

Effect of Variations in the Acyl Moiety on Herbicidal Activity of *N*-Substituted Alpha-Chloroacetamides

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A single α -halogen atom other than fluorine is necessary for practical herbicidal activity in the *N*-substituted acetamides. Replacement of the α -halogen atom with other functional groups nullifies activity. Extension of the acyl moiety to include halo-propionamides and butyramides results in complete inactivity under the conditions of these tests.

THE LIMITS OF ACTIVITY of *N*-substituted- α -chloroacetamides as grass-specific pre-emergence herbicides have been clearly defined with respect to the amide moiety (7). The determination of the limits of the acyl moiety of the most active chloroacetamides is reported here in the elucidation of the relation of structure to herbicidal activity.

Chemical and physical properties as well as methods of preparation of the new compounds discussed in this paper will be reported elsewhere (4).

Method of Testing

The results discussed here are based on greenhouse screening studies, and simple screening evaluation methods for pre-emergence herbicidal action. The chemical to be tested is applied in spray form to soil seeded to representative grass and broadleaf plants. An aluminum pan, perforated on the bottom, 13 × 9 × 2 inches, is level filled with standard soil preparation to a depth of 3/8 inch from pan top. Twenty seeds each of three weedy grasses—wild oat, cheat grass, and rye grass—and five

corn seeds are scattered over one third of the soil surface area. Twenty seeds of five or six representative broadleaf plants—buckwheat, mustard, red clover, beet, cotton, and cucumber—are scattered on the remaining two thirds of the soil area. The seeds are covered with soil to the pan top. The planted pans are placed in an exhaust hood and sprayed with 30 cc. of an aqueous solution containing 1% of a 20-20-20 water-soluble fertilizer (Monsanto's Folium) and 0.1% octamethyl pyrophosphoramidate. The pan is next sprayed with 30 cc. of an organic solvent (usually acetone) containing the chemical to be tested. The spray volume is kept constant, the rate per acre of active materials is varied as desired.

The prepared pan is next placed in an aluminum greenhouse bench containing 0.5 inch of water. The pan is sub-irrigated in this manner until moisture is evident on two thirds of the soil surface. The pan is then removed and placed on a moist soil bench in the greenhouse. The seeds germinate and emerge in 3 to 4 days, and observations on the degree of activity are made on the tenth day after planting.

The herbicidal ratings are determined for each grass specie according to the following scale.

Germination and Emergence, %	Herbicidal Rating
0-25	3
26-50	2
51-75	1
76-100	0

The herbicidal ratings reported in the tables are achieved by a summation of the herbicidal ratings for each weedy grass specie. The maximum score possible is 9, assuming three ratings for each grass specie. Any rating from 9 to 0

Summation of Individual Grass Ratings	Summation, Herbicidal Rating
9	4
7-8	3
5-6	2
3-4	1
1-2	0

Table I. Herbicidal Activity of α -Haloacetamides

R ₁	R ₂	Y						
		CH ₃	CH ₂ F	CH ₂ Cl	CH ₂ Br	CH ₂ I	CHCl ₂	CCl ₃
Herbicidal Rating at Lb. Per Acre								
Hydrogen	Hydrogen	0 at 15	0 at 25	0 at 5
Methyl	Methyl	4 at 5	4 at 25	...	0 at 25	0 at 5
Ethyl	Ethyl	4 at 5	0 at 25	0 at 25
Hydrogen	Propyl	3 at 5	0 at 25
Hydrogen	Allyl	0 at 25	...	3 at 5	0 at 25	...
Propyl	Propyl	0 at 25	...	4 at 5	0 at 25	0 at 25
Allyl	Allyl	...	0 at 25	4 at 2.5	2 at 5	2 at 5	2 at 25	1 at 25
Hydrogen	Butyl	0 at 25	...	4 at 25
Hydrogen	Cyclohexyl	0 at 25	...	4 at 5	...	3 at 5
Hydrogen	Furfuryl	0 at 25	...	3 at 5	...	2 at 5
3-Oxapentamethylene		0 at 25	...	4 at 2.5	...	4 at 5
Pentamethylene		4 at 5	...	4 at 5
1-Methylpentamethylene		0 at 25	...	4 at 2.5

Table II. Herbicidal Activity of α -Substituted *N,N*-Diallyl Acetamide

$$(\text{CH}_2=\text{CH}-\text{CH}_2)_2\text{N}\overset{\text{O}}{\parallel}\text{CCH}_2\text{Y}$$

α -Substituent, Y	Herbicidal Rating at 25 Lb. Per Acre
Cl	4
-SCN	1
-OH	2
-OC ₂ H ₅	0
-OC ₂ H ₃ Cl ₂ 2,4	0
-SSO ₃ Na	0
-SCH ₂ CH ₂ NH ₂	0
-SCH ₂ CH ₂ NHCOCH ₂ Cl	4
-SO ₂ CH ₂ CH ₂ NHCOCH ₂ Cl	1
-SCH ₂ CH(NH ₂)CO ₂ H	0
-NH ₂	0
-C ₆ H ₄ CONCO	1,2
-C ₆ H ₄ CON(CH ₂ CONH-)CO	1,2
C ₆ H ₅	0
C ₆ H ₅	1
4-ClC ₆ H ₄	2

is possible. A simple arbitrary scale was used to arrive at a summation herbicidal rating for the three weedy grasses used in the tests.

Results

The herbicidal activities of some α -haloacetamides are listed in Table I. These compounds are derived from the parent acetamide (column 1) by replacement of the α -hydrogen atoms with halogen. The α -chloroacetamides are included for comparison purposes.

The herbicidal activities of a number of α -substituents other than halogen are listed in Table II for *N,N*-diallyl-acetamide.

Table III presents data on the herbicidal activity of *N*-substituted halo-propionamides and butyramides compared with the corresponding acetamides.

Discussion

The outstanding activity of the *N*-substituted- α -chloroacetamides as compared with the other halogen analogs is clearly illustrated in Table I. The necessity of an α -halogen atom is shown by the lack of activity of the parent acetamides (column 1) at 25 pounds per acre. With the monohalogen derivatives, the general order of activity is Cl > I > Br > F. The bromo and iodo acetamides are slightly less active than the chloro analog. Activity increases with the iodo derivative. 4-(Iodoacetyl) morpholine and 1-(iodoacetyl)piperidine are as active as the chloro analogs. Specificity of action, however, decreases in the order of chlorine, bromine, iodine, with the iodo compounds showing more general phytotoxic behavior.

Whereas the diallyl- α -chloroacetamide

is active at the low rate of 1 pound per acre, the α -fluoro analog is completely inactive at 25 pounds per acre. This inactivity may be due to the stability of the carbon-fluorine bond. This would indicate that the lability of the α -halo atom is a prerequisite for activity. It is likely that the α -chlorine atom possesses the optimum degree of lability not only for phytotoxicity but also for grass-specificity, since the more chemically reactive iodo compounds show less grass specificity. Bond energies and interatomic distances (3) which are a measure of the relative stabilities of the carbon-halogen bonds are given in Table IV. The values for the carbon-hydrogen bond are listed for comparison.

The toxiphoric nature of the ClCH₂-group is also shown in Table I. Replacement of the other α -hydrogen atoms with chlorine leads to less active di- and trichloroacetamides. While the *N*-substituted α -chloroacetamides exhibit pre-emergence activity at 5 pounds per acre or less, the *N*-substituted di- and trichloroacetamides are practically devoid of activity at even the high rate of 25 pounds per acre.

The order of activity of trichloroacetamide (0 at 5; 3 at 15) is comparable to that of trichloroacetic acid. When substituents are attached to the nitrogen atom, activity in all cases tested is reduced almost to zero at 25 pounds per acre. *N*-Substituents on trichloroacetamide nullify activity, while *N*-substituents on monochloroacetamide enhance activity. This may indicate a different metabolic pathway to the final toxic action or simply an absorption and penetration difference.

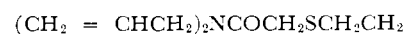
The role of the α -chlorine atom is further emphasized by the lack of activity of the series of compounds listed in Table II in which the α -chlorine atom has been replaced by a wide variety of groups. Groups such as SCN and CN, which are comparable in their electronegativity effects to chlorine, do not impart activity to the α -substituted acetamides. It is evident that part of the activity of the α -chloroacetamides is

Table IV. Bond Energies and Distances of Carbon-Halogen Bonds

Bond	Bond Energies, Kcal./Mole	Bond Distances A
C—H	87.3	1.09
C—F	107.0	1.42
C—Cl	66.5	1.77
C—Br	54.0	1.91
C—I	45.5	2.10

due to the phytotoxic properties of the chloroacyl moiety.

The inactivity of the —SCH₂CH₂NH₂ group and the relatively high order of activity of the —SCH₂CH₂NHCOCH₂Cl grouping in the compounds listed in Table II is further confirmation of the phytotoxicity of the chloroacyl moiety. The toxicity of the compound



shown in Table II to have a rating of 4 at 25 pounds per acre, can be explained by considering the compound to be a

$$\text{O}$$

monosubstituted amide, R₁NHCCH₂Cl, rather than a derivative of diallyl- α -chloroacetamide. R₁ owes its activity despite its length, to the interruption of the carbon chain by a sulfur atom after only two carbon atoms. This explanation is in accordance with a previous observation (7) that a three-carbon *N*-substituent can be lengthened considerably without loss of action providing a hetero atom such as N, O, or S is introduced after the third carbon. A simple example is the highly active *N*-isopropoxypropyl- α -chloroacetamide (7).

The α -chlorine atom has also been replaced in other highly active α -chloroacetamides such as 1-chloroacetyl piperidine, 4-chloroacetyl morpholine and α -chloro-*N,N*-diethylacetamide. The α -substituents in these cases included CN, SSO₃Na, SR, SO₂R, NH₃⁺X⁻, NR₂, and NR₃⁺X⁻ in addition to those

Table III. Herbicidal Activity of Halo-Propionamides and Butyramides

<i>N</i> -Substituents	Herbicidal Rating at 25 Lb. per Acre						
	α -Chloroacetamide	Propionamides			Butyramides		
		α -Cl	β -Cl	α,α -diCl	α,β -diCl	α,β -diCl-iso	γ -Cl
Ethyl	4	0	0
Allyl	4	0
3-Methoxypropyl	4	0	..	0	..
Cyclohexyl	4	0	0	0	..
Furfuryl	4	0	0	..	0	1	0
Dimethyl	4	0	0
Diethyl	4	..	0	0
Dipropyl	4	..	0	..	0
Diallyl	4	1	0	0	0
3-Oxapentamethylene	4	0	0	..	0	0	0

listed in Table II. Without exception the α -substituted acetamides thus formed were completely inactive as pre-emergence herbicides at the high rate of 25 pounds per acre.

If the activity of the α -chloroacetamides were due solely to the chemical reactivity of the chlorine atom, the α -chloropropionamides would be expected to possess activity, since the chemical reactivity of the chlorine atom in the two types of compounds should not differ greatly. Table III clearly illustrates that the α -chloropropionamides are completely lacking in pre-emergence herbicidal activity at 25 pounds per acre. It may well be that enzymatic processes are operative which are incapable of utilizing the α -chloropropionamides.

Table III also indicates that the position and number of chlorine atoms in the propionamides are not important in enhancing the activity of this class of

compounds. The diallyl and 3-methoxypropyl amides of α,α -chloropropionic acid (Dalapon) show no activity as pre-emergence herbicides in these tests. The chlorobutyramides are similarly devoid of activity, as illustrated by examples in Table III.

Biological activity involves not only structural considerations as illustrated above, but also biochemical and physicochemical considerations. The relative activities of the haloacetamides are undoubtedly the composite result of numerous properties of the chemicals and plants. Work is in progress in these laboratories to determine the importance and interrelationship of these various factors with respect to herbicidal activity (2).

Acknowledgment

The authors are indebted to A. H. Schlesinger and E. J. Prill for the syn-

thesis of many of the propionamides and butyramides. The help of D. B. MacKenzie and J. H. Nolan in preparing the herbicidal tests is gratefully acknowledged.

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Received for review April 4, 1956. Accepted July 17, 1956. Presented in part before the Division of Agricultural and Food Chemistry, 127th Meeting, ACS, Cincinnati, Ohio, March-April 1955.

PESTICIDAL ACTIVITY AND STRUCTURE

Structural Effect of Some Organic Compounds on Soil Organisms and Citrus Seedlings Grown in an Old Citrus Soil

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A study was made of the effect of saturated and unsaturated alcohols, halides, acids, esters, amides, and some commercial fumigants on the soil organisms and growth of sweet orange seedlings in an old citrus soil. The organisms examined included the citrus nematode, *Tylenchulus semipenetrans* Cobb, fungi, and bacteria. It was concluded that high toxicity to these organisms, and citrus, is associated with halides and alcohols containing α,β -unsaturation. Several halogen derivatives were more effective against the citrus nematode than some of the commercial fumigants now in use. Some chemicals were found to stimulate growth of *Trichoderma viride*, and indirect biological control of certain pathogenic soil organisms might be achieved by exploitation of this observation.

SOIL FUMIGATION for the control of nematodes, pathogenic fungi, bacteria, and other detrimental soil organisms is coming into increasing agricultural use (75). Fumigation of old citrus land before planting is becoming a common practice in California because of the substantial increases in

yields obtainable (3, 7). The fumigants commonly used for citrus soils are D-D (dichloropropene-dichloropropane mixture), EDB (1,2-dibromoethane), and carbon disulfide.

When a citrus grove becomes unproductive because of nematodes or other detrimental organisms, the trees must

be removed before the land is fumigated and replanted. These trees would not be lost if they could be treated in place with some nonphytotoxic fumigant. Alternate row fumigation with the trees in place is now being tried by some growers (8) and tested experimentally, but the practicability of this is yet unknown.