).

5 C. Methyl 4-amino-6-bromo-3-chloropyridine-2-carboxylate (Compound 15)

To a solution of titanium tetrachloride (0.015 mol, 2.8 g) in tetrahydrofuran (50 mL) was added lithium aluminum hydride (0.0175 mol, 0.7 g). The black slurry was stirred 15 minutes before adding methyl 6-bromo-3-chloro-4-nitropyridine-2-carboxylate, N-oxide (0.007 mol, 2.3 g) in THF (25 mL). The solution was stirred one hour before pouring into 1:1 H₂O/NH₄OH and filtering. The filtrate was extracted with EtOAc (2 x 75 mL). The organic phase was dried (Na₂SO₄), and concentrated. The red solid was chromatographed over silica in 4:1 EtOAc/hexane to give methyl 4-amino-6-bromo-3-chloropyridine-2-carboxylate (0.003 mol, 0.8 g); mp 194-5 °C. ¹H NMR(CDCl₃): δ 3.95 (3H, s), 5.3 (2H, bs), 6.9 (1H, s).

20 D. 4-amino-6-bromo-3-chloropyridine-2-carboxylic acid (Compound 14)

To methyl 4-amino-6-bromo-3-chloropyridine-2-carboxylate (200mg; 0.8 mmol) in 10 mL of methanol was added excess 2N NaOH (10 mL). The mixture was stirred for 1 h at ambient temperature and then evaporated to dryness in vacuo. The residue was dissolved in water and diethyl ether. After separation of the phases, the aqueous layer was acidified with 1N HCl to a pH=2. The aqueous layer was evaporated to dryness and the residue was dissolved in 50 mL of methanol and filtered. The filtrate was evaporated under reduced pressure and the residue was triturated with 5 percent diethyl ether in petroleum ether to give 70 mg of 4-amino-6-bromo-3-chloropyridine-2-carboxylic acid, mp 182-183 °C.

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6. Preparation of Methyl 4-amino-3-chloro-6-fluoropyridine-2-carboxylate (Compound 16)

A. Methyl 3-chloro-4,6-difluoropyridine-2-carboxylate

To a solution of methyl 3,4,6-trichloropyridine-2-carboxylate (0.010 mol, 2.4 g) in DMSO (10 mL) was added cesium fluoride (0.038 mol, 3.8 g) and the suspension was heated for 2 h at 100 °C. The reaction mixture was dissolved in dilute HCl and extracted with ethyl acetate (EtOAc). The organic layer was treated with (trimethylsilyl)diazomethane (TMSCHN₂) to re-esterify any hydrolyzed ester. The mixture was concentrated and the resultant residue was chromatographed over silica with 10 percent EtOAc/hexane to give methyl 3-chloro-4,6-difluoropyridine-2-carboxylate (0.0072 mol, 1.5 g). ¹H NMR(CDCl₃): δ 4.00 (3H, s), 6.95-6.90 (1H, m). ¹⁹F NMR {¹H}: δ -65.0 (d, J = 17 Hz), 95.8 (d, J = 17 Hz).

B. Methyl 4-amino-3-chloro-6-fluoropyridine-2-carboxylate (Compound 16)

Sodium azide (0.0086 mol, 0.60 g) was added to a solution of methyl 3-chloro-4,6-difluoropyridine-2-carboxylate (0.0072 mol, 1.5 g) in 15 mL dimethyl formamide (DMF). The solution was stirred 10 min at ambient temperature before pouring into 350 mL water and extracting the aqueous mixture with EtOAc (2 x 100 mL). The organic phase was dried (Na₂SO₄) and then treated with excess NaBH₄ for 30 min. The excess NaBH₄ was quenched with aqueous EtOH and the mixture was diluted with water (200mL). The organic layer was separated and the aqueous layer extracted with EtOAc (2 x 200 mL). The combined organic layers were dried (Na₂SO₄) and concentrated to an off-white powder which was purified by reversed-phase HPLC to give methyl 4-amino-3-chloro-6-fluoropyridine-2-carboxylate (0.0059 mol, 1.2 g). ¹H NMR(CDCl₃): δ 3.95 (3H, s), 5.2-5.1 (2H, bs), 6.36 (1H, s). ¹⁹F NMR {¹H}: δ -72.7.

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7. Preparation of Methyl 4-amino-3,5,6-tribromopyridine-2-carboxylate (Compound 17)

Methyl 4-amino-3,5,6-tribromopyridine-2-carboxylate was prepared by amination of methyl 3,4,5,6-tetrabromopyridine-2-carboxylate following the procedure of Example 6B. ¹H NMR(CDCl₃): δ 3.95 (3H, s), 6.9-6.8 (2H, bs).

8. Preparation of 4-Amino-3,6-dichloro-5-fluoropyridine-2-carboxylic acid (Compound 18)

To a solution of 4-amino-3,6-dichloropyridine-2-carboxylate (1.5 g, 6.8 mmol) in 20 mL of dry acetonitrile was added 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis (tetrafluoroborate) (Selectfluor[™] from Aldrich Chemical Company, Inc.; 2.9 g, 2.59 mmol [F⁺]/g). The resulting mixture was heated at reflux for 3 h, then allowed to cool to room temperature. This material was taken up in Et₂O and washed with H₂O. The organic layer was dried over MgSO₄, filtered and concentrated to yield a brown oil. The crude product was purified via reverse phase HPLC (50% acetonitrile/water) to give 0.37 g of white solid which was stirred in 1N NaOH for 1 h then made acidic with conc. HCl. The precipitated white solid was collected with suction, washed with H₂O and dried under vacuum to give 170 mg of 4-amino-3,6-dichloro-5-fluoropyridine-2-carboxylic acid (11% yield); mp 214 °C dec.

9. Preparation of 4-Amino-3,6-dichloro-5-bromopyridine-2-carboxylic acid (Compound 19)

To a solution of methyl 4-amino-3,6-dichloropyridine-2-carboxylate (18 g, 81 mmol) in 100 mL fuming sulfuric acid was added bromine (15 mL, excess). The resulting mixture was heated to 70 °C for 30 min, then allowed to cool to room temperature. This material was poured into ice water (1000 mL) and extracted with EtOAc (4

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x 500 mL). The combined organic extracts were dried (MgSO₄), filtered and concentrated to yield a brown solid. The crude product was purified via reverse phase HPLC (50% acetonitrile/water) to give 21 g of 4-amino-3,6-dichloro-5-bromopyridine-2-carboxylic acid as a white solid (91% yield); mp 201-202 °C.

10. Preparation of 4-amino-3,6-dichloro-5-methoxypyridine-2-carboxylate (Compound 20)

10 A. Methyl 3-chloro-5-methoxypyridine-2-carboxylate, N-oxide

In a dry 3-neck round bottom flask was added methyl 3,5-dichloropyridine-2-carboxylate, N-oxide (5.0 g, 22.5 mmol) to 25 mL of methanol to give a slurry. A 25% solution of sodium methoxide in methanol (5.40 mL, 23.62 mmol) was added and heated to reflux for 1.5 h. The reaction mixture was diluted in ethyl acetate and added to H₂O. The layers were separated and the aqueous layer was saturated with brine and extracted 2 more times in ethyl acetate. The combined organic layers were dried (MgSO₄) and concentrated to give a white solid. Purification by column chromatography (silica gel) using an eluent of 50% Et₂O/Petroleum ether (1.5 L) then 100% Et₂O to give 1.76 g of a white solid; mp 154-156 °C.

25 B. Methyl 3-chloro-5-methoxy-4-nitropyridine-2-carboxylate, N-oxide

To methyl 3-chloro-5-methoxypyridine-2-carboxylate, N-oxide (1.41 g, 5.97 mmol) in H₂SO₄ cooled to 0 °C was slowly added a 50/50 mixture of 30% oleum and fuming HNO₃. Reaction mixture stirred for 30 minutes at room temperature and then heated to 70 °C for 3 days. The reaction mixture was diluted with ethyl acetate and cooled to 0 °C. Saturated sodium bicarbonate was carefully added and the layers were separated. Aqueous layer was washed 2 more times with ethyl acetate. The combined organic layers

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were dried (MgSO₄) and concentrated to dryness. Purification by column chromatography (silica gel) using an eluent of 20% ethyl acetate/hexane gave 300 mg of a yellow solid; mp 160 °C

5 C. Methyl 3,6-dichloro-5-methoxy-4-nitropyridine-2-carboxylate

To methyl 3-chloro-5-methoxy-4-nitropyridine-2-carboxylate, N-oxide (0.300 g, 1.12 mmol) in 5 mL of chloroform was added PCl₃ (0.664 mL, 7.62 mmol). The
10 reaction mixture was heated to reflux for 8 h and then concentrated to dryness in vacuo to give 300 mg of a white solid.

D. Methyl 4-amino-3,6-dichloro-5-methoxypyridine-2-carboxylate

15 To methyl 3,6-dichloro-5-methoxy-4-nitropyridine-2-carboxylate (0.300 g, 1.06 mmol) in 5 mL of ethyl acetate was added SnCl₂ · 2H₂O (1.60 g, 7.1 mmol). The reaction mixture was heated to 70 °C for 30 min and then cooled to room temperature. Saturated sodium bicarbonate and a
20 saturated solution of KHF₂ were added to reaction mixture. The mixture was extracted with ethyl acetate and the layers were separated. The aqueous layer was washed 2 more times with ethyl acetate. The combined organic layers were dried (MgSO₄) and concentrated to dryness to give 0.250 g of a
25 yellow solid.

E. 4-Amino-3,6-dichloro-5-methoxypyridine-2-carboxylate (Compound 20)

4-Amino-3,6-dichloro-5-methoxypyridine-2-carboxylate was prepared by saponification of the methyl ester
30 according to the procedure of Example 12(D); mp 154-156 °C.

11. Preparation of 4-Amino-3,6-dichloro-5-methylthiopyridine-2-carboxylic acid (Compound 21)

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4-Amino-3,6-dichloro-5-methylthiopyridine-2-carboxylic acid was prepared by analogy to the preparation of 4-amino-3,6-dichloro-5-methoxypyridine-2-carboxylic acid following the procedure of Example 10; mp 160 °C dec.

5 12. Preparation of 4-N-Methylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 22)

A. Methyl 3,6-Dichloropyridine-2-carboxylate

To a 3-neck round bottom flask equipped with a reflux condenser was added 3,6-dichloropyridine-2-carboxylic acid (50.0 g, 260.42 mmol) in methanol (200 mL). HCl(g) was bubbled in until solution became saturated and stirred at room temperature for 2 h. The solution was concentrated to dryness in vacuo. Diethyl ether was added to make a slurry that was subsequently added to a flask filled with a 1:1 mixture of saturated sodium bicarbonate/diethyl ether and stirred for 10 min. The aqueous phase was extracted with diethyl ether (3 X 300 mL). The combined extracts were dried (MgSO₄) and concentrated to give 46.6 g of a light yellow solid. ¹H NMR(CDCl₃): δ 4.00 (s, 3H); 7.41 (d, 1H); 7.80 (d, 1H).

B. Methyl 3,6-Dichloropyridine-2-carboxylate, N-oxide

Methyl 3,6-dichloropicolinate (20.0 g, 97.07 mmol) was dissolved in a minimum amount of trifluoroacetic acid (TFA). In a separate flask was stirred trifluoroacetic anhydride (TFAA, 38 mL) and 50% H₂O₂ (9.9 g, 145.61 mmol) which was added to the TFA solution. The reaction mixture was stirred at reflux for 1 h and concentrated to dryness. The orange oil was dissolved in ethyl acetate and saturated sodium bicarbonate. The phases were separated and the aqueous phase was extracted with ethyl acetate (2 X 200mL). The combined extracts were dried (MgSO₄) and concentrated to a yellow solid. Purification by column chromatography (silica gel) using an eluent of 50% ethyl acetate/hexane gave 12.13 g of a yellow

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solid. ^1H NMR(CDCl_3): δ 4.00 (s, 3H); 7.25 (d, 1H); 7.50 (d, 1H).

C. Methyl 3,4,6-Trichloropyridine-2-carboxylate

To methyl 3,6-dichloropicolinate N-oxide (5.0 g, 22.52 mmol) dissolved in 15 mL of acetonitrile was added POCl_3 (4.20 mL, 45.04 mmol). The reaction mixture was stirred at reflux for 5 h, cooled to room temperature and concentrated to dryness in vacuo. The resultant orange oil was dissolved in diethyl ether. Carefully, saturated sodium bicarbonate was added and the aqueous phase was extracted with diethyl ether (2 X 100mL). The combined extracts were dried (MgSO_4) and concentrated to dryness. Purification by column chromatography (silica gel) using an eluent of 20% ethyl acetate/hexane gave 5.89 g of a light yellow solid. ^1H NMR(CDCl_3): δ 4.00 (s, 3H); 7.55 (s, 1H).

D. 3,4,6-Trichloropyridine-2-carboxylic acid

To methyl 3,4,6-Trichloropicolinate (3.57 g, 14.85 mmol) in 20 mL of methanol was added 1N NaOH (14.85 mL, 14.85 mmol). The reaction mixture was stirred at room temperature for 1 h and then concentrated to dryness in vacuo. 100 mL each of diethyl ether and H_2O were added. Aqueous layer was acidified with 1N HCl until pH=2. CH_2Cl_2 was added and the aqueous phase was extracted with CH_2Cl_2 (2 X 100 mL). The combined extracts were dried (MgSO_4) and concentrated to give 3.13 g of a white solid. ^1H NMR(CDCl_3): δ 7.50 (s, 1H).

E. 4-N-Methylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 22)

3,4,6-Trichloropyridine-2-carboxylic acid (1.56 g, 6.89 mmol) was dissolved in methylamine and placed in a Parr bomb at 80° for 2 days. The reaction mixture was cooled to room temperature and diluted with ethyl acetate. 1N HCl was added until pH=2. The aqueous phase was

extracted with ethyl acetate (2 X 50 mL) and the combined extracts were dried (MgSO₄) and concentrated to dryness. Desired product was triturated from 5% diethyl ether/pet ether; the solid was filtered and dried to give 0.600 g of a light yellow solid. ¹H NMR(CDCl₃): δ 2.75 (s, 3H); 5.70 (s, 1H); 6.30 (s, 1H); mp 170-172 °C.

The following N-alkyl analogs of 4-amino-3,6-dichloropyridine-2-carboxylic acid were prepared according to the procedure of Example 12:

10 4-N-Ethylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 23); mp 136-137 °C.

4-N-isopropylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 24); mp 146-147 °C.

15 4-N-Methoxyethylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 25); mp 97-99 °C.

4-N-Butylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 26); mp 96-97 °C.

4-N,N-Dimethylamino-3,6-Dichloropyridine-2-carboxylic acid (Compound 27); mp 110 °C.

20 4-pyrrolidino-3,6-Dichloropyridine-2-carboxylic acid (Compound 28); mp 153-5 °C.

4-Morpholino-3,6-Dichloropyridine-2-carboxylic acid (Compound 29); mp 183-4 °C.

25 13. Preparation of 4-amino-6-bromo-3-methoxypyridine-2-carboxylic acid (Compound 30)

A. Methyl 4,6-dibromo-3-methoxypyridine-2-carboxylate

To methyl 4,6-dibromo-3-hydroxypyridine-2-carboxylate 3.98 g (3.98 g, 12.81 mmol) in 40 mL of acetone was added K₂CO₃ (2.0 g, 14.47 mmol) and dimethyl sulfate (1.20 mL, 12.37 mmol). The reaction mixture was refluxed

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overnight and concentrated to dryness. The residue was dissolved in ethyl acetate and saturated sodium bicarbonate. The phases were separated and the aqueous phase was extracted with ethyl acetate (3 X 100 mL). The combined extracts were dried (MgSO₄) and concentrated to dryness. The residue was purified by chromatography (silica gel). Elution with 15% ethyl acetate/hexane gave 0.980 g, of a white solid. ¹H NMR(CDCl₃): δ 3.95 (s, 3H); 3.90 (s, 3H); 7.80 (s, 1H).

10 B. Methyl 4-azido-6-bromo-3-methoxypyridine-2-carboxylate

Methyl-4,6-dibromo-3-methoxypyridine-2-carboxylate (0.980 g, 3.02 mmol) was dissolved in a minimum amount of DMF. Slowly sodium azide (0.216 g, 3.32 mmol) was added followed by H₂O to form a homogeneous solution. The reaction mixture was heated to 60° and stirred for 2 days. Reaction mixture added to a flask filled with ice water and extracted with ethyl acetate (3 X 50 mL). Extracts were combined and back washed with H₂O, dried (MgSO₄) and concentrated to give 0.500 g of an orange oil. ¹H NMR(CDCl₃): δ 3.90 (s, 3H); 3.95 (s, 3H); 7.20 (s, 1H).

20 C. Methyl 4-amino-6-bromo-3-methoxypyridine-2-carboxylate

To methyl 4-azido-6-bromo-3-methoxypyridine-2-carboxylate (0.500 g, 1.74 mmol) in 10 mL of methanol was added NaBH₄ (0.046 g, 1.22 mmol). The reaction mixture was stirred at room temperature for 10 min. Ethyl acetate and water were added and the phases were separated. The organic phase was washed with H₂O, dried (MgSO₄) and concentrated to dryness in vacuo. The residue was purified by chromatography (silica gel). Elution with 100% ethyl acetate gave 0.300 g of a white solid. ¹H NMR(CDCl₃): δ 3.90 (s, 1H); 3.95 (s, 1H); 4.60 (s, 2H); 6.85 (s, 1H).

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D. 4-amino-6-bromo-3-methoxypyridine-2-carboxylic acid (Compound 30)

To methyl 4-amino-6-bromo-3-methoxypyridine-2-carboxylate (0.300 g, 1.15 mmol) in 10 mL of methanol was added 1N NaOH (1.15 mL, 1.15 mmol). The reaction mixture was stirred at room temperature for 1 h and concentrated to dryness in vacuo. Diethyl ether and H₂O were added. The aqueous layer was acidified with 1N HCl until pH=2 and concentrated to dryness. Methanol (50 mL) was added to the white solid. The mixture was filtered and the filtrate concentrated to dryness. Triturating with 5% diethyl ether/pet ether gave 0.180 g of a light pink solid. ¹H NMR(DMSO): δ 3.60 (s, 3H); 6.80 (s, 1H).

14. Preparation of 4-amino-6-bromo-5-chloro-3-methoxypyridine-2-carboxylic acid (Compound 31)

A. Methyl 4-amino-6-bromo-5-chloro-3-methoxypyridine-2-carboxylate

To methyl 4-amino-6-bromo-3-methoxypyridine-2-carboxylate (1.45 g, 5.56 mmol) in 10 mL of acetonitrile was added sulfuryl chloride, in excess, via pipette until the solution remained yellow. The solution was heated to reflux for 5 min. The reaction mixture was added to saturated sodium bicarbonate and aqueous phase was extracted with diethyl ether (3 x). The combined organic extracts were dried (MgSO₄), filtered and concentrated in vacuo to give a yellow solid. Solid was washed in 10% diethyl ether/petroleum ether and solid filtered to give 0.580 g of a white solid.

B. 4-amino-6-bromo-5-chloro-3-methoxypyridine-2-carboxylic acid (Compound 31)

To methyl-4-amino-6-bromo-5-chloro-3-methoxypyridine-2-carboxylate (0.300 g, 1.02 mmol) in 10 mL of methanol was added 1 N NaOH (1.10 mL, 1.10 mmol). The

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reaction mixture was stirred at room temperature for 4 h and was then concentrated to dryness in vacuo. The resulting aqueous layer was acidified with concentrated HCl. The white solid was collected by filtration and was
5 rinsed with H₂O. The solid was dried at 50 °C under vacuum to give 0.230 g of a white fluffy solid; mp 154-156 °C.

15. Preparation of 4-Amino-5,6-dichloro-3-fluoropyridine-2-carboxylic acid (Compound 32)

A. 4-Amino-5,6-dichloro-2-trichloromethylpyridine

10 To a solution of 4,5,6-trichloro-2-trichloromethylpyridine (2 g, 6.7 mmol) in aqueous DMF was added NaN₃ (0.5 g, 7.7 mmol). The resulting mixture was heated at 70°C for 2 h, added to H₂O and extracted (3x) with Et₂O. Organic layer was concentrated to yield a white
15 solid, which was dissolved in 10 mL of MeOH. Excess NaBH₄ was added and the reaction mixture was stirred at room temperature for 0.5 h. This material was added to H₂O, extracted (3x) with Et₂O, dried over MgSO₄ and concentrated in vacuo. The resulting solid was washed several times
20 with hexane to give 1.3 g of 4-amino-5,6-dichloro-2-trichloromethylpyridine.

B. 4-Amino-5,6-dichloro-3-fluoropyridine-2-carboxylic acid (Compound 32)

To a solution of 4-amino-5,6-dichloro-2-
25 trichloromethylpyridine (1.25 g, 4.46 mmol) in 20 mL of dry acetonitrile was added Selectfluor™ (1.9 g, 2.59 mmol [F⁺]/g). The resulting mixture was heated at reflux for 72 h, then allowed to cool to room temperature. This material was taken up in Et₂O and washed with H₂O. The organic layer
30 was dried over MgSO₄, filtered and concentrated to yield a dark oil. The crude product was purified via reverse phase HPLC (75% acetonitrile/water) to give 0.2 g of white solid which was stirred in 80% H₂SO₄ at 155°C for 0.5 h. Reaction mixture was allowed to cool and extracted several times

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with 10% MeOH/CH₂Cl₂. Organic layer was dried over MgSO₄, filtered and concentrated to give a white solid which was washed several times with hexane-diethyl ether to give 60 mg of 4-amino-5,6-dichloro-3-fluoropyridine-2-carboxylic acid; mp 208°C dec.

16. Preparation of 4-Amino-3-bromo-6-chloropyridine-2-carboxylic acid (Compound 33)

A. Methyl 3-Bromo-4-chloropyridine-2-carboxylate

To a solution of 3-bromo-4-chloropyridine-2-carboxylic acid (1.75 g, 7.4 mmol) in MeOH was added anhydrous HCl. The resulting mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated to give a solid, which was partitioned between Et₂O and saturated NaHCO₃. Organic layer was dried over MgSO₄, filtered and concentrated to give a brown residue. This material was purified via flash column chromatography to yield 1.35 g of product as a pale yellow oil.

B. Methyl 3-Bromo-4,6-dichloropyridine-2-carboxylate

To a solution of methyl 3-bromo-4-chloropyridine-2-carboxylate (1.35 g, 5.4 mmol) in 5 mL of TFA was added 30% H₂O₂ (1 g, 9.8 mmol). The resulting mixture was stirred at 75°C for 0.5 h and allowed to cool to room temperature. Et₂O was added and the organic layer was washed carefully with saturated NaHCO₃, dried over MgSO₄, filtered and concentrated to give the corresponding N-Oxide intermediate as a white solid. This material was taken up in acetonitrile (5 mL), POCl₃ (2-3 mL) and heated at reflux for 2 h. The reaction mixture was allowed to cool, added to Et₂O and washed carefully with saturated NaHCO₃, dried over MgSO₄, filtered and concentrated to give 0.9 g of product as a light brown oil. This material was sufficiently pure to carry on to the next step.

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C. 4-Amino-3-bromo-6-chloropyridine-2-carboxylic acid
(Compound 33)

To a solution of methyl 3-bromo-4,6-dichloropyridine-2-carboxylate (0.9 g, 3.2 mmol) in aqueous
5 DMF was added NaN_3 (0.25 g, 3.8 mmol). The resulting
mixture was heated at 60 °C for 1 h, added to H_2O and
extracted (3x) with Et_2O . Organic layer was concentrated
to yield a white solid, which was dissolved in 10 mL of
MeOH. Excess NaBH_4 was added and the reaction mixture
10 stirred at room temperature for 0.5 h. This material was
added to H_2O , extracted (3x) with Et_2O , dried over MgSO_4 and
concentrated. The resulting solid was stirred in 1N NaOH
for 1 h, made acidic with conc. HCl and concentrated to
dryness. This material was extracted with MeOH,
15 concentrated to give 220 mg of 4-amino-3-bromo-6-
chloropyridine-2-carboxylic acid; mp 175 °C dec.

17. Preparation of 4-Amino-3,5-dichloro-6-
trifluoromethylpyridine-2-carboxylic acid (Compound 34)

20 A. Methyl 4-chloro-6-trifluoromethylpyridine-2-
carboxylate

To a solution of 6-trifluoromethylpicolinic acid
(8.6 g, 45 mmol; prepared from the corresponding 6-
25 trifluoromethyl-2-cyanopyridine) in 25 mL of TFA was added
30% H_2O_2 (7.8 g, 67.5 mmol). Reaction mixture was stirred
at 70°C for 18 h and concentrated to give 8.0 g of the N-
oxide. This material was stirred in HCl/MeOH solution for
18 h. The reaction mixture was concentrated to give an
30 oily residue which was partitioned between Et_2O and
saturated NaHCO_3 . The organic layer was dried over MgSO_4 ,
filtered and concentrated to give 5.0 g of a yellow oil.
Neat POCl_3 was added and stirred at reflux for 2 h. The
mixture was allowed to cool, added carefully to saturated
35 NaHCO_3 and extracted (3x) with Et_2O . The organic layer was

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dried over MgSO_4 , filtered and concentrated to give a brown solid. This material was purified via flash column chromatograph to give 2.64 g of product as a white solid (mp $62-3^\circ\text{C}$).

5

B. Methyl 4-Amino-6-trifluoromethylpyridine-2-carboxylate

To a solution of methyl 4-chloro-6-trifluoromethylpyridine-2-carboxylate (2.44 g, 10.2 mmol) in aqueous DMF was added NaN_3 (0.7 g, 10.8 mmol). The resulting mixture was heated at 70°C for 18 h, added to H_2O and extracted (3x) with Et_2O . The organic layer was concentrated to yield a white solid that was dissolved in 10 mL of MeOH. Excess NaBH_4 was added and the reaction mixture stirred at RT for 0.5 h. This material was added to H_2O , extracted (3x) with Et_2O . The extract was dried over MgSO_4 and concentrated. The resulting residue was purified via flash column chromatography to give 0.95 of product as a white solid (mp 114°C).

C. Methyl 4-Amino-3,5-dichloro-6-trifluoromethylpyridine-2-carboxylate

To a solution of methyl 4-amino-6-trifluoromethylpyridine-2-carboxylate (0.75 g, 3.4 mmol) in 5 mL of dry acetonitrile was added SO_2Cl_2 (0.55 mL, 6.8 mmol). The resulting mixture was heated at reflux for 0.5 h, then allowed to cool to room temperature. This material was taken up in Et_2O and washed with saturated NaHCO_3 . The organic layer was dried over MgSO_4 , filtered and concentrated to give solid. The crude material was purified via flash column chromatography to yield 0.28 g of product as a white solid (mp $135-6^\circ\text{C}$).

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D. Preparation of 4-Amino-3,5-dichloro-6-trifluoromethylpyridine-2-carboxylate (Compound 34)

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To a solution of methyl 4-amino-3-5-dichloro-6-trifluoromethylpyridine-2-carboxylate (0.16 g, 0.56 mmol) in 5 mL of MeOH was added excess 1N NaOH. The resulting reaction mixture was stirred at room temperature for 1 h, then made acidic with conc. HCl. The precipitated white solid was collected with suction, washed with H₂O and dried under vacuum to give 80 mg of compound 34; mp 178°C dec.

18. Preparation of 4-Amino-3-chloro-6-trifluoromethylpyridine-2-carboxylic acid (Compound 35)

4-Amino-3-chloro-6-trifluoromethylpyridine-2-carboxylic acid was prepared by analogy to the preparation of 4-Amino-3,5-dichloro-6-trifluoromethylpyridine-2-carboxylic acid but using only one equivalent of SO₂Cl₂ to perform mono-chlorination rather than bis-chlorination in procedure 17C Preparation of Herbicidal Compositions

19. Preparation of Herbicidal Compositions

In the following illustrative compositions, parts and percentages are by weight.

EMULSIFIABLE CONCENTRATES

<u>Formulation A</u>	
	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	26.2
Polyglycol 26-3	
	5.2
Nonionic emulsifier-(di-sec-butyl)-phenyl-poly(oxypropylene)block polymer with (oxyethylene). The polyoxyethelene content is about 12 moles. Witconate P12-20 (Anionic emulsifier-	
calcium dodecylbenzene	5.2

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sulfonate-
60 wt. % active)
Aromatic 100 (Xylene range
aromatic
solvent) 63.4

Formulation B

	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	3.
Sunspray 11N (paraffin oil)	40.0
Polyglycol 26-3	19.0
Oleic acid	1.
Xylene range aromatic solvent	36.5

Formulation C

	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	13.2
Stepon C-65	25.7
Ethomeen T/25	7.7
Ethomeen T/15	18.0
Xylene range aromatic solvent	35.4

- 5 These concentrates can be diluted with water to give emulsions of suitable concentrations for controlling weeds.

WETTABLE POWDERS

10

Formulation D

	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	26.0
Polyglycol 26-3	2.0
Polyfon H	4.0
Zeosyl 100 (Precipitated hydrated SiO ₂)	17.0
Barden clay + inerts	51.0

Formulation E

	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	62.4
Polyfon H (sodium salt of lignin)	6.0

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sulfonate)
Sellogen HR (sodium naphthalene
4.0
sulfonate)
Zeosyl 100 27.6

5 The active ingredient is applied to the corresponding carriers and then these are mixed and ground to yield wettable powders of excellent wettability and suspension power. By diluting these wettable powders with water it is possible to obtain suspensions of suitable concentrations for controlling weeds.

10 WATER DISPERSIBLE GRANULES

<u>Formulation F</u>	
	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	26.0
Sellogen HR	
	4.0
Polyfon H	
	5.0
Zeosyl 100	17.0
Kaolinite clay	48.0

15 The active ingredient is applied in a liquid state to the hydrated silica, which is then mixed with the other ingredients and ground to a powder. The powder is agglomerated with water and sieved to provide granules in the range of -10 to +60 mesh. By dispersing these granules in water it is possible to obtain suspensions of suitable
20 concentrations for controlling weeds.

GRANULES

25

<u>Formulation G</u>	
	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	5.0
Celetom MP-88	95.0

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The active ingredient is applied in a liquid state to the Celetom MP 88 carrier or to other suitable carriers. The resulting granules can be applied by hand, granule applicator, airplane, etc. in order to control weeds.

5

<u>Formulation H</u>	
	<u>WT%</u>
4-Amino-3,6-dichloropicolinic acid	1.0
Polyfon H	8.0
Nekal BA 77	2.0
Zinc Stearate	2.0
Barden Clay	87.0

All materials are blended and ground to a powder then water is added and the clay mixture is stirred until a paste is formed. The mixture is extruded through a die to provide granules of proper size.

10

20. Evaluation of Postemergence Herbicidal Activity

Seeds of the desired test plant species were planted in Grace-Sierra MetroMix® 306 planting mixture, which typically has a pH of 6.0 to 6.8 and an organic matter content of about 30 percent, in plastic pots with a surface area of 64 square centimeters. When required to ensure good germination and healthy plants, a fungicide treatment and/or other chemical or physical treatment was applied. The plants were grown for 7-21 days in a greenhouse with an approximate 15 hr photoperiod which was maintained at about 23-29°C during the day and 22-28°C during the night. Nutrients and water were added on a regular basis and supplemental lighting was provided with overhead metal halide 1000-Watt lamps as necessary. The plants were employed for testing when they reached the first or second true leaf stage.

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A weighed amount, determined by the highest rate to be tested, of each test compound was placed in a 20 mL

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glass vial and was dissolved in 4 mL of a 97:3 v/v (volume/volume) mixture of acetone and dimethyl sulfoxide (DMSO) to obtain concentrated stock solutions. If the test compound did not dissolve readily, the mixture was warmed and/or sonicated. The concentrated stock solutions obtained were diluted with an aqueous mixture containing acetone, water, isopropyl alcohol, DMSO, Atplus 411F crop oil concentrate, and Triton X-155 surfactant in a 48.5:39:10:1.5:1.0:0.02 v/v ratio to obtain spray solutions of known concentration. The solutions containing the highest concentration to be tested were prepared by diluting 2 mL aliquots of the stock solution with 13 mL of the mixture and lower concentrations were prepared by serial dilution of the stock solution. Approximately 1.5 mL aliquots of each solution of known concentration were sprayed evenly onto each of the test plant pots using a DeVilbiss atomizer driven by compressed air pressure of 2 to 4 psi (140 to 280 kiloPascals) to obtain thorough coverage of each plant. Control plants were sprayed in the same manner with the aqueous mixture. In this test an application rate of 1 ppm results in the application of approximately 1 g/Ha.

The treated plants and control plants were placed in a greenhouse as described above and watered by sub-irrigation to prevent wash-off of the test compounds. After 2 weeks the condition of the test plants as compared with that of the untreated plants was determined visually and scored on a scale of 0 to 100 percent where 0 corresponds to no injury and 100 corresponds to complete kill.

By applying the well-accepted probit analysis as described by J. Berkson in *Journal of the American Statistical Society*, 48, 565 (1953) and by D. Finney in *"Probit Analysis"* Cambridge University Press (1952), the above data can be used to calculate GR_{50} and GR_{90} values, which are defined as growth reduction factors that

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correspond to the effective dose of herbicide required to kill or control 50 percent or 80 percent, respectively, of a target plant.

5 Some of the compounds tested, application rates employed, plant species tested, and results are given in Tables 1-2. Selectivity to rice, corn and wheat are illustrated in Tables 3-5.

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Table 1
Post-emergent % Control

#	M	R1	R2	X	Y	Z	XANST	STEME	POLCO	Rate (ppm)
1	OH	H	H	H	Cl	Cl	95	100	100	125
2	Oethyloxy	H	H	H	Cl	Cl	95	80	100	250
3		H	H	H	Cl	Cl	100	100	100	125
4	OEt	H	H	H	Cl	Cl	100	100	100	125
5	On-Pr	H	H	H	Cl	Cl	100	100	100	125
6	On-Pr	H	H	H	Cl	Cl	100	100	100	125
7	On-Bu	H	H	H	Cl	Cl	100	100	100	250
8	On-pentyl	H	H	H	Cl	Cl	100	90	100	250
9	On-hexyl	H	H	H	Cl	Cl	100	100	100	250
10	OPh	H	H	H	Cl	Cl				
11	NHEt	H	H	H	Cl	Cl	0	0	0	125
12	OMe	H	C(O)Me	H	Cl	Cl	90	30	100	125
13	OMe	C(O)Me	C(O)Me	H	Cl	Cl	95	100	80	250
14	OH	H	H	H	Br	Cl	85	90	50	250
15	OMe	H	H	H	Br	Cl	95	95	100	250
16	OMe	H	H	H	F	Cl	90	80	95	250
17	OMe	H	H	Br	Br	Br	85	90	75	250
18	OH	H	H	F	Cl	Cl	95	95	100	125
19	OH	H	H	Br	Cl	Cl	85	90	50	250
20	OH	H	H	OMe	Cl	Cl	80	70	100	250
21	OH	H	H	SMe	Cl	Cl	90	90	98	125
22	OH	H	Me	H	Cl	Cl	90	90	95	125
23	OH	H	Et	H	Cl	Cl	85	100	90	125
24	OH	H	i-Pr	H	Cl	Cl	95	90	95	250
25	OH	H	EtOMe	Cl	Cl	Cl	80	90	100	250
26	OH	H	n-Bu	H	Cl	Cl	95	90	90	250
27	OH	Me	Me	H	Cl	Cl	100	100	100	250
28	OH	pyrrolidine		H	Cl	Cl	30	50	100	250
29	OH	morpholine		H	Cl	Cl	0	0	0	250
30	OH	H	H	H	Br	OMe	80	90	100	125
31	OH	H	H	Cl	Br	OMe	85	90	90	250
32	OH	H	H	Cl	Cl	F	90	85	90	125
33	OH	H	H	H	Cl	Br	90	90	95	125
34	OH	H	H	Cl	CF3	Cl	90	0	80	250
35	OH	H	H	H	CF3	Cl	90	60	100	250

XANST = cocklebur (*Xanthium strumarium*)

STEME = chickweed (*Stellaria media*)

POLCO = wild buckwheat (*Polygonum convolvulus*)

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TABLE 2
POSTMERGENCE HERBICIDAL ACTIVITY & CONTROL

Qpd. No.	Rate, Ppm	STEME	XANST	CHEAL	AMARE	ABUTH	VIOTR	POLCO	ALOMY	ECHCG	DIGSA	SETFA	SORBI	AVEFA
1	125	90	100	100	95	70	80	100	50	45	60	75	50	50
4	125	70	100	100	100	70	70	100	40	50	70	75	40	40
14	125	65	100	95	90	85	75	100	50	65	65	65	60	40
18	125	60	95	95	60	50	50	100	20	10	30	20	10	20

STEME=chickweed (*Stellaria media*)
CHEAL=lambquarters (*Chenopodium album*)
ABUTH=velvetleaf (*Abutilon theophrasti*)
POLCO=wild buckwheat (*Polygonum convolvulus*)
ECHCG=barnyardgrass (*Echinochloa crus-galli*)
SETFA=giant foxtail (*Setaria faberi*)
AVEFA=wild oats (*Avena fatua*)

XANST=cocklebur (*Xanthium strumarium*)
AMARE=pigweed (*Amaranthus retroflexus*)
VIOTR=viola (*Viola tricolor*)
ALOMY=blackgrass (*Alopecurus myosuroides*)
DIGSA=crabgrass (*Digitaria sanguinalis*)
SORBI=Rox orange sorghum (*Sorghum bicolor*)

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Table 3

Control of Several Key Weeds in Rice

post emergent evaluation - % control			
ORYZA	ECHCG	CYPES	Rate (ppm)
10	75	75	250
10	65	75	250
40	70	50	250

ORYZA = rice (*Oryza sativa*)
ECHCG = Barnyardgrass (*Echinochloa crus-galli*)
CYPES = yellow nutsedge (*Cyperus esculentus*)

Table 4

Control of Several Key Weeds in Corn

Post-emergent Evaluation - % control					
compd #	ZEAMX	ABUTH	AMARE	XANST	Rate (ppm)
16	0	40	75	90	250
19	10	70	90	85	250
27	20	80	50	100	125
32	0	70	90	85	250

ZEAMX = corn (*Zea mays*)
ABUTH = velvetleaf (*Abutilon theophrasti*)
AMARE = pigweed (*Amaranthus retroflexus*)
XANST = cocklebur (*Xanthium strumarium*)

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Table 5

Control of Several Key Weeds in Wheat

cmpd #	Post-emergent Evaluation - % control				Rate (ppm)
	TRZAS	STEME	CHEAL	POLCO	
15	0	50	80	95	250
21	20	30	90	98	125
30	10	20	90	100	250
35	10	50	100	100	31

TRZAS = wheat (*Triticum aestivum*)
STEME = chickweed (*Stellaria media*)
CHEAL = lambsquarters (*Chenopodium album*)
POLCO = wild buckwheat (*Polygonum convolvulus*)

21. Evaluation of Preemergence Herbicidal Activity

Seeds of the desired test plant species were
5 planted in a soil matrix prepared by mixing a loam soil (43
percent silt, 19 percent clay, and 38 percent sand, with a
pH of about 8.1 and an organic matter content of about 1.5
percent) and sand in a 70 to 30 ratio. The soil matrix was
contained in plastic pots with a surface area of 113 square
10 centimeters. When required to ensure good germination and
healthy plants, a fungicide treatment and/or other chemical
or physical treatment was applied.

A weighed amount, determined by the highest rate
to be tested, of each test compound was placed in a 20 mL
15 glass vial and was dissolved in 4 mL of a 97:3 v/v
(volume/volume) mixture of acetone and dimethyl sulfoxide
to obtain concentrated stock solutions. If the test
compound did not dissolve readily, the mixture was warmed
and/or sonicated. The stock solutions obtained were
20 diluted with a 99.9:0.1 mixture of water and Tween® 155
surfactant to obtain application solutions of known

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concentration. The solutions containing the highest concentration to be tested were prepared by diluting 2 mL aliquots of the stock solution with 15 mL of the mixture and lower concentrations were prepared by serial dilution of the stock solution. A 2.5 mL aliquot of each solution of known concentration was sprayed evenly onto the soil surface (113 sq. cm) of each seeded pot using a Cornwall 5.0 mL glass syringe fitted with a TeeJet TN-3 hollow cone nozzle to obtain thorough coverage of the soil in each pot. Control pots were sprayed in the same manner with the aqueous mixture.

The treated pots and control pots were placed in a greenhouse maintained with an approximate 15 hr photoperiod and temperatures of about 23-29°C during the day and 22-28°C during the night. Nutrients and water were added on a regular basis and supplemental lighting was provided with overhead metal halide 1000-Watt lamps as necessary. The water was added by top-irrigation. After 3 weeks the condition of the test plants that germinated and grew as compared with that of the untreated plants that germinated and grew was determined visually and scored on a scale of 0 to 100 percent where 0 corresponds to no injury and 100 corresponds to complete kill or no germination. Some of the compounds tested, application rates employed, plant species tested, and results are given in Tables 6-7.

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Table 8

Pre-emergent % Control

#	M	R1	R2	X	Y	Z	IPOHE	% Control		Rate
								AMARE	ABUTH	(g/ha)
1	OH	H	H	H	Cl	Cl	100	100	100	280
2	Oethylhexyl	H	H	H	Cl	Cl	100	100	100	280
3	OMe	H	H	H	Cl	Cl	100	100	100	280
4	OEt	H	H	H	Cl	Cl	100	100	100	560
5	On-Pr	H	H	H	Cl	Cl	100	100	100	560
6	Ol-Pr	H	H	H	Cl	Cl	100	100	100	280
7	On-Bu	H	H	H	Cl	Cl	100	100	100	280
8	On-pentyl	H	H	H	Cl	Cl	100	100	100	280
9	On-hexyl	H	H	H	Cl	Cl	98	100	100	560
10	OPh	H	H	H	Cl	Cl				
11	NHEt	H	H	H	Cl	Cl	0	0	0	280
12	OMe	H	C(O)Me	H	Cl	Cl	95	100	95	280
13	OMe	C(O)Me	C(O)Me	H	Cl	Cl	95	100	95	280
14	OH	H	H	H	Br	Cl	100	100	100	280
15	OMe	H	H	H	Br	Cl	100	100	100	280
16	OMe	H	H	H	F	Cl	100	100	100	560
17	OMe	H	H	Br	Br	Br	80	100	100	560
18	OH	H	H	F	Cl	Cl	100	100	100	560
19	OH	H	H	Br	Cl	Cl	100	100	100	560
20	OH	H	H	OMe	Cl	Cl	100	100	100	560
21	OH	H	H	SMe	Cl	Cl	90	95	70	560
22	OH	H	Me	H	Cl	Cl	100	100	100	560
23	OH	H	Et	H	Cl	Cl	100	100	100	560
24	OH	H	i-Pr	H	Cl	Cl	100	100	100	560
25	OH	H	EtOMe	Cl	Cl	Cl	90	100	90	560
26	OH	H	n-Bu	H	Cl	Cl	100	100	100	560
27	OH	Me	Me	H	Cl	Cl	100	100	98	560
28	OH	pyrrolidine		H	Cl	Cl	80	95	100	560
29	OH	morpholine		H	Cl	Cl	0	0	80	560
30	OH	H	H	H	Br	OMe	100	90	98	560
31	OH	H	H	Cl	Br	OMe	100	100	100	560
32	OH	H	H	Cl	Cl	F	90	70	70	280
33	OH	H	H	H	Cl	Br	100	100	100	560
34	OH	H	H	Cl	CF3	Cl	100	100	90	560
35	OH	H	H	H	CF3	Cl	100	100	95	560

IPOHE = morningglory (*Ipomoea hederacea*)

AMARE = pigweed (*Amaranthus retroflexus*)

ABUTH = velvetleaf (*Abutilon theophrasti*)

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TABLE 7
PREEMERGENCE HERBICIDAL ACTIVITY & CONTROL

Cpd. No.	Rate, g/Ra	XANST	CHEAL	AMARE	ABUTH	EPHHL	ALOMY	ECHCG	DIGSA	SEFFA	SORBI	AVEFA
1	35	99	99	88	95	62	36	17	20	40	60	37
3	35	90	100	90	95	20	nt	20	40	40	30	10
14	35	100	100	100	100	70	60	40	80	98	50	40
31	35	98	90	60	80	40	30	30	30	30	20	30

nt=no test
XANST=cocklebur (*Xanthium strumarium*)
ABUTH=velvetleaf (*Abutilon theophrasti*)
ALOMY=blackgrass (*Alopecurus myosuroides*)
DIGSA=crabgrass (*Digitaria sanguinalis*)
SORBI=Rox orange sorghum (*Sorghum bicolor*)
CHEAL=lambquarters (*Chenopodium album*)
AMARE=pigweed (*Amaranthus retroflexus*)
EPHHL=wild poinsettia (*Euphorbia heterophylla*)
ECHCG=barnyardgrass (*Echinochloa crus-galli*)
SEFFA=giant foxtail (*Setaria faberi*)
AVEFA=wild oats (*Avena fatua*)

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22. Range & Pasture Crop Testing

Rates are calculated based upon 5 doses being applied. The high rate (X), followed by serial dilutions of 1/2X, 1/4X, 1/8X and 1/16X. Compound requirements are based upon the 187 l/ha carrier volume, specifications of the delivery system (Mandel track sprayer) and generating 24 mL of technical spray material to allow for the dilutions and overage in the sprayer.

10 Rate g/ha - X mg
 187 L/ha 24 mL

Example:

	<u>Starting X rate (g/ha)</u>	<u>mg required</u>
	560	71.9
15	280	35.9
	140	17.95
	70	8.9

20 All technical materials were formulated in 97:3 (acetone:DMSO) with 0.25% X-77. The total volume of solvent is maintained at less than 7%. An overhead Mandel track sprayer calibrated to deliver 187 l/ha was used for all treatment applications (post-emergence). Picloram was included as a comparison treatment.

25 Solutions were applied with a mechanized track-sprayer at the following settings:

Nozzle: 8002E

Speed: 2 mph

Spray Pressure: 40 psi

30 Spray height: 17 inches above top of plants

This provides an application volume of 187 l/ha

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Percent weed control (burn down) was evaluated 3 weeks after treatment. Visual control on a 0-100 linear scale was used, with 0 representing no control and 100 representing total control. Burn down ratings were taken for annual and perennial weed species. Some of the compounds tested, application rates employed, plant species tested, and results are given in Tables 8-10.

Table 8

Salts of Compound 1

salt	Post-emergent GR ₅₀ g/Ha		
	CASOB	CONAR	CIRAR
free acid	11	59	47
potassium salt	<8.8	36	27
amine salt	<8.8	34	37
dimethylamine salt	11.8	>140	43
monoethanolamine salt	11	20	18
triethylamine salt	<8.8	18	<8.8
trisopropanolamine salt	11	20	43

CASOB=sicklepod (*Cassia obtusifolia*)
CONAR=field bindweed (*Convolvulus arvensis*)
CIRAR=Canada thistle (*Cirsium arvense*),
3 week evaluation

Table 9

Control of Several Key Weeds In Pasture

Cmpd #	Post-emergent Evaluation - % control				Rate (g/Ha)
	AGRCR	CIRAR	RUMOB	AMBEL	
3	30	90	100	100	70
6	30	95	100	93	70
22	10	90	100	nt	70
27	30	80	100	85	70

AGRCR = crested wheatgrass (*Agropyron cristatum*)
CIRAR = Canada thistle (*Cirsium arvense*)
RUMOB = broadleaf dock (*Rumex obtusifolia*)
AMBEL = common ragweed (*Ambrosia artemisiifolia*)
3 week evaluation
nt = not tested

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Table 10

Control of Several Key Weeds in Clover
Pasture

Cmpd	GR ₂₀	g/ha GR ₂₀	GR ₂₀
	TRFRE	CONAR	CIRAR
3	<17.5	127.7	<17.5
4	<17.5	59	<17.5
5	<17.5	140.1	<17.5
6	98.8	98.8	<17.5
7	15.3	116.6	17.3
9	20.7	66	20.7

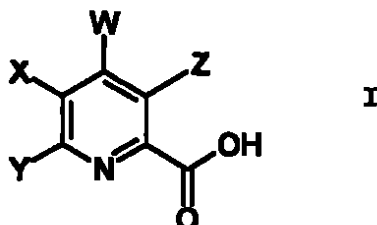
TRFRE=White Clover (*Trifolium repens*)
CONAR=Field Bindweed (*Convolvulus arvensis*)
CIRAR=Canada thistle (*Cirsium arvense*)

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WHAT IS CLAIMED IS:

1. A compound of Formula I:



wherein

- 5 X represents H, halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl;

Y represents halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl;

- 10 Z represents halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl;

W represents -NR₁R₂, -N=CR₃R₄ or -NHN=CR₃R₄

where

- 15 R₁ and R₂ independently represent H, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl, heteroaryl, hydroxy, C₁-C₆ alkoxy, amino, C₁-C₆ acyl, C₁-C₆ carboalkoxy, C₁-C₆ alkylcarbonyl, C₁-C₆ alkylsulfonyl, C₁-C₆ trialkylsilyl or C₁-C₆ dialkyl phosphonyl or R₁ and R₂ taken together with N represent a 5- or 6-membered saturated or unsaturated ring which may contain additional O or N heteroatoms; and

- 20 R₃ and R₄ independently represent H, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl or heteroaryl or R₃ and R₄ taken together with -C represent a 5- or 6-membered saturated ring; and

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agriculturally acceptable derivatives of the carboxylic acid, with the proviso that when X represents H or Cl, then Y and Z are not both Cl.

2. A compound of claim 1 wherein:

5 X represents H, halogen, cyano or trifluoromethyl;

Y represents halogen, cyano or trifluoromethyl;

Z represents halogen, cyano or trifluoromethyl;

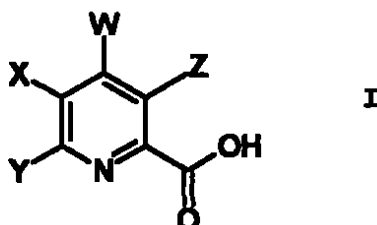
W represents $-NR_1R_2$

10 where

R_1 and R_2 independently represent H, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl or R_1 and R_2 taken together with N represent a 5- or 6-membered saturated ring which may contain additional O or N heteroatoms; and

15 agriculturally acceptable salts, esters or amides of the carboxylic acid.

3. A composition comprising an herbicidally effective amount of a 4-aminopicolinate of Formula I:



20

wherein

X represents H, halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

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Y represents halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl;

Z represents halogen, C₁-C₆ alkoxy, C₁-C₆ alkylthio, aryloxy, cyano or trifluoromethyl;

5 W represents -NR₁R₂, -N=CR₃R₄ or -NHN=CR₃R₄

where

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10 R₁ and R₂ independently represent H, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl, heteroaryl, hydroxy, C₁-C₆ alkoxy, amino, C₁-C₆ acyl, C₁-C₆ carboalkoxy, C₁-C₆ alkylcarbonyl, C₁-C₆ alkylsulfonyl, C₁-C₆ trialkylsilyl or C₁-C₆ dialkyl phosphonyl or R₁ and R₂ taken together with N represent a 5- or 6-membered saturated or unsaturated ring which may contain additional O or N heteroatoms; and

15 R₃ and R₄ independently represent H, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl or heteroaryl or R₃ and R₄ taken together with =C represent a 5- or 6-membered saturated ring; and

20 agriculturally acceptable derivatives of the carboxylic acid, with the proviso that when X represents Cl, then Y and Z are not both Cl, in admixture with an agriculturally acceptable adjuvant or carrier.

4. A composition of claim 3 wherein:

X represents H, halogen, cyano or trifluoromethyl;

25 Y represents halogen, cyano or trifluoromethyl;

Z represents halogen, cyano or trifluoromethyl;

W represents -NR₁R₂

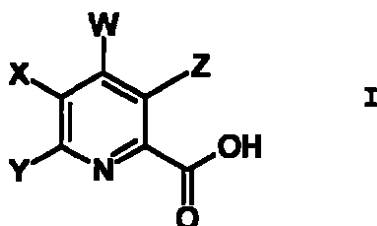
where

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R_1 and R_2 independently represent H, C_1-C_6 alkyl, C_3-C_6 alkenyl, C_3-C_6 alkynyl or R_1 and R_2 taken together with N represent a 5- or 6-membered saturated ring which may contain additional O or N heteroatoms; and

- 5 agriculturally acceptable salts, esters or amides of the carboxylic acid.

5. A method of controlling undesirable vegetation which comprises contacting the vegetation or the locus thereof or applying to the soil to prevent the
10 emergence of vegetation with an herbicidally effective amount of a 4-aminopicolinate of Formula I:



15 wherein

X represents H, halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

Y represents halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

20 Z represents halogen, C_1-C_6 alkoxy, C_1-C_6 alkylthio, aryloxy, cyano or trifluoromethyl;

W represents $-NR_1R_2$, $-N=CR_3R_4$ or $-NHN=CR_3R_4$

where

R_1 and R_2 independently represent H, C_1-C_6 alkyl,
25 C_3-C_6 alkenyl, C_3-C_6 alkynyl, aryl, heteroaryl, hydroxy, C_1-

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C₆ alkoxy, amino, C₁-C₆ acyl, C₁-C₆ carboalkoxy, C₁-C₆ alkylcarbonyl, C₁-C₆ alkylsulfonyl, C₁-C₆ trialkylsilyl or C₁-C₆ dialkyl phosphonyl or R₁ and R₂ taken together with N represent a 5- or 6-membered saturated or unsaturated ring which may contain additional O or N heteroatoms; and

R₃ and R₄ independently represent H, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, aryl or heteroaryl or R₃ and R₄ taken together with =C represent a 5- or 6-membered saturated ring; and

10 agriculturally acceptable derivatives of the carboxylic acid, with the proviso that when X represents Cl, then Y and Z are not both Cl.

6. A method of claim 5 wherein:

15 X represents H, halogen, cyano or trifluoromethyl;

Y represents halogen, cyano or trifluoromethyl;

Z represents halogen, cyano or trifluoromethyl;

W represents -NR₁R₂

where

20 R₁ and R₂ independently represent H, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl or R₁ and R₂ taken together with N represent a 5- or 6-membered saturated ring which may contain additional O or N heteroatoms; and

25 agriculturally acceptable salts, esters or amides of the carboxylic acid.

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ABSTRACT

- 5 4-Aminopicolinic acids, having halogen, alkoxy, alkylthio, aryloxy, cyano or trifluoromethyl substituents in the 3-, 5- and 6-positions, and their amine and acid derivatives are potent herbicides demonstrating a broad spectrum of weed control.

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