

Influence of Substituents of Multivalent Halogen on Activity of Anilide, Carbamate, and Urea Herbicides

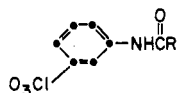
Kurt H. Pilgram,* Earl K. Jackson, and Lawrence E. Wittsell

The strongly electron withdrawing, meta-directing perchloryl (ClO_2) and iodoxy (IO_2) groups have been evaluated for their influence on the herbicidal activity and crop selectivity of anilide, *N*-phenylcarbamate, and phenylurea herbicides. *N*-Methoxy-*N*-methyl-*N'*-(3-perchlorylphenyl)urea, **8f**, is herbicidally most active and is safe on cotton. It controls a wide variety of grass and broadleaf weed species at low dosages and is more active when incorporated in the soil or applied on the soil surface before emergence than when applied to the soil surface and plant foliage after emergence. Administration of **8f** to susceptible plants causes severe bleaching (albinism), and treated plants are unable to direct the synthesis of chlorophyll.

Scores of anilides, *N*-phenylcarbamates, and ureas have been synthesized, and many have shown outstanding herbicidal properties. Both activity and crop selectivity in these three classes of herbicides are highly dependent on the position and nature of the substituents on phenyl.

In an effort to explore activity and further to improve crop selectivity in the anilide, carbamate, and urea herbicides, a selected number of structures carrying the strongly electron withdrawing, meta-directing perchloryl (ClO_2 , $\sigma_m +0.89$, $\sigma_p +1.07$) (Gardner et al., 1963) and iodoxy (IO_2 , $\sigma_m +0.68$, $\sigma_p +0.78$) (Chapman and Shorter, 1972) groups have been prepared and their herbicidal activity and crop selectivity evaluated in greenhouse and field tests.

Other than the preparation of one anilide, **6a** (Inman



(**6a**: R = CH₃; **7c**: R = OCH(CH₃)₂; **8g**: R = N(CH₃)₂)

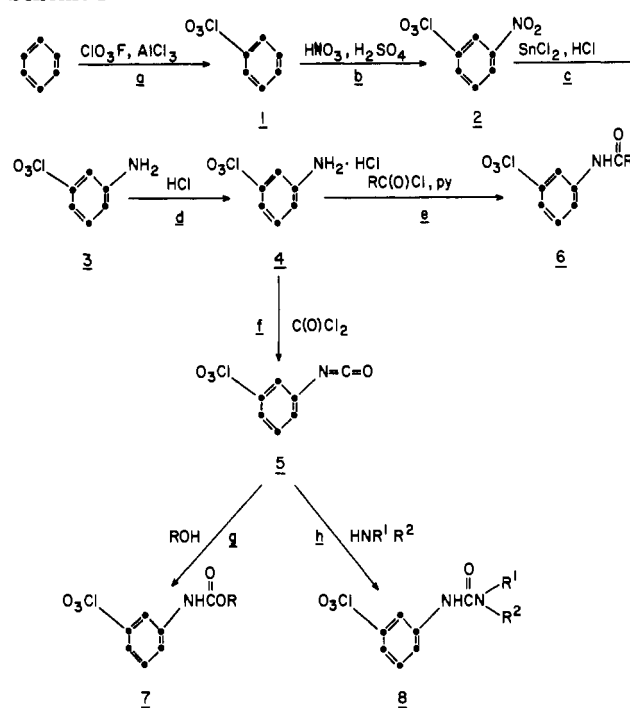
et al., 1962, 1963), and algicidal, herbicidal, and growth-modifying properties of one carbamate, **7c** (Scherer et al., 1961), and one urea, **8g** (Raasch, 1961), no properties of other anilides, carbamates, and ureas containing perchloryl and iodoxy substituents have yet been described.

MATERIALS AND METHODS

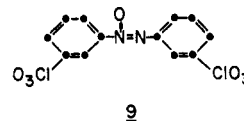
Chemical Methods. The synthetic procedure of Inman et al. (1958) was used for the preparation of the intermediate 3-perchlorylaniline hydrochloride **4** (Scheme I). Reaction of **4** in pyridine (-20 to +20 °C) with acid chlorides gave the anilides **6a-g** listed in Table I. Reaction of **4** in benzene or toluene with phosgene followed by treatment of the intermediate 3-perchlorylphenyl isocyanate **5** with alcohols gave the carbamates **7a-c**. Reaction of **5** with an amine or hydroxylamine gave the ureas **8a-h** (Table II).

All of the intermediates **1-5** must be treated with great caution because of their explosive tendencies (Inman et al., 1964). So that potential hazards (mechanical shock, local overheating) could be minimized or eliminated, none of the intermediates **1-6** was isolated in a pure or dry state. More specifically, removal of excess benzene (step a) was conducted in a falling film rotary evaporator at 65 °C (28 min) to give 70-75% of **1** as a brownish bottom product. As the reduction, step c (**2** → **3**), can be carried out in the

Scheme I




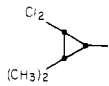


presence of solvents, complete removal of the solvent used for extraction in step b appears unnecessary. Introduction of hydrogen chloride into a solution of **3** in toluene or ether caused the hydrochloride **4** to precipitate as a light tan solid. In one instance, the filtrate from step d was concentrated. Purification of the residual tar by silica chromatography gave a small amount (1.3%) of 3,3'-diperchlorylazoxybenzene, **9**.



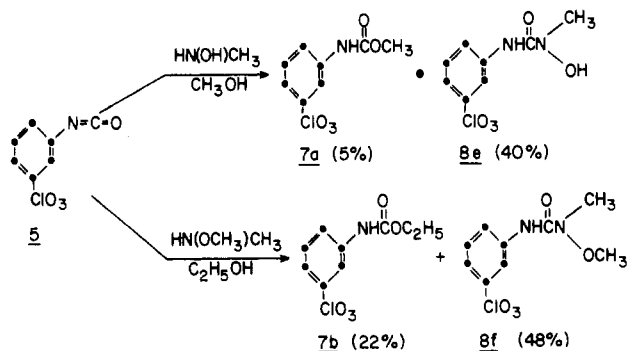
Reaction of a slurry of **4** in toluene with an excess of phosgene, at a moderately elevated temperature (40-100 °C), until the salt has dissolved followed by removal of phosgene and about two-thirds of the solvent gave a brownish solution containing 3-perchlorylphenyl isocyanate, **5**, which was used directly in steps g and h. Largely reduced yields were obtained in steps f and g when the phosgenation of **4** was carried out in ethyl acetate. The phosgenation of **4** is usually accompanied by the formation

Table I. *m*-Perchloryl Anilides and Carbamates: Properties and Herbicide Screen Results

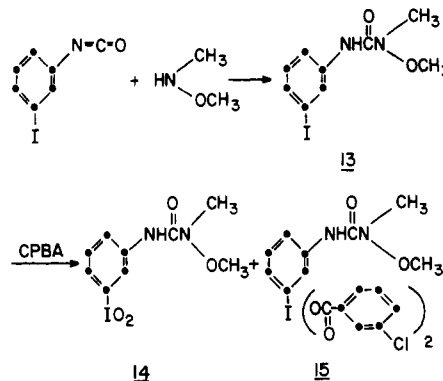
compd	R	% yield	mp, °C	phytotoxicity index ^a							
				pre				post			
				Bygr ^b		Gacr ^c		Lacg ^d		Rrpw ^e	
1 ^f	2 ^g	1	2	1 ^h	2 ⁱ	1	2				
6a	CH ₃	72	119-130	5	6	9	9	7	8	2	9
6b	C ₂ H ₅	81	90-91	2	7	9	9	7	9	4	9
6c	<i>n</i> -C ₃ F ₇	63	94-95	0	5	0	7	0	9	2	7
6d		87	160-163	0	5	9	9	8	9	3	9
6e		37	138-140	4	6	9	9	7	9	7	9
6f		62	137-138	0	4	6	9	4	7	4	9
6g		91	150-152	0	0	0	0	0	1	1	5
7a	OCH ₃	5	108-109	5	7	9	9	6	9	7	9
7b	OC ₂ H ₅	22	<i>j</i>	7	9	9	9	7	9	8	9
7c	OCH(CH ₃) ₂	17	<i>j</i>	7	9	9	9	9	9	8	9

^a O = no effect; 9 = death. ^b Barnyard grass. ^c Garden cress. ^d Large crabgrass. ^e Redroot pigweed. ^f Rate 1: soil treated with 2.4 kg/ha active ingredient/tube based on surface area. ^g Rate 2: soil treated with 24 kg/ha active ingredient/tube based on surface area. ^h Rate 1: sprayed to runoff with 250 ppm of active ingredient. ⁱ Rate 2: sprayed to runoff with 2500 ppm of active ingredient. ^j Liquid at room temperature.

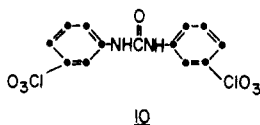
Scheme II



Scheme III

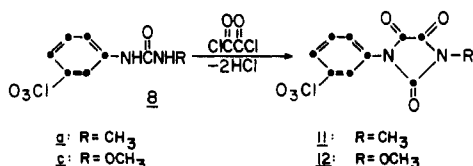


of very small amounts of *N,N'*-bis(3-perchlorylphenyl)urea, 10.



The carbamates 7a and 7b were obtained as coreaction products in low yield when a solution containing 5 in benzene was allowed to react with a solution of *N*-methylhydroxylamine in methanol, and a solution of *O,N*-dimethylhydroxylamine in ethanol, respectively (Scheme II).

The reaction of the ureas 8a and 8c with oxalyl chloride



proceeded smoothly in refluxing benzene (3 h) and toluene (2 h) to give parabanic acid derivatives 11 and 12 in good yield (Biltz reaction).

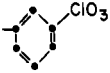





Per acid oxidation of aromatic iodo compounds can lead to derivatives of multivalent iodine (Roedig, 1955). Treatment of 3-iodophenyl isocyanate with *O,N*-di-

methylhydroxylamine gave *N*-(3-iodophenyl)-*N'*-methoxy-*N'*-methylurea, 13, from which 3-[[[(methoxymethylamino)carbonyl]amino]phenyliodosobis(3-chlorobenzoate), 15, and *N*-(3-iodoxyphenyl)-*N'*-methoxy-*N'*-methylurea, 14, were produced by oxidation with *m*-chloroperbenzoic acid (CPBA) in chloroform (Scheme III). Ureas 14 and 15 are the first reported examples of a phenylurea carrying an iodoso or iodoxy function. The formation of 15 is rationalized on the basis that the intermediate, iodoso, oxidation stage reacts, in part, with the coreaction product 3-chlorobenzoic acid; the basic nature of the iodoxy group and its ability to form diesters with organic acids are well established.

Structures and purities were ascertained by combinations of GC, TLC, IR, NMR, and MS techniques; satisfactory elemental analyses ($\pm 0.4\%$) were obtained for all new compounds. Illustrative synthetic procedures are outlined below.

3-Perchlorylaniline Hydrochloride, 4, and 3,3'-Di-perchlorylazoxybenzene, 9. To a solution of 268 g (1.3 mol) of crude 2 in 1.5 L of ethanol and 1.5 L of concentrated hydrochloric acid was added portionwise, and with stirring at 50–60 °C, 850 g (4.5 mol) of stannous chloride. After 2 h, the reaction mixture was concentrated under reduced pressure (25 min, 75–85 °C) to half of its original volume, poured into ice water, and neutralized to pH 5–6

Table II. (*m*-Perchlorylphenyl)ureas: Properties and Herbicide Screen Results

compd	R ₁	R ₂	% yield	mp, °C	phytotoxicity index ^a							
					pre				post			
					Bygr ^b		Gacr ^c		Lacg ^d		Rrpw ^e	
					1 ^f	2 ^g	1	2	1 ^h	2 ⁱ	1	2
8a	H	CH ₃	95	162-164	6	9	9	9	7	9	7	9
8b	H	<i>i</i> -C ₄ H ₉	93	141-142	5	6	8	9	6	8	8	9
8c	H	OCH ₃	29	152-153	6	8	7	9	2	8	2	9
8d	H		<i>j</i>	234-235	0	0	0	1	1	3	2	7
8e	OH	CH ₃	40	162 ^k	7	7	9	9	3	8	5	9
8f	OCH ₃	CH ₃	72	125-126	9	9	9	9	9	9	8	9
8g	CH ₃	CH ₃	29	164-166	9	9	9	9	9	9	7	9
8h			63	140-150	0	1	5	9	7	9	0	5
11			55	173-176	3	8	8	9	0	5	0	7
12			54	132-135	8	9	9	9	6	7	8	9

^{a-i} Defined as in Table I. ^j Obtained as a byproduct in step f (Scheme I). ^k With decomposition.

with aqueous sodium hydroxide. The mixture was extracted repeatedly with ether. The combined ether extracts were dried and treated with hydrogen chloride to yield 95 g (34%) of 4 as a light tan solid: mp 184-185 °C dec. Anal. Calcd for C₆H₇Cl₂NO₃ (212.0): C, 34.0; H, 3.3; N, 6.6. Found: C, 34.2; H, 3.3; N, 7.0.

Concentration of the filtrate and purification of the residue by silica chromatography gave 3.3 g (1.3%) of 9 as a tan solid: mp 154-156 °C; IR (KBr) no NH, 1220 cm⁻¹ (ClO₃); NMR (Me₂SO-*d*₆) δ 7.5-9.0 (m, CH=); mass spectrum *m/z* 362 (M⁺), 346 (M⁺ - O), 187 (O₃Cl - C₆H₄ - N₂⁺), 159 (O₃Cl - C₆H₅⁺). Anal. Calcd for C₁₂H₈Cl₂N₂O₇ (363.0): C, 39.7; H, 2.2; N, 7.7. Found: C, 40.0; H, 2.2; N, 8.0.

3-Perchlorylphenyl Isocyanate, 5, and *N,N'*-Bis(3-perchlorophenyl)urea, 10. To a stirred solution containing 39.4 g (0.4 mol) of phosgene in 500 mL of toluene was added 31.8 g (0.15 mol) of 4. After 10 h at ambient temperature, the reaction mixture was briefly heated to reflux, cooled, and filtered. The filter cake consisted of 0.25 g (0.9%) of 10; mp 234-235 °C dec; IR (KBr) 1670, 1550 (C=, amide II), and 1195 cm⁻¹ (ClO₃); NMR (Me₂SO-*d*₆) δ 7.8 (6, m, CH=), 8.63 (2, m, CH=), and 9.48 [2, s, (NH)₂]. Anal. Calcd for C₁₃H₁₀Cl₂N₂O₇ (377.0): C, 41.4; H, 2.7; N, 7.4. Found: C, 41.4; H, 2.7; N, 7.4.

The filtrate when concentrated under reduced pressure gave 30.0 g (99%) of 5 as a dark mobile liquid.

3'-Perchlorylcyclopropanecarboxanilide, 6d. To a stirred and cold (0 °C) solution of 4.5 (0.022 mol) of 4 in 50 mL of pyridine was added 2.44 g (0.24 mol) of cyclopropanecarbonyl chloride. The reaction mixture was poured into 300 mL of ice water and extracted with ether. The extract was washed with 5% hydrochloric acid and with water and dried. After evaporation of the ether,

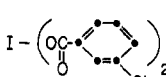
recrystallization from ether-hexane (1:1) gave 3.2 g (87.5%) of 6d as a colorless crystalline solid: mp 160-163 °C; IR (KBr) 3430, 3340 (NH), 1705 (C=O), and 1200 cm⁻¹ (ClO₃); NMR (Me₂NSO-*d*₆) δ 0.8 (4, m, CH₂CH₂), 1.8 (1, m, CH), 7.7 (4, m, CH=), and 8.9 (1, s, NH). Anal. Calcd for C₁₀H₁₀ClNO₄ (243.5): C, 49.3; H, 4.1; N, 5.8. Found: C, 49.6; H, 4.2; N, 6.0.

***N*-Methoxy-*N'*-methyl-*N'*-(3-perchlorylphenyl)urea, 8f.** To a solution of 12.9 g (64 mmol) of 5 in 250 mL of ether was added a solution of 4.9 g (80 mmol) of *O,N*-dimethylhydroxylamine in 350 mL of methanol. The mixture was concentrated under reduced pressure and washed with water. Recrystallization of the residue from acetone-hexane (5:1) gave 11.8 g (72%) of 8f as a crystalline solid: mp 125-126 °C; IR (KBr) 3420 (NH), 1210 (ClO₃), 1705 (C=O), and 1530 cm⁻¹ (amide II); NMR (CDCl₃) δ 3.2 (3, s, NCH₃), 3.8 (3, s, OCH₃), 7-8.5, (5, m, CH= and NH). Anal. Calcd for C₉H₁₁ClN₂O₅ (262.6): C, 41.1; H, 4.2; N, 10.7. Found: C, 41.2; H, 4.3; N, 10.8.

1-Methoxy-3-(3-perchlorylphenyl)imidazolidine-2,4,5-trione, 12. A solution containing 5.0 g (0.02 mol) of 8c and 2.0 g (0.026 mol) of oxalyl chloride in 100 mL of benzene was refluxed until TLC indicated complete disappearance of 8c (4 h). Removal of solvent under reduced pressure followed by crystallization of the residual solid from benzene-hexane gave 3.3 g (54%) of 12 as a crystalline solid: mp 132-135 °C; IR (KBr) 1760 (C=O); NMR (Me₂SO-*d*₆) δ 4.0 (3, s, OCH₃) and 7.8-8.3 (4, m, CH=). Anal. Calcd for C₁₀H₇ClN₂O₇ (302.5): C, 39.7; H, 2.3; N, 9.3. Found: C, 39.7; H, 2.5; N, 9.2.

***N*-(3-Iodophenyl)-*N'*-methoxy-*N'*-methylurea, 13.** To a stirred and chilled (5-7 °C) solution containing 39.0 g (0.4 mol) of *O,N*-dimethylhydroxylamine hydrochloride and 21.2 g (0.2 mol) of sodium carbonate in 300 mL of

Table III. *N*-(3-Iodophenyl)-*N'*-methoxy-*N'*-methylurea and Oxidation Products: Properties and Herbicide Screen Results

compd	X	% yield	mp, °C	phytoxicity index ^a							
				pre				post			
				Bygr ^b		Gacr ^c		Lacg ^d		Rrpw ^e	
1 ^f	2 ^f	1	2	1 ^h	2 ⁱ	1	2				
13	I	85	82-83	8	9	9	9	6	7	2	8
14	IO ₂	29.6	148 ^j	9	9	9	9	0	5	1	7
15	I - 	44.6	124-125 ^j	2	9	9	9	2	7	3	5

^{a-i} Defined as in Table I. ^j With decomposition.

water was added a solution of 49.0 g (0.2 mol) of 3-iodophenyl isocyanate in 160 ml of tetrahydrofuran. After 2 h, 150 mL of ether was added. The organic layer was dried and concentrated. Trituration of the residue with hexane gave 52.0 g (85%) of 13 as a white crystalline solid: mp 82-83 °C; IR (KBr) 3420 (NH), 1700 (C=O), and 1525 cm⁻¹ (amide II); NMR (Me₂SO-*d*₆) δ 3.1 (3, s, NCH₃), 3.6 (3, s, OSH₃), 6.8-8.2 (4, m, CCH=), and 9.1 (1, s, NH). Anal. Calcd for C₉H₁₁IN₂O₂ (306.0): C, 35.3; H, 3.6; N, 9.1. Found: C, 35.4; H, 3.6; N, 9.1.

***N*-(3-Iodoxyphenyl)-*N'*-methoxy-*N'*-methylurea, 14, and 3-[[[(Methoxymethylamino)carbonyl]amino]phenyliodoso Bis(3-chlorobenzoate), 15.** To a stirred solution containing 6.12 g (0.02 mol) of 13 in 50 mL of chloroform was added, in one portion, a solution containing 9.0 g (0.044 mol) of 85% 3-chloroperbenzoic acid in 100 mL of chloroform. After 1 h, the mixture was filtered to give 2.0 g (29.6%) of 14 as light brown solid: mp 148 °C dec; IR (KBr) 3260 (NH), 1655 (C=O), and 1525 cm⁻¹ (amide II); NMR (Me₂SO-*d*₆) δ 3.1 (3, s, NCH₃), 3.6 (3, s, OCH₃), 7.4 (3, m, CH=), 8.2 (1, s, CH=), and 9.4 (1, s, NH). Anal. Calcd for C₉H₁₁IN₂O₄ (338.0): C, 31.9; H, 3.2; N, 8.3; equiv wt, 84.5. Found: C, 31.7; H, 3.1; N, 7.9; equiv wt, 82.2.

The filtrate was washed 3 times with 5% aqueous sodium bicarbonate, dried, and concentrated. Trituration of the residual red oil, 9 g, with 500 mL of ether gave 5.5 g (44.6%) of 15 as a light tan solid: mp 124-125 °C dec; IR (KBr) 3310 (NH), 1660 (C=O), and 1520 cm⁻¹ (amide II); NMR (Me₂SO-*d*₆) δ 3.1 (3, s, NCH₃), 3.6 (3, s, OCH₃), 7.0-8.7 (12, m, CH=), and 9.4 (1, s, NH). Anal. Calcd for C₂₃H₁₉Cl₂IN₂O₆ (617.0): C, 44.7; H, 3.1; Cl, 11.5; N, 4.5. Found: C, 44.9; H, 3.2; Cl, 11.5; N, 4.7.

Biological Methods. The preemergence herbicidal activity was evaluated by planting seeds of barnyard grass and garden cress in test tubes, nominally measuring 25 × 200 mm, filled about three-quarters full of untreated soil, in each case covered on top with about 2.5 mL of soil treated with the test compound as the rates of 0.1 and 0.1 mg/tube, designated in Tables I-III as rates 1 and 2, respectively. The planted soil was held under controlled conditions of temperature, moisture, and light for 13-14 days. The amount of germination and condition of the plants were then noted, and the effectiveness of the test compound was rated on the basis of a 0-9 scale, the 0 rating indicating no effect and 9 indicating death of all the seedlings or no germination.

The postemergence activity of the compounds was evaluated by spraying 10-day-old redroot pigweed plants and 7-day-old large crabgrass plants to runoff with a liquid

formulation of the test compound at the rates of 0.62 mL of an 0.04% solution designated rate 1 in Tables I-III and 0.56 mL of an 0.5% solution designated rate 2 in Tables I-III. The sprayed plants were held in chambers with fluorescent light (43 000 lx) at 21-23 °C and watered as needed for 10 days, monitoring twice daily. Phytotoxicity of the test compound was then rated visually on a 0-9 scale, with 0 indicating no effect and 9 indicating death of all the plants of the given species.

Compounds showing appreciable activity in the initial pre- and postemergence screens were included in additional light chamber tests involving logarithmic dilution, variable rate spray applications. Activity of the compounds was determined with respect to several common species of weeds by spraying a formulation of the test compound onto the soil in which the weed seeds had been planted (preemergence) or onto the foliage of the plants (postemergence). In each series of tests, the soil was held in 3-in. pots kept in standard 6 × 24 in. shallow trays. The solution of test chemical was sprayed in a 10-fold log dilution from one end of the tray to the other, the concentration of the test compound varying logarithmically from a higher value at one end of the band to a lower value at the other end of the band. The effect of the test compound was evaluated visually and reported as the nominal rate of application, in kilograms per hectare, at which 90% inhibition of the growth of the weeds occurred. This is referred to as the 90% growth inhibition, or GI₉₀, dosage. Results of these pre- and postemergence tests, as well as the weed species involved, are listed in Table IV.

Additional light chamber tests, summarized in Table V and VI, were carried out by comparing the activity of 8f and 8g with that of diuron, linuron, and fluometuron. A log dilution of 8f, from 5.5 to 0.55 kg/ha, was applied preemergence to Webster silty clay loam soil (3-4% organic matter content) containing weed species not included in previous tests. For determination of the effect of soil incorporation on herbicidal activity, a log dilution spray pattern was applied as a layer 0.64 cm below the untreated soil surfaces consisting of Webster silty clay loam and Hanford sandy loam (<1% organic matter) soils, respectively (Table V). A similar test was carried out to determine the effective end point for preemergence weed control in the Hanford soil. Four grass and four broadleaf weed species were included with each chemical applied from 1.1 to 0.011 kg/ha (Table VI). Included in Table VI is a comparison of the herbicidal activity of 8f with that of 8g, diuron, linuron, and fluometuron.

Abbreviations for all herbaceous weeds used in Tables I-VII are listed in Table VIII. The table includes ab-

Table IV. Response of Six Plant Species to Pre- and Postemergence Application of Test Compounds (GI₉₀ in Kilograms per Hectare)^a

compd	application	Chgr	Lacg	Bygr	Rrpw	Wimu	Cudo
6b	pre	3.1+ ^b	3.1+	3.1+	3.1+	2.3	2.8
	post	5.5+	3.1	5.5+	3.1	1.8	5.5+
6d	pre	3.1+	3.1+	3.1+	0.55-	1.3	1.3
	post	5.5+	5.5+	5.5+	5.5+	0.9	5.5+
6e	pre	3.1+	1.3	3.1+	0.55-	0.55-	0.55
	post	5.5+	3.6	5.5+	1.8	0.66-	5.5+
Stam	pre	1.2+	1.2+	1.2+	1.2+	1.2+	1.2+
	post	5.5+	5.5+	5.5+	0.66	5.5+	1.2
cypromid	pre	3.1+	3.1+	3.1+	0.13	0.275	1.0
	post	1.8	0.66	0.77	0.33	0.33	0.55
7a	pre	3.1+	1.0	1.8	0.55-	0.55-	0.55-
	post	5.5+	5.5+	5.5+		1.0	1.8
7b	pre	0.9+	0.05-	0.7	0.55-	0.55-	0.55-
	post	5.5+	0.66-	3.1	0.66-	0.66-	3.1
7c	pre	2.0-	0.39-	1.3	0.39-	0.39-	0.39-
	CIPC	1.0	2.2+		2.2+	2.2+	0.44+
8a	pre	3.1+	0.55-	0.9	0.55-	0.55-	0.55-
	post	5.5+	1.8	5.5+	2.3	0.66-	5.5+
8f	pre	0.77	0.08	0.23	0.055	0.055	0.055
	post	5.5+	0.31	5.5+	0.18	0.066	1.0
8g	pre	1.0	0.07	0.55	0.18	0.13	0.055
	post	5.5+	4.2	5.5+	0.18	5.5+	5.5+
11	pre	3.1+	0.7	2.0	0.55-	0.66	0.55-
	post	5.5+	4.2	5.5+	1.8	5.5+	5.5+
12	pre	3.1+	3.1+	3.1+	1.0	2.8	3.1+
	13	pre	0.42	1.3	0.23	0.13	0.31
14	pre		1.5	4.2	1.5	1.3	1.5
	post		1.3	2.3	0.42	0.23	0.42
15	pre		2.8	5.5+	2.3	0.55	2.3
	post		1.1	3.1	0.42	0.31	0.42
diuron	pre	0.22	0.15	0.22	0.1	0.18	0.055-
	post	0.55	0.15	5.5+	0.055-	0.31	0.42
linuron	pre	0.55-	0.22	0.55-	0.06	0.13	0.08
	post	0.44	0.06	0.48	0.13	0.18	0.18

^a GI₉₀ = 90% growth inhibition by visual observation. ^b (+) = greater than; (-) = less than.

Table V. Comparison of 8f with 8g, Diuron, and Linuron^a (GI₉₀ in Kilograms per Hectare)

weed species	PE (Webster) ^b			layered (Webster) ^b				layered (Hanford) ^c			
	8f	diuron	linuron	8f	8g	diuron	linuron	8f	8g	diuron	linuron
Bygr	0.55- ^d	5.5+	5.5+	0.55-	3.1	3.1	4.2	0.1	0.33	0.44	0.55+
Grft	0.55-	1.0	2.3	0.55-	0.55-	0.55-	1.3	0.05+	0.22	0.22	0.33
Wimu	0.55-	0.55-	0.55-	0.55-	0.55-	0.77	0.55-	0.05+	0.22	0.22	0.11
Rrpw	0.55-	0.77	0.55-	0.55-	0.55-	0.88	0.55-	0.05-	0.05	0.22	0.11
Colq	0.55-	0.55-	0.55-	0.55-	0.55-	0.55-	0.55-	0.05-	0.07	0.07	0.11
Soth	0.55-	1.3	1.3	0.55-	0.55-	0.55-	0.55-	0.05-	0.05-	0.10	0.08
Cudo	0.55-	1.3	1.1	0.55-	0.55-	0.6	1.1	0.05-	0.08	0.11	0.11
Bhpl	0.55-	1.1	2.0	0.55-	1.8	2.0	2.3	0.05-	0.11	0.33	0.22

^a log dilution (5.5-0.055 kg/ha). ^b Webster silty clay loam soil: 3-4% organic matter content. ^c Hanford sandy loam soil: less than 1% organic matter content. ^d (+) = greater than; (-) = less than.

Table VI. Comparison of 8f with 8g, Diuron, Linuron, and Fluometuron^a

weed species	GI ₉₀ , kg/ha					calcd ratios of act.			
	8f	8g	diuron	linuron	fluometuron	8f/8g	8f/diuron	8f/linuron	8f/fluometuron
Grft	0.04	0.05	0.3	0.4	0.3	0.80	0.13	0.10	0.13
Qugr	0.1	0.08	0.2	0.04	0.04	1.25	0.50	2.50	2.50
Bygr	0.2	0.4	0.4	0.9	1.0	0.50	0.50	0.22	0.20
Lacg	0.04	0.05	0.2	0.4	0.2	0.80	0.20	0.10	0.20
Rrpw	0.01-	0.2	0.04	0.06	0.1	0.50 ^b	0.25 ^b	0.17 ^b	0.10 ^b
Colq	0.04	0.03	0.04	0.08	0.04	1.33	1.00	0.50	1.00
Wimu	0.02	0.8	0.04	0.1	0.3	0.25	0.50	0.20	0.07
Bhpl	0.06	0.2	0.3	0.6	0.3	0.30	0.20	0.10	0.20
						av: 0.72	0.41	0.49	0.55

^a Preemergence, log dilution (1.1-0.011 kg/ha). ^b The end point of control was not attained for 8f; the figures represent minimum values.

Table VII. Field Activity Screen with 8f^a

weed species	preplant incorporated		preemergence		postemergence	
	1 ^b	2 ^c	1 ^b	2 ^c	1 ^b	2 ^c
Rygr	0.1- ^f	0.1-	2.3-	0.5	0.3	1.6
Bygr	0.1-	0.1-	0.1-	0.5	0.3	1.6
Lacg	0.1-	0.1-	0.1-	0.5	0.3	1.6
Rrpw	0.1-	0.1-	0.1-	0.1-	0.1-	2.2
Wimu	0.1-	0.1-	0.1-	0.1-	0.1-	0.1-
Bhpl	0.1-	0.1-	0.1-	0.1-	0.3	1.1
Puns	0.3	0.3		0.3		2+

^a Minimum rate in kg/ha giving growth inhibition at the level indicated; GI₅₀ for weeks. ^b Evaluated 21 days after treatment. ^c Evaluated 33 days after treatment. ^d Evaluated 4 days after treatment. ^e Evaluated 12 days after treatment. ^f (+) = greater than; (-) = less than.

Table VIII. Abbreviations for Herbaceous Weeds

ab- brevi- ation	common name	botanical name
Bygr	barnyard grass (water grass)	<i>Echinochloa crus-galli</i> L. Beauv.
Lacg	crabgrass, large	<i>Digitaria sanguinalis</i> L. Scop.
Chgr	cheat (chess)	<i>Bromus secalinus</i> L.
Gacr	cress, garden	<i>Lepidium sativum</i> L.
Cudo	curly dock	<i>Rumex crispus</i> L.
Grft	foxtail, green	<i>Setaria viridis</i> L. Beauv.
Wimu	mustard, wild	<i>Brassica kaber</i> (DC.) L. C. Wheeler var.
Colq	lamb's-quarters, common	<i>Chenopodium album</i> L.
Rrpw	pigweed, redroot	<i>Amaranthus retroflexus</i> L.
Bhpl	plantain, buckhorn	<i>Plantago lanceolata</i> L.
Puns	nut sedge, purple	<i>Cyperus rotundus</i> L.
Yens	nut sedge, yellow	<i>Cyperus esculentus</i> L.
Qugr	quack grass	<i>Agropyron repens</i> L. Beauv.
Rygr	ryegrass	<i>Lolium multiflorum</i> Lam.
Soth	sow thistle, common	<i>Sonchus oleraceus</i> L.

Abbreviations for weeds reported in recent editions of the "Research Report of the North Central Weed Control Conference" (Calvin, 1979).

RESULTS AND DISCUSSION

The results in Table I-IV suggest certain structure-activity relationships within the three classes of herbicides.

(1) **Anilides.** Of the seven anilides evaluated for preemergence and foliar herbicide activity, the 1-methylcyclopropanecarboxanilide, 6e, appears to be most active. Less than 0.55 kg/ha applied preemergence controlled broadleaf weeds. This activity is similar to cypromid and greater than propanil. Similar to propanil, none of the perchorylanilides shows foliar activity against grasses. Cypromid, on the other hand, maintained excellent control of cheat, crabgrass, and barnyard grass. Of the broadleaf species tested, mustard was readily controlled by most compounds. Overall, 6e appears to be less potent than cypromid.

(2) **Carbamates.** Within the carbamates, 7, highest activity is found in the ethyl (7b) and isopropyl (7c) esters. All three carbamates control broadleaf weeds in pre- and postemergence applications. Preemergence, grasses are controlled at less than 0.55 kg/ha with all three perchloryl carbamates. In all laboratory screens, the 7 compounds are more active than chlorpropham.

(3) **Ureas.** Oxidation of iodine in 13 to iodoxy (14) and to the iodoso dibenzoate (15) lead to a decrease in overall

herbicidal activity (Tables III and IV).

Within the perchloryl ureas 8a-h, 8f and 8g are clearly the most active compounds. The "bridged" ureas, 11 and 12, do not appear to have any advantages over their acyclic precursors, 8a and 8c, respectively. The methoxymethylurea, 8f, controls green foxtail, barnyard grass, redroot pigweed, wild mustard, common lamb's-quarters, sow thistle, curly dock, and buckhorn plantain at less than 0.55 kg/ha in preemergence tests. Diuron and linuron are less active and fail to control barnyard grass (Table V). When layered under Webster soil, 8f again killed all weed species present. The urea 8g appears equally active when layered except for control of barnyard grass and buckhorn plantain. The ratio of herbicide activity, kilograms per hectare 8f per kilograms per hectare 8g, on barnyard grass is 0.18. This is a great enough difference that 8g may fail to control barnyard grass in field tests, while 8f may effectively control this species. The activity of both diuron and linuron is less than that of either 8f or 8g; both fail to control barnyard grass and buckhorn plantain. 8f was extremely active (0.055 kg/ha required for weed control) when layered under Hanford (sandy loam) soil (Table V).

In a preemergence test, 8f controlled yellow nut sedge grown from tubers at 1.1 kg/ha and caused chlorosis down to 0.22 kg/ha. Purple nut sedge appeared more resistant early in this test, but after 3 weeks was controlled at 1.4 kg/ha; many purple nut sedge leaves were chlorotic down to 0.44 kg/ha.

For determination of the effective end point for preemergence weed control in Hanford soil, four grass and four broadleaf weed species were included in a test with each chemical applied from 1.1 to 0.011 kg/ha. The herbicidal activity of 8f was compared to that of 8g, diuron, linuron, and fluometuron by calculation of the ratio of activity (Table VI). For control of the grasses and broadleaf weeds, 8f was approximately 4 times more active than diuron and 5-6 times more active than linuron and fluometuron.

The two anilides, 6b and 6d, the ureas 8f-h, and the parabanic acid derivative, 11, were included in preemergence, preplant incorporated, and postemergence field screens. The urea 8f was most active controlling nearly all weeds at 0.11 kg/ha (Table VII). In these tests, cotton exhibited no phytotoxicity at 2.2 kg/ha, the highest rate applied. Other field tests have demonstrated that slightly increased dosages of 8f are effective either preemergence or postemergence for the control of several economically important species of grass and broadleaf weeds (Pilgram, 1976).

Soil Relationships and Mode of Action. The urea 8f is nonvolatile (determined by weight loss from glass filter paper). Only 0.4% was lost after 14 days. The movement of 8f through Hanford soil with water was measured by the "slotted-tube" test technique (Lambert et al., 1965). When a rate of 2.2 kg/ha of 8f was banded at the top of a slotted tube and 5, 10, or 15 cm of water was percolated through the soil column, the front of activity was measured 13, 19, and 25 cm, respectively, from the origin.

Urea 8f has dimensions of molecular size that closely resemble linuron on the one hand and diuron and fluometuron on the other hand. Substituted *N*-phenylureas specifically affect the Hill reaction. More specifically, it is suggested that the mode of action of 8f is the inhibition of carotenoid synthesis. This explanation seems to accommodate our observations and is in agreement with observations on fluometuron, which also bleaches plants.

Stability Studies. The determination of the sensitivity of a compound includes studies of its behavior under

Table IX. Stability Test Results with 8f

- (1) differential thermal analysis
endotherm peaks: 113 °C
exotherm peaks: 216 °C
- (2) spark sensitivity: 50% fire point = 0.650 J (HMX standard = 0.7 J)
- (3) rotary friction: negative (4-kg load at 3000 rpm)
- (4) impact sensitivity: 50% fire point = 100 cm (Bureau of Mines apparatus, 2-kg weight)
- (5) drop weight test: 50% fire point = 5-6 in. (Janaf standard tests, 2-kg weight); RDX = 7 in.
- (6) explosive power: 0 cm³/g (Trunzl block test, No. 8 blasting cap); RDX = 25 cm³/g

well-defined conditions of impact, shock, vibration, friction, sparks, flame, or heat. Shock sensitivity and detonation studies, as well as thermal stability and rotary friction tests, were carried out on all intermediates and most products. The results indicate that all intermediates 1-3 and 5 are very sensitive to shock and impact [see also Inman et al. (1964)]. By use of proper precautions, compounds such as 8f can be handled safely. Stability tests results with 8f are included in Table IX.

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Verification of Structures of Chloroethyl *N*-Heptafluorobutyryl Derivatives of Glyphosate and (Aminomethyl)phosphonic Acid by Chemical Ionization and Electron Impact Mass Spectrometry

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Glyphosate (a highly effective herbicide with a low mammalian toxicity) is currently being studied on a wide range of agricultural commodities. The most commonly utilized residue procedure which quantitates this compound and its major metabolite, (aminomethyl)phosphonic acid, depends on the formation of the methyl *N*-trifluoroacetyl derivatives of both compounds following an extensive cleanup procedure. This study reports on the structural verification of the chloroethyl *N*-heptafluorobutyryl derivatives which were synthesized, resulting in the simplification of this residue analysis. Chemical ionization mass spectrometry with both isobutane and methane reagent gases is used to obtain reliable molecular weights for both derivatives. Electron impact mass spectrometry is then used to identify the fragmentation of the compounds.

Glyphosate [*N*-(phosphonomethyl)glycine] is the active ingredient of the herbicidal formulation ROUNDUP (a product of Monsanto Co.). This is an effective, broad-spectrum, nonselective herbicide which has a low mammalian toxicity (LD₅₀ = 4320 mg/kg). These factors have led to the widespread field trial study of this compound on a variety of agricultural commodities. A sensitive, widely applicable residue analysis for glyphosate and its major metabolite, (aminomethyl)phosphonic acid, is therefore necessary for the quantitation of these two compounds in a wide range of treated crops. A procedure developed by Monsanto and suggested by the Environ-

mental Protection Agency (U.S. EPA, 1977) has been adapted and used in this laboratory since 1975 (Thompson et al., 1980). This method involves extensive cleanup including solvent partitioning, charcoal elimination of pigments, large volume anion exchange, and separation of the pesticide and its metabolite by cation exchange. This is followed by separate acylation with trifluoroacetic anhydride, alkylation with diazomethane, and detection by gas chromatography with flame photometric detection. Reproducible results are sometimes difficult to obtain with this tedious methodology, especially on crops which present extreme cleanup problems (i.e., blueberries, strawberries, and okra).

A recent study from this laboratory (Guinivan et al., 1982) has reported the use of aqueous gel permeation chromatography and the formation of two new derivatives, presumably the chloroethyl *N*-heptafluorobutyryl esters, of glyphosate and (aminomethyl)phosphonic acid as a means for simplifying the complex existing procedures for the analysis of residues on blueberries. Smaller sample

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