Synthesis, Herbicidal Activity, and Mode of Action of IR 5790

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IR 5790, an arylthiadiazolone herbicide structurally related to oxadiargyl and oxadiazon, was synthesized. The herbicidal activity and mode of action of IR 5790 were investigated. This herbicide has broad-spectrum pre-emergence activity against both dicotyledonous and monocotyledonous weeds. The phenotypic responses of susceptible plants, such as interruption of growth and light-dependent development of necrotic areas on the foliage, are consistent with those observed with protoporphyrinogen oxidase-inhibiting herbicides. Tissues exposed to IR 5790 in darkness accumulated protoporphyrin IX, which led to a photodynamic loss of membrane integrity upon exposure to light. Consistent with these physiological symptoms, IR 5790 strongly inhibited protoporphyrinogen oxidase, with an I_{50} value of 3 nM. The presence of a sulfur atom did not significantly alter the molecular properties of the thiadiazolone ring, relative to the oxadiazolone ring of oxadiargyl, which explains why IR 5790 has the same mode of action as this herbicide.

Keywords: *Herbicide; thiadiazolone; cellular leakage; protoporphyrinogen oxidase; protoporphyrin; Protox; peroxidizing herbicides; computer modeling*

INTRODUCTION

The experimental arylthiadiazolone herbicide IR 5790, 5-*tert*-butyl-3-[2,4-dichloro-5-(2-propynyloxy)phenyl]-1,3,4-thiadiazol-2(3*H*)-one (**3**) (Figure 1), has recently been discovered by Isagro Ricerca Srl for broad-spectrum pre-emergence weed control in rice and winter cereals (*1*, *2*).

IR 5790 has structural similarities with the herbicides of the aryloxadiazole class, such as oxadiazon, 3-[2,4-dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2-(3*H*)-one, and oxadiargyl, 3-[2,4-dichloro-5-(2-propynyloxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2-(3*H*)-one, that are known to inhibit the enzyme protoporphyrinogen oxidase (Protox) (*3*). Inhibition of this highly regulated enzymatic conversion of protoporphyrinogen IX (Protogen) to protoporphyrin IX (Proto) leads to an unregulated extraplastidic accumulation of Proto (*4*−*7*). Accumulation of this photodynamic chlorophyll precursor is responsible for the light-dependent herbicidal action of Protox-inhibiting herbicides (*8*). All known Protox inhibitors apparently compete with Protogen at or near the catalytic site on the enzyme (*9*−*17*). The structural similarity between IR 5790 and oxadiazolone herbicides and the phenotypic response exhibited by treated susceptible plants suggest that the molecular target of IR 5790 is the enzyme Protox.

This paper reports the synthesis of IR 5790, its weed spectrum and crop selectivity of pre-emergence and postemergence application, and the description of its mode of action at the physiological and biochemical levels.

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MATERIALS AND METHODS

Melting points were determined using a Büchi SMP-20 apparatus and are reported uncorrected. Microanalyses were obtained using a Perkin-Elmer 2400 CHN element analyzer. Mass spectra were obtained using a Finnigan MAT INCOS 50 spectrometer with an electron impact source at 760 eV. IR spectra were obtained using a Perkin-Elmer 1420 spectrophotometer as KBr disks. The NMR spectra were recorded with a Bruker AC 200 spectrometer at 200.13 MHz with TMS as the internal standard.

Synthesis of IR 5790. *N′-[2,4-Dichloro-5-(2-propynyloxy)-phenyl]-N-thiopivaloylhydrazine (**2**).* Tetraphosphorous decasulfide (P_4S_{10}; 0.720 g, 1.6 mmol) was added to a solution of *N′*-[2,4-dichloro-5-(2-propynyloxy)phenyl]-*N*-pivaloylhydrazine (**1**) (2 g, 6.4 mmol) in dioxane (40 mL) at room temperature (22 °C), and the resulting mixture was stirred at 60 °C for 3 h (*1*). The reaction mixture was poured into water and extracted with diethyl ether. The organic phase was washed with water, dried (Na_2SO_4), and concentrated in vacuo. The residue (2.8 g) was dissolved in diethyl ether/*n*-hexane (1:1), filtered through silica gel, and concentrated in vacuo. Crystallization from *n*-hexane afforded 1.7 g of yellowish powder (80.2%): mp 126−128 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.31 (1H, s), 6.64 (1H, br s), 4.69 (2H, d, J = 2.3 Hz), 2.53 (1H, t, J = 2.3 Hz), 1.14 (9H, s); IR ν_{max} cm^{-1} 3247, 3020, 2923, 1272. Anal. Calcd for $C_{14}H_{16}Cl_2N_2OS$: C, 50.76; H, 4.87; N, 8.46. Found: C, 50.18; H, 4.61; N, 8.33.

*5-tert-Butyl-3-[2,4-dichloro-5-(2-propynyloxy)phenyl]-1,3,4-thiadiazol-2(3H)-one (**3**).* Pyridine (0.2 mL) and trichloromethylchloroformate (0.5 g, 2.5 mmol) were added to a solution of *N′*-[2,4-dichloro-5-(2-propynyloxy)phenyl]-*N*-thiopivaloylhydrazine (**2**) (1.65 g, 5 mmol) in dioxane (25 mL), under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 3 h.

The reaction mixture was poured into water (250 mL) and extracted with diethyl ether (100 mL × 3). The combined extracts were washed to neutrality with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by silica gel column chromatography with *n*-hexane/ethyl acetate (9:1) as the eluent to give 1.4 g of white to yellowish powder

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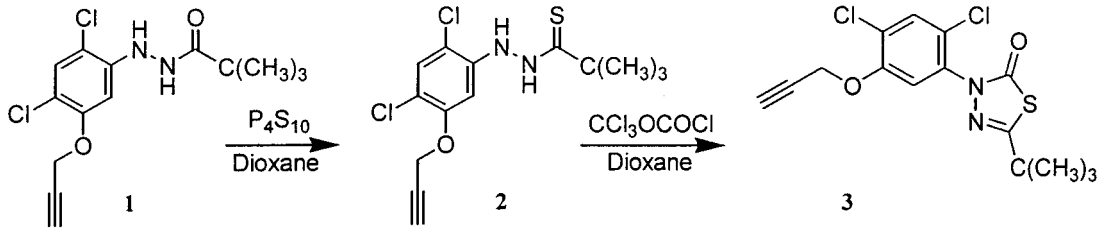

Figure 1. Synthesis of IR 5790.

(78.4%): mp 102−104 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (1H, s), 7.20 (1H, s), 4.81 (2H, d, J = 2.4 Hz), 2.67 (1H, t, J = 2.4 Hz), 1.36 (9H, s); IR ν_{max} cm^{-1} 3290, 3050, 2925, 2120, 1660, 1630; MS, m/z 356 (M^+), 321 ($M^+ - Cl$), 296 ($M^+ - COS$), 101, 57. Anal. Calcd for $C_{15}H_{14}Cl_2N_2O_2S$: C, 50.43; H, 3.95; N, 7.84. Found: C, 50.28; H, 3.72; N, 7.76.

Determination of Postemergence and Pre-emergence Activity of IR 5790 in the Greenhouse. Herbicidal activity was evaluated against both monocotyledonous and dicotyledonous weeds grown in greenhouses. Plants were grown in 10 × 10 cm pots containing sandy soil. There were 10 pots for each species. All of the pots were uniformly watered every 2 days and kept in a greenhouse environment at 24 °C and 60% relative humidity. The light cycle was 16 h light (luminous intensity at 143 μmol s^{-1} m^{-2} photon flux density) and 8 h dark. Each species was divided into two groups of five pots. The first group was treated 15 days after sowing with a hydroacetonic dispersion containing IR 5790 at the desired concentration, acetone (10 vol %), and Tween 20 (0.5%). The herbicide was applied over the top with a TJ 60-8002 EVS flat fan nozzle at the pressure of 3 bar and dispensing a volume of 430 L/ha. The second group (control) was treated with a hydroacetonic solution containing only acetone (10 vol %) and Tween 20 (0.5%). Plants were 10−15 cm high (depending on the species) at the time of treatment.

Herbicidal activity was evaluated 15 days after treatment on a visual rating scale ranging from 0 for no effect to 5 for complete control (see Table 1 for complete description). Visual rating refers to the percentage of leaf damage observed on treated plants relative to the controls.

Pre-emergence activity was tested on plants grown as described above except that IR 5790 was applied to the soil 24 h after sowing. Herbicidal activity was evaluated 28 days after the treatment as described above.

Laboratory Plant Material. Cucumber seedlings (*Cucumis sativus* L. cv. Long Green Improved) used for the leakage and Proto accumulation studies were grown in a growth chamber maintained at 25 ± 2 °C and with 200 μmol s^{-1} m^{-2} photon flux density (PFPD) of continuous illumination. Barley (*Hordeum vulgare* L.) seedlings used as a source of etioplasts for the Protox inhibition assay were grown in the dark.

Cellular Damage. Electrolyte leakage induced by IR 5790 was determined as described by Duke and Kenyon (*18*) using 7-day-old cucumber cotyledons. Fifty 4-mm cucumber cotyledon disks (~0.1 g of fresh weight) were placed in a 6-cm-diameter disposable Petri dish containing 5 mL of 1% (w/v) sucrose and 1 mM 2-(*N*-morpholino)ethanesulfonic acid (MES; pH 6.5) with 10 and 100 μM IR 5790 dissolved in acetone. Controls received the same amount of acetone as the treated tissues but without the test compounds. The final concentration of acetone in the dishes was 1% (v/v). The Petri dishes were placed in the dark at 25 °C for 16 h and then exposed to 325 μmol m^{-2} s^{-1} of photosynthetically active radiation for the remainder of the experiment.

Cellular damage was determined by measuring electrolyte leakage into the bathing medium with a conductivity meter capable of assaying 1 mL of bathing medium (*19*). Conductivity was monitored for 20 h in darkness, followed by 8 h of continuous light (375 μmol m^{-2} s^{-1} photon flux density). Because of differences in background conductivity between different treatment solutions, results are expressed as a change in the conductivity after initial measurement at the beginning of the dark period. All treatments for electrolyte leakage measurements were performed in triplicate, and the experiment was repeated. Both experiments yielded similar results, but the data could not be pooled because of differences in overall changes in conductivity. The data presented are representative examples of the experiment. Each point is the mean of three measurements, and the error bars represent the standard deviation. Maximum electrolyte leakage was estimated by boiling samples for 10 min and measuring the conductivity of the bathing medium.

Table 1. Pre-emergence and Postemergence Activities of IR 5790 on Selected Weeds and Crops[a]

	postemergence (g/ha)				pre-emergence (g/ha)	
species	150	50	15	5	150	50
dicotyledonous weeds						
Abutilon theophrasti	5	4.7	2.5	−	0.1	0
Amaranthus retroflexus	5.0	3.5	−	−	5.0	3.3
Amni maius	1.0	0.5	0.2	−	0.2	0
Capsella bursa−pastoris	3.5	1.5	−	−	5.0	4.2
Chenopodium album	5.0	5.0	4.5	1.5	5.0	4.7
Convolvulus sepium	5.0	4.5	3.5	1.0	0	0
Galium aparine	3.0	2.0	−	−	0.5	0
Geranium dissectum	3.5	3.0	−	−	0	0
Ipomea purpurea	5.0	5.0	5.0	3.0	0	0
Matricaria chamomilla	1.0	0.2	−	−	3.1	0.5
Papaver rhoeas	2.5	0.5	−	−	5.0	4.7
Polygonum persicaria	5.0	5.0	4.7	2.0	3.2	0.7
Portulaca oleracea	5.0	5.0	4.5	3.5	5.0	4.5
Sida spinosa	4.5	3.0	−	−	0.5	0
Solanum nigrum	5.0	5.0	1.5	0.2	4.7	2.0
Stellaria media	0.5	0.2	0	−	2.5	0
Veronica persica	3.5	0.5	−	−	3.0	2.0
Xanthium strumarium	−	1.0	−	−	0	0
monocotyledonous weeds						
Alopecurus myosuroides	4.5	2.5	0.5	0.2	4.2	1.5
Avena fatua	2.5	0.5	0	−	0	0
Digitaria sanguinalis	4.7	3.5	−	−	5.0	4.5
Echinochloa crus-galli	1.5	0.5	0	−	4.6	2.7
Panicum dichotomiflorum	5.0	3.0	0	−	5.0	5.0
Phalaris arundinacea	2.5	2.0	−	−	0	0
Setaria viridis	4.5	1.5	−	−	4.0	2.7
Sorghum bicolor	1.0	0.5	1.0	−	3.0	0
crops						
Zea mays	0.5	0.2	−	−	0	−
Oriza sativa	0.2	0.2	0.5	−	0	0
Glycine max	2.5	1.5	0.5	−	0	−
Brassica napus	−	−	−	−	0	0
Triticum aestivum	3.5	−	0.2	0	0	−
Beta vulgaris	5.0	3.5	−	−	1.5	1.0
Gossypium hirsutum	4.5	2.5	−	−	−	−

[a] 0 = 0−9% injury; 1 = 10−29% injury; 2 = 30−49% injury; 3 = 50−69% injury; 4 = 70−89% injury; 5 = 90% injury−death of the plant treated; −, not tested.

Protox Inhibition. Crude etioplast preparations were obtained from etiolated barley seedlings according to the method of Sherman et al. (*7*) and kept at −80 °C until used. No loss of activity was observed in samples stored under these conditions (for up to 1 month). Protein concentration was adjusted to 4 mg/mL prior to storage.

The procedures for Protogen preparation and Protox enzyme assays were derived from Jacobs and Jacobs (*20*). The assay mixture consisted of 100 mM *N*-[2-hydroxyethyl]piperazine-*N*′-[2-ethanesulfonic acid] (HEPES), 5 mM ethylenediamine-

tetraacetic acid (EDTA), 2 mM dithiothreitol (DTT), and 20 μL of substrate. The I_{50} values were determined under saturated substrate conditions (2 mM Protogen) in the presence of 0, 0.01, 0.1, 1, 10, 100, and 1000 nM technical grade IR 5790 (>95% purity).

The reaction was initiated by adding 20 μL of Proto to the etioplasts/assay mixture, which had been preincubated with or without the inhibitors for 15 min on ice prior to the assay. The rate of formation of Proto was measured continuously for 60 s at 30 °C using a spectrofluorometer (model RF-5301 PC, Shimadzu) with excitation and emission wavelengths set at 395 and 630 nm, respectively. Excitation and emission bandwidths were set at 1.5 and 20 nm, respectively.

Proto Determination. All extractions for HPLC determinations of Proto were made under dim, green light after 2 h of incubation in the presence of either 10 and 100 μM technical grade IR 5790 or acifluorfen-methyl in darkness at 25 °C. Cucumber cotyledon disks (~0.1 g each) were homogenized in 2 mL of HPLC grade methanol/0.1N NH_4OH (9:1 v/v) with a Brinkman Polytron at full speed for 15 s and sonicated for 10 min. The supernatant was collected after centrifugation at 3000*g* for 3 min. The pellet was resuspended in 1 mL of basic methanol and sonicated for 5 min, and the supernatant was collected after centrifugation as above. Supernatants were pooled and filtered through a 0.2 μm nylon syringe filter and stored in light-tight glass vials at −20 °C until analysis by HPLC.

The HPLC system was composed of Waters Associates components (Milford, MA) that included a model 717 plus autosampler, a model 600 controller, and models 474 fluorescence and 996 photodiode array detectors. The column used was a 3.9 × 300 mm (i.d.) μBondapak C18 reversed-phase column preceded by a Bio-Rad ODS-5S guard column. The solvent system consisted of a gradient beginning at 70% HPLC grade methanol and 30% double-distilled H_2O, reaching 100% methanol within 20 min in a linear mode, holding 100% methanol 20 min to clean the column, and re-equilibrated to the original settings. Injection volume was 100 μL. Pigment detection was performed with fluorescence detector with excitation and emission wavelength settings at 400 and 630 nm, respectively, and the peaks were confirmed by scanning them from 300 to 700 nm with the photodiode array detector. Proto concentration in samples was calculated from a standard curve determined using an authentic Proto standard. The data are expressed on a molar basis per gram of fresh weight (FW). All treatments were performed in triplicate, and the experiment was repeated. Data from both experiments were pooled and expressed as mean followed by standard deviation.

Molecular Properties. The structure of IR 5790 was built using fragments from the fragment library provided in SYBYL 6.3 (Tripos Associates, St Louis, MO) on a Silicon Graphics O_2 250 MHz R10000. Charges were calculated using Gasteiger-Hückel, and the structures were minimized using the Tripos force field to obtain a low-energy conformer. Minimization was initiated with Simplex (a nonderivative-based procedure) for 100 iterations, followed by Powell (a first-derivative-based method) for 1000 iterations, until convergence criteria of 0.005 were met. The structure was subjected to full geometry optimization via MOPAC (Quantum Chemistry Program Exchange 560, version 6.0, Department of Chemistry, Indiana University, Bloomington, Indiana) using AM1 (Austin Model) parametrization (*21*).

RESULTS AND DISCUSSION

IR 5790 is a broad-spectrum herbicide discovered by Isagro Ricerca. Its synthesis is described in detail under Materials and Methods and is illustrated in Figure 1. It has pre-emergence activity against annual broadleaf weeds, grasses, and sedges. The product has particularly good weed control in rice, sunflowers, vegetables, sugarcane, perennial crops, and turf (*2*) (N. Fossati and E. Signorini, personal communication).

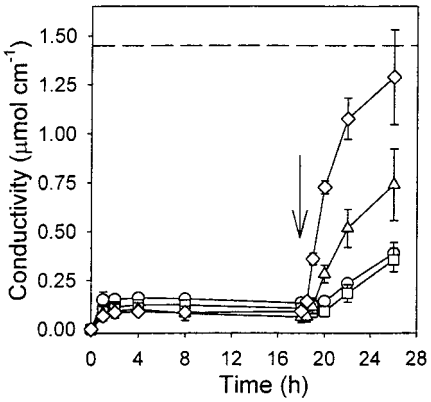

Figure 2. Electrolyte leakage from cucumber cotyledon disks exposed to IR 5790 as measured by change in conductivity in the bathing medium: (○) control; (□) 1 μM IR 5790; (△) 10 μM IR 5790; (◇) 100 μM IR 5790. Disks were incubated in the presence of IR 5790 for 20 h in darkness and then exposed to continuous light (375 μmol m^{-2} s^{-1}). Arrow indicates beginning of light exposure. Dotted line represents maximum conductivity obtained after boiling samples.

IR 5790 has a soil half-life of ~45 days but is not expected to leach to groundwater because it has very low soil mobility. The acute oral LD_{50} in rats is >4000 mg/kg, suggesting that this herbicide poses a low risk to mammals. Protox inhibitors are in general considered to have low toxicological problems, and many of the newer Protox inhibitors have been registered as reduced-risk pesticides.

Herbicidal Activity. The primary weed targets are the broadleaf species *Amaranthus* spp., *Abutilon theophrasti* (L.), *Capsella bursa-pastoris* (L.) Med., *Chenopodium album* L., *Galium aparine* L., *Matricaria* spp., *Papaver rhoeas* L., *Poligonum persicaria* L., *Portulaca oleracea* L., *Solanum nigrum* L., *Veronica persica* Poir. and the grasses *Alopecurus myosuroides* Huds., *Digitaria sanguinalis* (L.) Scop., *Phalaris arundinacea* L., and *Echinochloa crus-galli* (L.) Beauv.

Extensive greenhouse experiments with IR 5790 showed that this herbicide possesses good pre- and postemergence activities on both annual monocotyledonous and dicotyledonous species. Pre-emergence activity is associated with excellent selectivity to major crops, even at the higher rates (Table 1). Growth of susceptible plants exposed to IR 5790 was reduced, and the foliage developed necrotic areas sometimes called bronzing that is often associated with diphenyl ether and triazolinone herbicides (*22*).

Electrolyte Leakage. As with most Protox inhibitors, IR 5790 induced a light-dependent loss of membrane integrity as observed by the leakage of electrolytes from herbicide-treated cotyledon disks (Figure 2). The level of electrolyte leakage was proportional to the concentration of the herbicide, with no leakage at 1 μM, moderate leakage at 10 μM, and massive leakage at 100 μM. Conductivity of the bathing medium exposed to 100 μM IR 5790 was 90% of potential maximum (obtained from boiled samples), indicating that this herbicide caused an almost total loss of cellular electrolytes at that concentration. Despite the dramatic loss of membrane integrity observed in the cotyledon disk assay, no photobleaching symptoms were observed in the herbicide-treated disks after 8 h of exposure to 400 μmol m^{-2} s^{-1} light.

Duke et al. (*23*) have reported a similar loss of membrane integrity in tissues exposed to the structur-

Table 2. Accumulation of Proto in Cucumber Cotyledon Disks

treatment	Proto[a] (pmol g^{-1} of FW h^{-1})	fold increase
control	6.7 ± 16.2[b]	0
IR 5790		
10 μM	1577.7 ± 359.3	234
100 μM	2481.5 ± 511.1	369
acifluorfen-methyl		
10 μM	1964.1 ± 851.7	292
100 μM	2622.0 ± 581.4	390

[a] Proto levels were determined after 2 h of dark incubation. [b] Means are pooled from two experiments (n = 6) followed by standard deviation.

ally related oxadiazole herbicide oxadiazon. Relatively little information is available on the more recent oxadiazole herbicide oxadiargyl. However, this compound, which differs from IR 5790 by a substitution of a sulfur atom to an oxygen in the diazole ring, is also classified as a Protox inhibitor that should induce electrolyte leakage in treated tissues (*24*).

Proto Accumulation and Protox Inhibition. Cucumber cotyledon disks exposed to IR 5790 accumulated large amounts of Proto, relative to the untreated samples (Table 2). Proto levels in tissues exposed to 10 and 100 μM IR 5790 were 234- and 369-fold greater than the baseline amount detected in controls. A similar increase in Proto level was observed in a parallel study using acifluorfen-methyl (AFM). Such dramatic increases in cellular concentrations of Proto are common to all Protox-inhibiting herbicides (*22*). Accumulation of Proto was commensurate with the concentration of the inhibitors used (Table 2). The accumulation of this photodynamic pigment in response to IR 5790 was similar to that obtained with the diphenyl ether herbicide AFM (Table 2).

Two other porphyrin intermediates appeared in cucumber cotyledons after 20 h of dark incubation. The exact nature of these porphyrins has not been determined, but their spectra and relative retention times suggest that they may be Mg-Proto and Mg-Proto-methyl ester (data not shown).

The herbicidal activity of IR 5790 and the symptoms developing on susceptible plants, its structural similarity to oxadiargyl and oxadiazon, its ability to cause light-dependent leakage, and the induction of Proto accumulation were strong indications that this herbicide acted like a Protox inhibitor. Accordingly, the in vitro activity of Protox from crude barley etioplasts was sensitive to IR 5790, with an I_{50} of 3 nM (Figure 3). Numerous Protox inhibitors have been generated, but few of them have such a low I_{50} (e.g., refs *15* and *25*). However, the overall in vivo activity of IR 5790 is relatively low compared to the excellent in vitro inhibition of its molecular target site. Similar results reported with other Protox inhibitors have been attributed primarily to rapid metabolic degradation of the herbicides (*7*, *16*, *26*, *27*). Although other physiological factors such as uptake and translocation do not usually play important roles in the resistance of plants to Protox inhibitors, they sometimes influence their overall activity. For example, the foliar penetration and herbicidal activity of unformulated sulfentrazone (a triazolinone Protox inhibitor) were inversely proportional to the cuticle thickness (*28*). No difference in uptake of this herbicide was observed when surfactants were added to the sulfentrazone spray mixtures. Furthermore, physicochemical characteristics such as lipophilicity could play an important role in

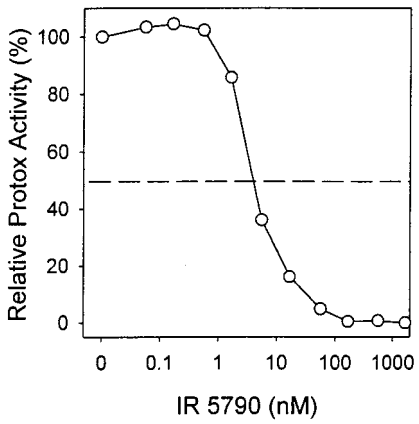

Figure 3. Effect of IR 5790 on Protox activity of barley etioplasts measured under initial-velocity conditions. Dotted line represents 50% inhibition of activity.

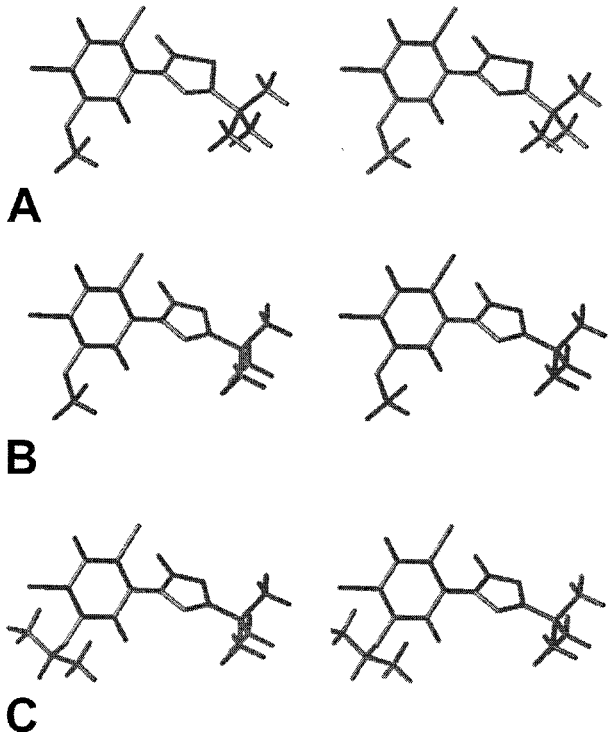

Figure 4. Relaxed stereoview of (A) IR 5790, (B) oxadiargyl, and (C) oxadiazon following structure optimization and energy minimization of the herbicides. Notice the longer bonds in the thiadiazolone ring of IR 5790, relative to the oxadiargyl and oxadiazon. The structures were orientated to optimize the view of the heterobicyclic backbones. The *m*-oxypropargyl side chains of oxadiazon and IR 5790 extend behind the plane of the structures.

limiting the concentration of the inhibitor at the target site, especially for a membrane-localized enzyme such as Protox (*14*). Because the greenhouse test presented in the paper was done with unformulated IR 5790, one should consider that the overall performance of this herbicide may be greatly enhanced via formulation.

Computer modeling of the diphenyl ether class of Protox inhibitors has indicated that the diphenyl ether backbone of these herbicides apparently mimics half of the tetrapyrrole ring of Protogen (*13*). Protox inhibitors with heterobicyclic backbones, such as the triazolinones, phenylimides, oxadiazoles, and IR 5790, do not resemble half of the tetrapyrrole as much, yet these compounds still act as competitive enzyme inhibitor. Moreover, heterobicyclic Protox inhibitors also compete for the

Table 3. Physical and Molecular Properties of IR 5790

property	IR 5790	oxadiargyl	oxadiazon
physical			
molecular weight	357.2	341.2	345.2
melting point, °C	103	131	87
solubility			
water, mg/L	1.1	0.37	0.70
organic, g/L	>250	>250	>250
volatility, mmHg at 25 °C	n/a	1.87×10^{-8}	7.76×10^{-7}
K_{ow}	25120[a]	8915	63100
molecular			
VDW_{area}, [b] Å^2	415.91	409.63	415.96
VDW_{vol},[b] Å^3	527.36	509.55	531.67
dipole moment, Debye	3.48	4.748	4.93
heat of formation, kcal	85.965	67.88	50.50
ionization potential, eV	9.29	9.30	9.44
partial $charge_{15}$,[c] eV	0.2440	−0.1875	−0.1899
VDW_{vol} [b] of heterocycle, Å^3	77.3	58.2	58.2

[a] Estimated by HPLC measurement. [b] VDW_{area} and VDW_{vol}, van der Waals area and volume, respectively. [c] Atom 15 was a sulfur for IR 5790 and an oxygen for oxadiargyl and oxadiazon.

binding of the diphenyl ether herbicides, suggesting that they act at or near the same site.

Structural comparison of IR 5790 to the oxadiazole herbicides oxadiazon and oxadiargyl highlights the similarities among these compounds (Figure 4). Except for the phenyl side chain changing from an isopropyloxy of oxadiazon, IR 5790 differed from the other compounds only by the sulfur atom in the thiadiazolone ring. The molecular characteristics of sulfur are similar to those of oxygen, so the thiadiazolone ring was expected to have molecular properties similar to those of oxadiargyl. The only differences observed were a slightly lower electronegative partial charge, a smaller dipole moment, and a larger van der Waals volume associated with the sulfur atom of IR 5790, relative to the oxygen atoms found in the other herbicides (Table 3). The slightly longer bonds associated with the sulfur atoms can be observed by comparing the heterocyclic rings of the three compounds displayed in Figure 4. These minor differences probably have little effect on the biological activity of these compounds, and it is not surprising that IR 5790 has a mode of action similar to that of the structurally related oxadiazole class of herbicide.

Conclusion. The new thiadiazolone herbicide IR 5790 possesses a broad spectrum of activity and can be applied both pre- and postemergence. It is a potent, competitive inhibitor of Protox and induces physiological responses normally associated with the inhibition of this target site, such as light-dependent electrolyte leakage and Proto accumulation. Substitution of an oxygen atom for a sulfur did not affect the overall molecular properties of the heterocyclic ring. IR 5790 should provide another alternative in the control of weeds in rice and winter cereals.

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